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The effect of bipolar I disorder and major depressive disorder on workforce function

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Abstract

This investigation was undertaken to explore and compare the effect of bipolar I disorder (BD) and major depressive disorder (MDD) on workforce function. The data for this analysis were procured from the Canadian Community Health Survey (CCHS 1.2). The sample consisted of 20 747 individuals (≥ 18 years old and currently working); the proportions screening positive for lifetime BD and MDD were 2.4% and 11.2%, respectively. Individuals with BD or MDD had a significantly lower mean annual income, compared to people without these disorders. Individuals with BD had a significantly lower annual income when compared to MDD ($p < 0.05$). Results from a multiple logistic regression also indicate that employed individuals with BD had greater odds of reporting one or more mental health disability days in the past two weeks, compared with those with MDD (OR = 1.6; 95% CI = 1.0 to 2.6). Currently employed individuals with BD had lower odds of "good job security" relative to those with MDD (OR = 0.6 95% CI = 0.5 to 0.9). The data herein underscore the pernicious effect of BD on workforce function, and suggest that opportunistic screening for BD in all individuals utilizing employment assistance programs for depression might be warranted.

Key words: bipolar disorder, major depressive disorder, workforce function, human capital

Introduction

Mounting evidence indicates that mood disorders are a leading cause of disability and premature mortality.^(1,2) Cost-of-illness studies indicate that mood disorders impart staggering direct and indirect costs in both developed and developing nations.⁽³⁾ Decrements in workforce productivity comprise a significant component of the overall cost of illness.⁽⁴⁾ Improved recognition and management of mood disorders

have important implications for averting expenditures and reducing cost.⁽⁵⁾

Most cost-of-illness studies focus on individuals diagnosed with major depressive disorder (MDD) with relatively fewer studies separately evaluating the effect of bipolar disorder (BD).⁽⁶⁻⁸⁾ During the past decade, the estimated lifetime prevalence of BD has increased considerably largely due to the broadening diagnostic boundaries.⁽⁹⁾ Taken together, the total cost of

mood disorders attributable to BD may be considerably higher than previously estimated.^(6,10)

The only study to present comparative information on the workforce costs of MDD and BD reported that BD was associated with more lost work days per ill worker per year.⁽⁴⁾ This effect was mediated by greater severity and persistence of depressive symptoms in BD versus MDD. It was also reported that presenteeism (i.e., low performance while at work) accounted for approximately two-thirds of the total workforce cost of illness.

This investigation was undertaken to describe and compare the effect of BD, relative to MDD and the general population, on workforce function. The data for this post hoc analysis was from a Canadian cross-national mental health survey.

Methods

The data for this analysis were procured from the 2002 Canadian Community Health Survey: Mental Health and Well-being (82-617-XIE); a component of the Canadian Community Health Survey (CCHS), conducted by Statistics Canada. Information about the survey is available at <http://www.statcan.ca:8096/bsolc/english/bsolc?catno=82-617-X>.

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The survey employed the World Health Organization (WHO) World Mental Health 2000 version of the Composite International Diagnostic Interview (WMH-CIDI). The questionnaire used can be found at http://www.statcan.ca/english/sdds/instrument/5015_Q1_V1_E.pdf.

Respondents were residents of private dwellings; a multistage stratified cluster design was used to sample dwellings. Most interviews (86%) were conducted in person; the remainder by telephone. The responding sample totaled 36 984 people aged 15 or older; the participation rate was high (77%). The data were weighted to be representative of the household population of the ten provinces of Canada in 2002. The analysis herein was limited to individuals aged 18 or older and currently working.

The CCHS collected information on determinants and correlates of mental health such as socio-demographics, income, self-reported distress, level of leisure-time physical activity, medication use, and social support. Based on WHM-CIDI screening criteria, the survey collected information on lifetime and past 12-month prevalence of various mental disorders and behaviours (i.e. major depressive episode, manic episode, panic disorder, agoraphobia, social phobia, alcohol and drug dependence, gambling, suicide, and abnormal eating behavior), self-reported height and weight, and previously diagnosed medical disorders. Work-related variables included current employment status, self-perceived job security and the number of “mental health disability days” experienced in the past two weeks. The latter variable was measured by asking respondents if, in the past 2 weeks, they had “stayed in bed all or most of day or cut down on activities because of illness or injury,” or had days that “took extra effort to perform up to their usual level at work or in other daily activities due to emotional or mental health or use of alcohol or drugs.”

Statistical analyses were calculated by producing frequencies, cross-tabulations and multiple regression models. All analyses were based on data weighted to be representative of the Canadian population aged 18 or older in 2002. Based on data for those screened positive for lifetime mood disorder (bipolar I or depression), multiple logistic regression modeling was used to compare the associations of lifetime bipolar I disorder and lifetime depressive disorder with self-reported job security, and with mental health disability days in the past two weeks. For the analysis, mutually exclusive groups were created as follows: persons screened positive for lifetime bipolar I disorder (BD); persons screened positive for lifetime major depressive disorder (without bipolar I disorder) (MDD); and persons with neither mood disorder.

The models controlled for the effects of sex, age group, level of education, presence of physician-diagnosed chronic medical disorders (arthritis, asthma, back problems excluding fibromyalgia and arthritis, high blood pressure, migraine, chronic bronchitis, emphysema or chronic obstructive pulmonary disease, diabetes, epilepsy, heart disease, cancer, stomach or intestinal ulcers, effects of a stroke, bowel disorder/Crohn’s disease or colitis, Alzheimer’s disease or other dementia, cataracts, glaucoma, and thyroid disorder) and body mass index. Preliminary analysis revealed a relatively high prevalence of substance (alcohol or illicit drugs) dependency in persons with BD or MDD. Twelve-month dependency estimates were 23% and 7%, respectively, compared with 3% in the general population (data not shown). Therefore, to avoid multicollinearity, no variable for substance dependency was included in the multivariate regression models.

All statistical analyses were performed using SAS statistical software, release 9.1 (SAS Institute, Cary, NC). Variables

for analysis were selected *a priori*, based on previous research. To account for the complex sampling design of the CCHS, coefficients of variation on estimates and significance of differences between estimates were calculated using the bootstrap technique. The level of statistical significance was defined as $p < 0.05$.

Results

A positive screen for a lifetime manic episode (i.e. DSM-IV-defined bipolar I disorder) was ascertained in an estimated 2.4% of the currently employed Canadian population aged 18 or older. Lifetime history of BD was more frequent in younger respondents, in persons not married or living with a partner, and in those with incomplete post-secondary education (Table 1). The proportion of the employed population aged 18 or older with a positive screen for lifetime MDD (without BD) was estimated at 11.2%.

Among Canadians aged 18 or older in 2002, the proportion of people who were currently employed did not differ significantly according to the presence of lifetime mood disorder, nor did it differ between persons with lifetime BD and those with lifetime MDD. In persons with no history of mood disorder, 70% were employed; the proportion in those with BD was 68%, and in those with MDD, 69% reported employment at the time of the survey (data not shown). In all three groups, most individuals who were employed had full-time jobs (86% in those with no mood disorder; 87% in those with lifetime BD; 84% in those with lifetime MDD; the differences between proportions were not statistically significant) (data not shown).

The mean annual income of employed persons with mood disorder was substantially lower than that for those who were unaffected. Persons with lifetime BD had an average income of \$32,000—nearly

\$5,000 less than the average income (\$36,800) of those with MDD ($p < 0.05$) (Table 2). For persons with neither mood disorder, the average yearly income was \$40,300—substantially and statistically higher than that of either of the mood disorder groups ($p < 0.05$).

The results of multivariate modeling indicated that the odds of having experienced at least one mental health disability day within the past two weeks was significantly higher in persons with lifetime BD (OR = 8.8; 95% CI = 5.9 to 13.1) or lifetime MDD (OR = 5.6; 95% CI = 4.1 to 7.7), compared

with the odds for persons with neither disorder (Table 3a). In comparison with persons with lifetime MDD, those with lifetime BD had significantly higher odds of having experienced at least one mental health disability day within the past two weeks (OR = 1.6; 95% CI = 1.0 to 2.6)

TABLE 1
Prevalence of lifetime bipolar I disorder (BD) and major depressive disorder (MDD) (excluding BD) by selected socio-demographic characteristics, employed household population aged 18 or older, Canada excluding territories, 2002

	Lifetime BD		Lifetime MDD (excl. BD)		Neither lifetime BD nor lifetime MDD	
	Est'd number	%	Est'd number	%	Est'd number	%
Total	371 000	2.4	1 737 000	11.2	13 320 000	86.3
Sex						
Males [†]	207 000	2.5	677 000	8.1	7 506 000	89.5
Females	164 000	2.3	1 060 000	15.0*	5 814 000	82.6*
Age group						
18 to 34	146 000	2.8*	529 000	10.0*	4 592 000	87.2
35+ [†]	225 000	2.2	1 208 000	11.9	8 728 000	85.9
Level of education						
Secondary graduation or less	140 000	2.6	512 000	9.7*	4 628 000	87.6
Some post-secondary	50 000	3.7*	152 000	11.4	1 134 000	84.8*
Post-secondary graduation [†]	173 000	2.0	1 046 000	12.0	7 450 000	85.9
Marital status						
Married/living with partner [†]	177 000	1.7	1 503 000	10.1	9 195 000	88.2
Separated/divorced/widowed	77 000	5.7*	293 000	21.4*	997 000	72.9*
Never married	117 000	3.2*	390 000	10.8	3 110 000	86.0

[†] Reference group.

* Estimate is significantly different from estimate for reference category ($p < 0.05$).

Because of rounding and data not available (level of education), detail does not always sum to total.

Source: 2002 Canadian Community Health Survey: Mental Health and Well-being.

TABLE 2
Mean annual income, by presence of mood disorder (lifetime bipolar I disorder (BD) or major depressive disorder (MDD)), employed household population aged 18 or older, Canada excluding territories, 2002

Disorder	Mean income (C\$)
Lifetime BD	32,000*
Lifetime MDD (excluding BD)	36,800
General population without mood disorder	40,300

* Estimate is significantly lower than estimates for other categories ($p < 0.05$)

Source: 2002 Canadian Community Health Survey: Mental Health and Well-being.

TABLE 3a
Adjusted odds ratios for one or more mental health disability days in past two weeks in relation to presence of mood disorder (lifetime bipolar I disorder (BD) or lifetime major depressive disorder (MDD)), controlling for selected characteristics, currently employed household population aged 18 or older, Canada excluding territories, 2002

	Odds ratio	95% confidence interval
Mood disorder		
Lifetime BD	8.8*	5.9 to 13.1
Lifetime MDD (excluding BD)	5.6*	4.1 to 7.7
None [†]	1.0	–
Sex		
Males	0.8	0.6 to 1.0
Females [†]	1.0	–
Age group		
18 to 34	1.6*	1.2 to 2.1
35+ [†]	1.0	–
Level of education		
High school graduation or less [†]	1.0	–
Some post-secondary education	0.8	0.5 to 1.3
Post-secondary graduation	0.7*	0.5 to 1.0
Comorbidity		
Chronic condition present [§]	2.0*	1.5 to 2.8
Body mass index category		
Underweight/normal weight/ overweight (BMI < 30.0) [†]	1.0	–
Obese (BMI 30.0+)	0.8	0.5 to 1.1

* Estimate is significantly different from estimate for reference category ($p < 0.05$)

[†] Reference group, for which the odds ratio is always 1.0

– Not applicable

[§] Reference group is absence of arthritis, asthma, back problems excluding fibromyalgia and arthritis, high blood pressure, migraine, chronic bronchitis, emphysema or COPD, diabetes, epilepsy, heart disease, cancer, stomach or intestinal ulcers, effects of a stroke, bowel disorder/Crohn's disease or colitis, Alzheimer's disease or other dementia, cataracts, glaucoma, and thyroid disorder.

Odds ratios have been rounded; some with 1.0 as the lower or upper confidence limit are statistically significant (as indicated).

Model is based on records of 20 431 respondents.

Source: 2002 Canadian Community Health Survey: Mental Health and Well-being.

(Table 3b). Similarly, the odds of reporting good job security were significantly lower in persons with BD (OR = 0.4; 95% CI = 0.3 to 0.6) or MDD (OR = 0.7; 95% CI = 0.6 to 0.8) than in persons without either mood disorder (Table 4a). As well, those with BD (OR = 0.6; 95% CI = 0.5 to 0.9) compared unfavorably to those with MDD (Table 4b). These associations were present after controlling for the effects of the potentially confounding influences of sex, age group, level of education, medical comorbidity and body mass index category.

Discussion

These results suggest that, on several indices of workforce function, individuals with either BD or MDD are strikingly more impaired than persons without mood disorder. These data further suggest that individuals with BD may be more impaired than individuals with MDD as evinced by annual income, more mental health disability days, and job security.

The only other investigation to present comparative information on the workforce costs of MDD and BD also reported that mood disorders predicted overall lost work performance with an estimated 65.5 lost workdays per worker with BD and 27.2 lost workdays per worker with MDD.⁽⁴⁾ No significant differences in the association of BD and MDD with work performance were found by sex or age. Work loss associated with BD affected all occupational groups with a significantly greater effect noted among technical and professional workers in the case of absenteeism and among laborers and professional workers in the case of presenteeism.

During the past decade, several observations in mood disorders provide a relevant context to workforce dysfunction studies. Firstly, the estimated lifetime prevalence of bipolar spectrum disorders is considerably higher than previously estimated.⁽⁹⁾ For example, it is now estimated that 2 to 5% of the general population may be affected by BD.^(11,12) In keeping with this view, the percentage of employable individuals with BD may be higher than previously estimated. Secondly, similar to MDD, the longitudinal symptomatic structure of BD is dominated by chronic subsyndromal depressive symptoms.⁽¹³⁻¹⁶⁾ It is increasingly recognized that depressive symptoms are a more impairing aspect of BD when compared to manic symptoms.⁽¹⁷⁾ Moreover, individuals with bipolar spectrum disorders (a predominantly depressive phenotype) exhibit impairment in functioning intermediate between those with bipolar I disorder and of non-cases in the general population.^(9,18) Thirdly, several cost-of-illness studies indicate that mood disorders are associated with substantial decrement in work performance, as well as appreciable caregiver burden, medical service utilization, and premature mortality.^(1,7,19) Improved recognition and management of non-bipolar depression has been shown to reduce overall illness burden and reduce costs.⁽²⁰⁾

Several factors limit the interpretations and inferences that can be drawn from this analysis. The major limitation of this post hoc analysis is that the CCHS was not designed *a priori* to evaluate and compare the effects of mood disorders on workforce function. The CCHS did not have a specific

TABLE 3b
Adjusted odds ratios for one or more mental health disability days in past two weeks in relation to lifetime bipolar I disorder (BD) and lifetime major depressive disorder (MDD), controlling for selected characteristics, currently employed household population aged 18 or older with mood disorder, Canada excluding territories, 2002

	Odds ratio	95% confidence interval
Mood disorder		
Lifetime BD	1.6*	1.0 to 2.6
Lifetime MDD [†] (excluding BD)	1.0	–
Sex		
Males	0.9	0.5 to 1.4
Females [†]	1.0	–
Age group		
18 to 34	1.5	0.9 to 2.5
35+ [†]	1.0	–
Level of education		
High school graduation or less [†]	1.0	–
Some post-secondary education	0.5*	0.2 to 1.0
Post-secondary graduation	0.5*	0.3 to 0.8
Comorbidity		
Chronic condition present [§]	2.0*	1.2 to 3.3
Body mass index category		
Underweight/normal weight/overweight (BMI < 30.0) [†]	1.0	–
Obese (BMI 30.0+)	1.2	0.7 to 1.9

* Estimate is significantly different from estimate for reference category ($p < 0.05$)

[†] Reference group, for which the odds ratio is always 1.0

– Not applicable

[§] Reference group is absence of arthritis, asthma, back problems excluding fibromyalgia and arthritis, high blood pressure, migraine, chronic bronchitis, emphysema or COPD, diabetes, epilepsy, heart disease, cancer, stomach or intestinal ulcers, effects of a stroke, bowel disorder/Crohn's disease or colitis, Alzheimer's disease or other dementia, cataracts, glaucoma, and thyroid disorder.

Odds ratios have been rounded, some with 1.0 as the lower or upper confidence limit are statistically significant (as indicated).

Model is based on records of 2 999 respondents screened positive for lifetime BD or MDD.

Source: 2002 Canadian Community Health Survey: Mental Health and Well-being

TABLE 4a
Adjusted odds ratios for good job security in relation to presence of mood disorder (lifetime bipolar I disorder (BD) or lifetime major depressive disorder (MDD)), controlling for selected characteristics, currently employed household population aged 18 or older, Canada excluding territories, 2002

	Odds ratio	95% confidence interval
Mood disorder		
Lifetime BD	0.4*	0.3 to 0.6
Lifetime MDD (excluding BD)	0.7*	0.6 to 0.8
None [†]	1.0	–
Sex		
Males	1.0	0.9 to 1.1
Females [†]	1.0	–
Age group		
18 to 34	1.0	0.9 to 1.1
35+ [†]	1.0	–
Level of education		
High school graduation or less [†]	1.0	–
Some post-secondary education	0.9	0.8 to 1.1
Post-secondary graduation	0.9*	0.8 to 1.0
Comorbidity		
Chronic condition present [§]	0.9	0.8 to 1.0
Body mass index category		
Underweight/normal weight/ overweight (BMI < 30.0) [†]	1.0	–
Obese (BMI 30.0+)	1.0	0.9 to 1.2

* Estimate is significantly different from estimate for reference category ($p < 0.05$)

[†] Reference group, for which the odds ratio is always 1.0

– Not applicable

[§] Reference group is absence of arthritis, asthma, back problems excluding fibromyalgia and arthritis, high blood pressure, migraine, chronic bronchitis, emphysema or COPD, diabetes, epilepsy, heart disease, cancer, stomach or intestinal ulcers, effects of a stroke, bowel disorder/Crohn's disease or colitis, Alzheimer's disease or other dementia, cataracts, glaucoma, and thyroid disorder.

Odds ratios have been rounded, some with 1.0 as the lower or upper confidence limit are statistically significant (as indicated).

Model is based on records of 20 251 respondents.

Source: 2002 Canadian Community Health Survey: Mental Health and Well-being

quantitative measure of work performance (e.g., World Health Organization Health and Work Performance Questionnaire). We are also unable to comment on components of impaired function and their contribution to overall performance and cost. For example, presenteeism may account for a larger component of workforce cost than absenteeism in the BD population.⁽⁴⁾ In keeping with this view, the CCHS does not have detailed longitudinal ratings of mood symptoms which prevents us from commenting on the relative contribution of depressive (or manic) symptoms to overall work performance. A symptomatic analysis of the comparative study by Kessler et al. indicates that the greater severity and persistence of depressive symptoms in the BD population mediates the greater effect of BD on workforce performance. The restriction of the study sample to persons currently employed also limits the interpretation of the results of the analysis. Specifically, any tendency for persons with BD or MDD to have disproportionately exited (or never entered) the labour force, relative to persons without these disorders, would result in diluting the strength of the observed association of mood disorder with work impairment from its true magnitude.

Other limitations of the CCHS include: identification of mood disorder was based on the CIDI which is less able to distinguish mixed episodes and bipolar spectrum conditions from MDD;⁽²¹⁾ insufficient information regarding prior work history and details of effects across different occupational groups; no objective measures of workforce performance; reliance on self-reporting for all dependent variables; the inclusion of persons whose manic episodes may have been due to

substance abuse; and inability to control for the effect of treatment. As well, although previous versions of the CIDI have been validated for use in community-based surveys, a version updated for the 2000 World Mental Health Initiative was used by the CCHS, and its validation has not been completed. Therefore, the extent to which assessments made by trained clinicians would correspond with CCHS findings is unknown. Nevertheless, individuals screening positive for MDD or BD in the CCHS survey are representative of other individuals with these disorders with respect to their lifetime prevalence, demographics, patterns of comorbidity, functional medical service utilization, and functional outcome.⁽²²⁻²⁴⁾

There is general awareness that mood disorders differentially affect disabled workers.⁽³⁾ The higher prevalence of MDD versus BD in the general population (and workforce) indicates that the aggregate cost of MDD is greater.⁽⁴⁾ Nevertheless, at an individual level, the study herein as well as the results from the Kessler et al. investigation, suggest that BD may be a more costly disorder. Emanating from this observation, screening and intervention programs for individuals with bipolar I disorder, and bipolar spectrum, may be more cost-effective than such programs for those with MDD.⁽⁶⁾ Behavioural health providers and employment assistance programs should incorporate opportunistic facile screening for BD.

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TABLE 4b
Adjusted odds ratios for good job security in relation to lifetime bipolar I disorder (BD) and lifetime major depressive disorder (MDD), controlling for selected characteristics, currently employed household population aged 18 or older with mood disorder, Canada excluding territories, 2002

	Odds ratio	95% confidence interval
Mood disorder		
Lifetime BD	0.6*	0.5 to 0.9
Lifetime MDD [†] (excluding BD)	1.0	–
Sex		
Males	0.8*	0.6 to 1.0
Females [†]	1.0	–
Age group		
18 to 34	0.9	0.7 to 1.1
35+ [†]	1.0	–
Level of education		
High school graduation or less [†]	1.0	–
Some post-secondary education	0.6*	0.4 to 0.9
Post-secondary graduation	0.8	0.6 to 1.1
Comorbidity		
Chronic condition present [§]	0.9	0.7 to 1.2
Body mass index category		
Underweight/normal weight/overweight (BMI < 30.0) [†]	1.0	–
Obese (BMI 30.0+)	0.8	0.6 to 1.2

* Estimate is significantly different from estimate for reference category ($p < 0.05$)

[†] Reference group, for which the odds ratio is always 1.0

– Not applicable

[§] Reference group is absence of arthritis, asthma, back problems excluding fibromyalgia and arthritis, high blood pressure, migraine, chronic bronchitis, emphysema or COPD, diabetes, epilepsy, heart disease, cancer, stomach or intestinal ulcers, effects of a stroke, bowel disorder/Crohn's disease or colitis, Alzheimer's disease or other dementia, cataracts, glaucoma, and thyroid disorder.

Odds ratios have been rounded, some with 1.0 as the lower or upper confidence limit are statistically significant (as indicated).

Model is based on records of 2 966 respondents screened positive for lifetime BD or MDD.

Source: 2002 Canadian Community Health Survey: Mental Health and Well-being

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A new population-based measure of the economic burden of mental illness in Canada

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Abstract

This paper presents a comprehensive measure of the incremental economic burden of mental illness in Canada which incorporates the use of medical resources and productivity losses due to long-term and short-term disability, as well as reductions in health-related quality of life (HRQOL), for the diagnosed and undiagnosed population with mental illness. The analysis was based on the population-based Canadian Community Health Survey Cycle 2.1 (2003). For all persons, we measured all health services utilization, long-term and short-term work loss, and health-related quality of life and their dollar valuations, with the economic burden being the difference in dollar measures between the populations with and without mental health problems. In total, the economic burden was \$51 billion in 2003. Over one-half was due to reductions in HRQOL. The current accepted practice in economic assessments is to include changes in medical resource use, work loss, and reductions in HRQOL.

Key words: *Economic burden, cost of illness, mental health, quality of life*

Introduction

Mental illness is a class of conditions which incur a significant use of health care resources, lost productivity, and human suffering. Two recent reports, one by Health Canada⁽¹⁾ and the other by the Senate,⁽²⁾ have underscored the large economic burden of mental illness in Canada.

Health Canada, in its 2002 Economic Burden of Illness in Canada Report,⁽³⁾ identified a large economic burden of mental illness from the use of direct government-funded health care services (\$4.7 billion in 1998), and the indirect cost of lost productivity due to short- and long-term disability and premature mortality (\$3.2 billion). A 1997 study by Health Canada,⁽⁴⁾ using several types of admini-

strative and survey data, estimated the economic burden (both direct and indirect costs) of mental disorders in Canada at \$7.8 billion in 1993 (or \$8.4 billion in 1998). Stephens and Joubert,⁽⁵⁾ using the same data as the 1997 Health Canada study as well as data from certain questions asked in the 1996/1997 National Population Health Survey (NPHS) regarding depression and distress, estimated that direct costs were \$6.3 billion (which included non-government insured health care services of \$278 million). The indirect costs of short-term and long-term productivity losses and early death associated with depression and distress were about \$8.1 billion. The estimated (recalculated) total burden was \$14.4 billion in 1998. All these estimates included only mental health services in the direct cost component.

However, the measured economic burden depends on how the concept is defined. We illustrate the concept of economic burden in Figure 1. As can be seen from this figure, economic burden includes both direct and indirect costs. The concept of economic burden, as recently formulated, also includes losses in health-related quality of life (HRQOL) (e.g., increases in pain and suffering) as an essential component.⁽⁶⁻⁹⁾ These losses from the HRQOL component add to the overall economic burden of illness, and the most recent measures of mental health economic burden incorporate it.⁽¹⁰⁾ The studies on economic burden mentioned above do not include losses in health-related quality of life. In addition, the above-mentioned estimates focus on mental health services costs, rather than on the excess costs of all health services, as the direct cost burden. Persons with mental health problems use both, and so the question of health service use is of considerable importance. In this paper, we report on our attempt to produce such a comprehensive measure for Canada.

The three significant features of our paper are (1) that it includes a measure of the burden of those with undiagnosed mental illness, (2) that the measures are based on the concept of excess costs and losses in outcomes that are attributable to mental illness, not simply measures of gross costs and losses, and (3) that it includes costs for all health services, not just those for mental health.

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Methods

Data

Data for this analysis came from the 2003 Canadian Community Health Survey (CCHS Cycle 2.1) public-use microdata file.⁽¹¹⁾ The CCHS is a cross-sectional survey conducted bi-annually by Statistics Canada which provides person-level information on the health status, health system utilization, and health determinants of Canadians living in private occupied dwellings. Sampling weights provided by Statistics Canada were applied to obtain population estimates.

Study population

The study was confined to the adult population aged 20 and above. We sought to classify individuals into one of three mental health categories (Diagnosed Mental Health Problems, Undiagnosed Mental Health Problems, or No Mental Health Problems) based upon their responses to particular questions selected from the CCHS Cycle 2.1. However, because not all questions were asked of all survey participants, we developed prevalence estimates based upon aggregated data for the three categories, as described in detail below.

For each of the following diagnostic categories, participants were asked whether they had been diagnosed by a health professional as having a major mental health problem in a common content Chronic Disease module. Persons were classified into the category Diagnosed Mental Health Problems if they said yes to any of the following questions: “Do you have schizophrenia?”, “Do you have a mood disorder such as depression, bipolar disorder, mania or dysthymia?”, or “Do you have an anxiety disorder such as a phobia, obsessive-compulsive disorder or a panic disorder?”

Our method for calculating undiagnosed mental illness follows that of Starkes, et al.⁽¹²⁾ but is broader in scope. Persons who had not been classified into the Diagnosed Mental Health category were classified into the Undiagnosed Mental Health

category if they had nevertheless met at least one of the following criteria in the past twelve months:

- a. In the self-rated mental health question, had reported their mental health as poor;
- b. In a module asking about contacts with mental health professionals, had reported 2 or more contacts in person or by telephone to a health professional about emotional or mental health;
- c. In a depression screening module consisting of many questions (taken from the Composite Diagnostic Interview Schedule),^(13,14) had been scored as having a probability of 0.8 or greater of being a clinical case of depression, or
- d. In a module about suicidal ideation or attempts, had indicated having ever seriously considered committing suicide or taking own life.

Only sub-segments of the survey population had been given the optional content questionnaire modules for sub-criteria *b*, *c*, and *d*. Specifically, only individuals from Newfoundland and Labrador, Prince Edward Island, New Brunswick, Quebec, Ontario, Alberta, and the North West Territories – a total of 77.1% of the weighted sample – had been asked the questions in *b* above; only individuals from Newfoundland and Labrador, Prince Edward Island, New Brunswick, some regions of Ontario and Saskatchewan, Alberta, Yukon, North West Territories and Nunavut – a total of 41.8% of the weighted sample – had been asked the questions in *c* above; and only individuals from New Brunswick, some regions of Ontario, Saskatchewan, Alberta, North West Territories, and Nunavut – a total of 32.2% of the weighted sample – had been asked the questions in *d* above.

The solution to estimating the three mental health categories involved a sequential process. First we estimated the prevalence of Diagnosed Mental Health Problems category from the full data. Then we estimated the prevalence of persons who

met criterion *a* for inclusion in the Undiagnosed Mental Health Problems category from the full data from the self-rated mental health question. From the group that had been administered both the question under criterion *a* and the questions under criterion *b*, we estimated the proportion which met criterion *b* but not criterion *a*. Similarly, from the set of persons administered all of the questions from *a*, *b*, and *c*, we estimated the proportion that met criterion *c* without meeting criterion *a* or *b*. This was repeated for the final set of questions, where the estimate was the proportion of persons meeting criterion *d* without meeting criterion *a*, *b* or *c*. These proportions were then added together to get a single prevalence estimate of persons in the Undiagnosed Mental Health Problems category.

There are two important aspects to note about this procedure. First, it makes the assumption that where the questions were not asked of all subjects, the sub-sample to which they were administered was nevertheless a representative one. And second, the proportion of persons that met each successive criterion is smaller, and therefore estimation errors due to sample bias should also be successively smaller at each stage.

Finally, the number of persons in the No Mental Health Problems category was estimated by subtraction. The results are presented in the first row of Table 1.

Outcome Measures

All outcome measures were estimated for each of the age-sex groups for all three Mental Health Problems categories defined above.

Utilization

Medical cost measures were derived from health care utilization during a one-year period measured as the number of all (i.e., not just mental health-oriented) general practitioner visits, specialist visits, and hospital days, as self-reported by each person in the survey. Use of physician services was determined based on the

question which asked the number of times (excluding hospital stays) the person had seen/talked on the telephone with the health professional (general practitioner and specialist) about his/her physical, emotional or mental health in the past year. Use of hospital resources was determined based on questions about the number of nights spent in a facility. Utilization was estimated for each age-sex group for all three mental health categories.

Unit Costs

Unit costs of services for age-sex groups were based on Alberta provincial statistics provided by Alberta Health and Wellness (AHW) for the budget year 2000 to 2001,⁽¹⁵⁾ adjusted for inflation and national levels, where appropriate. AHW maintains a database of physician claims which typically contains over 30 million records each year. The database records the location/type of service provided and the specialization of the physician for each claim. Average cost per visit to a general practitioner contained both the physician fee and the costs of laboratory tests. Specialist visits comprised visits made in specialists' offices and those made in hospital outpatient clinics (including emergency room). Average cost per specialist office visit included both the physician fee and the costs of diagnostic services. For specialist outpatient visits in a hospital setting, a hospital outpatient facility fee (based on the province-wide Alberta Ambulatory Care Classification System cost per visit) was added to the physician fee. Hospital inpatient stays included both facility and physician components. We used the province-wide per diem cost of \$809 (\$780 in 2000 to 2001 adjusted by 6.5% for the change in the Consumer Price Index to 2003 to 2004) for a typical hospital day and added the average physician billing per day of hospitalization. Physician fees for Alberta were downward adjusted by 18% because Alberta's fees per service level were higher than the national average by this amount.⁽¹⁶⁾ The unit costs of services according to age-sex groups were applied to each unit of service. Total medical cost per person is the sum of the costs for the three types of services.

Work Loss – measurement and valuation

Work loss due to long-term disability is estimated based on unemployment data in the past year. The proportion of people in each age-sex group who did not work throughout the year was obtained by tabulating answers to the question in the CCHS which asked each respondent for the number of weeks he/she worked at a job or business during the past year (including paid vacation leave, paid maternity leave, and paid sick leave). Lost work due to long-term disability (unemployment) was valued by an average annual wage, by sex, obtained from Statistics Canada [www.statcan.ca, Table 202-0102] for the year 2003. For 2003, the annual earnings were \$25,300 for women and \$40,200 for men.

In addition, work loss due to short-term disability (absenteeism) was also estimated based on questions that asked for the number of days spent in bed for all or most of the day (including hospitalization) in the 14-day period prior to the interview. The mean number of disability days in the two-week period for each age-sex group was multiplied by 5/7 assuming that the disability days were distributed equally across weekdays and weekends and further multiplied by 26 weeks to obtain the annualized figure. This annualized figure was then multiplied by a daily wage obtained from Statistics Canada. The average weekly earnings for all industries was \$690.57 in 2003, averaged over fulltime and part-time workers. This figure was divided by 5 working days to obtain a daily figure of \$138.11 which was then applied to both men and women in each age-sex group.

TABLE 1
Unit values for outcomes by mental health status in Canada (2003) in population 20 and over

	No mental illness	Diagnosed mental illness	Undiagnosed mental illness	Population
Frequency	23 261 558	1 877 163	1 605 238	26 743 959
Percent total	87.0%	7.0%	6.0%	100.0%
Male				
20 to 34 years	3 179 784	150 433	215 549	
35 to 49 years	3 822 703	235 545	246 683	
50 to 64 years	2 727 415	195 830	120 105	
65+ years	1 659 625	71 528	40 779	
Female				
20 to 34 years	3 154 711	302 591	332 724	
35 to 49 years	3 840 586	433 365	396 629	
50 to 64 years	2 751 214	330 160	190 324	
65+ years	2 125 520	157 711	62 445	
Per person values (weighted averages)				
GP visits	2.9	6.7	4.8	
Specialist visits	0.7	2.5	1.7	
Hospital days	0.5	2.2	1.2	
Health utility index	0.91	0.71	0.8	
Percent not working (long-term work loss)	0.33	0.46	0.26	
Disability days per year (short-term work loss)	10	33	27	

Health Utilities – measurement and valuation

Health-related quality of life (HRQOL) for each person was assessed using the Health Utilities Index Mark 3 (HUI3). HUI3 is a preference-based, multi-attribute measure of HRQOL that uses a multiplicative utility function to assign valuations to different health states.^(17,18) In the HUI3 system, health status is defined by 8 attributes – vision, hearing, speech, mobility, dexterity, emotion, cognition and pain. Each attribute has a number of different levels, and utility-based preference scores assigned to each attribute level are then combined multiplicatively to arrive at an overall utility score or index which measures the HRQOL associated with each individual's health state. Overall HUI scores range in the CCHS Cycle 2.1 from -0.36 to 1.0, with -0.36 representing the worst possible health state, 0.0 representing death and 1.0 representing full health. One year in full health is equivalent to one Quality Adjusted Life Year (QALY). According to Drummond,⁽⁷⁾ differences in overall utility scores of 0.03 are considered to be clinically significant.

In the CCHS, health status is an optional content questionnaire module which was only selected by 5 provinces – Newfoundland and Labrador, Prince Edward Island, Nova Scotia, New Brunswick and Quebec. As such, the analysis used sample weights of the 5 provinces to project HUI scores for the populations in the three mental health categories. To obtain a dollar value for the reductions in health utilities, the lost QALYs were multiplied by a figure of \$50,000, a dollar valuation commonly used in policy making.¹⁹

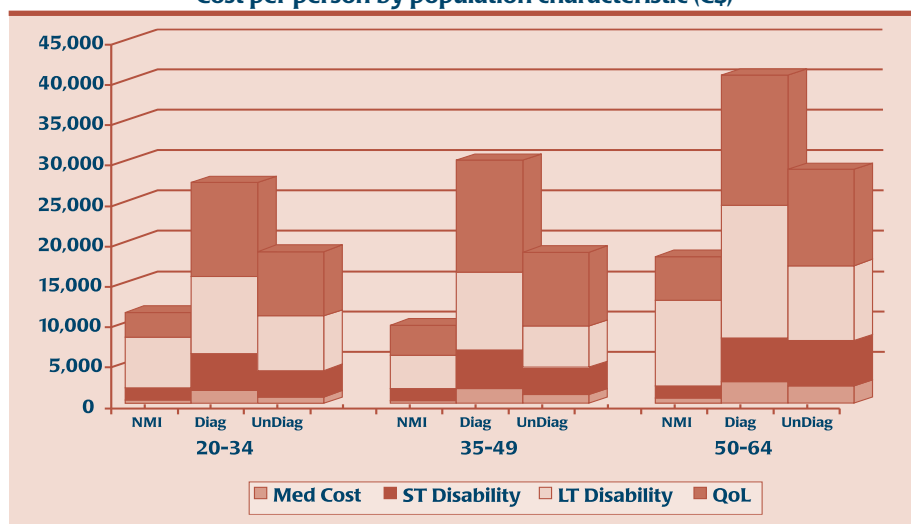
Analysis Methods

Our definition of economic burden focuses on the excess costs and losses in outcomes that are attributable to mental illness. It incorporates (1) the excess costs of the use of medical services resulting from mental illness, (2) the excess of work loss, both long term (unemployment) and short term (absenteeism), as a result of the disorder,

FIGURE 1
Classification of the components of economic burden

Health care resources	Direct (government) costs		Out-of-pocket and insurance costs
Lost productivity	Short-term disability	Long-term disability	Premature mortality cost
Health outcomes	Losses in health-related quality of life from morbidity		

FIGURE 2
Cost per person by population characteristic (C\$)



N MI = no mental illness, Diag = diagnosed mental illness, Un Diag = undiagnosed mental illness, Med Cost = direct medical cost, ST Disability = short-term disability, LT Disability = Long-term disability, QoL = quality of life.

TABLE 2
Economic burden of mental illness, Canada, 2003

	Diagnosed (C\$m)	Undiagnosed (C\$m)	Total burden (C\$m)	Per cent of total
Direct medical cost	3,518	1,447	4,965	9.8
Dollar value of work loss (long-term)	8,386	68	8,454	16.6
Dollar value of work loss (short-term)	5,724	3,551	9,275	18.2
Dollar value of loss in health unit	18,750	9,403	28,153	55.4
Total burden	36,378	14,469	50,847	100.0%

and (3) the excess loss in health utilities attributable to mental illness. All three components are expressed in terms of the differences in these measures between the populations which have Mental Health Problems (Diagnosed and Undiagnosed) and the one with No Mental Health Problems.

Excess of or net medical costs due to mental illness were estimated in the way stated above for each age-sex group and aggregated to obtain the total excess cost for each mental health problem category. In the case of health utilities, non-mentally ill persons generally have higher HUI scores than mentally ill persons, diagnosed and undiagnosed (Table 1). Taking the differences in the scores gives us the losses or reductions in health utilities attributable to the disorder. Starting with the diagnosed category, we multiplied the losses in health utilities for each age-sex group by the number of persons in each sub-group to obtain the number of lost QALYs for each sub-group. The lost QALYs for all the age-sex sub groups were then aggregated to obtain the total number of lost QALYs for the diagnosed category. The same was repeated for the undiagnosed category. The excess of income lost from long-term disability (work loss due to unemployment) in the past year and from short-term disability (work loss due to absenteeism annualized) were estimated in a similar way and added to the above costs to arrive at the total economic burden of diagnosed and undiagnosed mental illness population groups in Canada in 2003.

Results

The adult population of Canada, broken down by component, is shown in Table 1. Of the total population, 7% or nearly 1.9 million people have been diagnosed with mental illness and a further 6% or 1.6 million people are undiagnosed. The largest portion of mentally ill individuals, for both males and females, falls in the 35 to 49 age range; with females having a higher prevalence rate (between 1.5 and 2

times more) in all age groups for both the diagnosed and undiagnosed categories.

Utilization of all health care services is highest for the diagnosed mentally ill, lowest for the non-mentally ill, with those in the undiagnosed category in the middle. The same is true for health utility and absenteeism. Employment is lower for the diagnosed, but more undiagnosed are working than those without mental illness. The dollar values of these estimates follow the physical measures, as shown in Figure 2. The average medical cost per capita was \$643 for the non-mentally ill and \$2,515 for the diagnosed and \$1,442 for the undiagnosed.

On a per capita basis, the value of work loss (unemployment) is the highest component; this is the result of the high unit cost of an annual loss of employment (an average of \$32,750 per person).

The incremental economic burden of mental illness of persons over the age of 20 is shown in Table 2. The total burden for 2003 was about \$51 billion, with close to 30% of the cost incurred by the undiagnosed mentally ill population. Loss of health utilities, valued at \$50,000 per quality-adjusted life year (QALY), was by far the dominating effect, accounting for more than 50% of the total burden or around \$28 billion. The value of work loss from absenteeism (short-term disability) was about 10% higher than the value of work loss from unemployment (long-term disability); and together they account for about 35% of the burden. Medical expenses accounted for less than 10% of the total burden.

Discussion

We have constructed a comprehensive measure of the incremental economic burden of persons with mental illness aged 20 and above in Canada in 2003. Our total estimate of the burden was \$51 billion. The main components are shown in Table 2, with the loss in health utilities

accounting for more than one-half of the total burden.

Our results and analysis differ conceptually from those of Health Canada⁽³⁾ and Stevens and Joubert (SJ).⁽⁵⁾ Health Canada's analysis identified specific mental health services, while ours examines all health care services (used by persons with mental illness) for all causes, to measure direct health care costs. The Health Canada approach, however, could not be used to identify the numbers of persons who received services. Health Canada conducted its estimate using a top-down approach, by which costs were assigned to mental health (and other conditions) according to how services were used; patients were not identified. Only services which were specifically coded (in billings and abstracts) to mental health were included. Further we included only hospital and medical services, whereas Health Canada included medicines as well. Both Health Canada and SJ, as well as our study, excluded community mental health. SJ used the Health Canada estimates for direct cost, but they used a similar approach to ours for indirect costs (i.e., excess costs as derived from the CCHS).

SJ have a definition of mental illness that includes depression and distress, while ours focused on diagnosed and undiagnosed mental illness.⁽⁵⁾ However, their definitions of both short- and long-term time-loss costs differ from ours. Our short-term time loss includes only time lost from work; SJ included time lost from all activities. We measure long-term costs as the value of the difference in employment between those with and without mental illness. SJ included only the inactivity days within the net time of unemployment. As we defined the entire loss of employment during a single year as our work-loss measure, our number is much larger than that of SJ.

One of the major benefits of our approach, as pointed out by SJ,⁽⁵⁾ is that resources used are traced to persons. This allows the overall burden to be assigned to a variety

of specific risk factors, such as age, sex and socio-economic indicators, that is, a population health approach. A second benefit of our approach, which stems from the first, is that it allows us to estimate the net additional use of all healthcare resources, even if they have not been identified as “mental health” resources. Persons with mental illness may use more general health services, and this will be reflected in our analysis.

Our approach is also significant in identifying and including the undiagnosed mentally ill population (of around 1.6 million persons) in the cost estimate. More than one-fourth of the total burden was attributed to this population, and they accounted for about 30% of the direct medical cost. Sareen, et al.⁽²⁰⁾ have shown using the Mental Health Supplement of the Ontario Health Survey that in addition to the explicit criteria of an accepted diagnostic system, self-perceived need for mental health treatment provides valuable information for estimating the number of people in the population who need mental health services, and in devising public health strategies to minimize the burden of mental illness in Canada.

Several key assumptions should be highlighted, because the results are influenced by the approach taken. First, the health utility effect depends on the value placed on a QALY. It would have been substantial even if the valuation per QALY was very conservatively valued at \$20,000, as was suggested by Laupacis.⁽²¹⁾ In this case, the burden of HRQOL would still be over \$11 billion and nearly 35% of the total burden. A value of \$50,000 placed on the loss of a QALY is the most widely used, but it is still arbitrary. If the value were \$10,000 lower/higher, this would deduct/add about \$1,500 to the difference per person. In any event, it is clear that HRQOL poses the major component of the economic burden of mental illness and cannot be ignored.

Second, the calculation of the annual loss placed on persons who are out of work in the long term depends on the perspective of the study. Using the current method, value lost is equal to lost wages for each

“incremental” year of work lost. There is an alternative approach, the “friction cost” approach: if the worker is replaced by another who would, otherwise, not have been employed, there is an offset to the lost work. The societal measure of work loss is equal to the income lost by the disabled worker minus the gains made by the replacement worker. One method placed the friction cost estimate at about one-half that of the current method.⁽²²⁾ If this were the case, long term losses would be closer to \$9 billion, rather than \$16 billion and the total burden would be reduced by this amount as well.

Our approach which is based on community survey has several limitations which will also influence our total estimate. Firstly, utilization estimates are based on personal recall, which are not as reliable as provider encounter records. However, a previous analysis using this data indicated that the estimate of global costs using this method is consistent with other methods.⁽¹⁵⁾

A second limitation is related to our use of unit costs. Our costs represent general health care costs, not those for mental health services. Per diem hospital costs, in particular, are lower for psychiatric admissions than they are for general admissions. In 2004 mental health inpatient services cost were roughly \$600 per day, compared to our estimate for general health services of \$800. Our estimate for hospital costs is somewhat higher, though some of these hospitalizations will be for non-mental health care and should be costed at the higher rate. We have no information what this percentage is.

A third and related, limitation is that we do not explicitly account for the contribution of physical comorbidities to the effects of mental illness on productivity. The literature indicates that the combination of physical and mental illness have a greater impact on disability.^(23,24) Using our approach to estimating undiagnosed cases, it would prove very difficult to estimate the net contribution of comorbidities.

A final limitation deals with the persons identified in the CCHS survey. As this was a household-based survey, it excluded

persons with mental illness who were permanently institutionalized. According to estimates obtained from CIHI, there were 403 long-term psychiatric beds in specialty psychiatric hospitals in 2003 to 2004 in Ontario.⁽²⁵⁾ Assuming that Canada-wide the beds to population ratio were the same as in Ontario, there would be 1,039 long-term residents in Canada. At 365 days per patient, the total bed days would be 379 000. At a very rough daily (Ontario) cost of between \$300 and \$400 for institutionalized mental health persons [Source: Alberta Mental Health Board] (\$109,500 - \$146,000 per person yearly), these institutionalized persons would cost between \$113 million and \$151 million. If this calculation is correct, then institutionalization costs would add about 3% to our estimates of direct costs.

Apart from the estimation and sampling errors, our investigation has left out mortality differences in indirect costs. Though they would be higher for the mentally ill population, these would likely not be very different between the groups. In direct costs, we have left out services of non-medical mental health professionals such as social workers and psychologists. This would add about 4 per cent to our estimate (SJ⁽⁵⁾). The most important of these omissions are outpatient prescription drugs because they cannot be calculated from the CCHS. Health Canada⁽³⁾ estimates mental health drug costs to be 22% of total health care costs; this implies that the total direct costs with drugs would be about \$6 billion, up from about \$5 billion.

In conclusion, the economic burden of persons with mental illness as we have measured it is substantial. Losses in HRQOL, normally excluded, are substantial in this measure. While these are not costs (i.e., resource use items) as usually defined, they do impose hardship, and people are willing to pay to reduce the burden, i.e., they have economic value. However, it should be stressed that there are different ways of defining and measuring economic burden, and which one is appropriate depends on the purpose of the study. And finally, data have improved enormously in recent years, but while we are closer to a comprehensive estimate,

better data in the area of institutional care, community care, and pharmaceuticals are needed to provide global estimates of cost that will be helpful to policy-makers.

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The evolution of HPV-related anogenital cancers reported in Quebec – Incidence rates and survival probabilities

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Abstract

Non-cervical anogenital cancers (i.e. anal, vulvar, vaginal and penile cancers) associated with the human papillomavirus (HPV), for which HPV is known to be the necessary cause of carcinogenesis, are poorly documented due to their relatively low incidence rate. The aim of this study is to describe the incidence rates of these cancers between 1984 and 2001, and their relative survival probabilities, in Quebec (Canada) between 1984 and 1998. The incidence of these cancers is on the rise, particularly anal cancer in women and, more recently (since 1993-95), vulvar cancer. Between 1984-86 and 1993-95, the 5-year relative survival probability for men with anal cancer decreased from 57% to 46%, while that for penile cancer dropped from 75% to 59%. However, during the same period, the 5-year relative survival probability for women with anal cancer rose from 56% to 65%, and remained stable for cervical and vulvar cancers, at 74% and 82%, respectively.

Key words: *alphapapillomavirus, uterine cervical neoplasm, anal neoplasm, vaginal neoplasm, vulvar neoplasm, penile neoplasm, survival probability*

Introduction

The fight against the human papillomavirus (HPV) has taken a major turn since this infection was identified as the necessary cause of cervical cancer. In fact, in addition to including HPV-detection tests in the screening or follow-up of cytological anomalies, the battle against this disease has been bolstered by the development of prophylactic vaccines.⁽¹⁾

HPV is associated with a spectrum of diseases other than cervical cancer. It is now believed to be associated with other anogenital cancers, including over 80% of anal cancers and approximately 40% to 50% of penile, vulvar and vaginal cancers.^(2,3) It is also associated with a significant proportion of oropharyngeal cancers,^(2,3) and may be associated with other cancers⁽⁴⁾ as well.

To date, non-cervical anogenital cancers associated with HPV have been poorly documented due to their low incidence rate. A few studies have reported an increase in the incidence rate of anal cancer in the U.S.,⁽⁵⁻⁷⁾ Sweden⁽⁸⁾ and Denmark⁽⁹⁾ over the past several decades; however, population data are scarce for the other types of anogenital cancers (vulvar, vaginal, penile).⁽¹⁰⁻¹²⁾

The aim of this study is to describe the significance and evolution of HPV-related anogenital cancers in Quebec. More specifically, this epidemiological portrait will address the incidence rates of cervical, anal, vulvar, vaginal and penile cancers in Quebec from 1984 to 2001, as well as the relative survival probabilities associated with these cancers from 1984 to 1998. The evolution of the incidence rate of cancer may provide insight into

the changes in causal risk factors. It may also help evaluate the effects of screening, diagnostic and prevention procedures for these types of cancers.

Method

Data source

The data on the incidence rate of cancers diagnosed in Quebec between 1984 and 2001, inclusively, were taken from the Fichier des tumeurs du Québec (FiTQ) [Quebec tumour registry]. The population data used to calculate the rates are Institut de la statistique du Québec (ISQ) [Quebec statistics centre] estimates, based on national censuses (Statistics Canada) and corrected to account for under-enumeration, over-enumeration and non-permanent residents.

With respect to the calculation of survival probabilities, the vital status of individuals whose cancers were reported to the FiTQ between 1984 and 1998 was determined by linking their case reports with the Quebec death registry from 1984 to 1999, inclusively. The linking of these two registries is described in the report entitled “Cancer survival of newly diagnosed cases, Quebec, 1992”⁽¹³⁾ in the section on the quality of data used. The cancers addressed in this study are anal (ICD-9 154.2, 154.3 and 154.8), cervical (ICD-9 180), vaginal (ICD-9 184.0), vulvar (ICD-9 184.1, 184.2, 184.3 and 184.4) and penile cancers (ICD-9 187.1, 187.2, 187.3 and 187.4, 187.7 and 187.8).

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Calculation of standardized incidence rates

The reference population used to calculate the standardized incidence rates was that of the 1991 Canadian census, distributed by age group, both sexes combined. For each type of cancer, the incidence rate was calculated based on three categories of morphology (squamous-cell, adenocarcinoma and other). Squamous-cell cancers are the most frequent (67%, 58%, 64%, 57% and 74%, respectively, for cancers of the vulva, vagina, cervix, anus and penis).

Calculation of survival probabilities

The calculation of survival probabilities was based on newly diagnosed cases of cancer reported to the Quebec tumour registry, involving individuals under 100 years of age at diagnosis. Only the first primary cancer reported in an individual between 1984 and 1998, inclusively, was retained. Subsequent primary cancers were excluded.

The relative survival probability is a ratio of the probability of survival observed in a group of patients to the expected probability of survival of a comparable group within the general population that, hypothetically, does not have the cancer being studied and has the same demographic characteristics as the group of cancer patients. The observed survival probability is calculated according to the actuarial method, i.e. the

ratio of the number of survivors at the end of the follow-up period to the number of living individuals at the beginning of that same period. The expected survival probability was estimated using three mortality tables for the general population of Quebec,⁽¹⁴⁻¹⁶⁾ based on the Ederer II method.⁽¹⁷⁾ The calculation of the relative survival probability is described in detail by Louchini et al.⁽¹⁸⁾

Findings

Incidence rates of and relative survival probabilities for anogenital cancers

From 1984 to 2001, there were 9556 reported cases of primary anogenital cancers, all types combined: 988 (10%) in men and 8568 (90%) in women. This large proportion observed in women is attributable mainly to cases of cervical cancer, which alone represents 65% of all anogenital cancers. Table 1 presents the distribution of these cancers by site, sex and time period. Figure 1 presents this distribution by site, sex and age, for the entire period. With the exception of cervical cancer, which is most common in women aged 40-59, anogenital cancers are most common in the 60-79 age group, which accounts for roughly 50% of all such cancers observed.

Cervical cancer has the highest incidence rate among all anogenital cancers, followed by vulvar cancer. For example, between 1999 and 2001, the incidence rate was 5.6

per 100 000 women for cervical cancer and 1.3 per 100 000 women for vulvar cancer. Incidence rates for the other cancers range from 0.2 to 0.8 per 100 000 (Figure 2).

A total of 7201 cases of anogenital cancer reported as the first primary cancer were used to calculate the relative survival probabilities between 1984 and 1998. They are distributed as follows: 4822 cases of cervical cancer, 900 cases of vulvar cancer, 290 cases of vaginal cancer, 360 cases of penile cancer and 759 cases of anal cancer (338 men and 421 women). Relative survival probabilities vary by site and sex. The 5-year relative survival probability is highest for vulvar cancer (81%) followed by cervical cancer (72%), penile cancer (67%), anal cancer (53% in men and 60% in women) and, finally, vaginal cancer (49%). Figure 3 presents the relative survival probabilities for each site, up to 15 years post-diagnosis. While relative survival probabilities for vulvar cancer and vaginal cancer have reached a plateau at 6 years and 9 years post-diagnosis, respectively, those for penile cancer and anal cancer have decreased to 59% and 42% at 15 years post-diagnosis, respectively.

Relative survival probabilities also vary by age group, decreasing with age for most sites (Figure 4); however, the relative survival profiles for vaginal cancer, anal cancer in men and penile cancer are different for the youngest age group. In fact, the relative survival probability for this age

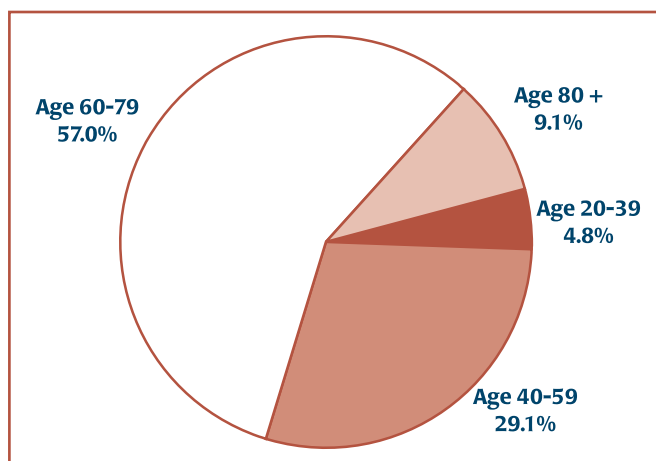
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TABLE 1
Distribution of the number of new cases (% in parentheses) of cancer, by site (all morphologies), sex, and time period, Quebec, 1984-1986 to 1999-2001

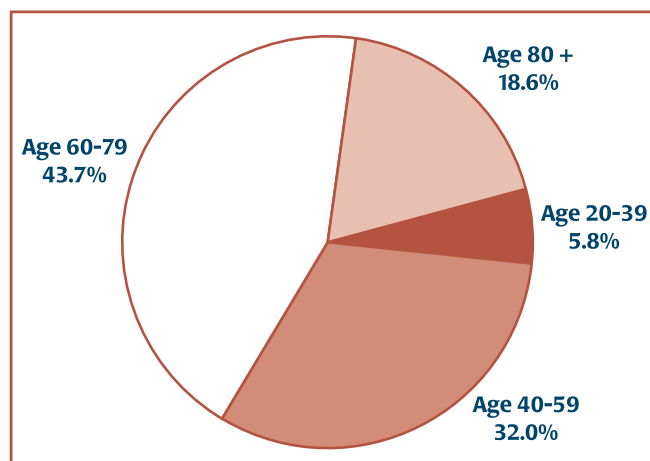
Site	Sex	1984-86		1987-89		1990-92		1993-95		1996-98		1999-01		Total	
Anus	Men	53	(3)	59	(4)	80	(5)	107	(7)	79	(5)	82	(5)	460	(5)
	Women	70	(4)	69	(5)	101	(7)	111	(7)	101	(7)	139	(9)	591	(6)
Cervix	Women	1 229	(72)	1 057	(68)	1 003	(65)	1 011	(64)	939	(61)	976	(60)	6 215	(65)
Vagina	Women	103	(6)	95	(6)	86	(6)	79	(5)	67	(4)	57	(4)	487	(5)
Vulva	Women	182	(10)	189	(12)	181	(12)	196	(12)	264	(17)	263	(16)	1 275	(13)
Penis	Men	77	(4)	79	(5)	93	(6)	78	(5)	93	(6)	108	(7)	528	(6)
Total	Men	130	(8)	138	(9)	173	(11)	185	(12)	172	(11)	190	(12)	988	(10)
	Women	1 584	(92)	1 410	(91)	1 371	(89)	1 397	(88)	1 371	(89)	1 435	(88)	8 568	(90)
	Total	1 714	(100)	1 548	(100)	1 544	(100)	1 582	(100)	1 543	(100)	1 625	(100)	9 556	(100)

FIGURE 1
Distribution of new cases of cancer, by site (all morphologies), sex and age, Quebec, 1984-2001

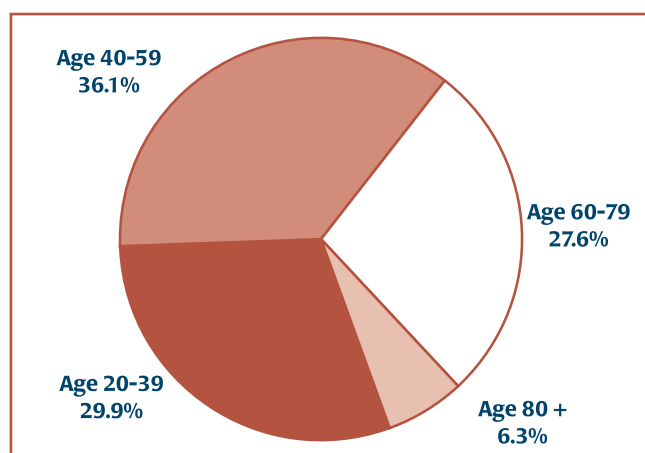
a) Anal cancer in men



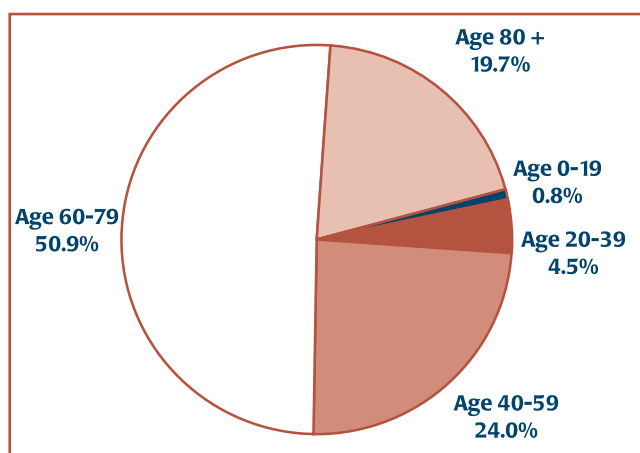
b) Anal cancer in women



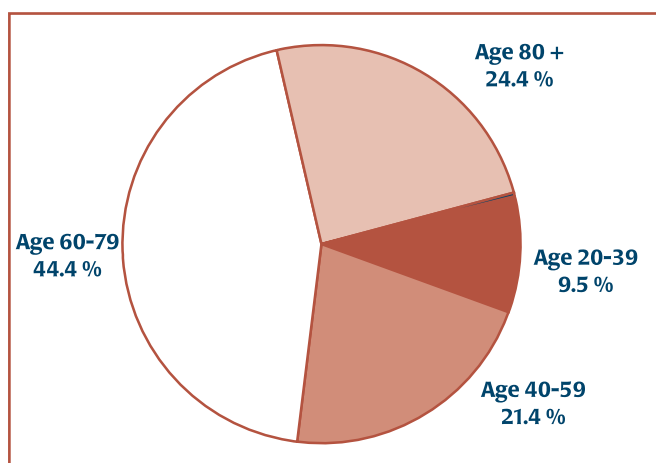
c) Cervical cancer



d) Vaginal cancer



e) Vulvar cancer



f) Penile cancer

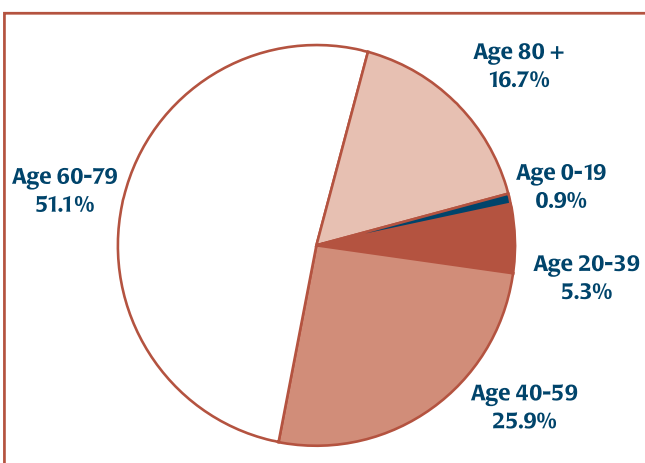
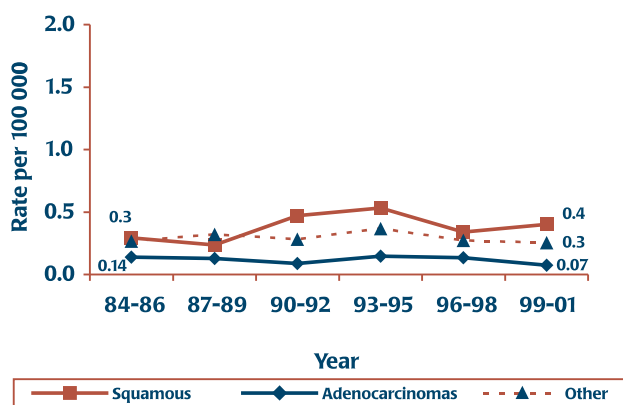
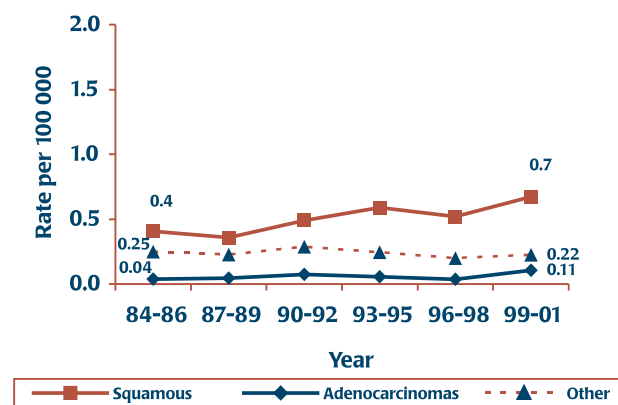


FIGURE 2
Evolution of standardized incidence rates of anogenital cancers, by sex, Quebec, from 1984-1986 to 1999-2001

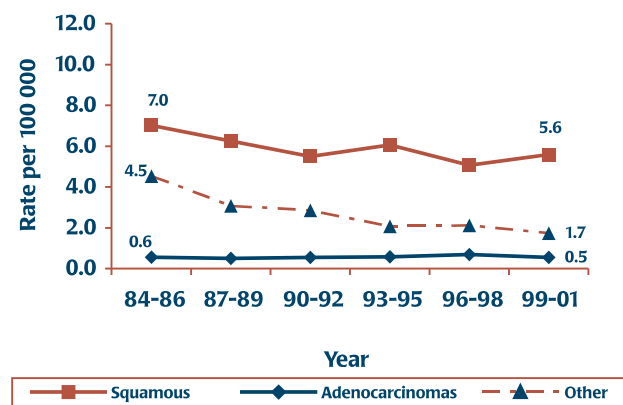
a) Anal cancer in men



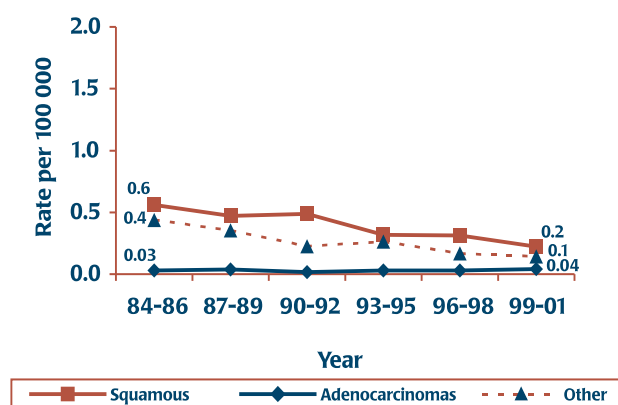
b) Anal cancer in women



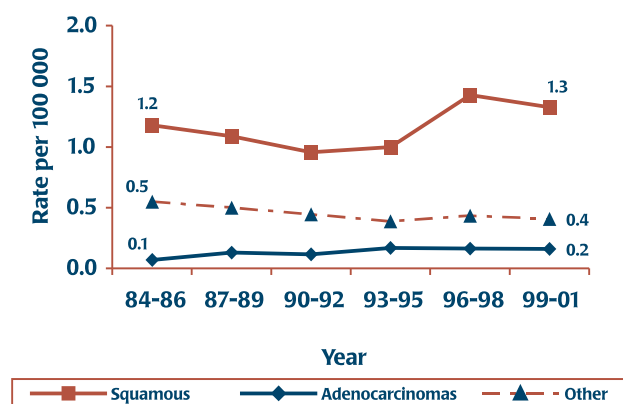
c) Cervical cancer



d) Vaginal cancer



e) Vulvar cancer



f) Penile cancer

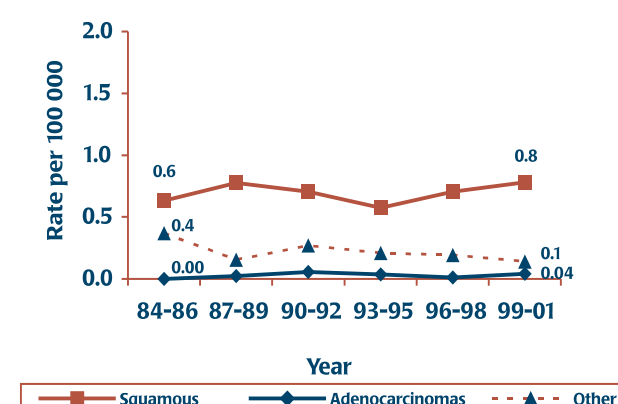
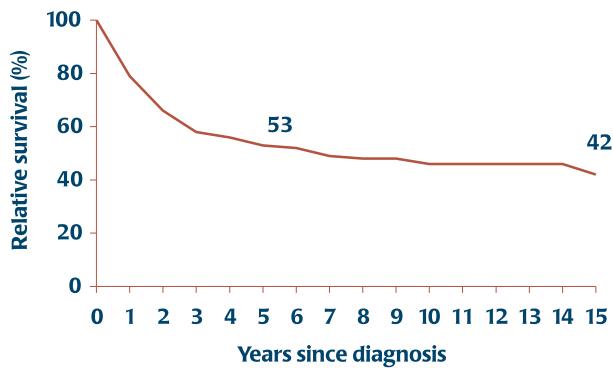
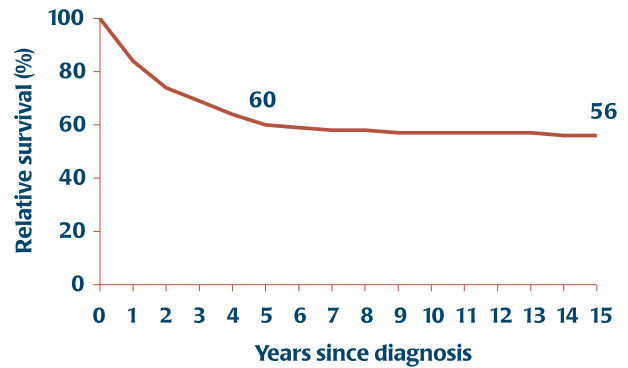


FIGURE 3
Relative survival (%), by site (all morphologies) and sex, Quebec, 1984-1998

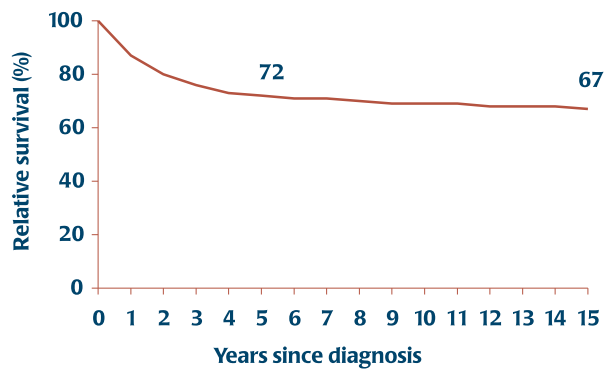
a) Anal cancer in men



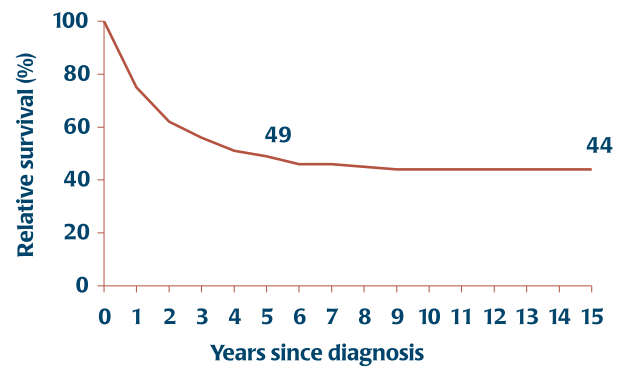
b) Anal cancer in women



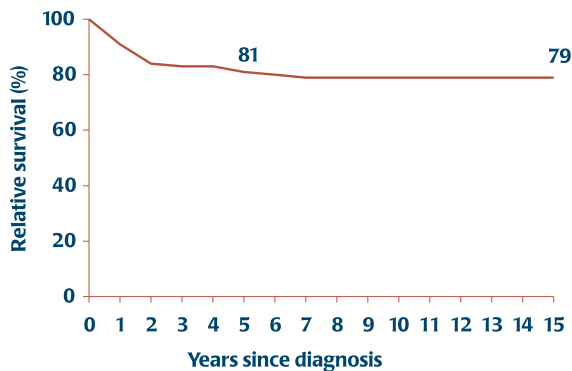
c) Cervical cancer



d) Vaginal cancer



e) Vulvar cancer



f) Penile cancer

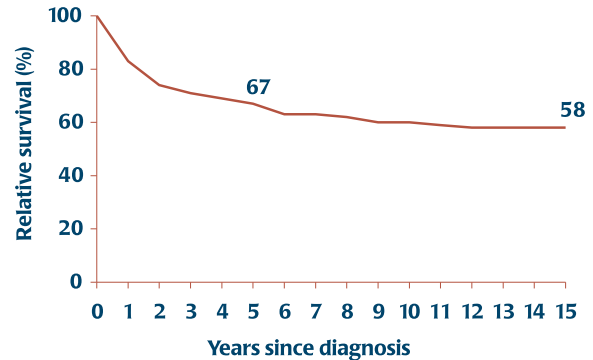
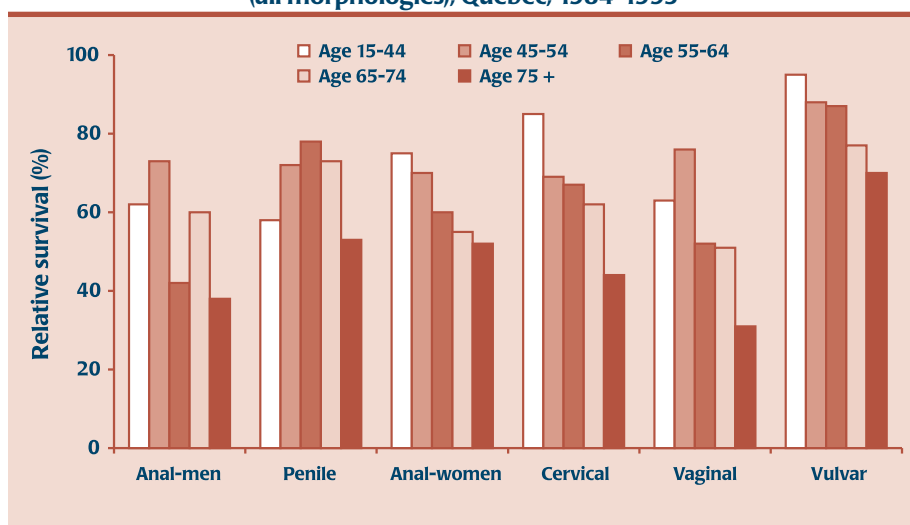


FIGURE 4
Five-year relative survival (%), by age group and site
(all morphologies), Quebec, 1984-1995



group is not the highest, as compared with the other anogenital cancer sites.

Evolution of the incidence of anogenital cancers

The incidence rate of anal cancer increased between 1984-1986 and 1999-2001, particularly in women (Figure 2), and the incidence of vulvar cancer has increased slightly since 1993-95. However, there has

been a decline in the incidence of cervical and vaginal cancers.

Evolution of the relative survival probabilities for anogenital cancers

The relative survival probabilities for men with anal or penile cancer dropped from 57% and 75%, respectively, in 1984-86, to 46% and 59% in 1993-95. However, the 5-year relative survival

probability for women with anal cancer increased from 56% to 65%. The 5-year survival probability for cervical and vulvar cancers remained stable at 74% and 82%, respectively (Figure 5).

Relationship between the incidence of anal cancer and cervical cancer in women in Quebec between 1984 and 1999: incidence rate of a second cancer site

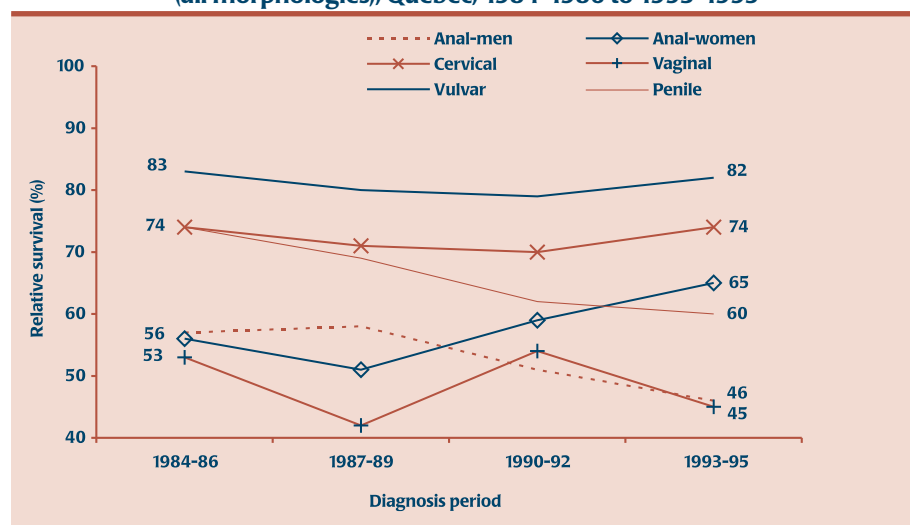
We also studied the relationship between anal cancer and cervical cancer in women. Only 3 women in 5818 who had either cervical cancer or anal cancer also had a second cancer at a different site (cervix or anus) during the 17-year observation period in Quebec.

Discussion

The results of this study show that, between 1984 and 2001, the incidence of anogenital cancers in Quebec, particularly anal cancer in women and vulvar cancer since 1993-95, was low but rising. The same trend was observed for anal cancer in several countries, specifically the U.S., Denmark and Sweden,^(5,6,8,9,19,20) and for vulvar cancer in Sweden⁽²¹⁾ between 1958-69 and 1990-96 and in Austria⁽²²⁾ between 1985-88 and 1994-97. However, the latter increase was not observed in Norway, Switzerland or the U.S.^(11,23,24) The surge in vulvar intraepithelial neoplasia (VIN), a precursor to vulvar cancer,⁽²⁴⁾ particularly in young women,⁽²⁵⁾ may explain the observed increase in the incidence of vulvar cancer. A New Zealand study reported that 87.5% of 113 untreated cases of grade-3 VIN evolved into invasive cancer.⁽²⁶⁾

In contrast to other anogenital cancers, the incidence rates of cervical cancer and vaginal cancer dropped markedly. This drop in the incidence of vaginal cancer was also observed in Switzerland. In fact, the incidence rate of vaginal cancer (per 100 000) dropped from 0.8 in 1974-84 to 0.4 in 1985-94,⁽¹¹⁾ conversely, a slight increase was observed in Sweden.⁽²¹⁾ Early screening with the introduction of the Pap test in

FIGURE 5
Five-year relative survival (%), by diagnosis period and site
(all morphologies), Quebec, 1984-1986 to 1993-1995



the 1960s accounts for the reduction in the number of cervical cancers. Similarly, the withdrawal of diethylstilbestrol (DES) from the market in 1971 may also explain the lower incidence of cervical and vaginal cancers. DES, a synthetic form of estrogen, was found to be associated with a higher risk of squamous intraepithelial neoplasia and clear cell adenocarcinoma of the cervix and vagina in girls whose mothers were treated with this drug during pregnancy.⁽²⁷⁾ This hormone was prescribed between 1941 and 1971 to women who experienced bleeding during pregnancy, had had previous miscarriages or were diabetic.⁽²⁸⁾

Genital HPV infection raises the issue of the risk of multiple cancers, particularly anal cancer in women and cervical cancer. In Quebec, only 3 women had both anal cancer and cervical cancer over a 17-year study period. While this result does not enable us to establish a clear link between these two cancer sites, a retrospective study measuring the standardized incidence ratios of low- and high-grade cervical intraepithelial neoplasia (CIN 1, 2 and 3) and the incidence of concomitant and subsequent anogenital cancers (cervical, anal, vulvar and vaginal) indicates a strong relationship.⁽²⁹⁾

The findings also indicate that the relative survival probability is lower in the youngest age group for anal cancer in men and for penile and vaginal cancers. Contrasting results for anal cancer were reported in 2006 in a study conducted by Jeffreys et al. in England and Wales.⁽³⁰⁾ Moreover, our study revealed a marked difference between men and women in the relative survival probability for anal cancer, a gap which continued to widen, reaching 19% in 1993-95. Whereas the relative survival probability increased for women, it decreased for men. The same trend was observed in the U.S.;⁽⁷⁾ however, in England and Wales, the 5-year survival probability for men with anal cancer improved between 1986 and 2001.⁽³⁰⁾

Anal cancer is more common in men who have receptive anal sex and who are infected with HIV.⁽⁹⁾ A 2005 Quebec study conducted by Goggin et al. found that the incidence rate of squamous-cell anal

cancer in men had risen dramatically in the Montreal area.⁽³¹⁾ In fact, between 1984 and 2001, the incidence of squamous-cell anal cancers in the metropolitan Montreal area rose by 353% in men and 134% in women; however, no increase in the incidence of anal adenocarcinoma—representing approximately 21% of cases—was observed during the same period. Antiretroviral therapy can prolong the life expectancy of HIV-positive individuals with chronic immunodeficiency, a condition that promotes the development of anal cancer, thereby increasing its incidence. However, these individuals risk having a poor prognosis following their diagnosis of cancer, which could partly explain the low survival probability observed for these cancers.

Secondary prevention through early screening of precancerous cervical lesions and primary prevention through vaccination are the best courses of action to reduce the burden of this disease by reducing its incidence. Generally speaking, once at the cancer stage, the efficacy of treatment seems to reach a plateau at which point mortality no longer decreases. Moreover, in Quebec, the relative survival probability, an indicator of the efficacy of treatment, has remained unchanged over the years for both cervical cancer and the majority of the main cancer sites.⁽¹⁸⁾

In conclusion, although in Quebec the number of cases of anogenital cancers is relatively low compared to other cancer sites, it is continuously on the rise, and the associated survival probability is mediocre in men and is continuously decreasing. HPV continues to represent a heavy burden. The development of prophylactic HPV vaccines is a primary prevention measure which, when combined with screening as a secondary prevention measure (in the case of cervical cancer), should provide protection against HPV.

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First title page: Concise title; full names of all authors and institutional affiliations; name, postal and e-mail addresses, telephone and fax numbers for corresponding author; separate word counts for abstract and text.

Second title page: Title only; start page numbering here as page 1.

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Text: Double-spaced, 1 inch (25 mm) margins, 12 point font size.

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