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**INCREASING INCIDENCE OF CANCER OF THE  
CORPUS UTERI IN THE ELDERLY IN CANADA?  
ANALYSIS OF DESCRIPTIVE DATA,  
HYSTERECTOMY ADJUSTMENT AND CHART REVIEW**

by

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**Thesis submitted to  
the School of Graduate Studies and Research  
in partial fulfilment of the requirements for the  
MSc degree in Epidemiology**

**University of Ottawa**

**January 1995**

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UNIVERSITÉ D'OTTAWA  
UNIVERSITY OF OTTAWA

"Well, grandson," said the Lone Ranger, "that's about as much as we can do for you. How do you feel?"

Lionel jammed his hands into his pockets. "I feel fine."

"Fixing up the world is hard work," said Ishmael.

"Even fixing up the little things is tough," said Robinson Crusoe.

Thomas King *Green Grass, Running Water*

## **Acknowledgements**

Many others have helped with this work in one way or another. I thank the following for their contributions:

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**Abstract**

*Background.* Incidence of cancer of the corpus uteri (of which 89% is endometrial adenocarcinoma) in Canada is declining in women under 70 years of age; in women 70 and over incidence increased from 1969 until 1982 since when it has been stable. These incidence data use as a denominator all women in the population, rather than just women with intact uteri, who constitute the real population at risk. Several of the known risk factors could potentially lead to a cohort effect. Some other cancers have had increased incidence related to better diagnosis. Therefore we need this study to describe the disease patterns in elderly women, correct incidence data to reflect hysterectomy prevalence, perform a cohort analysis, and look for evidence of improved diagnosis in these elderly women.

*Methods.* A descriptive analysis was done using data from national databases on incidence, mortality, morphology, method of diagnosis, surgical procedures and population numbers, focussing on incidence in women  $\geq 70$  years of age. Adjustment for prior hysterectomy modelled surgical rates before 1969 and used actual surgical rates from 1969 to 1990 to estimate proportions of women with intact uteri for different age groups and years. A chart review of incident cases in three periods (1969-72, 1980-81, 1990-91) in the Ottawa Regional Cancer Centre looked for evidence of increased diagnosis in elderly women in more recent periods.

*Results:* A variety of models for the hysterectomy adjustment all resulted in a trend

of increasing incidence in women over 70 years of age; this effect is most important in the most recent period, where the adjustment changes stable crude rates into increasing adjusted ones. The cohort analysis showed a birth cohort effect (greatest for the 1915-19 birth cohort) for incidence but not mortality. Analysis of adjusted incidence data was consistent with a persistent increased risk for that birth cohort even in the most recent data points, 14 years after the peak in sales of unopposed estrogen in Canada. Decreasing proportions of diagnosis by death certificate only, and decreasing mortality/incidence ratios in recent periods suggest some improvement in diagnosis in elderly women. The chart review showed a trend of a greater proportion of stage I disease in more recent periods ( $\chi^2$  for linear trend 10.676,  $p=.001$ ). Endometrial biopsy, a technique not available in the earliest two periods, played a minor role in diagnosis in cases (6.7%) from 1990-91.

*Conclusions:* Incidence of cancer of the corpus uteri, adjusted for hysterectomy prevalence, is increasing in women over 70 years of age in Canada. There is a cohort effect which may represent residual increased risk from unopposed estrogen use in the 1970s. There is also some (weak) evidence to suggest improved diagnosis of this cancer in elderly women in recent periods. Absolute numbers of cases in women  $\geq 70$  years are definitely increasing as the population ages. Epidemiologic monitoring and clinical research need to emphasize study of this disease in older age strata.

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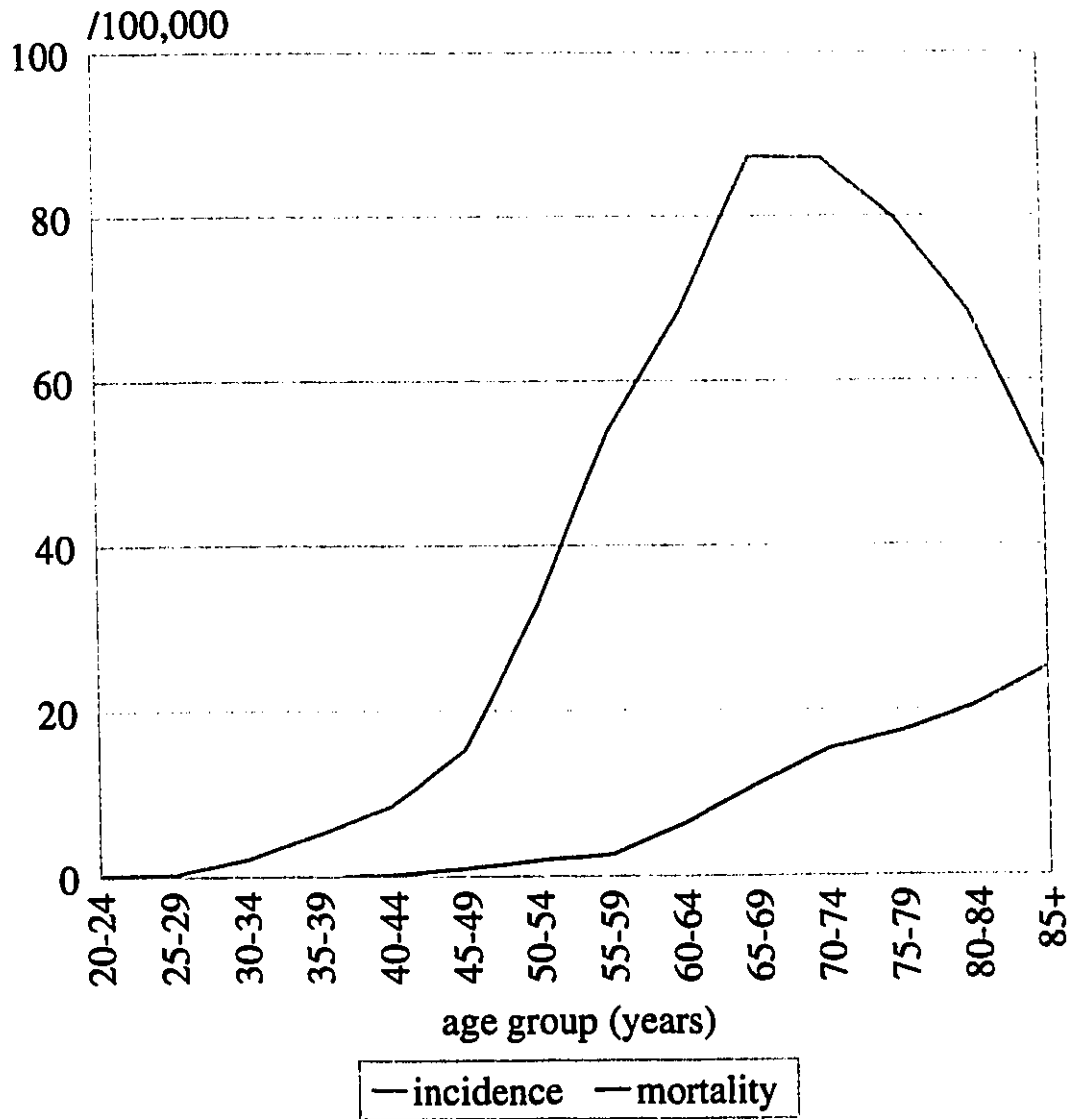
## **Introduction**

Cancer of the corpus uteri is cancer occurring in the anatomic body of the uterus. In the 9th revision of the International Classification of Diseases (ICD9), this is clearly distinguished from both cancer of the cervix and cancer of the uterus, site unspecified, at the three digit level (see Appendix A).

It is the most common female genital cancer in Canada, with an expected lifetime probability for women of developing the cancer of 2.4% and of dying from it of 0.6%.<sup>1</sup> It is usually diagnosed at an early stage due to vaginal bleeding. The good prognosis is reflected in a five year relative survival of 85% (Canada, both for 1970-74 & 1980-84).<sup>1</sup> The highest incidence rates are in the 65-74 year age groups (see Figure 1).<sup>2</sup> This is reflected in low ranking when impact is assessed by potential years of life lost: 9000 PYLL based on life expectancy for 1990, compared with 94,000 for breast cancer, 76,000 for lung cancer in women, or 11,000 for cervical cancer.<sup>1</sup>

When classified histologically, the great majority of cases are adenocarcinomas or variants thereof (89% in Canada for 1989).<sup>2</sup> It was endometrial adenocarcinomas like these that were the subject of intense study in the mid 1970s when they were linked to the use of unopposed estrogens.

# incidence and mortality, Canada<sup>2</sup> 1989 by 5 year age group



cancer of the corpus uteri, ICD9 182

Figure 1: Incidence and mortality, Canada, by age group.

### ***Canadian trends***

Overall (age 0-85+) age standardised incidence rates of cancer of the corpus uteri (ICD9 182) in Canada rose from 1969 to a peak in 1978, with the annual rate of increase being 3.7% (see Figure 2). These summary rates subsequently declined by 1.8% per year up to 1990. Analysis by region confirms a mid 1970s peak followed by a decline in all areas with the exception of the Atlantic region where there is no obvious trend. The remarkable peak in 1978 for Quebec is likely artefactual, representing some backreporting of cases from previous years.

Analysis of the age ranges 35-69 and 70-84 (also standardised to Canada 1971) reveals two distinct patterns. The rise to a mid 70s peak (3.5% per year) followed by a gradual decline (2.6% per year) is striking in the younger age range. In elderly women, however, the pattern is of increased incidence until around 1982 (2.9% per year) followed by stability. The regional patterns are once again similar except for the Atlantic region, where the 1970s peak for the 35-69 year age range was not as high. Incidence rates in the elderly in the Atlantic region have been lower during most of the period. The rise in incidence for this age range between 1969 and the early 1980s in all other regions is not present in data from the Atlantic provinces.

Age-standardised (0-85+ years) mortality from cancer of the corpus uteri in Canada has declined steadily from 1950 to 1990. This is most marked in the truncated (35-69

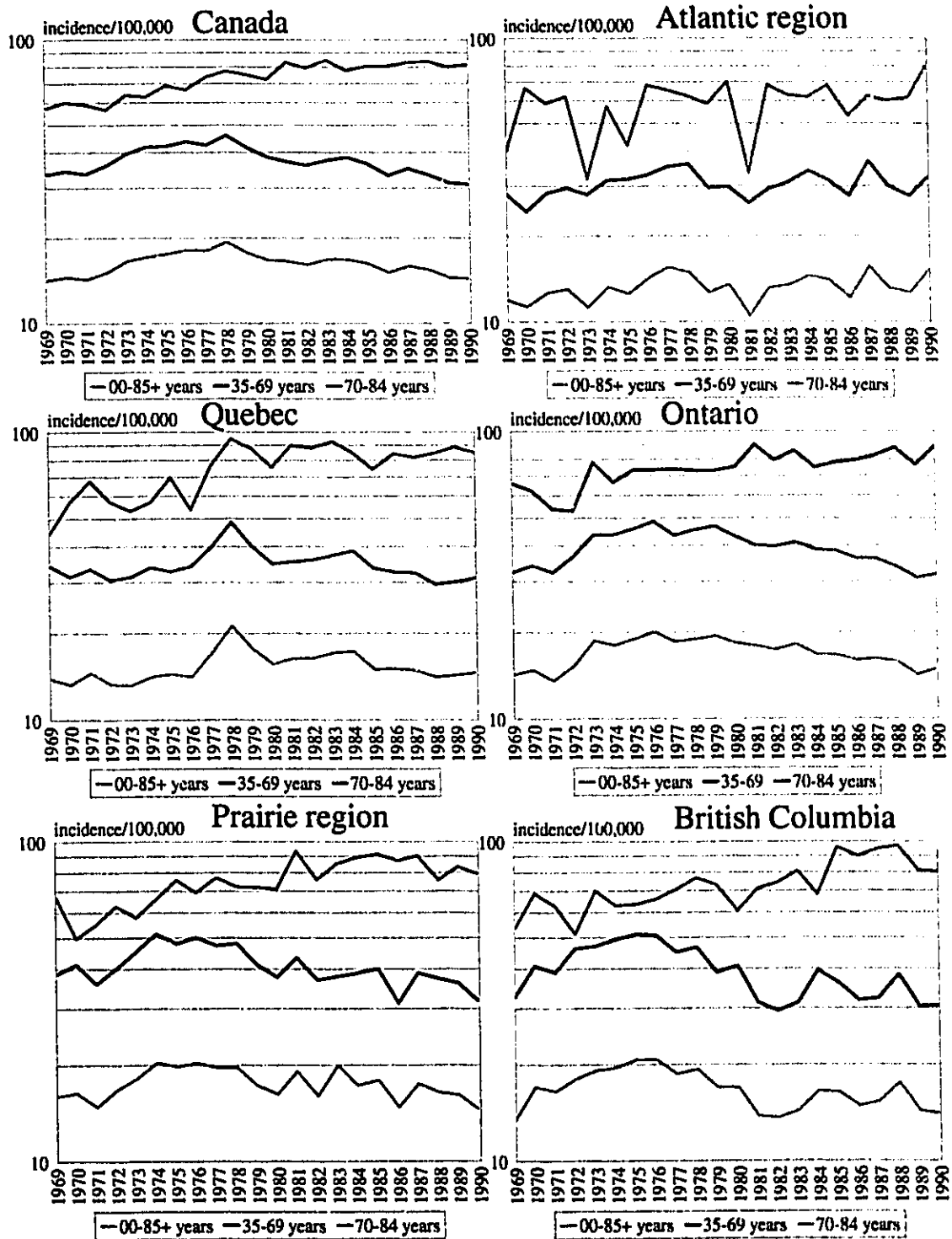
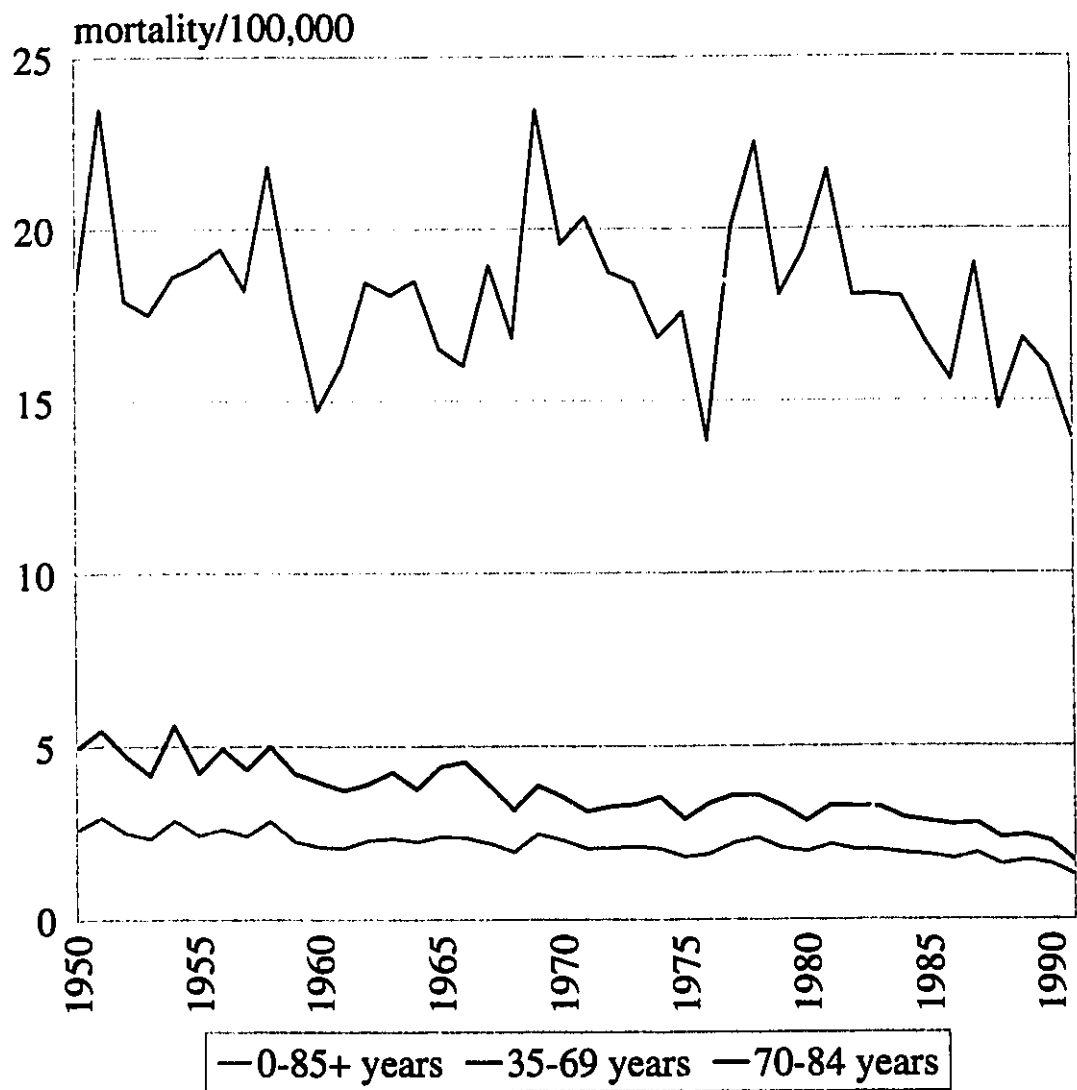


Figure 2: Age standardised (Canada 1971) incidence of cancer of the corpus uteri, ICD9 182, by age range and region.

# Canada, mortality, ICD9 182 <sup>5</sup>

in standardised age ranges



standard Canada 1971

Figure 3: Mortality, ICD9 182, standardised in various age ranges.

years) standardised rate. In the 70-84 year age range, in contrast, there is decreased mortality in the most recent years, but no clear long term trend (see Figure 3).

## **Background**

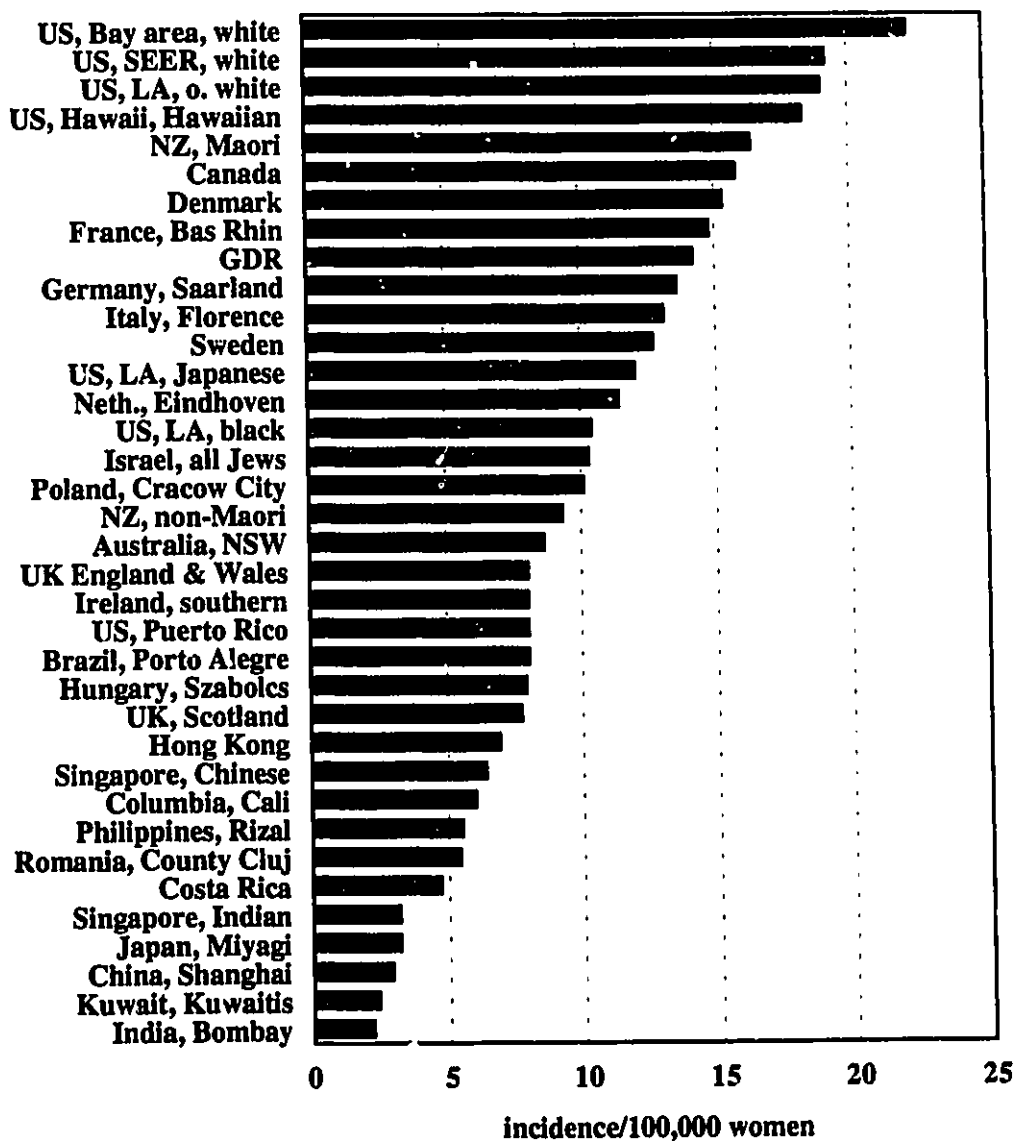
### ***International trends***

There are marked international differences in incidence and mortality; unfortunately, these differences are confounded by variations in hysterectomy patterns, diagnostic coding practices (chiefly the frequency of using ICD9 179, uterus not otherwise specified, in some countries, rather than the more specific ICD9 182), pathologic interpretations, intensity of diagnostic efforts (especially in older age groups), and not least of all, differences in reporting systems and quality of registries. Nonetheless, there appear to be important geographic differences.

Cancer of the corpus uteri is in general a disease of affluent societies, with an estimated two-thirds of known cases arising in developed countries.<sup>3</sup> The highest incidence rates (age-adjusted to a world standard population) are found in the United States and Canada (see Figure 4).<sup>4,5,6</sup> In Europe the highest rates are reported from Switzerland, Denmark and Germany, with lower rates being reported from the UK, east European countries, France and Spain.<sup>4</sup> The ratio between the highest and lowest European rates is about 3:1. Asian countries including Japan have rates lower than the lowest European rates, while Australia and white New Zealanders have intermediate rates. Maoris have a higher rate than whites in New Zealand (16.4 vs 9.3/100,000).<sup>5,6</sup>

# ICD9 182, age standardised

## selected countries



world standard population

Figure 4: Standardised incidence of ICD9 182, data from mid 1980s. Source: *Cancer Incidence in Five Continents, Vol VI, 1992* (reference 6).

Age specific incidence patterns are consistent internationally, rising sharply from 30 years of age to a peak incidence between 60-70 years and usually declining thereafter.<sup>5</sup>

The most striking temporal trends in incidence have been in North America. US data shows a marked increase in incidence in the early 1970s to a peak in 1975, followed by a decline in age standardised rates.<sup>5,6</sup> The Surveillance Epidemiology and End Results Program of the National Cancer Institute (SEER) collects data from 11 locations representing 10% of the US population. Analysis of age-specific rates from this program show that most of the recent decrease up until 1986 is in 45-64 year old women, with no clear trend in older or younger age groups.<sup>7,8</sup> The same pattern is still apparent after a correction to reflect previous hysterectomy.

Data on endometrial cancer from a population-based registry in the Swiss canton of Vaud from 1974-88 present a similar picture of declining rates in 30-59 year old women with no apparent trend in women  $\geq 60$  years old.<sup>9</sup> A Swedish study of endometrial cancer covering the period 1960-1984 showed a peak in the age standardised incidence rate in the 1975-9 time period followed by a decrease. Age specific rates showed a pattern like the US data: a mid 1970s peak followed by decline for ages 35-59, while rates for women aged 60 years or more were stable.<sup>10</sup>

*Trends in Cancer Incidence and Mortality*<sup>3</sup> presents data from cancer registries on five continents which, for cancer of the body of the uterus, cover the period 1973-87. For

incidence of ICD9 182 the patterns are complex and cannot be summarised in a few words. Mortality on the other hand has been consistently decreasing in North America, Australia and most of Europe. There is no mid 1970s peak in US mortality data to match the incidence pattern.

### ***The true denominator: women with intact uteri***

Hysterectomy is a common operation in developed countries, particularly in North America. Rates of performing this operation may vary markedly from one region to another even within one country, as well as by socioeconomic status.<sup>11,12,13,14,15</sup> The US and Canadian hysterectomy rates are very similar, and are twice that of England and Wales, and over three times those of Norway and Sweden.<sup>16</sup> Age-specific hysterectomy rates in the US and Canada peak in the 35-44 year age group.

As a result of these operations a proportion of women in each population is not at risk for developing cancer of the body of the uterus, and incidence and mortality data using the entire female population for the denominator underestimate the true rates. In the US, surveys have estimated that up to 35-40% of women in strata over the age of 55 do not have intact uteri;<sup>15,17,18</sup> a mathematical model combining survey and hospital separation data showed similar proportions.<sup>12</sup>

Recent work on incidence or mortality trends for cancer of the corpus uteri frequently involves adjusting the data to reflect the real denominator at risk (women with intact

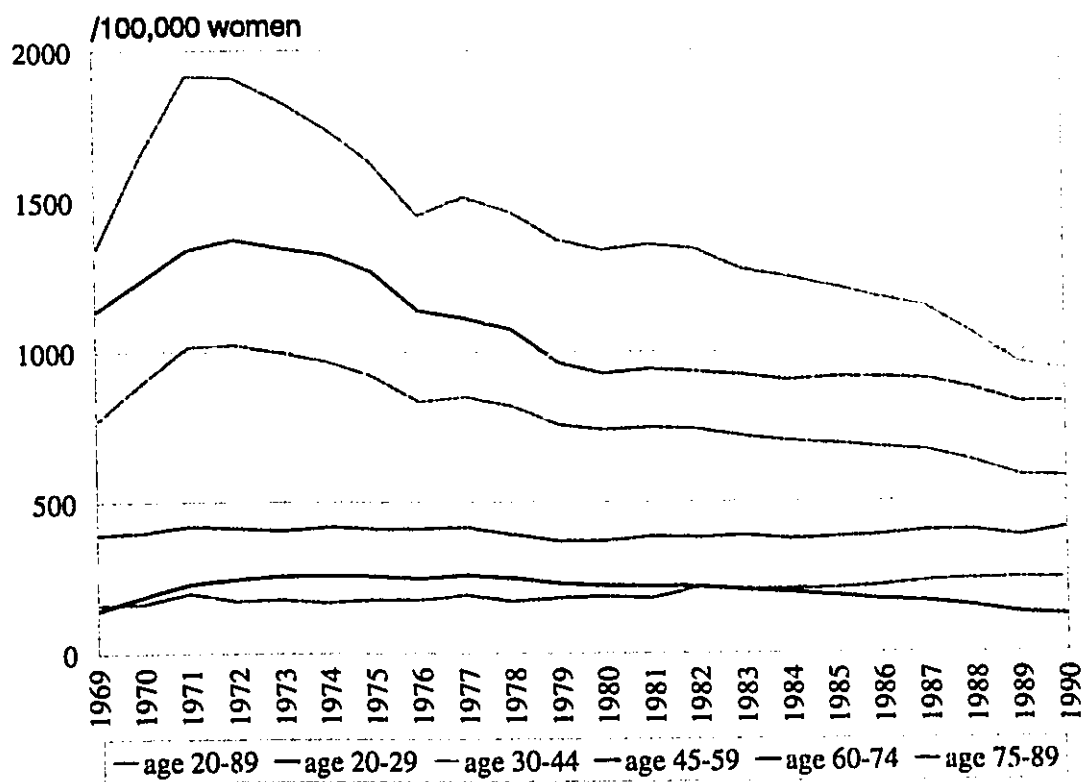
uteri). This is particularly important in North America where clear temporal trends in hysterectomy rates may confound the data. Age standardised hysterectomy rates peaked in Canada in 1971-72 (see Figure 5), and in the US in 1975 and have declined since.<sup>11,12,19,20</sup>

Since hysterectomy rates vary widely by time and place it is desirable to use data for the adjustment from the same population whose disease patterns are being studied. Unfortunately there are no cross sectional studies of 'hysterectomy prevalence' in Canada.

This paper will only correct incidence (and not mortality) data for 'hysterectomy prevalence' since trends in incidence data are the focus of this study. The rationale for correction of mortality data is less clear in that almost all women who die of cancer of the body of the uterus will have had a hysterectomy shortly after diagnosis, and thus not be represented in the adjusted denominator at the time of their death. The risk of dying from cancer of the corpus uteri is related to the proportion of women with intact uteri at the time the cancer began, rather than the proportion with intact uteri at the time of death. As well, in women over the age of 70, 20% of those having hysterectomies have a discharge diagnosis of cancer of the corpus uteri (Figure 6).

## hysterectomies in Canada

### standardised by age range

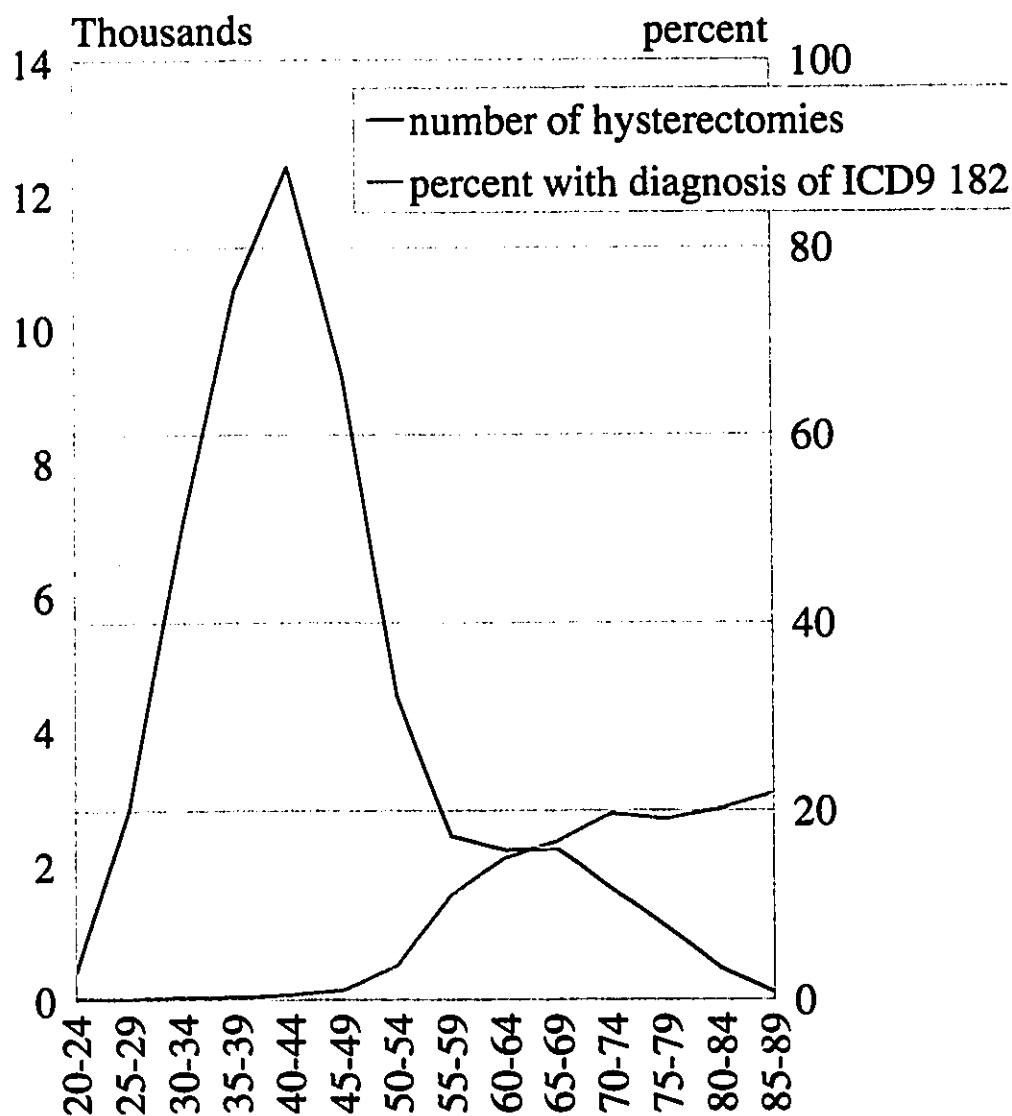


**Figure 5: Standardised hysterectomy rates by age range; includes subtotal hysterectomies.**

standard Canada 1971

# hysterectomies, 1989

## by age group



**Figure 6:** Hysterectomies (crude numbers) for 1989 by age group, and percent of hysterectomies done on patients for whom the diagnosis was ICD9 182 (hospital separation data).

### ***Hysterectomy adjustment methods***

Hysterectomy adjustments described in recent literature are of two types: those using *cross sectional* data on proportions of women with intact uteri, and those relying on *modelling* of temporal patterns of hysterectomy rates to estimate those proportions.

Both techniques then estimate the proportions for later periods using procedural data: for each cohort of women they subtract the proportion who have hysterectomies within the period of interest.

#### ***US methodology***

US adjustments have been able to use cross-sectional data from the US Health Examination Survey (HES) of 1960-1962<sup>11,12,18,21</sup> or the 1970 National Fertility Survey<sup>22</sup> and procedure data from the National Hospital Discharge Survey (NHDS).

The most relevant survey question was about menopause in the first cycle of the HES mentioned above. It was part of a self-administered medical questionnaire. It asked if periods had stopped, and, if yes, the age at which they had stopped and whether this had been due to an operation.<sup>23</sup>

The NHDS gathers yearly data from a sample of all hospitals in the Master Facility Inventory of Hospitals and Institutions; in 1965 this sample size was 315 out of 6965 hospitals. Although sample size increased to 553 by 1984, the proportion participating in the survey dropped from 94% to 73% over the same period.<sup>12</sup>

Other US surveys such as the 1988 Behavioral Risk Factor Surveillance System<sup>15</sup> and a large sample 1982 survey in upstate New York have provided estimates of hysterectomy prevalence similar to those calculated on the basis of surgical procedure data.

US hysterectomy corrections by Lyon & Gardner<sup>18</sup>, Marrett<sup>21</sup>, and Pokras & Hufnagel<sup>12</sup> have all been based on answers to the 1960 menopause question mentioned above plus NHDS procedures figures. In 1980 Marrett suggested a modification to the survey results for women over the age of 50 to account for those who had had hysterectomies after a natural menopause. Hysterectomy rates were only available from 1965 onward, and she assumed that the pre 1960 age-specific hysterectomy rates were comparable to those in 1965. Her method calculated person-years at risk (of surgery) by subtracting age at interview from average age of natural menopause, and applied the 1965 age-specific operative rates to these.

Thus the US longitudinal methods have the advantage of early survey data, but use only a sample of all hospital separations, and make the assumption that hysterectomy rates for women over 50 remained stable over time.

#### *Canadian methodology*

In Canada there have been no similar surveys. On the other hand hospital separation data on procedures are available from 1969 forward for virtually 100% of hospitals.

In Canada the options for a hysterectomy adjustment are to use US data or to model early patterns of hysterectomy rates to replace cross sectional data.

In 1981 Miller published a method for estimating prevalence of previous hysterectomy by combining actual procedure data from 1969 to 1976 with various models of the patterns of hysterectomy rates over time prior to 1969.<sup>11</sup> The models assumed that no hysterectomies took place before age 20; for each (single year of age) birth cohort, it cumulated the risk of hysterectomy year by year until age 84. The proportion ( $P$ ) of women of age  $K$  in year  $L$  with intact uteri was calculated as:

$$P_{K,L} = 1 - \sum_{i=20}^K \frac{h_{i,L-i+20}}{N_{i,L-i+20}}$$

where  $h_{ij}$  = number of hysterectomies in women of age  $i$  in year  $j$  and  $N_{ij}$  = population count for women of age  $i$  in year  $j$ .

Miller used three models of early hysterectomy trends: an exponential model fitted to British Columbia hospital separation data, a high linear model in which the rates were assumed to have been zero before 1950 and then constant from 1950 to 1969 (at 1969 rates), and a low linear model in which rates were assumed to increase linearly from zero in 1950 up to the actual rates in 1969 (and have been zero prior to 1950).

The BC data points were from a study by Boyes et al. which estimated age-specific

hysterectomy rates in BC for two cohorts of women in the 1950s and 1960s: those born in 1914-18 and 1929-33.<sup>24</sup> These were based on provincial hospital separation data. The estimated hysterectomy rate for age group 36-40 of the early cohort was 7.29/1000 women in 1954; the rate for the later cohort applying to the same age group was 16.35/1000 in 1969.

All three models assume that the pattern of hysterectomy rates over time is the same for all age groups. In the 1970s in Canada, however, hysterectomy rates varied little for those over the age of 55, but there were striking fluctuations in women under the age of 45.<sup>11</sup>

#### *Historical information on early hysterectomy rates*

A similar problem exists for study of carcinoma of the cervix: a need for a hysterectomy adjustment, and a lack of procedural data for the period prior to 1969. To supplement the BC data mentioned above, P. Holowaty reviewed historical data on hysterectomies in Canada and the US. She concluded that a model consisting of two exponential curves intersecting around 1950 was a reasonable one to adjust Canadian cervical cancer data.<sup>79</sup> Hysterectomies were performed only rarely prior to 1930; they became gradually more common during the 1930s and early 1940s, followed by a rapid increase in the late 1940s.<sup>25</sup>

There are published Saskatchewan data for the period 1964-75 which show an increase

in crude numbers of procedures from close to 1700/year in 1964 to just over 3000/year in 1971 (up 76%), followed by a decline back to the same baseline by 1975. The information is also displayed as a rate/100,000 women 15 years of age and over, but no age standardised or age specific rates are included.<sup>20</sup>

US 'all ages' hysterectomy rates/100,000 women rose from 439 in 1965 to 490 in 1968 (an 11% increase) and 651 in 1973 (up 48% from 1965).<sup>18</sup> The youngest age groups showed the greatest increase in age specific rates.

*When is a hysterectomy a hysterectomy?*

Even where there are data there remains the issue of what types of hysterectomies to count. The major problem is that in earlier periods subtotal abdominal hysterectomies (which removed the corpus and left a cervical stump) were common because the surgical technique was easier.<sup>25</sup> In one 1946 US paper on hysterectomies 65.8% of 246 hysterectomies were subtotal.<sup>26</sup> These are uncommon now because of the persistent risk of the cancer in the residual cervical tissue.

In published papers on hysterectomy adjustments, however, there is little discussion of what constitutes a hysterectomy. Including subtotal hysterectomies in the adjustment model is reasonable for cancer of the body of the uterus but not for cervical cancer. The procedure code which includes partial and subtotal hysterectomies in Canada decreased from 11-12% of all hysterectomies in 1969 and 1970 to 3% in 1978 (see

# hysterectomies in Canada

subtotal or partial vs all types

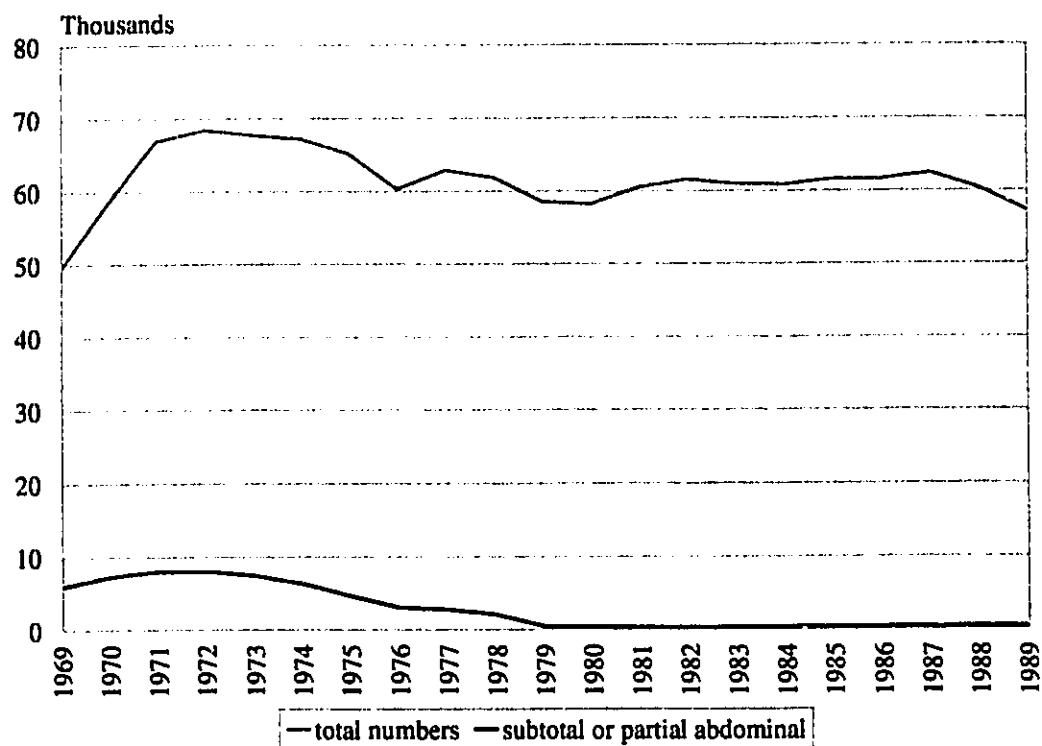


Figure 7: Hysterectomies in Canada: subtotal or partial contrasted with total counts.

Figure 7). In 1979 Statistics Canada changed its procedure coding from an ICD8A based system to the Canadian Classification of Diagnostic, Therapeutic, and Surgical Procedures (CCP), and since then the corresponding code has accounted for .6-.9% each year (until 1989).

### *Hysterectomies done for cancer of the corpus uteri*

Another issue related to these adjustments is that some of the hysterectomies are done as treatment for cancer of the corpus uteri. Between 1979 and 1989 in Canada these accounted for only 2.8-3.5% of the total number done per year. Since the proportions are small it is usually assumed to be reasonable to disregard this in the hysterectomy counts.

### *Risk factors*

This discussion of risk factors will apply mostly to endometrial carcinomas, which comprise 90% or more of most series of cancer of the corpus uteri; sarcomas and related tumours usually comprise less than 10% of cases, and less is known about their epidemiology.<sup>27</sup> A great deal of evidence has been accumulated on risk factors for endometrial cancer in the past 25 years. Several recent reviews summarise the available evidence well.<sup>27,28,29,30,31,32</sup>

The most clearly established risk factors are the use of unopposed estrogens, obesity, nulliparity, and a variety of menstrual factors (early menarche, late menopause,

amenorrhea or long menstrual cycles). Combined oral contraceptive use and smoking have been associated with reduced risk.

The increase in incidence of endometrial cancer in the mid 1970s in North America resulted in multiple studies which showed a relationship between unopposed estrogen use and endometrial cancer which is duration dependant and consistent across many different study designs. A recent review (not a formal metaanalysis) of studies published in English language journals listed 2 cohort and 17 case-control studies.<sup>32</sup> Women who used estrogens for less than six months have no measurable increase in risk. After 1 year of use the relative risk increased with increasing length of exposure; studies of medium-term use (12-60 months) have yielded odds ratios of 1.0-5.6. Long term use ( $\geq 60$  months) has been associated with ORs of between 1.8 and 63, with half the studies of 96 months or greater use having ORs of greater than 10. In the eight reviewed studies which addressed recency of use all showed a decrease in risk after cessation of estrogen therapy. Seven of the eight showed some long term residual increased risk.<sup>33,34,35,36,37,38,39,40,50</sup> Table I displays the risk estimates from those studies for lengths of time  $\geq 5$  years after cessation of estrogens.

Progestogens have clearly been shown to prevent or reverse estrogen induced endometrial hyperplasia (thought to be a precursor to endometrial carcinoma).<sup>28, 29</sup> There is epidemiological evidence that the risk of endometrial cancer from estrogens is similarly decreased or eliminated by adding progestogens, but the literature is not

**Table I: Studies of long term risk after cessation of estrogen use**

<b>Duration of use</b>	<b>Time since cessation of estrogens</b>	<b>Odds ratio from study</b>	<b>95% C.I.</b>
unadjusted :			
	≥5 years	4.5 <sup>38</sup>	1.4-15
adjusted (for duration of use):			
	≥8 years	3.0 <sup>40</sup>	0.9-11
stratified by duration:			
≤1 year	≥10 years	1.2 <sup>34</sup>	0.4-3.6
<2 years	≥6 years	1.4 <sup>33</sup>	0.4-5.2
≤3 years	≥15 years	6.2 <sup>*,36</sup>	2.3-17
1-4 years	≥10 years	3.5 <sup>34</sup>	1.4-8.3
5-9 years	≥10 years	4.1 <sup>34</sup>	1.1-15
4-14 years	≥15 years	4.0 <sup>*,36</sup>	0.9-17
≥2 years	≥6 years	5.4 <sup>33</sup>	1.6-19
≥10 years	≥5 years	3.7 <sup>34</sup>	0.8-18
≥15 years	≥15 years	7.2 <sup>*,36</sup>	1.8-28

\*relative risk (cohort studies); all other values are odds ratios from case/control studies

source: condensed from Herrinton & Weiss<sup>32</sup>

extensive.<sup>32,39,41,42,43</sup>

An article by Horwitz in 1978<sup>44</sup> started a debate about the importance of detection bias in the apparent association between estrogens and endometrial carcinoma. Among postmenopausal women, taking estrogens may precipitate uterine bleeding. This could

result in diagnosis of endometrial cancer which would have remained otherwise undetected, or in misdiagnosis of estrogen-induced hyperplasia as carcinoma.

Estimates of the importance of asymptomatic endometrial cancer are available from necropsy prevalence data,<sup>45</sup> and it is currently thought that this does not account for a significant amount of the apparent association.<sup>32,46</sup>

Estrogen associated tumours occur in younger patients and have an earlier stage and histologic grade; patients with them have improved survival rates.<sup>29,47</sup> Because of these characteristics the issue of pathologic misdiagnosis within the grey zone between endometrial hyperplasia and endometrial carcinoma arose. It was assessed by two pathology studies in the late 1970s with the conclusion that the amount that existed was not great enough to account for the observed trends. The estrogen-carcinoma association was also present for cases in which all of a panel of pathologists independently agreed on the diagnosis of endometrial carcinoma.<sup>48,49</sup>

The issue of misdiagnosis was also addressed by epidemiologic studies which found that although the association between estrogens and adenocarcinoma of the endometrium is strongest with low grade cancers, there is also an increased risk for more invasive types of cancer.<sup>27, 29,50</sup>

Obesity has been repeatedly shown to be a risk factor for endometrial cancer, supposedly because of increased peripheral conversion of androstenedione to estrone

and lower levels of sex hormone binding globulin.<sup>29,51,52</sup> Relative risks associated with being overweight (body mass index  $>25$  kg/ m<sup>2</sup>) in a recent study by La Vecchia ranged from 1.2 to 8.1, increasing with higher BMI and age.<sup>52</sup> Obesity close to the age of tumour diagnosis is important, while weight as a young adult is probably not.<sup>53</sup>

Nulliparity has consistently been found to be a risk factor, with relative risks of parous women usually being .3-.8; some studies have found a trend for decreasing risk with increasing parity, as well.<sup>28,54</sup>

A number of different menstrual factors have been associated with increased risk. Early menarche has been associated with relative risks of 1.2 -3.9. Late menopause has been associated with relative risks of 1.5-2.5 in North American studies.<sup>28</sup> Similarly amenorrhea and long menstrual cycles have been found to increase risk.

A number of other associations have been investigated in the past whose status is not as clear. Diabetes is a commonly cited association with evidence both for and against.<sup>29</sup> For hypertension, as well, the evidence is inconsistent. Dietary fat has been linked in ecologic studies to increased risk, but the interpretation of this is unclear.<sup>52</sup>

Tamoxifen was first used as adjuvant chemotherapy for breast cancer, but primary prevention trials are now underway using it for asymptomatic women at high risk of breast cancer. It competes with estrogen for binding sites in target tissues, and

although usually classified as an estrogen antagonist, it also has weak estrogen agonist properties. A 1991 analysis of pooled results from 7 trials concluded that the relative risk of endometrial carcinoma associated with tamoxifen use was 5.0<sup>55</sup>, while a more recent RCT of adjuvant therapy yielded a relative risk of 7.5.<sup>56</sup> It has recently been shown to induce atypical hyperplasia (a premalignant lesion) in a cohort of women involved in one of the primary prevention trials.<sup>57,58</sup>

Alcohol as a risk factor has been assessed in two recent studies, one of which showed a trend to lower risk in heavier drinkers.<sup>59,60</sup>

Repeated studies have confirmed a protective effect of combined oral contraceptives with a typical relative risk of 0.5; the effect is duration-related and lasts 15 years or more after stopping.<sup>28,61,62</sup>

Smoking cigarettes has consistently been associated with decreased risk of endometrial cancer of about 50%; there is evidence for a dose-related effect.<sup>28,29</sup> It is thought to be mediated through an anti-estrogenic effect of smoking.

Population attributable risk from all known risk factors combined has been estimated at 30-60% in various populations.<sup>28</sup>

### ***Cohort effects***

A cohort effect is defined in Lasts' Dictionary of Epidemiology as a variation in health status that arises from the different causal factors to which each birth cohort in the population is exposed as the environment and society change (synonymous with generation effect).<sup>87</sup> Several of the well documented risk factors could result in a cohort effect: use of unopposed estrogens is associated with increased risk, while use of oral contraceptives and cigarette smoking are associated with reduced risk. There are distinctive temporal trends in prevalence of all three for certain age groups.

### ***Cancer in the elderly***

Age is a strong risk factor for most types of cancer. Current US estimates are that over 50% of cancer cases occur in patients over the age of 65.<sup>63</sup> Analysis of all cause cancer incidence (excluding non-melanoma skin cancer) for Canada shows that from 1969 to 1989 the proportion of patients over the age of 65 has climbed steadily from 48.2% to 57.9%.<sup>2</sup>

There is an urgency to the study of cancer in the elderly as the oldest age groups (especially women) comprise an increasingly large proportion of populations in industrialised countries. For Canada, Statistics Canada has projected that by the year 2000 women over the age of 65 will make up 14.7% of the female population, and that by 2011 this will grow to 16.6%.<sup>64</sup> In a review of current literature related to cancer in the elderly, the following issues emerge:

### *Quality of information*

The quality of information is poorer for the elderly, especially for those in the oldest age strata.<sup>65</sup> This is typified by high rates of disease diagnosed by death certificate only, lower proportions of histologically confirmed cancer, and higher error rates on death certificates.<sup>65, 101, 66</sup> A study done in Japan found that death certificate errors in general were becoming less frequent over time, and that this change was most marked in people over the age of 75.<sup>66</sup> As well population estimates of the oldest age strata may be less accurate.<sup>75</sup>

### *Improving diagnostic methods*

Some trends in cancer incidence may be explained by changes in diagnostic methods. Incidence of brain cancer climbed following introduction of CT scanners, and some of the increase was likely due to improved diagnosis.<sup>67</sup> Greater numbers of pathologic specimens from treatment of benign prostatic disease may have resulted in increased diagnosis of prostatic cancer.<sup>68</sup> Widespread adoption of screening with prostate specific antigen (PSA) will contribute to a further apparent increase: 39% of new prostate cancer cases in eight Quebec City hospitals between October 1990 and December 1992 were discovered after PSA assay.<sup>69</sup>

### *Age bias in research*

In the past, little research has been done on the oldest age groups which are at highest risk of developing cancer; most studies of response to treatment have been done in

younger patients, often using age above 65 as an exclusion criterion.<sup>70</sup>

### *Age related clinical patterns*

Patterns of stage at diagnosis, relative survival, and to some extent diagnostic delay may be different in the elderly, and do vary with tumour type. The available evidence suggests that breast cancer is diagnosed at a more advanced stage in the elderly, and lung and pancreatic cancer at an earlier stage, while for cancer of the colon and prostate there was no relationship between age and stage.<sup>71,72</sup>

### *Age related management patterns*

The elderly may be less likely to be seen by clinical oncologists or to receive curative treatment, even with comparable comorbidity.<sup>73</sup> Some of this may be related to accessibility: older patients who no longer drive must find someone else to drive them for radiotherapy, for example.<sup>74</sup>

### *Issues related to standardisation*

Epidemiologic literature describing trends in cancer incidence and mortality over time must deal with the problem of changes in the age structure of the population over time in deciding how to present the information. These changes in age structure act as a confounder, since most types of cancer have strong age related incidence and mortality patterns.

Displaying age specific statistics is one way to deal with this problem. This is a stratified analysis based on age ranges. The amount of confounding removed depends on the change in risk within the age strata chosen: if the age related risk is fairly uniform within strata, most of the confounding will be removed. In simpler terms, the narrower the age strata, the more confounding will be removed. The disadvantage of presenting age-specific rates is the large mass of information which must be assimilated by the reader. However, a much better understanding of the variation of the cancer rates over time can be gained. Trends in different directions in different age strata, for instance, will be obscured in summary figures.

A more common method of dealing with the changing age structure is to use summary rates based on the age structure of a particular population. The standardised rates which Statistics Canada publishes are an example of direct standardisation using the age-specific rates pertaining to the population of interest and applying to them weights derived from the reference population (I have used Canada 1971 as the reference population in this paper). The advantage of having a single summary figure to compare is counterbalanced by the loss of detail, and the inherent assumption that it is reasonable to use a single summary figure to represent trends in many different age strata. To the extent that trends in different age strata are not uniform, a single summary figure is misleading.

Doll & Peto, among others, have made the point that both population estimates and

death certification are less reliable in older age strata,<sup>75</sup> and for this reason a truncated standardised rate has frequently been used, with the age span 35-64 years being common.<sup>76</sup>

Another limitation of both age-standardised summary figures and age specific rates is that, with confounding of the change in age structure removed, one loses an appreciation for the impact of the crude incidence and mortality numbers on the medical care system. In planning resources for the medical care system the crude numbers are more important. The difference is illustrated in data from the present study: the overall (0-85+) standardised incidence rates are clearly declining (see Figure 2) while the crude case numbers in 1990 were at about the same level as in 1978 (Figure 8). Crude numbers of cases in the 70-84 year age range have increased linearly from 1969 to 1990, and the proportion of total cases from that age range has increased from .2 to .32 over the same period.

### *Summary of relevant issues*

Temporal trends in incidence of endometrial cancer in Canada are different for women 70 years and older than they are for younger age groups. In these elderly women incidence (unadjusted for hysterectomy prevalence) increased from 1969 to 1982 and has been stable since; in younger women incidence peaked in 1978 and has declined since.

# ICD9 182 incidence

crude numbers, by age range

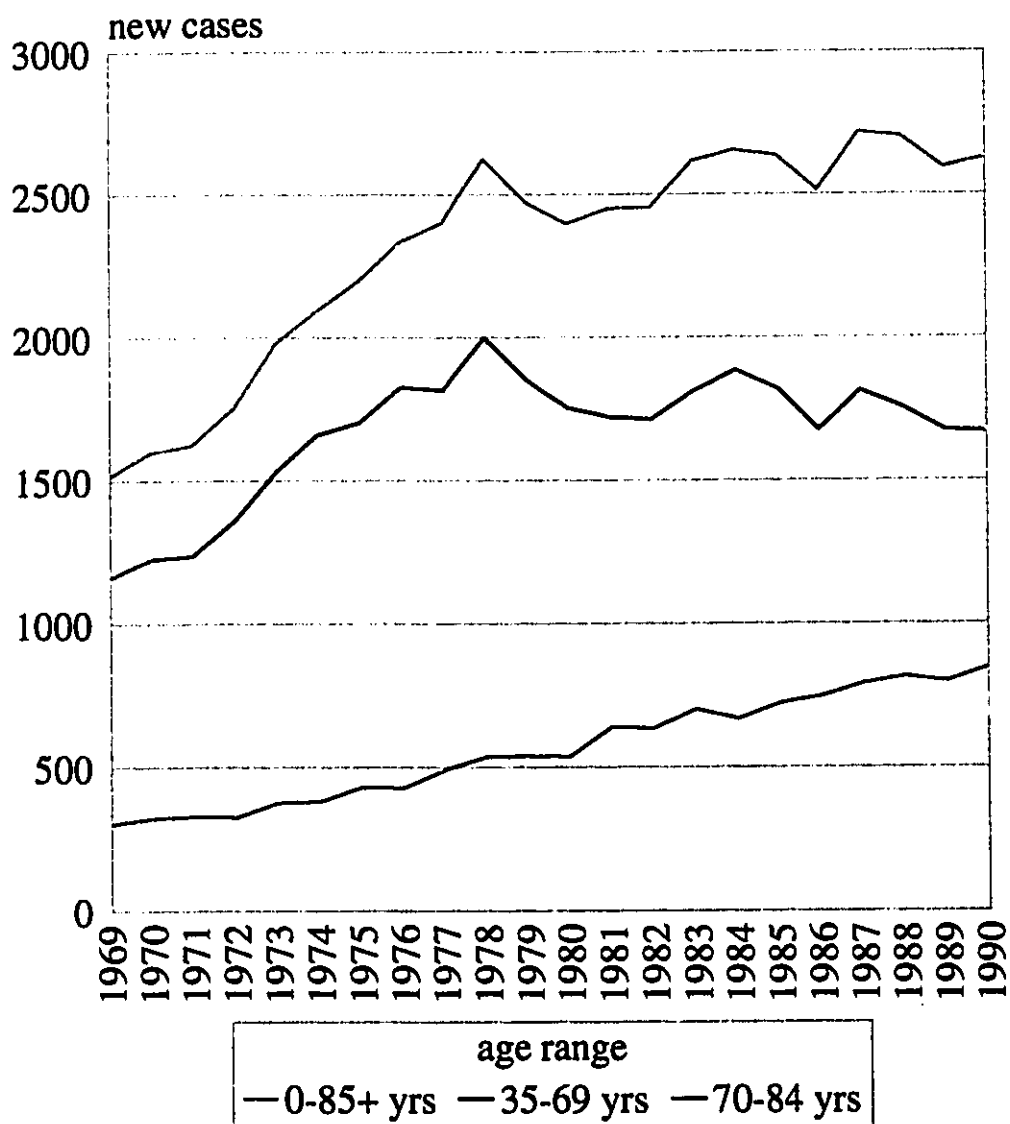


Figure 8: Incidence of ICD9 182 in Canada, crude numbers by age range.

To analyse trends in the real population at risk, the incidence data need to be adjusted to reflect the proportion of women with intact uteri in different age groups and for different years.

There are many risk factors which could result in a cohort effect: use of unopposed estrogens, use of oral contraceptives and prevalence of cigarette smoking, for instance.

With some other cancers increased diagnosis (as opposed to increased disease) has contributed to an apparent increase in incidence. This can be through earlier diagnosis (as diagnostic techniques are introduced, disseminated or intensified), diagnosis of asymptomatic cases (which would have otherwise remained undetected), or more precise diagnosis (less misclassification of brain tumours, for instance). This may be accompanied by a shift to an earlier stage disease.

## **Objectives & Hypotheses**

### ***Objectives***

This paper focuses on incidence of cancer of the corpus uteri (ICD9 182) in women 70 years and over in Canada. It will:

- describe trends over time in incidence and mortality in different age groups in Canada; this will include data on trends in morphology for elderly women
- adjust incidence data to reflect previous hysterectomy
- perform a cohort analysis for incidence (adjusted and unadjusted) of and mortality from ICD9 182 to try to explain the trends
- assess the role of increased diagnosis for women  $\geq 70$  years by:
  - analysing temporal trends in diagnostic procedures (D&Cs) in hospital separation data
  - analysing cancer registry data for indicators of greater precision in diagnosis (trends in most confirmed method of diagnosis, diagnosis by death certificate only, mortality/incidence ratios)
  - a chart review of incident cases of ICD9 182 from three time periods to assess evidence for earlier diagnosis (shift to an earlier stage, decreased length of symptoms, more asymptomatic cases) and use of new diagnostic methods

### ***Hypotheses***

The hypotheses related to these objectives are:

- (1) with a hysterectomy correction applied, incidence rates of ICD9 182 in women  $\geq 70$  years old will be increasing;
- (2) there is a birth cohort effect involved in incidence trends of cancer of the corpus uteri, with increased risk in women who were postmenopausal during a period centring on the mid 1970s;
- (3) there is increased diagnosis (as opposed to increased disease) of ICD9 182 for elderly women in the most recent periods.

## **Materials and methods**

This is a descriptive study of trends related to cancer of the corpus uteri in Canada, focussing on elderly women, using incidence, mortality, surgical procedure and population data (among others) from national databases, and a chart review of incident patients from a regional cancer centre.

### ***National database materials***

Incidence, mortality, population and surgical procedures data were supplied by Statistics Canada.

The National Cancer Incidence Reporting System (NCIRS) is a database managed by the Canadian Centre for Health Information (CCHI); it supplied incidence and morphology data, as well as method of diagnosis (see Appendix A). The morphology data presented use data from five provinces (Newfoundland, Ontario, Saskatchewan, Alberta and British Columbia) from 1969 to 1989; the other choice would have been to use all provinces from 1982 onward.

Mortality data came from the Canadian Mortality Database (CMDB), a consolidated computerised file containing information based on all death registrations in Canada back to 1950.<sup>77</sup> Although its coverage has not been formally tested, it is assumed to approach 100% because of Canadian legal requirements related to death certification.<sup>78</sup>

The National Hospital Morbidity Statistics Database (also at CCHI) provided numbers of surgical procedures by single year of age, province and four digit ICD code from 1969 to 1990. These are collated from provincial hospital separation data representing all hospitals other than National Defence, Worker's Compensation hospitals and psychiatric hospitals, but do not include data from the Yukon or North West Territories. Although it was established in 1960, it only started collecting surgical procedure data in 1968.

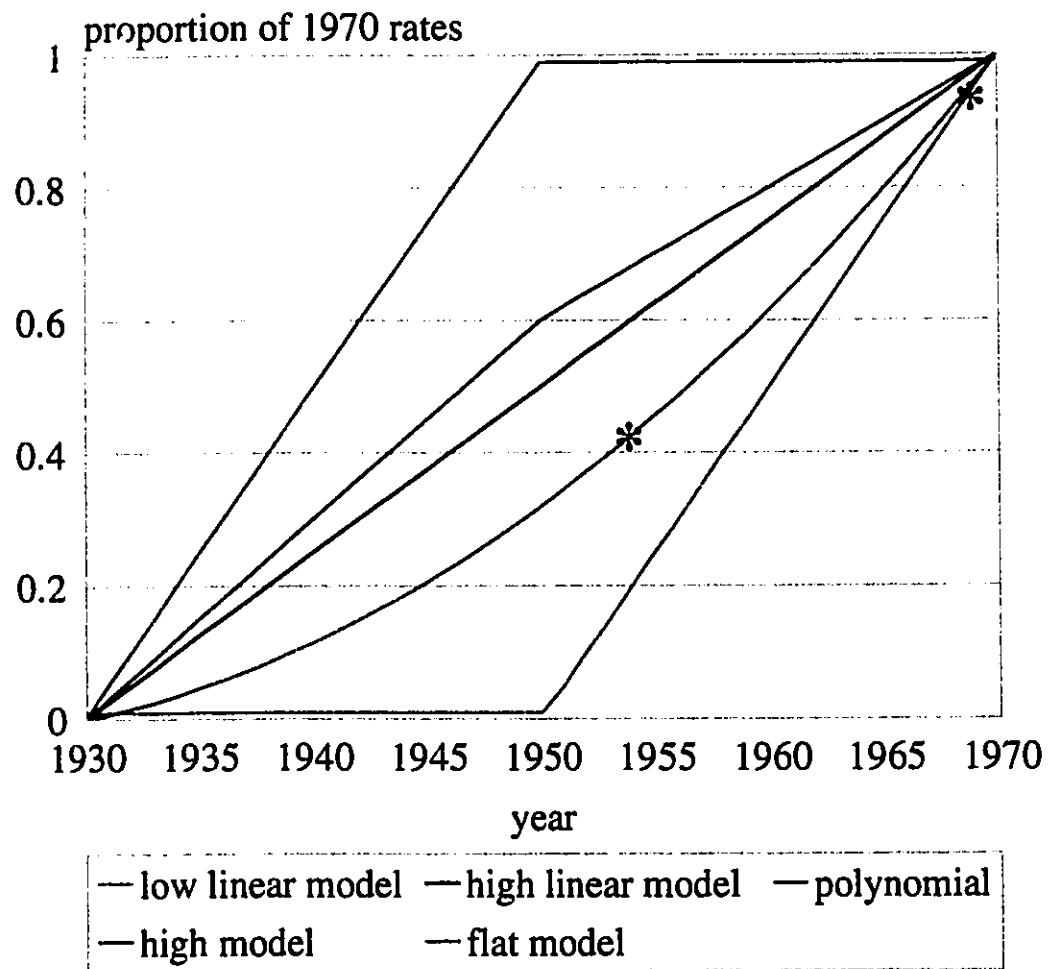
Population numbers were supplied by Statistics Canada by single year, sex, single year of age, and province for the period 1969 to 1990.

### *Hysterectomy adjustment*

The method used in this paper is based closely on a technique used by Miller in 1981 to adjust cervical cancer mortality data, with some modifications.<sup>11</sup> A comparison was also made with a recent (as yet unpublished) version of that model by P. Holowaty.<sup>79</sup> The method defines birth cohorts by single year of age and subtracts from them the proportion each year who have had a hysterectomy in that calendar year at the age appropriate for that cohort. It assumes that the mortality rate is the same for women with and without hysterectomies.

Actual hysterectomy rates are only available from 1969 to 1990, which correspond to the incidence data. For the years prior to 1969 it is necessary to model the pattern of

# hysterectomy models



\* correspond to B.C. data points

**Figure 9:** Hysterectomy models: the vertical axis represents the proportion of 1970 age specific hysterectomy rate which would apply to the same age group for the years stated. The same proportion is assumed to apply to all age groups for that year. The flat model is used only as one component in a mixed model.

age-specific hysterectomy rates over time. The data-based model, partly on the basis of some British Columbia estimates and partly based on history, uses a second degree polynomial equation to estimate these rates. As a sensitivity analysis, I have included a high model (linear, with a change in slope in 1950), a high linear model, and a low linear model (see Figure 9). The ideal data to add to the cohort methodology would be cross sectional data in 1969 giving hysterectomy prevalence by single year of age. The various models are substitutes for that missing information.

The method used in this paper assumes that no hysterectomies were done prior to 1930. For the period 1930-1968 age-specific (by single year of age) hysterectomy rates are calculated as a proportion of the 1970 age-specific rates according to the various models. Reference rates from 1970 are used rather than 1969 rates as likely representing more complete reporting to the database in the second year of its full operation. The proportion is a function of which model is being used, and is assumed to apply uniformly to all age groups in that calendar year for that model.

The *polynomial model* uses a second degree polynomial equation to describe a curve through three data points: two based on the BC study mentioned above (a rate of 7.29/1000 in 1954 and 16.35/1000 in 1969), the third being a value of 0 set arbitrarily based on the historical review mentioned above. The equation used is:

$$y=0.1190x+0.0077x^2$$

where y is the hysterectomy rate/1000 women, x is the time in years (0 in 1930 and

39 in 1969).

This is used to generate hysterectomy rates for the years from 1950 to 1970. These rates are then divided by the 1970 rate, yielding a hysterectomy rate for each year as a proportion of the rate in 1970. The polynomial equation above predicts a rate of 17.08/1000 women for 1970, compared with the actual rate of 18.13 for the 35-39 year age group.

The *high model* has two linear components with different slopes, one before 1950 (from 0 in 1930 to .6 of the 1970 rate in 1950) and one after (from .6 in 1950 to 1 in 1970). It provided a model with rates intermediate between the high linear and flat models.

In the *high linear* model hysterectomy rates increase from 0 in 1930 to 1 in 1970 in a linear fashion. It models higher rates than the 'polynomial' model to account for inclusion of incomplete hysterectomies which were proportionately more common in earlier years.

The *low linear* model is a low model in which the rates prior to 1950 are assumed to be 0, and increase from 0 in 1950 to 1 in 1970 linearly. It acts as a lower bound of possible models.

A *flat* model was developed for use only as one component in a mixed model which used different models for temporal patterns of different age ranges (discussed on pages 14, 41 and 79) . It assumed that hysterectomy rates increased from 0 in 1930 to 1 in 1950 and remained constant at that level thereafter. The proportions for all models are shown in Figure 9.

The proportion ( $P$ ) of women of age  $k$  in year  $l$  with intact uteri was calculated as:

$$P_{k,l} = 1 - \sum_{i=0}^k \frac{h_{i,l-k+i}}{N_{i,l-k+i}}$$

where:  $h_{i,j}$  is the number of hysterectomies carried out on women of age  $i$  in year  $j$ , and  $N_{i,j}$  is the population count for age  $i$  in year  $j$ . These calculations are carried out for ages from 0 to 89. This formula is similar to what is described in Miller's text, but differs from the formula shown in Miller's article. The technique in this paper differs from Miller's in that I have included hysterectomy rates in women less than 20 years old, whereas Miller assumed that they were zero. The hysterectomies in the adjustment in this paper include subtotal hysterectomies.

As a comparison to this method, I have also included a less elegant hysterectomy adjustment which uses as a baseline the prevalence of intact uteri in 1970 according to a US study (it assumes that the 1970 US data apply to Canada). That study, by Pokras and Hufnagel, used the 1960 USHES menopause data with Marrett's suggested modification for post menopausal women. From that baseline, for each five year age

cohort, I have subtracted the proportion of women having had hysterectomies in that birth cohort in Canada for each five year period, yielding a total of five data points for each model.

To assess the magnitude of the bias built into these models by assuming that hysterectomy rates follow the same temporal pattern for all age groups, I have included a mixed model which uses the polynomial model for age groups less than 60 years, the 'flat' model for women 60-74 and the 'high linear' model for women 75+. The reasons for these particular choices will be described in the discussion section (page 80).

The hysterectomy adjustment is done as follows: Each model is used to estimate the proportion of women with an intact uterus by single year of age for each year of interest (1969-1990). Values for 5 year age groups are then derived by weighting these proportions to reflect the age structure of each 5 year age group for each year. This results in proportions of women with intact uteri by 5 year age group and year. Incidence rates of ICD9 182 are available by 5 year age group. The adjusted incidence rates are calculated by dividing the crude (unadjusted) incidence rates by the proportion of women with intact uteri for each age group and year. Unless the proportion of women with intact uteri for an age group is 100%, this will result in the adjusted incidence rate being higher.

Trends in these adjusted and unadjusted age specific incidence rates are then displayed by means of line charts showing temporal patterns of three year moving averages.

### ***Analysis of temporal trends***

Analysis of temporal trends in data is usually done by simple visual display or by complex modelling methods. Multiple regression techniques look at the relationships between independent variables. They are not appropriate for analysis of temporal trends in a single variable because in a time series the values are serially correlated, and the temporal order of the data points is important.

The simplest technique to perform and for a reader to understand involves visual display using a line chart, and is used in the present study. The major advantage of simplicity is counterbalanced by a degree of subjectivity in interpretation, and a lack of statistical testing.

The alternative to this involves ARIMA (autoregressive integrated moving averages) modelling. It deals with the autocorrelation and trends in an iterative process of model identification.<sup>80</sup> The effect of an intervention can be analysed by comparing models developed separately for the pre- and post-intervention data. It is a complex process which is both difficult to learn and difficult for a reader to understand, and for these reasons has not be used in this study.

The most significant source of uncertainty in the adjusted incidence data is that due to the models, and different models are used as a sensitivity analysis.

### ***Probability, incidence measures & hysterectomy adjustments***

The method used in this paper for the hysterectomy adjustment cumulates the year by year hysterectomy probabilities for a birth cohort from the birth year until the year of interest. To adjust one age specific cancer incidence rate in a particular year, the cohort of interest is limited to those ( $n$ ) women of the birth cohort who have survived till that year. For this fixed cohort the year by year hysterectomy probabilities would be  $h_0/n, h_1/n, h_2/n, \dots, h_k/n$ , where  $h_k$  is the number of hysterectomies done at age  $k$ .

The actual hysterectomy probabilities are not available for the fixed cohort, and I assume that the age specific 'hysterectomy rate' for the appropriate single year, calculated with national data, is a reasonable estimate of the hysterectomy probability of our fixed cohort of  $n$  women. A real hysterectomy probability for a cohort for a single year would involve defining the population of interest at the beginning of the period, counting the procedures done in the next 12 months, and adjusting the denominator to reflect withdrawals. This would be similar to calculating a cumulative incidence by the actuarial method:<sup>81</sup>

$$\hat{Pr}_{t_0}^t = \frac{I}{N_0 - (W/2)}$$

which estimates the probability for the time from  $t_0$  to  $t$ ,  $N_0$  being the population at

time 0 and  $W$  the number of withdrawals during the period. The national age specific hysterectomy rates use a mid-year population estimate as the denominator, which is what the term  $(N_0 - W/2)$  is estimating; the procedures, however, are provided for a 12 month period from April 1 to March 31 rather than the calendar year.

The assumption is inherent in this technique that mortality and emigration are not affected by hysterectomy status, and that immigrants have the same 'hysterectomy experience' as native born women.

The hysterectomy probability which is cumulated for each birth cohort is closely related to, but distinct from, cumulative incidence and incidence density. The hysterectomy probability for each year for each cohort has as its denominator the total population for that birth cohort in that year (includes women with and without uteri). The cumulative incidence (CI) for the year is the risk of having a hysterectomy during that period for those women in the cohort who have intact uteri at the beginning of the year. For the first year of the birth cohorts this will be identical to the hysterectomy probability, but thereafter the denominator of the CI will exclude women with previous hysterectomies. The incidence density (ID) is an average rate per unit time of procedures performed on women with uteri. For the ID calculated for a year, the denominator should exclude women with previous hysterectomies and also half the women who have hysterectomies in that year: operations are distributed over the twelve months, and women are no longer 'at risk' once they have had a hysterectomy.

Table II: Hysterectomy probability (Pr), CI and ID for a fixed cohort (N) with no withdrawals or losses						
Year	No. of hysterectomies	Total population	Population with intact uteri	Pr	CI	ID
0	$h_0$	N	N	$h_0/N$	$h_0/N$	$h_0/(N-h_0/2)$
1	$h_1$	N	$N-h_0$	$h_1/N$	$h_1/(N-h_0)$	$h_1/(N-(h_0+h_1)/2)$
2	$h_2$	N	$N-(h_0+h_1)$	$h_2/N$	$h_2/(N-(h_0+h_1))$	$h_2/(N-(h_0+h_1+h_2)/2)$
k	$h_k$	N	$N-(h_0+h_1+h_2)$	$h_k/N$	$h_k/(N-(h_0+h_1+\dots+h_k))$	$h_k/(N-(h_0+\dots+h_k)/2)$

The different denominators are shown in Table II.

The year by year probabilities are mutually exclusive, and thus are additive.

The cumulative probability for a cohort from age 0 to age  $k$  would be:

$$\sum_{i=0}^k \frac{h_i}{N_i}$$

where  $h_i$  is the number of hysterectomies performed on women of age  $i$  in the year which corresponds to age  $i$  for that birth cohort, and  $N_i$  is the total population of women age  $i$  in that same year.

A more common epidemiologic method to calculate cumulative incidence over time is: where  $CI_i$  is the cumulative incidence for the year  $i$ .<sup>82</sup> The equivalence of these two methods is shown below:

$$CI_{0-k} = 1 - \prod_{i=0}^k (1 - CI_i)$$

$$\begin{aligned} CI_{0-k} &= 1 - \left(1 - \frac{h_0}{N}\right) \left(1 - \frac{h_1}{N-h_0}\right) \left(1 - \frac{h_2}{N-(h_0+h_1)}\right) \dots \left(1 - \frac{h_k}{N-(h_0+h_1+\dots+h_{k-1})}\right) \\ &= 1 - \left(\frac{N-h_0}{N}\right) \left(\frac{N-h_0-h_1}{N-h_0}\right) \left(\frac{N-h_0-h_1-h_2}{N-h_0-h_1}\right) \dots \left(\frac{N-h_0-h_1-\dots-h_{k-1}-h_k}{N-(h_0+h_1+\dots+h_{k-1})}\right) \\ &= 1 - \left(\frac{N-(h_0+h_1+\dots+h_k)}{N}\right) = \left(\frac{h_0+h_1+\dots+h_k}{N}\right) \end{aligned}$$

Thus the cumulative probability method used in this paper is mathematically equivalent to calculating a cumulative incidence by the method above (simple cumulative method).

The assumption that the hysterectomy rate calculated from national databases is a reasonable estimate of hysterectomy probability is analogous to assuming that a CI for one year is equal to the ID. The CI is a measure of risk, and the ID a rate. The relationship between the two is:

$$CI = 1 - e^{-ID\Delta t}$$

For rare diseases, where  $ID\Delta t < .10$ , the assumption can be made that  $CI \approx ID$ .<sup>82</sup> There is error introduced by equating the hysterectomy rate with a hysterectomy probability, but other potential sources of error in the method (e.g., the modelling of early hysterectomy rates) seem to be a greater problem, and the degree of error introduced would best be judged by validating the estimated hysterectomy prevalence by a survey.

### ***Cohort analysis***

An age-period-cohort analysis attempts to disentangle the effects of age, period and birth cohort in longitudinal data. An inherent limitation in this analysis is the linear dependency of each variable on the other two. Thus each set of data has at least two explanations (the "identification problem"). Separating the three effects empirically depends on a priori knowledge and is not solved by using statistical techniques.<sup>83</sup>

This can be done by displaying the three elements using line charts (often referred to simply as a 'cohort analysis'). This technique is simple to perform, makes few assumptions and is more easily understood than the alternative method. In the present study birth cohorts are defined by five year age groups in 1969; later data points for that cohort are the values appropriate for the aging of that birth cohort at five year intervals. The analysis involves interpretation of line charts of that data.

An alternative method involves analysis of the same elements using a computer program. This involves using a model, and the assumptions inherent in that model. Using three separate variables in the model for age, period and cohort makes the assumption that the three elements are independent, and it is now common to include only two. This method does offer the advantage that it can be used to adjust the data (e.g., to remove the cohort effect), but does not solve the basic problem of the 'identification problem'; as well, its shortcomings may be less obvious to the reader. There do not appear to be significant advantages to the modelling technique that

outweigh the simplicity of the simple graphical technique for the present study.

### ***Chart review at Ottawa Regional Cancer Centre***

A chart review of incident cases of cancer of the corpus uteri at both branches of the Ottawa Regional Cancer Centre (ORCC) was done to assess the role of increased diagnosis in elderly women in more recent periods. It looked for evidence of earlier diagnosis (shift to an earlier stage, decreased length of symptoms before diagnosis), and more frequent diagnosis of asymptomatic cases, as well as use of new diagnostic techniques.

The Ottawa Regional Cancer Centre is an organisation providing clinical oncology services to western Quebec and eastern Ontario during the period of study through two branches situated in the Ottawa Civic (OCH) and Ottawa General Hospitals (OGH). It is part of a system of regional cancer centres in Ontario. Hospital-based tumour clinics at OCH and OGH became part of the Ontario Cancer Treatment and Research Foundation in 1953. The satellite clinic at the Ottawa General Hospital has been a separate division since 1958.<sup>84</sup> It has a smaller volume of patients and draws a significant proportion of its clientele from western Quebec.

Permission for the chart review was obtained from the clinical research committee of the Ottawa Regional Cancer Centre. Charts were pulled from both divisions of the ORCC for three time periods: 1969-72, 1980-81, and 1990-91. Criteria for inclusion in

the study were: age of 65 or greater at the time of admission to the clinic, a new diagnosis of cancer of the corpus uteri (ICD9 182) during the time periods of interest, and that the patient had been seen within a six month period after the date of the definitive diagnostic procedure. Patients whose usual residence was not within the ordinary catchment area of the ORCC were excluded. All eligible charts within each time period were included.

The information gathered included clinical stage, presenting symptoms, length of symptoms before diagnosis, method of diagnosis, and histologic diagnosis. Initially, as well, 5 charts from each time period were examined to assess the feasibility of collecting risk factor information.

Analysis was done by performing  $\chi^2$  for linear trend of proportions over the three time periods, and unpaired t-tests,  $\chi^2$  and Fisher exact tests where appropriate comparing the later periods to the earliest period. Some tests were further stratified by age (65-74,  $\geq 75$ ). Where tests of statistical significance are done in this paper, they are tests of the relevant null hypotheses.

### ***Staging for endometrial cancer***

In 1988 the International Federation of Gynecology and Obstetrics (FIGO) changed the staging for endometrial cancer from a clinical staging system to a surgicopathologic one which offered better precision in terms of prognosis and treatment decisions.

Although that system is the one in current use and is thought to be more accurate than the previous clinical staging, it involves histologic grading and surgical staging information which were not available from the charts of the two earliest periods in this study.<sup>85</sup> This meant that a clinical staging scheme was the only appropriate method for this chart review.

Since 1950 there have been three staging plans drawn up by FIGO. The most 'developed' one which could be supported by the chart data is the 1961 staging:

- Stage I: confined to the corpus
- Stage II: involving the corpus and the cervix
- Stage III: extending outside the uterus but not outside the true pelvis
- Stage IV: outside the true pelvis or involving the mucosa of the bladder or rectum

This was modified by not considering the results of fractional D&Cs in the staging; these have been shown to be a significant source of misclassification in the past<sup>65, 101</sup> (see Appendix E for more detailed discussion of staging issues).

## **Results**

### ***Hysterectomy patterns***

Age standardised hysterectomy rates in Canada peaked in 1971-72 and have declined continuously since. Underlying this simple trend are marked changes in rates for women under 60 years of age, peaking in the early 1970s, stable rates for the age group 60-74 and slowly increasing rates in the 75-89 year age group. Rates for these age ranges have been standardised to the 1971 Canadian age distribution (see Figure 5).

Even within the three youngest age ranges, the proportionate increase in rates from 1969 to 1972 was inversely related to age: the increase from 1969 rates was 72% for the 20-24 year age group, 43% for 30-44 year old women, and 20% for the 45-59 year old group. Hysterectomy rates by five year age group for the period 1969-90 are included in Appendix F.

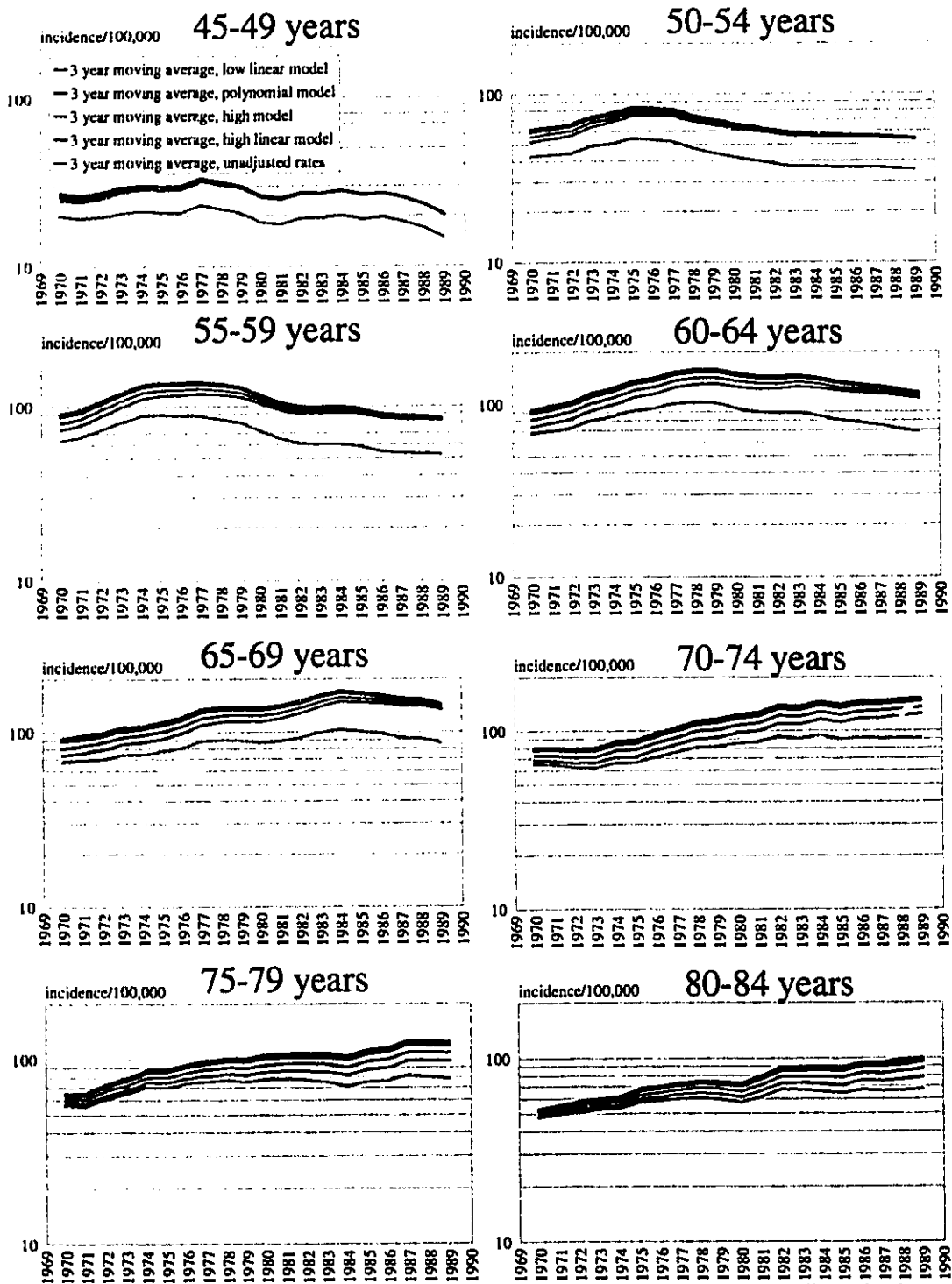
Subtotal and partial hysterectomies only contributed significantly during the first years of the period, as can be seen in Figure 7. There was a coding change in 1979, but even before that, the proportion of subtotal and partial hysterectomies had fallen dramatically.

***Trends in age-specific incidence of cancer of the corpus uteri;  
hysterectomy adjustment***

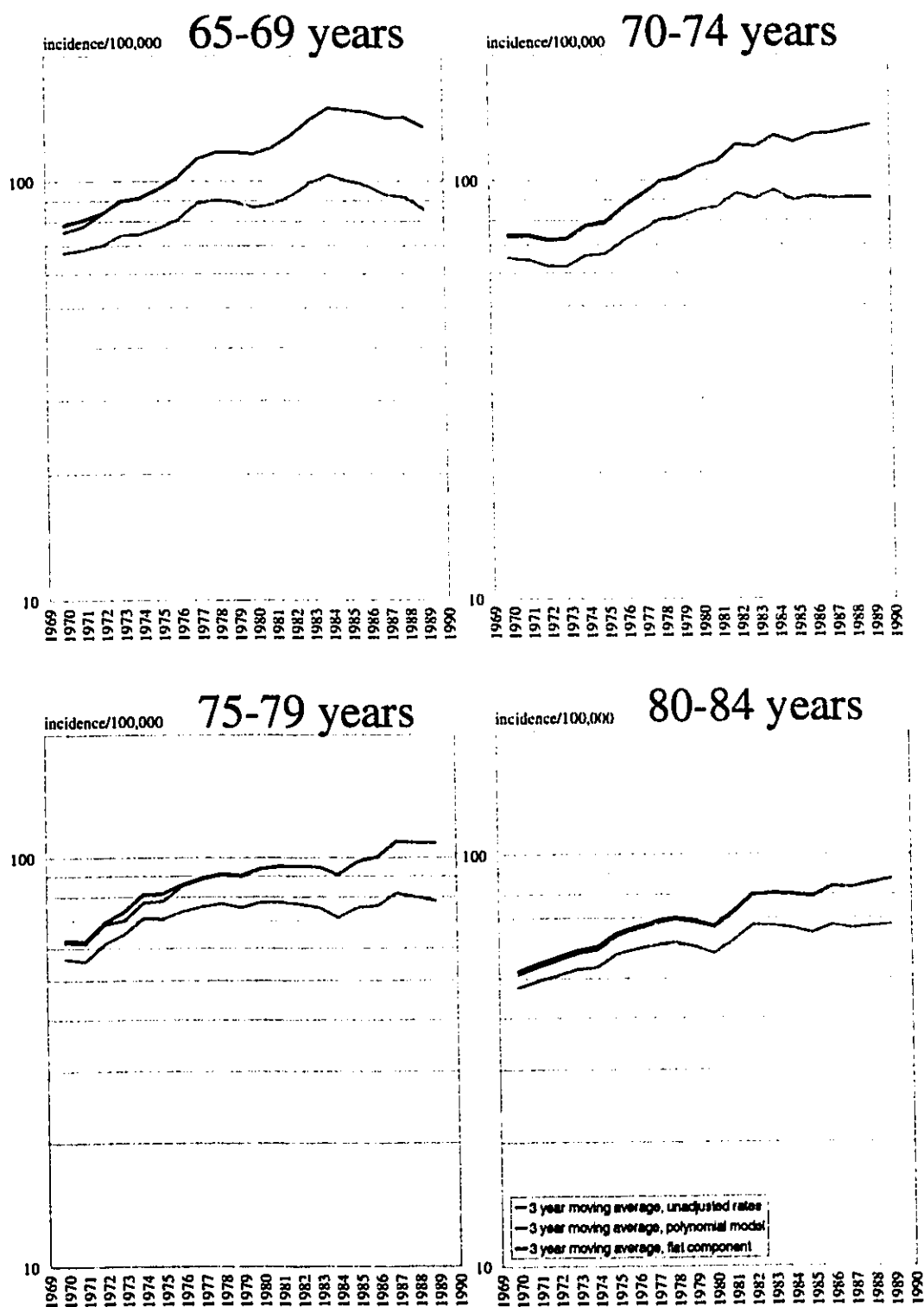
Age specific incidence rates of ICD9 182 in Canada both with and without hysterectomy adjustments are displayed in Figure 10. In age groups under 70, cancer of the corpus uteri is clearly declining after peaking in the mid 1970s. In age groups over 70, however, unadjusted incidence rates have been fairly stable since around 1982, after rising during the 1970s.

After adjustment for hysterectomy prevalence using the modelling technique derived from Miller, incidence rates in age groups under 70 still show declining trends for all models, although the slopes are not as steep. For age groups over 70, after adjustment using this technique, all age groups show a rising incidence. This was true for all models tested, even the improbably low linear model which assumed no hysterectomies prior to 1950.

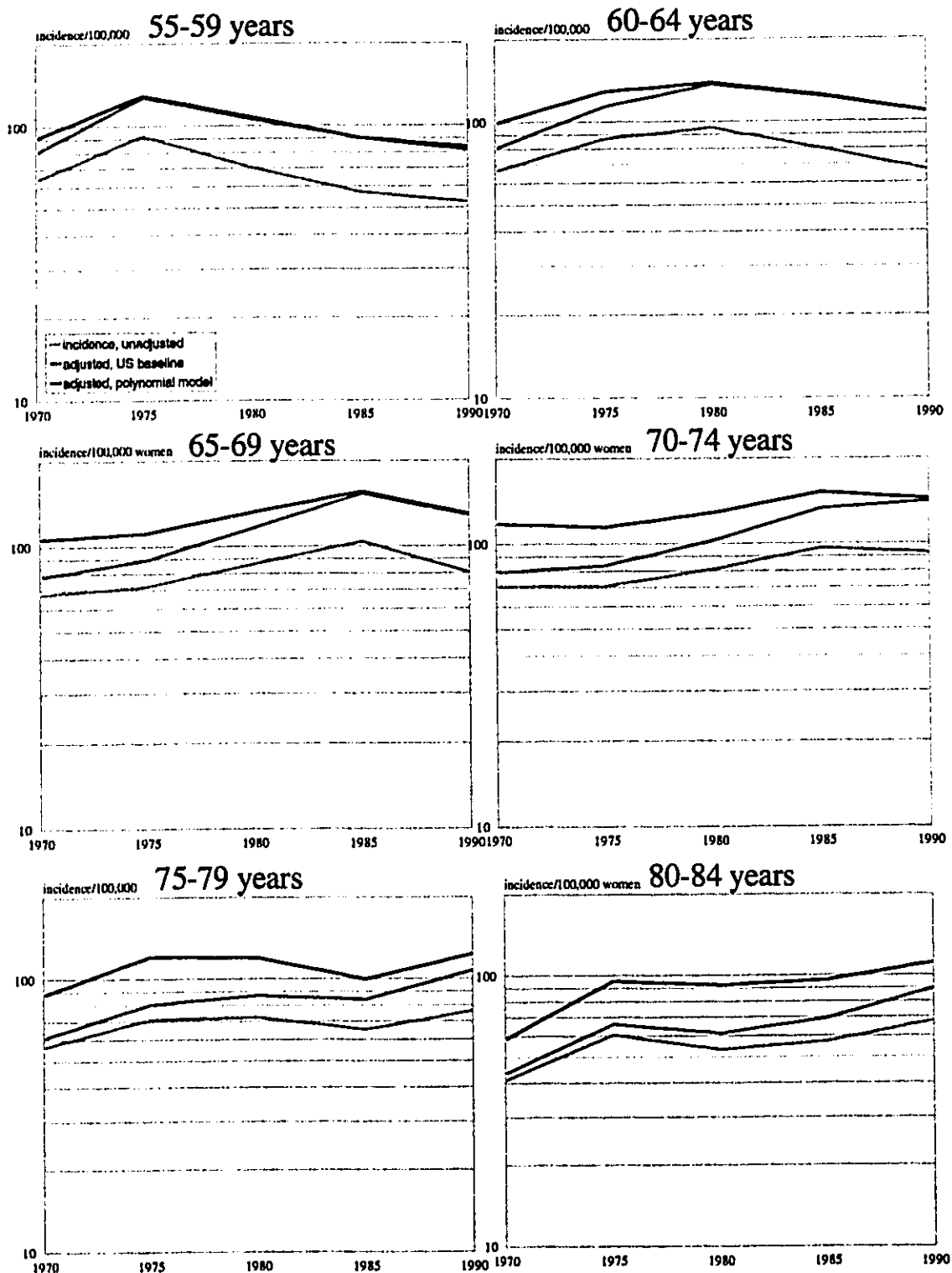
The mixed model was done to demonstrate the effect on adjusted trends of overestimating hysterectomy rates in older women relative to the estimates in younger women (see Figure 11). It raises the 1969 (adjusted) incidence rates by 1.8%, 2.9% and 3.7% for age groups 70-74, 75-79 and 80-84 years, and thus decreases the slope of the initial segment of the incidence curves. This make little difference to the



**Figure 10: Incidence rates for Canada of ICD9 182, unadjusted and adjusted using various simple models using the technique described in this paper.**



**Figure 11:** Incidence of ICD9 182 adjusted using a mixed model with the polynomial model for age <60 years, flat model for age 60-74, and linear model for age 75-84 of each cohort; unadjusted rates and polynomial model included for comparison. This uses higher estimates of hysterectomy rates in older age groups for earlier periods. All data displayed as three year moving averages.



**Figure 12:** Hysterectomy adjustment using US baseline hysterectomy prevalence for 1970 and Canadian procedure rates in the same birth cohort in Canada; unadjusted rates, and adjusted rates using second degree polynomial model also shown. Each presents only five data points.

adjusted rates for the 1980s in which period the adjustment technique yields increasing incidence rates in women over 70, rather than the stable pattern seen with unadjusted rates.

The other crude hysterectomy adjustment presents five data points, using US baseline prevalence rates and Canadian procedure data for five year age groups. It shows a different picture (Figure 12). Using this method, incidence in age groups below 70 years is decreasing in the most recent period. In 70-74 year old women incidence increased from 1975 to 1985 and then declined slightly to 1990. In the 75-79 year age group adjusted incidence rates were quite stable from 1975 onwards, whereas in the 80-84 year age group a similar stability was replaced by an increase of 16.4% from 1985 to 1990. Overall the adjustment does not change the picture much.

### ***Morphology***

Trends in morphologic subtypes of ICD9 182 in women aged 70-84 were analysed to see whether one particular morphologic type was increasing in that age group. The analysis was done on data from five provinces from 1969 to 1989 (Newfoundland, Ontario, Saskatchewan, Alberta, British Columbia), age standardised to the 1971 Canadian female population. This information is displayed in Figure 13. The largest diagnostic group, adenocarcinomas (ICDO-M 814), showed the only important increase over the whole period increasing from 47.5/100,000 to 58.8/100,000 or 86% of the total increase among carcinomas. Sarcomas increased from 3 to 3.6/100,000 over the

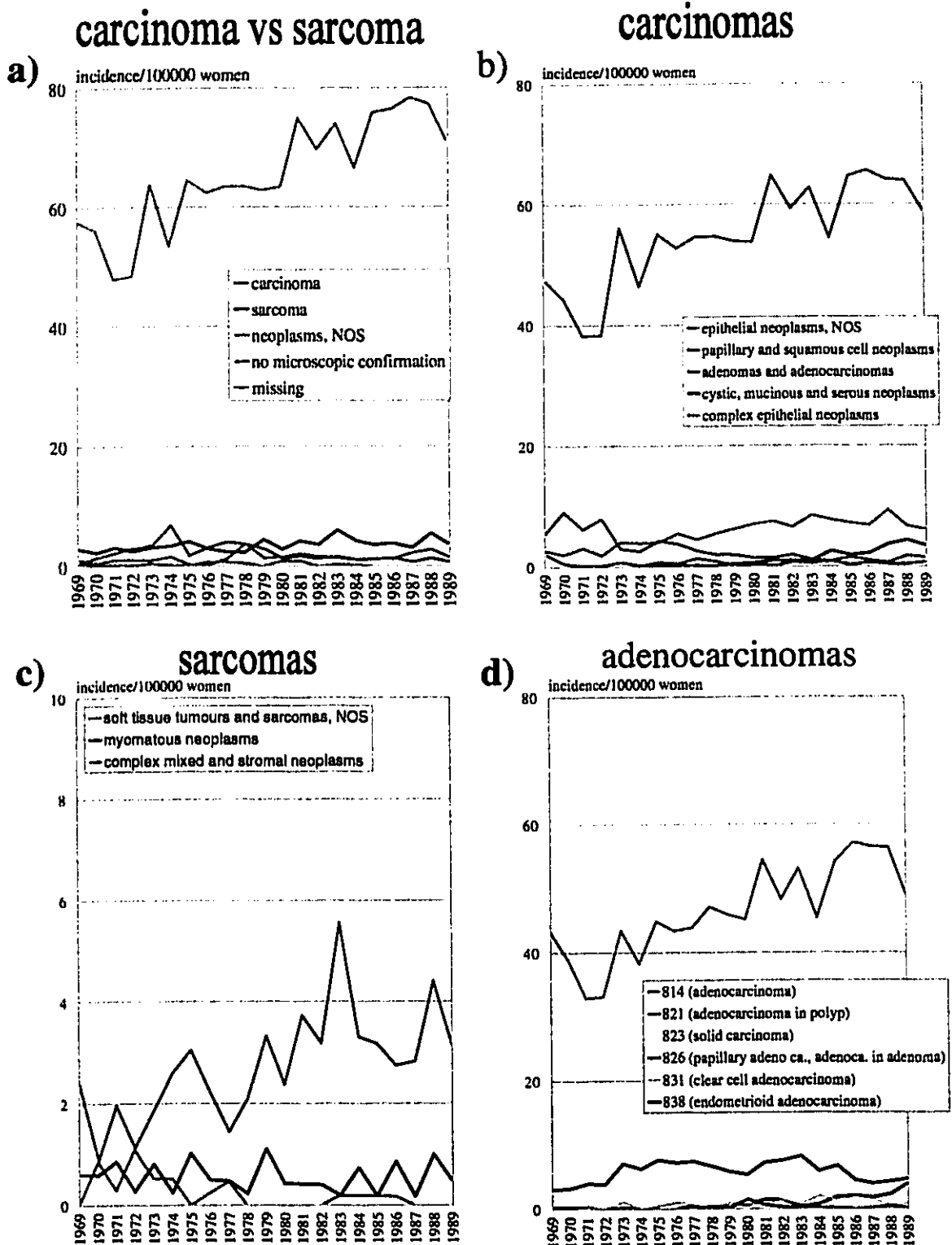


Figure 13: Standardised incidence rates of histological subtypes (ICDO-M), age group 70-84 years ICD9 182; based on five provinces (Newfoundland, Ontario, Saskatchewan, Alberta & British Columbia); standard Canada 1971. Figures b and c describe one line each of a, and d one line of b.

same time.

It should be noted that the incidence rates in this morphology section do not add up to the same total as the national incidence figures: although they are standardised to the 1971 Canadian population, the morphology data represent the experience of only five provinces.

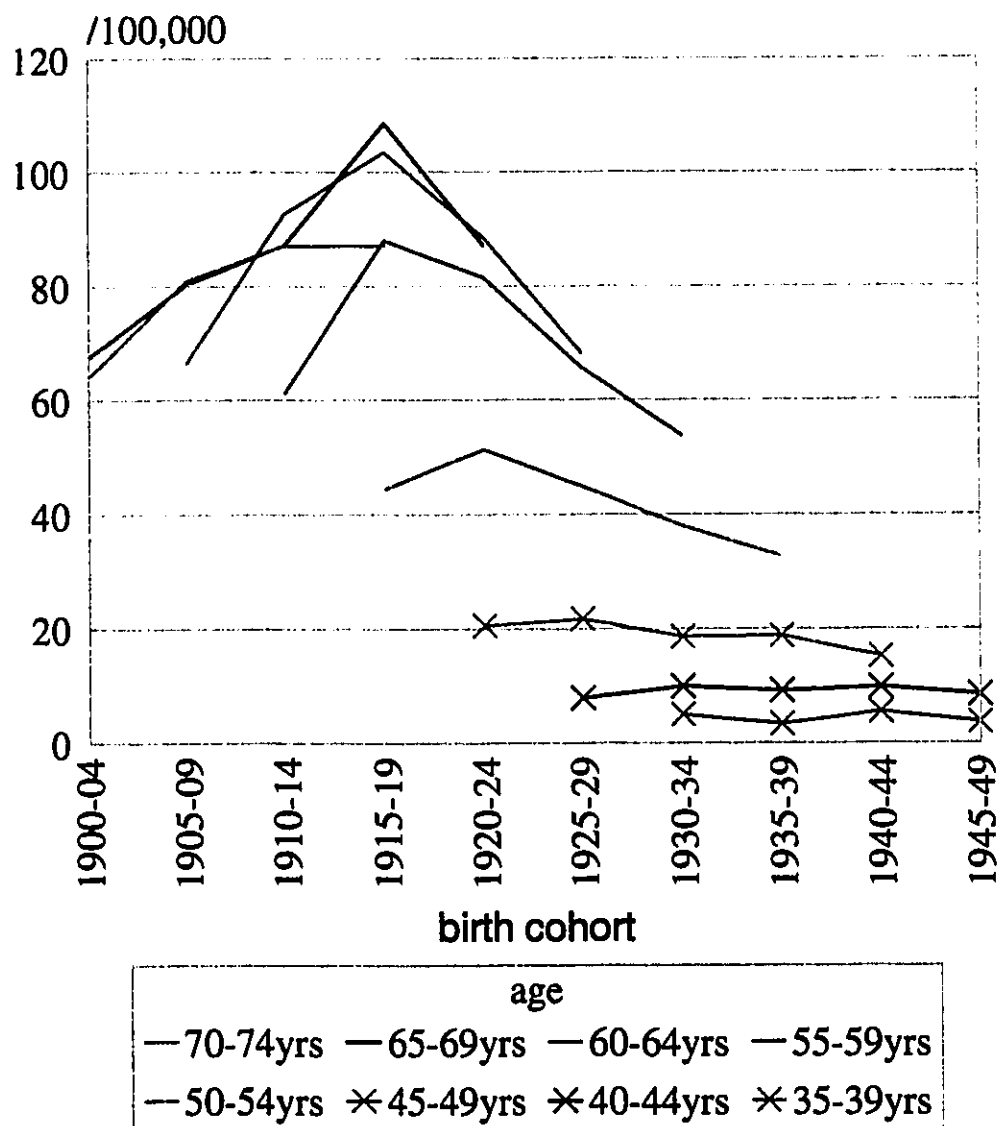
### ***Cohort analysis***

The cohort analysis presents information from birth cohorts in five year age groups in an attempt to disentangle the effects of age, period and birth cohort. This information can be displayed in a number of different manners, two of which are used in this paper.

In Figure 14 age specific incidence rates are presented by birth cohort. These rates have not been adjusted to reflect hysterectomy prevalence. Each data point represents the incidence for that birth cohort when it reaches the stated age. In a stable situation (no cohort or period effect) this type of graph should consist of a series of parallel horizontal lines with the highest one being that of the age group with the highest age specific incidence rate (65-74 years). A strong birth cohort effect on this graph will show as peaking of the age-specific incidence curves for that birth cohort. This appears to be the case for age groups greater than 55 years of age, which peak for the

# incidence, ICD9 182

## birth cohort analysis



**Figure 14:** Incidence of ICD9 182; birth cohort analysis displayed as age specific curves.

# mortality, ICD9 182

## birth cohort analysis

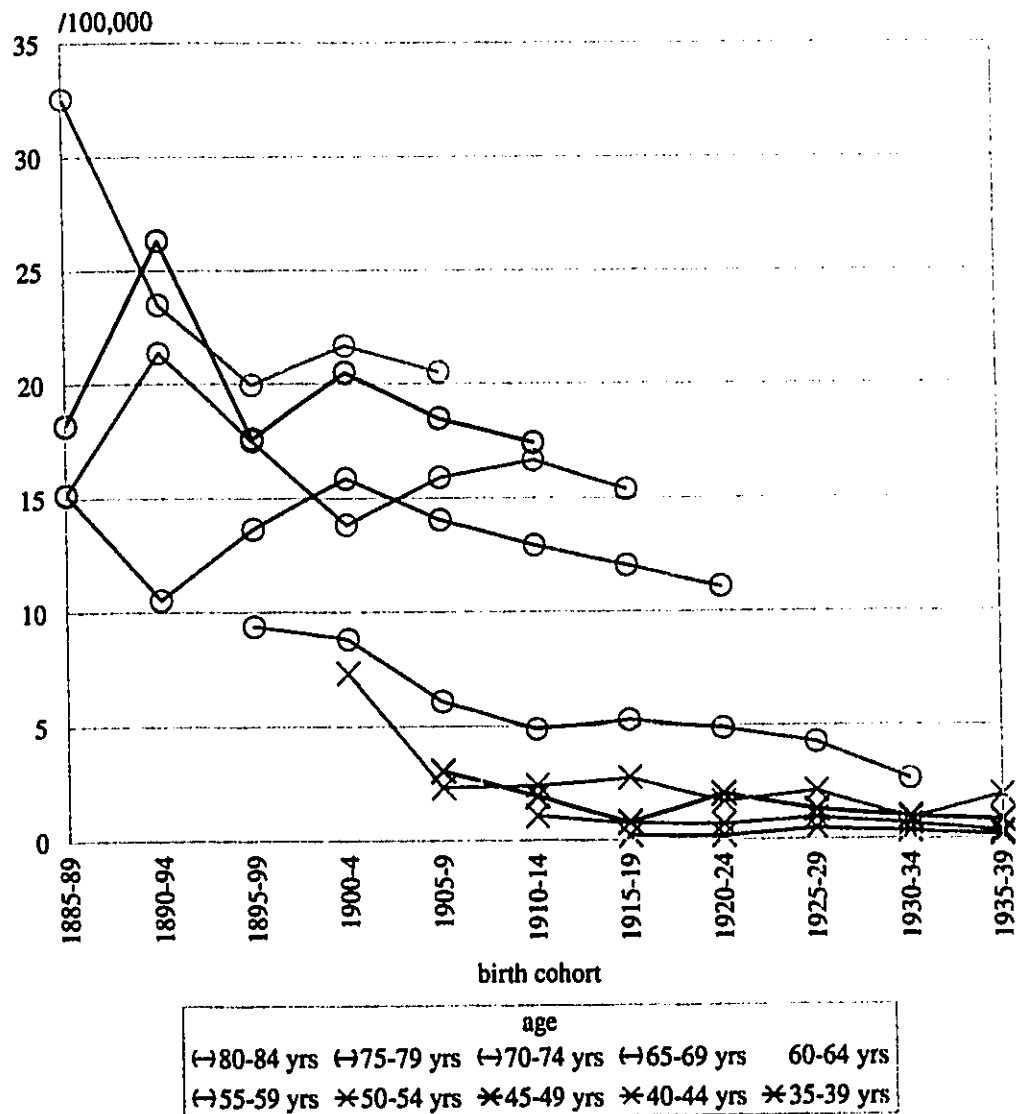


Figure 15: Birth cohort analysis of ICD9 182 mortality, displayed as age specific curves.

1915-19 birth cohort. The risk decreases for birth cohorts earlier than that.

A strong period effect on the graph would appear as a peak in the age specific incidence curves marching down and to the right: moving one birth cohort to the right for each decrease in the age group. The curves covering age groups 45-59 years fit that pattern: an increased risk for the 'period' 1974.

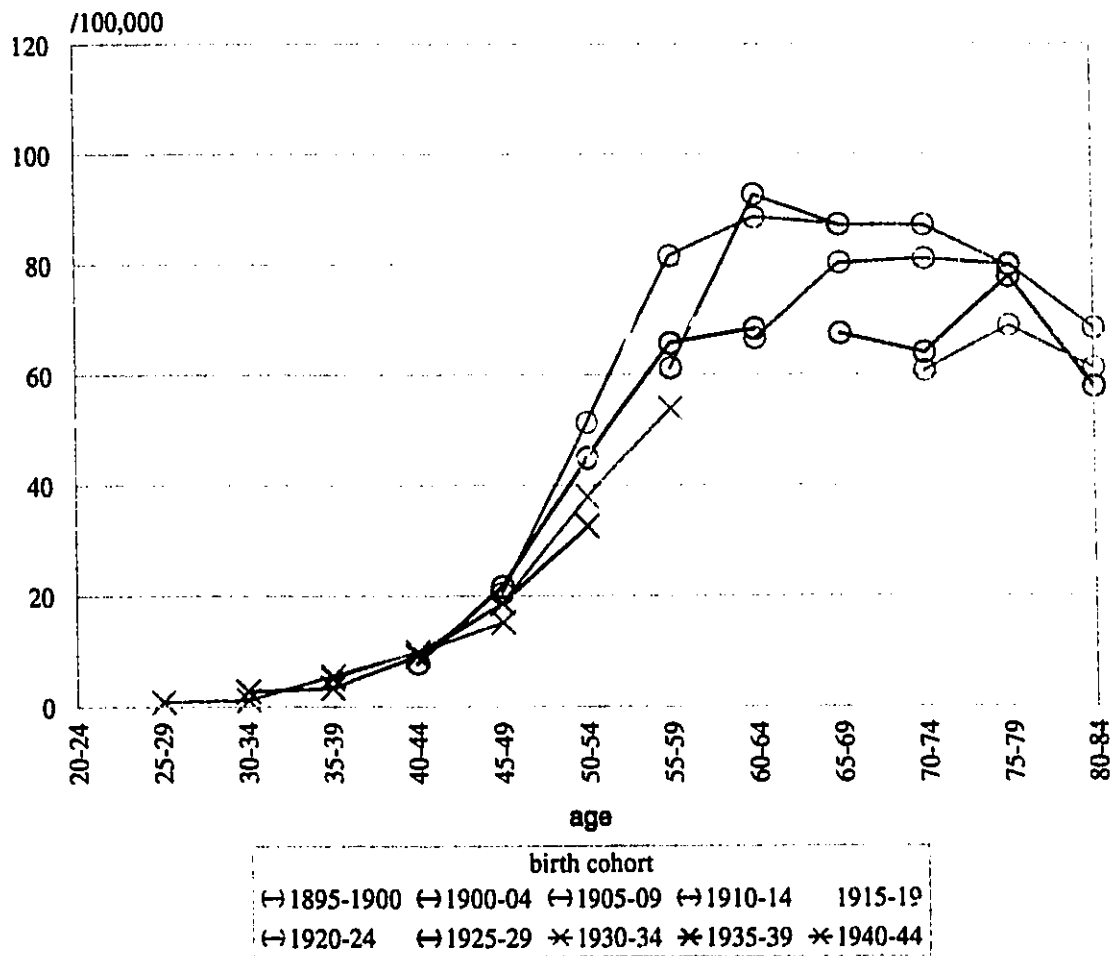
The data can be interpreted as a combination of birth cohort effect (in older women) and a smaller period effect in younger women.

Figure 15 is a similar analysis of mortality by birth cohort, not adjusted for hysterectomy prevalence. The highest mortality tends to be in the oldest birth cohorts for the oldest age groups. To some extent the wild fluctuations in mortality for birth cohorts prior to 1900-04 represent the unstable rates associated with small numbers of cases. In birth cohorts from 1900-04 onwards, mortality for all age groups other than 70-74 year old women is declining. There is no peak in mortality for the 1915-19 birth cohort corresponding to the peak in incidence.

Figures 16, 17 & 18 present the birth cohort information as incidence or mortality by five year age group, with each line representing a birth cohort. In a period of stable incidence and mortality these should yield a smooth curve resembling the age specific curves for a single year (Figure 1), with the birth cohort lines overlapping.

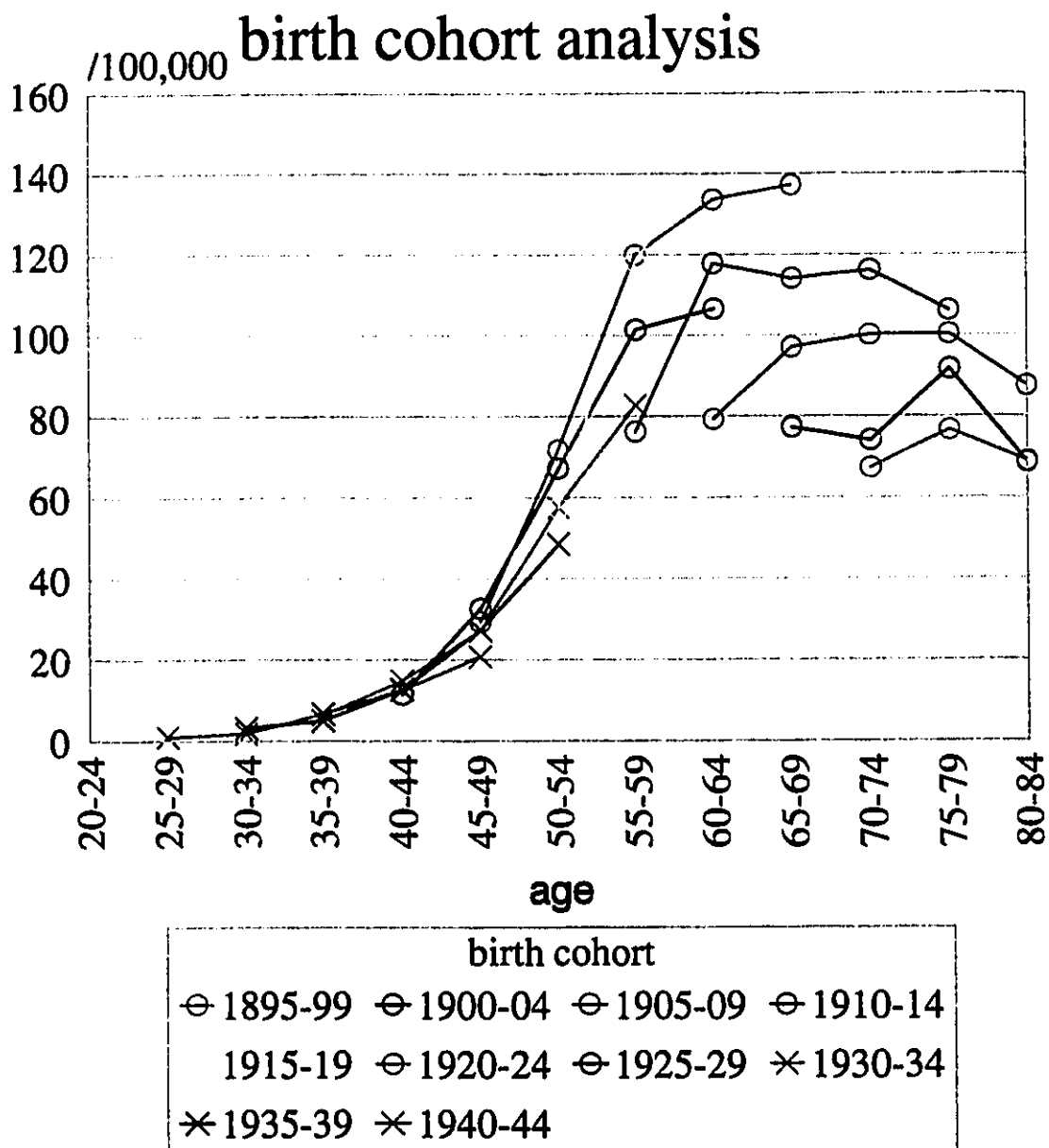
# incidence, ICD9 182

## birth cohort analysis



**Figure 16:** Birth cohort analysis of incidence of ICD9 182 in Canada. Each curve represents the age-specific incidence associated with that birth cohort.

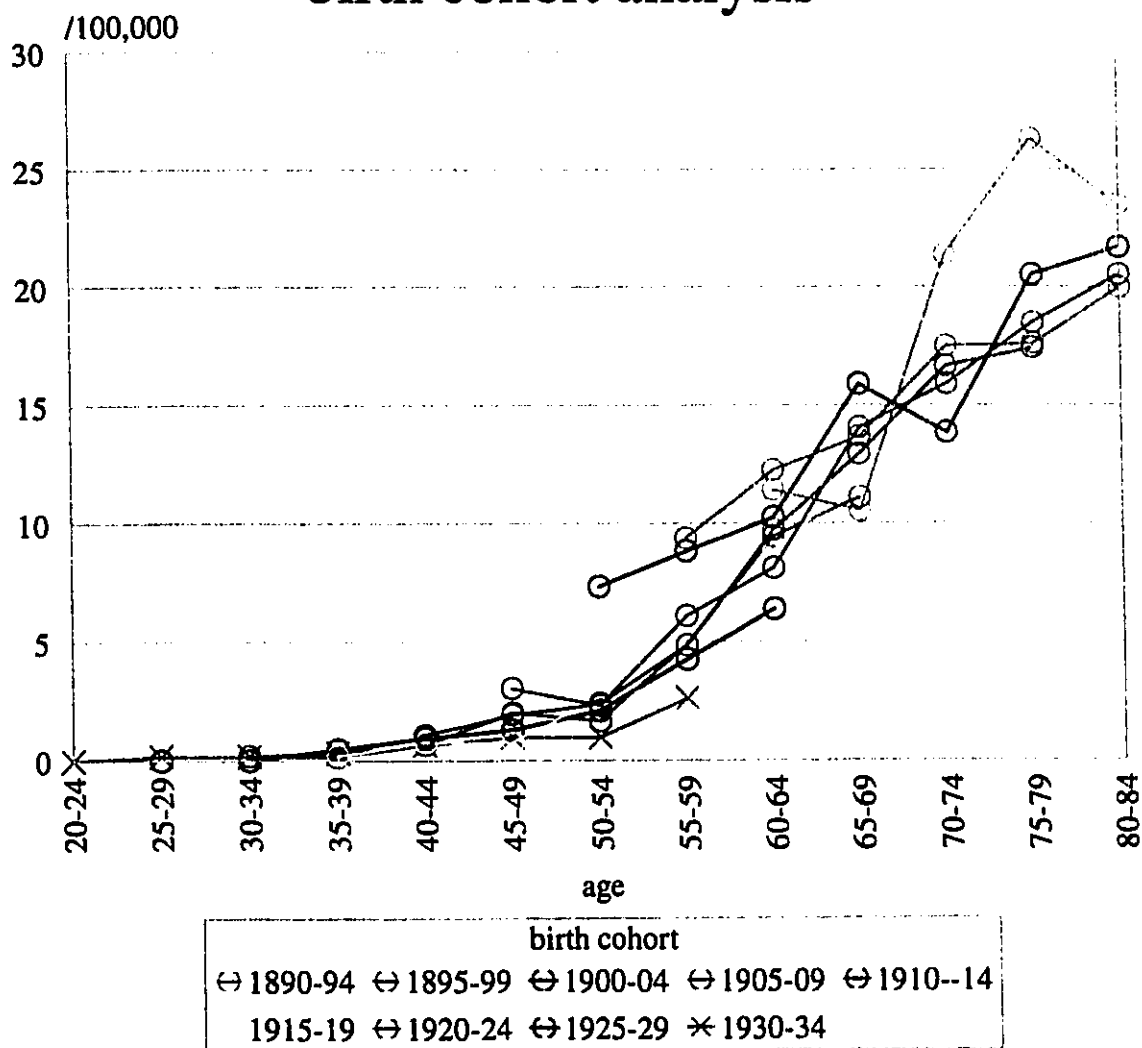
# incidence, adjusted



**Figure 17:** Birth cohort analysis of incidence of ICD9 182, adjusted for hysterectomy prevalence using second degree polynomial model. Each curve represents the age specific incidence (adjusted) of one birth cohort.

# mortality, ICD9 182

## birth cohort analysis



**Figure 18:** Birth cohort analysis, mortality, ICD9 182. Each curve represents the age specific mortality of one birth cohort.

It is possible to tease a few useful pieces of information out of these colourful tangles of lines. The incidence chart (Figure 16) demonstrates that the 1915-19 birth cohort had the highest age specific rates from ages 50-74, followed by the birth cohorts on either side of it. Age specific rates for these three birth cohorts were higher than for either earlier or later birth cohorts. As these three high risk birth cohorts age, their incidence rates are converging towards those of earlier birth cohorts if they are constructed with unadjusted data. If the same type of birth cohort analysis is constructed with incidence rates adjusted using the second degree polynomial model (Figure 17), the two highest risk birth cohorts (1915-19 & 1920-24) still carry an excess risk for the most recent period.

The highest mortality (see Figure 18) is in the earliest birth cohorts: for 70-84 year old women in the 1890-94 cohort, and for women in their 50s in the 1895-99 and 1900-04 cohorts. Recent birth cohorts are associated with lower mortality.

### ***Trends in D&Cs***

Increased diagnostic intensity in older women might result in increased diagnosis of cancer even if there were no real increase. Dilatation and curettage of the uterus (D&C) is the most common initial test done which provides tissue for histologic examination.

Age specific rates of D&Cs done as inpatients are published on an annual basis by

the Canadian Centre for Health Information, and are displayed in Figure 19. The procedure codes used are those for 'other' D&Cs as distinguished from D&Cs related to pregnancy or therapeutic abortions. There was a change in coding system in 1979 from ICD8 based procedure codes to Canadian Classification of Diagnostic, Therapeutic, and Surgical Procedures (CCP) codes.

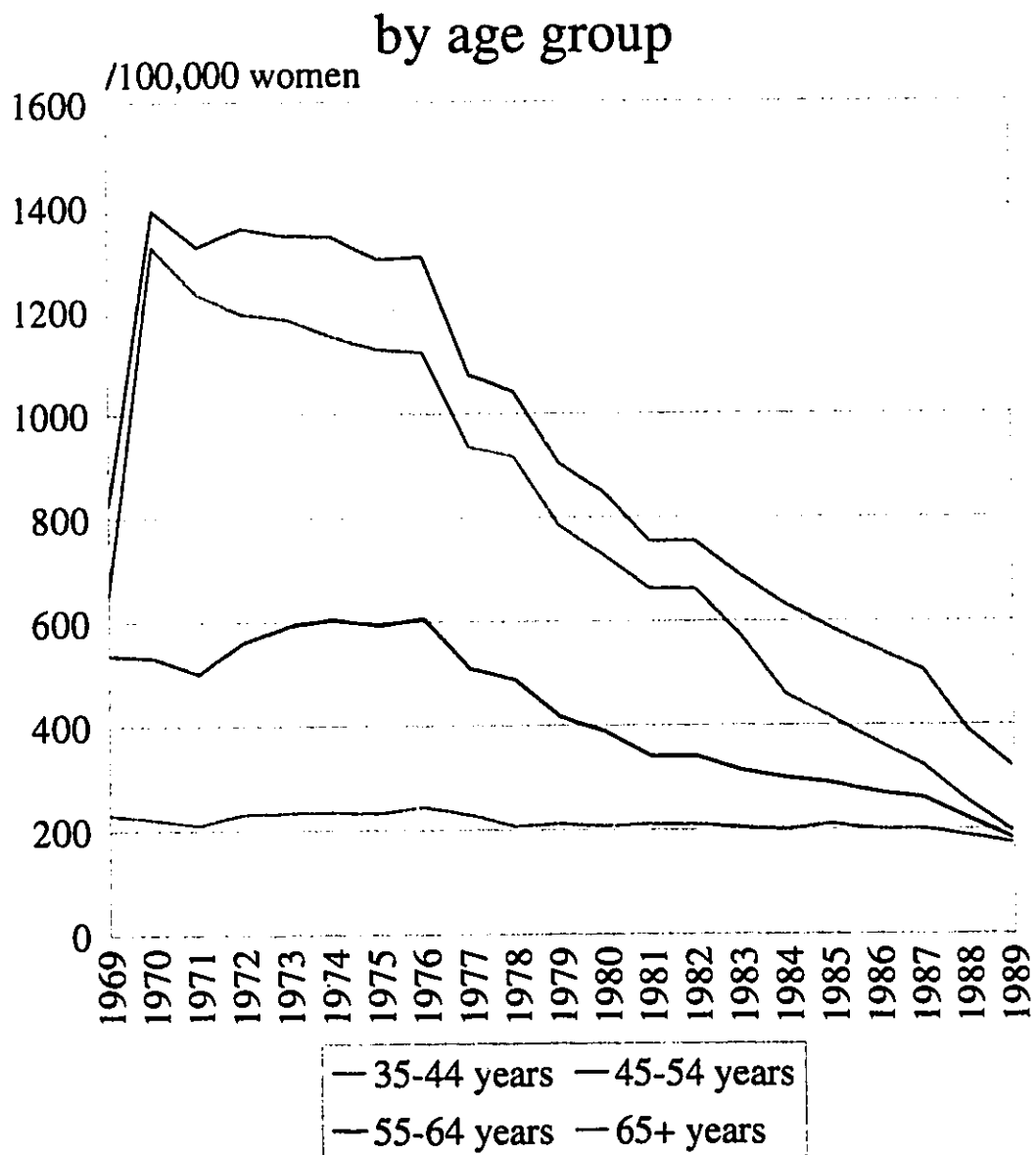
The remarkable rise from 1969 to 1970 in the two youngest age groups is likely artefactual, due to incomplete reporting in the first year or a change in coding procedures. For 55-64 year old women there is a decrease in the rate of D&Cs during the period of study. The rate for women  $\geq 65$  years decreases slightly from 1969 to 1989.

### ***Mortality/Incidence ratios***

Mortality/incidence ratios (MIRs) are included here as a measure of completeness of cancer registration (higher MIRs may indicate underreporting of incident cases). Other factors which influence these ratios are discussed below.

These ratios for Canadian data are shown in Figure 20 based on age standardised rates for the three age ranges. There are decreases from 1969 to 1975 for all three age ranges. For women 70-84 years, there is a fairly consistent decline from 1978 to 1990, while for the younger age range the pattern is fairly stable since 1982.

# 'other' D&Cs, Canada



coding change in 1979 from ICD8 based codes to CCP codes

Figure 19: Age specific rates of 'other' D&Cs (not related to pregnancy), Canada.

# mortality/incidence ratios

ICD9 182 by standardised age ranges

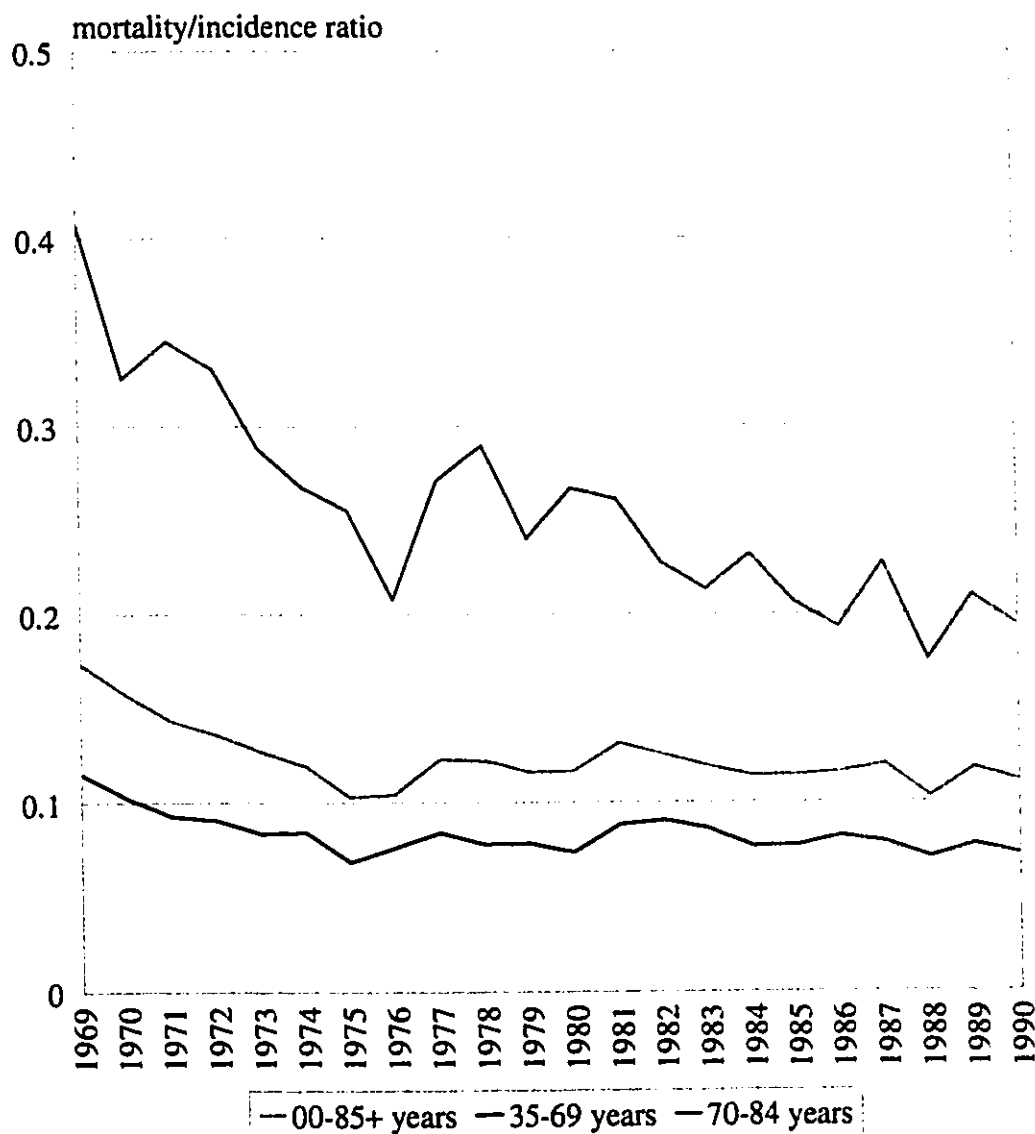


Figure 20: Mortality/incidence ratios by standardised age range (Canada 1971) over time.

## diagnosis by death certificate only

### by 10 yr age group

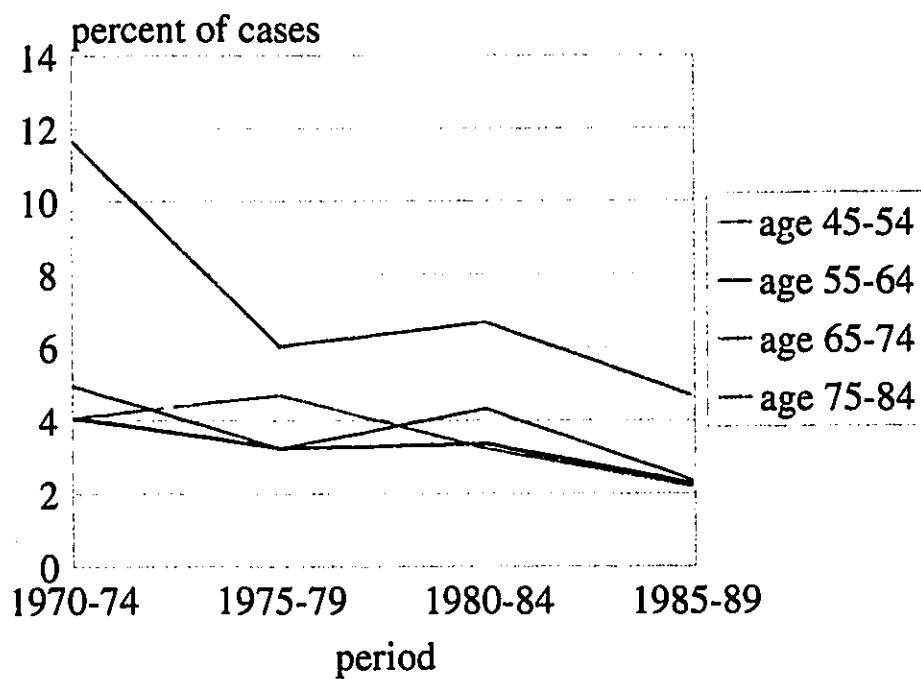


Figure 21: Diagnosis of ICD9 182 by death certificate only in Canada for four periods, by 10 year age groups.

## most confirmed method of diagnosis

age 70 and over

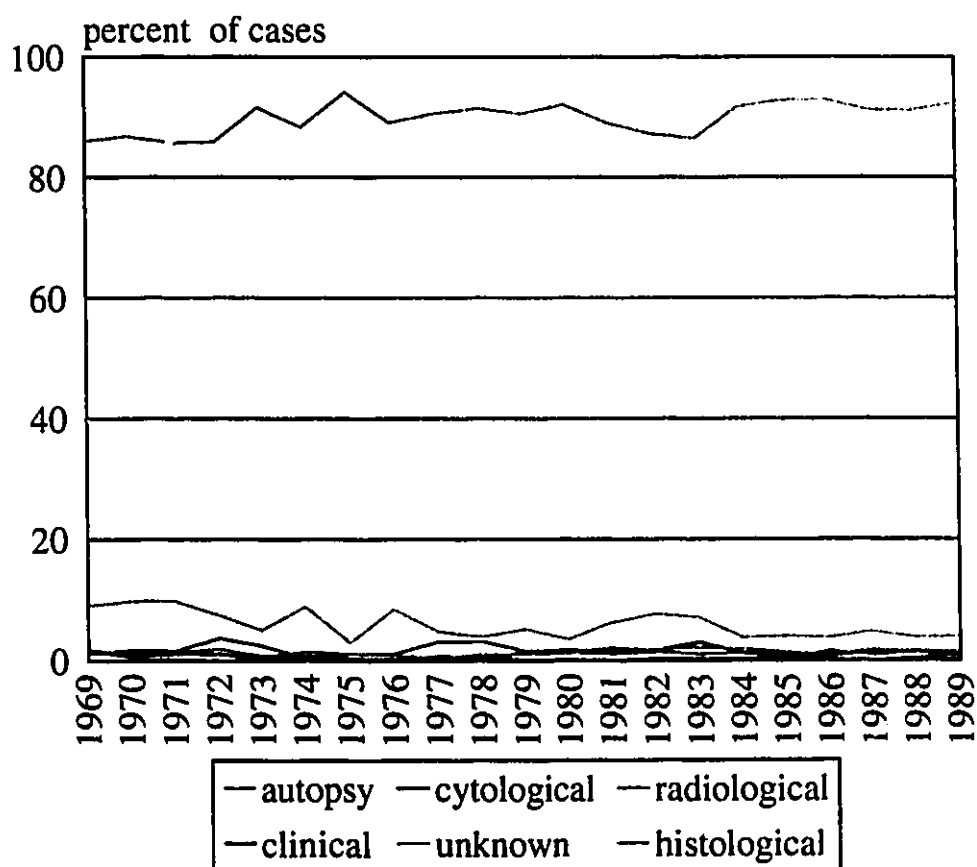


Figure 22: Methods of diagnosis over time, for women with ICD9 182, Canada.

### ***Most confirmed method of diagnosis***

The NCIRS file lists the most confirmed method of diagnosis for each case. One obvious age-related problem with the data is the increased frequency of diagnosis by death certificate only (dco) in the elderly. In the NCIRS 'death certificate only' is a composite of two codes ('unknown' on method of diagnosis or a 'yes' code for the vital statistics source variable). The results by period for 10 year age groups from age 45 to 84 are in Figure 21. The age group 75-84 consistently has a higher proportion of dco than the other age groups, even though it is markedly improved since 1970-74.

Figure 22 is a line chart presenting the most confirmed method of diagnosis for women  $\geq 70$  years of age for data from 1969 to 1989. The percent confirmed by histologic diagnosis rose from 86% in 1969 to 92.4% in 1989, while 'unknown method of diagnosis' fell from 9.1% to 3.8% over the same period.

### ***Chart review***

The chart review was primarily designed to assess the role of better diagnosis of cancer of the corpus uteri in women 65 years and over in more recent periods.

Of an original list of 341, 8 charts could not be located (3 from period 1 and 5 from period 2). After applying the exclusion criteria a total of 183 charts were eligible: 38 from period 1 (1969-72), 54 from period 2 (1980-81) and 91 from period 3 (1990-91).

**Table III**

<b>Risk factor information</b>	<b>mean (sd)</b>		
	<b>1969-72</b>	<b>1980-81</b>	<b>1990-91</b>
	<b>age (n=183)</b>	<b>71.7 years(5.8)</b>	<b>71.8 years(7.0)</b>
<b>parity (n=173)</b>	<b>1.94(2.9)</b>	<b>2.04(2.6)</b>	<b>2.14(2.6)</b>

The type and quality of information present in the charts varied with time period. This was particularly true of risk factor information, which seemed to be most consistently recorded when it was the responsibility of a non-physician (usually a nurse or nutritionist). Unfortunately this "routinely" collected information was different in the three time periods; only parity, marital status and age were consistently available (mean age and parity are listed in Table III). Even weight (within a month of first admission) and height were only available for 71% and 44% of the cases respectively. The quality of some information varied markedly from period to period: there was no information at all about hormone use in 83% of charts from period 1, vs 43% in period 2 and 30% in period 3. The information present only rarely included dose or duration.

The distribution of clinical stages in the three periods is shown in Table IV.

**Table IV**

<b>Clinical stage by period</b>				
<b>Stage</b>	<b>Period</b>			<b>Total</b>
	<b>1969-72</b>	<b>1980-81</b>	<b>1990-91</b>	
I	27(71.1%)	40(74.1%)	84(92.3%)	151(82.5%)
II	5(13.2%)	4(7.4%)	1(1.1%)	10(5.5%)
III	4(10.5%)	7(13.0%)	5(5.5%)	16(8.7%)
IV	2(5.3%)	3(5.6%)	1(1.1%)	6(3.3%)
<b>Total</b>	<b>38</b>	<b>54</b>	<b>91</b>	<b>183</b>

In Table V stage is analysed as a dichotomous variable, early (stage I) vs late (all others). Relative risks of early stage disease in the later periods (using the earliest period as a reference) are listed. There is a significant trend for a greater proportion of early stage disease in more recent periods ( $\chi^2$  for linear trend=10.676,  $p = .001$ ). Stratifying by age (65-74, 75+) does not materially change the results. A greater proportion of cases are stage I in more recent periods.

Duration of symptoms before diagnosis could be estimated for 156 women. The mean number of complete months of symptoms was 7.1(sd 13.5) in period 1, 3.8(6.2) in

Table V

Early (stage I) vs late stage disease		
	unstratified	stratified (65-74, ≥75)*
RR period 2 vs period 1	1.04(.81-1.35)	1.05(.82-1.35)
RR period 3 vs period 1	1.25(1.01-1.55)	1.32((1.06-1.63)
$\chi^2$ for linear trend	10.676, $p=.001$	12.798, $p=.0004$

\*RR<sub>MH</sub> or extended Mantel-Haenszel  $\chi^2$

Table VI

Length of symptoms by period				
length of symptoms	period 1 (1969-72)	period 2 (1980-81)	period 3 (1990-91)	total
<1 month	12	17	25	54
1-3 months	8	14	21	43
4-6 months	5	7	11	23
>6 months	7	9	20	36
total	32	47	77	156

Kruskal-Wallis  $H=.754$ ,  $p=.69$

period 2 and 6.7(10.9) in period 3. The quality of the data was so poor that it is most reasonable to present them in broad categories (see Table VI). There is no evidence that length of symptoms before diagnosis is shorter in more recent periods.

Information on presenting symptoms was present in 182 charts, and is summarised in Table VII. In period 2, of the two patients with no symptoms referable to the

Table VII

<b>Presenting symptom by period</b>				
<b>symptom</b>	<b>period 1 (1969-72)</b>	<b>period 2 (1980-81)</b>	<b>period 3 (1990-91)</b>	<b>total</b>
No symptoms	0	2(3.7%)	2(2.2%)	4(2.2%)
Any symptoms	38(100%)	52(96.3%)	88(97.8%)	178(97.8%)
vaginal bleeding	34(89.5%)	48(88.9%)	85(94.4%)	167(91.8%)
abdominal pain	1(2.6%)	2(3.7%)	1(1.1%)	4(2.2%)
mass	1(2.6%)	0	1(1.1%)	2(1.1%)
vaginal discharge	0	2(3.7%)	0	2(1.1%)
cough	1(2.6%)	0	0	1(0.5%)
diarrhea	1(2.6%)	0	0	1(0.5%)
abnormal ultrasound	0	0	1(1.1%)	1(0.5%)
<b>total</b>	<b>38</b>	<b>54</b>	<b>90</b>	<b>182</b>

\*percentage refers to the total cases in that period

\*expressed as a dichotomous variable, asymptomatic/symptomatic,  $p = .671$  by Fisher's exact test (two-tail) on the  $3 \times 2$  table (periods  $\times$  symptoms)

cancer, one had a suspicious Pap smear done essentially for screening purposes during a visit for uterine prolapse, and the other was diagnosed as an incidental finding on pathology after a vaginal hysterectomy for uterine prolapse. The two asymptomatic women in period 3 also consisted of one woman diagnosed on a 'routine' Pap smear and a second diagnosed incidentally after a vaginal hysterectomy. The woman listed as presenting with an abnormal ultrasound in period 3 was being investigated for an abnormal endometrial echo on ultrasound. Although she did have some vaginal bleeding just before her D&C, the D&C had already been arranged prior to the onset

of symptoms. The reason for doing the initial ultrasound was not clear from the chart.

**Table VIII**

<b>Initial method of diagnosis by period</b>				
<b>method of diagnosis</b>	<b>period 1 (1969-72)</b>	<b>period 2 (1980-81)</b>	<b>period 3 (1990-91)</b>	<b>total</b>
D&C	27(71%)	36(67%)	70(78%)	133(73%)
Pap smear	3(7.9%)	7(13%)	6(6.7%)	16(8.8%)
laparotomy	5(13.2%)	5(9.3%)	3(3.3%)	13(7.1%)
cervical biopsy	2(5.3%)	4(7.4%)	2(2.2%)	8(4.4%)
endometrial biopsy	0	0	6(6.7%)	6(3.3%)
incidental finding on path.specimen	0	2(3.7%)	1(1.1%)	3(1.6%)
ultrasound	0	0	2(2.2%)	2(1.1%)
vaginal biopsy	1(2.6%)	0	0	1(.5%)
<b>total</b>	<b>38</b>	<b>54</b>	<b>90</b>	<b>182</b>

The initial method of diagnosis lists the first tests done which were clearly abnormal (see Table VIII); this usually involves a pathology specimen and a pathologic or cytologic diagnosis. Ultrasounds, however, were listed as the initial method for two patients in whom they were clearly abnormal and for whom a hysterectomy was the next procedure done, as a direct result of the ultrasound findings.

New diagnostic techniques are playing a role in the most recent period, endometrial biopsy in 6.7%(6) of cases and ultrasound in 2.2%(2). Endometrial biopsy in

particular is a technique suitable for outpatient use in a hospital or in a physician's office, and was not in use in earlier periods. For 6 women in period 3 endometrial biopsies were the first positive confirmatory tests.

**Table IX**

Pathology: carcinomas vs sarcomas				
	period 1 (1969-72)	period 2 (1980-81)	period 3 (1990-91)	total
carcinomas	36(97.3%)	52(96.3%)	84(92.3%)	172(94.5%)
sarcomas	1(2.7%)	2(3.7%)	7(7.7%)	10(5.5%)
total	37	54	91	182

$p=.51$ , Fisher's exact test;  $\chi^2$  for linear trend 1.573,  $p=.21$

Fourteen different pathologic diagnoses were listed in 182 charts. These can be divided into carcinomas and sarcomas as in Table IX. The apparent trend of increasing proportions of sarcomas in more recent periods is not statistically significant (this may of course be due to the small numbers).

## **Discussion**

### ***Age specific trends and hysterectomy adjustments***

The clearest aspect of the age-specific trends is that they are different in women above and below the age of 70. In age groups below the age of 70 the incidence of cancer of the corpus uteri is decreasing whether or not previous hysterectomies are taken into account.. For age groups above 70 unadjusted incidence rates have been stable since around 1982 after increasing over the previous 10 years.

After using the modelling technique to adjust for previous hysterectomies, incidence in age groups above 70 is increasing regardless of whether a 'high' or 'low' model is used. Modelling the early hysterectomy rates provides an estimate of cross sectional hysterectomy prevalence rates for 1968. Two possible types of errors may introduce a trend into the adjusted data and need to be considered: error in estimating the average hysterectomy rate for a year or period (whether the model is in general low or high), and error resulting from the assumption of uniform rates of change in all age groups. I find it easiest to think of them in terms of their effects on the cross sectional estimates.

If the model provides estimates that are in general lower than actual hysterectomy prevalence the errors will be cumulated over the 'lifetime' of the birth cohort, and the absolute value of the underestimation will be highest for the oldest women (since they

have accumulated more of their lifetime risk of hysterectomy by 1968 than younger women). An age-specific hysterectomy prevalence for a later period (for example, the 80-84 year age group in 1978 as compared with the 'cross sectional' estimate for 1968) represents the 1968 estimate for 70-74 year old women and 10 years of good quality procedural data. The 1968 estimate for the 70-74 year age group will not have cumulated as much of the lifetime risk for that age group, and thus not be as low in absolute terms. This will show up as a trend of increasing hysterectomy prevalence, and consequently, incidence of adjusted data. This change of slope will be steepest in the earliest period of study which relied more on the models and less on the procedure data for the estimates.

The 'high' model (0 in 1930, .6 in 1950 and 1 in 1970) gives higher hysterectomy rates in the past than are likely to have been the case, and still shows increasing incidence in elderly women.

One assumption of these models is that hysterectomy rates for all age groups changed at the same rate from 1930 to 1970. An examination of the hysterectomy rates for Canada from 1969 to 1990 shows that this is not strictly true. Whereas rates in age groups under 60 in general rose to a peak in 1971 or 1972 followed by a gradual decline, rates for women from age 60 to 74 have been more uniform, and rates in women over 75 have risen during most of the 1980s.

If rates in older women prior to 1969 did not fall off as fast as those in younger women, estimates of hysterectomy rates for older women derived from the models would be lower relative to their true values than the estimates for younger women. These relatively low values would result in high estimates of the proportion of women with intact uteri in these age strata, and consequently an adjusted incidence rate that was low. These low values would appear as the adjusted values for higher age strata in the earliest years of the study period. Similar to the situation discussed above, values later on in the study period for the same age stratum represent progressively younger age cohorts whose estimates of hysterectomy rates (and adjusted incidence rates) were not as relatively low. This would appear as a temporal trend of increasing incidence in the elderly, with the extent depending on the degree of underestimation of operative rates in the elderly relative to that in younger age groups. This affects only the lifetime cumulative risk of hysterectomy left after age 60.

The importance of this effect was tested by using a mixed model which overestimated early hysterectomy rates in older women by using different (higher) models for older age ranges. The magnitude of this effect in the mixed model was small, and did not greatly affect the adjustments to the data in the 1980s, which were more dependent on the procedure data.

The US method used by Pokras and Hufnagel makes the assumption that hysterectomy rates for women prior to 1960 were similar to the age-specific rates in 1965. This

assumption will result in an overestimation of operative rates in the elderly, particularly in the oldest age groups. Women aged 75 in 1960 were 50 in 1935, and calculation of their risk of hysterectomy would involve 25 years at 1965 age-specific rates. This will result in an overestimate of hysterectomy rates, an underestimate of the real proportion of women with intact uteri, and a resultant overcorrection of the incidence rates. Corrected incidence rates for older women in the early years with this method will be too high.

**Table X:** estimates of proportions of women with intact uteri, US baseline vs modelling technique.

Proportions of women with intact uteri in 1970, various methods					
Age group	method or model used				
	Pokras, US	low linear	polynomial	high linear	high
20-24 yrs	.997	.999	.999	.999	.999
25-29 yrs	.983	.990	.990	.990	.990
30-34 yrs	.945	.959	.958	.956	.955
35-39 yrs	.915	.904	.899	.891	.889
40-44 yrs	.826	.842	.827	.809	.802
45-49 yrs	.769	.807	.775	.741	.728
50-54 yrs	.751	.817	.762	.712	.691
55-59 yrs	.701	.866	.791	.728	.701
60-64 yrs	.670	.912	.828	.760	.729
65-69 yrs	.636	.941	.863	.796	.767
70-74 yrs	.602	.956	.894	.837	.813
75-79 yrs	.642	.965	.922	.877	.860
80-84 yrs	.705	.974	.944	.913	.901

\*the low linear, polynomial, high linear and high models are all from the present study

The resulting biases can be kept in mind in comparing estimates of the proportions of

women with intact uteri for the Pokras method and the models described in this paper.

The US baseline technique shows a stable incidence since 1975; the bias inherent in that method would overestimate the prevalence of hysterectomy in older women, and this would appear as a declining incidence over time. Stable incidence rates using this correction method are therefore consistent with some degree of underlying real increase over time in the elderly.

Using the modelling technique, adjusted incidence rates with all models show an increase in the elderly over time. The actual procedural data used are very good, covering very close to the entire Canadian population, and estimates produced using the technique in this paper will continue to improve as greater proportions of the hysterectomy rates are from the procedural data and less from the modelling. Visually this can be seen as a convergence of the curves from various models. This is already apparent for younger age groups. On balance, it seems likely that incidence is increasing in women over 70; quantifying it is a matter of speculation.

Overall the polynomial model is the most reasonable to use, since it uses the two data points from the BC study. However, it is also possible that the 'high linear' model is closer to the truth: if the BC data points represent only total hysterectomies, an adjustment for cancer of the corpus uteri should use higher values as it includes

subtotals which were more common in earlier periods.

The model-based hysterectomy adjustments in this paper have inherent biases which may affect trends in elderly women. A more sophisticated model with different temporal patterns for different age groups would be useful but is limited by the lack of data and the rapidly changing hysterectomy rates in the early 1970s, making it hard to develop a believable model. A large sample survey of Canadian hysterectomy prevalence rates by age group would be useful, but would not help for the most uncertain period (the earliest)

The present method of hysterectomy adjustment in Canada is an imprecise tool, and not much faith can be put in the exact adjusted rates for older women or for the early years for which the method is used (close to 1969). However the pattern of increasing incidence in the elderly seems clear since it is insensitive to the model being used.

### *A cohort effect, still?*

Both uncorrected and corrected age specific incidence rates are compatible with a birth cohort effect for age groups 55 and over, with the effect not yet having worked its way through to age groups 70 and older. With data adjusted for hysterectomy prevalence, there still appears to be an excess risk for two birth cohorts for the most recent period (1989). For women 55 and younger, the data are more compatible with

a period effect in the mid 1970s. The most plausible explanation is that this is related to unopposed estrogen use: the affected birth cohorts (1910-14, 1915-19, and 1920-24) were 51-65 years of age at the time of the peak in estrogen sales in Canada.<sup>86</sup> This is consistent with the evidence mentioned above (page 22) that excess risk may persist for 15 years or more after estrogen use. Other factors which may present as a cohort effect are the use of oral contraceptives, and the prevalence of cigarette smoking; both of these are protective, and both will affect younger birth cohorts than those discussed in this paper.

Terminology in describing age, period and cohort effects is not as simple as it might at first seem. A cohort effect is defined in Last's Dictionary of Epidemiology as variation in health status that arises from different causal factors to which each birth cohort in the population is exposed as the environment and society change.<sup>87</sup> On the other hand Kleinbaum, Kupper & Morganstern state that a cohort effect is present when disease rate varies by year of birth, regardless of age.<sup>83</sup>

According to the data presented in this study the 1910-24 birth cohorts are at excess risk for incidence of cancer of the corpus uteri from the age of 55 onwards, but not before. Although this does not meet the stricter of the two definitions above, the term 'cohort effect' conveys the idea of a risk which persists over time for a population defined by its age at a particular period. For these data this involves being in the age group 51-65 in 1974, rather than being born in a particular year. If the 'exposure' does

not occur until after menopause, there will be no excess risk before about age 50. An analysis by 'menopause cohort' rather than by birth cohort might fit the stricter definition more closely.

A combination of age and period effects can also explain the findings, but does not convey the idea of an ongoing increased risk. These descriptions are all simplifications: they take for granted the age effect which is a consistent finding in studies of cancer of the corpus uteri (peak incidence in elderly women), for example.

### ***Is there increased diagnosis in the elderly?***

There is some weak evidence both from the chart review and national database material that increased diagnosis is playing some role in the trends.

While over 90% of cases at the ORCC presented with vaginal bleeding, there was a trend of greater proportions of stage I disease in the most recent periods, but no decrease in duration of symptoms that might accompany earlier diagnosis. Other explanations for this finding are also possible: a change in aggressivity of tumours over time, or a change in referral patterns (the latter will be discussed in the section which follows). Although D&Cs are still the most important method of diagnosis, endometrial biopsy is a new technique used in the most recent period.

Some role for improved diagnosis in elderly women is suggested by lower percentages

of diagnosis by 'death certificate only' in women 75-84 and decreasing mortality/incidence ratios in women 70 and over. In a situation where disease patterns and cancer registration are stable, MIRs provide an estimate of case fatality. The interpretation of changing ratios, however, is not clearcut. A decrease in MIRs can be due to a number of factors including more complete reporting of incident cases to the registry, better diagnosis, better treatment (less mortality), or a change in the biology of disease (estrogen associated tumours are less biologically aggressive, for example).

Trends in age specific rates of D&Cs in Canada (Figure 19) do not support increased diagnostic intensity in the elderly, but there are important limitations to the data. The rate for women 65+ years decreased slightly from 1969 to 1989. These figures are not age standardised, and the 65+ population in 1989 would have had an older mean age than in 1969. In effect, then, it is possible that a standardised rate for women 65 and over would have increased slightly.

Unfortunately availability of diagnostic techniques (D&Cs and endometrial biopsies) was not well assessed by hospital separation data, as they are often done as outpatients, or in physicians' offices. A more complete assessment of the intensity of the relevant diagnostic procedures would need some other source of information, such as physician billing data.

### *Limitations of using cancer clinic data*

The regional cancer clinic had the advantage of being a centralised source of data for the region. Incident cases were easy to select from the total caseload for the three periods of interest, and the relevant information for clinical staging was consistently present. Within each period the data in the charts was collected in a fairly consistent manner.

The primary purpose of the cancer clinic charts is to serve as an information base for and record of treatment decisions. Patients are referred to the clinic by their primary treating physicians (usually gynecologists, sometimes family physicians). There are limitations to the data related to both these factors.

Information relevant to treatment decisions is clearly recorded, as are the details of the therapy decided upon. Detailed risk factor information is not as relevant to treatment decisions, and thus is not as well recorded. There is a particular problem in studying temporal trends, since the type and quality of information varied from period to period. This depended both on who was responsible for recording information, and the state of medical knowledge (estrogens were not known to be associated with endometrial cancer in 1969-72, for example).

Changes in referral patterns over time may affect disease patterns seen at a regional cancer clinic: if there is a tendency in more recent years to refer elderly women with

early stage disease who would not have been referred in an earlier period this will lead to an apparent shift to earlier stage disease in the most recent period. This is one possible explanation for the data in the present study. On the other hand early stage disease in 1969-72 was often treated with radiation, and now is not, which would have created a bias in the other direction.

### ***Conclusions***

Incidence of cancer of the corpus uteri, adjusted for hysterectomy prevalence, is increasing in women over 70 years of age in Canada. This finding is present using a variety of models for temporal patterns in hysterectomy rates for the period prior to 1969. Birth cohorts from 1910 to 1924 are at increased risk from age 55 onwards; this may represent residual increased risk from unopposed estrogen use in the 1970s in postmenopausal women. There is also some (weak) evidence to suggest improved diagnosis of this cancer in elderly women in recent periods: there is a shift to earlier stage disease in more recent periods at the Ottawa Regional Cancer Centre, as well as decreasing mortality/incidence ratios and decreasing proportions of cases diagnosed by 'death certificate only' in national administrative data. Alternative explanations for these findings are also possible. Absolute numbers of cases in women  $\geq 70$  years are increasing as the population ages.

### ***Recommendations***

The impact of this disease in older women on the health care system is hidden in

overall standardised rates. Older age groups need to be targeted specifically in monitoring trends, either by following age specific rates, or by presenting standardised data in appropriate age ranges (70-84 in the present study). For Canada's fastest growing age group it is important to follow trends in crude numbers as well.

Clinical researchers need to focus on the elderly as well: age as an exclusion criterion may make the research less relevant to the age group which needs it most.

To validate the method involved in the hysterectomy adjustment and choose the most appropriate model a large sample survey of hysterectomy prevalence by age needs to be done, with specific oversampling of the elderly population. The absence of data on early hysterectomy rates could be partly remedied by counting hysterectomies done in a hospital (or hospitals) with a known catchment area.

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## Appendices

### *Appendix A: ICD Revisions and Cancer of the Corpus Uteri*

The chief difficulty with ICD revisions is to distinguish clearly between cancer of the body of the uterus, cancer of the cervix (with markedly different epidemiology) and cancer of the uterus, site unspecified. Within the time frame of the Canadian incidence data in this paper (1969-90), uterus, site unspecified, is uncommon compared with cancer of the body of the uterus.<sup>88</sup> In the data used for this study trends of the pooled diagnostic grouping of cancer of the corpus uteri and uterus, site unspecified (ICD9 179 + 182) showed no appreciable difference from those of ICD9 182 alone, although uterus site unspecified formed a greater proportion in the oldest age groups (see Figure 23).

King & Wigle in 1982 studied death certificate misclassification in Alberta women who died of uterine cancer between 1969 and 1978. By examining Alberta Cancer Registry records they were able to reclassify all but 16 of 136 cases of uterus unspecified; of these 96 (71%) were reclassified as cancer of the corpus uteri.<sup>89</sup>

The ratio of cancer of the uterus, site unspecified, to cancer of the body of the uterus is considerably higher in some countries than in others. This may reflect differing

degrees of sophistication of pathology services, reporting systems, or perhaps disease epidemiology. It makes international comparisons more problematic.<sup>90</sup>

**ICD9:**

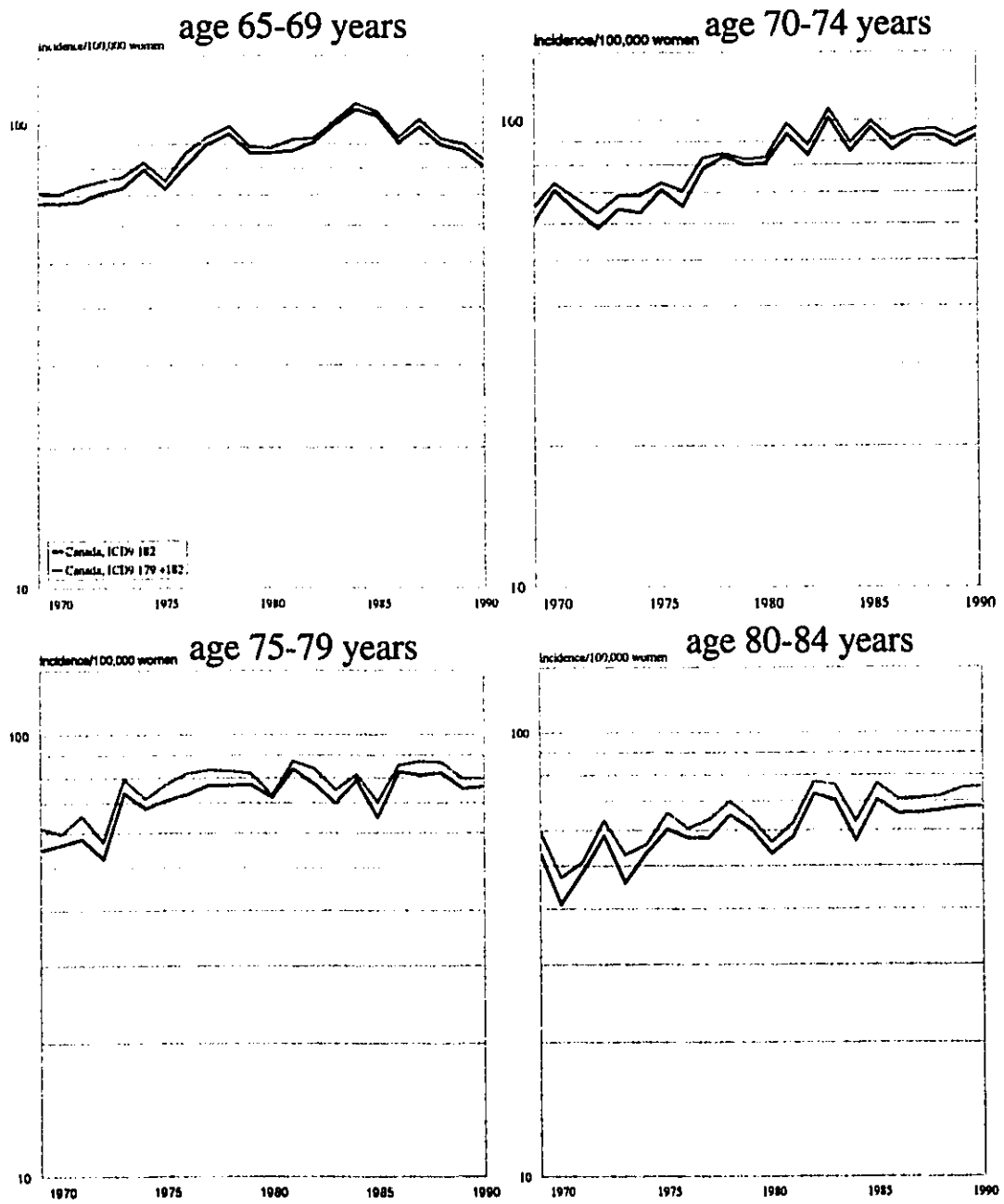
This is the currently used version, soon to be superseded by ICD10, which has already been published. ICD9 was based on recommendations of a conference in 1975, published in 1977, and was used by Statistics Canada starting in 1979. It separates cancer of the corpus uteri (ICD9 182) from cancer of the cervix (ICD9 180) and uterus, part unspecified (ICD9 179) at the three digit coding level. This paper, unless otherwise stated, uses ICD9 182, with older coding converted to ninth revision codes.

**ICD8:**

The distinction between cancer of the corpus uteri (ICD8 182.0) and those with site unspecified (ICD8 180.9) was made at the four digit level. Cancer of the cervix was assigned ICD8 180. The ICD8 was used in Statistics Canada data starting in 1969 up to and including 1978. Information at the four digit level is needed to ensure comparability with ICDs 7 and 9.

**ICD7:**

Distinguished at three digit level between cancer of the corpus uteri (ICD7 172), cervical cancer (ICD7 171) and those with site unspecified (ICD7 174). Used for Canadian data from 1958-1968.<sup>91</sup>



**Figure 23:** Incidence of ICD9 182 alone vs combined ICD9 179 (cancer of the uterus, not otherwise specified) & 182.

***Appendix B: National Cancer Incidence Reporting System & ICD-O  
Morphology Coding***

The National Cancer Incidence Reporting System began operating in 1969, and up to 1978 collected information on incident cancers classified according to ICD code. The NCIRS was established at Statistics Canada with the help of the National Cancer Institute of Canada. The original 9 participating provincial cancer registries were joined in 1981 by the Ontario registry which has now back reported all cases to 1969. The Northwest Territories similarly back reported cases up to 1969 after a cancer registry was established there.<sup>93</sup>

The NCIRS is a population-based tumour registry currently covering 100% of the country's population. New primary sites of cancer are reported to the cancer registry belonging to the province or territory in which the patient resides.

Starting in 1979 morphology (histologic type) was reported by most provinces, classified according to the International Classification of Diseases of Oncology (ICDO). In 1981 Quebec began reporting ICDO morphology, and since 1982 (when Manitoba did as well) all provinces have consistently reported it.<sup>93</sup>

There are differences between provinces both with regard to sources of data used, and

coding practices used: use or non-use of death certificates or cytology reports as sources of cases, whether or not "other skin cancers" (ICD9 173) are reported, for example. Quebec is an outlier in using only hospital data as a source. These differences are well described in recent publications.<sup>92,94</sup> However, uniformity has increased over time, and measures of quality have become more similar as well as improving. The percentage of cancers microscopically confirmed has increased from 82 to 85% over the four five-year periods since the start of the NCIRS, while the percent diagnosed on death certificate only has dropped from 4 to 2%; mortality/incidence ratios have decreased from 60 to 51%, with less variability between registries.<sup>94</sup>

Estimated coverage is over 95% at the national level.<sup>92</sup>

*Appendix C: Year by year proportions in hysterectomy models*

<b>Table 1: Hysterectomy rates as a proportion of 1970 rates, 1930-1970</b>				
<b>year</b>	<b>low linear model</b>	<b>second degree polynomial model</b>	<b>high linear model</b>	<b>high model</b>
1930	.000	.000	.000	.000
1931	.000	.007	.025	.030
1932	.000	.016	.050	.060
1933	.000	.025	.075	.090
1934	.000	.035	.100	.120
1935	.000	.046	.125	.150
1936	.000	.058	.150	.180
1937	.000	.071	.175	.210
1938	.000	.085	.200	.240
1939	.000	.099	.225	.270
1940	.000	.115	.250	.300
1941	.000	.131	.275	.330
1942	.000	.149	.300	.360
1943	.000	.167	.325	.390
1944	.000	.186	.350	.420
1945	.000	.206	.375	.450
1946	.000	.227	.400	.480
1947	.000	.249	.425	.510
1948	.000	.272	.450	.540
1949	.000	.295	.475	.570
1950	.000	.320	.500	.600

<b>year</b>	<b>low linear model</b>	<b>polynomial model</b>	<b>high linear model</b>	<b>high model</b>
1950	.000	.320	.500	.600
1951	.050	.345	.525	.620
1952	.100	.371	.550	.640
1953	.150	.399	.575	.660
1954	.200	.427	.600	.680
1955	.250	.456	.625	.700
1956	.300	.486	.650	.720
1957	.350	.517	.675	.740
1958	.400	.548	.700	.760
1959	.450	.581	.725	.780
1960	.500	.615	.750	.800
1961	.550	.649	.775	.820
1962	.600	.685	.800	.840
1963	.650	.721	.825	.860
1964	.700	.758	.850	.880
1965	.750	.796	.875	.900
1966	.800	.835	.900	.920
1967	.850	.875	.925	.940
1968	.900	.916	.950	.960
1969	.950	.957	.975	.980
1970	1.00	1.00	1.00	1.00

### *Appendix D: Surgical procedures coding*

In the hospital separations data used for this study, ICD8 procedure codes were used from 1969 to 1978, inclusive and codes from the Canadian Classification of Diagnostic, Therapeutic, and Surgical Procedures (CCP) from 1979 to 1990.<sup>95,96</sup>

Only one coding space was available for surgical procedures from 1969 to 1980, whereas from 1981 to 1990 there were three. Although additional information was present in the second and third coding spaces the hysterectomy models and data on trends in hysterectomy rates were restricted to the first surgical code which was available throughout the study period. For the nine years for which three surgical coding spaces were available, the extra two contributed between 2.2 and 5.6% of the total.

Unfortunately there is an age related trend: in age groups between 20 and 49 years the extra two codes contribute about 3% of the total; thereafter the proportion increases monotonically, reaching 8.8% in the 80-84 year age group and 11.1% in the 85-89 year age group. This method will underestimate hysterectomy rates to a greater degree with increasing age above 50 years. Repeating the analysis and comparing the first four years and the last years merely confirmed these results and did not show any temporal trend.

*Hysterectomy codes*

The following codes were used construct hysterectomy rates:

**Table I: Hysterectomy codes**

<b>Procedure</b>	<b>ICD8A code</b>	<b>CCP code</b>
Subtotal hysterectomy	69.1	80.2
Total abdominal	69.2	80.3
Radical abd. hysterectomy	69.3	80.5
Vaginal hysterectomy	69.4	80.4
Radical vag. hysterectomy	69.5	80.6
Pelvic evisceration	69.7	80.7

To generate the hysterectomy rates where only complete hysterectomies were counted, the category of subtotal hysterectomies was not included.

Under the code 80.2 in CCP (subtotal abdominal hysterectomy) the following types of operation are listed:

- Bell-Beuttner operation
- Bisection
- Supracervical
- Supravaginal
- Uterine fundectomy

These are aggregated in the one code number. The supracervical and supravaginal hysterectomies are much more common than the other categories<sup>97</sup>, and basically leave the patient with a cervical stump.

***Appendix E: International Federation of Gynecology and Obstetrics***

***(FIGO) Staging Issues***

The FIGO staging system for cancer of the corpus uteri has developed from simple clinical staging to a complex surgicopathological classification over forty years.

The earliest FIGO staging (1951-1961) was defined by clinical examination and the results of a diagnostic dilatation and curettage (D&C) with endocervical curettage.<sup>98</sup>

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**Table I: Early staging 1951-61**

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Stage 0	Pathologist considers it likely carcinomatous, but no definitive microscopic diagnosis
Stage I	Confined to the corpus
Stage II	Spread outside the corpus

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In 1961 this was revised to include a separate stages for cervical involvement and spread within the pelvis only:

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**Table II: Staging 1962-71**

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Stage 0	histology suspicious but not proven
Stage I	confined to the corpus
Stage II	involving the corpus and the cervix
Stage III	spread outside the uterus but not outside the true pelvis
Stage IV	outside the true pelvis, or involving the mucosa of bladder or bowel

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The next revision in 1971 took into account the size of the uterus and subdivided

Stage 1 tumours by histologic grade:

**Table III: Staging 1971-1988**

Stage 0	carcinoma-in-situ
Stage I	confined to the corpus G1 highly differentiated adenocarcinoma G2 differentiated adenocarcinoma, partly solid G3 undifferentiated adenocarcinoma or mostly solid
Stage Ia	length of uterine cavity $\leq 8$ cm
Stage Ib	length of uterine cavity $> 8$ cm
Stage II	involving corpus and cervix
Stage III	spread outside the uterus but not outside true pelvis
Stage IV	spread outside the pelvis

Again in 1988 a new FIGO surgicopathologic staging system was put in place to reflect a need for more precise classification for prognosis and treatment decisions:

**Table IV: 1988 staging**

Stage I	Confined to the corpus Ia. limited to endometrium Ib. invasion $< \frac{1}{2}$ of endometrium Ic. invasion $> \frac{1}{2}$ of endometrium
Stage II	Involvement of the cervix IIa. glandular involvement only IIb. cervical stromal involvement
Stage III	Spread outside the uterus, confined to pelvis IIIa. involvement of uterine serosa, adnexae, positive peritoneal cytology IIIb. spread to vagina IIIc. spread to retroperitoneal nodes
Stage IV	Spread to bladder, rectum, distant sites IVa. bladder or rectal mucosa IVb. distant sites, intrabdominal spread or inguinal nodes

Within each stage the tumours are classified as G1, G2, or G3 on the basis of histologic criteria.

It was necessary for the chart review in this study to use the 1962-1971 staging system because data for the more precise staging schemes were usually not present in charts from earlier periods.

Misclassification in clinical staging systems has been shown to be a problem. A study in Italy reported by de Palo found that of 1055 stage I cases (1971 criteria) who underwent surgicopathological staging similar to the 1988 classification, 92 (8.7%) were reclassified to stage II, 72 (6.8%) to stage III and 5 (0.5%) to stage IV.<sup>99</sup> A similar study by Gal et al. in New York found that 22% of 93 clinical stage I patients were reclassified higher with surgicopathological staging.<sup>100</sup> Cowles et al. retrospectively reclassified 62 consecutive patients of all clinical stages, and found that the stage changed in 14/46 (30.4%) of stage I patients, 5/8 (62.5%) of stage II patients, 3/5 (60%) of stage III patients and 0/3 stage IV patients.<sup>101</sup> One particular problem is the fractional D&C which is incorporated into the earlier 'clinical' staging systems: Cowles cites previous work showing that 37-70% of patients with clinical stage II are overstaged.

For the chart review in the present study information from D&Cs was not used in the staging.

A clinical staging system was the only practical option to assess whether less

advanced disease is being diagnosed in later periods. If there is no temporal trend in misclassification it should provide useful, if biased, measurements to analyse for trends

*Appendix F: Proportions of female population by age group, Canada**1971*

0-4 yrs	.08206894
5-9 yrs	.10129422
10-14 yrs	.10404715
15-19 yrs	.09742017
20-24 yrs	.09048949
25-29 yrs	.07364001
30-34 yrs	.06007505
35-39 yrs	.05710435
40-44 yrs	.05747656
45-49 yrs	.05745632
50-54 yrs	.04923729
55-59 yrs	.04439649
60-64 yrs	.03647826
65-69 yrs	.02989306
70-74 yrs	.02320998
75-79 yrs	.01711122
80-84 yrs	.01093026
85+yrs	.00766918

**Appendix G: Proportions of women with intact uteri calculated using various models**

- These all include subtotal hysterectomies in the adjustment.
- Five year age groups.

**Proportion of women with intact uteri, using low linear model**

age group	1969	1970	1971	1972	1973	1974	1975	1976	1977	1978	1979
20-24 yrs	0.9990061	0.9989056	0.9986899	0.9984802	0.9983224	0.9981772	0.998106	0.998066	0.9979423	0.9978571	0.9978545
25-29 yrs	0.9910054	0.9902357	0.9891307	0.9882209	0.9873244	0.9864326	0.9855229	0.9850371	0.9847169	0.9849187	0.9852846
30-34 yrs	0.9619471	0.9594141	0.9557026	0.952368	0.9502529	0.9488088	0.9481469	0.948468	0.9486781	0.9483352	0.9481388
35-39 yrs	0.9102002	0.903897	0.8954035	0.8884419	0.8836031	0.8801629	0.8783998	0.8792535	0.8785835	0.8796614	0.8810563
40-44 yrs	0.8530631	0.8419775	0.8293173	0.8175849	0.8072717	0.7991889	0.7943937	0.7929433	0.7916892	0.7909288	0.7925085
45-49 yrs	0.8222923	0.8066309	0.7903131	0.7744146	0.7597381	0.7457261	0.7341547	0.7255796	0.7192897	0.7141975	0.7113357
50-54 yrs	0.8342586	0.8167899	0.7979492	0.7795528	0.7623351	0.7459853	0.7303602	0.7169357	0.7038964	0.6923998	0.6829259
55-59 yrs	0.8817752	0.8661935	0.8501776	0.832696	0.8143838	0.7958296	0.7759183	0.756764	0.7396196	0.7245841	0.7110195
60-64 yrs	0.9243946	0.912709	0.9001033	0.8865396	0.8721202	0.8565846	0.8406211	0.8242749	0.8063745	0.7887706	0.7712466
65-69 yrs	0.9489436	0.9412239	0.9326933	0.9234048	0.913755	0.9029743	0.8912488	0.8783652	0.8647744	0.8503263	0.8353302
70-74 yrs	0.9608821	0.9560297	0.950165	0.9446886	0.9382661	0.9310759	0.9233653	0.9149657	0.9058014	0.8959773	0.8853751
75-79 yrs	0.9689484	0.9651998	0.9607891	0.956411	0.9518429	0.9474176	0.9424297	0.9366105	0.9309736	0.9245626	0.9177724
80-84 yrs	0.9774942	0.974365	0.971166	0.9676037	0.9641119	0.9604375	0.9563246	0.9520718	0.9474243	0.9429362	0.9385019
85-89 yrs	0.9849845	0.9829286	0.9804834	0.9780989	0.9752759	0.9723302	0.9695069	0.9663344	0.9627141	0.959004	0.9546993
1980	1981	1982	1983	1984	1985	1986	1987	1988	1989	1990	
0.9978452	0.9979141	0.9979615	0.9980802	0.9982177	0.9983021	0.9984362	0.9985806	0.9986221	0.998734	0.998859	
0.9856768	0.9857631	0.9858214	0.9859606	0.9864142	0.986996	0.9877	0.9883832	0.9889286	0.9903019	0.9910536	
0.9481819	0.9484648	0.9493022	0.95097	0.9526576	0.9540333	0.9551569	0.9565824	0.9583451	0.9609681	0.9636098	
0.8825175	0.8839604	0.8860144	0.8875498	0.8885659	0.8898284	0.8926058	0.895999	0.9004215	0.9054177	0.9098681	
0.7941333	0.7957815	0.7967553	0.8000391	0.8025646	0.8056833	0.8081923	0.8124321	0.816451	0.8208821	0.8253822	
0.7108915	0.7111394	0.7123916	0.7122626	0.7146298	0.7160503	0.718723	0.7208252	0.7255622	0.7308901	0.7361449	
0.6733874	0.6684702	0.6636083	0.660908	0.6589497	0.6582893	0.6590177	0.660338	0.6604463	0.6630616	0.6656185	
0.6983488	0.6870968	0.6760662	0.6662853	0.6572235	0.6499451	0.6432854	0.6386991	0.6361297	0.6340266	0.6333192	
0.7523717	0.7340796	0.7182812	0.7043712	0.6913452	0.679221	0.6683563	0.657075	0.6475296	0.6388295	0.6314068	
0.8198163	0.8015249	0.7863252	0.7688223	0.7510042	0.7319046	0.713784	0.6982968	0.6843509	0.6712342	0.6591536	
0.8735123	0.8608584	0.8472563	0.8322953	0.8170839	0.8011958	0.7845235	0.7667315	0.7489412	0.7311636	0.7112847	
0.9092355	0.9007666	0.89145	0.8813961	0.8703644	0.8578914	0.8449467	0.8310879	0.8157078	0.7997223	0.783648	
0.9335337	0.9274572	0.9214912	0.9146004	0.906677	0.8987778	0.8898963	0.8805428	0.8700557	0.8584356	0.8454843	
0.9503951	0.9464334	0.9417032	0.9367275	0.9323844	0.9271008	0.9210267	0.9148506	0.9075797	0.8998036	0.8915122	



*Proportion of women with intact uteri, high linear model*

age group	1969	1970	1971	1972	1973	1974	1975	1976	1977	1978	1979
20-24 yrs	0.9989423	0.9988676	0.9986657	0.9984658	0.9983142	0.9981728	0.9981039	0.9980652	0.9979421	0.9978571	0.9978545
25-29 yrs	0.9902804	0.98977	0.9888389	0.9880325	0.9872193	0.9863695	0.9854847	0.9850132	0.9847025	0.9849104	0.9852802
30-34 yrs	0.9574204	0.9561037	0.9533587	0.9507439	0.9491605	0.9480905	0.9476829	0.948177	0.9485012	0.9482304	0.9480762
35-39 yrs	0.894384	0.891181	0.8852928	0.8805512	0.8775848	0.8756553	0.8751029	0.8769137	0.8769619	0.8785681	0.8803359
40-44 yrs	0.8141863	0.8087406	0.8012766	0.7941463	0.7879466	0.783374	0.7816593	0.7828415	0.783803	0.784919	0.7880083
45-49 yrs	0.7493281	0.741168	0.7318406	0.7229165	0.7147932	0.7068725	0.7009873	0.6975828	0.6958827	0.6948774	0.6956958
50-54 yrs	0.7216748	0.711889	0.7013675	0.6910907	0.6816397	0.6728166	0.6646559	0.6584484	0.6523807	0.6476495	0.6440732
55-59 yrs	0.7391134	0.7282062	0.71755	0.706065	0.6943826	0.6831547	0.6713057	0.6602772	0.6512537	0.6439224	0.6378149
60-64 yrs	0.7713749	0.7598928	0.7484266	0.7369772	0.7255809	0.7139412	0.7026395	0.6916468	0.6798038	0.6687823	0.6585441
65-69 yrs	0.808027	0.7962633	0.7843948	0.772686	0.7614393	0.7499493	0.7384334	0.7267356	0.7152486	0.7038113	0.6927305
70-74 yrs	0.8482587	0.8370388	0.8249492	0.8136925	0.8019688	0.7900698	0.778314	0.7666143	0.7550336	0.7436298	0.7323418
75-79 yrs	0.8870856	0.8774869	0.8668921	0.8562149	0.8452695	0.8344333	0.8230725	0.8110126	0.7997077	0.7880683	0.7758899
80-84 yrs	0.9204615	0.9128991	0.9052091	0.8966224	0.887712	0.8783066	0.8682645	0.8577972	0.8468174	0.835944	0.8251583
85+ yrs	0.9447417	0.9398146	0.9342872	0.9285389	0.92196	0.9148984	0.9077006	0.8997717	0.8911904	0.8820237	0.8719367
	1980	1981	1982	1983	1984	1985	1986	1987	1988	1989	1990
	0.9978452	0.9979141	0.9979615	0.9980802	0.9982177	0.99831021	0.9984362	0.9985806	0.9986221	0.998734	0.998859
	0.9856746	0.9857623	0.9858212	0.9859606	0.9864142	0.986996	0.9877	0.9883832	0.9892856	0.9903019	0.9910536
	0.9481439	0.9484409	0.9492878	0.9509618	0.9526533	0.9540311	0.9551561	0.9565822	0.9583451	0.9609681	0.9636098
	0.8820508	0.8836693	0.8858383	0.8874454	0.8889303	0.8897903	0.8925819	0.8959847	0.9004133	0.9054134	0.909866
	0.7908429	0.7934459	0.7951324	0.7989449	0.8018443	0.8032174	0.8079012	0.8122558	0.8163466	0.8208196	0.8255443
	0.6981405	0.701054	0.7045322	0.7062638	0.7101269	0.7127557	0.7163879	0.7192072	0.7244709	0.7301709	0.7356793
	0.6422418	0.6405051	0.6402112	0.6415711	0.6430883	0.6455251	0.6489204	0.6524709	0.654442	0.65856	0.6623276
	0.6326488	0.6286908	0.6246165	0.6213746	0.618409	0.616822	0.6133298	0.6153144	0.6168066	0.6181848	0.6207636
	0.6477748	0.6376728	0.6299429	0.6236755	0.6181142	0.6135268	0.609999	0.6056907	0.6026697	0.6000397	0.5982963
	0.6819557	0.6710525	0.6598108	0.6489028	0.6383997	0.627448	0.617481	0.6100288	0.6037337	0.5980948	0.5935518
	0.7207154	0.7092474	0.6977483	0.685853	0.6745893	0.6634507	0.6521567	0.6403568	0.629181	0.6187403	0.6070167
	0.7640267	0.7522886	0.740605	0.7290097	0.7173198	0.7051161	0.6933913	0.6816702	0.6693806	0.6573663	0.6460634
	0.8138351	0.8016106	0.7899324	0.7777853	0.7652196	0.7533367	0.7412688	0.7295925	0.7176013	0.7053753	0.6927437
	0.8616354	0.8515177	0.8404987	0.8291815	0.8185252	0.8068738	0.7945962	0.7827357	0.7702955	0.7579807	0.7458016

*Proportion of women with intact uteri, using high model*

age group	1969	1970	1971	1972	1973	1974	1975	1976	1977	1978	1979
20-24 yrs	0.9989296	0.9988601	0.9986609	0.9984629	0.9983126	0.998172	0.9981035	0.998065	0.9979421	0.9978571	0.9978545
25-29 yrs	0.9901354	0.9896768	0.9887805	0.9879972	0.9871985	0.9863569	0.9854771	0.9850084	0.9846996	0.9844088	0.9852794
30-34 yrs	0.9565151	0.9544416	0.95289	0.9504191	0.9489421	0.9479469	0.9475901	0.9481188	0.9484659	0.9482095	0.9480637
35-39 yrs	0.8912207	0.8886378	0.8832706	0.8789731	0.8763811	0.8747538	0.8744436	0.8764457	0.8766376	0.8783494	0.8801918
40-44 yrs	0.8064109	0.8020933	0.7956685	0.7894586	0.7840815	0.780211	0.7791124	0.7808211	0.7822257	0.783717	0.7871082
45-49 yrs	0.7347352	0.7280754	0.7201461	0.7126169	0.7058043	0.6991017	0.6943539	0.6919834	0.6912013	0.6910134	0.6925278
50-54 yrs	0.699158	0.6909088	0.6820512	0.6733983	0.6655007	0.6581829	0.651515	0.6467509	0.6420776	0.6386595	0.6363027
55-59 yrs	0.710581	0.7006087	0.6910245	0.6807388	0.6703823	0.6606197	0.6503832	0.6409798	0.6335805	0.62779	0.623174
60-64 yrs	0.7407709	0.7293296	0.7180912	0.7070647	0.6962731	0.6854126	0.6750432	0.6651212	0.6544896	0.6447846	0.6360036
65-69 yrs	0.7798437	0.7672712	0.754735	0.7425422	0.7309762	0.7193443	0.7078703	0.6964096	0.6853435	0.6745083	0.6642106
70-74 yrs	0.825734	0.8132406	0.799906	0.7874933	0.7747094	0.7618686	0.7493037	0.736944	0.72488	0.7131603	0.7017352
75-79 yrs	0.8707131	0.8599443	0.8481127	0.8361756	0.8239548	0.8118364	0.7992011	0.785893	0.7734545	0.7607694	0.7476534
80-84 yrs	0.9090549	0.9006039	0.8920178	0.8824261	0.872432	0.8618804	0.8506325	0.8389423	0.826696	0.8145455	0.8024895
85-89 yrs	0.9366932	0.9311918	0.925048	0.9186269	0.9112968	0.903412	0.8953393	0.8861592	0.8768856	0.8666276	0.8553842
	1980	1981	1982	1983	1984	1985	1986	1987	1988	1989	1990
	0.9978452	0.9979141	0.9979615	0.9980802	0.9982177	0.9983021	0.9984362	0.9985806	0.9986221	0.998734	0.998859
	0.9856742	0.9857622	0.9858212	0.9859606	0.9861142	0.986996	0.9877	0.9883832	0.9882856	0.9903014	0.9910536
	0.9481363	0.9484361	0.949285	0.9509602	0.9526525	0.9540307	0.955156	0.9565821	0.9583451	0.9609681	0.9636098
	0.8819575	0.8836111	0.8858031	0.8874246	0.8884908	0.8897827	0.8925771	0.8959818	0.9004117	0.9054126	0.9098655
	0.7901848	0.7929788	0.7948079	0.798726	0.8017002	0.8051242	0.807843	0.8122205	0.8163257	0.8208071	0.8255367
	0.6955903	0.6990369	0.7029603	0.705064	0.7092263	0.7120968	0.7159208	0.7188835	0.7242527	0.730027	0.7355862
	0.6356126	0.6349121	0.6355318	0.6377037	0.6399161	0.6429722	0.6469009	0.6508975	0.6552412	0.6576596	0.6616694
	0.6195088	0.6170096	0.6143266	0.6123924	0.6106462	0.6101974	0.6097386	0.6106375	0.612942	0.6150164	0.6182124
	0.6268554	0.6183914	0.6122752	0.6075363	0.603468	0.600388	0.5983276	0.5954139	0.593698	0.5922818	0.5916742
	0.6543836	0.6445581	0.6345079	0.6249189	0.6158788	0.6065567	0.5982204	0.5923753	0.5876103	0.5834669	0.5804315
	0.690156	0.6789252	0.6678467	0.6565646	0.6460904	0.6359017	0.6256833	0.6150819	0.605229	0.5962557	0.5881631
	0.7349849	0.722593	0.710436	0.6985324	0.6867109	0.674561	0.6630803	0.6517867	0.6401151	0.6288951	0.6185465
	0.7899194	0.7764413	0.7636206	0.7504222	0.736921	0.7242849	0.7115433	0.6994025	0.6871104	0.6747632	0.6621956
	0.8438835	0.8325246	0.8202578	0.8076722	0.7957534	0.7828283	0.7693101	0.7563127	0.7428386	0.7296157	0.7166994

*Proportions of women with intact uteri, mixed model*

•age <=59 polynomial model

•age 60-74 flat model

•age 75-89 high linear model

age group	1969	1970	1971	1972	1973	1974	1975	1976	1977	1978	1979
20-24 yrs	0.998983	0.998892	0.998681	0.998475	0.99832	0.998176	0.998105	0.998066	0.997942	0.997857	0.997855
25-29 yrs	0.99074	0.990067	0.989023	0.988146	0.987287	0.98641	0.985509	0.985029	0.984712	0.984916	0.985283
30-34 yrs	0.960191	0.958148	0.954818	0.951762	0.94985	0.948546	0.947978	0.948363	0.948615	0.948298	0.948116
35-39 yrs	0.903548	0.898637	0.891289	0.885283	0.881232	0.878414	0.877139	0.878371	0.877979	0.879258	0.880793
40-44 yrs	0.835241	0.827004	0.816906	0.807388	0.799007	0.792537	0.789126	0.788833	0.788532	0.788561	0.790763
45-49 yrs	0.786044	0.774587	0.762119	0.74999	0.738779	0.727916	0.719215	0.713189	0.709108	0.705936	0.704872
50-54 yrs	0.774821	0.761972	0.748066	0.734419	0.721686	0.709621	0.698182	0.688733	0.679462	0.671638	0.665116
55-59 yrs	0.803694	0.79105	0.778394	0.764647	0.750426	0.736336	0.721271	0.706936	0.694542	0.683954	0.674635
60-64 yrs	0.838988	0.827831	0.816188	0.804084	0.791611	0.778514	0.765481	0.752491	0.738363	0.724821	0.711737
65-69 yrs	0.866641	0.857589	0.848033	0.838112	0.828203	0.817572	0.806376	0.794484	0.782343	0.769832	0.757288
70-74 yrs	0.887986	0.881148	0.873226	0.865781	0.857536	0.848743	0.839702	0.83029	0.820498	0.810423	0.799982
75-79 yrs	0.903443	0.898595	0.892864	0.886967	0.880698	0.874413	0.867429	0.859542	0.851972	0.843764	0.83468
80-84 yrs	0.916114	0.912149	0.90822	0.903887	0.899542	0.894886	0.889651	0.884062	0.877877	0.871676	0.865389
85-89 yrs	0.929029	0.92561	0.921973	0.918521	0.914712	0.910869	0.90723	0.903295	0.898918	0.894345	0.889038
	1980	1981	1982	1983	1984	1985	1986	1987	1988	1989	1990
	0.997845	0.997914	0.997962	0.99808	0.998218	0.998302	0.998436	0.998581	0.998622	0.998734	0.998859
	0.985676	0.983763	0.983821	0.983961	0.986414	0.986996	0.9877	0.988383	0.989286	0.990302	0.991054
	0.948168	0.948456	0.949297	0.950967	0.952656	0.954033	0.955157	0.956582	0.958345	0.960968	0.96361
	0.882348	0.883855	0.885951	0.887512	0.888543	0.889815	0.892597	0.895994	0.900419	0.905416	0.9099867
	0.792875	0.7949	0.79615	0.799635	0.802301	0.805514	0.808087	0.812369	0.816413	0.82086	0.825569
	0.705616	0.707036	0.709246	0.7099	0.712883	0.714791	0.717842	0.720222	0.725159	0.730627	0.735976
	0.660438	0.656095	0.653431	0.652639	0.652277	0.653008	0.654909	0.657189	0.658081	0.661315	0.66436
	0.666173	0.658939	0.651668	0.645344	0.639433	0.635028	0.630915	0.628528	0.627867	0.627363	0.628241
	0.697734	0.684299	0.67322	0.663722	0.654946	0.647048	0.640225	0.632711	0.626615	0.621052	0.616496
	0.744753	0.731838	0.718349	0.704915	0.691553	0.677351	0.664064	0.653277	0.643747	0.634887	0.627032
	0.788659	0.776992	0.764836	0.751846	0.739108	0.726205	0.712903	0.698842	0.685132	0.671823	0.656843
	0.825522	0.816054	0.806128	0.795839	0.784981	0.773063	0.761121	0.748726	0.73533	0.721833	0.708758
	0.858429	0.850304	0.842388	0.83369	0.824192	0.814999	0.80514	0.795195	0.784493	0.77307	0.760697
	0.883583	0.878281	0.872008	0.865313	0.859115	0.851818	0.843675	0.835554	0.826506	0.817196	0.807637

**Appendix H: Hysterectomy rates/100,000 women by 5 year age group**

•includes subtotal hysterectomies

age group	1969	1970	1971	1972	1973	1974	1975	1976	1977	1978	1979
15-19 yrs	3.53	4.63	7.89	7.32	8.92	10.45	11.97	11.83	13.67	6.71	7.91
20-24 yrs	38.68	49.75	64.48	79.5	81	84.58	85.27	79.96	86.05	87.15	81.08
25-29 yrs	269.42	357.34	428.51	444.89	466.15	467.97	462.93	448.34	467.23	443.42	411.1
30-34 yrs	796.95	1032.71	1244.74	1253.81	1196.84	1163.09	1116.66	1008.08	1045.42	1017.17	974.39
35-39 yrs	1451.02	1812.99	2107.71	2085.42	1983.93	1874.49	1738.89	1562.55	1635.94	1565.38	1461.39
40-44 yrs	1771.9	2127.42	2419.27	2413.91	2340.46	2213.1	2048.21	1794.79	1880.78	1828.73	1695.1
45-49 yrs	1687.25	1892.9	2051.86	2052.58	2004.67	1973.89	1852.24	1652.07	1637.82	1600.18	1466.88
50-54 yrs	1023.3	1084.74	1189.94	1243.06	1200.91	1179.74	1140.44	1009.82	978.36	942.98	827.07
55-59 yrs	533.6	548.71	574.11	629.27	643.82	637.32	647.47	604.81	575.27	535.56	463.44
60-64 yrs	429.51	450.13	465.44	471.56	476.67	490.99	482.86	465.92	470.63	434.31	414.26
65-69 yrs	409.91	409.04	425.12	413.77	398.03	411.32	399.97	414.86	414.89	392.24	370.13
70-74 yrs	316.52	307	345.91	322.33	306.94	313.19	316.02	317.42	334.9	325.12	306.85
75-79 yrs	223.93	216.39	267.36	228.47	242.19	221.24	235.11	231.3	257.79	234.34	216.44
80-84 yrs	105.85	131.86	145.16	133.76	124.64	128.43	142.81	148.55	147.31	119.59	153.77
85-89 yrs	69.68	70.63	87.56	74.57	77.82	80.52	62.32	62.06	84.11	78.63	76.21
1980	5.88	5.3	6.79	4.33	5.35	4.82	4.24	3.76	2.92	1.97	2.43
80-24	74.31	70.41	64.71	64.58	58.07	54.53	52.3	50.25	41.44	35.14	228.84
395.58	397.77	399.36	384.72	363.26	345.92	317.93	308.78	271.16	235.44	228.84	562.99
928.51	919.98	920.23	855.48	826.08	798.49	757.43	729.17	674.53	594.04	562.43	972.43
1436.94	1456.94	1428.7	1370.18	1330.73	1300.32	1226.72	1203.13	1089.47	990.05	972.43	1281.73
1659.5	1707.49	1689.32	1608.75	1596.42	1562.24	1562.6	1524.36	1418.68	1306.13	1246.8	732.2
1410.27	1457.35	1441.53	1442.35	1413.43	1426.19	1425.42	1393.31	1350.11	1254.38	719.72	397.45
798.12	807.32	811.38	776.94	748.99	778.77	774.49	780.47	754.35	719.72	397.45	384.34
441.22	422.12	407.07	406.76	409.21	399.52	394.29	413.02	386.98	396.41	431.8	424.07
412.95	406.87	396.53	395.89	369.13	373.42	379.43	405.32	388.12	373.26	384.34	431.8
366.49	395.45	383.94	408.31	418.34	405.82	410.57	413.55	423.56	398.97	431.8	424.07
311.34	341.93	357.49	355.23	333.55	368.31	379.46	386.39	399.06	382.92	317.24	209.99
243.18	237.57	279.69	265.32	267.74	276.09	297.06	316.8	309.32	317.24	314.14	209.99
145.02	143.98	179.98	175.97	184.08	171.5	173.62	186.12	195.64	209.63	209.99	100.51
93.79	85.15	98.01	103.68	84.76	101.86	78.14	93.09	120.76	88.09	100.51	



17. history of oral contraceptive use: ever .....
- total years .....
- sequential .....
- comments .....
- .....

***Coding summary for endometrial cancer chart review***

Sept 20, 1993

If missing data, leave blank.

1. Study number        3 digits, eg 006, 089 131
2. Hospital                1. Civic Hospital  
2. General Hospital
3. Area                    1.Regional municipality of Ottawa-Carleton  
2.Cornwall  
3.Hull  
4.Pembroke  
5.other eastern Ontario  
6.other western Quebec  
7.other
4. Age
5. Symptoms              1.vaginal bleeding  
2.abdominal pain  
3.mass  
4.vaginal discharge  
5.no symptoms  
6.other
6. Complete months before diagnosis
7. Initial method of diagnosis                1.D&C  
2.endometrial biopsy  
3.cervical biopsy  
4.laparotomy  
5.surprise on path. from other OR  
6.other
- 8.Endometrial biopsy                            1.yes, done and negative  
2.yes, done and positive  
3.not done
9. Clinical stage
10. Parity
11. Marital status                                1.single

2.other

12. Weight in kg
13. Height in cm
14. Year of admission to cancer centre