ENDOMETRIAL CANCER AND PRE-MALIGNANT CONDITIONS IN YOUNG WOMEN:

SURVEY OF ENDOMETRIAL SAMPLING PRACTICES BY CANADIAN GYNECOLOGISTS

by

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Abstract

Objective: To identify the physician-, patient- and health-system-related factors that influence gynecologists' decision to recommend endometrial sampling in young women (less than 40 years) with abnormal uterine bleeding

Study methods: A mail-based survey study was conducted using the Salant-Dillman method with 4 points of contact over 9 weeks. All Canadian obstetrician/gynecologists were initially surveyed (N=1746), receiving either French or English questionnaires. Eligible respondents were gynecologists practicing in Canada who treat these young women (N=834). Order response bias was taken into consideration by mailing two versions of the survey. Categorical data were analyzed using Pearson's Chi-square statistics. A logistic regression with mixed effect model was performed to determine the odds of sampling the endometrium, using physician as random factor.

Results: Overall response rate was 56.5%. The majority of respondents were generalists (83.6%). 70.3% of respondents have had young patients with malignant or pre-malignant endometrial conditions. Physicians ≤ 39 years have had less experience with these patients (59.6%, p=0.002) as have physicians practicing in communities without ob/gyn residents (35.2%, p=0.006). Sampling method was predominantly by office pipelle (79.7%), with younger physicians and female respondents employing this method most frequently (p=0.0001).

In case scenarios which explored the importance of four patient-related risk factors (obesity, irregular cycles, nulliparity and older age), on the decision to sample, 98.8% of respondents would sample a young woman presenting with all four risk factors, as opposed to 8.8% who would sample if the patient did not have any of these characteristics. Obesity and irregular cycles was the next most important combination of risk factors prompting sampling in 87.3% of physicians.

In the logistic regression, the odds ratio to proceed with endometrial sampling was 2.23 (95% CI 1.64-3.03) if a physician had previous experience with young women diagnosed with endometrial cancer or a pre-malignant condition, and was 1.45 (95% CI 1.05-2.01) if the physician was female.

Conclusion: Patient and physician factors influenced the decision to proceed with sampling the endometrium of young women with abnormal uterine bleeding, whereas the health-system factors studied in this survey did not seem to play a strong role.

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Chapter 1
Introduction

1.1 Overview

Endometrial cancer occurs with a lower incidence in young women as compared to their post-menopausal counterparts. However, the impact of early diagnosis in this age group may be even more profound, than in older women, as women less than 40 years of age would benefit from avoiding early menopause as a result of treatment, and potentially maintaining fertility. Clinicians must balance the frequency of menstrual dysfunction in women of reproductive age, the relative protective effect of younger age on the risk of developing endometrial cancer, and the discomfort of an endometrial biopsy, with a young woman's individual risk factors and the benefits of early diagnosis. The decision to investigate young women, for endometrial cancer is likely based on a myriad of factors (see Figure 1).

Understanding the decision process that leads to young women being investigated for endometrial cancer would offer insight into the gaps in knowledge, physician biases, and environmental factors that influence patient management. This information will help tailor further educational opportunities and shed light on areas in need of additional research.

1.2 Objectives

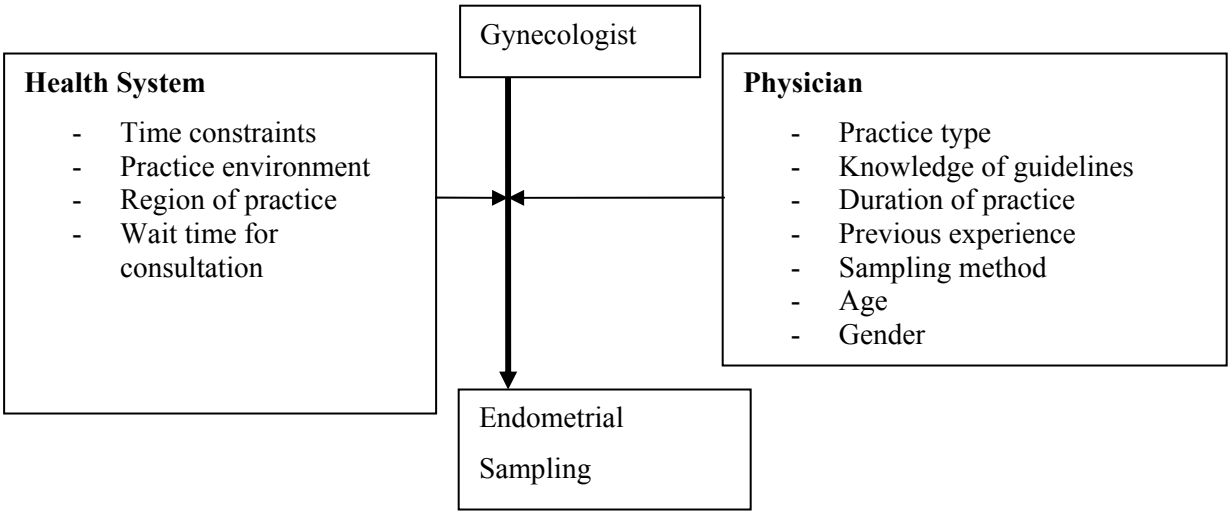
The primary objectives are to describe the specific clinical circumstances in which Canadian gynecologists proceed with endometrial sampling in young (less than 40 years old) women, presenting with abnormal uterine bleeding; and to identify patient, physician, and health-system-related factors that influence gynecologists' decision to proceed with endometrial sampling in young women with abnormal uterine bleeding.

1.3 Hypothesis

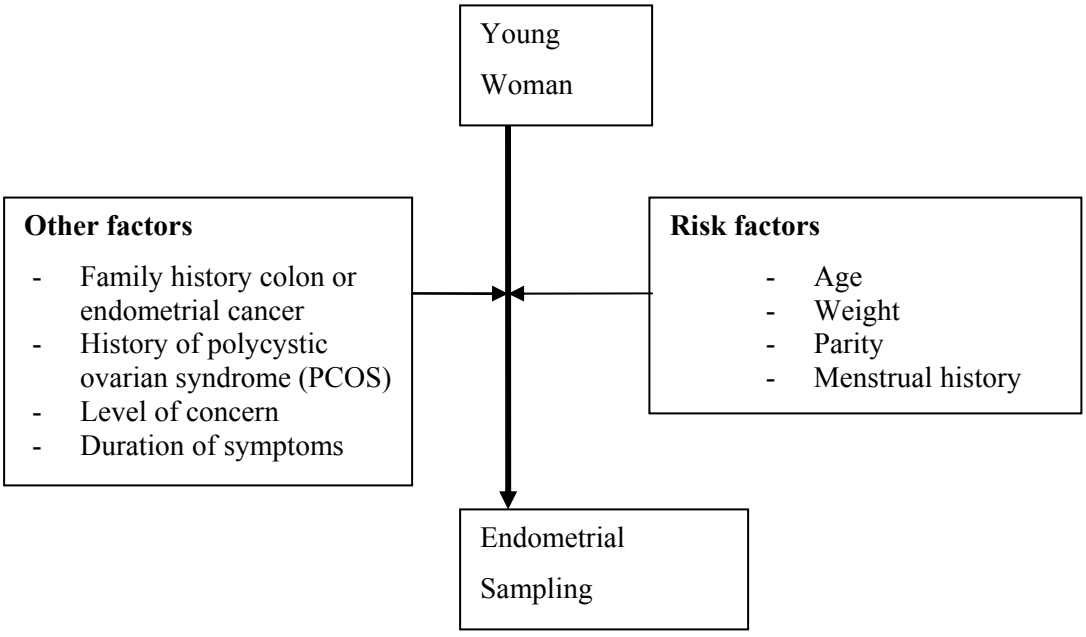
We hypothesize that previous experience with young women diagnosed with endometrial cancer, or pre-malignant conditions, will prompt more liberal use of endometrial sampling. As they are well recognized risk factors, the presence of obesity, irregular menses, and nulliparity, secondary to infertility, will also prompt gynecologists to recommend endometrial sampling.

Figure 1: **Conceptual framework of physician-, health-system- and patient- related factors that influence gynecologists to recommend endometrial sampling in young women presenting with abnormal uterine bleeding**

a) Physician- and health-system-related factors



b) Patient- related factors



Chapter 2

Literature Review

2.1 Incidence of Endometrial Cancer

Endometrial cancer, also referred to colloquially as cancer of the uterus, is the fourth most common cancer affecting women. The histological type is nearly always adenocarcinoma. Though this disease occurs primarily in post-menopausal women, 20-25% of cases are diagnosed in young women before menopause. The incidence of endometrial cancer increases rapidly with age: 5.17, 9.14 and 19.15 cases per 100,000 women in age groups 35-39, 40-44 and 45-49 years respectively (Public Health Agency of Canada, Cancer surveillance, Canada 2004).

In pre-menopausal women, endometrial cancer can present with abnormal menstrual bleeding. However in this age group, abnormalities of menstrual function are quite common, accounting for 20% of office visits to gynecologists, and 25 % of gynecologic surgeries (Goldstein 2004). Triaging women that require further investigations prior to initiation of menstrual management is a clinical conundrum. Given the low probability of malignancy, more invasive investigations such as an endometrial biopsy are often deferred.

The decision to proceed with sampling the endometrium, to determine if an endometrial pathology is present, is frequently based on known risk factors (section 2.3). Endometrial cancer is thought to originate in situations of either endogenous (such as obesity) or exogenous (e.g. unopposed post-menopausal estrogen therapy or prolonged pre-menopausal anovulation) estrogen excess (Amant et al. 2005). This malignancy may start de novo, or can result from the progression of hyperplasia: atypical complex hyperplasia evolves into endometrial

adenocarcinoma in approximately 41-45% of cases, if left untreated (Jadoul and Donnez, 2003). Though less common, some endometrial cancers are genetically linked to other familial cancers (Amant et al. 2005).

2.2 Management of Endometrial Cancer

In post-menopausal women, endometrial cancer usually presents with abnormal bleeding. Treatment and staging is surgical: hysterectomy with bilateral removal of Fallopian tubes and ovaries. Depending on stage, grade and type of the malignancy, adjuvant therapy with radiation and/or chemotherapy is occasionally required (Amant et al. 2005).

Though the incidence of endometrial cancer is lower in young women, early diagnosis is essential for conservative (medical) management in women desiring to maintain fertility. The time interval preceding development of endometrial cancer, from atypical complex hyperplasia, was found to range from 1 to 11 years, with mean of 4 years (Jadoul and Donnez, 2003). Progestin treatment has been used in the context of atypical complex hyperplasia and endometrial adenocarcinoma with response rates of 83-94% and 57-75% respectively. Median time to response was 12 weeks (range 4-60 weeks) (Ramirez et al. 2004). In Jadoul and Donnez's review of the literature from 1970 to 2001, 26 patients younger than 40 years of age were reported to have had 31 pregnancies, following conservative treatment of their endometrial adenocarcinoma. The majority of these women (twenty) were noted to be nulliparous, highlighting that conservative therapy is usually reserved for women who have not yet had the opportunity to conceive. This review concluded that conservative management was acceptable in young women, diagnosed with early stage endometrial cancer wishing to preserve their fertility, when close monitoring for recurrence was possible.

2.3 Risk Factors for Endometrial Cancer in Premenopausal Women

In a retrospective study by Farquhar et al. (1999) risk factors for endometrial hyperplasia and cancer were identified from 51 charts. In addition to age ≥ 45 years, weight ≥ 90 kg (OR 5.5, 95% CI 2.9-10.6), infertility (OR 3.6, 95% CI 1.3-9.9) and nulliparity (OR 2.8, 95% CI 1.1-7.2) were significant independent risk factors. A family history of colon cancer was a genetic risk factor (OR 5.0, 95% CI 1.3-19.1). Hereditary non-polyposis colon cancer (HNPCC), which is a known genetically linked family of cancers, imparts a 40-60% lifetime risk of endometrial cancer (Amant et al. 2005). In 2005, Soliman et al. published a chart review of 188 pre-menopausal women less than 50 years of age at the time of diagnosis of endometrial cancer. In women less than 40 years of age (n=79), 75% of women were overweight (BMI 25-29.9 kg/m^2) or obese (over 30 kg/m^2). The mean age of this group was 35 years of age, and these women were more likely to be nulliparous (71%). In a subanalysis of the same group of women, Schmeler (2005) showed that irregular menses was the most common presenting symptom in women under 50 years of age.

Hardiman et al. (2003) published a literature review investigating polycystic ovarian syndrome (PCOS) as an independent risk factor for endometrial cancer in premenopausal women. As obesity and infertility are common hallmarks of PCOS, the independent link between this condition and endometrial cancer remains controversial. Pillay (2006) noted an association between polycystic appearing ovaries in premenopausal women and endometrial cancer. However, multiple cysts on ovaries are only one of three possible criteria for diagnosing PCOS, thus not pathognomonic.

Though most studies investigating risk factors for endometrial cancer in young women are based on retrospective chart reviews, Parslov et al. (1999) conducted a case control study surveying 319 affected women and 642 matched controls, aged 25-49 years. The survey return rate was over

90%. Interestingly endometrial cancer risk decreased with increasing age of first birth (adjusted OR 0.02, 95% CI 0.01-0.02 for age ≥ 30yrs). Parity ≥ 1 tended to reduce the risk of endometrial cancer but was only significant when at least 2 pregnancies were achieved (adjusted OR 0.3, 95% CI 0.2-0.6), echoing nulliparity as a risk factor. Androgen excess, which is one criteria of the diagnosis of PCOS, was present in 3% of cases but only 0.6% of controls.

As previously discussed, menstrual dysfunction is a common presentation in pre-menopausal women. As a likely result, Evans-Metcalf et al. (1998), in a cross-sectional study of 289 women with endometrial cancer, found that women aged ≤45 years had a mean duration of menstrual irregularities of 12 months prior to diagnosis, as opposed to women over 45 years where the mean duration was 4 months. In this study, women ≤45 years were more frequently diagnosed in stage Ia (cancer confined to the endometrium) than older women. However, the overall distribution among stages I to IV was similar between the two groups of women, which agreed with findings from an Australian retrospective study of 17 women, 45 years or younger, with endometrial cancer (Gitsch, 1995).

A later diagnosis in young women, as indicated by the prolonged duration of symptoms prior to sampling the endometrium, could shift the distribution to more advanced cancers, hindering the chances at conservative treatment. Duska (2001), in a chart review of 95 women ≤ 40 years with endometrial cancer, found that 12 % were diagnosed during investigations for infertility. Overall 12.6% were treated medically; however 2 out of these 12 patients did require further surgical intervention for failure of medical management.

2.4 Physician- and Health-System-related Factors Influencing Physician Utilization of Endometrial Assessment

A physician's decision to proceed with endometrial assessment will likely be influenced by variables other than patient-related risk factors. Grol and Grimshaw's paper (2003) discusses barriers that exist in practice environments: financial disincentives, lack of time, perception of liability, and patients' expectations. Standards of care, opinion leaders, medical training and types of advocacy were also found to be influential.

In a study to explain physicians' practice pattern variations, O'Neill and Kuder (2005) hypothesized that physicians' clinical decision and propensity to treat, under conditions of uncertainty, could be described in three stages of influence. The first stage is a clinical baseline heuristic decision structure where decisions were based on clinical training and experience of the physician, rather than setting and patient characteristics. In the second stage, the baseline clinical heuristics are adapted to the environment where organizational setting and resources, practice population, and rewards and censure framework play a role. Lastly the practice specific heuristic is altered by patient clinical characteristics and preferences. Similarly, Eisenberg (2002) suggests that motivations influencing physicians' prescription of medical services include physicians' personal interests and desires, patient benefit and social good.

2.5 Endometrial Assessment for Endometrial Cancer and Pre-malignant Conditions

A histological sample is required for definitive diagnosis (Amant 2005). An office endometrial biopsy can provide sufficient tissue for diagnosis (SOGC 2000), and is frequently chosen given its simple technique and overall low cost. The procedure involves placing a pipelle in the uterine cavity and removing a random sample of endometrial tissue. Side effects are minimal but do involve cramping and the uncommon risks of infection and perforation of the uterus. In a

systematic review of outpatient endometrial biopsy, for the detection of endometrial cancer, Clark et al. (2002) found a failure rate of the office pipelle of 8% (histologically inadequate sample). The pooled likelihood ratios for all methods of endometrial biopsy were 66.48 (95% CI 30.04-147.13) for a positive result, and 0.14 (95% CI 0.08-0.27) for a negative sample. However in the context of symptoms, the post test probability was 81.7% (95% CI 59.7-92.9%) and 0.9% (95% CI 0.4-2.4%) for a positive and negative result, respectively. The authors thus concluded that office endometrial sampling had a high overall accuracy in detecting endometrial cancer, but a negative test was only moderately useful.

Alternatively hysteroscopy, with dilatation and curettage, is the gold standard for diagnosis. This operative technique may be performed under local sedation, or under general anesthetic, and includes risks of infection, bleeding and uterine perforation (Te Linde's, 1997).

2.6 Recommendations for Endometrial Assessment in Young Women

Both the Society of Obstetricians and Gynecologists of Canada (SOGC) and the American College of Obstetricians and Gynecologists (ACOG) have evidence-based recommendations to guide the practice of their members.

With respect to the evaluation of the endometrium, to rule out malignant or pre-malignant conditions in young women presenting with abnormal menstrual bleeding, the SOGC (2001) has suggested performing an endometrial biopsy of all symptomatic women ≥ 40 years old, or "those with an increased risk of endometrial cancer" including: weight ≥ 90kg, nulliparity from infertility, new onset irregular heavy bleeding, PCOS, family history of endometrial or colon cancer, and/or tamoxifen use. The guidelines also suggest investigation of any woman who has not responded to 3 months of treatment.

The ACOG (2000) recommends that women over 35 years of age should have an endometrial biopsy if "anovulatory bleeding" is suspected. In women of 19-35 years, endometrial evaluation is recommended if there is no response to medical therapy or if anovulation is present for a "prolonged period".

It is important to highlight that the SOGC recommendations, for instance, are based primarily on one retrospective chart review (Farquhar 1999). The ACOG guideline is not specifically referenced, thus more an "expert opinion".

2.7 Assessing Physicians Practice Patterns

Peabody et al. (2000) performed a prospective validation study of 3 methods for measuring health care quality: vignettes, standardized patients, and chart abstraction, in 98 physicians working in outpatient primary care clinics. Clinical vignettes consistently produced results close to the gold standard of standardized patients, suggesting that this method was a useful way to measure practice pattern in an outpatient setting. They concluded that vignettes directly measured the process of care where interventions could be targeted. In a later study, Peabody et al (2004) performed a prospective evaluation of vignettes compared to standardized patients, in outpatient centres with 144 physicians. Vignettes were found to accurately measure unnecessary utilization of health care.

Veloski et al. (2005) reviewed the use of clinical vignette-based surveys as a tool for assessing physician practice variations. They emphasized that physicians should be reassured that the vignettes are not a test of knowledge or competence, but a method of measuring practice pattern. Three important issues were highlighted: the vignette-based survey needs unambiguous instructions, realistic clinical situations, and distinctive strategy for data analysis. Vignette-based surveys were felt to offer a simple and economical tool for characterizing physicians' practice variations.

2.8 Changing Physicians' Behavior

Discrepancies between the established practice pattern and that guided by clinical guidelines would lead to opportunities to modify physician behavior, or potentially modify the guidelines themselves. Eisenberg's review in 2002 noted six methods of changing physician practice patterns: education, feedback, participation, administrative changes, incentives and penalties. Through a vignette-based survey, physicians would have the opportunity to participate in the information- gathering process, and dissemination of results would provide feedback. In Davis and Taylor-Vaisey's systematic review of theoretic concepts, practical experience and research evidence in the adoption of clinical guidelines (1997), part of the steps in developing and disseminating guidelines is to define and refine the problem, such as with the proposed survey. In addition, having physicians participate in the development of their own guidelines was found to improve their attitude towards the guidelines themselves.

Chapter 3

Study Design and Methods

3.1 Survey Overview

A mail-based census survey of Canadian gynecologists was performed to investigate the practice of endometrial sampling in young women, presenting with abnormal uterine bleeding. Respondents were asked whether or not they would perform endometrial sampling in a series of clinical scenarios designed to represent patients with varying risk factors of endometrial cancer. Respondents were also asked about aspects of their background and experience which were considered to be potential modifiers of their behavior.

3.2 Survey Content

At the beginning of the survey (Appendix A), physicians were first introduced to the context of the study. Young women were defined as less than 40 years of age. Subsequently, the participants were asked if their practice involves young women with menstrual problems such that the decision to sample the endometrium is a relevant issue. If not, the physician was asked to return the questionnaire after identifying their practice type. The rest of the survey contained three sections addressing the issues outlined in Figure 1 (Chapter 1).

The first section began with an assessment of the overall frequency with which physicians use endometrial sampling in this population: never, infrequently (< 50% of these patients), frequently (≥ 50%) or always. This question was also an overall measure of the controversy associated with

the practice of sampling these young women, i.e. if the majority of gynecologists never or always sampled these patients there may not be a strong role played by the individual physician-, patient- and health-care-related factors.

If physicians sampled at least infrequently, they were directed to a series of 16 cases where patient-risk factors for endometrial cancer, and pre-malignant conditions, such as obesity, older age, nulliparity and irregular cycles, were sequentially altered. Participants were asked if they would sample such patients. The importance of other patient-factors such as a history of polycystic ovarian disease, family history of endometrial or colon cancer and their level of concern was investigated, as was the influence of time constraints in the decision to sample. This section also asked physicians what duration of symptoms they felt was sufficient to warrant proceeding with endometrial sampling.

To assess for response-order effect in the responses to the cases, two versions of the questionnaire were created, with different orders to the cases presented, and these were mailed to physicians in the mail-out list in an alternating fashion.

In the second section, a physician's previous experience with young women diagnosed with endometrial cancer or pre-malignant conditions was ascertained. Other aspects of their practice pattern such as whether they operate on women with endometrial cancer was determined. Their knowledge of the SOGC guidelines on the management of abnormal bleeding, and their opinion of these recommendations, were questioned. Though physicians who "never" sampled were asked to forgo answering the first section, they were re-directed to continue the survey with this section.

In the third section, demographic information on the participants was obtained including practice type (generalist, subspecialist or other), practice environment, time in practice, age and gender.

Two comment sections were present in this survey. The first was with respect to the SOGC recommendations, asking physicians how they could be improved. The last section allowed for

comments and suggestions on the question of endometrial sampling in these young women, and on the study itself.

As participants would be either English or French speaking, the survey was translated into French by the principal investigator (Appendix B). Both the English and French surveys were reviewed by a French speaking colleague in order to assure accurate translation and appropriate grammar and spelling. As the questions themselves were simple, back translation was not felt to be necessary.

3.3 Pilot Study

After the initial construction of the survey, a pilot study was performed investigating the survey for clarity, and ease of response. The 15 members of the department of Obstetrics and Gynecology at Queen's University were provided with the survey and asked to respond as actual participants. Comments were received regarding time to complete the survey (approximately 5-10 minutes), as well as suggestions to improve the content of the questions. The principal modification of the survey was to the questions in the case scenarios. Each question was changed to offer systematic variations in the four patient-related risk factors. As this group of physicians did not receive the survey in its final form, they were removed from the mail-out list, and their responses were not used in the final data set.

3.4 List Frame

According to a Health Canada paper of "Supply, Distribution and Migration of Canadian Physicians, 2006" 1674 obstetricians/gynecologists were practicing in Canada. As an a priori knowledge of the number of eligible physicians for this survey was not available a sample size calculation could not be performed. Thus a census survey of all practicing Canadian gynecologists was chosen in order to obtain a comprehensive overview of the Canadian practice

pattern. A census would also have the advantage of seeking representation from the smallest provinces, with the fewest gynecologists.

The Cornerstone List Brokerage was approached in order to obtain a list frame. Their most comprehensive list was generated from the Canadian Medical Directory with a total of 1762 physicians (1385 English- and 377 French-speaking gynecologists). After eliminating the physicians from this list that were practicing in Kingston (the principal investigator, and those surveyed in the pilot study: 1 French- and 14 English-speaking physicians), 1,746 physicians were offered participation in the study: 1370 had English as their preferred language, and 376 had French.

The remaining list was divided into regional groupings of provinces. Regions and provinces, with number of physicians as per list frame (E=English, F= French) were thus:

Atlantic:	Newfoundland, Nova Scotia, Prince Edward Island and New Brunswick
	Total physicians: E = 119; F = 11
Quebec	Total physicians: E = 90; F = 339
Ontario	Total physicians: E = 680; F = 20
Prairies	Manitoba, Saskatchewan, Alberta
	Total physicians: E = 266; F = 3
West	British Columbia, North West Territories, Yukon
	Total physicians: E = 215; F = 3

Ideally physicians providing exclusively obstetrical care, or other subspecialties that do not have young women with menstrual dysfunction as patients, would be excluded from the population surveyed. Unfortunately an accurate list (or even an estimation) of these physicians was not available a priori. The survey thus asked physicians that do not have a patient population relevant to this questionnaire to identify themselves in the first question.

3.5 Survey Methodology

A mail-based survey was chosen, over an electronically distributed survey, as this study was intended to reach a diverse population of physicians, where access to electronic documents may vary.

The survey methodology was based on the Salant-Dillman "Total Design" approach (1994), with four points of contact in order to maximize the response rate. According to this design, the survey was printed on legal sized non-white paper, folded in half, booklet-style (Survey in Appendix A modified in form to fit letter size paper). All letters were printed on Queen's University letterhead, and signed by the principal investigator in blue ink. A "true" stamp was used instead of a metered stamp on the return envelopes. The two versions were assigned in an alternating fashion throughout the original list frame (assembled in a geographical order from east to west). Surveys were coded with numbers and letters identifying region, province, unique survey number, language and version. These codes were the only link to the physician names and addresses. When surveys were returned, the physician's personal identifiers were removed from the database itself. Consent to participate was felt to be implicit when the completed survey was returned.

In the first mail-out, physicians received a letter (Appendix C), explaining the study and inviting them to participate, along with the survey, a self-addressed stamped return envelope, and a Queen's University bookstore pen to assist in completing survey (week 0). Three weeks later (week 3) a reminder letter (Appendix D), doubling as a thank you to respondents, was sent to all gynecologists. At week 6, a package was sent to all non-respondents including a letter emphasizing the importance of the study (Appendix E), and encouraging participation, a second copy of the survey and a self-addressed stamped return envelope. A final package including a

similarly worded letter (Appendix F), a third copy of the survey and a self-addressed stamped return envelope was sent to the remaining non-respondents at week 9. By week 20, accrual of completed surveys was stopped to proceed with analysis. Surveys were marked to identify from which mail-out they came. As surveys were returned, time of receipt and mail-out number was recorded.

3.6 Data Management

As surveys were received, the original physician database was updated, removing physician's personal information, and indicating if the physician was eligible for the study. If the initial mail-out was "returned to sender", an internet search for a current practice address was undertaken. If unsuccessful, an attempt was made at contacting their previous workplace for a forwarding address. Physicians were designated as not practicing in Canada if they were in fellowship training (not independent practice), had moved outside the country, were retired or were deceased. Ineligible respondents were physicians who identified themselves as not seeing young women with abnormal uterine bleeding in their practice.

The remaining physicians were considered eligible participants, and their responses were then entered in an Excel database. Attention was paid to the questionnaire version physicians had received, and after adjusting for different case ordering, data was pooled (Version code, A or B, was still identified for later analysis). Once the final database was completed, data entry was checked for errors by re-entering, in an independent fashion, 10% of the surveys from each region. Errors were found in less than 1% of surveys re-entered, generally in only the entry of 1 to 2 questions per survey.

3.7 Data analysis

Analysis was undertaken using SAS Enterprise Guide 4 and SAS 9.1. Physician and health-system variables were analyzed with Pearson Chi-square statistics to test for association. A p-value of less than 0.05 was statistically significant.

In the case scenarios, physicians were asked whether or not they would sample the endometrium in each clinical situation. When the responses for each case were examined in a bivariate analysis, by physician and health-system variables, the Cochran-Mantel-Haenszel statistics were used for the analysis, in order to stratify by version of survey. In this portion of the analysis, given the multiple comparisons, only a p-value less than 0.01 was considered statistically significant.

Lastly, a logistic regression with mixed effects model was performed on the pooled data. Patient, physician and health-system factors were entered into the regression, as was survey version. Interaction terms were not considered. Physicians themselves were included as random effects to account for the multiple repeated measures which occurred in the case scenarios. The odds ratio, and 95% confidence interval, of sampling the endometrium was thus obtained for the patient, physician and health-system variables.

3.8 Ethical Consideration

Approval was obtained through Queen's University research ethics board (Appendix G). Confidentiality was assured to respondents. The original list frame was password protected, and only accessed by the principal investigator and a research assistant. The surveys were kept in a locked office, and the only link to the list frame was through the survey code.

Chapter 4

Results

4.1 Distribution of Potential Participants

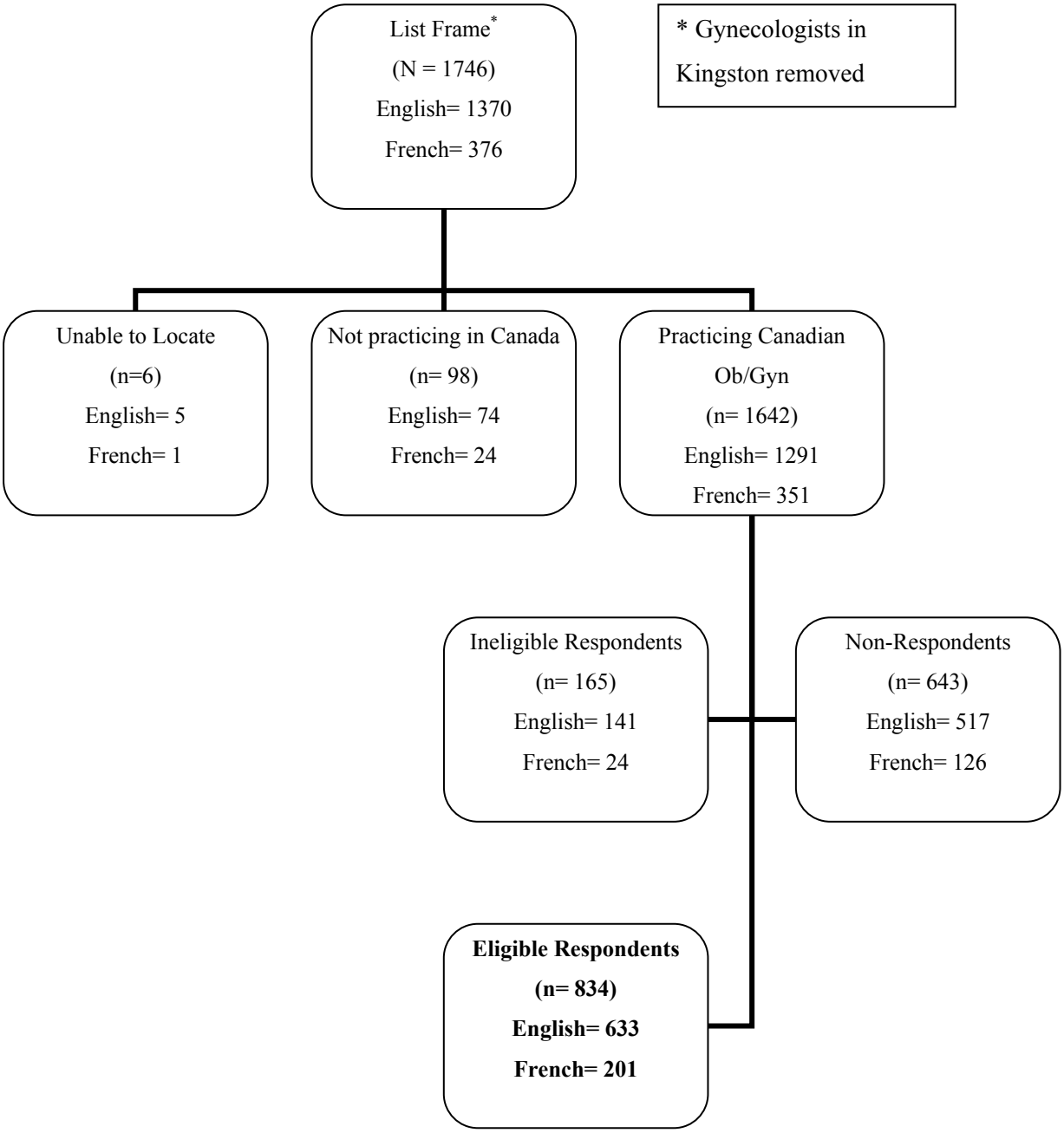
The list of Canadian obstetricians/gynecologists (Ob/Gyn) initially consisted of 1,746 physicians, after removing participants in the pilot study and the principal investigator (see Figure 2). A valid work address could not be obtained for 6 physicians (unable to locate), despite repeated searches. 98 physicians were not practicing in Canada, were retired or deceased, or continued in post-graduate training. Thus a total of 1,642 obstetrician/gynecologists were currently practicing in Canada. With 643 physicians not responding, and 165 physicians considered ineligible, the remaining 834 gynecologists were the eligible respondent group. In the French group, 362 were practicing in Quebec (96.3 %).

The distribution of surveys received, by version, was 420 (50.4%) for A and 414 (49.6%) for B, respectively.

4.2 Response Rate

The response rate was calculated as the ratio of eligible respondents over the total number of eligible obstetricians/gynecologists practicing in Canada (i.e. practicing Canadian Ob/Gyn minus ineligible respondents). The overall response rate was 56.5 %. The response rate for the French survey was greater than the English survey: 61.5% versus 55.0 % respectively.

Figure 2: Distribution of Potential Participants

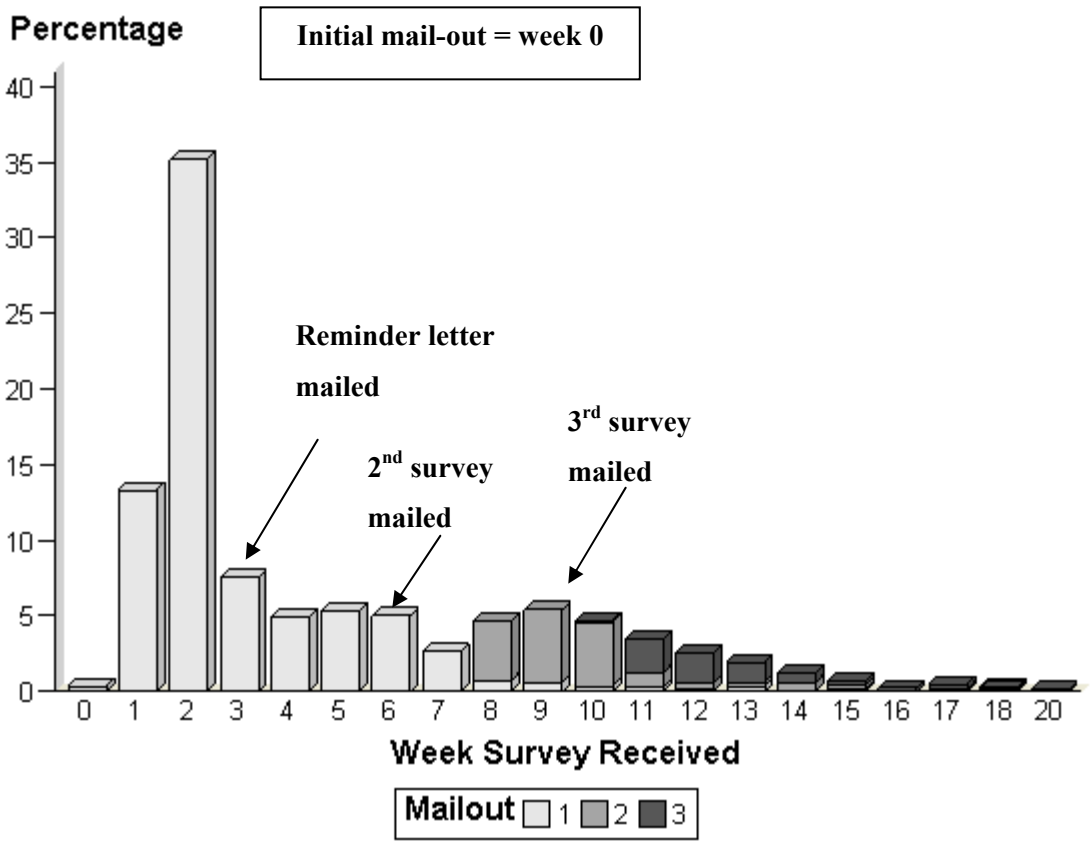


Overall Response Rate **= 834/ (1642- 165)**
= 56.5%
English Response Rate = 55.0%
French Response Rate = 61.5%

4.3 Chronology of Surveys Received

Figure 3 demonstrates the chronology of eligible surveys received. The initial package was sent on week 0. The largest number of surveys received in one week was in week 2 (35.2% of total number of surveys received). Sending the second survey in week 6 did generate an increase in response by week 8 that was sustained until week 10. Though a third survey was sent on week 9, its improvement on response rate was modest. Accrual ended by week 20.

Figure 3: Chronological Distribution of Received Eligible Surveys



4.4 Non-respondent analysis

Information on non-respondents, from the initial list frame, was limited to geographic location, and preferred language. Gender could not be accurately assessed from the physician names themselves. Table 1 looks at response rates across region, province and language.

The Atlantic region showed the greatest proportion of respondents. The remaining four regions had similar proportions of respondents (from 51.2% in Ontario to 59.7% in Quebec). When the regions were separated into their provinces, a statistically significant difference remained, with Nova Scotia having the highest proportion of respondents (81.6%), and Ontario the lowest (51.2%).

Language preference (thus language of survey) was also statistically different with a greater number of French physicians responding than English: 61.5% versus 55.0 % respectively.

Table 1: Response rate across categories

	NUMBER OF RESPONDENTS (N= 834)	RESPONSE RATE (%)	CHI-SQUARED (P-VALUE)
Region			19.38 (0.0007)
Atlantic (n = 98)	71	72.4	
Quebec (n = 376)	225	59.7	
Ontario (n = 598)	306	51.2	
Prairies(n = 225)	124	55.1	
West (n = 183)	108	59.0	
Province			25.52 (0.008)
Newfoundland (n = 19)	13	68.4	
Nova Scotia (n = 38)	31	81.6	
PEI (n = 8)	6	75.0	
New Brunswick (n = 33)	21	63.6	
Quebec (n = 376)	225	59.8	
Ontario (n = 598)	306	51.2	
Manitoba (n = 48)	31	64.6	
Saskatchewan (n = 40)	21	52.5	
Alberta (n = 137)	72	52.6	
West* (n = 185)	108	59.0	
Language			4.16 (0.04)
English (n = 1152)	633	55.0	
French (n = 329)	201	61.3	

p-value from Pearson Chi squared statistic

* West = British Columbia, Northwest Territories and Yukon

4.5 Eligible Respondent Characteristics

Table 2 represents both the physician- and health-system-related characteristics (as described in Figure 1) of the eligible participants. Given that Quebec and Ontario were the largest regions surveyed, it is not surprising that these provinces together represent 63.7% of respondents.

As the vast majority of physicians seeing young women with abnormal uterine bleeding (AUB) are generalists (83.6%), practice type was not be investigated as a potential explanatory variable in further analyses. With respect to practice environments, 39.0% of respondents worked in community-based environments without Ob/Gyn resident teaching commitments, 34.3% work in a university-affiliated or academic centre and 22.7% are in a community environment with a role in training Ob/Gyn residents.

Year of graduation from Ob/Gyn residency ranged from 1952 to 2008. The median time since graduation was 16.0 years, with 25th to 75th quartile of 8.0 to 27.0 years (range 1 to 57 years). The median duration of independent practice in Canada was 15.0 years with 25th to 75th quartile of 8.0 to 27.0 years (range 1 to 53 years; N=818). Time since graduation and duration of independent practice are highly correlated (Pearson correlation coefficient 0.98) confirming that most physicians responding to the survey have not pursued further fellowship training and thus function as generalist Ob/Gyn. Physician age and time in practice are also highly correlated with a Pearson correlation coefficient of 0.91 (where the categorical variable of age was approximated as continuous using 35, 45, 55 and 65 years to represent the four categories: $\leq$ 39 years, 40-49 years, 50-59 years and $\geq$ 60 years respectively). Physician age was thus used as the marker of both time since graduation and duration of independent practice.

Table 2: Physician and Environment Characteristics of Participants

	PARTICIPANTS	PERCENT (%)
Gender (n = 830)		
Male	435	53.0
Female	385	47.0
Age (years) (n = 820)		
≤ 39	203	24.8
40-49	226	27.6
50-59	215	26.2
≥ 60	176	21.5
Regions (n = 834)		
Atlantic	71	8.5
Newfoundland	13	1.6
Nova Scotia	31	3.7
PEI	6	0.7
New Brunswick	21	2.5
Quebec	225	27.0
Ontario	306	36.7
Prairies	124	14.9
Manitoba	31	3.7
Saskatchewan	21	2.5
Alberta	72	8.6
West	108	13.0
Type of Practice (n = 825)		
Generalist	690	83.6
Reproductive Endocrinology and Infertility	43	5.2
Gynecology Oncology	19	2.3
Urogynecology	28	3.4
Other	45	5.5
Practice Environment (n = 820)		
University affiliated or academic centre	282	34.3
Community-based with Ob/Gyn residents	187	22.7
Community-based without Ob/Gyn residents	321	39.0
Other	33	4.0

4.6 Practice Pattern

4.6.1 Overview of practice pattern of respondents

All survey respondents were asked to answer questions related to their practice pattern. Variables that might influence their decision to sample young women presenting with abnormal uterine bleeding were investigated (Table 3).

The majority (70.3%) of physicians had experience with young women with endometrial cancer or complex hyperplasia with atypia (pre-cancerous endometrial abnormality). The median time since having had a patient with these conditions was 2.0 years with 25^{th} to 75^{th} quartile of 1 to 4 years (range= less than 1 - 29.0 years). Approximately half (50.3%) of all physicians treated these patients medically, to preserve fertility. In this group, the median time since last medically managing a case was 2.0 with 25^{th} to 75^{th} quartile of 1 to 4 years (range= less than 1 – 21 years). Only 33.2% of respondents did not operate on their own patients diagnosed with these conditions, with 64.7% of them needed to refer these patients to another centre for surgical treatment.

The majority of gynecologists (79.7%) used the office pipelle for sampling. 16.1% (N=133) of physicians described alternative choices for sampling: a small number (18) of physicians used other types of curettes and 99 gynecologists used a combination of pipelle and dilation and curettage. It was difficult to ascertain from the data if these D & C (dilation and curettage) procedures were performed in outpatient clinics, as opposed to in-hospital. Responses to this question also highlighted the use of ultrasound in the decision process that lead to endometrial sampling. This will be revisited in the review of comments derived from the questionnaires.

When asked the length of time patients waited to see a gynecologist for abnormal uterine bleeding, after being referred from their primary care practitioner, 87.2% stated these women would be seen within 6 months.

With respect to the duration of symptoms in young women that should prompt endometrial sampling, the greatest proportion of respondents (55.7%) stated that they would evaluate the endometrium at 12 months of symptoms. For this question most qualitative responses in the "other" option stated that an absolute time factor did not influence their decision as much as the rest of the clinical scenario.

The SOGC "Guidelines for Management of Abnormal Uterine Bleeding", which offers some recommendations for the sampling of these young women, was familiar to 69.8% of respondents, with most of these physicians finding these guidelines helpful (68.2%).

Table 3: Overview of practice pattern of respondents

	YES N (%)
Have you ever had a patient less than 40 years of age with endometrial cancer or complex hyperplasia with atypia? (N = 829)	583 (70.3)
Have you ever medically treated a young woman with endometrial cancer, or complex hyperplasia with atypia to preserve fertility? (n = 584)	294 (50.3)
Do you operate on women with endometrial cancer? (N = 825)	551 (66.8)
Do you need to refer affected patients to a different hospital for care? (n = 275)	178 (64.7)
Do you primarily sample the endometrium by: (N = 827)	
Office pipelle	659 (79.7)
Hysteroscopy, D&C	35 (4.2)
Other	133 (16.1)
How long would young women with abnormal uterine bleeding wait to see you in consultation, after being referred from their primary care health practitioner? (N = 826)	
Less than 6 months	720 (87.2)
6-12 months	99 (12.0)
More than 12 months	7 (0.8)
What duration of symptoms do you feel is sufficiently significant to warrant an endometrial biopsy in a young woman with abnormal uterine bleeding? (N = 799)	
12 months	445 (55.7)
18 months	99 (12.4)
24 months	46 (5.8)
Other	209 (26.2)
Are you familiar with the recommendations from the SOGC's "Guidelines for the Management of Abnormal Uterine Bleeding" 2001? (N = 828)	578 (69.8)
Do you find the guidelines helpful with respect to its recommendations for sampling the endometrium, to exclude malignancies or pre-malignant conditions, for women less than 40 years of age? (N = 576)	
Very helpful	143 (24.8)
Somewhat helpful	393 (68.2)
Not at all	40 (6.9)

4.6.2 Physician-related factors that influence the decision to sample the endometrium in young women with abnormal uterine bleeding

4.6.2.1 Have you ever had a patient less than 40 years of age with endometrial cancer or complex hyperplasia with atypia?

Younger physicians (≤ 39 years), physicians in Quebec and Ontario, and gynecologists working in community without Ob/Gyn residents were less likely to have had experience with these cases. Table 4 demonstrates that gender did not have a significant effect on whether physicians had experience with these patients.

4.6.2.2 Do you operate on young women with endometrial cancer?

Table 5 shows that older physicians (≥ 60 years) were least likely to operate on these patients. There were significant differences according to region of practice: gynecologists practicing in the Atlantic region and in Quebec were less likely to operate than those in Ontario, the Prairies and Western provinces. Practice environment also demonstrated an influence, with university based physicians (51.6%) and those classifying their practice environment as “other” (42.4%) being the least likely to operate.

Table 4: Have you ever had a patient less than 40 years of age with endometrial cancer or complex hyperplasia with atypia?

	YES N (%)	NO N (%)	P-VALUE*
Gender			
Male	312 (72.1)	121 (27.9)	0.18
Female	261 (67.8)	124 (32.2)	
Age (years)			
≤ 39	121 (59.6)	82 (40.4)	
40 – 49	172 (76.1)	54 (23.9)	0.002
50 – 59	155 (72.1)	60 (27.9)	
≥ 60	125 (71.8)	49 (28.2)	
Region			
Atlantic	54 (76.1)	17 (23.9)	
Quebec	147 (65.9)	76 (34.1)	
Ontario	205 (67.4)	99 (32.6)	0.006
Prairies	86 (69.9)	37 (30.1)	
West	91 (84.3)	17 (15.7)	
Practice Environment			
University	206 (73.6)	74 (26.4)	
Community with Ob/Gyn residents	141 (75.4)	46 (24.6)	0.006
Community without Ob/Gyn residents	203 (35.2)	118 (36.8)	
Other	26 (78.8)	7 (21.2)	

* Pearson Chi square statistics

Table 5: Do you operate on women with endometrial cancer?

	YES **N (%)**	**NO** **N (%)**	**P-VALUE***
Gender			
Male	301 (69.7)	131 (30.3)	0.05
Female	241 (63.2)	140 (36.8)	
Age (years)			
≤ 39	138 (68.3)	64 (31.7)	
40 – 49	148 (66.4)	75 (33.6)	0.01
50 – 59	156 (72.9)	58 (27.1)	
≥ 60	100 (57.5)	74 (42.5)	
Region			
Atlantic	40 (56.3)	31 (43.7)	
Quebec	109 (50.0)	109 (50.0)	
Ontario	214 (70.4)	90 (29.6)	<0.0001
Prairies	96 (77.4)	28 (22.6)	
West	92 (85.2)	16 (14.8)	
Practice Environment			
University	144 (51.6)	135 (48.4)	
Community with Ob/Gyn residents	159 (85.0)	28 (15.0)	
Community without Ob/Gyn residents	227 (71.6)	90 (28.4)	<0.0001
Other	14 (42.4)	19 (57.6)	

* Pearson Chi square statistics

4.6.2.3 Do you primarily sample the endometrium by: office pipelle, hysteroscopy and D&C, or "other"

Table 6 reveals that female physicians relied on office pipelle more than their male counterparts (82.9% versus 76.5% respectively). Across the age groups, a trend was seen with older physicians using the pipelle less than younger gynecologists. The opposite trend was seen with hysteroscopy and D&C.

Gynecologists from Quebec were least likely to use the office pipelle for sampling, and most likely to describe their pattern as "other".

Table 6: Do you primarily sample the endometrium by:

	OFFICE PIPELLE N (%)	**HYSTEROSCOPY, D&C N (%)**	**OTHER N (%)**	**P-VALUE***
Gender				
Male	332 (76.5)	32 (7.4)	70 (16.1)	<0.0001
Female	316 (82.9)	2 (0.5)	63 (16.5)	
Age (years)				
≤ 39	176 (87.1)	2 (1.0)	24 (11.9)	
40-49	187 (82.7)	4 (1.8)	35 (15.5)	0.0001
50-59	160 (75.1)	11 (5.2)	42 (19.7)	
≥ 60	126 (72.4)	16 (9.2)	32 (18.4)	
Region				
Atlantic	63 (88.7)	3 (4.2)	5 (7.0)	
Quebec	150 (66.7)	11 (4.9)	64 (28.4)	<0.0001
Ontario	252 (83.7)	10 (3.3)	39 (13.0)	
Prairies	104 (84.6)	7 (5.7)	12 (9.8)	
West	90 (84.1)	4 (3.7)	13 (12.2)	
Practice Environment				
University	227 (81.4)	7 (2.5)	45 (16.1)	
Community with Ob/Gyn residents	149 (80.1)	13 (7.0)	24 (12.9)	0.15
Community without Ob/Gyn residents	249 (77.6)	13 (4.1)	59 (18.4)	
Other	27 (84.4)	0	5 (15.6)	

* Pearson Chi square statistics

4.6.2.4 How long would young women (less than 40 years old) with abnormal uterine bleeding wait to see you in consultation, after being referred from their primary care health practitioner?

The clinical concern physicians have for young women with dysfunctional bleeding, developing an endometrial cancer, may in part be reflected by how long these patients wait to be seen in consultation, once referred by their primary care practitioner.

As shown in Table 7 , these young women are reported to be seen in a shorter time frame by male physicians, older gynecologists in the 50-59 years and ≥ 60 years age groups, and in the province of Quebec and the Western region, where the interval from referral to consultation was less than 6 months.

Physicians' practice environment did not influence the time within which they report seeing these young women in consultation.

Table 7: How long would young women (less than 40 years old) with abnormal uterine bleeding wait to see you in consultation, after being referred from their primary care health practitioner?

	WAIT TIME FOR CONSULTATION WITH GYNECOLOGISTS (MONTHS)			
	< 6 **N (%)**	**6-12** **N (%)**	**>12** **N (%)**	**p-value***
Gender				
Male	400 (92.6)	30 (6.9)	2 (0.5)	< 0.0001
Female	309 (80.9)	68 (17.8)	5 (1.3)	
Age (years)				
≤ 39	164 (80.8)	37 (18.2)	2 (1.0)	
40-49	192 (85.0)	31 (13.7)	3 (1.3)	0.002
50-59	187 (88.2)	23 (10.8)	2 (0.9)	
≥ 60	166 (96.0)	7 (4.0)	0	
Region				
Atlantic	53 (74.6)	17 (23.9)	1 (1.4)	
Quebec	198 (88.4)	24 (10.7)	2 (0.9)	0.02
Ontario	258 (86.0)	39 (13.0)	3 (1.0)	
Prairies	107 (87.0)	15 (12.2)	1 (0.8)	
West	104 (96.3)	4 (3.7)	0	
Practice Environment				
University	242 (87.0)	34 (12.2)	2 (0.7)	
Community with Ob/Gyn residents	160 (86.0)	23 (12.4)	3 (1.6)	0.89
Community without Ob/Gyn residents	282 (87.8)	37 (11.5)	2 (0.6)	
Other	27 (84.4)	5 (15.6)	0	

*Bivariate analyses with small expected cell size limits validity of Pearson Chi-square statistics, however analysis repeated without category time > 12 months shows similar p-values

4.6.2.5 What duration of symptoms do you feel is sufficiently significant to warrant an endometrial biopsy in a young woman with abnormal uterine bleeding?

Overall 55.7% of gynecologists recommended sampling after 12 months of symptoms (Table 3). The duration of symptoms sufficient to prompt an endometrial sampling was then analyzed by physician and health-system variables (Table 8).

Region was a significant variable influencing physicians' opinion: fewer physicians in Quebec and Ontario suggested proceeding with sampling at 12 months of symptoms (48.4% and 55.2% respectively) than in other regions. In both Ontario and the Prairies, a greater proportion of physicians would suggest sampling later at 18 months. More gynecologists in Quebec did not select a specific time frame for sampling (i.e. "other" category). When comments were provided on the "other" category, physicians frequently noted that duration of symptoms did not necessarily influence their decision to sample.

Table 8: What duration of symptoms do you feel is sufficiently significant to warrant an endometrial biopsy in a young woman with abnormal uterine bleeding?

	12 MONTHS N (%)	18 MONTHS N (%)	24 MONTHS N (%)	OTHER N (%)	P-VALUE*
Gender					
Male	225 (54.5)	45 (10.9)	23 (5.6)	120 (29.1)	0.19
Female	215 (57.2)	53 (14.1)	22 (5.8)	86 (22.9)	
Age (years)					
≤ 39	110 (55.3)	32 (16.1)	13 (6.5)	44 (22.1)	
40-49	130 (59.1)	24 (10.9)	11 (5.0)	55 (25.0)	0.32
50-59	119 (57.5)	23 (11.1)	12 (5.8)	53 (25.6)	
≥ 60	80 (49.1)	18 (11.0)	10 (6.1)	55 (33.7)	
Region					
Atlantic	41 (61.2)	6 (9.0)	4 (6.0)	16 (23.9)	
Quebec	105 (48.4)	19 (8.8)	13 (6.0)	80 (36.9)	0.01
Ontario	160 (55.2)	45 (15.5)	18 (6.2)	67 (23.1)	
Prairies	74 (62.7)	17 (14.4)	7 (5.9)	20 (17.0)	
West	65 (60.8)	12 (11.2)	4 (3.7)	26 (24.3)	
Practice Environment					
University	148 (54.4)	40 (14.7)	13 (4.8)	71 (26.1)	
Community with Ob/Gyn residents	106 (57.9)	23 (12.6)	10 (5.5)	44 (24.0)	0.46
Community without Ob/Gyn residents	168 (55.4)	34 (11.2)	22 (7.3)	79 (26.1)	
Other	18 (54.6)	1 (3.0)	1 (3.0)	13 (39.4)	

* Pearson Chi square statistics

4.6.2.6 Are you familiar with the recommendations from the SOGC's "Guidelines for the Management of Abnormal Uterine Bleeding" 2001?

As shown in Table 9, male physicians were less likely to be familiar with the guidelines, as were older physicians 50-59 years and ≥ 60 years. No significant differences in familiarity were noted across regions or practice environment.

More Quebec physicians found the guidelines very helpful as opposed to the Atlantic and Western regions where more physicians found them not at all helpful. P-values for variations across age and practice environment were not significant ($p = 0.05$ and 0.76 respectively).

Table 9: Are you familiar with the recommendations from the SOGC's "Guidelines for the Management of Abnormal Uterine Bleeding" 2001?

	ARE YOU FAMILIAR WITH THE GUIDELINES?			DO YOU FIND THE GUIDELINES HELPFUL?			
	Yes N (%)	No N (%)	p-value*	Very helpful N (%)	Somewhat helpful N (%)	Not at all N (%)	p-value*
Gender							
Male	286 (65.9)	148 (34.1)	0.01	79 (27.2)	192 (66.2)	19 (6.6)	0.39
Female	282 (73.8)	100 (26.2)		62 (22.4)	194 (70.0)	21 (7.6)	
Age (years)							
≤ 39	173 (85.2)	30 (14.8)		33 (19.6)	128 (76.2)	7 (4.2)	
40-49	160 (70.8)	66 (29.2)	<0.0001	41 (25.6)	103 (64.4)	16 (10.0)	0.05
50-59	127 (59.9)	85 (40.1)		31 (23.7)	89 (67.9)	11 (8.4)	
≥ 60	107 (61.1)	68 (38.9)		36 (33.3)	66 (61.1)	6 (5.6)	
Region							
Atlantic	55 (77.5)	16 (22.5)		11 (19.6)	40 (71.4)	5 (8.9)	
Quebec	156 (69.3)	69 (30.7)		56 (36.6)	89 (58.2)	8 (5.2)	
Ontario	206 (68.7)	94 (31.3)	0.68	45 (22.3)	144 (71.3)	13 (6.4)	0.02
Prairies	85 (68.6)	39 (31.4)		19 (21.6)	63 (71.6)	6 (6.8)	
West	76 (70.4)	32 (29.6)		12 (15.6)	57 (74.0)	8 (10.4)	
Practice Environment							
University	193 (68.9)	87 (31.1)		48 (24.9)	130 (67.4)	15 (7.8)	
Community with Ob/Gyn residents	137 (73.3)	50 (26.7)	0.69	30 (22.1)	100 (73.5)	6 (4.4)	0.76
Community without Ob/Gyn residents	219 (68.4)	101 (31.6)		57 (25.9)	145 (65.9)	18 (8.2)	

* Pearson Chi square statistics

4.6.2.7 In your practice, would you sample the endometrium of young women that present with abnormal uterine bleeding: Never, Infrequently, Frequently or Always

At the beginning of the survey, participants were asked to rate how frequently they perform endometrial sampling in women less than 40 years of age presenting with abnormal uterine bleeding. This question was meant to assess the overall role of endometrial sampling, in gynecologists' management of young women. Table 10 shows that most respondents (61.2%) use endometrial sampling infrequently in this clinical scenario (defined as less than 50% of cases). As over 25% of cells were smaller than 5 in the age and region bivariate analyses, they were recalculated removing the smaller "never" category. For the regional variation, the p-value did not change. In the analysis with physician age, however, the p-value changed from 0.007 to 0.31. Thus endometrial sampling frequency did not vary significantly across age groups, with this correction. Gender, and practice environment did not have a significant influence on sampling frequency ($p>0.05$).

When physicians' overall description of their endometrial sampling frequency was compared to their responses in the case scenarios, all gynecologists that stated "never sample" also never sampled in the case scenarios. Only 11 of the 44 physicians that stated "always sample" chose to always sample the women in the case scenarios however.

For subsequent analyses of the influence of physician-, health-system- and patient-related factors on decision to sample, physicians that never sample were removed from the dataset, as they were asked not respond to section 1 of the survey.

Table 10: In your practice, would you sample the endometrium of young women that present with abnormal uterine bleeding:

	NEVER N (%)	INFREQUENTLY (<50% of patients) N (%)	FREQUENTLY (≥50% of patients) N (%)	ALWAYS N (%)	P-VALUE*
Participants N (%)	15 (1.8)	502 (61.2)	259 (31.6)	44 (5.4)	
Gender					
Male	13 (3.0)	263 (61.3)	129 (30.1)	24 (5.6)	0.06
Female	2 (0.5)	231 (61.3)	125 (33.2)	19 (5.0)	
Age (years)					
≤ 39	0	125 (62.5)	66 (33.0)	9 (4.5)	
40-49	2 (0.9)	134 (59.8)	75 (33.5)	13 (5.8)	0.31#
50-59	4 (1.9)	137 (64.9)	64 (30.3)	6 (2.8)	
≥ 60	9 (5.2)	99 (57.6)	50 (29.1)	14 (8.1)	
Region					
Atlantic	0	40 (57.1)	24 (34.3)	6 (8.6)	
Quebec	6 (2.7)	131 (59.0)	73 (32.9)	12 (5.4)	0.24#
Ontario	7 (2.3)	204 (67.3)	79 (26.1)	13 (4.3)	
Prairies	2 (1.6)	66 (54.6)	46 (38.0)	7 (5.8)	
West	0	61 (58.6)	37 (35.6)	6 (5.8)	
Practice Environment					
University	4 (1.4)	177 (63.7)	81 (29.1)	16 (5.8)	
Community with Ob/Gyn residents	1 (0.5)	104 (55.9)	70 (37.6)	11 (5.9)	0.33
Community without Ob/Gyn residents	10 (3.2)	194 (61.6)	96 (30.5)	15 (4.8)	
Other	0	20 (66.7)	9 (30.0)	1 (3.3)	

* Pearson Chi square statistics
# p-value after removing "never" category

4.6.2.8 Influence of Other Characteristics

Other patient- and health-system-related characteristics were investigated by asking respondents if these factors were considerations in their decision to biopsy these young women.

Women with polycystic ovarian syndrome were likely to have an endometrial sampling performed by 82.8% of 812 respondents. Similarly a family history of endometrial or colon cancers led to obtaining a histological sample of the endometrium by 79.8% of 814 physicians. Physicians felt strongly that time constraints did not play a role in their management (93.8% or 761/811 respondents). Level of patient concern however influenced their action: 67.7% of 809 respondents would biopsy if the patient was worried about her symptoms and her risk of endometrial pathology.

4.7 Analysis of case scenarios

4.7.1 Influence of patient-related factors

In Table 11, each case scenario from the survey (Appendix A) is described by its patient-related risk factors. (Note that the cases are numbered according to Version A: data from Version B was reordered when merged with Version A). Cases are numbered by descending order of agreement, amongst respondents, on the decision to sample.

Cases 1.5.3 and 1.4.3 showed the highest degree of agreement with 98.8% and 98.4% of physicians, respectively, choosing to sample the women presenting with these risk factors. As nulliparity was the only difference between these two cases, it would appear that its presence, or absence, was not a strong influence on behavior. Similarly, cases 1.2.1 and 1.3.1, 1.3.3 and 1.2.3, and 1.5.2 and 1.4.2, only differed by the risk factor of nulliparity. Little difference existed between physicians' decision in each case pair: respondents strongly agreed not to biopsy in cases 1.2.1 and 1.3.1 (91.2 and 91.1% respectively), and to biopsy in cases 1.3.3 and 1.2.3 (88.3% and 87.3%), and 1.5.2 and 1.4.2 (81.7% and 79.7%). Consequently, nulliparity was not felt to have an important influence on the decision to proceed with sampling. Table 11 also showed agreement with the SOGC "Guideline on Management of Abnormal Uterine Bleeding", as patients' presenting with all risk factors, such as case 1.5.3, were almost always sampled, whereas women with no risk factors, as in case 1.2.1, were unlikely to be sampled.

The combination of obesity and irregular cycles was the most likely pair of risk factors that led to sampling (87.3%), as in case 1.2.3. Irregular cycles and older age (39 years as opposed to 32 years) were the next most influential combination with 79.7% of physicians deciding to sample.

The last significant pairing of patient-related risk factors was obesity and older age where 67.5% of physicians agree to sample.

Table 11: Influence of patient-related risk factors on decision to sample the endometrium

	PATIENT-RELATED RISK FACTORS					
Cases	**Obesity**	**Irregular cycles**	**Nulliparity**	**Older Age**	**Would you sample the endometrium?**	**N (%)**
1.5.3	X	X	X	X	Yes	807 (98.8)
1.4.3	X	X		X	Yes	800 (98.4)
1.2.1					No	738 (91.2)
1.3.1			X		No	737 (91.1)
1.3.3	X	X	X		Yes	718 (88.3)
1.2.3	X	X			Yes	710 (87.3)
1.5.2		X	X	X	Yes	665 (81.7)
1.4.2		X		X	Yes	647 (79.7)
1.5.4	X		X	X	Yes	583 (71.7)
1.4.1				X	No	561 (69.3)
1.4.4	X			X	Yes	547 (67.5)
1.5.1			X	X	No	544 (67.0)
1.2.4	X				No	430 (52.9)
1.3.4	X		X		No	429 (52.9)
1.2.2		X			No	413 (51.0)
1.3.2		X	X		Yes	407 (50.4)

4.7.2 Influence of physician- and health-system- related variables on decision to sample in case scenarios

Physician gender, age, region of practice, practice environment, previous experience with young women with malignant or pre-malignant conditions, whether the physician operates on these patients, and familiarity with guidelines were explored as potential influential variables, on the decision to sample in the case scenarios. In order to decrease the chance that the associations found were due to chance, given the large number of comparisons, a significant p-value in this analysis was designated as <0.01.

The survey version received by physicians was found to frequently have an effect on the decision to sample in the case scenarios. Consequently, Cochran-Mantel-Haenszel statistics were used to give a stratified analysis of the relationship between the decision whether or not to sample, in each case, and the physician- and health-system-related variables, controlling for the survey version.

Table 12 shows the Cochran-Mantel-Haenszel statistic p-values from the bivariate analyses for each case by the physician- and health-system- related variables.

The physician's practice environment and whether the physician operates on young women with malignant or pre-malignant endometrial conditions had no significant effect on the decision to sample in any cases. Having previously had a young patient with endometrial cancer or a pre-cancerous lesion was the most common modifier of behavior where previous experience prompted a physician to sample more frequently in the case scenarios. In two cases (1.3.3 : a 32 year old nulliparous obese woman with irregular periods, and 1.3.4: a 32 year old nulliparous obese woman with regular heavy periods), familiarity with the SOGC guidelines was associated with a greater preponderance to sample these young women. Region of practice was only

significant in case 1.3.2, where the patient was a 32 year old nulliparous woman of normal weight with irregular periods. Physicians from Quebec, and Ontario were the least likely to sample in Version A and B respectively.

Decisions in cases 1.5.3, 1.4.3, 1.4.1 and 1.4.4 were not altered by any of physician and health-system variables. In cases 1.5.2, 1.4.2, 1.5.1, 1.2.4 and 1.2.2, the only significant influence prompting a physician to sample more frequently was the gynecologist having had a previous experience with young women diagnosed with malignant or pre-malignant conditions.

In order to explore how the physician and health-system variables influence the decision to sample in the remaining cases, the bivariate analyses of cases 1.2.1, 1.3.1, 1.3.3, 1.2.3, 1.5.4, 1.3.4, and 1.3.2 are presented in tables 13 to 19. Practice environment, and whether the physician operates on these young women, was not shown in these tables as they were consistently found not to be associated with the decision to sample.

Table 12: Cochran-Mantel-Haenszel statistic p-value for bivariate analysis of physician- and health-system- related variables on decision to sample in case scenarios

Cases	Physician Gender	Age	Region	Practice Environment	Experience*	Operate#	Familiarity with guidelines
1.5.3	0.08	0.02	0.8	0.1	0.03	0.7	0.04
1.4.3	0.03	0.1	0.3	0.2	0.4	0.2	0.2
1.2.1	0.02	**0.001**	0.6	0.2	**0.006**	0.3	0.2
1.3.1	**0.004**	**0.0006**	0.4	0.07	**0.0007**	0.2	0.9
1.3.3	**0.0002**	**0.0007**	0.02	0.04	**0.006**	0.06	**0.004**
1.2.3	**<0.0001**	**0.003**	0.02	0.04	**0.0001**	0.2	0.5
1.5.2	0.2	0.08	0.2	0.6	**0.0003**	0.2	0.8
1.4.2	0.1	0.7	0.06	0.7	**0.002**	0.9	0.1
1.5.4	0.01	**0.008**	0.08	0.4	0.01	0.9	0.2
1.4.1	0.3	0.6	0.03	0.9	0.08	0.4	0.9
1.4.4	0.01	0.02	0.09	0.4	0.2	0.7	0.2
1.5.1	0.4	0.06	0.1	0.8	**0.008**	0.4	0.03
1.2.4	0.3	0.6	0.07	0.4	**0.005**	0.6	0.02
1.3.4	0.6	0.2	0.2	0.1	**0.003**	0.9	**0.0002**
1.2.2	0.2	0.4	0.03	0.03	**<0.0001**	0.6	0.8
1.3.2	0.3	0.8	**0.005**	0.3	**<0.0001**	0.8	0.4

Bold = $p<0.01$

*Experience= physicians having had a young patient with endometrial cancer or atypical complex hyperplasia

Operate= Physicians who operate on women with endometrial cancer

4.7.3 Analysis of individual cases with significant influence of physician- and health-system related factors

In case 1.2.1 (a 32 year old multiparous woman of normal weight with regular heavy periods), younger physicians (≤ 39 years and 40-49 years) were more likely not to sample women with no patient-related risk factors than their older counterparts, as shown in Table 13. Physicians that had had a patient with a malignant or pre-malignant endometrial condition, however, were more likely to sample women when the only potential factor was heavy regular periods.

Similar trends are observed in case 1.3.1 (a 32 year old nulliparous woman of normal weight with regular heavy periods), however in addition male physicians were observed to sample more frequently than their female colleagues (Table 14).

Table 15 demonstrates that, in case 1.3.3, a 32 year old nulliparous obese patient with irregular cycles was more likely to be sampled by female gynecologists, those aged ≤ 49 years, physicians who had had experience with malignant and pre-malignant conditions and physicians who were familiar with the SOGC guidelines. If the same patient was multiparous, as in case 1.2.3, the same findings were obtained (Table 16) except that familiarity with the SOGC guidelines was not significant.

Analysis of case 1.5.4 (Table 17), with a 39 year old nulliparous obese woman with regular heavy periods, showed that physician age was a significant factor: for version A, physicians ≤ 49 years and for Version B, those ≤ 39 years, sampled more frequently than the older respondents.

Cases 1.3.4 and 1.3.2 demonstrated the greatest controversy with respect to the decision to proceed with sampling. In Table 18 (case 1.3.4), previous experience with malignant and pre-malignant conditions in young women and familiarity with the SOGC guidelines resulted in an increased likelihood of proceeding with endometrial sampling, in a 32 year old nulliparous obese woman with regular heavy periods. Case 1.3.2, which had a 32 year old patient with irregular

heavy cycles, normal weight and nulliparity, was the only situation where region was associated with the decision to sample (Table 19): physicians in Quebec and Ontario were less likely to proceed with sampling in this clinical situation.

Table 13: Influence of physician- and health-system- related factors on case 1.2.1

(32 year old multiparous woman of normal weight with regular heavy periods)

	VERSION A		**VERSION B**		**P-VALUE***
	Sample the endometrium		**Sample the endometrium**		
	Yes N (%)	**No N (%)**	**Yes N (%)**	**No N (%)**	
Overall	43 (10.5)	367 (89.5)	28 (7.0)	371 (93.0)	
Physician Gender					0.02
Male	27 (12.2)	194 (87.8)	18 (9.1)	18 (90.9)	
Female	15 (8.2)	168 (91.8)	8 (4.1)	187 (95.9)	
Physician Age					0.001
≤ 39	3 (3.3)	87 (96.7)	4 (3.6)	108 (96.4)	
40-49	12 (10.0)	108 (90.0)	6 (5.9)	96 (94.1)	
50-59	10 (9.0)	101 (91.0)	9 (9.2)	89 (90.8)	
≥60	17 (21.0)	64 (79.0)	8 (9.6)	75 (90.4)	
Region					0.6
Atlantic	6 (16.2)	31 (83.8)	3 (8.8)	31 (91.2)	
Quebec	9 (7.8)	107 (92.2)	9 (8.9)	92 (91.1)	
Ontario	15 (10.0)	135 (90.0)	7 (4.9)	137 (95.1)	
Prairies	7 (12.7)	48 (87.3)	4 (6.1)	62 (93.9)	
West	6 (11.5)	46 (88.5)	5 (9.3)	49 (90.7)	
Previous Experience					0.006
Yes	36 (12.6)	250 (87.4)	24 (8.2)	268 (91.8)	
No	6 (4.9)	116 (95.1)	4 (3.8)	102 (96.2)	
Familiar with Guidelines					0.2
Yes	27 (9.6)	255 (90.4)	18 (6.3)	267 (93.7)	
No	16 (12.7)	110 (87.3)	10 (8.8)	103 (91.2)	

***** Cochran-Mantel-Haenszel statistics

Table 14: Influence of physician- and health-system- related factors on case 1.3.1 (32 year old nulliparous woman of normal weight with regular heavy periods)

	VERSION A		VERSION B		P-VALUE*
	Sample the endometrium		Sample the endometrium		
	Yes N (%)	No N (%)	Yes N (%)	No N (%)	
Overall	42 (10.3)	366 (89.7)	30 (7.5)	371 (92.5)	
Physician Gender					0.004
Male	25 (11.4)	195 (88.6)	23 (11.6)	176 (88.4)	
Female	16 (8.8)	166 (91.2)	5 (2.6)	190 (97.4)	
Physician Age					0.0006
≤ 39	4 (4.5)	85 (95.5)	3 (2.7)	109 (97.3)	
40-49	10 (8.6)	107 (91.4)	7 (6.8)	96 (93.2)	
50-59	12 (10.7)	100 (89.3)	7 (7.2)	90 (92 .8)	
≥60	14 (17.1)	68 (82.9)	12 (14.3)	72 (85.7)	
Region					0.4
Atlantic	7 (18.9)	30 (81.1)	2 (5.9)	32 (94.1)	
Quebec	10 (8.7)	105 (91.3)	9 (8.7)	94 (91.3)	
Ontario	12 (8.2)	135 (91.8)	8 (5.6)	136 (94.4)	
Prairies	6 (10.7)	50 (89.3)	5 (7.6)	61 (92.4)	
West	7 (13.2)	46 (86.8)	6 (11.1)	48 (88.9)	
Previous Experience					0.0007
Yes	36 (12.6)	249 (87.4)	27 (9.3)	264 (90.7)	
No	5 (4.1)	116 (95.9)	3 (2.8)	105 (97.2)	
Familiar with Guidelines					0.9
Yes	28 (10.0)	252 (90.0)	23 (8.1)	262 (91.9)	
No	14 (11.10	112 (88.9)	7 (6.1)	107 (93.9)	

* Cochran-Mantel-Haenszel statistics

Table 15: Influence of physician- and health-system- related factors on case 1.3.3

(32 year old nulliparous obese woman with irregular heavy periods)

	VERSION A		**VERSION B**		**P-VALUE***
	Sample the endometrium		**Sample the endometrium**		
	Yes N (%)	**No N (%)**	**Yes N (%)**	**No N (%)**	
Overall	376 (90.8)	38 (9.2)	342 (85.7)	57 (14.3)	
Physician Gender					0.0002
Male	198 (89.2)	24 (10.8)	156 (78.8)	42 (21.1)	
Female	173 (93.0)	13 (7.0)	180 (92.3)	15 (7.7)	
Physician Age					0.0007
≤ 39	87 (96.7)	3 (3.3)	105 (93.8)	7 (6.2)	
40-49	111 (92.5)	9 (7.5)	88 (86.3)	14 (13 .7)	
50-59	97 (85.8)	16 (14.2)	79 (81.4)	18 (18.6)	
≥60	75 (90.4)	8 (9.6)	66 (78.6)	18 (21.4)	
Region					0.02
Atlantic	35 (94.6)	2 (5.4)	31 (91.2)	3 (8.8)	
Quebec	107 (92.6)	9 (7.8)	90 (87.4)	13 (12.6)	
Ontario	133 (87.5)	19 (12.5)	113 (79.0)	30 (21.0)	
Prairies	52 (92.9)	4 (7.1)	59 (89.4)	7 (10.6)	
West	49 (92.4)	4 (7.6)	49 (92.4)	4 (7.6)	
Previous Experience					0.006
Yes	269 (93.4)	19 (6.6)	253 (86.9)	38 (13.1)	
No	105 (84.7)	19 (15.3)	88 (82.2)	19 (17.8)	
Familiar with Guidelines					0.004
Yes	262 (92.2)	22 (7.8)	251 (88.4)	33 (11.6)	
No	111 (87.4)	16 (12.6)	90 (79.0)	24 (21.1)	

* Cochran-Mantel-Haenszel statistics

Table 16: Influence of physician- and health-system- related factors on case 1.2.3

(32 year old multiparous obese woman with irregular heavy periods)

	VERSION A		**VERSION B**		**P-VALUE***
	Sample the endometrium		**Sample the endometrium**		
	Yes N (%)	**No N (%)**	**Yes N (%)**	**No N (%)**	
Overall	276 (90.8)	38 (9.2)	334 (83.7)	65 (16.3)	
Physician Gender					<0.0001
Male	196 (88.3)	26 (11.7)	154 (77.4)	45 (22.6)	
Female	175 (94.1)	11 (5.9)	175 (90.2)	19 (9.8)	
Physician Age					0.005
≤ 39	86 (95.6)	4 (4.4)	100 (89.3)	12 (10.7)	
40-49	111 (92.5)	9 (7.5)	88 (87.1)	13 (12.9)	
50-59	95 (84.1)	18 (15.9)	78 (79.6)	20 (20.4)	
≥60	78 (94.0)	5 (6.0)	64 (76.2)	20 (23.8)	
Region					0.02
Atlantic	35 (94.6)	2 (5.4)	30 (88.2)	4 (11.8)	
Quebec	106 (91.4)	10 (8.6)	84 (83.2)	17 (16.8)	
Ontario	133 (87.5)	19 (12.5)	112 (77.8)	32 (22.2)	
Prairies	52 (92.9)	4 (7.1)	58 (87.9)	8 (12.1)	
West	50 (94.3)	3 (5.7)	50 (92.6)	4 (7.4)	
Previous Experience					0.0001
Yes	269 (93.4)	19 (6.6)	253 (86.6)	39 (13.4)	
No	105 (84.7)	19 (15.3)	80 (75.5)	26 (24.5)	
Familiar with Guidelines					0.5
Yes	259 (91.2)	25 (8.8)	241 (84.3)	45 (15.7)	
No	114 (89.8)	13 (10.2)	92 (82.1)	20 (17.9)	

* Cochran-Mantel-Haenszel statistics

Table 17: Influence of physician- and health-system- related factors on case 1.5.4

(39 year old nulliparous obese woman with regular heavy periods)

	VERSION A		VERSION B		P-VALUE*
	Sample the endometrium		Sample the endometrium		
	Yes N (%)	No N (%)	Yes N (%)	No N (%)	
Overall	312 (75.5)	101 (24.5)	271 (67.8)	129 (32.2)	
Physician Gender					0.01
Male	161 (72.5)	61 (27.5)	127 (63.5)	73 (36.5)	
Female	148 (80.0)	37 (20.0)	139 (71.6)	55 (28.4)	
Physician Age					0.008
≤ 39	74 (82.2)	16 (17.8)	87 (78.4)	24 (21.6)	
40-49	93 (77.5)	27 (22.5)	63 (60.6)	41 (39.4)	
50-59	78 (69.0)	35 (31.0)	61 (62.9)	36 (37.1)	
≥60	61 (74.4)	21 (25.6)	56 (66.7)	28 (33.3)	
Region					0.08
Atlantic	28 (75.7)	9 (24.3)	21 (61.8)	13 (38.2)	
Quebec	89 (76.7)	27 (23.3)	75 (72.8)	28 (27.2)	
Ontario	104 (68.9)	47 (31.1)	92 (63.9)	52 (36.1)	
Prairies	48 (85.7)	8 (14.3)	47 (71.2)	19 (28.8)	
West	43 (81.1)	10 (18.9)	36 (67.9)	17 (32.1)	
Previous Experience					0.01
Yes	228 (79.2)	60 (20.8)	201 (68.8)	91 (31.2)	
No	82 (66.7)	41 (33.3)	69 (64.5)	38 (35.5)	
Familiar with Guidelines					0.2
Yes	221 (77..8)	63 (22.2)	195 (68.4)	90 (31.6)	
No	89 (70.6)	37 (29.4)	76 (66.7)	38 (33.3)	

* Cochran-Mantel-Haenszel statistics

Table 18: Influence of physician- and health-system- related factors on case 1.3.4

(32 year old nulliparous obese woman with regular heavy periods)

	VERSION A		VERSION B		P-VALUE*
	Sample the endometrium		Sample the endometrium		
	Yes N (%)	No N (%)	Yes N (%)	No N (%)	
Overall	213 (51.8)	198 (48.2)	169 (42.2)	231 (57.8)	
Physician Gender					0.6
Male	110 (49.8)	111 (50.2)	86 (43.4)	112 (56.6)	
Female	102 (55.4)	82 (44.6)	80 (40.8)	116 (59.2)	
Physician Age					0.2
≤ 39	42 (46.7)	48 (53.3)	55 (49.1)	57 (50.9)	
40-49	67 (56.3)	52 (43.7)	36 (35.0)	67 (65.1)	
50-59	50 (44.2)	63 (55.8)	39 (40.2)	58 (59.8)	
≥60	51 (63.0)	30 (37.0)	37 (44.1)	47 (56.0)	
Region					0.2
Atlantic	19 (51.4)	18 (48.6)	16 (47.1)	18 (52.9)	
Quebec	63 (54.8)	52 (45.2)	40 (38.8)	63 (61.2)	
Ontario	71 (47.3)	79 (52.7)	53 (36.8)	91 (63.2)	
Prairies	33 (58.9)	23 (41.1)	33 (50.0)	33 (50.0)	
West	27 (50.9)	26 (49.1)	27 (50.9)	26 (49.1)	
Previous Experience					0.003
Yes	163 (57.0)	123 (43.0)	127 (43.5)	165 (56.5)	
No	49 (39.8)	74 (60.2)	41 (38.3)	66 (61.7)	
Familiar with Guidelines					0.0002
Yes	158 (55.8)	125 (44.2)	133 (46.7)	152 (53.3)	
No	53 (42.4)	72 (57.6)	36 (31.6)	78 (68.4)	

* Cochran-Mantel-Haenszel statistics

Table 19: Influence of physician- and health-system- related on case 1.3.2

(32 year old nulliparous woman of normal weight with irregular heavy periods)

	VERSION A		VERSION B		P-VALUE*
	Sample the endometrium		Sample the endometrium		
	Yes N (%)	No N (%)	Yes N (%)	No N (%)	
Overall	222 (54.2)	188 (45.8)	185 (46.5)	213 (53.5)	
Physician Gender					0.3
Male	114 (52.1)	105 (48.0)	89 (45.2)	108 (54.8)	
Female	104 (56.2)	81 (43.8)	93 (47.7)	102 (52.3)	
Physician Age					0.8
≤ 39	46 (51.7)	43 (48.3)	54 (48.2)	58 (51.8)	
40-49	68 (57.6)	50 (42.4)	46 (45.1)	56 (54.9)	
50-59	57 (50.4)	56 (49.6)	43 (44.8)	53 (55.2)	
≥60	46 (56.1)	36 (43.9)	40 (47.6)	44 (52.4)	
Region					0.005
Atlantic	23 (62.2)	14 (37.8)	18 (52.9)	16 (47.1)	
Quebec	54 (47.4)	60 (52.6)	47 (45.6)	56 (54.4)	
Ontario	76 (50.7)	74 (49.3)	54 (37.8)	89 (62.2)	
Prairies	39 (69.6)	17 (30.4)	33 (50.8)	32 (49.2)	
West	30 (56.6)	23 (43.4)	33 (62.3)	20 (37.7)	
Previous Experience					<0.0001
Yes	167 (58.4)	119 (41.6)	153 (52.8)	137 (47.2)	
No	53 (43.4)	69 (56.6)	31 (29.0)	76 (71.0)	
Familiar with Guidelines					0.4
Yes	154 (55.0)	126 (45.0)	134 (47.2)	150 (52.8)	
No	66 (52.0)	61 (48.0)	50 (44.2)	63 (55.8)	

* Cochran-Mantel-Haenszel statistics

4.8 Mixed effect logistic regression of the decision to sample by patient-, physicians- and health-system-related factors

A multiple logistic regression analysis was performed to assess the effect of patient-, physician-, and health-system-related factors jointly. An effect of multiple repeated measures needed to be taken into consideration as the results from all respondents were pooled, but answers from each physician may not be independent. A mixed effect logistic model was thus performed with patient, physician, and health-system factors as fixed variables, but using physician as the random effect. The model fit was statistically significant with $p < 0.0001$.

When compared to the multiple logistic regression, without the random term, the value of the odds ratio and confidence interval was altered with addition of the random term, but the order of magnitude was similar. The mixed effects logistic regression data is presented in Table 20.

All patient-related risk factors, studied in this survey, were significant with weight and cycle irregularity being the strongest factors leading to a decision to biopsy. As highlighted in the analysis of the individual cases, female gynecologists appeared to be more likely to biopsy than their male colleagues: OR 1.45, 95% CI 1.05 – 2.01.

Previous experience with a young woman with endometrial cancer or a pre-cancerous lesion was associated with an increased likelihood of proceeding with an endometrial sample, as seen in the case scenario analyses, with OR 2.23, 95% CI 1.64 – 3.03. Other physician- and health-system-related variables did not have a significant impact on the decision to biopsy, in this logistic model.

Table 20: Mixed effect logistic regression of patient-, physician- and health-system-related variables on the decision to sample the endometrium in young women with abnormal uterine bleeding

		OR	95% C I
Patient-related factors			
	Weight (obese vs. normal)	9.58	8.56 – 10.72
	Cycles (irregular vs. regular)	19.61	17.30 – 22.23
	Parity (nulliparous vs. multiparous)	1.84	1.66 – 2.05
	Age (39 vs. 32 years)	3.96	3.57 – 4.41
Physician-related factors			
Gender	Male	1	
	Female	1.45	1.05 – 2.01
Age (years)	≤39	0.79	0.50 – 1.24
	40-49	0.86	0.63 – 1.16
	50-59	0.92	0.80 – 1.08
	≥60	1	
Experience with a young patient with endometrial cancer or pre-malignant condition	Yes	2.23	1.64 – 3.03
	No	1	
Operate on woman with endometrial cancer	Yes	0.84	0.62 – 1.14
	No	1	
Familiar with guidelines	Yes	1.35	0.99 – 1.83
	No	1	

Table 20 (cont.)

	OR	**95% C I**
Health-system-related factors		
Region		
Atlantic	1	
Quebec	1.05	0.93 – 1.19
Ontario	1.11	0.86 – 1.42
Prairies	1.16	0.80 – 1.70
West	1.23	0.74 – 2.03
Practice Environment		
University	1	
Community with Ob/Gyn residents	0.93	0.80 – 1.07
Community without Ob/Gyn residents	0.86	0.64 – 1.15
Other	0.79	0.51 – 1.24
Version A vs. B	1.78	1.35 – 2.35

Model fit statistics: Generalized Chi Square = 8918.98; DF = 13,116, $p < 0.0001$

4.9 Respondent comments on SOGC guidelines "Management of Abnormal Uterine Bleeding"

Participants were invited to provide comments and suggestions with respect to the SOGC guidelines on management of abnormal uterine bleeding. Comments were reviewed by the principal investigator, and themes were extracted.

- Many participants felt that the guidelines needed to be updated and include the role of ultrasound in triaging young women with abnormal bleeding, as well as the impact of diabetes and hypertension on the decision to obtain a histological sample.
- Guidelines were not felt to contain information on women less than 40 years of age.
- Concerns arose that the guidelines may not be evidence-based, and that differences exist between SOGC and ACOG guidelines.
- An algorithm for management of these women was requested.
- A comment was made that if the guidelines became too rigid general practitioners may no longer manage these patients, or initiate biopsies, and would need to refer all women with abnormal uterine bleeding.
- Questions existed on the need for sequential testing if symptoms persist.
- Questions arose if the absolute weight or BMI was the important risk factor.

4.10 Respondent suggestions on management of young women with abnormal uterine bleeding

- The overwhelmingly frequent comment was on the use of ultrasound and/or sonohysterography in the management of these women to exclude polyps or fibroids, and to assist in the decision to sample the endometrium.

- Many participants stated that the change in menstrual pattern is more important than the actual risk factors, in addition to the presence of intermenstrual bleeding and/or postcoital bleeding.
- Minimal age for investigating women varied between 30 to 37 years of age.
- Frequently management was started in these young women first, and sampling the endometrium would be undertaken if treatment was unsuccessful at controlling symptoms. Some would only biopsy prior to proceeding with destruction of the endometrium (endometrial ablation).
- Physicians that have had a young patient diagnosed with endometrial cancer state that this experience has influenced their practice to be more proactive with endometrial sampling.

4.11 Comments/Suggestions on Survey

- Frequent comments noted that the survey was difficult to answer as cases were limited in information and no option was provided to individualize management. The cases were not felt to offer a realistic clinical picture as other variables that could influence a physician's decision were not presented. "Maybe/Depends" was requested as a possible answer on whether to biopsy the women portrayed in the cases.
- The most common criticism was that ultrasound was not a modality available to triage women.
- Participants felt that diabetes and hypertension were risk factors that were not included in the survey.
- Many physicians stated that duration of symptoms did not significantly influence their judgment, nor did the presence of regular periods.

- There was concern raised that the introduction to the survey, and the questions themselves, could have biased the results.

Chapter 5

Discussion

5.1 Practice pattern

Despite an incidence of endometrial cancer and atypical complex hyperplasia, in women 35-39 years, of only 5.17 (Public Health Agency of Canada, 2004) and 6.96 (Reed et al. 2009) per 100,000 women/year respectively, 70.3% of gynecologists reported having had a young patient with a malignant or pre-malignant endometrial condition. Finding that younger physicians had less experience with these patients was likely a direct reflection of their time in practice. Interestingly, gynecologists working in communities without ob/gyn residents reported less experience than their counterparts working with residents in community or academic centres, perhaps reflecting the influence of the learners themselves on practice pattern.

With respect to methods of obtaining a histological sample of the endometrium, most physicians employed the office pipelle, which has been shown to be readily available and demonstrates diagnostic accuracy, according to guidelines from the SOGC (2000).

This survey asked gynecologists the duration of symptoms they felt was sufficient to warrant sampling the endometrium. This question has not previously been addressed in the literature. Sampling after 12 months of symptoms was suggested by 55.7% of gynecologists. Given that 87.2% of respondents see young women with abnormal uterine bleeding within 6 months of receiving the referral, if a primary care practitioner asks a gynecologist to see a young woman in consultation within 6 months of symptom presentation, timely investigation of the endometrium could be undertaken. However, 26.2% of physicians indicated that other factors, such as failure of

previous medical management, and pre-existing menstrual pattern, took precedence, over duration of symptoms, in their decision to proceed with sampling.

5.2 Patient-related factors that influence the decision to sample the endometrium in young women with abnormal uterine bleeding

The case scenarios demonstrated agreement with the SOGC guidelines as 98.8% of physicians would sample young women presenting with the four patient-related risk factors investigated: older age, obesity, nulliparity and irregular cycles. Similarly, a young woman without any of these characteristics would not be sampled by 91.2% of gynecologists.

The cases also pointed to "nulliparity" as a relatively insignificant factor in swaying physicians to evaluate the endometrium. Previous studies have shown that nulliparity secondary to infertility is an independent risk factor for endometrial cancer in young women (Farquhar 1999, Parslov 1999, Soliman 2005). The lack of importance of nulliparity in this study might be due to the interpretation of the clinical context as infertility was not specified. However, in the logistic regression, when the responses of all the cases are pooled, the history of nulliparity prompted physicians to sample with an odds ratio of 1.84 (95% CI 1.66-2.05).

Obesity and irregular cycles were the combination leading most frequently to sampling in the analysis of the case scenarios followed by older age and irregular cycles, and obesity and older age. As individual factors, obesity, older age and irregular cycles did not commonly prompt endometrial evaluation suggesting young women need to have at least two of the three factors to result in a sample being performed, in the case scenarios. The mixed effect logistic regression, however, showed that the presence of irregular cycles was the strongest individual factor influencing physicians to perform an endometrial biopsy (OR 19.61, 95% CI 17.30-22.23), followed by obesity (OR 9.58, 95% CI 8.56-10.72). Indirectly this implies that women with

PCOS are more likely to be biopsied as amenorrhea or oligomenorrhea is one of three diagnostic criteria, and the majority of women with PCOS struggle with obesity.

These practice patterns supported the findings from a retrospective review of 310 endometrial biopsies, from women of mean age of 39 years ("older age" in our study), where the additional presence of irregular cycles conveyed a 14.3% probability of abnormal histology, and obtaining a histological sample in this context was suggested (Ash 1996).

A woman's age was felt to prompt evaluation in the logistic regression. Physicians agreed that the age of 39 years was a more significant risk factor than age 32 years. The resulting odds ratio may be somewhat attenuated as the gap in age range is limited. It is likely that a wider difference in age would offer a greater odds ratio.

5.3 Physician-related factors that influence the decision to sample the endometrium in young women with abnormal uterine bleeding

When physician- related factors were taken into consideration in the analysis of case scenarios, a gynecologist's previous experience with young women with malignant or pre-malignant endometrial conditions was the most common factor prompting an endometrial biopsy. This finding was echoed in the mixed effect logistic regression where physicians having had experience with these young women were over twice as likely to proceed with sampling than physicians that had not had previous contact with these patients. Previous experience prompted the decision to proceed with an endometrial sample more than a patient's history of nulliparity. Potentially, if physicians are more likely to sample young women because of previous experience, they may ultimately be more likely to diagnose women with these conditions, reinforcing their practice pattern. Previous studies have demonstrated that physicians' clinical experience will alter their perception of patient's risk. Tudiver et al (2001) studied focus groups

of family physicians to determine important factors that influence their decision to screen for cancer, in situations where the guidelines are not clear. With respect to physician factors they found that clinical practice experience played a significant role particularly if they had a previous experience missing a diagnosis. They also noted that physicians were more likely to screen earlier in their career. Davis and Taylor-Vaisey (1997) also demonstrated that clinical experience influences the adoption of guidelines.

In cases where factors other than previous experience influenced the decision to evaluate the endometrium, younger age and female gender of the physicians were associated with an increased probability of sampling in three and two of the seven cases, respectively. Both these physician characteristics were also associated with greater use of the office pipelle for endometrial sampling, and longer wait times from referral by the primary care practitioner to consultation with the gynecologist. The ease of the office pipelle may facilitate sampling on a more frequent basis. In addition, if women wait longer to see these physicians, their symptoms would have had a longer duration, thus physicians may be more likely to perform an endometrial biopsy, as 55.7%, 68.1% and 73.9% of physicians would biopsy at 12, 18 and 24 months respectively. Bertakis et al (1995), in a study that observed patient-physician interactions of 250 patients attending primary care and internal medicine clinics, found that female physicians engaged in more preventative services. Though endometrial sampling is not a form of primary prevention, its use in symptomatic women would be an example of secondary prevention. This association of female physicians performing more endometrial biopsies is supported in the logistic regression (OR 1.45, 95% CI 1.05-2.01).

Though familiarity with guidelines was only a significant factor to prompt endometrial sampling in the case where the patient was obese and nulliparous, and the case where she was obese,

nulliparous and had irregular cycles, both younger and female physicians were also found to be more familiar with the SOGC guidelines, in the previous bivariate analysis.

In cases where none of the four patient risk factors, or only nulliparity, was present, both older and male physicians were found to sample more than their younger and female counterparts. Again this may be an indirect reflection of familiarity with the SOGC guidelines, as in the absence of significant risk factors, sampling was not recommended. Choudhry et al (2005) concludes, in a systematic review of the relationship between clinical experience and quality of health care, that older physicians may be more likely to have poorer adherence to standards of care.

5.4 Health-system-related factors that influence the decision to sample the endometrium in young women with abnormal uterine bleeding

Region of practice was only a significant factor influencing the decision to sample the endometrium in the case where the patient was 32 years of age, nulliparous, of normal weight and had irregular cycles. When other factors were controlled in the logistic regression, region did not exert a significant influence on the physician's practice. Thus, there did not seem to be an important practice variation across the country.

Similarly, a specific practice environment was not found to prompt gynecologists to proceed with endometrial sampling, in case scenarios or the regression. Consequently, the presence of ob/gyn residents or the academic milieu did not influence the overall practice pattern.

5.5 Strengths

This study was the first census survey study in the Canadian gynecologist population. Being a mail-based study, access to technology was not a barrier. A census approach had the advantage of obtaining representation from all provinces. The Salant-Dillman survey methodology resulted in

an overall response rate of 56.5%. This is comparable previous estimated response rates of 54% (Asch 1997), but lower than a study with anesthesiologists, with similar methodology (70%, Turner et al. 2006). The Atlantic region had the greatest regional response rate (72.4%) likely due to the principal investigator's previous ties to this area. From the distribution of received eligible surveys (Figure 3), the second survey package mailed was noted to result in a sustained response until week 10. The third survey package however did not significantly increase the number of surveys received.

As opposed to previous retrospective studies, physician and health-system variables, and not only patient factors, were investigated for their impact on patient management. This resulted in the first study of its kind to provide a comprehensive overview of Canadian gynecologists' intended practice pattern of endometrial sampling, with respect to young women presenting with abnormal uterine bleeding.

The influence of case scenario order was taken into consideration by using two versions of the survey itself. This proved an important advantage of this study as an order bias was discovered, and thus, controlled in the bivariate analysis of the cases, and in the mixed effect logistic regression itself.

5.6 Limitations

As in most survey studies, non-response is a limitation. With an overall response rate of 56.5%, there may be a response bias that cannot be accounted for in the non-respondent analysis: particularly in view that gender and practice environment of non-respondents could not be elucidated. Given the discrepancy between the incidence of malignant and pre-malignant endometrial conditions, in women less than 40 years of age, and the number of respondents stating that they had had clinical experience with these patients, there is likely a bias towards

gynecologists that have had such patients, being more motivated to answer a survey on the matter.

Patient-variables such as a history of polycystic ovarian syndrome, family history of endometrial or colon cancer, or level of concern were not incorporated in the case scenarios, to reduce the permutations of variables. Investigating these variables with close-ended questions could however have been leading. A similar effect occurred when physicians were asked if time constraints were an influence in their practice.

With respect to the physician and health-system factors, in the regression analysis, only a previous experience with young women diagnosed with malignant or pre-malignant conditions and female gender were a significant influence. However, other variables not measured in this survey could also alter a gynecologist's decision.

As noted in the respondents' comments, the cases were limited in the variables presented to the physicians, and the responses did not allow for variations in clinical practice. It is acknowledged that this is a limitation imposed to allow for clearer interpretation of responses, and a quantitative analysis, particularly in the context of a large survey. Consequently the results may be limited in their representation of gynecologists' true practice.

The main criticism from the respondents was that ultrasound was not offered as a modality for triaging patients. Though not a method discussed in the SOGC "guidelines for management of abnormal uterine bleeding", transvaginal ultrasound and/or sonohysterography has been studied in this context. In a systematic review of the literature, Farquhar et al. (2003) concluded that, from eight studies, transvaginal ultrasound was a sensitive test in diagnosing endometrial hyperplasia in premenopausal women if an endometrial thickness cut-off greater or equal to 12 mm was used. Whether the endometrial thickness was measured in the early follicular phase of the menstrual cycle (when the lining would be at its thinnest) or at other times was not stated.

Farquhar et al suggested an algorithm where a sonohysterogram be performed if the endometrial thickness is at or above this thickness, to rule-out the presence of polyps or submucosal fibroids. The authors acknowledge that the studies cited do not indicate whether ultrasound use has ultimately changed clinical outcome or patient management. With respect to endometrial cancer or pre-malignant conditions, of interest in this study, endometrial thickness has not been specifically studied as a diagnostic predictor. Furthermore, the availability of this modality may vary by practice environment.

5.7 Implications for further educational and research opportunities

From the bivariate analyses of the case scenarios and the mixed effect logistic regression, women's risk factors for developing a malignant or pre-malignant condition appeared to be well recognized by gynecologists. A bias was present, however, in physicians who have had young patients with these conditions. Further discussion at meetings of the presence of endometrial abnormalities and impact of early diagnosis in young women could bring these issues to the forefront.

Education and future research is needed on the role of transvaginal ultrasonography and/or sonohysterography in the triaging of women with abnormal uterine bleeding as, in some areas, these modalities may be readily available, however in other circumstances may lead to delay in diagnosis.

This study only touched on the issue of length of symptoms which would prompt sampling by physicians. Further research is needed to clarify if the practice of obtaining a histological sample at 6 months of symptoms is appropriate.

Given these emerging questions, the SOGC's 2001 "Guidelines for management of abnormal uterine bleeding" should be updated specifically considering the management of women less than

40 years of age. Given that the majority of physicians responding to this survey have had experience with young women diagnosed with malignant or pre-malignant conditions, evidence-based information on conservative management of women seeking fertility should be provided. The role of ultrasound in these patients could be addressed, as could the lack of evidence with respect to the duration of symptoms warranting a histological sample.

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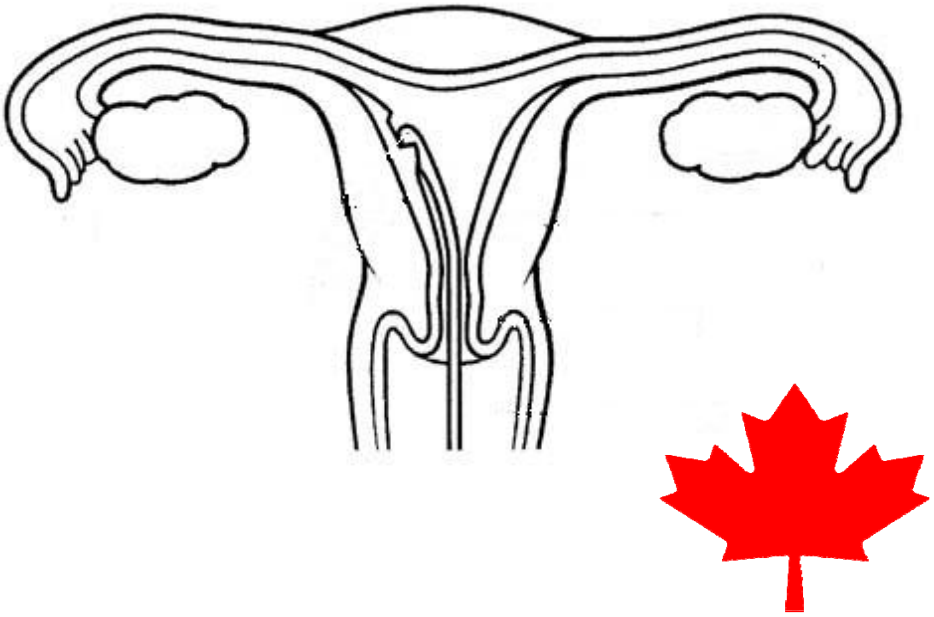
Appendix A

Survey (Version A)

Endometrial Cancer and Pre-malignant Conditions in Young Women:

Survey of Endometrial Sampling Practices by Canadian Gynecologists



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Endometrial Cancer and Pre-malignant Conditions in Young Women:

Survey of Endometrial Sampling Practices by Canadian Gynecologists

As you are aware, endometrial cancer and pre-malignant conditions are uncommon in women less than 40 years of age. Symptoms may be indistinguishable from other more prevalent causes of abnormal uterine bleeding. Early diagnosis, however, is important if conservative treatment is sought, as with women seeking fertility.

The purpose of this study is to determine characteristics that would prompt you to sample the endometrium (obtain a histological sample of the endometrial tissue by your method of choice) in a young woman presenting with abnormal uterine bleeding (prior to initiating medical management). For the purpose of this study, "Young women" refers to women less than 40 years of age.

Thank you in advance for your contribution.

Before you start:

Would you see young women with abnormal uterine bleeding in an office setting?

a. Yes – Please continue the survey at Section 1 on page 5

b. No

If No:

What does your practice entail?

a. Perinatology
b. Urogynecology
c. Gyne/oncology
d. Reproductive Endocrinology and Infertility
e. Research
f. Other: _____

Thank you for your response. For the physicians who do not manage women with dysfunctional bleeding, **please return your questionnaire in the pre-addressed envelope.**

Section 1: Decision Making

1.1 In your practice, would you sample the endometrium of young women (less than 40 years of age) that present with abnormal uterine bleeding :

- **a.** Never (Go to Section 2 on page 11)
- **b.** Infrequently (in less than 50% of these patients)
- **c.** Frequently (in 50% or more of these patients)
- **d.** Always

Case Scenarios:

Case A: A **32** year old **G2P2** woman presents with abnormal uterine bleeding for **18 months**. Would you sample the endometrium **if:**

1.2.1 She is of **normal weight** (70kg,BMI=23*) with heavy **regular** periods :

a. Yes

b. No

1.2.2 She is of **normal weight** (70kg,BMI=23*) with heavy **irregular** periods :

a. Yes

b. No

1.2.3 She is **obese** (100kg, BMI=35*) with heavy **irregular** periods:

a. Yes

b. No

1.2.4 She is **obese** (100kg, BMI=35*) with heavy **regular** periods:

a. Yes

b. No

* ***WHO Classification of weight by BMI (kg/m^2)*** *2004*

Normal	*18.5-24.9*
Overweight	*≥ 25*

Case B: A **32** year old **nulligravid** woman presents with abnormal uterine bleeding for **18 months**. Would you sample the endometrium **if:**

1.3.1 She is of **normal weight** (70kg, BMI=23*) with heavy **regular** periods:

- **a.** Yes
- **b.** No

1.3.2 She is of **normal weight** (70kg, BMI=23*) with heavy **irregular** periods:

- **a.** Yes
- **b.** No

1.3.3 She is **obese** (100kg, BMI=35*) with heavy **irregular** periods:

- **a.** Yes
- **b.** No

1.3.4 She is **obese** (100kg, BMI=35*) with heavy **regular** periods:

- **a.** Yes
- **b.** No

Case C: A **39** year old **G2P2** woman presents with abnormal uterine bleeding for **18 months**. Would you sample the endometrium **if:**

1.4.1 She is of **normal weight** (70kg, BMI=23*) with heavy **regular** periods:

- **a.** Yes
- **b.** No

1.4.2 She is of **normal weight** (70kg, BMI=23*) with heavy **irregular** periods:

- **a.** Yes
- **b.** No

1.4.3 She is **obese** (100kg, BMI=35*) with heavy **irregular** periods:

- **a.** Yes
- **b.** No

1.4.4 She is **obese** (100kg, BMI=35*) with heavy **regular** periods:

- **a.** Yes
- **b.** No

Case D: A **39** year old **nulligravid** woman presents with abnormal uterine bleeding for **18 months**. Would you sample the endometrium **if:**

1.5.1 She is of **normal weight** (70kg, BMI=23*) with heavy **regular** periods:

- **a.** Yes
- **b.** No

1.5.2 She is of **normal weight** (70kg, BMI=23*) with heavy **irregular** periods:

- **a.** Yes
- **b.** No

1.5.3 She is **obese** (100kg, BMI=35*) with heavy **irregular** periods:

- **a.** Yes
- **b.** No

1.5.4 She is **obese** (100kg, BMI=35*) with heavy **regular** periods:

- **a.** Yes
- **b.** No

1.6 What duration of symptoms do you feel is sufficiently significant to warrant an endometrial biopsy in a young woman with abnormal uterine bleeding:

- **a.** 12 months
- **b.** 18 months
- **c.** 24 months
- **d.** Other: Specify (in months) _____

1.7 Does a family history of endometrial or colon cancer influence your choice to sample the endometrium of a young woman with abnormal uterine bleeding:

- **a.** Yes
- **b.** No

1.8 Do time constraints influence your choice to sample the endometrium of a young woman with abnormal uterine bleeding:

- **a.** Yes
- **b.** No

1.9 Does the level of patient concern influence your choice to sample the endometrium of a young woman with abnormal uterine bleeding:

- **a.** Yes
- **b.** No

Section 2: Practice Pattern

2.1 Have you ever had a patient less than 40 years of age ("young" woman) with endometrial cancer or complex hyperplasia with atypia?

a. Yes: When was the most recent encounter (number of days, months or years)

_____

b. No (Go to Question 2.3)

2.2 Have you ever medically treated a young woman with endometrial cancer, or complex hyperplasia with atypia to preserve fertility?

a. Yes: When was the most recent encounter (number of days, months or years)

_____

b. No

2.3 Do you operate on women with endometrial cancer?

a. Yes (Go to Question 2.5)

b. No

2.4 If **No**, do you need to refer affected patients to a different hospital for care?

a. Yes: If to a different city, what is the distance in kilometers?

_____

b. No

2.5 Do you primarily sample the endometrium by:

- **a.** Office pipelle biopsy
- **b.** Hysteroscopy, dilatation and curettage
- **c.** Other:_____

2.6 How long would young women (less than 40 years old) with abnormal uterine bleeding wait to see you in consultation, after being referred from their primary care health practitioner?

- **a.** Less than 6 months
- **b.** 6-12 months
- **c.** More than 12 months

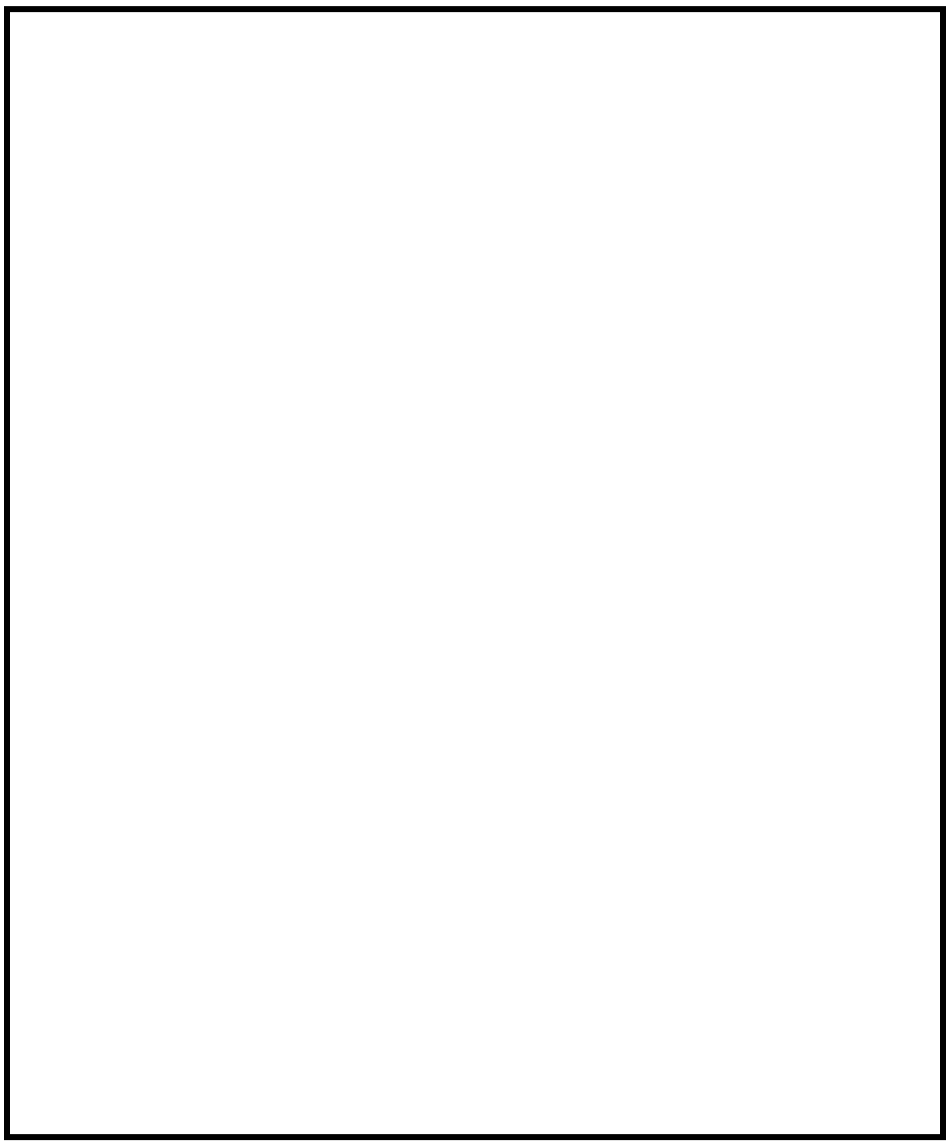
2.7 Are you familiar with the recommendations from the SOGC (Society of Obstetricians and Gynecologists of Canada)'s "Guideline for the Management of Abnormal Uterine Bleeding" 2001?

- **a.** Yes
- **b.** No (Go to Section 3, page 14)

2.8 Do you find the guideline helpful with respect to its recommendations for sampling the endometrium, to exclude malignancies or pre-malignant conditions, for women less than 40 years of age?

- **a.** Very helpful
- **b.** Somewhat helpful
- **c.** Not at all helpful

2.9 How could the guidelines be clarified?



Section 3:

3.1 In your practice do you primarily function as a:

- **a.** Generalist
- **b.** Reproductive endocrinologist
- **c.** Gynecology oncologist
- **d.** Urogynecologist
- **e.** Other_____

3.2 In what year did you graduate from training as a generalist OB/GYN?

_____

3.3 How long have you been in practice (in years)?

_____

3.4 In what kind of setting do you practice?

- **a.** University affiliated or academic centre
- **b.** Community-based with Ob/Gyn resident involvement
- **c.** Community-based without Ob/Gyn resident involvement
- **d.** Other:_____

3.5 Are you: **a.** Male **b.** Female

3.6 How old are you?

a. ≤ 39 years

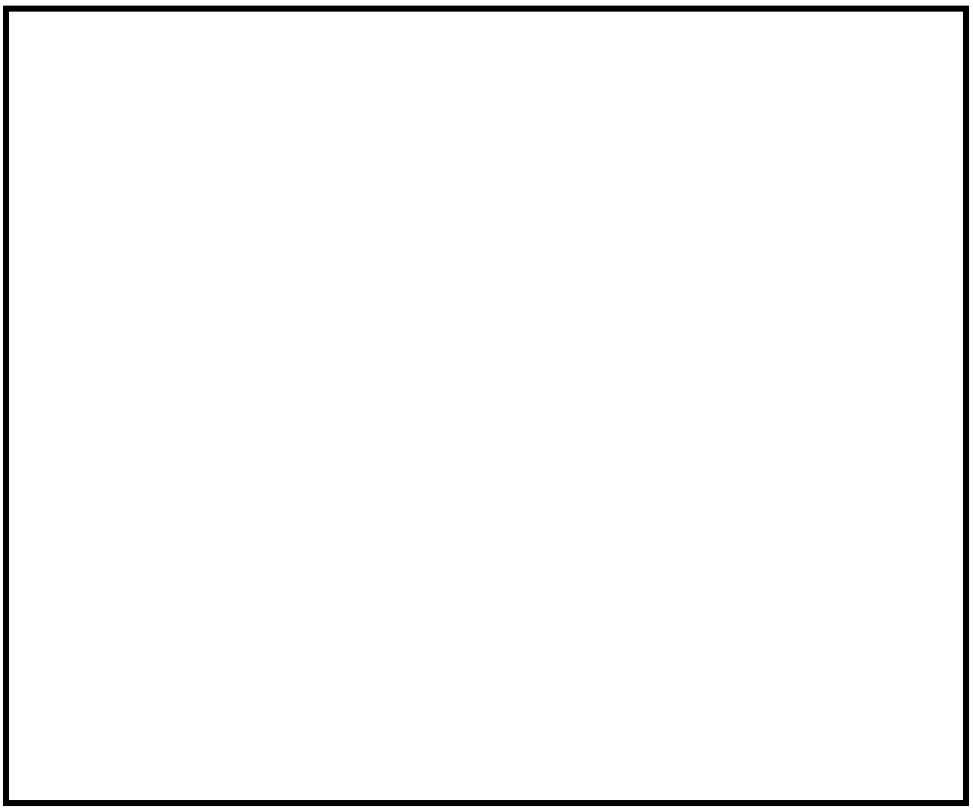
b. 40-49 years

c. 50-59 years

d. ≥ 60 years

Section 4: Comments

You have completed the questionnaire. Please use the remaining space in this booklet for any comments/questions on this survey, or on assessing women less than 40 years of age for endometrial cancer and pre-malignant conditions.



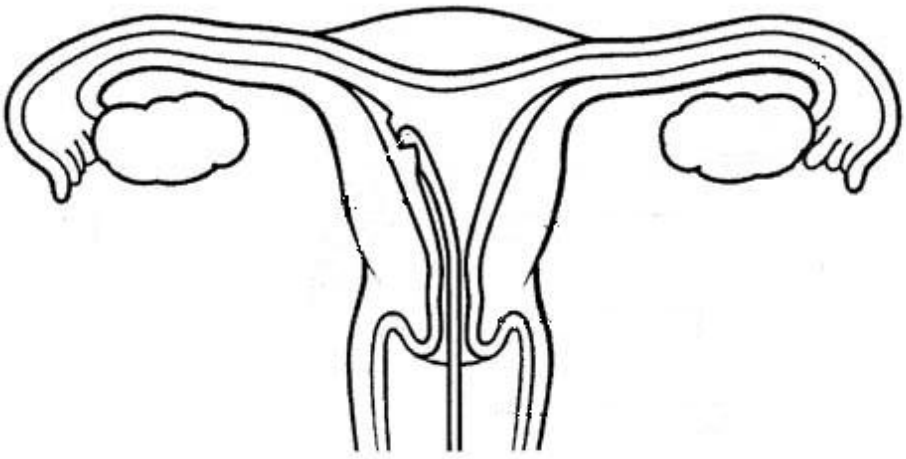
Thank you for your participation

Appendix B

French Survey (Version A)

Le Cancer de l'Endomètre et ses Conditions Précurseurs:

Sondage de l'Investigation de l'Endomètre Pratiquée par les Gynécologues Canadiens



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Le Cancer de l'Endomètre et ses Conditions Précurseurs:

Sondage de l'Investigation de l'Endomètre Pratiquée par les Gynécologues Canadiens

Comme vous le savez, le cancer de l'endomètre et ses conditions précurseurs ne sont pas communs chez les femmes âgées de moins de 40 ans. Les symptômes peuvent être difficiles à distinguer d'autres causes plus communes de saignement utérin anormal. Par contre, un diagnostic précoce est important pour permettre un traitement conservateur, particulièrement chez les femmes désirant préserver leur fertilité.

La raison d'être de ce projet de recherche est de déterminer les caractéristiques des patientes qui vous conduiraient à obtenir un échantillon histologique de l'endomètre (par votre méthode de choix) chez une jeune femme qui présente avec des saignements utérins anormaux (avant d'entreprendre des traitements médicaux). Pour cette étude, le terme « jeune femme » indique une femme âgée de moins de 40 ans.

Merci en avance pour votre contribution.

Avant de commencer:

Dans votre pratique, est-ce que vous voyez des jeunes femmes (moins de 40 ans) qui se présentent avec des saignements utérins anormaux?

c. Oui – veuillez passez à la section 1, page 5

d. Non

Si non:

Comment décrirez-vous votre pratique ?

g. Périnatalogie

h. Urogynécologie

i. Exclusivement gynéco-oncologie

j. Endocrinologie de la reproduction et infertilité

k. Recherche

l. Autre: _____

Merci pour votre collaboration. Si vous ne voyez pas ces jeunes femmes, **veuillez retournez le sondage dans l'enveloppe inclus.**

Section 1: Décisions

1.1. Dans votre pratique, est-ce que vous faites des biopsies de l'endomètre dans des jeunes femmes qui présentent avec des saignements anormaux ?

e. Jamais (Allez à la Section 2 sur page 11)
f. Occasionnellement (dans moins de 50% des cas)
g. Fréquemment (dans 50% ou plus des cas)
h. Toujours

Cas Cliniques:

Cas A: Une femme âgée de **32** ans, **G2P2**, se présente avec des saignements utérins anormaux depuis **18 mois**. Lui feriez-vous une biopsie de l'endomètre **si** :

1.2.5 Elle est de poids **normal** (70kg,IMC=23*) avec des saignements **réguliers** et abondants :

c. Oui

d. Non

1.2.6 Elle est de poids **normal** (70kg,IMC=23*) avec des saignements **irréguliers** et abondants:

c. Oui

d. Non

1.2.7 Elle est **obèse** (100kg, IMC=35*) avec des saignements **irréguliers** et abondants:

c. Oui

d. Non

1.2.8 Elle est **obèse** (100kg, IMC=35*) avec des saignements **réguliers** et abondants:

c. Oui

d. Non

* ***Classification du WHO de poids par IMC (kg/m^2)*** *2004*

Normal	*18.5-24.9*
Surpoids	*≥ 25*

Cas B: Une femme âgée de **32** ans, **nullipare**, se présente avec des saignements utérins anormaux depuis **18 mois**. Lui feriez-vous une biopsie de l'endomètre **si**:

1.3.1 Elle est de poids **normal** (70kg,IMC=23*) avec des saignements **réguliers** et abondants:

- **c.** Oui
- **d.** Non

1.3.2 Elle est de poids **normal** (70kg,IMC=23*) avec des saignements **irréguliers** et abondants:

- **c.** Oui
- **d.** Non

1.3.3 Elle est **obèse** (100kg, IMC=35*) avec des saignements **irréguliers** et abondants:

- **c.** Oui
- **d.** Non

1.3.4 Elle est **obèse** (100kg, IMC=35*) avec des saignements **réguliers** et abondants:

- **c.** Oui
- **d.** Non

Cas C : Une femme âgée de **39** ans, **G2P2**, se présente avec des saignements utérins anormaux depuis **18 mois**. Lui feriez -vous une biopsie de l'endomètre **si** :

1.4.1 Elle est de poids **normal** (70kg,IMC=23*) avec des saignements **réguliers** et abondants:

a. Oui

b. Non

1.4.2 Elle est de poids **normal** (70kg,IMC=23*) avec des saignements **irréguliers** et abondants:

a. Oui

b. Non

1.4.3 Elle est **obèse** (100kg, IMC=35*) avec des saignements **irréguliers** et abondants:

a. Oui

b. Non

1.4.4 Elle est **obèse** (100kg, IMC=35*) avec des saignements **réguliers** et abondants:

a. Oui

b. Non

Cas D : Une femme âgée de **39** ans, **nullipare**, se présente avec des saignements utérins anormaux depuis **18 mois**. Lui feriez-vous une biopsie de l'endomètre **si :**

1.5.1 Elle est de poids **normal** (70kg,IMC=23*) avec des saignements **réguliers** et abondants:

a. Oui

b. Non

1.5.2 Elle est de poids **normal** (70kg,IMC=23*) avec des saignements **irréguliers** et abondants:

a. Oui

b. Non

1.5.3 Elle est **obèse** (100kg, IMC=35*) avec des saignements **irréguliers** et abondants:

a. Oui

b. Non

1.5.4 Elle est **obèse** (100kg, IMC=35*) avec des saignements **réguliers** et abondants:

a. Oui

b. Non

1.6 Les symptômes doivent durer depuis combien de temps pour vous inciter à faire une biopsie de l'endomètre chez une jeune femme avec des saignements utérins anormaux (SUA)?

e. 12 mois

f. 18 mois

g. 24 mois

h. Autre: Spécifiez (en mois) _____

1.7 Est-ce qu'une histoire familiale de cancer de l'endomètre ou du côlon influence votre décision de faire une biopsie de l'endomètre chez une jeune femme avec des SUA ?

c. Oui

d. Non

1.8 Est-ce que les contraintes de temps influencent votre décision de faire une biopsie de l'endomètre chez une jeune femme avec des SUA?

c. Oui

d. Non

1.9 Est-ce que le niveau d'inquiétude de la patiente influence votre décision de faire une biopsie de l'endomètre chez une jeune femme avec des SUA?

c. Oui

d. Non

Section 2: Sommaire de votre Pratique

2.1 Avez-vous déjà eu une patiente âgée de moins de 40 ans (« jeune femme ») avec un cancer de l'endomètre ou hyperplasie complexe avec atypie?

c. Oui: Quand étais la dernière fois (en jours, mois ou années)

_____

d. Non (Allez à la Question 2.3)

2.2 Avez-vous déjà traité une jeune femme avec un cancer de l'endomètre d'une façon médicale pour maintenir sa fertilité?

c. Oui: Quand étais la dernière fois (en jours, mois ou années)

_____

d. Non

2.5 Est-ce que vous faite la chirurgie pour le cancer de l'endomètre vous-même?

c. Oui (Allez à la Question 2.5)

d. Non

2.6 Si **Non**, Avez-vous besoin de référer la patiente à un autre hôpital pour les soins?

c. Oui: Si à une autre ville, quelle est la distance en kilomètre?

_____

d. Non

2.5 Est-ce que vous faites des biopsie de l'endomètre par:

d. Biopsie de l'endomètre en cabinet

e. Hystéroscopie, dilatation et curetage

f. Autre:_____

2.6 Quelle est la durée d'attende pour une consultation d'une jeune femme avec des saignements utérins anormaux, référée par son praticien de la santé ?

d. Moins que 6 mois

e. 6-12 mois

f. Plus de 12 mois

2.7 Etes-vous au courrant des recommandations du document (2001) de la SOGC (Société des Obstétriciens et Gynécologues du Canada) "Lignes Directrices sur la Prise en Charge du Saignement Utérin Anormal"?

c. Oui

d. Non (Allez à la Section 3, page 14)

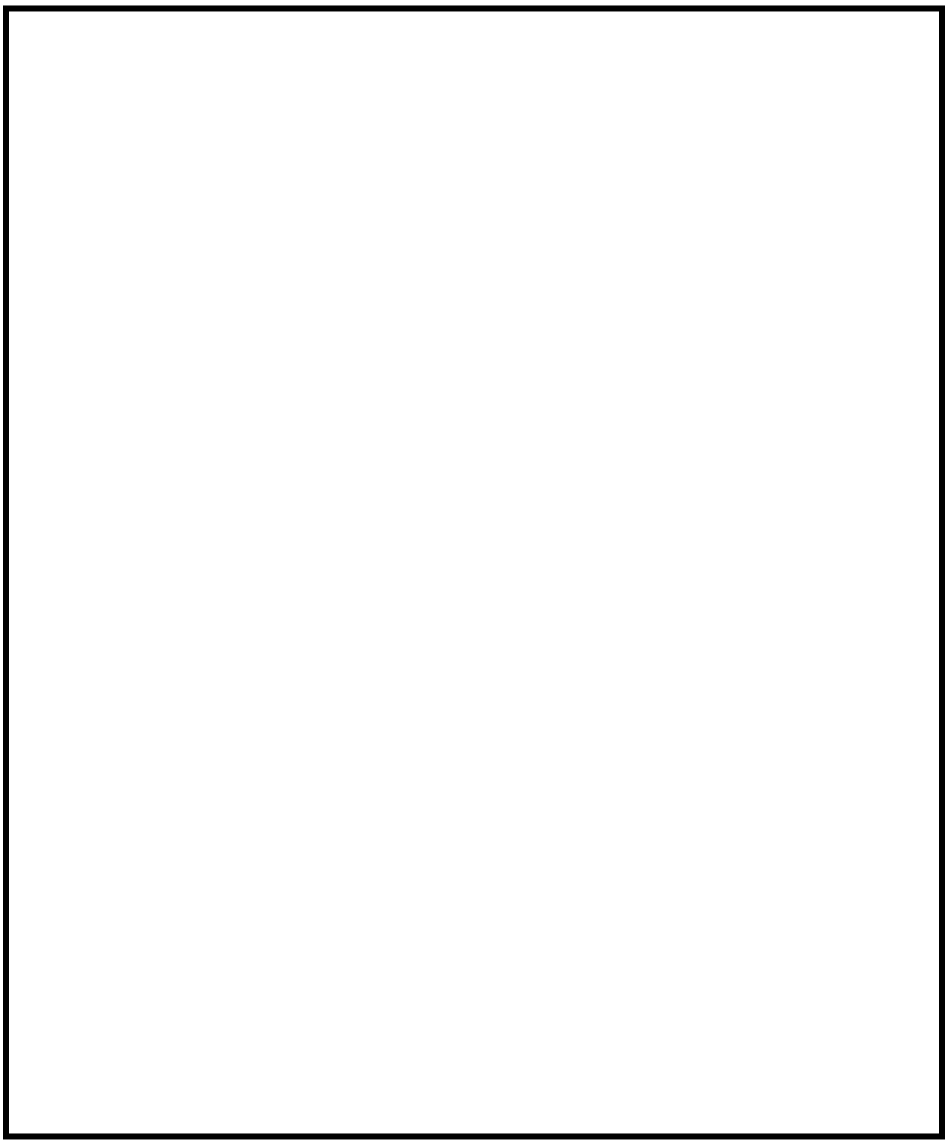
2.8 Avez-vous trouvé ce document utile en fait de ses recommandations sur l'évaluation de l'endomètre, pour exclure le cancer et ses conditions précurseurs, chez les femmes âgées de moins de 40 ans?

d. Très utile

e. Un peu utile

f. Pas du tous utile

2.9 Comment ces lignes directrices pourraient-elles être clarifiées?



Section 3:

3.1 Dans votre pratique, fonctionnez-vous principalement en:

- **f.** Gynécologie et obstétrique générale
- **g.** Endocrinologie de la reproduction
- **h.** Gynéco oncologie
- **i.** Urogynécologie
- **j.** Autre_____

3.2 En quelle année avez-vous complété votre résidence en gynécologie et obstétrique?

_____

3.3 Depuis combien d'année êtes-vous en pratique?

_____

3.4 Dans quel milieu pratiquez-vous?

- **e.** Centre universitaire ou académique
- **f.** En communauté avec des résidents en Ob/Gyn
- **g.** En communauté sans résidents en Ob/Gyn
- **h.** Autre:_____

1.1 Êtes vous: **a**. Homme **b.** Femme

1.2 Quel est votre âge? **a**. ≤ 39 ans

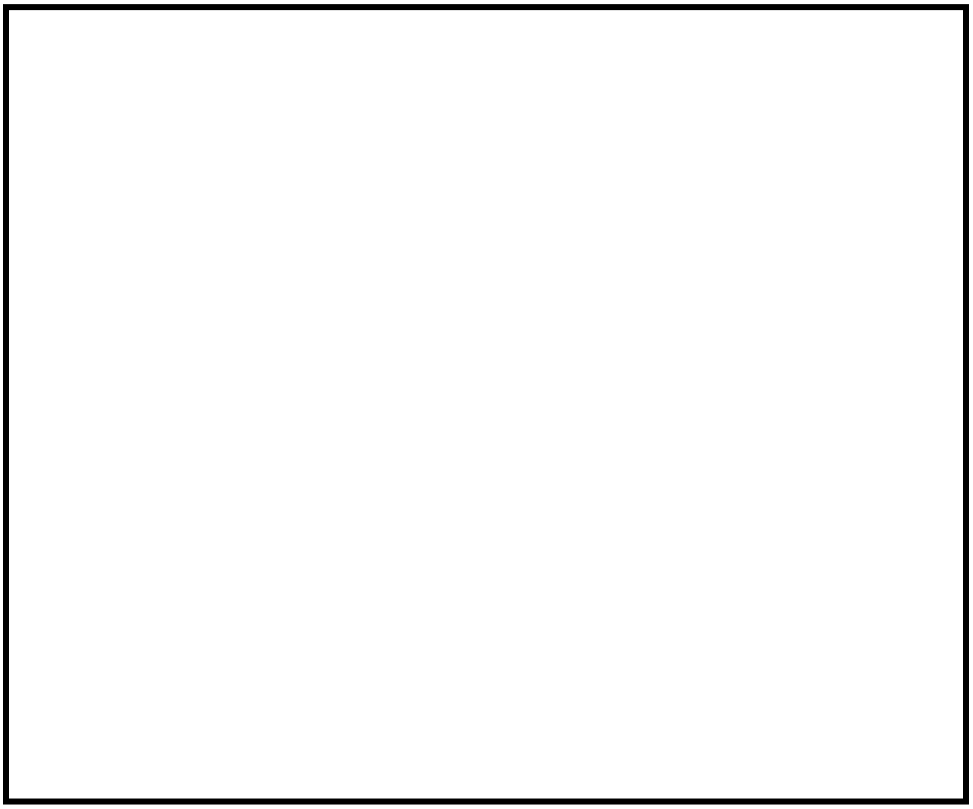
b. 40-49 ans

c. 50-59 ans

d. ≥ 60 ans

Section 4: Commentaires

Vous avez complété le questionnaire. Veuillez partager vos commentaires ou questions sur le sondage, ou sur l'évaluation des femmes de moins de 40 ans pour le cancer de l'endomètre et ses conditions précurseurs dans l'espace ci-dessous.



Merci de votre participation

Appendix C

Letter of Invitation

STEPHANIE PALERME, MD, FRCSC
Department of Obstetrics & Gynecology
Department Head: Dr. M. McGrath (613) 548-1372
Kingston General Hospital
Kingston, Ontario, K7L 2V7

613-542-9473 Fax 613-533-6779

Dear Dr.[last name],

As you are aware, abnormal uterine bleeding (AUB) is a common problem in young women (less than 40 years of age). Despite the myriad of benign causes, endometrial cancer and pre-malignant conditions need to be considered in some women.
There is little information, however, on which factors prompt gynecologists to sample the endometrium in these women.

I would thus like to invite you to participate in this National survey study on endometrial sampling practices by Canadian gynaecologists, dealing with young women presenting with AUB. Your completed questionnaire is important in order to obtain a comprehensive understanding of the Canadian practice pattern, and potentially identify areas of controversy that would benefit from further research. The survey should only require a few minutes of your time.

Please return your survey in the self addressed envelope. Upon receipt of the questionnaire, your name will be removed from the mailing list and you will receive no further correspondence. Your responses will be completely confidential as they will only be used in summarized form. The final results of this study will be submitted for publication to a National journal.

This study has been reviewed for ethical compliance by the Queen's University Health Sciences and Affiliated Teaching Hospitals Research Ethics Board, and is part of my Master's thesis in clinical Epidemiology. If you have any questions or comments with respect to this study, please do not hesitate to contact me at the above number, or by Email: palerme@queensu.ca. For any concerns about your rights as a research subject please contact – Dr. Albert Clark – Chair of the Queen's University Health Sciences and Affiliated Teaching Hospitals Research Ethics Board at (613) 533-6081.

Thank you in advance for your contribution to this study.

Yours Sincerely,

Stephanie Palerme, MD

Appendix D

Reminder/Thank You Letter

STEPHANIE PALERME, MD, FRCSC
Department of Obstetrics & Gynecology
Department Head: Dr. M. McGrath (613) 548-1372
Kingston General Hospital
Kingston, Ontario, K7L 2V7

613-542-9473 Fax 613-533-6779

Dear Dr.[last name],

3 weeks ago I sent you a survey investigating endometrial sampling practices of Canadian gynaecologists in the context of young women (less than 40 years of age) presenting with abnormal uterine bleeding. If you have already returned the questionnaire, please accept my sincere gratitude.

If you have not yet had the opportunity to complete the survey, I would ask for a few moments of your time for this important study. Your response is essential in order to obtain results that reflect the Canadian practice pattern and help identify potential areas of research that could improve the care of these women.

If you have any questions or comments with respect to this study, please do not hesitate to contact me at the above number, or by Email: palerme@queensu.ca. For any concerns about your rights as a research subject please contact – Dr. Albert Clark – Chair of the Queen's University Health Sciences and Affiliated Teaching Hospitals Research Ethics Board at (613) 533-6081.

Thank you in advance for your contribution to this study.

Yours Sincerely,

Appendix E

Letter with 2nd Mail-out

STEPHANIE PALERME, MD, FRCSC
Department of Obstetrics & Gynecology
Department Head: Dr. M. McGrath (613) 548-1372
Kingston General Hospital
Kingston, Ontario, K7L 2V7

613-542-9473 Fax 613-533-6779

Dear Dr.[last name],

Approximately 6 weeks ago you received a survey on endometrial sampling practices of Canadian gynaecologists in the context of young women (less than 40 years of age) presenting with abnormal uterine bleeding. I would like to emphasize the importance of your participation in order to obtain results that reflect the Canadian practice pattern and contribute to our knowledge on this issue.

As I have not yet received your response I am forwarding you an additional copy of the survey. Completing this questionnaire should only require a few minutes from your busy schedule. If you have already returned the questionnaire, I am very grateful for your time.

The surveys are identified only by code. Once the survey is received your name will be withdrawn from the mailing list and no further contact will be made. Your responses will be completely confidential.

If you have any questions or comments with respect to this study, please do not hesitate to contact me at the above number, or by Email: palerme@queensu.ca. For any concerns about your rights as a research subject please contact – Dr. Albert Clark – Chair of the Queen's University Health Sciences and Affiliated Teaching Hospitals Research Ethics Board at (613) 533-6081.

Thank you in advance for your contribution to this study.

Yours Sincerely,

Appendix F

Letter with 3rd Mail-Out

STEPHANIE PALERME, MD, FRCSC
Department of Obstetrics & Gynecology
Department Head: Dr. M. McGrath (613) 548-1372
Kingston General Hospital
Kingston, Ontario, K7L 2V7
613-542-9473 Fax 613-533-6779

Dear Dr.[last name] ,

I am writing to you one last time to invite you to participate in the study on endometrial sampling practices of Canadian gynaecologists in the context of young women (less than 40 years of age) presenting with abnormal uterine bleeding.

Your completed questionnaire is essential to obtain a comprehensive understanding of the Canadian practice pattern, and to identify areas requiring further research. The information you provide is completely confidential.

As this study is drawing to a close, I would sincerely appreciate if you could complete the included questionnaire, which should only require a few minutes of your time. If you have already returned the questionnaire, I am very grateful for your time.

If you have any questions or comments with respect to this study, please do not hesitate to contact me at the above number, or by Email: palerme@queensu.ca. For any concerns about your rights as a research subject please contact – Dr. Albert Clark – Chair of the Queen's University Health Sciences and Affiliated Teaching Hospitals Research Ethics Board at (613) 533-6081.

Thank you in advance for your contribution to this study.

Yours Sincerely,

Appendix G

Ethics Approval

QUEEN'S UNIVERSITY HEALTH SCIENCES & AFFILIATED TEACHING HOSPITALS RESEARCH ETHICS BOARD

March 10, 2009

This Ethics Application was subject to:

☐ Full Board Review
Meeting Date:
☒ Expedited Review

Dr. Stephanie Palerme
Department of Obstetrics & Gynaecology
Room 3022, Etherington Hall
Queen's University

Dear Dr. Palerme,

Study Title: **Endometrial Cancer and Pre-Malignant Conditions in Young Women: Survey of Endometrial Sampling Practices By Canadian Gynecologists**
Co-Investigators: **Dr. W. Mackillop, Dr. P. Peng, Ms. H. Ouellette-Kuntz**

I am writing to acknowledge receipt of your recent ethics submission. We have examined the protocol, information letter and survey for your project (as stated above) and consider it to be ethically acceptable. This approval is valid for one year from the date of the Chair's signature below. This approval will be reported to the Research Ethics Board. Please attend carefully to the following list of ethics requirements you must fulfill over the course of your study:

- **Reporting of Amendments:** If there are any changes to your study (e.g. consent, protocol, study procedures, etc.), you must submit an amendment to the Research Ethics Board for approval. (see http://www.queensu.ca/vpr/reb.htm).

- **Reporting of Serious Adverse Events:** Any unexpected serious adverse event occurring locally must be reported within 2 working days or earlier if required by the study sponsor. All other serious adverse events must be reported within 15 days after becoming aware of the information.

- **Reporting of Complaints:** Any complaints made by participants or persons acting on behalf of participants must be reported to the Research Ethics Board within 7 days of becoming aware of the complaint. Note: All documents supplied to participants must have the contact information for the Research Ethics Board.

- **Annual Renewal:** Prior to the expiration of your approval (which is one year from the date of the Chair's signature below), you will be reminded to submit your renewal form along with any new changes or amendments you wish to make to your study. If there have been no major changes to your protocol, your approval may be renewed for another year.

Yours sincerely,

Albert Clark
Chair, Research Ethics Board

March 11, 2009
Date

ORIGINAL TO INVESTIGATOR - COPY TO DEPARTMENT HEAD- COPY TO HOSPITAL(S) /P&T (If appropriate) - FILE COPY

Study Code: OBGY-188-09

- **Investigators please note that if your trial is registered by the sponsor, you must take responsibility to ensure that the registration information is accurate and complete**

QUEEN'S UNIVERSITY HEALTH SCIENCES & AFFILIATED TEACHING HOSPITALS RESEARCH ETHICS BOARD

The membership of this Research Ethics Board complies with the membership requirements for Research Ethics Boards as defined by the Tri-Council Policy Statement; Part C Division 5 of the Food and Drug Regulations, OHRP, and U.S DHHS Code of Federal Regulations Title 45, Part 46 and carries out its functions in a manner consistent with Good Clinical Practices.

Federalwide Assurance Number : #FWA00004184
#IRB00001173

Current 2008 membership of the Queen's University Health Sciences & Affiliated Teaching Hospitals Research Ethics Board

Dr. A.F. Clark	Emeritus Professor, Department of Biochemistry, Faculty of Health Sciences, Queen's University (Chair)
Dr. H. Abdollah	Professor, Department of Medicine, Queen's University
Dr. C. Cline	Assistant Professor, Department of Medicine Director, Office of Bioethics, Queen's University Clinical Ethicist, Kingston General Hospital
Rev. T. Deline	Community Member
Dr. M. Evans	Community Member
Dr. S. Irving	Psychologist, Providence Care, St. Mary's of the Lake Hospital Site
Prof. L. Keeping-Burke	Assistant Professor, School of Nursing, Queen's University
Mrs. J. Kotecha	Research & Programs Manager, Centre for Studies in Primary Care, Department of Family Medicine, Queen's University
Dr. J. Low	Emeritus Professor, Department of Obstetrics and Gynaecology, Queen's University and Kingston General Hospital
Dr. W. Racz	Emeritus Professor, Department of Pharmacology & Toxicology, Queen's
Dr. B. Simchison	Assistant Professor, Department of Anesthesiology, Queen's University
Dr. A.N. Singh	WHO Professor in Psychosomatic Medicine and Psychopharmacology Professor of Psychiatry and Pharmacology Chair and Head, Division of Psychopharmacology, Queen's University Director & Chief of Psychiatry, Academic Unit, Quinte Health Care, Belleville General Hospital
Dr. E. Tsai	Associate Professor, Department of Paediatrics and Office of Bioethics, Queen's University
Rev. J. Warren	Community Member
Ms. K. Weisbaum	LL.B. and Adjunct Instructor, Department of Family Medicine (Bioethics)
Dr. S. Wood	Director, Office of Research Services (Ex-Officio)