EXTENDED-USE ORAL CONTRACEPTIVES AND MEDICALLY-INDUCED AMENORRHEA: ATTITUDES, KNOWLEDGE AND PRESCRIBING HABITS OF OREGON WOMEN'S HEALTH PHYSICIANS.

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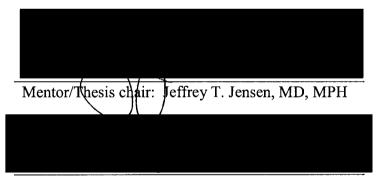
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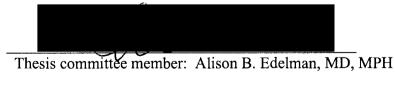
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List of abbreviations

ARHP: Association of Reproductive Health Professionals
BTB: Breakthrough bleeding
EOC: Extended-use oral contraceptives
FM: Family Medicine
Ob/Gyn: Obstetrics and Gynecology
OC: Oral contraceptives
OHSU: Oregon Health and Science University
OMA: Oregon Medical Association
PCOS: polycystic ovarian syndrome
URL: Uniform Resource Locators

Abstract

Background: Although numerous patient surveys have demonstrated that women are interested in contraceptive methods that would decrease the frequency of menses, the majority of women surveyed are unaware that such methods exist and may be available to them. Extended-use oral contraceptives may not only be effective for contraception, but are also helpful for relieving much of the morbidity and inconvenience associated with menstruation. It is unclear whether providers who prescribe oral contraceptives are aware of this potential interest. Research is needed to investigate whether barriers to greater prescribing, such as lack of knowledge about risks and benefits of extended-use OCs, or negative attitudes toward medically-induced amenorrhea, exist among women's health providers.

Objective: The purpose of this investigation is to determine whether prescribing habits of Oregon Obstetrics & Gynecology and Family Medicine physicians regarding extendeduse OCs are influenced by geographic location, primary specialty, and knowledge regarding extended-use oral contraceptives or attitudes regarding medically-induced amenorrhea.

Study Design: A cross-sectional survey of Oregon Obstetrics & Gynecology (Ob/Gyn) and Family Medicine (FM) physicians who are members of the Oregon Medical Association (OMA).

Methods: This study used a web-based survey instrument. A URL link to the survey was sent by e-mail to all 575 members of the OMA who identified as either Obstetrician-Gynecologists or Family Medicine physicians and provided e-mail addresses to the OMA. In addition, a smaller random sample of 138 physicians in the same specialties

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who did not have e-mail addresses on file with the OMA were sent a paper survey by standard mail.

Analysis: Relationships between prescribing and geographic location, primary specialty, gender, knowledge and attitudes were examined using chi-square, Mann-Whitney U, t-tests for independent samples and multiple logistic regression. Groups of variables were examined using multiple logistic regression to evaluate for confounders of primary specialty and geographic location.

Results: Of 713 providers surveyed, 233 completed the survey for an overall response rate of 32.7%. The web-based survey achieved a significantly lower response rate (26.3%) than the paper survey (59.4%) (p=0.005). Subjects responding to the e-mail survey tended to be younger, female and more urban than the paper survey respondents (p > 0.05). Most respondents (211/233) indicated that they prescribe oral contraceptives. Of these, 73.9% prescribe extended-use OCs either often (22.9%) or sometimes (51.0%). Without adjusting for other factors, an Ob/Gyn was eight times more likely to prescribe often often or sometimes compared with a FM physician (OR 8.02, 95% CI: 3.40, 18.91) and urban physicians were almost three times as likely to prescribe extended-use OCs (OR 2.75, 95% CI: 1.42, 5.30) compared with rural physicians. A significant positive association exists between providers' attitudes about medically-induced amenorrhea and their willingness to prescribe extended-use OCs (OR 1.84, 95% CI: 1.41, 2.42). After controlling for attitudes, knowledge, gender and age, neither primary specialty nor geographic location was associated with prescribing habits.

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Conclusions:

This study demonstrates that positive attitudes regarding medically-induced amenorrhea are the strongest factor influencing extended-use OC prescribing and that a small increase in positive attitudes about medically-induced amenorrhea results in increased prescribing (e.g. for a one point increase in attitudes score, a provider is almost twice as likely to prescribe extended-use OCs). A large proportion of providers report that they do prescribe extended-use OCs, and overall, providers had positive attitudes about medically-induced amenorrhea. Many providers remain uncertain about the safety of extended-use oral contraceptives and about the need for monthly menstruation in a woman taking oral contraceptives. Because there are still insufficient data to assess safety compared to traditional cyclic OCs, and because long-term health effects of extended-use OCs have not been documented, providers must rely on their attitudes and knowledge to guide their prescribing patterns. This study suggests that efforts to improve awareness and knowledge about the potential non-contraceptive benefits of extended-use OCs may be fruitful in improving the attitudes and prescribing patterns of those remaining providers who may be hesitant to prescribe this method for patients who may desire it.

Introduction

Approximately 80% of women use oral contraceptives sometime during their reproductive years¹. The standard FDA approved oral contraceptive regimen using 21 days of active pills followed by 7 hormone free days for withdrawal bleeding has no true scientific basis; in fact it has been suggested that the decision to mimic the natural 28 day menstrual cycle was made in an attempt to appeal to the Catholic church, rather than for physiologic reasons $^{2-4}$. This design was intended to reassure the user of normal menstrual cycle function and the absence of pregnancy. For many women, monthly menstruation is simply an annoyance; for others, there is substantial inconvenience and morbidity associated with menses ⁵⁻⁸. Nonetheless, many women and health care providers continue to believe that monthly menstruation is necessary for health, despite suggestions that it may actually increase the risk of breast and gynecologic cancers ⁹. Although clinicians have prescribed oral contraceptives in extended dosing regimens for years to suppress menstruation for medical indications such as endometriosis, extended use for nonmedical indications remains somewhat controversial. The reasons for this controversy are unclear. Other forms of hormonal contraception, such as the medroxyprogesterone acetate injection (Depo-Provera®) and the levonorgestrel releasing intrauterine device (Mirena®) frequently produce amenorrhea as a side effect, and this has been embraced as a potential advantage to many women. Over the last 30 years, there has been considerable discussion about whether using oral contraceptives to shorten or eliminate menses altogether would be a safe and acceptable alternative for women ^{4-7, 10-16}. Numerous surveys have now demonstrated that women would be interested in decreasing the frequency of menses if it were shown to be safe ¹⁷⁻²¹. Perhaps it is time for us to

reexamine our attitudes about menstruation and medically induced amenorrhea in the interest of improving the health and quality of life for our female patients.

Extended and continuous use oral contraception

For this research, it is important to explicitly define the terms "extended" and "continuous" with respect to oral contraceptive regimens. In general, an extended regimen involves taking hormone-containing pills for longer than the traditional 21 days, with a periodic hormone-free interval to allow a withdrawal bleed. For example, Seasonale® is an extended formulation with 84 days of active pills, followed by an interval of 7 days of inactive pills²². Loestrin-R-24® has 24 days of active pills, and four days of iron-containing placebo pills²³. Some regimens, such as Seasonale® are intended, at least in part, to produce amenorrhea for intervals beyond 28 days (e.g. for the entire 84 day duration of active pill exposure in the case of Seasonale®). Others do not interfere with the occurrence of monthly menses but are intended to decrease the likelihood of ovulation by decreasing or eliminating the hormone-free interval (more about this below). For purposes of this survey I defined an "extended" regimen as one that uses hormone-containing pills for 28 or more days in a row, to better distinguish it from the regimens that include some combination of hormone containing pills during days 21-28 of the cycle. In a continuous regimen, the user would continue to take hormone-containing pills indefinitely, with no scheduled interruption.

Physiology of the normal menstrual cycle

The normal menstrual cycle lasts an average of 28 days and is divided into two phases: the follicular phase and the luteal phase ²⁴. These phases are a function of hormonal changes occurring in the hypothalamic-pituitary-gonadal axis, a complex system involving the hypothalamus of the brain, the pituitary gland and the gonads or ovaries.

Day one of menses defines the first day of the menstrual cycle and also the beginning of the follicular phase ²⁴. The follicular phase lasts 10-14 days and is a process of preparing a mature follicle or oocyte for ovulation. Early in the follicular phase, levels of the hormones estradiol (estrogen) and progesterone are low. The hypothalamus releases gonadotropin-releasing hormone (GnRH), which stimulates the pituitary gland to release follicle-stimulating hormone (FSH) and luteinizing hormone (LH). FSH in turn stimulates maturation of premature oocytes, which begin to secrete estradiol. The release of estradiol has two main functions: feedback inhibition of FSH and LH release from the pituitary, and thickening of the endometrium in preparation for implantation of a fertilized egg. Estradiol levels continue to rise during the follicular phase until they reach a peak around day 10-14 and a switch from negative to positive feedback on LH occurs resulting in a surge in LH levels. This LH surge marks the beginning of the luteal phase and leads to release of a mature ovum from the ovary, or "ovulation" ²⁴.

During the luteal phase, there is a gradual increase in progesterone production by the corpus luteum, a structure formed in the ovary after it has released the ovum ²⁴. At the same time, LH and FSH levels are falling. If the ovum is not fertilized, the corpus luteum

begins to dissolve, estrogen and progesterone levels fall, and the hormonal support of the endometrial lining disappears, leading to sloughing of the endometrial tissue and menses ²⁴.

Physiology of oral contraception

Combination oral contraceptives contain synthetic estrogen (in the form of ethinyl estradiol) and progesterone (known as a class as progestins). Individual pill formulations vary by estrogen and progestin dose as well as the type of progestin (most currently prescribed pill formulations contain the same estrogen component, ethinyl estradiol). Pill formulations also may vary in the dose of hormone given over the course of the cycle. Monophasic formulations have a consistent dose of ethinyl estradiol (EE) and progestin throughout the cycle. Triphasic or multiphasic formulations have varying doses of EE and progestin as the cycle progresses ²⁴. Hormones in the combination pill act in synergy to prevent ovulation by suppressing the hypothalamic-pituitary-gonadal axis. Progestin suppresses LH, thereby preventing the LH surge that leads to ovulation²⁴. Estrogen acts to suppress FSH, hindering the development of a dominant follicle²⁴. Estrogen and progestin, when given in combination, also have important effects on the uterine endometrium that warrant discussion here: estrogen has a stabilizing effect on the endometrium, meaning that irregular shedding of endometrial tissue is decreased, thereby decreasing the likelihood of breakthrough bleeding between periods ²⁴. Estrogen also potentiates the action of progesterone, possibly by upregulating progestin receptors, allowing for lower doses of progestin in the combination pill²⁴. When given in a combination formulation, the progestin effects of the pill dominate. It is the withdrawal

of these hormones, particularly progestin, which results in bleeding during the placebo week of pills²⁴. This bleeding is actually a "pseudo" menstruation and occurs because of hormone withdrawal, not because of endometrial lining buildup. Estrogen, if given alone, stimulates proliferation of the endometrium, greatly increasing the risk of endometrial cancer²⁵⁻²⁸. Progestin balances the estrogenic effect, causing the endometrium to become inactive and actually decreasing this risk. In addition, elevated doses of estrogen have been implicated in increased risk of thrombosis associated with oral contraceptives ²⁹⁻³¹, so keeping the estrogen dose low is crucial in order to minimize adverse effects. Because today's pill formulations contain such low doses of estrogen and progestin, and additionally because of the dominance of the progestin effects of the pill, long-term use of the oral contraceptive pill often results in a thin, inactive endometrium. In some women, this results in amenorrhea, even with traditional cyclic use of the pill 24 . When active pills are taken continuously for greater than 28 days, the atrophic effect of the pill on the endometrium appears to persist, resulting in amenorrhea with decreasing frequency of breakthrough bleeding as the duration of use increases 5, 6, 14.

The lower doses of estrogen and progesterone in today's oral contraceptive pill formulations have resulted in a much more favorable side-effect profile than that seen with early OCs such as breast tenderness, nausea, fluid retention and moodiness ³². There is concern, however, that because the current formulations' hormone doses are so low, ovulation may occur if a woman forgets to take her pills, particularly at the beginning of a new cycle after the 7-day placebo week. Schlaff et al found that women on a traditional 21/7 day OC regimen had evidence of decreased ovarian suppression compared with

women taking 28 days of active pills or women taking 21 days of estrogen and progesterone, followed by two days of placebo, then five days of estrogen alone ¹⁶. The decrease in ovarian suppression was particularly prominent in overweight women in their study. The concern raised by this physiologic study of an increased risk of oral contraceptive failure in overweight women was supported in a case-control study by Holt et al, which found that OC failure was inversely proportional to the dose of steroid hormones in OCs, with failures occurring most often in women taking "very low" (defined as <35µg) doses of ethinyl estradiol ¹³.

Additionally, low dose oral contraceptives are more frequently associated with irregular or breakthrough bleeding between periods ¹². Breakthrough bleeding (BTB) is the most common reason cited for discontinuation of oral contraceptives ¹⁵. Since BTB occurs in users of standard OC regimens, researchers hypothesized that by eliminating the hormone-free interval, one might decrease BTB and therefore increase the acceptability and therefore the use of oral contraceptives as a birth-control method ^{6, 14}. A number of randomized, unblinded studies have been performed comparing bleeding profiles and patient acceptability of standard 21/7 day OC regimens with extended continuous regimens. The duration of hormone use varied among studies from 49 days (considered "extended cycle") to 365 days ("continuous use"). A study by Miller ⁷ looking at 49 day extended use oral contraceptives found no significant difference between groups in terms of mean number of bleeding or spotting days, except that the traditional cyclic group had a mean of 4.5 more bleeding days (95% CI 1.9-7.1) in the first trimester (84 day reference period) than the continuous use group. However, the two studies looking at

continuous regimens of 336 days or 168 days of active pills found that women using continuous oral contraceptive regimens have significantly fewer bleeding days requiring sanitary protection than women on traditional cyclic regimens, and that amenorrhea rates increase with longer durations of use ^{6, 14}. Both studies found overall satisfaction to be high, with no statistically different difference shown in satisfaction or compliance between women randomized to standard vs. continuous regimens.

Side effects associated with the hormone-free interval

With the traditional 21/7 day regimen, cycle related symptoms and side effects (pelvic pain, headaches, bloating, breast tenderness) have been shown to be more common during the 7-day hormone-free interval (HFI) rather than during the 21 hormone containing pills ^{8, 33}. Three randomized studies comparing standard to continuous dosing of OCs looked at menstrual-associated side effects and found that side effects were improved with extended use oral contraceptives ⁵⁻⁷. Symptoms shown to improve with continuous dosing included headache ^{5, 7}, genital irritation ⁷, tiredness ⁷, bloating ⁶ and menstrual pain ⁶.

Adverse events related to OCs

Oral contraceptives have been linked to an increased risk of venous thrombosis that is directly related to estrogen dose and seen mainly in the first years of use ²⁹⁻³¹. There are theoretical concerns that extended or continuous dosing regimens may increase a woman's overall estrogen exposure, thus increasing her risk of venous thrombosis, but no difference in adverse events has been documented in studies comparing extended

regimens with cyclic OC regimens ³⁴. There is also a risk of myocardial infarction or stroke associated with OC use in smokers ³⁵⁻³⁹, but studies have failed to document this in healthy non-smoking women ^{40, 41}.

Non-contraceptive Health Benefits

The health benefits of oral contraception have been well documented. For example, use of oral contraceptives has been shown to decrease the risk of ovarian ⁴²⁻⁴⁸ and endometrial cancers ⁴⁹⁻⁵¹ and may decrease benign breast disease ^{52, 53}. There is also growing evidence that oral contraceptive use decreases the risk of colorectal cancer in women ⁵⁴⁻⁵⁶. In addition, women with androgen excess due to polycystic ovarian syndrome have noted improved menstrual patterns as well as decreased acne and hirsutism through the use of OCs ⁵⁷. Oral contraceptives have also been shown to decrease symptoms of dysmenorrhea and menorrhagia ⁵⁸⁻⁶⁰ and symptoms associated with endometriosis ⁶¹⁻⁶³. There has also been shown to be a decreased risk of osteoporosis associated with OC use ⁶⁴⁻⁷¹. Decreased menstruation, achieved with extended cycle oral contraceptives, may have additional positive health benefits, such as decreased iron deficiency ^{72, 73} and hereditary anemias ⁷⁴. Oral contraceptives also have cosmetic effects, resulting in decreased cycle related acne in many women ⁷⁵⁻⁸¹.

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Formulations

In September, 2003, the Food and Drug Administration approved a dedicated extended oral contraceptive regimen, Seasonale®, consisting of 84 days (12 weeks) of active pills, followed by a 7 day hormone-free interval. A randomized, multicenter, open-label trial compared Seasonale with Nordette®, a conventional 21/7 day cycle preparation containing the same hormonal combination of 30mcg ethinyl estradiol (EE) and 150mcg levonorgestrel (LNG) in the active pills. Women in the Seasonale group reported more unplanned bleeding and spotting during the initial cycles than women on the conventional regimen, but this decreased with each cycle and by the fourth cycle was similar to the conventional regimen group. Safety and efficacy was similar among groups ²².

Other extended regimens utilizing off-label administration of existing OC formulations have also been shown to be well tolerated and safe in comparison to the standard 28 day regimen. While none of these studies have been sufficiently powered to study efficacy, it is reassuring that no difference in efficacy, as measured by the number of unintended pregnancies occurring during the study time period, has been reported ^{5-7, 14}. One study found that pregnancy rates were lower with extended cycle OCs, although not statistically significant, as the lower bound of the 95% confidence interval was 1.0 ⁸². Two studies looked for evidence of endometrial hyperplasia by ultrasound measurement of the endometrial stripe or endometrial biopsy ^{6, 14}. No evidence of hyperplasia was found on biopsy and all endometrial stripe measurements were less than 5mm, consistent with inactive endometrium. There were no serious adverse events reported in these studies ^{5-7, 14, 82}.

Morbidity associated with menstruation

While there is no evidence to suggest that monthly menstruation improves health, there is substantial morbidity, loss of productivity and direct economic costs associated with menstruation. Menstrual related symptoms such as heavy menstrual bleeding (menorrhagia), menstrual migraine, breast tenderness and menstrual related pelvic pain (dysmenorrhea) account for significant cost to women in terms of lost productivity and personal expense. Based on data from the 1984-1992 National Health Interview Survey. the annual prevalence of menstrual disorders is 53 per 1,000 women aged 18 to 50. In 1996, when these data were published, this was estimated to be about 2.5 million women ⁸³. A study by Cote et al in 1999 found that women with heavy menstrual flow missed 6.9 percent (3.6 weeks) more work per year compared with women with light menses. The annual lost income from this was estimated at approximately \$1,692 per woman⁸⁴. It has even been estimated that U.S. industry loses 8% of its annual wages because of menstrual disorders ¹¹. An analysis looking at the personal expenses associated with standard 21/7 day OC therapy compared with trimonthly OC therapy such as Seasonale® suggested that the trimonthly regimen may be less expensive than the standard 21/7 day cycle based on reduction in the need for sanitary supplies, pain relievers and physician visits for menstrual related concerns⁸⁵.

Womens' attitudes towards menstruation and amenorrhea

In spite of considerable morbidity and inconvenience associated with menstruation, many surveys of women's attitudes demonstrate that women feel that monthly periods provide them reassurance of the absence of pregnancy and a feeling of health or cleansing ¹⁸⁻²⁰. In

addition, some women cite concerns about unexpected bleeding as a reason for not wanting to use regimens that may decrease the frequency of menses ¹⁸. In these same surveys, however, the majority of women also say they would prefer to have a period less than monthly if it had no negative impact on their health ¹⁷⁻²¹. A 2004 survey by Andrist of a geographically diverse convenience sample of reproductive age women found that 59% of women reported they would be interested in menstruating less frequently than once a month and 33% would choose not to have periods ever ¹⁷. In a multinational survey, 57% of women in Edinburgh, Scotland, 36-55% in Cape Town, South Africa and 45% in Hong Kong and Shanghai would prefer to have periods every 3 months or not at all. However, this preference for less frequent menses is not universal; 71% of Nigerian women surveyed said they would prefer to have monthly periods ¹⁹.

Despite this apparent interest, it seems that many women are not aware that menstrual suppression with extended use oral contraceptives exists as an option. Most (62%) of respondents to the Andrist survey had never used any birth control method for reasons other than to prevent pregnancy. Although 78% had never heard of using OCs to suppress menses, 20% said that a provider had offered extended OCs to suppress their period ¹⁷.

Provider attitudes towards menstruation and amenorrhea

There have been five published studies looking at the attitudes and/or prescribing habits of providers regarding extended use oral contraception in the United States. In 2002, the Association of Reproductive Health Professionals ⁸⁶ and the National Association of Nurse Practitioners in Women's Health polled a sample of their annual meeting

registrants, finding that 81% had heard of extended use oral contraceptives for suppression of menstruation ⁸⁶. Most (77%) of them prescribed extended use oral contraceptives, citing the following reasons for prescribing: endometriosis, patient request, lifestyle, menorrhagia and dysmenorrhea. This population includes many professionals who work primarily in family planning and therefore have generally favorable attitudes towards the use of extended OCs.

The recent study by Andrist et al examined attitudes of a larger sample of ARHP members toward extended use oral contraception ¹⁷. This study found that 44% of providers surveyed felt that menstrual suppression was a good idea; 52% said they prescribe extended use oral contraceptives to their patients. Medical reasons for prescribing cited included dysmenorrhea, menorrhagia and endometriosis. Although many indicated that they would prescribe extended regimens on patient request, providers cited many of the same concerns about delaying menses as their patients have. A great many of the providers surveyed (88%) stated that they would like to see more research confirming the absence of negative side effects or an impact on future fertility associated with extended OC use ¹⁷. This study was also subject to similar selection bias as the above mentioned AHRP study. The vast majority of respondents to the Andrist survey were advance practice providers, physician assistants, certified nurse midwives and osteopathic physicians. Only 13% were allopathic physicians. An additional limitation of this study was a poor response rate of near 10%, and the fact that respondents were not representative of women's health care providers, the majority of whom are not ARHP members.

Glasier surveyed health care providers at family planning clinics in Shanghai, Hong Kong, Sagamu, Nigeria, Cape Town, South Africa and Edinburgh, Scotland about factors influencing their choice of contraception for patients and their beliefs about the importance of menstruation to patients using contraceptives ¹⁹. This study found that providers tended to overestimate their patients' feelings about the importance of menstruation, with more than 75% of providers reporting that they thought monthly menstruation was either "quite important" or "very important" to their patients. Despite this, more than half of all providers at each site except for Shanghai said they would be willing to recommend a method of contraception which produced amenorrhea. Surveys were either hand-delivered or mailed by postal mail to health care providers, and the resulting response rate was 83%. The level of training of respondents (i.e. physician, nurse, etc) was not noted.

A 2003 postal survey of the attitudes of German women and gynecologists about extended-use OCs found that nearly all (99.5%) respondents had prescribed OCs to postpone withdrawal bleeding, and 97% reported having prescribed extended-use OCs to suppress menstruation "at least for a limited period of time" ²¹. Reasons cited for prescribing were either for medical indications or patient request. Although 9000 German gynecologists were surveyed, only 1623 surveys (18%) were returned, and 471 of those were excluded because of inconsistent or incomplete data, leaving only 13% of the originally sampled population. This resulted in obvious selection bias.

Sulak et al surveyed a varied population of health care providers attending six medical meetings in 2004 about their prescribing patterns and attitudes regarding extended-use oral contraceptives ⁸⁷. Almost 82% of providers indicated that they have recommended extended-use OCs to patients and 29% of those said they have done so "frequently." Over 87% of respondents indicated that they thought that extended-use OCs "should be routinely offered to patients who want the option of eliminating monthly bleeding and other associated problems." Ob/Gyn physicians were significantly more likely (p<0.0002) than non-Ob/Gyn physicians to agree with this statement. Age, geographic location and patient population size were not associated with attitudes toward extendeduse OCs. More than half (52%) of those surveyed thought that withdrawal bleeding was unnecessary and did not confer health benefits. The majority (83%) did not feel that there were significant health risks associated with extended-use OCs, although 13% were concerned about an increased risk of deep venous thromboembolism or pulmonary embolism; concerns about an increased risk of breast cancer were noted in 7% and infertility in 3%. This study achieved greater than a 90% participation rate and succeeded in surveying a wide range of providers including Ob/Gyns, nurse midwives. physician assistants and primary care physicians, but was distributed to attendees of a contraceptive update lecture, therefore resulting in a biased population.

Use of electronic survey methods

This study utilized both a traditional paper survey method and a newer web-based survey which involved sending a URL link to providers via e-mail. E-mail surveys have been in use since 1986, and since the widespread introduction of the World Wide Web in 1994, the use of e-mail and the internet has grown exponentially ⁸⁸. A major advantage of electronic survey methods is the reduction in cost and increase in efficiency as compared with traditional paper methods ⁸⁸. Electronic surveys prevent unnecessary use of paper, save on postage and office supply costs, allow much faster responses and can often streamline data collection and prevent data entry error ⁸⁸. It remains unclear, however, whether e-mail methods are a viable alternative or complement to the use of paper surveys.

A number of studies have investigated whether e-mail and web-based surveys achieve the same response rate as mailed paper surveys do ⁸⁹⁻⁹¹. McMahon looked at response rates to a survey of physician members of the Georgia chapter of the American Academy of Pediatrics which used postal, fax and e-mail survey methods. Although the main subject of this survey was rotavirus vaccination, it included questions about whether providers had computers and internet access at work. Response rates after two mailings were 41% for postal, 47% for fax and 26% for e-mail surveys. Greater than 85% of providers reported having a computer at work and 70% said they had access to the internet. Unfortunately, however, only 39% of the total member population of the Georgia AAP had e-mail addresses listed in the member directory. A review of 17 internet-based surveys of health professionals published between 1999 and 2002 found response rates

ranging from nine to 94% ⁸⁹. This article also reported results of the authors' own internet-based survey of general practitioners in the United Kingdom, which achieved a 52.4% response rate after five e-mail reminders. Leece et al published a report comparing response rates among a population of surgeons in Ontario, Canada to a web-based and a paper version of the same survey. The web-based survey achieved a significantly lower response rate (45%) than the paper survey (58%) after three follow-up reminders in each arm (absolute difference 13%, 95% CI: 4-22%, p < 0.01) ⁹⁰. It is not always the case, however, that postal mail surveys always achieve better response than e-mail surveys. In her review of studies comparing e-mail and postal survey methods, Sheehan found that in some cases, the response rate to e-mail surveys was improved over postal survey methods; specific reasons were not mentioned ⁸⁸.

A problem frequently encountered in electronic survey methods is non-receipt of the survey by a portion of the population due to incorrect spelling of e-mail addresses or e-mail addresses that are no longer valid. In the internet-based survey of general practitioners in the UK by Braithwaite, over one-fourth of e-mail invitations sent were rejected due to misspelled or invalid e-mail addresses ⁸⁹. In the survey of pediatricians in Georgia, groups receiving the survey by e-mail were much more likely to have invalid addresses/numbers compared to postal and fax surveys (16% compared to 4% and 8% respectively) ⁹¹. In addition, check-all that apply type questions are reported to be more frequent in internet-based surveys ⁹². This format has been shown to result in less frequent selection of answer choices than when a simple Yes/No answer format is used ⁹³.

It is also important to consider what factors improve response rate in both postal and electronic surveys. A review by Sheehan (2001) looking at whether response rates to both e-mail and postal surveys are influenced by year of survey, survey length, respondent pre-notification, follow-up contacts and issue salience found that the year in which the survey was performed was a negative predictor of response (i.e. response rates have declined since the introduction of e-mail surveys) and the number of follow-up notices positively influenced survey response rates ⁸⁸. Opinions on the influence of survey length were mixed: Sheehan concluded that survey length alone may not be sufficient to predict response. It was not mentioned what length is considered "long." Sheehan also found that pre-notification and issue salience were not significantly associated with response ⁸⁸. In the review by Braithwaite, follow-up reminders achieved a substantial increase in response rates ⁸⁹. Dillman warns against the use of pull-down menus or complex design options in web-based surveys, as these features tend to encourage novice Web users to prematurely discontinue completion of the survey ⁹⁴.

To address the limitations in the existing knowledge regarding provider attitudes, I designed a survey of a diverse sample of women's health care physicians in Oregon representing diverse geographic regions, social beliefs and practice styles. The goals of this study were to measure the attitudes, knowledge and prescribing habits of allopathic Obstetrician-Gynecologists and Family Medicine physicians and to assess whether specialty type or geographic location influence prescribing habits. In addition, I wished to exploit the cost savings and efficiency available with a web-based survey method for a portion of the survey population and planned to draw comparisons between responses to web-based and postal versions of the survey.

Materials and Methods

Approval for this study was obtained from the Oregon Health and Sciences University Institutional Review Board.

Study design

A cross-sectional self-administered survey developed specifically for this investigation (see appended survey).

Study population

The survey was distributed to a sample of Oregon Obstetrics and Gynecology (Ob/Gyn) and Family Medicine (FM) physicians who are members of the Oregon Medical Association (OMA). The OMA is a professional physicians' organization with greater than 7,400 members representing the spectrum of medical specialties in the state of Oregon. The board of the OMA approved the use of their member database for this study (see appendix for letter of cooperation from the OMA).

When the sample was obtained, a total of 1,240 Ob/Gyns and FM physicians were members of the OMA. This represents approximately 56% of the currently licensed Ob/Gyn and FM physicians in the state of Oregon. Of these, 575 had e-mail addresses on file. To obtain the sample needed to investigate the question of interest and to investigate various methods of surveying physicians, an additional random sample of the remaining member Ob/Gyns and FM physicians were sent a paper version of the survey. A sample of approximately 20% of the e-mail survey population - with a ratio of FM to Ob/Gyn

physicians similar to the e-mail sample - was chosen to obtain the needed sample size for this study.

Of the 713 providers who were surveyed, 233 completed the survey for an overall response rate of 32.7%. 151 of 575 e-mail surveys were returned, for a response rate of 26.3%. 82 of 138 paper surveys were returned, yielding a response rate of 59.4%. Of the 233, 22 indicated that they do not currently prescribe oral contraceptives and were excluded from analysis. Responses from the remaining 211 participants were used in this analysis. Groups responding to the e-mail and paper surveys did not differ by geographic location, primary specialty, gender, age or ethnicity and so the two groups were merged into one common database for analysis.

Inclusion criteria

Criteria for eligibility to participate in the study included being designated as a currently practicing Obstetrician-gynecologist or Family Medicine physician in the state of Oregon with either an e-mail or postal mail address on file with the OMA.

Exclusion criteria

Physicians who were members of the OMA but whose primary business address was not in Oregon were excluded from participation.

Survey design

Survey instrument:

The survey used in this study was designed specifically for this investigation. The series of questions investigating providers' prescribing habits and attitudes about menstruation and extended-use OCs were adapted from a survey distributed to physicians and advanced practice clinicians (i.e. nurse practitioners) on the Association of Reproductive Health Professionals ⁸⁶ membership roster by Linda Andrist (2004). Some questions were used exactly as Andrist had written them. The language of other questions was modified to be more neutral considering that the population surveyed in this study may have less favorable attitudes toward menstrual suppression overall than the population surveyed by Andrist.

The survey was piloted on OHSU Ob/Gyn residents at their Grand Rounds for feedback regarding question clarity, time needed to complete the survey, etc. 13 of 13 residents present at Grand Rounds completed the survey. Their responses to this pilot survey were not included as part of the overall sample.

The web-based surveys utilized Zoomerang software, MarketTools, Inc., Mill Valley, CA. (<u>www.zoomerang.com</u>). Zoomerang is an internet based survey tool which allows users to create and send surveys, or as in this case, send a URL link to a website for the survey. Results are compiled into a downloadable database by the program, which was easily converted into an SPSS database. There were two forms of the same survey distributed to the study population (the webbased version and a paper version). For all providers listed as Obstetrician-Gynecologists or Family Medicine physicians that had e-mail addresses in the Oregon Medical Association (OMA) member database (n=575), an e-mail was sent by the OMA, inviting them to participate in a web-based survey with a URL link to the Zoomerang site. The paper survey was sent by standard mail to 138 physicians sampled from the remaining 665 Ob/Gyn and FM providers without known e-mail addresses. An information sheet was provided with both the e-mail and paper survey explaining the survey intent as well as risks and benefits. Providers were to imply their consent to participate by completing the survey. Providers who wished not to participate were asked to submit the survey blank to avoid receiving follow-up surveys. Non-responders to the postal survey were sent two follow-up surveys at approximately four to six-week intervals after the initial mailing. All recipients of the web-based version were sent two e-mail reminders at approximately four to six-week intervals after the initial e-mail mailing.

As an incentive to encourage provider participation, I offered a \$1.00 donation for every survey completed to Northwest Medical Teams to aid in disaster relief efforts in South and Southeast Asia, as well as in other sites worldwide. This was stated in the attached information sheet that accompanied the e-mail and paper surveys. The funding for this endeavor was a generous gift from the Leon Speroff Endowed Professorship at Oregon Health and Sciences University.

Survey content and study measures

The survey was divided into four main sections: the first section asked subjects to provide information about their prescribing habits with regard to oral contraceptives and extended-use OCs. If subjects indicated that they do not prescribe oral contraceptives (extended or otherwise), they were asked not to complete the survey, and to return the survey blank to avoid being contacted further. The second section contained questions assessing providers' knowledge about morbidity associated with menstruation and with cyclic use of OCs, oral contraceptives effect on menstrual and uterine physiology. The third section examined providers' attitudes about menstruation and medically-induced amenorrhea. The fourth section asked for demographic information including age, ethnicity, gender, practice location, primary specialty, secondary specialty area (if applicable) and type of practice. At the end of the survey, space was provided for comments.

Prescribing habits

If subjects indicated that they do prescribe oral contraceptives, they were then asked whether they prescribe oral contraceptives for reasons other than to prevent pregnancy, and if so, for what reasons (to regulate menstrual cycle, to relieve menstrual symptoms such as bloating, headache, breast tenderness, PMS, to decrease menstrual bleeding or for medical problems including migraines, endometriosis, vonWillebrand's disease, chronic pelvic pain). Participants were asked if they prescribe oral contraceptives in an extended fashion "often," "sometimes," "rarely," or "not at all." To address the primary outcome responses were dichotomized such that "often" or "sometimes" was considered

prescribing, whereas the answers "rarely" or "not at all" were categorized as not prescribing. This was done because in looking at the data, "rarely" prescribers behaved similarly to "not at all" prescribers, as compared with physicians who prescribe "often" or "sometimes."

If respondents chose "often," "sometimes," or "rarely," they were asked what type of OC they prescribe (monophasic, triphasic, Seasonale® or "other"), for what duration they advise the patient to take active pills(using an ordinal 5-point scale ranging from "for up to one week [for total 28 days]" to "indefinitely"), and their reasons for prescribing extended-use OCs. This last question allowed respondents to choose from a variety of responses, listed below:

a. Patient asked me, for symptomatic relief of menstrual symptoms (i.e. heavy menses, pelvic pain, bloating, etc.).

- b. Patient asked me, for medical reasons (i.e. migraines, endometriosis).
- c. Patient asked me, for personal reasons (i.e. honeymoon, sports, etc.).
- d. Patient asked me, for employment reasons (i.e. military training).
- e. Patient asked me, for no particular reason.
- f. I offer extended OCs for symptomatic relief of menstrual symptoms.
- g. I offer extended OCs for medical reasons.
- h. I offer extended OCs for personal reasons.
- i. I offer extended OCs for employment reasons.
- j. I offer extended OCs as an option for any woman using oral contraceptives.
- k. Other (write in):

For the purposes of analysis, this last question was recategorized into four categories:

patient request (for specific reasons), patient request (for no particular reason), physician

offered (for specific reasons), physician offered (for any woman using OCs).

Questions then addressed what factors were important in physicians' choice of what kind

of pill formulation to use for extended-use, and what factors affected their decision to

prescribe extended-use OCs or not. Respondents were asked to rate the relative importance of estrogen dose, type of progesterone, cost, monophasic formulation, triphasic formulation or "whatever I happen to have samples of" using a 5-point Likert scale with choices ranging from "very unimportant" to "neutral" to "very important." This question was additionally meant to investigate whether physicians are using triphasic pill formulations in extended regimens. Studies comparing traditional cyclic use of OCs with extended or continuous regimens have primarily utilized monophasic regimens and the safety and efficacy of triphasic formulations in extended use remains unproven. Finally, providers were asked to rate the importance of concerns about cost, side effects, long-term health effects and potential impact on future fertility on their decision about whether or not to prescribe extended-use OCs using the same scale.

Knowledge

Five questions were intended to assess providers' knowledge about the effects of oral contraceptives on menstrual and uterine physiology, documented morbidity associated with hormone withdrawal, and benefits associated with oral contraceptives. Questions included "Menstrual symptoms can result in lost productivity at work/school for women (True/False)," "Oral contraceptives can relieve painful menses (True/False)," "Monthly bleeding on a cyclic oral contraceptive pill regimen is due to: (Endometrial proliferation, Hormone withdrawal, Release of an unfertilized ovum, or None of the above)," and "Extended/continuous use oral contraceptive use results in a thickened endometrium (True/False)." The fifth question asked "In women taking a traditionally dosed cyclic pill, menstrual associated side effects (nausea, bloating, pelvic pain, headaches) are most

common during: (The first 7 days of active pills, Days 8-14 of active pills, days 15-21 of active pills, the 7 day placebo week, or 'there is no relationship between the cycle week and associated side effects')." This last question was included because a 2000 study by Sulak published in the journal Obstetrics and Gynecology found that cycle-associated side effects in oral contraceptive users were significantly more common during the 7-day hormone free week compared with the 21 day period of active pills ³³.

For three of the five questions, respondents' answers were almost universally correct. 99% of those surveyed chose the correct answer ("True") to the question "Menstrual symptoms can result in lost productivity at work/school for women." The correct answer for the question "Oral contraceptives can relieve painful menses" was also "true," and 100% of respondents chose this answer. For the question that asked about the mechanism of monthly bleeding on cyclic OCs, the answer was "hormone withdrawal," and 95% of providers answered correctly. Because responses were so similar for these three questions, they were not analyzed further for differences in geography, gender or primary specialty.

For the remaining two knowledge questions, respondents answers differed, and these were included as separate variables in the analysis. The question which asked about the week in which menstrual-related side-effects were most common in users of cyclic oral contraceptives was coded as correct if subjects chose the answer "placebo week," or incorrect if they chose otherwise. The remaining question examined whether subjects were aware that extended OC use has been shown not to cause endometrial thickening.

This variable was coded as correct if subjects chose the answer "false," and incorrect if they chose "true."

Attitudes

In order to assess providers' attitudes toward menstruation and medically-induced amenorrhea, participants were asked to indicate their degree of agreement or disagreement with the following statements using five Likert-scale responses ranging from "strongly disagree" to "strongly agree":

- "Monthly menstruation is essential for health in women taking birth control pills,"
- "There are potential health benefits to hormonal suppression of ovulation"
- "There are potential economic benefits to hormonal suppression of ovulation"
- "Given the choice, many women would prefer to menstruate less than monthly"
- "I feel that hormonal suppression of menstruation with extended-use oral contraceptives is safe"

For the purposes of analysis, the five attitudes questions were recoded as appropriate so that the Likert scale values went in the same direction for all questions (e.g. a score of 5 indicated a favorable attitude towards menstrual suppression and a score of 1 indicated unfavorable attitudes). A total attitudes score was then computed by adding the Likert scale values for all five attitudes question for each respondent. The range was 5 to 25.

Demographic information

Age, gender, ethnicity

Participants were asked to circle the category corresponding to their age (e.g. 20-29, 30-39, 40-49, 50-59, 60-69, 70-79), their gender and their ethnicity (choices were Caucasian, African American, Hispanic, Asian/Pacific Islander, Native American or Other). For analysis, age was categorized into <40 years, 40-49 years, and \geq 50 years, based on the distribution in the data. Gender was coded as male or female. Ethnicity was recategorized into two groups (White and non-White) because of the small numbers of non-White physicians in Oregon.

Primary specialty

Participants were asked to indicate whether they are Obstetrics & Gynecology or Family Medicine physicians. In addition, if they identified themselves as Obstetrics & Gynecology, they were asked to indicate the specialty area in which they practice,(e.g. general obstetrics-gynecology, primarily obstetrics, primarily gynecology (including urogynecology), gynecologic oncology, family planning/reproductive health, or reproductive endocrinology). For analysis, only the main categories of primary specialty (Obstetrics & Gynecology vs Family Medicine) were examined.

Practice location

Respondents were asked to identify the county in which they practice most of the time by choosing it from a list of Oregon counties. Using criteria cited in the 2004 PRAMS study, the geographic location of respondents was categorized into "rural" or "urban" based on

the self-reported county of practice. The Oregon PRAMS or "Pregnancy Risk Assessment Monitoring System" study defines a rural county as one with less than 60 people per square mile based on 2001 United States Census data. In Oregon, there are 26 counties that meet this definition (Baker, Clatsop, Coos, Crook, Curry, Deschutes, Douglas, Gilliam, Grant, Harney, Hood River, Jefferson, Josephine, Klamath, Lake, Lincoln, Linn, Malheur, Morrow, Sherman, Tillamook, Umatilla, Union, Wallowa, Wasco, Wheeler) and 10 remaining counties classified as urban (Benton, Clackamas, Columbia, Jackson, Lane, Marion, Multnomah, Polk, Washington, Yamhill).

Participants were also asked to indicate the setting in which they practice, such as private practice, group practice, university setting, etc. They could choose more than one category.

Survey type

Two different survey methods were utilized in this study: a traditional paper survey sent by postal mail, and a newer web-based survey method. Considering there could be differences in categories of providers who would respond to one method over another and because differences in response rates to each method could impact observed prescribing patterns, this variable was included for consideration in statistical modeling. The type of survey for each subject was coded for analysis as e-mail or paper.

Data collection

Data management and recoding were done using SPSS version 13.0 (SPSS, Chicago, IL). Individual identifiers were known when the survey was initially mailed, but were removed from returned surveys and were not known when the data were analyzed. Surveys were labeled with a four-digit number which could be linked to each individual study participant and which indicated whether the returned survey was from the first mailing or from one of the two follow-up mailings. When data were entered in the database, the corresponding number was used as the subject ID.

Study variables

Outcome variable: Extended oral contraceptive prescribing. As described above, prescribing was defined as prescribing extended-use OCs either often or sometimes, while those who prescribe rarely or not at all were defined as non-prescribers.

Main covariates of interest

- Geography: rural vs. urban
- Primary specialty: Obstetrics & Gynecology vs. Family Medicine

Other factors of interest (covariates/confounders)

- Gender: male vs. female
- Knowledge about the most common week of side effects on cyclic oral contraceptive regimens
- Knowledge about whether extended-use OCs cause endometrial thickening

- Attitudes about medically-induced amenorrhea: continuous attitudes score
- Age: <40 years, 40-49, and ≥ 50 years old
- Ethnicity: White vs. non-White
- Survey type: e-mail vs. paper

Missing data

Answers that were left blank were coded as "missing" in SPSS. Missing data were not included in individual analyses, therefore, the total sample for certain comparisons varies somewhat depending on how many providers answered a particular question. In cases where the number of missing subjects was greater than 10% of the overall population, missing subjects were included as a separate category for comparisons.

Statistical analysis

211 providers were included in this analysis. First, descriptive statistics were obtained for the primary outcome variable, covariates of interest and additional factors. Next, 2x2 tables (or RxC tables where applicable) were created to evaluate whether there were associations between the covariates of interest (primary specialty, geographic location and gender) and the primary outcome. Chi-square statistics and Fisher's Exact test (when cell values were less than 5) were used to assess statistical significance as appropriate, with significance defined as a p-value <0.05. The Mann-Whitney U test was used to evaluate differences in ordinal Likert scale responses between groups (e.g. primary specialty and geographic location). A t-test for independent samples was used to examine whether a given respondent's overall attitudes score was associated with the outcome of interest as well as with other covariates of interest.

Description of model building

Logistic regression was used to try to further understand which factors were predictive of physician prescribing of extended use OCs after controlling for potential confounders. First, simple logistic regression models were used to assess for associations between prescribing habits and each independent variable: geographic location, primary specialty, gender, attitudes, the two knowledge variables, and age. Multivariable models were then fitted to assess the simultaneous effects of geographic location, primary specialty and gender after adjusting for other explanatory measures (attitudes and knowledge). Only factors with a p<0.25 in the simple logistic regression model. Both the p-value of the Wald statistic and the odds ratios of the main factors of interest were considered in evaluating the confounding effect

of covariates. If the adjusted odds ratio of one of the main factors of interest changed more than 10% from the unadjusted odds ratio in the presence of a particular covariate, that covariate was retained in the model as a potential confounder.

Given the confounding of geographic location and primary specialty in the sample, subanalyses were performed to examine the effect of geographic location among FM physicians only and the effect of primary specialty among urban physicians only, as there were approximately balanced populations of rural and urban physicians within the population of FM physicians in the sample, and similarly, urban physicians were balanced by practice type.

Power and sample size

Out of a possible 1240 Ob/Gyns and Family Medicine physicians that are members of the OMA, 575 had provided e-mail addresses. That number was supplemented with an additional 138 paper surveys as described above in the study population section. This gave a total sampled population of 713. A response rate of 35-40% was expected for this survey. This rate was based on another student's paper-based survey of the same population done approximately 5 years ago (Alicia Ahn, Oregon Providers' Knowledge, Attitudes and Practices Regarding Emergency Contraception, unpublished thesis). The overall urban/rural proportions of physicians in Oregon (of all specialties) is 80% urban, 20% rural. Applying that ratio to an n of 713 gives 571 urban and 142 rural physicians. The proportion of physicians who currently prescribe extended-use oral contraceptives was not known; reports in the literature range from 52-99.5%, but those estimates were obtained from populations who could be expected to have favorable attitudes towards

contraception, so I used a more conservative estimate for this population. The table below demonstrates power calculations for assumed prescribing proportions of 0.50 among urban providers. As an example, if a response rate of 50% were achieved, group sample sizes of 200 and 50 achieve 86% power to detect a difference of 0.20 between the null hypothesis that both urban and rural providers prescribe the same proportion (0.50) of extended-use OCs and the alternative hypothesis that the proportion in rural providers is 0.30 using a two-sided Chi-square test with continuity correction and a significance level of 0.05.

Assuming n=713 and 50% response rate							
Power	Urban MDs	Rural MDs	Allocation Ratio	P1	P2	Alpha	Detectable Difference
0.86	286	71	0.25	0.50	0.30	0.05	20%
0.58	286	71	0.25	0.50	0.35	0.05	15%
0.28	286	71	0.25	0.50	0.40	0.05	10%

P1 = Proportion of urban providers who prescribe extended-use OCs

P2 = Proportion of rural providers who prescribe extended-use OCs

Results

Of the 713 providers in the sample, 233 returned the survey for an overall response rate of 32.7%. A significantly lower proportion (151/575, response rate 26.3%) of e-mail surveys were returned than paper surveys (82/138, response rate 59.4%, p=0.005). Of these 233 responses, 22 indicated that they did not prescribe OCs and the remainder of the survey was not completed. Subjects responding to the e-mail survey tended to be younger, more urban, and more female than the paper survey respondents, although these differences were not significant (see Table 1). There were no significant differences within geographic or specialty groups with respect to gender, age or survey type (Table 2). Twenty-nine of the 36 Oregon counties were represented among respondents.

Of the 211 providers who do prescribe oral contraceptives, 98.1% said they would prescribe them for reasons other than to prevent pregnancy (Table 3). Reasons cited among these respondents included "to regulate the menstrual cycle" (98.1%), "to relieve menstrual symptoms such as bloating, headache, breast tenderness, PMS" (81.7%), "to decrease menstrual bleeding" (90.9%), and "for medical problems (migraines, endometriosis, von Willebrand's disease, chronic pelvic pain)" (81.3%). Urban and rural providers did not differ in their non-contraceptive reasons for prescribing OCs, but Ob/Gyns were significantly more likely to prescribe OCs to relieve menstrual symptoms $(X^2=16.56, p<0.001)$, to decrease menstrual bleeding ($X^2 = 4.97$, p=0.026), and for medical problems ($X^2 = 18.49$, p<0.001).

Overall, 155 (73.9%) of providers who do prescribe oral contraceptives indicate that they do prescribe extended-use OCs. Of those, 48 (22.9%) prescribe EOC "often" and 107 (51.0%) prescribe "sometimes." Ob/Gyns were more likely to indicate that they prescribe extended-use OCs often or sometimes, while many more FM physicians said they prescribe them rarely or not at all (X^2 =44.5, p <0.001) (Table 3). There were also statistically significant (X^2 =11.4, p=0.010) differences between rural and urban providers in their reported frequency of prescribing extended-use OCs, with urban providers being more likely to prescribe.

The majority of respondents, regardless of primary specialty or geographic location, were unaware of the most common week (correct answer = "placebo week") in which users of cyclic OCs experience menstrual-related side-effects (Table 4). Overall, respondents understood that use of extended-use OCs does not result in a thickened endometrium, however, a minority of those surveyed answered incorrectly (17%). Those who answered incorrectly were significantly more likely to be Family Medicine providers ($X^2 = 23.6$, p<0.001) (Table 4). Urban and rural providers did not differ in their responses to this question.

Compared with FM physicians, Ob/Gyns had significantly higher mean levels of agreement with the statements "There are potential health benefits to hormonal suppression of ovulation" (Mann-Whitney U p<0.001), "There are potential economic benefits to suppressing menstruation" (p<0.001), and "I feel that hormonal suppression of menstruation with extended-use OCs is safe (p<0.001) (Table 4). Their mean level of

disagreement with the statement "Monthly menstruation is essential for health in women taking birth control pills" was stronger than for FM physicians (p<0.001).Compared to rural physicians, urban physicians recorded a significantly stronger mean level of disagreement that monthly menstruation is essential for health (p=0.03), and a higher level of agreement that there are potential economic benefits to hormonal suppression of ovulation (p=0.004) and that hormonal suppression of menstruation is safe (p=0.03). Urban and rural providers did not differ in their mean agreement that menstrual suppression has potential economic benefits. Groups did not differ by geography or primary specialty in their mean level of agreement that "given the choice, many women would prefer to menstruate less than monthly." When an overall attitudes score was calculated, mean score for all providers was 21.32 ± 2.62 . Scores ranged from 13 to 25. Attitudes scores were significantly higher for Ob/Gyns (p<0.001) and for urban physicians (p=0.002).

Logistic regression

A summary of simple and multiple logistic regression models is shown in Table 5. In univariate analyses, geography and primary specialty were both significantly associated with prescribing (p=0.003 and p<0.001 respectively), as were gender (p<0.001), knowledge about the most common week of side-effects on a cyclic OC regimen (p=0.027), knowledge about the effect of extended-use OCs on the endometrium (p<0.001), attitudes about medically-induced amenorrhea (p<0.001), and age (p=0.042). Without adjusting for other factors, an Ob/Gyn was eight times more likely to prescribe often or sometimes compared with a FM physician (OR 8.02, 95% CI: 3.40, 18.91). The

association of geography with prescribing was not as strong, but still significant, with an urban provider being almost three times as likely to prescribe extended-use OCs (OR 2.75, 95% CI: 1.42, 5.30). Ethnicity and survey type were not associated with prescribing (p=0.456 and 0.275 respectively).

When controlling for other factors, the only variable that remained significantly associated with prescribing was providers' attitudes about medically-induced amenorrhea (Table 5). For a one unit increase in attitudes score, a provider is almost twice as likely to prescribe extended-use OCs often or sometimes (OR 1.8, 95% CI: 1.41, 2.42, p<0.001). When controlling for attitudes, primary specialty and geographic location were not significantly associated with prescribing extended-use OCs (p=0.090 and 0.256, respectively), although primary specialty approached statistical significance.

The following factors were found to significantly affect the association between primary specialty and prescribing habits: knowledge about endometrial thickening in users of extended-use OCs, age, attitudes and geographic location. Variability in age was found to negatively influence the relationship between primary specialty and prescribing: when adjusting for age, the odds of an Ob/Gyn prescribing often or sometimes increased from 8.02 to 10.1 (95% CI: 4.1, 24.9). When adjusting for either geography, knowledge about endometrial thickening or attitudes, the relationship between primary specialty and prescribing was no longer significant, and the odds ratio for primary specialty took on a similar value as in the full model (2.40, 95% CI: 0.87, 6.58).

Primary specialty and attitudes were the only factors to significantly change the association between geography and prescribing habits. Although geographic location became insignificant as a predictor with either factor in the model, of the two, attitudes had a stronger influence. Adjusting for gender, knowledge and age did not significantly affect the relationship of geographic location and prescribing habits.

There were no significant interactions between any variables.

As described above, primary specialty influences the association of geography with prescribing habits and vice versa. In order to determine which factor was more important in determining prescribing, subanalyses were done, looking at the influence of geographic location among Family Medicine physicians only (as there were relatively balanced numbers of urban and rural physicians in this group), and similarly, looking at the influence of primary specialty among urban physicians only (as the numbers of Ob/Gyn and FM physicians were approximately balanced in this group).

Among Family Medicine physicians (Table 6), geographic location was not significantly associated with prescribing (p=0.077). Female gender and knowledge about the most common week of side-effects on cyclic OC regimens were confounders of the relationship between geography and prescribing. When adjusting for knowledge about the effect of extended-use OCs on the endometrium, the relationship between geographic location and prescribing was strengthened, with the odds ratio increasing by approximately 10% and the p-value approaching statistical significance.

Among urban physicians (Table 7), Ob/Gyn as the primary specialty was significantly independently associated with prescribing (p<0.001). When adjusting for other factors, however, primary specialty was not a significant predictor of prescribing (p=0.163). Knowledge about the effect of extended-use OCs on the endometrium and attitudes about medically-induced amenorrhea were significant confounders of the relationship between being an Ob/Gyn and prescribing. When controlling for knowledge about endometrial thickening alone, the odds of an Ob/Gyn prescribing often or sometimes decreased by greater than 10%, but primary specialty remained significantly associated with prescribing. When adjusting for attitudes alone, the odds of an urban Ob/Gyn prescribing often or sometimes decreased by a greater than 10%. The results of these subanalyses suggest that primary specialty is a greater predictor of prescribing extended-use OCs than geographic location.

In addition, multiple logistic regression models were examined for web-based survey respondents only, and for paper survey respondents only. Among web-based survey respondents, attitudes remained the only factor significantly associated with prescribing. In fact, the association of positive attitudes was stronger than in the analysis examining all survey respondents, with an odds ratio of 2.89 (95% CI: 1.71, 4.89). When paper survey respondents were examined, no factors were significantly associated with prescribing.

Other findings

The length of time providers prescribe extended-use OCs depends on primary specialty and not geography (Table 8). FM physicians were more likely to advise the patient to take active pills for only two to twelve weeks beyond the initial 21 days, while Ob/Gyns were much more comfortable than FM physicians in advising the patient to take active pills indefinitely ($X^2 = 19.9$, p<0.001).

Among providers who do prescribe extended-use OCs, there were no significant differences by primary specialty or by geographic location in the proportions of providers who say that they offer extended-use OCs to patients for specific reasons (e.g. symptomatic, medical, personal or employment reasons), or for no particular reason (Table 9). Ob/Gyn physicians were more likely than FM physicians to report that they prescribe extended-use OCs because a patient asked, for specific reasons ($X^2 = 3.79$, p=0.052) and because a patient asked, for no particular reason ($X^2 = 7.11$, p=0.008). Urban providers were significantly more likely than rural providers to say they prescribe extended-use OCs because a patient asked, for specific reasons ($X^2 = 7.30$, p=0.007), but groups did not differ by geographic location in their likelihood of prescribing because a patient asked, for no particular reason (p=0.664).

In order to better characterize providers who indicated that they prescribe rarely (n=31), reasons for prescribing and preferred pill formulations were also examined for this group, although the numbers of physicians in this category were too small to allow for meaningful statistical analysis. Of these, 27 identified as FM and 4 identified as Ob/Gyn.

Of the 27 FM providers, 25 (92.6%) said they do prescribe extended-use OCs on patient request (for specific reasons), but 26 (96.3%) did not check the box corresponding to patient request (for no particular reason). 20 FM physicians (74.1%) said they offer extended-use OCs (for specific reasons), and 22 (81.5%) did not indicate that they offer extended-use OCs to all women on OCs. Of the four Ob/Gyn physicians who prescribe rarely, all four indicated that they prescribe extended-use OCs for specific reasons) and that they offer extended-use OCs for specific reasons. Additionally, none of the four indicated that they would prescribe on patient request (for no reason), nor that they would offer extended-use OCs to all patients already on OCs. 75% of Ob/Gyn and FM physicians said that when they prescribe OCs in an extended regimen, they prescribe a monophasic formulation. Of the 27 FM physicians, 17 (63.0%) said they also prescribe Seasonale®, and 2 (50%) of the Ob/Gyn physicians prescribe Seasonale®.

Among often or sometimes prescribers, providers did not differ by primary specialty or geographic location in their reported prescribing of Seasonale®. Similar proportions of Ob/Gyn and FM physicians reported that when they prescribe OCs in an extended fashion, Seasonale® is at least one of the formulations they prescribe (72.3% and 70.6% respectively, p=0.818). Similarly, 69.2% of urban physicians reported prescribing Seasonale®, compared with 81.8% of rural physicians (p=0.155). Seasonale® prescribing was also not necessarily linked to the duration for which a physician was willing to prescribe active pills in an extended fashion. Of those who are only willing to advise their patients to take active pills for 2-12 weeks (a time frame which would correspond to the 84 day Seasonale® regimen) beyond the initial 21 days, 75.3% said they prescribe

Seasonale®, while 76.9% of those who are comfortable prescribing active pills indefinitely also report prescribing Seasonale®.

There were no observed differences between groups of providers who do prescribe extended-use oral contraceptives in the relative importance of estrogen dose, type of progesterone or cost in their choice of which pill formulation to prescribe for extended use (lowest p=0.087). The mean level of importance of a monophasic formulation, was higher for Ob/Gyns and urban physicians (p<0.001 for primary specialty and p=0.009 for geographic location).

Ob/Gyns answered more frequently that "whatever I happen to have samples of" was a positive factor in their decision about which pill formulation to prescribe for extended use (p<0.001) compared with FM physicians.

Concerns about prescribing extended-use OCs

Among prescribers, the only observed differences were in the mean level of importance of concerns about potential long-term health effects, with FM physicians attributing a higher mean level of importance to this factor (p=0.01). Prescribers did not differ by geographic location in their concerns about prescribing.

Among non-prescribers, there were no differences in the relative importance of various factors between Ob/Gyns and FM physicians. There were insufficient data to analyze concerns among non-prescribers by geographic location.

Alternate definition of prescribing

When respondents who indicated that they prescribed extended-use OCs "rarely" were included in the category of prescribers, all variables remained significantly associated with prescribing in univariate analyses except for geographic location. When all variables were in the regression model, attitudes score was the only significant predictor of prescribing, and the odds ratio was almost identical (1.86, 95% CI: 1.31, 2.66) to the one obtained in the main analysis described in this survey.

Comments

The survey provided ample opportunity for providers to write in comments. The most frequent comments involved other reasons for prescribing extended OC regimens besides what was listed in the answer options. Many providers indicated that acne was a reason for recommending extended-use OCs. Other reasons included polycystic ovarian syndrome (PCOS), perimenopausal symptoms, prevention of menstrual cramps, ovarian cancer prevention and hirsutism. Many providers also commented that they were recommending the Nuva Ring® (a vaginal hormonal contraceptive ring) and Ortho-Evra® (a hormonal transdermal contraceptive patch) to their patients for extended-use.

Discussion

The purpose of this study was to examine the prescribing habits of Oregon Women's Health providers with regard to extended-use OCs, and to investigate providers' attitudes and knowledge about extended-use OCs and medically-induced amenorrhea. Additionally, the intent was to examine whether primary specialty, geographic location, knowledge or attitudes are related to prescribing.

This study found that 74% of providers prescribe extended-use OCs in their current practice (23% often and 51% sometimes). Reports of extended-use OC prescribing in the literature ^{17, 21, 86, 87} have ranged from 52% ¹⁷ to 99.5% ²¹, but all studies have suffered from varying degrees of selection bias, so it is difficult to evaluate the consistency of this finding. In this study, Ob/Gyn physicians were eight times more likely to prescribe extended-use OCs than FM physicians, and urban physicians were almost three times more likely to prescribe than rural physicians. Although primary specialty was not found to be a significant predictor of prescribing frequency when controlling for attitudes and other factors, the p-value approached statistical significance, and may have reached significance in a larger sample. The results of subanalyses among urban physicians and FM physicians also support the argument that primary specialty may be an important predictor in addition to attitudes. The only other study to look at primary specialty in relation to extended-use OC prescribing frequency found that Ob/Gyn providers were three times more likely to frequently prescribe extended-use OCs in their practice ⁸⁷. It is possible that the higher observed proportion of Ob/Gyn prescribers in my study results from having included providers who indicated that they prescribe extended-use OCs

"often" or "sometimes," while the above mentioned study only examined the relationship of primary specialty to prescribing "frequently" and did not include those who prescribe "occasionally." There are no known studies looking at prescribing by geographic location.

This study was also different from previous studies by Sulak and Andrist because it looked only at physicians, and only certain physician specialties. These categories of providers were chosen because they were thought to provide the majority of women's reproductive health care. Also considered for inclusion were advanced practitioners such as nurse practitioners and physician assistants, who arguably do provide a large proportion of women's health care, particularly in rural areas and in the county clinic setting. I decided that since physicians supervise these practitioners, a representative sample could still be obtained using only physicians.

The strongest factor predicting prescribing in this study was physicians' attitudes about menstruation and medically-induced amenorrhea. When controlling for differences in primary specialty, geographic location, gender, knowledge and age, attitudes remained significantly associated with prescribing. Overall, the women's health physicians surveyed had favorable attitudes towards extended-use oral contraception and medically-induced amenorrhea, with a mean attitudes score of 21.32 out of a possible 25, and this may help to explain the high percentage of providers reporting that they prescribe extended-use OCs in this population. Primary specialty and geographic location were found to influence attitudes about the need for monthly menstruation in users of OCs,

with Ob/Gyns and urban physicians indicating stronger beliefs that monthly menstruation is not necessary. These results are consistent with other literature looking at providers' attitudes. In the survey of health care providers performed by Sulak, 52% of respondents felt that withdrawal bleeding has no health benefits and is not necessary ⁸⁷. Only 11% of respondents to Andrist's survey thought that it was important for women to menstruate monthly ¹⁷. Neither study differentiated attitudes by specialty or geographic location. Glasier found cultural differences in providers' attitudes in her multi-national survey, with the majority of providers in Nigeria, Shanghai and Hong Kong reporting that they felt monthly menstruation on OCs was important, while providers in Scotland and South Africa felt that it was not important ¹⁹.

Glasier found that in every site except for South Africa, providers grossly overestimated the importance of monthly menstruation to their clients, and that their recommendations tended be much more consistent with their own attitudes, rather than the desires of their patients. This study found that although providers generally agree across specialties and geographic locations that women would prefer to menstruate less than monthly, their prescribing habits also tend to correspond to their attitudes about menstruation and medically-induced amenorrhea.

It would be reasonable to speculate that if certain populations of providers had more positive attitudes toward medically-induced amenorrhea, they might also be more likely to take a proactive approach to prescribing extended-use OCs, e.g. more frequently offering extended regimens to their patients. This was not borne out in this study,

however, with Ob/Gyn and FM physicians being equally likely to report that they offer extended-use regimens to their patients, whether for specific reasons or for no particular reason. Conversely, Ob/Gyns were more likely to report that patient request was a reason for prescribing extended-use OCs as compared with FM physicians. This may reflect a greater proportion of patients seeking contraception in general in Ob/Gyn practices as compared with Family Medicine practices.

To date, only six randomized controlled trials have compared extended or continuous-use OCs with traditional cyclic OC regimens, and these have not been consistent in the pill formulation or time-interval for extended/continuous dosing, so no established guidelines yet exist regarding the appropriate pill formulation or time interval ³⁴. Although the incidence of adverse side effects do not appear to differ between cyclic and extended-use OCs, trial numbers have been too small and of too short duration to draw conclusions about rare adverse events or long-term health effects associated with extended-use OCs ³⁴. As a result, providers must base prescribing decisions on their own attitudes and comfort level. In this study, there was a significant difference in prescribing between Ob/Gyn and FM physicians. These groups also differed in their attitudes about menstruation and medically-induced amenorrhea. Existing literature demonstrates that even when there are established guidelines, prescribing can vary significantly between Ob/Gyns and FM physicians. Levy looked at differences in hormone replacement therapy (HRT) use between women receiving care from Ob/Gyns and from FM physicians at the University of Iowa⁹⁵. In this study, women attending gynecology clinics were 2.6 times more likely to be using HRT than those attending FM clinics (95% CI 1.4, 4.6). In a

study by Yankowitz, also at the University of Iowa, obstetricians were significantly more likely to offer triple marker prenatal serum screening (p<0.05) than FM physicians ⁹⁶. What accounts for differences in prescribing patterns between specialty types? Levy and Yankowitz attributed differences in their studies to varying degrees of uncertainty between practice types, with specialists benefiting from a higher level of comfort and familiarity with complex considerations involved in recommending treatments or diagnostic tests, including recent scientific evidence, women's thoughts, concerns and individual risks and benefits. In my study, although FM physicians did not differ from Ob/Gyns in their agreement that many women would prefer to menstruate less than monthly, there is evidence that they feel more uncertain about the potential risks associated with extended-use OCs. FM physicians were more likely to think that extended OC use results in endometrial thickening and had a significantly lower level of agreement with the statement "I feel that hormonal suppression with extended-use OCs is safe." FM physicians were also more likely to report that concerns about long-term health effects were an important factor in their decision to prescribe extended-use OCs.

If, in fact FM physicians were more likely to have concerns about the safety of extendeduse OCs, would those that do prescribe extended regimens be more likely to prescribe an FDA approved regimen such as Seasonale®, assuming that FDA approval serves as a proxy for safety and provides some sort of guideline as to an agreed upon regimen duration? Among the eleven physicians in this study who reported exclusively prescribing Seasonale®, 91% were FM physicians, but it is not possible to draw conclusions with such a small group. Furthermore, the survey question that this

information was drawn from was a "check all that apply" question, and, as discussed above, the proportions of physicians who use Seasonale® as part of their prescribing repertoire were similar for Ob/Gyn and FM physicians, demonstrating that for the most part, FM physicians are familiar with off-label uses of other OC formulations and utilize those in addition to Seasonale®.

This survey utilized a combination of a traditional paper survey method, and a newer, somewhat unfamiliar web-based method, which achieved very different response rates. There were no significant differences in who responded to each method by geographic location, primary specialty, gender or age, but there was a trend towards younger, urban, female providers responding more to the e-mail survey. This reflects the current trend in the physician workforce in the United States ⁹⁷⁻⁹⁹ with ever increasing numbers of women graduating from medical school and practicing primarily in urban areas. It is not clear why these groups answered the web-based survey preferentially. It is possible that computer literacy is more pronounced in one of these populations, but a 2000 survey looking at internet use by rural physicians found that 85% of providers had internet access, and 75% reported using the internet either daily or one to four times per week ¹⁰⁰. There were no significant differences in frequency of internet use among groups by gender, age or specialty. There are no other known studies looking at demographics of computer use by physicians.

Strengths

There are several strengths of this study. I was successful in achieving an improved response rate over other mailed surveys addressing a similar question, although using a somewhat novel web-based survey technique resulted in a lower response. In addition, the sample for this survey was drawn from a general population of women's health physicians that would not be expected to have as favorable attitudes toward contraceptive use as the populations surveyed by Andrist, Glasier or Sulak. I also succeeded in capturing a geographically diverse group of providers, with responses coming from providers in 29 of 36 (80%) Oregon counties.

Limitations

A known problem in health care in the United States is the low numbers of rural providers, particularly Obstetrician/Gynecologists ¹⁰¹. Therefore, it is very difficult to accurately measure the prescribing habits of rural providers, and particularly to make comparisons between rural Ob/Gyns and FM physicians. One would have to do a much broader study, probably over multiple states to capture adequate numbers of rural providers with statistical weighting of Ob/Gyn physicians to accurately and reliably measure rural providers' prescribing habits, attitudes and knowledge with regard to extended-use OCs.

A significant limitation of this survey is the low response to the web-based survey. It could be argued that this resulted in response bias, with physicians having more favorable attitudes or a higher level of prescribing being more likely to return the survey. The

relationship of positive attitudes with prescribing was strengthened when looking only at web-based survey respondents, while attitudes was not a significant predictor among the much larger paper survey population, making responder bias in the web-based survey population a distinct possibility.

Although the response rate to the email survey was low, this finding was not entirely unexpected considering response rates found in other studies comparing web-based survey methods to postal mail surveys. The response rate was improved over that observed in Andrist's survey, which utilized postal mail surveys but not web-based surveys. There are several factors that may account for the low response to the web-based survey. It may be that many providers still do not regularly use e-mail or the internet in their practice, despite having e-mail addresses on file with the Oregon Medical Association. It is also plausible that the sheer volume of solicitations that a person receives by e-mail each day lead to a sort of burnout, where e-mails that come from an unknown party or seem to have been part of a mass mailing are simply deleted unopened. An estimate in 2000 was that some internet users receive more than 39 unsolicited emails per day at the workplace (NUA, E-mail driving growth of office workload, 2000, [Online] <u>www.nua.ie/surveys/?f=VS&art_id=905355873&rel-=true</u>). It is likely that this number has increased substantially in the past six years since that figure was published. Additionally, spam blockers may have rerouted some emails to providers' junk-mail folders, where the providers never noticed them. I was unable to obtain information from the OMA regarding the number of invalid e-mail addresses, but this cannot be presumed to account for a significant number of non-responses. I was also unable to query the

Zoomerang software regarding the number of participants who followed the link to the survey, but then opted not to participate, suggesting that the survey format appeared too complex or too long.

As mentioned in the introduction, other factors have been proposed as contributing to decreased response rates to web-based surveys. Dillman warns against using "fancy" or complex designs in web-based surveys as this may discourage participation by novice web users ⁹⁴. I took great pains in designing the web-based survey to ensure that both the survey methods were as identical in format and appearance as possible, but I cannot exclude complexity in the web-based survey style as being a factor in the lower response rate. It is unclear whether survey length is a factor in influencing response rates, but considering that both the web-based and paper versions of this survey were 26 questions in length, it is unlikely that this contributed significantly to the low web-based response while the paper survey achieved an impressive response.

Although primary specialty was not a significant predictor of prescribing when controlling for other factors, results from the main analysis as well as subanalyses suggest that with a larger sample, primary specialty may have reached statistical significance as a factor influencing prescribing. As discussed in the power and sample size section, a larger sample of 286 urban and 71 rural providers (as compared with the actual sample of 148 and 57 respectively) would have been necessary to detect a difference in prescribing of 20% between geographic groups. Power calculations were not done for primary

specialty, but it is likely that this study was underpowered to show differences between specialty types, particularly in smaller subgroups.

An additional limitation may be the way in which prescribing was defined, in that combining "rarely" and "not at all" as non-prescribers may have introduced bias. I chose to put "rarely" prescribers in the non-prescriber category, but it could be argued that they should have been categorized as prescribers. There was no existing literature on this subject to guide the classification of prescribing. The study by Sulak (2006) is the only study known to examine relative frequencies of prescribing, and it used different definitions of prescribing depending on whether comparisons by practice type were being made or not. My categorization could have introduced non-differential misclassification bias, which would tend to bias the observed relationship between main covariates and prescribing habits towards 1.0. However, when I performed multiple logistic regression with prescribing defined as "often," "sometimes" or "rarely," the observed odds ratio for attitudes was almost identical to the odds observed when prescribing was defined as "often" or "sometimes." Perhaps to better avoid this dilemma in the future one should phrase the question regarding prescribing frequency better to be able to discriminate between what providers mean by "rarely", and what their reasons are for prescribing when they say rarely. In the case of this survey, it appeared that providers who prescribe extended-use OCs rarely appear to only prescribe them for specific reasons (e.g. for medical, personal or employment reasons).

In addition, the terms often, sometimes, and rarely are subjective, and there may have been some variability in the way in which providers interpreted these terms. This could have, therefore, resulted in some misclassification of outcome. In the future, one could perform a more objective assessment of physicians prescribing patterns by utilizing an electronic record of prescriptions, which are becoming more common, but it may be difficult in this situation to link prescribing patterns to individual providers' attitudes and knowledge.

Generalizability

This study attempted to capture a diverse sample of women's health care physicians in Oregon representing a variety of geographic regions, social beliefs and practice styles. According to the Oregon Board of Medical Examiners, which bears the responsibility for licensing physicians in the state, there are currently 2,092 Obstetrician-gynecologists and Family Medicine physicians practicing in the state. The Oregon Medical Association had, at the time I distributed my survey, 1,240 physician members who were listed as one of these two specialties, or 59% of the total population of these physicians in the state. In addition to the population of OMA members that I sent my web-based survey to, I surveyed a sample of the remaining OMA members by paper survey in order to compare the characteristics of the respondents in each group. Although there were no statistically significant differences in the demographics of the web-based and paper survey populations, as stated above, the web-based survey respondents tended to be more urban, female and younger. The low response rate to the web-based survey limits some of the generalizability of this study, however, it may be balanced by an impressive response to

the paper survey. Additionally, Oregon physicians may have different characteristics than physicians in other states, so caution should be taken when extrapolating these results to other populations of physicians.

Summary and Conclusion

This study demonstrates that positive attitudes regarding medically-induced amenorrhea are the strongest factor influencing extended-use OC prescribing and that a small increase in positive attitudes about medically-induced amenorrhea results in increased prescribing. It is reassuring that a large proportion of providers report that they do prescribe extendeduse OCs, and overall, providers had positive attitudes about medically-induced amenorrhea. However, many providers remain uncertain about the safety of extended-use oral contraceptives and about the need for monthly menstruation in a woman taking oral contraceptives. Because there are still insufficient data to assess safety compared to traditional cyclic OCs, and because long-term health effects of extended-use OCs have not been documented, providers must rely on their attitudes and knowledge to guide their prescribing patterns. Although a low response rate limits the generalizability of this study's findings, the results are consistent with existing literature. It may be some time before there are sufficient data to document whether extended-use OCs are comparable to traditional OC regimens in safety and absence of long-term health effects. In the meantime, this study suggests that efforts to improve awareness and knowledge about the potential non-contraceptive benefits of extended-use OCs may be fruitful in improving the attitudes and prescribing patterns of those remaining providers who may be hesitant to prescribe this method.

Future applications of this study

This study identifies a need for additional evidence from well-designed clinical trials to support providers' attitudes about the advantages and disadvantages of medically-induced amenorrhea and clarify the real and perceived safety concerns about the use of extendeduse OCs to produce amenorrhea. Many providers indicated that they prescribe extendeduse OCs on patient request, yet the results of past studies looking at women's preferences about menstruation suggest that women are still unaware or unclear about extended-OC use. Therefore, to increase utilization of this strategy, it would be important to make use of media such as popular magazines, newspapers, television or radio to increase women's awareness and knowledge about the potential benefits (and risks, both perceived and theoretical) of extended-use OCs, so that they would more often ask their provider about these regimens. As an example, campaigns to increase awareness about emergency contraception (EC) have employed the popular media (e.g. the New York Times, Self magazine, etc) and in recent years, EC use has risen dramatically ¹⁰². Additionally, because providers play a key role in teaching patients about novel approaches for improving health, it would also be crucial to increase providers' awareness and knowledge about extended-use OCs through continuing medical education, including special courses, mailings and journal articles.

This study has raised a number of additional questions. First, this survey did not investigate in great detail the concerns of extended-use OC non-prescribers and the factors that influence their decisions or what their attitudes are toward medically-induced amenorrhea. It would be interesting in the future to more thoroughly assess a larger

sample of non-prescribing providers to more fully examine the reasons behind this practice pattern that represent potential barriers to access for some women.

Another area that remains unclear is the impact of the marketing of Seasonale on extended-use OC prescribing. In the future, it may be helpful to assess both providers' perceptions of changes in the frequency of patient requests for extended-use OCs because of publicity surrounding Seasonale®, and providers' acceptance of extended regimens as a valid method of contraceptive prescribing because of the existence of Seasonale®.

Although using extended-use OCs to produce amenorrhea is not for every woman, it is an option that is now available to those who wish to use it. Women desiring contraception or with hormonal symptoms deserve to be able to discuss all available options with their health care providers. To that end, providers need to be as familiar as possible with all available methods. Additionally, as this study demonstrates, providers need to be aware that their attitudes about extended-OC use and medically-induced amenorrhea influence their recommendations for their patients, whether for better or for worse.

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OREGON MEDICAL ASSOCIATION



December 30, 2004

To Whom It May Concern:

The Oregon Medical Association has agreed to allow Carrie Frederick to use its physician database to distribute her survey instrument to participants in her study for her master's thesis.

Should you have any questions, please contact Paige Webster $-\underline{paige@theOMA.org}$ or (503) 226-1555.

Thank you.

Regards,

Catherine Hotchkiss Director, Communications and Community Affairs



Trends in Oral Contraceptive Prescribing Survey

1. Do you currently prescribe oral contraceptive pills? (circle one) Yes No

If you answered "NO", you do not need to complete this survey, thank you for your time. Please return the survey blank in the provided envelope to ensure that you are not contacted again with a follow-up survey

Definition of terms used in this survey:

"Cyclic oral contraceptive pill" dosing is meant as 21 days of active pill followed by 7 days of placebo or no pills. "Extended oral contraceptive pill" dosing is meant as 28 or more consecutive days of active pills.

- 2. Do you prescribe oral contraceptive pills (OCPs) for reasons other than to prevent pregnancy?
 - □ Yes
 - D No

2a. If you answered "yes" to #2, please indicate for what reasons (check all that apply):

- To regulate menstrual cycle
 - To relieve menstrual symptoms such as bloating, headache, breast tenderness, PMS
- · □ To decrease menstrual bleeding
- □ For medical problems (i.e. migraines, endometriosis, von Willebrand's, chronic pelvic pain)
- □ Other (write in): _

3. Do you prescribe OCPs in an extended fashion (i.e. advising the patient to take active pills for longer than 28 days in a row)?

- 🖸 Often
 - □ Sometimes
 - □ Rarely
 - □ Not at all*
 - * If you answered "Not at all", please go on to question #8
- 4. If you have prescribed OCPs in an extended fashion, please indicate how you prescribe them (check all that apply):
 - □ Instruct patient to skip placebo week of monophasic pills (for example, Alesse, Ortho-Novum 135)
 - □ Instruct patient to skip placebo week of triphasic pills (for example, Ortho-Tricyclen, Triphasil)
 - □ Prescribe Seasonale®
 - □ Other (write in): _
- 5. When you have prescribed OCPs in an extended fashion, for what length of time do you advise patients to continue taking <u>active</u> pills beyond the initial 21 days?
 - For up to one week (total of up to 28 days of active pills)
 - For two to twelve weeks
 - □ For thirteen to 26 weeks
 - For 27 to 52 weeks
 - □ Indefinitely
 - Other (write in):

- 6. Please explain your reasons for prescribing extended regimen OCPs (check all that apply):
 - Patient asked me, for symptomatic relief of menstrual symptoms (i.e. heavy menses, pelvic pain, bloating, etc.).
 - D Patient asked me, for medical reasons (i.e. migraines, endometriosis).
 - □ Patient asked me, for personal reasons (i.e. honeymoon, sports, etc.).
 - Patient asked me, for employment reasons (i.e. military training).
 - □ Patient asked me, for no particular reason.
 - □ I offer extended OCPs for symptomatic relief of menstrual symptoms.
 - □ I offer extended OCPs for medical reasons.
 - □ 1 offer extended OCPs for personal reasons.
 - □ I offer extended OCPs for employment reasons.
 - □ I offer extended OCPs as an option for any woman using oral contraceptives.
 - Other (write in): _____

7. Please indicate the relative importance of the following features in your choice of which pill to prescribe for extended duration use.

	Very <u>Un</u> important	Somewhat <u>Un</u> important	Neutral	Somewhat Important	Very Important
a. Estrogen dose	1	2	3	4	5
b. Type of progesterone	1	2	3	4	5
c. Cost	1 -	. 2	3	4 .	5.
d. Monophasic formulation	1	2	3	4	5
e. Triphasic formulation	1	2	3	4	5
f. Whatever I happen to have samples of	1	2	3	4	5

8. How important are the following item	is in your decision to (o	r not to) prescribe	extended-use OCPs	š? .	
	Very <u>Un</u> important	Somewhat <u>Un</u> important	Neutral	Somewhat Important	Very Important
a. The cost	1 .	2	3	4	5
b. The side effects	1	2	. 3	4	5
a. Long-term health effects	1	2	3	4	5
d. Concerns about future fertility	1	2	3	4	5

9. Menstrual symptoms can result in lost productivity at work/school for women.

- True
- □ False

10. In women taking a traditionally dosed cyclic pill, menstrual associated side effects (nausea, bloating, pelvic pain, headaches) are most common during:

- □ The first 7 days of active pills
- Days 8-14 of active pills
- Days 15-21 of active pills
- □ The 7 day placebo week
- □ There is no relationship between the cycle week and associated side effects.

11. Oral contraceptives can relieve painful menses.

- □ True
- □ False

12. Monthly bleeding on a cyclic oral contraceptive pill regimen is due to:

- Endometrial proliferation
- □ Hormone withdrawal
- □ Release of an unfertilized ovum
- □ None of the above

13. Extended/continuous oral contraceptive use results in a thickened endometrium.

- True
- □ False

	Strongly disagree	Disagree	Neutral	Agree	Strongly agree
 Monthly menstruation is essential for health in women taking birth control pills. 	1	2	3	4	5
15. There are potential health benefits to hormonal suppression of ovulation	1	2	3	4	5
 There are potential economic benefits to suppressing menstruation. 	1	2	3	4	5
17. Given the choice, many women would prefer to menstruate less than monthly.	1	2	3	4	5
18. I feel that hormonal suppression of menstruation with extended use oral contraceptives is safe.	1	2	3	4	5
9. Your age (circle one): 20-29 30-39 40-49	50-59	60-69	70-79	80-89	
0. Gender (circle one): Male Female					

21. Ethnicity (circle one): Caucasian African American Hispanic Asian/Pacific Islander Native American Other-

22. Your primary specialty (circle one): Family Medicine OB/Gyn

23. If OB/Gyn, please indicate your secondary specialty (check all that apply).

- □ General
- □ Primarily obstetrics
- □ Primarily gynecology (including urogynecology)
- □ Gynecologic oncology
- □ Family planning/reproductive health
- □ Reproductive endocrinology

24. Please circle the county in which you practice the majority of the time:

Baker	Crook	Harney	Lake	Morrow	Union
Benton	Curry	Hood River	Lane	Multnomah	Wallowa
Clackamas	Deschutes	Jackson	Lincoln	Polk	Wasco
Clatsop	Douglas	Jefferson	Linn	Sherman	Washington
Columbia	Gilliam	Josephine	Malheur	Tillamook	Wheeler
Coos	Grant	Klamath	Marion	Umatilla	Yamhill

25. Is the patient population you serve in your practice primarily (check one):

- D Rural
- □ Suburban
- 🗆 Urban
- □ Combination of above categories
- 26. Type of Practice (check one):
 - □ Group
 - D Private
 - □ University
 - □ Community hospital
 - Other _____

Additional comments (feel free to write on the back of this page):

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Tables

		Survey type					
		Paper n(%)	E-mail n(%)	Total	X ²	OR(95% CI)	
Geogr	aphy						
	Urban	50(66.7)	98(75.4)	148(72.2)			
	Rural	25(33.3)	32(24.6)	57(27.8)	1.80		
Total		75	130	205	p=0.180	0.65(0.35,1.22)	
Prima	ry special	ty					
	Ob/Gyn	28(37.8)	62(47.7)	90(44.1)			
	Family	46(62.2)	68(52.3)	115(55.9)			
	Med				1.86		
Total		74	130	204	p=0.173	0.67(0.37,1.20)	
Gende	er						
	Female	40(53.3)	80(60.6)	120(58.0)			
	Male	35(46.7)	52(39.4)	87(42.0)	1.04		
Total		75	132	207	p=0.308	0.74(0.42, 1.32)	
Age	2						
-	<40	28(37.3)	59(44.7)	87(42.0)			
	40-49	23(30.7)	38(28.8)	61(29.5)			
	≥50	24(32.0)	35(26.5)	59(28.5)	1.18		
Total		75	132	207	p=0.555		
Ethni	city	8 12 1 2 12 12 1					
	White	68(91.9)	117(89.3)	185(90.2)			
	Non-	6(8.1)	14(10.7)	20(9.8)			
	white				0.357		
Total		74	131	205	p=0.550	0.737(0.271,2.01)	

Table 1: Demographic characteristics of survey respondents by survey method:

		All providers	providers Ob/Gyn Family Med Ob	Rural	Rural	p-value*		
					Ob/Gyn n=12	Family Med n=43	Primary specialty	Geography
Gender	Female	120(58.0)	51(66.2)	41(58.6)	6(50.0)	20(46.5)	0.198	0.054
construct other time to prove	Male	87(42.0)	26(33.8)	29(41.4)	6(50.0)	23(53.5)	0.355	6.210
Age	<40	87(42.0)	30(39.0)	33(47.1)	2(16.7)	20(46.5)	0.237	0.809
	40-49	61(29.5)	23(29.9)	22(31.4)	7(58.3)	9(20.9)		
	≥50	59(28.5)	24(31.2)	15(21.4)	3(25.0)	14(32.6)	1.	0.845
Survey type	Paper	75(35.5)	25(32.5)	25(35.7)	3(25.0)	21(48.8)	0.173	0.180
	Email	136(64.5)	52(67.5)	45(64.3)	9(75.0)	22(51.2)	- WERE	12725

Table 2. Comparison of demographic factors of interest and survey type by geography and primary specialty

*Chi-square p-values for categories collapsed by geography or primary specialty † Totals vary slightly among categories due to incomplete responses. No variable had >10% missing values.

Table 3. Comparison of prescribing habits for providers by primary specialty and geograp	phic location
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		All providers	Urban Ob/Gyn	Urban Family Mod	Rural	Rural	p-	value [*]
Knewtodge stood mine		providers	n=77 [†]	Family Med n=70	Ob/Gyn n=12	Family Med n=43	Primary specialty	Geography
Do you prescribe OCs for reasons other than to preven pregnancy?	t Yes No	207(98.1) 4(1.9)	74(96.1)	69(98.6)	12(100)	43(100)	0.209	0.210
If yes to above, for what reas	ons?		1 7500.70	19/70.61	12(10)0		- 1 (M)	0.046
To regulate the mens	trual cycle	204(98.1)	73(98.6)	69(98.6)	12(100)	42(97.7)	0.726	0.843
To relieve menstrual	symptoms	170(81.7)	70(94.6)	53(75.7)	12(100)	31(72.1)	< 0.001	0.197
To decrease menstru For medical problem	0	189(90.9) 169(81.3)	71(95.9) 71(95.9)	63(90.0) 51(72.9)	12(100) 12(100)	36(83.7) 30(69.8)	0.026 <0.001	0.215 0.246
Reported frequency of prescribing extended-use OCs	Often	48(22.9)	34(44.2)	7(10.0)	4(33.3)	3(7.0)	< 0.001	0.010
	Sometimes	107(51.0)	37(48.1)	39(55.7)	7(58.3)	18(41.9)	-0.001	0.010
	Rarely	31(14.8)	3(3.9)	14(20.0)	1(8.3)	13(30.2)		
	Not at all	24(11.4)	3(3.9)	10(14.3)	0(0)	9(20.9)		

*Chi-square p-values for categories collapsed by geography or primary specialty * Totals vary slightly among categories due to incomplete responses. No variable had >10% missing values.

		All	Urban	Urban	Rural	Rural	р-	value
		providers n=202	Ob/Gyn n=77	Family Med n=70	Ob/Gyn n=12	Family Med n=43	Primary specialty	Geography
Knowledge about most common week of side- effects	Correct Incorrect	62(32.0) 132(68.0)	n=73 28(38.4) 45(61.6)	n=66 19(28.8) 47(71.2)	n=9 3(33.3) 6(66.7)	n=41 11(26.8) 30(73.2)	0.115*	0.379*
Knowledge about endometrial thickening	Correct Incorrect	168(82.8) 35(17.2)	n=76 75(98.7) 1(1.3)	n=68 48(70.6) 20(29.4)	n=12 12(100) 0(0)	n=42 31(73.8) 11(26.2)	<0.001 [‡]	0.289*
Monthly menstruation is health in women taking b pills		Mean(SD) 1.47(0.70)	Mean (SD) 1.09(0.29)	Mean (SD) 1.76(0.75)	Mean (SD) 1.17(0.39)	Mean (SD) 1.77(0.87)	<0.001**	0.031**
There are potential health hormonal suppression of		4.17(0.90)	4.57(0.72)	4.00(0.78)	4.25(1.14)	3.74(1.05)	< 0.001**	0.004**
There are potential econo to suppressing menstruat		4.18(0.66)	4.42(0.66)	4.03(0.62)	4.25(0.45)	4.02(0.67)	< 0.001**	0.100**
Given the choice, many w prefer to menstruate less	omen would	4.16(0.75)	4.29(0.67)	4.13(0.82)	4.00(0.89)	4.05(0.69)	0.198**	0.147**
I feel that hormonal supp menstruation with extend safe	ression of	4.30(0.76)	4.69(0.49)	4.06(0.78)	4.58(0.67)	3.98(0.89)	<0.001**	0.031**
Mean attitudes score (range 13-25)		21.32(2.62)	22.8(1.96)	20.5(2.47)	21.9(2.46)	20.0(2.70)	< 0.001****	0.002***

Table 4. Comparison of knowledge and attitudes for providers by primary specialty and geographic location

Note: Totals vary slightly from subcategories due to incomplete responses. No variable had >10% missing values.

*Chi-square p-value *Fisher's Exact test (2-sided) **Mann-Whitney U p-value ***t-test for 2 independent samples

		Simple LR m	odels	Full model		
		OR (95% CI)	p*	OR (95% CI)	p**	
Geography	Urban	2.75 (1.42,5.30)	0.003	1.76 (0.67,4.64)	0.256	
Geography	Rural	1.00		1.00		
Primary specialty	Ob/Gyn	8.02 (3.40,18.9)	< 0.001	2.76 (0.86,8.90)	0.090	
Grader	Fam Med	1.00		1.00		
Gender	Female	3.75 (1.96, 7.19)	< 0.001	1.42 (0.55,3.65)	0.471	
	Male	1.00		1.00		
Knowledge: Week of	Correct	2.24 (1.06, 4.73)	0.027	1.71 (0.58,5.04)	0.335	
side-effects	Incorrect	1.00		1.00		
Knowledge: Effect on	Correct	7.48 (3.40, 16.5)	< 0.001	1.31 (0.40,4.27)	0.659	
endometrium	Incorrect	1.00		1.00		
Attitudes	<40 ·····	1.95 (1.59, 2.40)	< 0.001	1.85 (1.41,2.42)	< 0.001	
Age	<40	1.00	<0.001	1.00	0.484	
	40-49	0.88 (0.40, 1.93)	0.042	0.69 (0.23,2.07)	0.503	
	≥ 50	0.41 (0.20, 0.85)		0.33 (0.10,1.17)	0.086	
Survey	E-mail	0.70 (0.37, 1.32)	0.275			
	Paper	1.00				
Ethnicity	White	0.66 (0.21, 2.06)	0.456			
•	Non-white	1.00				

Table 5: Results of simple logistic regression and multivariate regression models for prescribing often or sometimes vs rarely or not at all.

* p-value for Likelihood Ratio Test ** p-value for Wald statistic

		Simple LR m	odels	Full model		
		OR (95% CI)	p*	OR (95% CI)	p**	
Geography	Urban	2.01 (0.93, 4.36)	0.077	2.15 (0.71, 6.53)	0.176	
	Rural	1.00		1.00		
Gender	Female	4.63 (2.07, 10.3)	< 0.001	1.50 (0.48, 4.71)	0.484	
	Male	1.00		1.00		
Knowledge: Week of	Correct	2.48 (0.99, 6.25)	0.046	3.93 (0.99, 15.5)	0.050	
side-effects	Incorrect	1.00		1.00		
Knowledge: Effect on	Correct	4.24 (1.76, 10.2)	0.001	1.32 (0.35, 4.89)	0.681	
endometrium	Incorrect	1.00		1.00		
Attitudes		1.79 (1.41, 2.27)	< 0.001	1.85 (1.35, 2.54)	< 0.001	
Age	<40	1.00	.0.157	1.00	0.115	
	40-49	4.63 (2.07, 10.3)	< 0.001	1.50 (0.48, 4.71)	0.484	
	≥ 50	0.30 (0.12, 0.76)		0.28 (0.06, 1.29)	0.102	

Table 6: Subanalysis for Family Medicine physicians only: Results of simple logistic regression and multivariate regression models for prescribing often or sometimes vs rarely or not at all.

* p-value for Likelihood Ratio Test ** p-value for Wald statistic

		Simple LR models		Full model		
		OR (95% CI)	p*	OR (95% CI)	p**	
Primary specialty	Ob/Gyn	6.17 (2.34, 16.3)	< 0.001	2.60 (0.68, 9.97)	0.163	
	Fam Med	1.00		1.00		
Gender	Female	4.09 (1.78, 9.42)	0.001	1.12 (0.34, 3.69)	0.851	
	Male	1.00		1.00		
Knowledge: Week of	Correct	4.40 (1.44, 13.5)	0.003	1.90 (0.47, 7.75)	0.371	
side-effects	Incorrect	1.00		1.00		
Knowledge: Effect on	Correct	7.0 (2.64, 18.6)	< 0.001	1.45 (0.33, 6.30)	0.620	
endometrium	Incorrect	1.00		1.00		
Attitudes		1.89 (1.48, 2.42)	< 0.001	1.95 (1.39, 2.75)	< 0.001	
Age	<40	1.00		1.00		
	40-49	0.58 (0.22, 1.58)	0.157	0.30 (0.07, 1.34)	0.115	
	≥ 50	0.39 (0.15, 1.03)		0.19 (0.04, 1.04)	0.056	

Table 7. Subanalysis for urban physicians only: Results of simple logistic regression and multivariate regression models for prescribing often or sometimes vs rarely or not at all.

*p-value for Likelihood Ratio Test ** p-value for Wald statistic

Table 8. Duration providers advise continuing extended-OC regimens, among prescribers, by geography and primary specialty

	All providers n=149	Urban Ob/Gyn n=67 [†]	Urban Family Med n=46	Rural Ob/Gyn n=11	Rural Family Med n=19	p-value*	
Designed to the same resigned for						Primary specialty	Geography
When you have prescribed OCs in an extended fashion, for what length of time do you advise patients to continue taking <u>active</u> pills beyond the intitial 21 days?	1040x.5	1.000 M	10,000 it 2	100 m	1385 m	91157 6.000	1007
For up to one week	0	0	0	0	0		
For two to twelve weeks	89(59.7)	32(47.8)	29(63.0)	8(72.7)	14(73.7)	0.001	0.165
For thirteen to 26 weeks	16(10.7)	5(7.5)	9(19.6)	0(0)	2(10.5)		
For 27 to 52 weeks	5(3.4)	1(1.5)	2(4.3)	0(0)	2(10.5)		
Indefinitely	26(17.4)	18(26.9)	5(10.9)	2(18.2)	1(5.3)		
Other	13(8.7)	11(16.4)	1(2.2)	1(9.1)	0(0)		

*Pearson's chi-square [†] Totals vary slightly among categories due to incomplete responses. No variable had >10% missing values.

	All providers n=152	Urban Ob/Gyn n=71	Urban Family Med n=46	Rural Ob/Gyn n=9	Rural Family Med n=20	p-value*	
						Primary specialty	Geography
Please explain your reasons for							
prescribing extended regimen OCs							
Patient asked me (for symp-	134(86.5)	66(93.0)	41(89.1)	8(88.9)	13(65.0)	0.052	0.007
tomatic, medical, employment or				. ,			
personal reasons)							
Patient asked me (for no reason)	52(33.5)	31(43.7)	9(19.6)	3(33.3)	6(30.0)	0.008	0.664
I offer extended-use OCs for	144(92.9)	69(97.2)	42(91.3)	9(100.0)	18(90.0)	0.141	0.666
symptomatic, medical,							
employment or personal reasons							
I offer extended-use OCs as an	81(52.3)	42(60.6)	21(45.7)	4(44.4)	10(50.0)	0.115	0.645
option for any women using OCs							

Table 9: Reasons for prescribing extended-use OCs among extended-use OC prescribers, by primary specialty and geography

Note: percentages do not sum to 100% because providers could choose more than one response *Pearson's Chi-square p-value