

Fertility Report: January, 2007

Good Concordance Found between Self-reported Start of Menses and WHO Algorithm

James Trussell from the Office of Population Research at Princeton University re-analyzed data from a previous study that described the menstrual bleeding patterns found after use of the emergency contraceptive pill (ECP) that contained 1.5 mg of levonorgestrel.^{1,2} The purpose for the re-analysis was to determine if there was concordance between the starting dates of menses as self-recorded by diary with the date of menses as determined retrospectively with an algorithm. The menstrual period algorithm was adapted from a formula developed by the World Health Organization (WHO) and stated that a menstrual period was any episode of at least 3 days of bleeding/spotting (either 3 consecutive days of bleeding/spotting or 2 days of bleeding/spotting separated only by one bleeding/spotting free day), preceded by at least 2 days without bleeding/spotting.

The participants in the study were women between the ages of 18-35, who had a usual menstrual cycle length of 23-32 days, and had taken the ECP on the day of enrollment into the study or the day before. There were 111 participants obtained from a Planned Parenthood clinic in the Boston area (between June 2004 and March 2005), met the criteria, and were asked to record in a paper diary any vaginal bleeding or spotting for the next 10 weeks and whether they thought that this bleeding was part of their menstrual period. In a follow-up interview at 9 weeks the participants were asked to verify or correct any discrepancies identified. The diaries were analyzed with the modified WHO algorithm to determine concordance.

There were a total of 261 periods identified with the algorithm of which 74% were in concordance with the self-identified start of menses. In another 13% the self-identified start of menses was 1 day later. In 8% of the cases the self-identified start of menses was more than 7 days later than the algorithm start date, and in 18 of these 21 cases the start date was more than 2 weeks later. The concordance was lower in the first menstrual period following ingestion of the ECP. There was only a 68% concordance between the WHO adapted algorithm determined date and the self-reported date and in 14% the cases the difference was more than 7 days.

The author concluded that there was good concordance between the WHO adapted algorithm date for the start of menses and the self-recorded start date as recorded in diaries. However, he also stated that some women struggle to interpret whether or not bleeding/spotting in a cycle following ECP constitutes a period. Furthermore, in analyzing the data from the self-reported diaries in comparison of the dates from the follow-up interviews, he stated that retrospective answers to questions about the start of the last menstrual period may be suspect.

Comments: The adapted WHO algorithm as presented in this article could be useful to NFP teachers to help women/clients interpret the beginning of menses, and in particular when there are 1-2 days of spotting. Findings from this study also have relevance to fertility awareness and NFP methods that rely on the correct identification of the menstrual period for determining the fertile phase.

1. Trussell J. **Bleeding after use of the levonogestrel regimen of emergency contraception: concordance between women's reports of their menstrual periods and an objective algorithm.** *Contraception* 2007;75:32-36.
2. Raymond EG, Goldberg A, Trussell J, Hays M, Roach E, Taylor D. **Bleeding patterns after use of levonogestrel emergency contraceptive pills.** *Contraception* 2006;73:376-81 [*Erratum. Contraception 2006;74:349 – 50*]

No Increased Risk of Depressive Symptoms found Among Young Oral Contraceptive Users

There is common knowledge among the public and natural family planning teachers that use of hormonal oral contraceptives (OCs) causes depression among users. One of the reasons that has been stipulated is due to a decrease in vitamin B6. However, there is little research to show that this is so. In fact, a study by Oddens has shown that there are higher levels of depression among NFP users.¹ Researchers from the University of Newcastle, Australia conducted a study for the purpose of determining if there was an association between use of OCs and depression among young Australian women.² A unique aspect of the study was that they also wanted to control for confounding factors of depression, such as, life changes, stress, limited social support, and previous depressive illness.

The subjects for this study were women who were participants in the Australian Longitudinal Study on Women's Health that involved 3 surveys, one in 1996, the next in 2000, and the 3rd survey in 2003. The current study involved 9,688 women between the ages of 22 and 27 in survey 2 and 9,081 of the women in survey 3. The survey items included a depressive symptoms scale, current use of OCs, a measure of health status, life events, and over all perceived stress.

Before adjusting for confounders, 23.3% of the OC users and 30.3% of the non-OC users reported depressive symptoms. This proportion was statistically significant by Chi square statistics. The odds ratio (OR) of a non-user experiencing a depressive symptom being 1.43 (95% CI=1.28-1.58) times that of the OC users. After adjusting for confounders of depression, there was no significant increased likelihood of the no-OC users reporting of depressive symptoms than the OC users, OR = 1.05 (95% CI = 0.90-1.21). However in comparison with women who were using OCs for contraceptive purposes, the odds ratio for depressive symptoms was significantly increased among women who used OCs for non-contraceptive purposes, i.e., the OR was 1.32 (95% CI = 1.07-1.62). The researchers also found that the amount of depressive symptoms decreased among the OC users as the number of years of use increased. They concluded that there was no evidence for the association between OC use and depression among young Australian women.

Comments Based on the evidence from this Australian study and the European study, it would not be recommended that NFP teachers mention an association between OC use and depression. This was a large population based longitudinal study with a representative sample of women. However, as the author points out, this was not a randomized controlled trial of OC users versus

non-users, which would be a better (but not necessarily feasible) research design to determine cause an effect.

1. **Oddens BJ. Women's satisfaction with birth control: a population survey of physical and psychological effects of oral contraceptives, intrauterine devices, condoms, natural family planning, and sterilization.** *Contraception*, 1999;59:277-286.
2. **Duke JM, Sibbritt DW, Young AF. Is there an association between the use of contraception and depressive symptoms in young Australian women?** *Contraception*, 2007;75:27-31.

Inconsistent Use of Oral Contraceptives Associated with having Occasional Sexual Partner

It is common knowledge among natural family planning (NFP) teachers that the use of NFP is more effective when used by a consistent and committed sexual partner -- so too with the use of oral contraceptives (OCs). Although OCs are highly effective when used correctly, there is an approximate 8% unintended pregnancy rate when used inconsistently. Researchers from the Office of Population Research at Princeton University in conjunction with researchers from the French Institute of Health and Medical Research conducted a study to determine social, demographic, and situational characteristics associated with inconsistent use of OCs. They cite the need to use conceptual models of consistent use that highlight the contextual and dynamic nature of contraceptive behavior and not just individual level ones, such as age, ethnicity, and social background.

The subjects for this study were 1,234 OC users who were randomly selected from a French population based (The Cohorte Contraception) survey that was conducted in 2000. This survey involved women aged 18-44 who were selected from 14,704 households. The eventual population was 2,863 women. The survey questionnaire included questions designed to collect information on social and demographic characteristics, contraceptive knowledge and use, sexual intercourse patterns, and information on OC pill compliance. The data for this study was based on the 4 weeks prior to the interview survey.

In the 4 weeks prior to the survey date, 20% of the women respondents missed at least 1 pill and 7% missed 2 or more. Furthermore, 10% missed at least 1 OC pill and did not use backup contraception. The odds ratio (OR) of an increased likelihood of missing a pill were among those women who had an occasional sexual partner (OR = 5.3), those who did not feel involved with the choice of the pill (OR = 8.3), having a young child in the household (OR = 2.9) and not having a regular pill-taking routine (OR = 1.9). Those women who felt they were not involved with the decision-making in the choice of contraceptive method and who took the pill inconsistently were also more likely not to have used a back up contraceptive (OR = 4.0). Based on these findings the authors recommended that family planning service providers need to assess and address women's preferences and needs in the context of their sexual, emotional, and social lifestyles in order to increase compliance and effectiveness during typical use.

Comments: Based on the findings of this study, service providers of NFP and fertility awareness based methods need to also assess and address the woman client's (and couple's) sexual, emotional, and social lifestyles. NFP teachers also need to help couples and clients determine what NFP method works best for them in their given situation and not just (or offer) one method for all situations. NFP teachers often work with clients that have small children and the consistent observation of natural biological indicators is not always possible. The results also suggest that the use of NFP would not be advisable with (outside of marriage) occasional sexual partners.

Moreau C, Bouyer J, Gilbert F, the CONCON Group, Bajos N. **Social, demographic and situational characteristics associated with inconsistent use of oral contraceptives: evidence from France.** Perspectives on Sexual and Reproductive Health, 2006;38:190-196.

Live Delivery Rate is Zero for Women Older than 45 years using Autologous Oocytes

It is well known that fertility decreases with age largely due to the decrease in the number of follicles (ovarian reserve) and to increased chromosomal abnormalities in the remaining oocytes. Women who seek IVF after the age of 42 are recommended to use donor oocytes but for many women this is not an acceptable option. Previous studies with IVF with women over 44 years of age and with use of homologous oocytes have shown no pregnancies. However, these were small studies with no more than 23-51 cycles of IVF. The conclusion, however, from these small studies was that no live pregnancy could be achieved for women over 45 years of age using autologous oocytes. Researchers from the Center of Reproductive Endocrinology and Infertility of the Cornell Medical Center reported the results (pregnancy rates) they experienced with a much larger pool of women over age 44 who were involved with autologous oocytes for IVF.

This was a retrospective study of 288 women between the age of 45-49 (mean 45.4) and who underwent 288 IVF cycles with autologous oocytes from October of 1991 through June of 2005. Of the 288 women, 57 were unable to start the IVF procedures because of an elevated FSH or ovarian cyst and 30% (70/231) had their IVF cycle cancelled due to low ovarian stimulation response (i.e., < 3 follicles). The mean number of follicles of the remaining women was 6.8 (SD=3.8) and the mean number of fertilized zygotes was 5.4 (SD=3.4). On average the mean number of embryos that were transferred was 3.2 (SD+1.5).

Of the 231 IVF cycles there were 116 IVF cycles among the 45 year old women of which 24.1% resulted in a positive pregnancy, 12.9% clinic pregnancies, and only 4.3% live deliveries. The remaining 46-49 year old women had 0 live deliveries. But the data from the 46-49 year old women was only from 45 IVF cycles. Thus, there was an overall live delivery rate of only 2.2% (5/231). The authors concluded that IVF using autologous oocytes in women over 44 years of age can be successful. However, they also said that this is limited to women with normal ovarian reserve and a response of a least 5 oocytes during ovarian hyperstimulation.

Comments: I would add to say that there still is no evidence that a live delivery could be achieved for a woman over 45 with autologous oocytes. I reviewed this article to reemphasize

the difficulty of achieving a pregnancy after 45 years of age. The authors of this study did not mention the expense of the 288 IVF cycles with an actual pregnancy rate of only 1.7% (5/288). I would imagine in the “real” world of 3rd party insurance that such a small success rate and the expense would preclude these procedures taking place for the poor. If these women had no anatomical defects (e.g., block tubes) I would like to have seen a comparison of using focused intercourse on days of high fertility as observed with natural indicators of fertility.

Spandorfer SD, Bendikson K, Dragisic K, Schattman G, Davis OK, Rosenwaks Z. **Outcome of in vitro fertilization in women 45 years and older who use autologous oocytes.** *Fertility and Sterility*, 2007;87:74-76.

There is no Evidence that Access to Emergency Contraceptive Pills Decreases Unintended Pregnancy and Abortion Rates

A trio of researchers from Family Health International, the Office of Population Research at Princeton University, and the Department of Family and Reproductive Health at Johns Hopkins Bloomberg School of Public Health systematically investigated the published literature to determine if increased access to emergency contraceptive (EC) pills influenced the pregnancy rates and use of the pills. After conducting an extensive search from 4 literature data sources they were able to identify 717 articles on the topic. They eliminated 694 of those articles that either did not contain primary data that compared interventions or were articles that had the same data from a prior publication. Thus, there were 23 articles (published between 1998-2006) that met their selection criteria. Of these, 10 were randomized control trials, 4 were cohort studies, and the others were population based studies. The results from the studies convincingly showed that greater access to EC increased the use of EC pills. However, there was no evidence that increased access led to decreased unintended pregnancy or abortion rates. They concluded that further research is needed to explain the best ways to use EC to produce a public health benefit.

Comments: Back in 1992 Trussell, Hatcher and others published an article in which they proposed that the wide spread use of EC will cut the number of induced abortions in the US in half. In this current article, Trussell and others are saying that EC is only relatively effective and that, at best, what access to EC does is help women to focus on more effective methods of contraception. As the authors stated in their article “previous expectations that improved access could produce a direct, substantial impact on a population level may have been overly optimistic.” What can we learn from this article about providing easier access to NFP methods? Greater use but maybe not better efficacy rates?

Raymond G, Trussell J, Polis CB. **Population effect of increased access to emergency contraceptive pills.** *Obstetrics and Gynecology*, 2007;109:181-188.

Menstrual Cycle Irregularity Related to Increased Risk for Cardiovascular Disease

University based researchers from Brazil conducted a case-control study to determine the association between cardiovascular risk factors and disease during the post menopausal years in

relation to menstrual cycle irregularity during the reproductive years. The participants were 414 postmenopausal women (mean age 60.4). The variables that were measured were menstrual cycle characteristics at age 20-35 (as the independent variable) with medical records of hypertension, diabetes mellitus, dyslipidemia, and coronary artery disease (as the dependent or outcome variables).

Participants who reported menstrual cycle irregularity during the reproductive years were associated with an increased risk for some cardiovascular risk factors compared to those women with regular menstrual cycles with an odds ratio (OR) = 2.14. Stratified analysis also identified women with irregular menstrual cycles to have a increased risk for: 1) arterial hypertension, OR = 2.74, 2) hypercholesterolemia, OR = 2.32, 3) hypertriglyceridemia, OR = 2.09, and 4) coronary angioplasty, OR = 6.82. The authors emphasized that the association between menstrual cycle irregularity and cardiovascular disease was indicative of polycystic ovary syndrome.

Comments: Although I have the complete article (in Portuguese) I was able to read only the English abstract with depth. The findings imply the health benefit of self-monitoring the menstrual cycle and the use of menstrual cycle charting to help evaluate treatments for polycystic ovary disease, i.e., regular length menstrual cycles as a positive outcome.

Azevedo GD, Duarte JM, Souza MO, Costa-E-Silva TD, Soares EM, Marandao TM. **Menstrual cycle irregularity as a marker of cardiovascular risk factors at postmenopausal years.** Brazilian Archives of Endocrinology and Metabolism (ARq Bras Endocrinol Metab) 2006;50:876-882.

Oral Hormonal Contraceptive Use and Risk of Cancer

Investigators from the Fertility and Infertility Research Center in Warszawa, Poland conducted a systematic review of the research literature to determine risk for all different types of cancers among women users of combined hormonal oral contraceptives. They provided a table of their findings which I have recreated below:

Table 1 The influence of combined oral contraceptives on the risk of cancer development

<i>Type of cancer</i>	<i>Decreased risk</i>	<i>Increased risk</i>
Ovarian cancer	40% decrease	None
Endometrial cancer	56-72% decrease	None
Breast cancer		Slight increase*
Cervical cancer		Slight increase*
Colon cancer	Slight decrease*	Not applicable
Liver cancer		Slight increase*
Melanoma		None (according to meta-analysis)

*Most probably – but difficult to estimate precisely.

Comments: I think that it is important for NFP/FAM teachers when discussing the use of OCs with clients or the public to not over state the associated risk of cancer with use of oral hormonal contraceptives – in particular with the risk of breast cancer.

Lech MM, Ostrowska L. **Risk of cancer development in relation to oral contraception.** The European Journal of Contraception and Reproductive Health Care, 2006;11:162-168.