Long-term, reversible, progestogenic contraceptive use in adolescents: an evaluation of common hesitations

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Long-term, reversible, progestogenic contraceptive use in adolescents:

An evaluation of common hesitations.

Erika Marie Simmermeyer

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2010
Dedication

This clinical review is dedicated to my family and fiancé, Alex, who supported and tolerated me throughout this extensive process.
Acknowledgments

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Introduction

The Youth Risk Behavior Surveillance-United States released by the Centers for Disease Control and Prevention (CDC) reports that on average 47.8% of U.S. high school students have had sexual intercourse. By age 15, 13% of teenagers have been sexually active which increases to 70% by 19 years of age. More specifically, a total of 35.0% of teenage students report current sexual activity, meaning within the last three months (Eaton, et al., 2008). Each year an average of 750,000 teenagers become pregnant with as many as 82% of the pregnancies being unplanned. This accounts for one-fifth of all unintended pregnancies in the U.S. and as of 2006, averaged to 71.5 pregnancies per 1000 women when looking specifically at 15-19 year olds. While there was a 41% decline from the peak pregnancy rate of 116.9 to 69.5 pregnancies per thousand 15-19 year olds in 1990 compared to 2005, a 3% increase occurred between 2005 and 2006 (Guttmacher Institute, 2010a). Regarding actual birth rates, as of 2008 the average birth rate was 41.5 births per thousand 15-19 year olds which is a decrease from 42.5 per thousand in 2007. Overall, teen birth rates have been decreasing since 1991 with the exception of a slight increase occurring between 2005 and 2007 (Hobson, 2010). Though U.S. teen pregnancy and birth rates are declining on the whole, these rates are still the highest among industrialized countries, remaining double the rates of England and Canada and eight times the rates of the Netherlands and Japan (Guttmacher Institute, 2006). Teen pregnancy rates can be attributed to unprotected sex or improper use of contraception. It is noted that teenage females who engage in unprotected sexual intercourse have a 90% chance of becoming pregnant within one year. Regarding contraceptive use in the adolescent population, nearly all sexually active adolescents have used at least one form of contraception (98%). A total of 74% of females and 82% of males used contraceptives at their first sexual encounter, whereas 83% of females and 91% of males used
contraceptives at their most recent sexual encounter (Guttmacher Institute, 2010a). Among the female adolescent population, 54% rely on oral contraceptive pills (OCPs) and 25% rely on condoms as their primary method of contraception (Guttmacher Institute, 2010b). Due to the need for daily or intercourse-dependent use, however, adherence with these methods is often difficult for adolescents. Poor adherence consequently leads to high failure rates and unwanted pregnancies. The Pearl Index, which is a method for discussing the efficacy of contraceptive methods, reports the percentage of women experiencing an unintended pregnancy within the first year of contraceptive use. Rates for both perfect and typical use are generally reported for each method. Perfect use of the male condom and combined oral contraceptive pill result in a Pearl Index failure rate of 2% and 0.3%, respectively, however typical use rates, which take user error and sporadic use into account, are poorer at 15% and 8%, respectively (Hatcher, et al., 2007).

With a majority of sexually active teens utilizing daily or intercourse-dependent contraceptive methods, often with poor adherence, or using no contraception at all, it is understandable that teen pregnancy is prevalent. Problems arise as teen mothers and their children are often found to have more physical problems, poorer living conditions, and fewer educational and employment opportunities than women who postpone childhood until later in life. Regarding maternal and infant birth outcomes, some studies note relatively rare complications among pregnant teens which remain comparable to 20-30 year old control counterparts. Several studies, however, have shown greater incidence of cervicovaginal infections during pregnancy, preterm delivery, low birth weight, and adverse neonatal outcomes including neonatal death among adolescent pregnancies compared to those of older control subjects (Chedraui, 2008). A Swedish study also noted that teenage mothers are more likely to have lower socioeconomic status later in life compared to women who waited until age 20-24
years to have children. Teen mothers were additionally found to have lower educational attainment and higher parity as well as single living arrangements. Furthermore, it was determined that teen mothers were more likely to be unemployed, collect disability pension and be dependent on public assistance such as welfare even when the collected data was adjusted for her family’s socioeconomic status. The incidences of these problems were determined to have an inverse correlation with the adolescent’s age, as teens becoming mothers at the youngest ages were more likely to experience such situations (Olausson, Haglund, Weitoft, & Cnattingius, 2001). Another study investigated these outcomes later in life comparing teenage mothers to those of the same age without children and dividing subjects based on race and ethnicity. This longitudinal study demonstrated that overall, females that become pregnant during their teenage years are more likely to have lower educational attainment and use public assistance than their non-pregnant equivalents. However, black adolescents are less likely to be disadvantaged by pregnancy than their white counterparts in terms of educational attainment. This study suggests that pregnancy causes disadvantage to the adolescent female, but the extent of disadvantage cannot not be generalized, as variation occurs across race/ethnicity (Casares, Lahiff, Eskenazi, & Halpern-Felsher, 2010).

Whatever the situation may be, adolescent pregnancy still creates disadvantages and hardships for women throughout their life. While teen pregnancy and birth rates are currently declining, it is important to support this trend. As long as adolescents continue to be sexually active, the promotion of safe sex and pregnancy preventative practices is of vital significance. While condoms and OCPs tend to be the most commonly used contraceptives, other available methods have been found to be highly effective and have strong adherence rates. Such methods include the injectable Depo Provera, the subdermal implant Implanon, and the Mirena
levonorgestrel intrauterine system (LNG-IUS). Depo Provera, Implanon, and Mirena were chosen as the methods of interest for this scholarly project because each are considered forms of long-term, reversible, progestogenic contraceptives that are comparable in terms of efficacy and adherence rates. Perfect use Pearl Index failure rates for Depo Provera, Implanon, and Mirena are reported as 0.3, 0.05, and 0.2%, respectively, while typical use failure rates are reported as 3, 0.05, and 0.2%, respectively (Hatcher, et al., 2007). While these methods are considered to be highly effective in preventing unwanted pregnancies, they are often regarded as underutilized by clinicians. For example, only 2% of all contraception users rely on the intrauterine system (IUS) (Guttmacher Institute, 2006). Reasons for low rates of usage may include out of date knowledge opposing the use of such methods in adolescents and misconceptions about adverse effects, as well as reliance on previous research and results on long-term, reversible methods that are no longer on the market. Other causes for low rates of use may merely be a lack of awareness of the current guidelines and committee opinions on such method use in the adolescent female and a lack of easy-to-use, clinician-aimed tools to help prescribe in such a population.

When examining the use of these methods of contraception in the adolescent female population, it is critical for clinicians to understand the current guidelines, indications, contraindications, and adverse effects as well as committee and patient attitudes toward such methods. Avoidance of misconceptions and irrelevant information is critical. The purpose of this article review is to address common hesitations clinicians and adolescent females have when considering long-term, reversible, progestogenic contraceptives like Depo Provera, Mirena, and Implanon. When taking into account the adolescent population, the most common reservations regarding Depo Provera include the potential for bone mineral density (BMD) loss and weight gain. Common hesitations for the use of Mirena in adolescents include concern with possible
increased risk of pelvic inflammatory disease (PID) and potentially higher expulsion rates. Regarding Implanon, concerns with early discontinuation due to side effects such as menstrual bleeding irregularity may limit clinicians’ use of this method in the adolescent population. This review aims to evaluate the validity of each of these hesitations in order to aid clinicians in decision making when considering these contraceptive options in the adolescent population.
Methods

The databases searched for this clinical article review included PubMed, using both of the quick search and MeSH database features, as well as the Science Citation Index/Social Science Citation Index, for all relevant articles from peer-reviewed journals. Sought-after journal articles that could not be found through these databases were requested from other libraries through the ILLiad Interlibrary Loan system of the University of Toledo. Reference sections of clinical guideline reports and original research articles as well as traditional and systematic review articles were also examined for additional relevant citations.

The search strategy included the following terms: adolescent, adolescent contraception, contraception, contraceptives, Depo Provera, DMPA, medroxyprogesterone acetate, Mirena, levonorgestrel, intrauterine device, IUD, intrauterine system, IUS, LNG-IUS, intrauterine contraception, IUC, intrauterine contraceptive device, IUCD, Implanon, implantable contraception, 3-keto-desogestrel, and etonogestrel. Other terms were searched more specifically for each method. Terms specific for Depo Provera included: bone mineral density, BMD, weight changes, weight gain, and adverse effects. Those terms specific for Mirena included: pelvic inflammatory disease, PID, sexually transmitted disease, STD, sexually transmitted infection, STI, gonorrhea, Chlamydia, expulsion, expulsion rates, parity, parous, nulliparous, adverse effects, and complications. Those specific for Implanon included: adverse effects, bleeding, bleeding irregularities, menstrual bleeding, dysfunctional uterine bleeding, discontinuation, and complications.

Types of journal articles utilized for this clinical review included systematic review articles as well as original research articles of prospective and retrospective designs including surveys or questionnaires and cross-sectional comparative and non-comparative studies.
Prescribing information for Depo Provera, Implanon, and Mirena was sought along with position statements and committee opinions from professional organizations concerning such contraceptive methods. Presentations, dissertations, and case studies were not considered.

For the purposes of this clinical review, journal articles utilized included only those written in English. Research articles within the last ten years, dating after 2000, were preferred, but articles dating before 2000 were utilized as well. Research involving the U.S. population was preferred, but due to the relatively small number of pertinent articles available, studies from other countries including New Zealand, the United Kingdom, Australia, and Canada as well as additional countries were also drawn upon. Due to the large number of original studies in this subject area involving research conducted on humans, those conducted on animals were excluded. Research specifically on the female adolescent was favored, but that conducted on adult women was also included due the limited number of studies focusing specifically on or including adolescents. While this clinical review focused on long-term, reversible progestogenic methods of contraception, specifically Depo Provera, Mirena, and Implanon, studies including similar methods such as the subdermal implant, Norplant, and various other intrauterine devices were also drawn upon when appropriate.
Pertinent Definitions

- “Adolescent” is defined as a person between the age of 13 and 18 years old for the purposes of this clinical review. This age range corresponds to that examined by the CDC’s Youth Risk Behavior Surveillance, which surveys students in grades 9-12.

- “Depo Provera,” also known as depot-medroxyprogesterone acetate (DMPA), is defined as a “non-daily hormonal contraceptive option” in the form of an intramuscular injection which provides contraception over a three month period (Bakry, et al., 2008).

- “DMPA” is an abbreviation for depot-medroxyprogesterone acetate, a derivative of progesterone and the active ingredient in Depo Provera (Pfizer, 2006).

- “Implanon” is defined as “a single-rod, nonbiodegradable implantable contraceptive that contains the progestin etonogestrel…, providing contraceptive protection for up to 3 years when inserted subdermally” (Funk, et al., 2005).

- “IUC” is an abbreviation for intrauterine contraception.

- “IUCD” is an abbreviation for intrauterine contraceptive device.

- “IUD” is an abbreviation for intrauterine device.

- “IUS” is an abbreviation for intrauterine system.

- “LNG-IUD” is an abbreviation for levonorgestrel-intratuterine device, which is synonymous with levonorgestrel-intrauterine system.

- “LNG-IUS” is an abbreviation for levonorgestrel-intrauterine system.

- “Mirena” is defined as a levonorgestrel-releasing intrauterine system which provides contraception over a five year period by “causing thickened cervical mucus and an atrophic endometrium” (Burkett & Hewitt, 2005). It is often abbreviated as “LNG-IUS.”
• “Multiparous” is defined as having given birth two or more times, or given birth to more than one offspring at a time.

• “Nulligravid” is defined as having never been pregnant.

• “Nulliparous” is defined as having never given birth.

• “Primiparous” is defined as having given birth only one time.

• “Progestogenic contraception” also known as “progestogen-only contraception” refers to contraceptive methods that contain only progestogen and do not contain estrogen.

• “STD” is an abbreviation for sexually transmitted disease.

• “STI” is an abbreviation for sexually transmitted infection.
A recurring theme in research and literature regarding Depo Provera (DMPA) use, especially in the adolescent population, is clinician concern with negative effects on bone mineral density (BMD). Adolescence is a time of significant bone accumulation, with a majority of bone mass accruing by the age of 18 after which there may be only slight gain in overall skeletal mass until the late twenties or early thirties. Increased estrogen levels during adolescence act as an important factor in bone formation and inhibition of bone resorption, as well as suppression of bone remodeling, thus affecting bone mineral density levels. DMPA’s mechanism of action increases progestin levels to the point of inhibiting the luteinizing hormone (LH) surge, thus preventing ovulation. Additionally, DMPA suppresses follicle stimulating hormone (FSH), thereby decreasing serum estrogen levels. A prolonged estrogen-deficient state allows for increased bone remodeling as well as a predomination of osteoclastic activity and bone resorption (Speroff & Fritz, 2005). The potential effects of DMPA on serum estrogen levels and bone activity may contribute to clinicians’ hesitation to prescribe DMPA during adolescence, which is such a pivotal time of bone accumulation.

Much research indicates significant bone mineral density decreases with initiation and continued use of DMPA. A study by Busen, Britt, and Rianon (2003) of an adolescent cohort using DMPA for 1-2 years tested serum estradiol levels and BMD levels based on dual-energy x-ray absorptiometry (DEXA) at baseline as well as at 1 and 2 years of DMPA use. Results revealed significant bone loss with a decrease of 3.31% (P=0.013) at the femoral neck and 3.52% (P=0.02) at the lumbar spine at year 1 with continued bone loss at the lumbar spine at year 2. Bone loss at the femoral head at year 2 of DMPA use varied between slight BMD gain, return to
baseline, and continued, though not significant, bone loss. There were no correlations found between estradiol and BMD levels. Limitations of this study include a small subject group of adolescents and poor continuation rates (Busen, Britt, & Rianon, 2003).

Other research studies contribute to the evidence that DMPA use can contribute to significant BMD loss. A similar, but slightly more populated, 12 month study by Cromer et al. (2004) demonstrated comparable results in a larger adolescent population. DEXA scan results at 12 months duration of DMPA use revealed significant BMD loss with a decrease in 1.414% at the lumbar spine and 2.172% at the femoral head when adjusted for race, chronological age and body weight. These results also showed a significant difference in BMD levels in adolescents using DMPA when compared to those using non-hormonal forms of contraception (Cromer, et al., 2004).

A non-randomized, prospective study by Lara-Torre, Edwards, Perlman, and Hertweck (2004) measured BMD changes using DEXA scanning every 6 months in new adolescent DMPA users between the ages of 11 and 21 years over a 24 month period. These subjects were compared to new oral contraceptive pill users as well as a control group of adolescents using non-hormonal forms of contraception. Results of this study exhibited a decrease in BMD values at the lumbar spine of 0.249, 1.59, 2.91 and 1.85% from baseline values at 6, 12, 18 and 24 months respectively in adolescents using DMPA. Data analysis also revealed statistically significant decreases in BMD values between DMPA users and the control group of 3.01, 3.02, 4.81, and 6.81% at 6, 12, 18 and 24 months respectively. Limitations of this study included a large dropout rate, though methods of analysis were adjusted to cope with the dropout rate. This study has advantages in that it contained a larger adolescent subject group of DMPA users as
well as hormonal and non-hormonal contraceptive comparison groups (Lara-Torre, Edwards, Perlman, & Hertweck, 2004).

A study by Scholes, Lacroix, Ichikawa, Barlow and Ott (2004) focusing specifically on adolescent DMPA use and BMD effects compared 14-18 year old DMPA users with non-users over a 24 month period. Data analysis of this study varied from those discussed previously in that users of DMPA showed decreased, though not statistically significant, changes in BMD when compared to non-users upon DEXA scan at the proximal femur, lumbar spine and whole body. This study also showed a dose-response trend between DMPA use duration and BMD. The trend demonstrated lower BMD values, especially at the spine, with greater number of DMPA injections suggesting that BMD continues to decrease with sustained use of DMPA. Limitations of this study include the limited amount of DMPA exposure in that few subjects received greater than 4 DMPA injections or 12 months DMPA exposure, thus limiting the dose-response trend analysis (Scholes, LaCroix, Ichikawa, Barlow, & Ott, 2004). Scholes, Lacroix, Ichikawa, Barlow, and Ott (2005) performed further analysis of the same data, revealing significant mean percentage change in BMD at the hip and lumbar spine at the 12, 18, and 24 month follow-up intervals for users of DMPA when compared to non-users. These values were statistically significant when adjusted for covariates, both baseline and time-dependent. It was also determined that changes in BMD at the hip and spine were greater with new DMPA users who had begun using DMPA during the actual study than those considered prevalent DMPA users who had begun the method before the beginning of the study. New users were found to have a 6.09% decrease at the hip after 24 months compared to a 2.04% decrease of prevalent users. Analysis of the data also revealed the greatest change in BMD “with the least cumulative use, but DMPA users continued to lose BMD at the hip and spine well beyond 24 months of
use,” (Scholes, LaCroix, Ichikawa, Barlow, & Ott, 2005) suggesting that changes in BMD were the greatest in the first 1-2 years, but continued beyond that time with sustained use.

Studies comparing DMPA users and non-users which are stratified by age are important in determining if those still actively accruing bone are more vulnerable to BMD effects than those who have already reached peak bone mass. A Scholes et al. (1999) study comparing non-users, new users, and continuing users of DMPA in the age ranges of 18-21, 22-29, and 30-39 years demonstrated a 2.5% lower total mean bone density by DEXA scanning at the lumbar spine in DMPA users when compared to non-users overall, which was considered statistically significant. BMD levels were also found to be significantly lower at the greater trochanter as well as lower, though not significantly, at the femoral neck and whole body. When stratifying the data by age groups, the greatest difference in BMD between DMPA users and non-users occurred in the 18-21 year age group, with significant difference found at every anatomical site (femoral neck, greater trochanter, lumbar spine, and whole body). The 22-29 and 30-39 year old age groups did exhibit BMD loss in DMPA users compared to non-users, however, the difference was not significant at any anatomical sight. The younger age group was also found to have a dose-response relationship between BMD levels and duration of DMPA exposure as greater lengths of DMPA exposure corresponded to lower bone mineral density values at all anatomical sites. This dose-response relationship was not found to occur within the older age groups (Scholes, Lacroix, Ott, Ichikawa, & Barlow, 1999). Further analysis of this data was reported in the Scholes, Lacroix, Ichikawa, Barlow and Ott (2002) study which revealed continued BMD decline at both the lumbar spine and hip with sustained DMPA exposure, thus suggesting that bone loss is likely to occur for the complete duration of DMPA use. The greatest amount of BMD loss, however, was found to be within the first 12 months of the study. The
amount of bone loss at each six month interval decreased with each additional DMPA injection, suggesting a greater rate of bone loss with beginning use in newer DMPA users than in continuous use in longer-term DMPA users (Scholes, LaCroix, Ichikawa, Barlow, & Ott, 2002).

Walsh, Eastell, and Peel (2008) also conducted an age stratified study on the effects of DMPA use on BMD and bone metabolism. The study compared DMPA users and non-users between the age ranges of 18-25 and 35-45 years to determine if BMD effects due to DMPA use were age specific. In the 18-25 year age group, results showed a significant decrease in BMD of 5.2% at the hip and 5.6% lumbar spine in users of DMPA when compared to non-users, however, no significant differences were seen in the 35-45 year old age group between DMPA users and non-users. The study also demonstrated that bone turnover markers including propeptide of type I procollagen (PINP) and collagen type 1 cross-linked N-telopeptide (NTX) were highest and statistically significant in the 18-25 year old age group as well as the DMPA user group by up to 40% suggesting that bone turnover and BMD effects could not only be contributed to normal active bone remodeling consistent with that age of life, but also to DMPA use (J. S. Walsh, Eastell, & Peel, 2008).

With numerous studies demonstrating statistically significant negative effects on BMD, especially in new, adolescent users of DMPA, it is important to determine if use of DMPA increases the risk of osteoporosis or fracture in the future. In order to investigate this concern, several studies have researched the extent of BMD recovery upon discontinuation of DMPA. In a Scholes et al. (2002) study involving reproductive age women between 18 and 39 years of age, continued BMD gain was observed at each six month follow up interval in subjects who discontinued DMPA use during the study. BMD values were found to be similar to those of non-users by the end of the 30 month follow up period. Discontinuers of DMPA were found to
demonstrate higher annualized mean rates of BMD gain than that of non-users. DMPA discontinuers revealed annualized rates of 1.41 and 1.03% gain at the lumbar spine and hip, respectively, compared to 0.40% gain and 0.005% loss at the hip and spine, respectively, in non-users. This illustrated that following DMPA discontinuation, BMD is regained at an accelerated rate than the normal rate of accumulation that occurs in a non-user. It was determined that the overall gain at the spine in DMPA discontinuers was similar to that of bone loss at the same anatomical area for continuous DMPA users for each six month follow up interval suggesting that BMD is regained at the amount that it is lost. BMD gain at the hip in DMPA discontinuers, however, was discovered to be less than BMD loss at the same anatomical site in continuous DMPA users at each six month follow up interval, suggesting that bone loss at the hip is recovered more slowly or may not be fully recovered, at least within the 30 month study period (Scholes, et al., 2002).

A later Scholes et al. (2005) study focusing specifically on adolescent use of DMPA demonstrated similar results revealing continuous BMD gain especially at the spine and whole body overall at each six month follow up interval for those discontinuing DMPA during the study. The mean gain at each six month follow up interval was found to be 0.0058, 0.0133, and 0.0186 g/cm² at the hip, spine, and whole body, respectively, with each value greater than the mean six month follow up interval of non-users at corresponding anatomical sites. The annualized adjusted mean percentage gain in BMD in DMPA discontinuers was found to be 1.34, 2.86, and 3.56% at the hip, spine, and whole body, respectively, compared to -0.19, 1.32 and 0.88% of nonusers. These differences were statistically significant at each anatomical site. Data analysis also showed no difference in the amount of BMD gain based on the duration of DMPA use at the time of discontinuation and that adjusted mean BMD values at 12 months post
discontinuation were at least as high as non-users at all measured anatomical sites (Scholes, et al., 2005).

A systematic review by Kaunitz, Arias, and McClung (2008) investigating BMD recovery after DMPA discontinuation included studies involving adolescents, premenopausal, and postmenopausal women. All studies concerning BMD recovery in premenopausal women demonstrated at least partial recovery of BMD either at the distal radius and ulna or spine and hip. Studies measuring BMD values at the spine and hip demonstrated faster recovery at the spine, with increases ranging from 1.41 to 3.4% in BMD per year, than at the hip which revealed 0.4 to 0.9% increases per year. One study involved in the review, reported mean BMD levels of DMPA discontinuers similar to those of non-users at 30 months post discontinuation. An additional study revealed full recovery of BMD to baseline values at the spine at 27-30 months post discontinuation, though full recovery had not occurred at the hip by the completion of the study with a value 2.0% lower than baseline for women who had used DMPA for 12-24 months duration. Unlike other studies mentioned previously, this study reported that rates of change in BMD recovery upon DMPA discontinuation were dependent upon duration of DMPA use. It was found that longer duration of use was associated with greater annual rates of BMD recovery. Finally, a seven year matched cohort study involved in the review investigated premenopausal women between 25 and 35 years of age which further supported at least partial recovery of BMD at the spine and hip after DMPA discontinuation. A 5.16% decrease at the hip and 5.38% decrease at the spine from baseline in DMPA users recovered to a 0.20% deficit at the hip and 1.19% deficit at the spine at 96 weeks post discontinuation follow up. Further recovery could not be determined due to the two year limitation of post-treatment follow up. All studies demonstrated that “BMD loss during DMPA use is at least partially reversible upon
discontinuation in premenopausal women, with BMD returning to levels at or near baseline depending on measurement site and length of follow up,” (Kaunitz, Arias, & McClung, 2008).

Kaunitz et al. (2008) also investigated studies concerning DMPA use and BMD recovery in adolescents which included the Scholes et al. (2005) study mentioned previously. As discussed earlier, this study demonstrated significant BMD increases at the hip and spine following discontinuation of DMPA use in 14 to 18 year olds. It was determined that rate of BMD recovery was not affected by duration of DMPA use and that at 12 months of discontinuation, BMD values in discontinuers were found to be at least as high as those of non-users at the hip and spine (Kaunitz, et al., 2008).

With much research in the area of BMD effect with DMPA use, several warnings, guidelines, and committee opinions have been released concerning the subject. In 2004, the U.S. Food and Drug Administration (FDA) issued a black box warning to the Depo Provera prescribing information stating that “women who use Depo-Provera Contraceptive Injection may lose significant bone mineral density,” which may not fully recover (Pfizer, 2006). The warning also states that “it is unknown if use of Depo Provera Contraceptive Injection during adolescence or early adulthood, a critical period of bone accretion, will reduce peak bone mass and increase the risk for osteoporotic fracture later in life,” (Pfizer, 2006). Due to the evidence of BMD loss with DMPA use and unknown amount of recovery and effect on peak bone mass and osteoporotic fracture risk, the FDA recommends that DMPA be used for no longer than two years and should only be used greater than two years if no other contraception methods are adequate. The World Health Organization (WHO) released a statement on hormonal contraception and bone health in 2006 which acknowledges studies demonstrating that DMPA reduces BMD in both women who have achieved peak bone mass as well as those, including
adolescents, who are actively accumulating bone. The WHO statement also acknowledges the data suggesting that BMD increase upon DMPA discontinuation with values appearing to be comparable to those of non-users within 2-3 years. It additionally notes that it is not known whether DMPA use during times of bone accumulation will increase fracture risk during postmenopausal years, but suggests that the risk is small due to the evidence of BMD recovery after DMPA discontinuation. In regards to use in adolescents specifically, the WHO suggests that “the advantages of using DMPA generally outweighs the theoretical safety concerns regarding fracture risk” and that “the overall risks and benefits for continuing use of the method should be reconsidered over time with the individual user” because data concerning long term use of DMPA in adolescents is still lacking (World Health Organization, 2005). The America College of Obstetrics and Gynecology (ACOG) also put forth a committee opinion in 2008 concerning DMPA and bone effects. The ACOG committee opinion states that DMPA should be considered a first line method of contraception in adolescents and that “concerns regarding the effect on BMD should neither prevent practitioners from prescribing nor limit its use to [two] consecutive years,” (American College of Obstetricians and Gynecologists, 2008). It also suggests that those considering beginning DMPA use should be counseled on potential BMD effects as well as methods of beneficial bone health such as adequate daily calcium and vitamin D intake as well as load-bearing exercise (American College of Obstetricians and Gynecologists, 2008).
Bone Mineral Density Discussion

The effects on BMD by DMPA use, especially in the adolescent population, bring to the surface many questions which can begin to be answered through investigation and review of the current literature, research and studies mentioned previously. First of all, does the use of DMPA cause negative effects on BMD? There is significant evidence that DMPA use does cause BMD loss. While varying by age, duration of use, and anatomical site of BMD measurement, all the studies reviewed exhibited at least decreased BMD with DMPA use, with most studies demonstrating statistically significant losses at various anatomical sites when compared to baseline measurements or control groups not using hormonal methods of contraception. Several of the studies also illustrated a dose-response trend of increased BMD loss with greater duration of DMPA use. Interestingly, a number of studies also reported trends of greater percentages of BMD loss in new users of DMPA when compared with prevalent or longer-term users suggesting that, while BMD loss continues with sustained use, the greatest amount of bone loss at the greatest rates occurs within the first 1-2 years of DMPA use.

Another question that arises with the subject of DMPA use and BMD effects is that of BMD recovery once DMPA use is discontinued. All of the studies discussed previously demonstrated at least some amount BMD gain at all anatomical sites providing strong evidence that at least partial recovery occurs upon discontinuation of DMPA. Several studies made mention that BMD gain occurred at each follow up measurement throughout the duration of the study suggesting that BMD would likely continue past study follow up. These studies cause one to contemplate if BMD is found to only recover partially due to limitations of length of study follow up and if BMD would be found to fully recover given adequate follow up time. While some studies revealed only partial recovery of BMD following DMPA discontinuation, there
were multiple studies which reported complete recovery of BMD to baseline values or to values comparable to DMPA non-users within time frames of 12 to 30 months post discontinuation. In terms of rates of BMD recovery, there was disagreement as to whether duration of DMPA use affected rates of BMD gain post DMPA continuation. One study reported no difference in rates of BMD gain with differing durations of DMPA use; however, another study reported greater rates of BMD gain in subjects with longer durations of use. So to answer the question posed earlier, it appears that BMD lost during DMPA use is at least partially recovered after DMPA discontinuation with trends toward full BMD recovery with adequate time allowance.

When considering DMPA use in adolescents and deciding whether it is an appropriate contraception method to prescribe in such a population, additional questions arise. First of all, are adolescents, who are actively accruing bone, more susceptible to the negative BMD effects caused by DMPA use? In the two studies that stratified data by age, it was apparent that the younger age groups were more vulnerable to BMD loss due to DMPA use. The younger groups exhibited significant changes in BMD when compared to control groups, whereas the older age groups did not manifest significant differences. Another question that comes about is whether or not adolescents using DMPA will be able to reach their peak bone mass as they would have without DMPA use. This question is more difficult to answer in that studies varied in terms of what they considered full recovery of BMD. While all studies concerning BMD recovery revealed at least partial bone recovery post DMPA discontinuation, those studies that reported “full recovery” differed. Some reported BMD values returning to baseline while others reported values comparable to DMPA non-users. Because bone is actively accumulating during adolescence, it would be more reassuring if studies reported full recovery of BMD to values similar to those of DMPA non-users rather than just to baseline values at DMPA initiation.
Because there are a limited amount of studies available concerning BMD recovery after discontinuation of DMPA, especially focusing specifically on adolescents, and because there are differing opinions as to what is considered full BMD recovery, it appears that more research is needed in this area to determine if peak bone mass is still achievable in an adolescent using DMPA. When considering the available data about BMD recovery at this point, the research tends to lean toward the notion that peak bone mass appears to still be attainable in adolescents using DMPA. A related question that arises in adolescent use of DMPA is whether or not the use of DMPA use during the time of adolescence increases osteoporotic fracture risk in the post-menopausal period of life. While no studies have investigated this directly, the research revealing that BMD is at least partially, if not fully, recovered after DMPA discontinuation seems to suggest that increased fracture risk is likely to be minimal as the WHO statement on hormonal contraception and bone density suggests.

The most important question concerning adolescents and the use of DMPA is whether or not this method of contraception is appropriate for adolescent use, especially since it will cause BMD loss at a time known for bone accumulation. To answer this, one must consider adolescents in general and their intentions for seeking DMPA. Adolescents are a population that in general is likely to have adherence issues with daily or intercourse-dependent contraceptive methods. Most adolescents seeking DMPA seem to do so because of its ease of use in pregnancy prevention. Pregnancy itself has its own effects on bone health, as well as other physical, social, and emotional burdens specific to each individual, therefore one must individually weigh the risk of unintended pregnancy with that of the theoretical or even potential increased osteoporotic fracture in the future. Adolescents, due to their age, are likely to be new users of DMPA and potentially undergo only short durations of use than older users, as evident by the large dropout
rates in studies specific to adolescent DMPA use; therefore they are likely to experience rather high rates of BMD loss when compared to older, more long-term users. However, due to the evidence that BMD loss during DMPA use is largely reversible with DMPA discontinuation, it appears, as mentioned previously, that the increased risk for osteoporotic fracture later in life is small. It seems, therefore, that with the current research, guidelines, and committee opinions available as well as consideration for the needs of adolescents seeking contraception methods, DMPA is an appropriate long-term, reversible method of contraception which clinicians should not hesitate to prescribe in the adolescent population.
Weight Gain Literature Review

Another common concern of both clinicians and patients is the potential for weight gain with DMPA use. This possibility may cause patients hesitation to initiate or continue the method due to concerns with physical appearance. At the same time, risk of weight gain may provoke concern in clinicians to prescribe this method due to the potential for negative health effects or medical problems associated with increased weight. This concern may seem to be increased for adolescents in that it is already a time of increased weight caused by puberty as well as a time of increased awareness of physical appearance. The Depo-Provera Contraceptive Injection (CI) prescribing information lists weight gain as a general precaution stating that “there is a tendency for women to gain weight while on therapy with Depo-Provera CI.” It references a study in which “from an initial body weight of 136 lb, women who completed 1 year of therapy with Depo-Provera CI gained an average of 5.4 lb. Women who completed 2 years of therapy gained an average of 8.1 lb.” It was also noted that “two percent of women withdrew from a large scale clinical trial because of excessive weight gain,” (Pfizer, 2006). However, there is controversy and variation of opinions as to whether weight gain is significant with DMPA use. Studies concerning DMPA use and effects on weight have reported conflicting results; some describing weight gain while other describing no significant weight change. The following is a review of studies involving women and, more specifically, adolescents using DMPA and its effects on weight. It attempts to answer the question of whether the concern for weight gain is warranted and to address potential risk factors or predictors for greater incidence of weight gain with DMPA use.

Few studies revealed no significant weight change with DMPA use. One study by Moore, Valuck, McDougall, and Fink (1995) involved a retrospective chart review of 150
women between 15 and 30 years of age divided equally between Depo-Provera, the Norplant subdermal implant, or oral contraceptive therapy groups. Results of this retrospective study revealed mean one-year weight gain of +0.1, -1.8, and -2.0 pounds or +0.06, -0.81, and -0.93kg for Depo-Provera, Norplant, and oral contraceptive users, respectively. Analysis of the data exhibited that the Depo-Provera therapy group weight gain over a 12 month period was slightly greater than that of the other two treatment groups, but did not differ significantly from zero. There were many limitations to this study including its design as a retrospective chart review which did not address therapy discontinuation or include subjects in the study which discontinued therapy before one year of use. It is possible that those who experienced significant weight gain discontinued the study before one year of use, and thus were not included in the study, while those who did not experience a significant amount of weight gain continued the therapy. Therefore, the design of the study may have contributed to the results that Depo-Provera users exhibited a small, insignificant amount of weight gain with one year of use (Moore, Valuck, McDougall, & Fink, 1995).

A non-randomized, prospective study by Lara-Torre et al. (2004) addressing bone mineral density in adolescents between 12 and 21 years of age noted no significant difference in body mass index (BMI) between DMPA users, oral contraceptives users, and normal menstruating girls using non-hormonal methods of contraception at any point during the two year study. The leaders of the study, however, discuss that the average BMI of all therapy groups was less than 25 and may have contributed to the explanation that study participants did not show a statistically significant BMI difference throughout the study. This study is limited in that it only mentions that no significant difference in BMI occurred between study groups throughout the study without providing actual measurements or figures (Lara-Torre, et al., 2004).
An overwhelming majority of the studies investigated regarding DMPA use and effects on weight demonstrated some form of significant weight gain or increased BMI in DMPA users. Such include a three year, non-randomized, longitudinal study by Berenson and Rahman (2009) which investigated changes in weight, total fat, percent body fat, and central-to-peripheral fat ratio in DMPA users compared to oral contraceptive and non-hormonal contraceptive users in females between the ages of 16 and 33. Weight measurements as well as total body fat, percent body fat, total lean mass, and body fat distribution measurements by DEXA scan were taken at baseline and six month intervals for three years. Results revealed increases of 5.1kg in weight, 4.1kg in body fat, 3.4% in percent body fat and 0.1 in central-to-peripheral fat ratio in DMPA users, all of which were significantly more than that of oral or non-hormonal contraceptive users. Data analysis also noted the highest amount of weight gain in DMPA users during the first 18 months of use with a mean value 4.4kg followed by a small gain of 0.7kg during the second 18 months. The trends were found to be similar for total body fat (3.6 versus 0.5kg), percent body fat (3.0 versus 0.4%), and central-to-peripheral fat ratio (0.08 versus 0.02). With analysis, DMPA users were found to be 2.13 times more likely to become obese by exceeding a BMI of 30 by the end of the three year study when compared with non-hormonal contraceptive users. It was also revealed that DMPA users who were found to have gained greater than 5% of their baseline body weight were significantly more likely to discontinue the method by the following six month interval than users who did not gain weight. This presents as a limitation to the study because the loss of participants gaining greater than 5% of baseline body weight may have affected the mean amount of weight gained by the DMPA users, causing the results to detect a lower value than what it actually may have occurred (Berenson & Rahman, 2009).
Further studies contribute to evidence that DMPA use may lead to weight gain or increased BMI. A three year retrospective study by Pantoja, Medeiros, Baccarin, Morais, Bahamondes, and Fernandes (2010) compared 18-35 year old DMPA and TCu380A intrauterine device (IUD) users matched for age and baseline BMI. When stratified by the type and amount of weight change, it was determined that a greater percentage of DMPA users gained weight than IUD users. Results demonstrated that 71.8% of DMPA users and 81.5% IUD users maintained their baseline BMI whereas 23.7% and 11.7% had increased BMI in DMPA and IUD users, respectively. This represented an increase in 9.3% of obese participants using DMPA meaning that of DMPA users who were not considered obese at the beginning of the study, 9.3% became obese by the end of the three years. This is compared to an increase of 3.6% in the IUD user group. Limitations to this study include the retrospective design which included only those subjects using DMPA for a complete three years (Pantoja, et al., 2010).

Other studies adding to the evidence that DMPA use causes weight gain or increased BMI focus specifically on adolescents and are likely to be more influential in determining if weight gain is a warranted concern for both patients and clinicians when prescribing DMPA for the adolescent population. A retrospective chart review by Risser, Gefter, Barratt, and Risser (1999) involving 13-19 year olds compared weight changes between DMPA and oral contraceptive users at one year of use. Results revealed a mean weight gain of 3.0kg in DMPA users compared to 1.3kg of oral contraceptive users at one year of use which was considered statistically significant. When stratified by amount of weight change, 24% of DMPA users gained greater than 10% of their baseline weight at one year of use, compared to 7% of oral contraceptive users. It was also discovered that a smaller percentage of DMPA users (56%) compared to oral contraceptive users (70%) lost weight or gained less than 5% of their baseline
weight after one year of contraceptive therapy. These differences between contraceptive groups were found to be statistically significant. Limitations to the study include a small DMPA subject group as well as the lack of a non-hormonal contraceptive group as a comparison. Because DMPA and oral contraceptives are both forms of hormonal contraception, the study is unable to determine if weight gain is due to the hormones of the contraceptive methods or other factors. Also because the study design was that of a retrospective chart review, patients who discontinued contraceptive use before one year were not considered for the study (Risser, Gefter, Barratt, & Risser, 1999).

Additional evidence involves another retrospective chart review study by Mangan, Larsen, and Hudson (2002) involving adolescents younger than the age of 19 years who were first time DMPA or oral contraceptive users that continued the contraceptive method for at least one year. By the end of the one year study, the mean weight gain for the DMPA users was 8.9 pounds which was significantly greater than the 4.7 pound gain of oral contraceptive users. BMI change from baseline in the DMPA users was also found to be significantly greater than that of oral contraceptive uses with a 1.51 ± 1.94 increase compared to 0.75 ± 1.65, respectively. When stratified by amount of weight change, 55% of DMPA users were found to gain greater than five pounds at one year of use compared to 44% of oral contraceptive users, while 45% of DMPA users were found to either lose weight or gain less than five pounds compared to 56% of oral contraceptive users. Limitations of this study are similar to other studies which used the retrospective chart review design and included no form of non-hormonal contraceptive comparison group. Also, it may be difficult to generalize the results of this study across all adolescents because the majority of subjects considered themselves black with only 8% of the subject population considering themselves white (Mangan, Larsen, & Hudson, 2002).
Also adding to the evidence of weight gain in adolescents with DMPA use is a longitudinal study by Beksinska, Smit, Kleinschmidt, Milford, and Farley (2010) which followed women age 15-19 years old beginning injectable contraceptives including DMPA or norethisterone enanthante (NET-EN), as well as combined oral and non-hormonal contraceptives. Subjects were weighed every six months for the course of four to five years. For data analysis, subjects were categorized into groups including injectable contraception (IC) users (defined as those using either of the two or both injectable contraceptives), combined oral contraceptive (COC) users, discontinuers, and nonusers. Subjects using DMPA, NET-EN, or both were combined into one group because the exclusive DMPA group was too small to analyze due to study drop-out or method switching. Results revealed weight and height gain across all groups. The IC group was found to gain a significantly greater amount of weight with a mean of 6.2kg compared to 2.8, 2.3 and 2.8kg of nonusers, COC users and discontinuers, respectively. When stratified by amount of weight gain, it was found that 68.52% of IC users gained greater than 2kg compared to 50.8%, 54.2%, and 50% of nonusers, COC users, and discontinuers, respectively. While DMPA and NET-EN users were combined into a group for analysis, exclusive DMPA users were found to gain more weight than exclusive NET-EN users or those subjects who used both throughout the four to five year follow up. This greater weight gain, however, was not found to be significant. Limitations with this study include the inability to analyze injectable methods separately. Discontinuation overall was also found to be a problem with only 42% of subjects completing between four and five years of follow up. Additionally, the study had little diversity with most subjects of African descent; therefore results may not be able to be generalized further (Beksinska, Smit, Kleinschmidt, Milford, & Farley, 2010).
Additional evidence is found in a prospective study by Bonny et al. (2006) which followed weight changes in obese and nonobese females between the ages of 12 and 18 years initiating DMPA, oral contraceptives, or a non-hormonal form of contraception. Weight changes were examined at 6, 12, and 18 months. After 18 months, nonobese DMPA users were found to gain 4.0 kg compared to 2.8 and 3.5 kg of nonobese oral and non-hormonal contraceptive users, respectively. While nonobese DMPA users gained more than nonobese oral and non-hormonal contraceptive users, this difference was not found to be significant. Obese DMPA users showed weight gain of 9.4 kg which was significantly greater than the 0.2 and 3.1 kg of obese oral and non-hormonal contraceptive users, respectively. Also, weight gain in obese DMPA users was significantly greater than in nonobese DMPA users or nonobese subjects using either other form of contraception. It was also revealed that of nonobese subjects using DMPA, 19.0% became obese by 18 months of use compared to 9.8 and 2.8% of oral and non-hormonal contraceptive users, respectively. Overall, the study found that “adolescent girls who initiated DMPA were more likely to gain weight over time than those who initiated [oral contraceptive] or no method, and this weight gain was accentuated by being obese at baseline.” Limitations to this study include the fact this study is secondary analysis of data from a previous study evaluating BMD changes with hormonal contraceptive use and also that most subjects were black, urban adolescents which may reduce the generalizability of results (Bonny, et al., 2006).

Since an overwhelming majority of the studies reported some form of weight gain or BMI increase with DMPA use, especially those specifically involving adolescents, it is important to further investigate risk factors or predictors of weight increase with DMPA use to aid in determining which adolescent patients may be more at risk. Many of the studies previously reviewed addressed risk factors or predictors of weight gain within their research. One of the
most commonly thought of risk factors for significant weight gain with DMPA use includes baseline obesity. Further investigations of the previously discussed studies address this risk factor to determine if the concern of significant weight gain is warranted even more in obese adolescents. Other risk factors addressed include race or ethnicity, age, appetite and dietary factors, parity, and early weight gain as a predictor of later weight gain to determine which adolescents are more at risk for weight gain and in which DMPA may be an appropriate method of pregnancy prevention.

The study by Berenson and Rahman (2009), which stratified 16-33 year old DMPA, oral contraceptive and non-hormonal contraceptive users by race and BMI obesity status, revealed that DMPA users who were nonobese, defined as BMI less that 30, gained more weight than those who were obese (BMI ≥ 30) at baseline. When DMPA users were stratified by race/ethnicity, it was found that white nonobese women gained significantly more weight than white obese women. Hispanic subjects showed similar, though not significant, trends. This trend was not visualized in black DMPA users. The DMPA users stratified by race, however, were not compared directly in terms of weight gain or body composition, therefore it could not be determined if one race/ethnicity was more likely to gain than another. The study also examined dietary habits such as total caloric intake as well as amount of fat, carbohydrate and protein intake per day revealing that increased protein intake was significantly protective against weight gain. Other dietary factors did not affect weight gain or body composition (Berenson & Rahman, 2009).

Further analysis of the previous study’s DMPA users, investigated in a study by Le, Rahman, and Berenson (2009), divided subjects into “early weight gainers,” defined as those gaining greater than 5% weight gain at six months of DMPA use, and “regular gainers” including
the rest of the DMPA user study participants. Regular gainers exhibited a weight gain of 0.63, 1.48, and 2.49 kg at 12, 24, and 36 months of use, respectively, whereas early weight gainers revealed significantly greater amounts with 8.04, 10.86, and 11.08 kg at 12, 24, and 36 months of use, respectively. When determining the amount of DMPA users who gained significant amount of weight, it was found that slightly over one-fourth of DMPA users gained greater than 5% baseline weight at six months of use. This study indicated that early weight gain in DMPA users was very much predictive of later weight gain. Additional risk factors investigated included baseline BMI, age, race, marital status, parity number, prior DMPA use, and lifestyle variables such as appetite. It was found that DMPA users with a BMI of less than 30 were significantly more likely to gain weight than those with BMI greater than 30. Other significant predictors of early weight gain, and thus, later weight gain, included parity of at least one and self reported increased appetite at six months of use (Le, Rahman, & Berenson, 2009).

The study by Pantoja et al. (2010), comparing 18-35 year old DMPA and IUD users additionally stratified subjects by baseline BMI status: group 1 (G1) with BMI <25, group 2 (G2) with BMI between 25 and 29.9, and group 3 (G3) with BMI ≥30. Results after 3 years of DMPA use showed a gain of 4.5 ± 4.5 kg in DMPA users compared to 1.2 ± 4.0 kg in IUD users in the G1 group. The G2 group DMPA users revealed a mean weight gain of 3.4 ± 5.5 kg compared to 0.2 ± 4.9 kg in IUD users; while the G3 group DMPA users gained a mean weight of 1.9 ± 6.7 kg compared to 0.6 ± 7.0 kg of IUD users. The mean weight gain of the DMPA users was found to be significantly greater when compared to IUD users in the nonobese G1 and G2 groups, though not significant in the obese G3 group. In terms of BMI, all three groups showed progressive increase in both DMPA and IUD users throughout the length of the study, though DMPA users had significantly greater BMI increase than the IUD users in groups G1 and G2,
though not G3. Additionally, the G1 and G2 DMPA users were found to have significant BMI increase trends with longer duration of use when compared against IUD users. The G3 group showed a similar trend, though it was not significant. In summary, and similarly to the previously discussed study, those DMPA users considered nonobese were found to gain significantly more weight compared to nonobese IUD users, whereas the obese DMPA users’ weight gain, while present, was not significantly greater than the obese IUD users. BMI was also found to significantly increase in DMPA users compared to IUD users in the nonobese subject group, however, not significantly in the obese subject group. Additionally, correlations between BMI increase with duration of use was significantly greater in the nonobese DMPA users than the obese DMPA users when compared to their IUD counterparts (Pantoja, et al., 2010).

The three previous studies focused more on adult women while the following spotlight adolescent DMPA use and associated risk factors for weight gain which may be more influential in determining if DMPA is an acceptable contraceptive method for the adolescent patient. The study by Risser et al. (1999) determined that baseline variables such as age, BMI, and race/ethnicity did not affect the likelihood of gaining greater than 5-10% of baseline body weight. It was found, however, that of adolescents who gained greater than 5% of baseline body weight at three months, 93% were found to gain more by 12 months of use suggesting that early weight gain is a predictor of later weight gain. It was also noted that adolescents using DMPA who gained greater than 6kg at 12 months of use had significantly greater baseline BMI than those who gained 2-6kg suggesting that those with higher BMI at baseline may have a greater risk of gaining more weight that those with smaller baseline BMI (Risser, et al., 1999).
The study by Beksinska et al. (2010), which stratified adolescents by baseline BMI status, placed subjects into groups considered normal (18.5-24.9 BMI), overweight (25.0-29.9 BMI), and obese (BMI $\geq 30$) which were later combined to form “normal” (18.5-24.9 BMI) and overweight/obese (BMI $\geq 25$). It was determined that there was no significant difference in mean weight gain among normal baseline BMI injectable contraceptive users compared to the overweight/obese group. However, the study noted that subjects who had discontinued a method of contraception were found to have a mean baseline weight of 3-4kg higher than the groups of contraceptive users or non-users and had the “highest proportion (50%) of women in the overweight/obese category” suggesting that “women who are already overweight when they start a contraceptive method may consider discontinuing contraception if they gain any further weight compared to a woman in the normal weight range who may be prepared to accept a small weight gain.” This study demonstrated that while there was no statistically significant difference in weight gain between subjects of differing BMI, weight gain of any sort may cause subjects with greater BMI a higher likelihood of contraceptive discontinuation than those with normal BMI. Limitations of this study include a small amount of obese subjects (10.7%) which is why overweight and obese subject groups were combined for data analysis. Also, as mentioned previously, the subjects were nearly all of African descent which may limit the generalizability of the study (Beksinska, et al., 2010).

In the study Mangan et al. (2002), baseline characteristics such as age, race, method of contraception, height, and weight were collected. Initial BMI was calculated and subjects were categorized as overweight if their initial BMI was greater than the 85th percentile for their age. Results of the study, when stratified by weight status, showed significantly greater weight gain in the overweight DMPA subjects with a mean gain of 13.6 pounds compared to the 6.9 pounds of
the non-overweight group. It was also discovered that 66% of the overweight DMPA group gained 10 or more pounds with one year of use whereas only 27% of the non-overweight group were found to gain more than 10 pounds. In addition, the DMPA users who gained greater than 10 pounds with one year of use had significantly higher baseline BMI than those who gained less than or equal to 10 pounds (25.4 versus 21.9 BMI). When the results were stratified by race, it was determined that in white subjects, baseline BMI was the only significant predictor of weight gain regardless of contraceptive method, whereas in black subjects, “initial BMI (P = .01) and the interaction between initial BMI and contraceptive method (P = .01) were both significant predictors of weight change” showing that there is much correlation between weight gain and black subjects who use DMPA and are initially overweight. Limitations of this study, as mentioned by the researchers, include inability to determine the effects of variables such as prior weight gain, diet, and exercise on weight gain during the study (Mangan, et al., 2002).

The study by Bonny et al. (2006), which investigated weight gain in obese and nonobese adolescents initiating DMPA, oral contraceptives, or non-hormonal contraceptive methods showed, as mentioned previously, that obese DMPA users, defined as a baseline BMI of 30 or greater, were found to have significantly greater weight gain than those considered nonobese. A significant interaction between baseline obesity status and contraceptive method was discovered in that DMPA users were more likely to gain weight than users of other contraceptive methods and this likelihood of weight gain was “accentuated by being obese at baseline.” When stratified by obesity status, results indicated that significant weight gain predictors for nonobese subjects, regardless of contraceptive method, included black race, younger gynecologic age, and duration of contraceptive use. For obese subjects, however, an interaction between contraceptive method and duration of use was found to be a significant risk factor for weight gain suggesting that
weight gain was likely to be greater in obese DMPA subjects with longer duration of DMPA use. Race and gynecologic age were not found to be weight gain predictors in obese DMPA users (Bonny, et al., 2006).

Another study investigating risk factors of weight gain in adolescent DMPA use is that by Bonny, Britto, Huang, Succop, and Slap (2004). Primary predictors of weight gain that were explored in women between the age of 12 and 21 years included baseline weight, BMI, total body fat and percent body fat. Secondary predictors that were examined included race, chronological age, menarcheal age, gynecological age, pregnancy history, medication use, dietary restraint (defined as the prevention of eating), dietary disinhibition (defined as the continuation of eating), as well as appetite. When results were stratified by race, both black and white subjects had an increase in mean weight, total body fat, and BMI at six months of DMPA use. However, it was discovered that black subjects had significantly greater increases in percent weight gain, percent BMI, and percent body fat than the null (zero change) over the six month study. White subjects did not show significant changes. It was found that black DMPA users had a 2.9kg or 4.2% weight increase compared to 0.9kg or 1.2% of their white counterparts. Additionally, black subjects revealed a 12.5% increase in total body fat compared to 1.2% of white subjects. Change in BMI of black subjects was 0.9 or 3.7% compared to 0.3 or 1.2% of white subjects, which was statistically significant. When reviewing baseline predictors of weight gain, it was also found that younger chronological age, higher baseline weight, BMI, and total body fat, as well as higher baseline eating restraint and disinhibition were found to have a statistically significant correlation with weight gain in black DMPA users. In white DMPA users, there were no statistically significant baseline predictors of weight gain throughout the six month study, however, baseline BMI and total body fat showed a statistically significant
correlation with weight gain for the first three months of contraceptive use. The study results also showed a trend in black subjects of continued weight gain with longer DMPA duration of use, which was not the case for white subjects. Limitations to this study include a small amount of white subjects (35%) compared to black subjects (65%). No other race/ethnicity was included. Other limitations include the small number of subjects as well as the lack of any sort of comparison group. Also, subjects with a BMI greater than or equal to 30 were excluded, therefore weight gain in obese subjects could not be investigated (Bonny, Britto, Huang, Succop, & Slap, 2004).

Common limitations in several of the studies investigating weight changes in DMPA users included designs like retrospective chart reviews, which can be problematic and limiting because subjects who have used contraception methods for a certain period of time are included, while those who have discontinued the method before that time are excluded. Therefore, due to the lack of inclusion of subjects discontinuing due to weight gain, weight gain results may actually be underestimated by many studies. Another common limitation that arose was the lack of a non-hormonal contraceptive comparison group in some of the studies which creates difficulty in determining if weight gain can be contributed to DMPA use specifically or hormonal contraceptive use in general. Also, several studies lacked racial/ethnic diversity throughout study subjects, limiting the generalizability of results.
Weight Gain Discussion

The question of the effect of DMPA use on weight gain, especially in the adolescent population, can begin to be answered through investigation and review of the current literature, research, and studies mentioned previously. The thought that DMPA use causes weight gain is a common one and is even listed in the Depo-Provera package insert as a general precaution. While a few studies noted no significant weight gain with DMPA use, an overwhelming majority of research, including that focusing specifically on adolescents, indicated statistically significant weight gain or BMI increase when contrasted against other hormonal and non-hormonal contraceptive methods. Several studies also reported significantly greater percentages of subjects who gained weight in the DMPA group, 9.3% - 19%, compared to those in other contraceptive groups. Some studies additionally determined significantly greater percentages or odds ratios of DMPA users actually becoming obese by achieving a BMI of greater than or equal to 30 throughout the course of the study when compared to other contraceptive methods.

Since a majority of studies revealed significant weight gain with DMPA use, it is important to investigate if risk factors or predictors of weight gain exist that patients and clinicians should be aware of. Awareness of such risk factors will aid in determining if significant weight gain is more likely in certain adolescent users compared to others, and thus assist in deciding if DMPA is an appropriate contraceptive method for an individual adolescent. One of the most commonly questioned risk factors of significant weight gain with DMPA use is baseline obesity. Interesting and varying results were noted in the studies which explored baseline weight status effect on weight gain with DMPA use. The three studies which included adult women as subjects actually found that nonobese DMPA subjects gained significantly greater weight than their obese counterparts. These results differed from adolescent-focused
studies. Two adolescent studies reported that baseline BMI had no affect on the likelihood of weight gain in subjects, however, one of these studies revealed that subjects who gained greater than 6kg at one year of use had a greater baseline BMI than those who gained 2-6kg suggesting that baseline BMI may actually affect amount of weight gain. Other adolescent-focused studies discovered that those DMPA users who were overweight or obese at baseline were found to gain a significantly greater amount of weight with DMPA use than those not considered overweight or obese at baseline. One these studies also found that a greater percentage of the overweight subject group gained more than ten pounds with one year of DMPA use compared to the non-overweight group. Additionally, it found that those gaining more than ten pounds at one year of DMPA use had a greater baseline BMI than those who did not gain ten pounds suggesting that baseline BMI significantly affects weight change with DMPA use. This is the stance that the WHO takes in that DMPA is given a category 2 rating defined as a condition where the advantages of using the method generally outweigh the theoretical or proven risks for obese adolescents (≥ Menarche to < 18 years and ≥ 30 kg/m2 body mass index) making the statement of evidence that “obese adolescents who used DMPA were more likely to gain weight than obese nonusers, obese COC users, and non-obese DMPA users. This relationship was not observed among adult women” (World Health Organization, 2009). This trend has also been noticed by a key informant health care provider from Planned Parenthood in Toledo, Ohio. She notes that about 15 adolescent Depo-Provera Contraceptive Injection users are seen each week at the Toledo, Ohio Planned Parenthood location with at least 10 being newly-initiating Depo-Provera users. It is her impression that obese adolescents using the Depo-Provera seem to gain more weight with continued use than nonbese adolescents.
Two studies also investigated early weight gain with DMPA use to determine if this was a risk factor for later weight gain. One study noted that in subjects who gained greater than 5% of their body weight at three months of DMPA use, 93% were found to gain even more weight at 12 months of use. The other study noted that subjects who gained greater than 5% of their baseline body weight at six months DMPA use gained significantly more weight at 12, 18 and 36 months than those who had gained less than 5% of baseline weight as six months of DMPA use. These studies demonstrated that early weight gain with DMPA use was a strong predictor of later weight gain with continued use. This is important because it suggests that DMPA could be prescribed to an adolescent and then re-evaluated at three or six months if the patient or clinician is unhappy with the amount of weight gain, at which point additional dietary and exercise counseling could be ensued.

Race or ethnicity was another investigated risk factor of weight change with DMPA use in several of the studies. Two studies that stratified results by race found that it was not a risk factor for significant weight gain with DMPA use. Other studies, however, revealed that race did have an effect on weight gain, but which races that were more likely to gain weight using DMPA varied between studies. One study noted that white nonobese subjects gained significantly more weight that white obese subjects. This was found to be a trend, though not significantly, in Hispanic women, but was not the trend in black subjects. Other studies noting disparity in weight gain in those of differing race found that black subjects had significant weight gain, BMI increase, and percent body fat increase compared to than their white counterparts, who showed no significant weight gain. Black subjects were also shown to have interactions between their race and other risk factors such as younger age, dietary factors, and longer duration of DMPA use, which was not the case with white subjects. This was similar for another study which
showed that white subjects were found to have baseline BMI as a risk factor for weight gain, regardless of contraceptive method, whereas black subjects were found to have a significant interaction between baseline BMI and actual DMPA method use. Because the investigated studies had such varied results, this suggests that more research is needed in this area to determine if race is a risk factor for weight gain with adolescent DMPA use.

Other risk factors mentioned in the various studies that were found to be significant predictors of weight gain included duration of use, parity of at least one, and self-reported increased appetite.

When considering DMPA as a potential contraceptive method for adolescents, weight gain may be an important concern for both of the patient and clinician, but one must also consider the reason an adolescent is seeking the method in the first place: pregnancy prevention. When determining the appropriateness of DMPA in the adolescent patient, one must weigh the potential for weight gain against the risk of teen pregnancy with its associated with its own physical effects including weight gain as well as the social, educational, and emotional consequences that may arise. It is important for clinicians to inform adolescents seeking DMPA as a potential form of pregnancy prevention, especially those concerned about weight gain, that not all users gain significant weight. Studies revealed that anywhere from 45 to 72% of DMPA users were able to maintain their weight or gain less than five pounds or 5% of their baseline weight. However, it is essential that clinicians also educate patients, especially those who may have risk factors for significant weight gain, such as a higher baseline BMI, that significant weight gain is a definite possibility that must be addressed and discussed. As the key informant from the Toledo, Ohio Planned Parenthood noted, weight gain is one of the more common reasons for DMPA discontinuation in adolescents in her personal experience. Letting adolescent
patients know of the potential for weight gain and questioning them about their ability or lack of ability to tolerate weight gain may help clinicians decide if DMPA would be a reasonable and acceptable method of contraception for an individual patient. Also, offering a three or six month trial of DMPA with assurance of adequate follow up of weight changes and education about the physical, emotional, and social risks and consequences that can occur with unplanned teenage pregnancy may cause the hesitant adolescent patient to agree to initiate the method. Strategies such as these, which provide education and take the individual patient into consideration, may aid in keeping some adolescents from discontinuing the method because of their awareness and acceptance of the possibility of weight gain upon initiation of the contraceptive. Additionally, discussing healthy diet, eating behaviors, and exercise with patient is imperative and may help ward off the potential weight gain, therefore possibly preventing method discontinuation in some patients and thus potentially preventing unwanted teen pregnancy. Regarding the evidence presented in the current research and committee opinions available, it appears that DMPA is an appropriate method of pregnancy prevention in adolescents, even those with risk factors such as higher baseline BMI, and that the risks of weight gain and associated health effects are minimal when weighed against the consequences of an unplanned teen pregnancy.
Mirena

Expulsion Rate Literature Review

Disclaimer: Mirena is considered a levonorgestrel-releasing intrauterine system (LNG-IUS) according to its prescribing information; however, it is also referenced as an IUS, IUD, LNG-IUD, IUC or IUCD in other information resources. The terms LNG-IUS or IUS will be used in reference to Mirena for the purposes of this project, but other terms listed above may be used interchangeably when directly quoted or when referring to other similar methods of contraception.

Concerns with higher expulsion rates may cause hesitation in the use of Mirena or other IUDs in the adolescent population. This concern may result from the generally smaller uterine size of younger women. If higher expulsion rates do occur in younger IUD users, this may lead to an increased number of unplanned pregnancies. Because there are few available studies and little information about Mirena in adolescents, studies concerning expulsion rates of copper IUDs and adult women were also utilized. Also, because parity may have an effect on uterine size, and thus, potentially IUS and IUD expulsion, this was investigated as well.

The Faculty of Family Planning and Reproductive Health Care Guidance (FFPRHC) on the LNG-IUS reports that expulsion is the most common cause for IUS failure occurring once in about every 20 insertions. Expulsion rates are reported as 4.5% at one year, 5.2% at two years, and 5.9% at five years of use. It also notes that LNG-IUSs are more likely to expulse than IUDs, but the difference is only significant after five years of use (Faculty of Family Planning and Reproductive Health Care Guidance, 2004).

A systematic review by Deans and Grimes (2009) regarding the use of various IUDs in adolescents found expulsion rates ranging widely from 5-22% over 6-48 months post-insertion.
Two studies included in the review were noted to have expulsion rates that were inversely related to age. With regard to gravidity and parity within these two studies, no pattern or relationship to expulsion rates was discovered. An additional study showed that nulligravid study participants had significantly higher expulsion rates than parous women reporting 8% for nulligravid, 5% for nulliparous, and 2-3% for parous participants over a 24-month follow up. Another study involving 13-22 year old women, however, reported a greater expulsion rate in parous participants compared to nulliparous over a 36-months follow up time (22% versus 17%). It is noted, though, that the studies did not control for age and populations of participants were small (Deans & Grimes, 2009).

A retrospective study by Diaz et al. (1993) investigated adolescent use of copper IUDs and reported expulsion rates stratified by age. A group of 995 parous adolescents age 12 to 20 years were each paired with a control subject 10 years older and of the same parity status so that age could be the main factor of interest with other factors controlled. Copper T 200 IUDs were inserted and participants were followed until removal of the device. Results demonstrated significantly higher expulsion rates in the adolescent group throughout four years of follow up. Rates were discovered to be 7.4, 8.9, 10.3, and 11.4% in the adolescent subject group compared to 4.2, 5.0, 5.8 and 5.8% in the older population for the subsequent four years. For the purposes of this paper, limitations of this study include the use of only parous subjects, as not all adolescents are parous and therefore results may not be able to be fully generalized. Also, the continuation rate throughout the four year follow up was small in the adolescent population at 31.3% compared to the 50% of the control participants (Diaz, et al., 1993).

There are few studies which concentrate specifically on age as a factor in IUD expulsion rates. A majority of studies rather investigate parity as a factor as it is thought that nulliparous
women have smaller uterine sizes and therefore may be more at risk for expulsion. Such research includes a nationwide cohort study by Paterson, Ashton, and Harrison-Woolrych (2009) examining LNG-IUS use by 175 New Zealand adolescents ages 11-19 years. Participants were sent a questionnaire following insertion of the IUS questioning indication of IUS use, adverse events encountered, and reason for removal if applicable. Of the 133 responders, 73% were nulliparous with 65% being nulligravid. Over the entire participant group, 11 expulsions occurred representing 8.3% of the responder population of 133 and 6.3% of the entire cohort of 175. The researchers noted that these rates fell within that of the general population of LNG-IUS users: 5.8 to 11.7%. Of the 11 expulsions within this study, five were found to occur in the nulligravid population representing 4.4% of the 114 nulligravid participants. While this study reported expulsion rates for nulligravid participants specifically, it is limited in that the rates for nulliparous and parous subjects were not reported. Other limitations include the use of self-reported questionnaires in that those with IUS complications such as expulsions may be less likely to report, therefore skewing the results (Paterson, Ashton, & Harrison-Woolrych, 2009).

Another study reporting expulsion rates in adolescents is that by Kaivola and Hirvonen (1984) in which the clinical performance of Fincoid copper IUD was investigated. A Helsinki outpatient clinic followed 646 nulliparous and 498 parous adolescents over a 12 month post-insertion period. Data revealed greater expulsion rates among younger participants than older, regardless of parity, though differences were not statistically significant. The researchers suggest that higher expulsion rates in younger IUD users are likely due to smaller uterine sizes in that population. Limitations to this study include the lack of reporting specific result values and limited discussion about age stratification of results (Kaivola & Hirvonen, 1984).
A study by Kulig, Rauh, Burket Cabot, and Brookman (1980) examined Cu-7 IUD use in nulliparous and parous adolescents over a three year period in a Cincinnati, Ohio adolescent clinic. A total of 147 Cu-7 IUDs were inserted into 120 adolescent females between the ages of 13 and 22 years with a mean age of 16.8 years. Of the participants, 81% were nulliparous with 16% being primiparous and 3% multiparous. After insertion, participants were required to return to the clinic for follow up at three month intervals for a total of three years. Results revealed 26 expulsions overall when combining both partial and total. Of these, 21 were partial expulsions occurring in the 116 participants completing at least six months of follow up, representing 18% of the entire study population. Of the 21 partial expulsions, 16 were found to occur in the 94 nulliparous participants (17%) and five in the parous participants (22%). A majority of the expulsions occurred within the first six months of insertion (15 of 26). It is noted that one pregnancy occurred with a partial expulsion of the IUD. Limitations of this study include the small study population and the poor continuation rate of 39% at 3 years (Kulig, Rauh, Burket, Cabot, & Brookman, 1980).

Another study by Hirvonen and Kaivola (1983) reported expulsion rates in adolescents and young nulliparous women using the copper IUD, Fincoid in a gynecological outpatient clinic in Helsinki, Finland. Fincoid IUDs were inserted into 241 nulliparous women less than 21 years of age with a 12 month follow up period. After one year of follow up, the IUD expulsion rate was found to be 10.4% of the participant population with 1.9% of the total population experiencing partial expulsions and 8.5% having total expulsions. The researchers suggest that high rates of expulsions in this age group is likely due to smaller uterine cavities and greater myometrial distention sensitivity causing increased contractions of the uterus upon IUD insertion (Hirvonen & Kaivola, 1983).
Studies involving IUD use in adolescents from 1980 and earlier vary widely in reported expulsion rates. Those involving nulligravid and nulliparous adolescents reveal rates from 0.67% to 24.8% over study periods ranging from 12 to 33 months. These studies involved anywhere from 30 to 243 subjects varying in age from 13 to 20 years and included the use of various IUDs such as Copper-7, Copper-T, Lippes loop A, Lippes loop C, Lippes loop D, LEM and the W device (J. A. Goldman, Dekel, & Reichman, 1979; J. A. Goldman & Reichman, 1980; Lane & Sobrero, 1975; Weiner, Berg, & Johansson, 1978). One study involving 82 parous adolescents between 11 and 17 years of age receiving the Lippes loop or Copper-T had four expulsions throughout a one-year follow-up resulting in an expulsion rate of 0.49% (Jorgensen, 1973). Problems with these studies include the lack of comparison groups and the use of types of IUDs that are no longer used, especially in the United States.

Data on IUD and IUS expulsion rates stratified by parity is limited in adolescents, therefore much information is taken from studies including adult women. A systematic review was compiled by Hubacher (2007) regarding copper IUD expulsion rates in nulliparous and parous women. The review included 15 studies with 20 comparisons between nulliparous and parous IUD users and nine studies involving only nulliparous women that fit the search inclusion criteria. In the contrast between nulliparous and parous women, 13 of the 20 comparisons reported higher rates of IUD expulsion in the nulliparous group. Hubacher notes that one study using the CuT380A reported only a small difference between nulliparous and parous women in terms of performance and expulsion rates. In the studies reporting solely on nulliparous women, expulsion rates were found to vary widely, ranging from 1.8 to 12.7% at 12 months post-insertion. Comparisons between different copper IUDs showed that smaller IUDs such as the MiniCu7 and CuT380Nul had lower expulsion rates than larger IUDs suggesting that expulsions
may be due to incongruity between the size of the device and the size of the uterine cavity.

Limitations to this systematic review include the lack of discussion about statistical significance of expulsion rate differences between nulliparous and parous women (Hubacher, 2007).

A retrospective chart review by Veldhuis, Vos and Lagro-Janssen (2004) investigated 332 parous and 129 nulliparous women between the ages of 17 and 52 years using the Multiload Cu375, Multiload Cu250, and Nova T as well as a levonorgestrel-releasing IUD between 1981 and 2000. The mean age of participants was 30.8 years with 23.7% of the population being nulliparous and 76.3% parous. Of the entire participant population, 18 expulsions were recorded, 17 of which occurred with a copper IUD. Five expulsions took place in nulliparous participants representing an expulsion rate 0-2.8% per year compared to the 12 expulsions occurring in parous participants representing an expulsion rate of 0-1.4% per year. The difference in expulsion rates between nulliparous and parous participants was not found to be statistically significant. One expulsion of the LNG-IUD occurred in a nulliparous women with none occurring in the parous population. This was also not statistically significant. Limitations to this study include the retrospective chart review study type in which information was only available for those who reported complications or concerns to their clinician. Also, for the purposes of this study, the study is limited in the average age of study participants and small amount of adolescents IUD users (Veldhuis, Vos, & Lagro-Janssen, 2004).

Similarly, an observational, prospective study by Ramirez Hidalgo and Pujol Ribera (2000), investigated 676 parous and 98 nulliparous women who were fitted with one of several copper IUDs and followed for two to five years. Participants were required to have a medical health history taken as well as a gynecological exam and hysterometry performed. High copper load IUDs were used in women with two or more children or women with less than one year
between children. Smaller IUDs were used on women with uterine sizes of greater than 5.0cm and less than 6.5cm on hysteroscopy. Analysis of the collected data showed a participant population consisting of 87.3% parous and 12.7% nulliparous women. The average age of the parous group was 32.8 years compared to the 27.4 years of the nulliparous group. Only two IUDs were placed in women under 18 years of age. Regarding IUD expulsions, 35 expulsions occurred throughout the study representing 3.2% of the entire participant population. Of these, four occurred in nulliparous participants (4.1%) and 21 in parous participants (3.1%). This difference was not statistically significant. It was also discovered that of the 25 expulsions, 17 occurred within the first year with 12 occurring within the first three months. This study is limited by the use of different sized IUDs for subjects based on uterine size or parity number. Information was not provided regarding which subjects received the smaller IUD and if these smaller devices were placed in only nulliparous participants, parous participants or both (Ramirez Hidalgo & Pujol Ribera, 2000).

Duenas, Albert, and Carrasco (1996) investigated the performance of various copper IUDs in 525 nulliparous and 2,770 parous women between the ages of 16 and 34 years over a four year period. The MLCu-250, a smaller copper IUD, was placed in the nulliparous participants, while parous women received the T Cu-200, 7 Cu-200, or Nova T IUDs. The expulsion rate for nulliparous, MLCu-250 IUD users was found to be 2.15% compared to the 2.55% of the parous participants. It is noted by the researchers that 64% of expulsions occurred within the first year of insertion. Limitations to this study include the lack of discussion about statistical significance between nulliparous and parous expulsion rates. Also, it is difficult to compare the expulsion rates as nulliparous women received a smaller IUD than parous participants, which may have had an effect on the collected rate of expulsion. However, this
may show that type and size of IUD may have an effect on the rates of expulsion, therefore the
type of IUD could potentially be tailored to the patient or subject based on their parity or uterine

A comparative, cross-sectional study by Lete, Morales, and Pablo (1998) in Vitoria, Spain compared Nova T IUD use and effectiveness in 227 nulliparous and 2080 parous women between the ages of 18 and 46 years. Results of the study revealed a mean age of nulliparous participants of 27 years compared to 33 years of the parous group. Upon hystermometry, nulliparous participants were discovered to have a mean uterine cavity length of 7cm in comparison to 7.5cm of the parous subject. Throughout the 12 year study, 48 expulsions occurred; two within the nulliparous group representing 1.6% of the nulliparous population and 46 within the parous group, representing 5.1% of the parous population. The researchers suggest that the very low expulsion rate in the nulliparous group compared to that of the parous may be due to more careful selection of IUD candidates in nulliparous women than in women who have already had children (Lete, Morales, & de Pablo, 1998).

A study by Baeyertz and Hartfield (1997) examined Nova-T IUD clinical performance in 383 parous and 42 nulliparous women over two years of follow up. The average age of nulliparous participants was found to be 24 years compared to 33 years of the parous subgroup. At one point during the eight year study, nulliparous women were no longer fitted with the Nova-T IUD, but rather the smaller Minigravigard IUD due to high removal rates and Pearl index failure rates early in the study. Collected data revealed 21 expulsions after an average of 23 months duration of use. This represents a 4.9% expulsion rate when considering the parous and nulliparous participants together. Of the 21 expulsions, 14 were complete expulsions that occurred during menstruation, while seven were partial expulsions detected by the study
participant. It is noted that one of the complete expulsions resulted in an accidental pregnancy at six months post-insertion. The researchers note that age and parity had no relevance regarding expulsion rates. While the researchers communicate that age and parity did not have a bearing on expulsions rates, data and results stratified by age and parity were not directly reported. Also, the fact that nulliparous women were fitted with a smaller IUD part of the way through the study may have had an effect on expulsion rates. Additionally, there was a very large disparity between the number of participants in the parous and nulliparous making comparison of expulsion rates difficult and thus limiting the generalizability of the study results (Baeyertz & Hartfield, 1997).

A one-year randomized study by Suhonen, Haukkamaa, Jakobsson, and Rauramo (2004) in Helsinki, Findland, compared the LNG-IUS with oral contraceptive pills in 200 nulligravid and nulliparous women age 18-25 years. The 200 participants were randomly assigned to the IUS and oral contraceptive subgroups with 99 in the IUS group and 101 in the oral contraceptive group. Follow up occurred every three months for one year and included a gynecological examination and recording of adverse events. Collected data revealed one partial IUS expulsion that occurred within the first six months after insertion, representing 1.2% of the IUS subgroup. The researchers noted that this rate is similar and slightly less than that of a comparable age group in a previous study investigating the clinical performance of the LNG-IUS. Limitations to this study include the small study population of IUS users and the lack of a proper comparison group such as parous women of a comparable age range (Suhonen, Haukkamaa, Jakobsson, & Rauramo, 2004).

Another study by Brockmeyer, Kishen, and Webb (2008) investigated IUD and LNG-IUS use in 113 nulliparous women 16-30 years of age at a sexual health clinic in Liverpool,
United Kingdom. Of these participants, 104 had one of several copper IUDs placed, while an IUS was placed in nine women. Following insertion, participants received either a postal or phone call questionnaire at three months and then one year of follow up. Collected data confirmed two expulsions within the first three months following insertion, representing 2% of the participant population. It is noted that both expulsions occurred in IUD users. At one year of follow up, a total of six expulsions had occurred, representing 7% of the study participants. A majority of the expulsions occurred more than three months post-insertion. Limitations to this study include the small study population and a lack of comparison group such as parous IUD and LNG-IUS users of comparable age range. Also the small number of IUS users compared to IUD users makes it very difficult to compare the two types of devices, and thus difficult to compare expulsion rates (Brockmeyer, Kishen, & Webb, 2008).

Srisupandit (1988) investigated the Cu-7 Minigravigard in nulliparous women at a family planning research center in Bangkok, Thailand. The study included 99 nulliparous participants with uterine axial length of 6-7cm. Follow up occurred at three and six months, as well as at one year and then yearly thereafter for a total of three years. The participants ranged in age from 17-32 years with a mean age of 27.87 years. A total of 19.2% of the participants fell within the age range of 17-19 years and 46.5% fell within the 20-24 year age range. Regarding IUD expulsions, a rate of 3.0% occurred at three months, 5.5% at six months, 6.0% at one year and 8.0% at two and three years post-insertion. One expulsion was determined a partial expulsion as it was found in the cervical canal three weeks after insertion. Limitations of this study include the small number of subjects and lack of a comparison group such as parous women of a comparable age range using the same IUD. Also, the Minigravigard is a smaller IUD than most
and was only placed in study participants with a uterine axial length of 6-7cm, therefore
expulsion rates may not be able to be generalized fully (Srisupandit, 1988).

Committee opinions about the use of IUSs and IUDs in adolescents include that by the
World Health Organization (WHO) which rates both the LNG-IUS and copper IUDs a category
2 for women within the age range of menarche to less than 20 years old meaning that “the
advantages of using the method generally outweigh the theoretical or proven risks,” (World
Health Organization, 2009). Regarding parity, the LNG-IUS and copper IUDs are given a
category 2 rating for nulliparous women and a category 1 rating for parous women meaning that
“there is no restriction for the use of the contraceptive method,” (World Health Organization,
2009). The disparity between ratings of parous and nulliparous users seems to stem from minor
concern about infertility risk associated with PID rather than potentially increased expulsion
rates. The ACOG Committee Opinion number 392 regarding the IUD and adolescents reports an
IUD failure rate due to expulsion of 1 in 20 adolescents and notes that younger age and previous
IUD expulsion may increase the risk of failure, but notes that prior expulsion should not be a
contraindication for IUD insertion. It also suggests that patients undergo appropriate counseling
and follow up with IUD or IUS insertion (American College of Obstetricians and Gynecologists,
2007).
Expulsion Rate Discussion

A review article by Prager and Darney (2007) notes that “clinicians are concerned that a smaller [uterine] cavity may increase the risk of failure due to expulsion, perforation or early discontinuation…” (Prager & Darney, 2007). Younger age and nulligravidity or nulliparity are considered to be associated with smaller uterine size, and therefore, could potentially have an effect on IUS and IUD expulsion rates. Of the studies reviewed, those involving adolescents using the LNG-IUS specifically reported expulsion rates ranging from 4.4-8.3% over follow up periods varying between one and five years. When including studies involving adolescent use of various other IUDs, expulsion rates were reported between 5-22% in studies occurring after 1980, while earlier studies noted rates anywhere from 0.49-24.8%. Only one study included both LNG-IUS and copper IUDs, but the small number of IUS subjects made comparisons between the two groups unfeasible. Regarding age as a potential factor in higher rates of expulsion, the systematic review by Dean and Grimes (2009) noted expulsion rates inversely related to age with higher incidence occurring in younger IUD users. This was also evident in the study by Diaz et al. (1993) which noted significantly higher expulsion rates in adolescent IUD users compared to the control subjects 10 years older. The study by Kaivola and Hirvonen (1984) also reported increased expulsion rates in younger IUD users.

Regarding parity as a factor affecting expulsion rates, studies reviewed in this paper revealed nulligravid and nulliparous expulsions rates ranging from 0.67-24.8% compared to 0.49-22% of parous users in the adolescent population. These rates appear rather similar, possibly suggesting that age may have more association with expulsion rates than parity in adolescents. The systematic review by Deans and Grimes (2007) noted one study in which parity did not affect expulsion rates, however, other reviewed studies noted results in which
nulliparous expulsion rates were found to be greater than those of parous subjects and vice versa. In studies comparing adult nulliparous and parous IUD/IUS users, expulsion rates ranged from 1.2-12.7% in nulliparous women contrasted with 1.4-5.1% of parous women. This suggests that parity may indeed have an effect on expulsion rates. One study involving adult women noted no expulsion rate disparity between parous and nulliparous users and two others reported parous expulsion rates slightly higher than those of nulliparous women. These two studies, however, used smaller IUD types in the nulliparous participants which may have affected expulsion rates. This could suggest that the type and size of the IUS/IUD may affect rates of expulsion. Unfortunately, this may not be of much bearing in the United States due to the availability of only the Mirena LNG-IUS and Paragard copper IUD.

The studies reviewed previously portray evidence that age and parity may have an effect on IUS and IUD expulsion rates in that younger, nulligravid and nulliparous IUD/IUS users may have slightly greater potential for expulsion risk. Due to the limited number of studies involving adolescents, and the LNG-IUS especially, however, more research is needed to determine if this is actually the case. Whatever the case may be, the potential risk for expulsion must be weighed against risks of unwanted teen pregnancy without proper contraceptives, as well as the social, education, and emotional complications that accompany unwanted teen pregnancy in order to determine if the IUS is a proper contraceptive option for adolescents. Based on the available data and current committee opinions available regarding adolescent use of IUSs, young, nulligravid and nulliparous women may have an increased risk of expulsion, it appears that the increase is only slight and that IUSs should not be withheld from adolescents seeking contraception merely due to the potential risk. Rather, adolescents receiving an IUS as a form of contraception must educated about the potential expulsion risk and the importance of checking
the position of the IUS/IUD by feeling for the device strings on a regular basis. It is this education that may help to prevent unknown expulsion, and thus potential accidental pregnancy.
Pelvic Inflammatory Disease Literature Review

Another common reason for underutilization of the IUS in the adolescent population is the concern for the risk of pelvic inflammatory disease (PID). Pelvic inflammatory disease is a condition which includes “acute salpingitis, often in association with endometritis,” (L. Goldman, MD & Ausiello, 2008). “C. trachomatis is the dominant cause of PID in the United States, but gonorrhea remains a common cause. …C. trachomatis infection can spread from the cervix to the endometrium and produce endometritis and salpingitis in 10 to 40% of women, and 10 to 20% of women infected with gonorrhea,” (L. Goldman, MD & Ausiello, 2008). Clinical manifestations include lower abdominal pain most commonly, but may also include fever, malaise, anorexia, and symptoms of lower genital tract infection such as vaginal discharge. Physical exam often demonstrates low abdominal tenderness, cervical motion tenderness, and bilateral adnexal tenderness, and often includes signs of cervicitis or bacterial vaginosis.

“Clinical diagnosis is inexact…both insensitive and nonspecific” in that “many cases of PID lack the classic signs and symptoms,” (L. Goldman, MD & Ausiello, 2008). Laparascopy showing visible salpingitis is used as the definitive test, however, may not show abnormality in some cases. Untreated PID can have severe consequences including infertility or ectopic pregnancy due to fallopian tube scarring. “Incidence of tubal infertility has been estimated at 15% after one episode of PID and up to 50% after three attacks” (L. Goldman, MD & Ausiello, 2008).

Concern about PID associated with the IUS, especially in the United States, seems to stem from past intrauterine systems, especially the Dalkon Shield. Introduced in 1970, the Dalkon Shield was found to cause a high incidence of pelvic infections due to the “multi filamented tail…[which] provided a pathway for bacteria to ascend protected from the barrier of cervical mucus” (Speroff & Fritz, 2005). Sales of the Dalkon Shield discontinued in 1975,
however, “a call for removal of all Dalkon Shields was not issued until the early 1980s.” This led to multiple lawsuits against the pharmaceutical company by women who developed pelvic infections. This seems to have created a stigma within the U.S. against all intrauterine systems. “Changes in sexual behavior in the 1960s and 1970s, and failure to use protective contraception (condoms and oral contraceptives), led to an epidemic of sexually transmitted infections (STIs) and pelvic inflammatory disease (PID) for which IUDs were held partially responsible.” This caused decreased IUD rates of use in the U.S. of 7.1% to 2% and then to 0.8% of contraceptive users in 1982, 1988, and 1992, respectively. The trend was not the same in the rest of the world with numbers of users totaling 60, 83, and 106 million in 1981, 1988, and 1995, respectively (Speroff & Fritz, 2005).

A review by David A. Grimes (2000), states that studies demonstrating “apparent increased risk of upper-genital-tract infection” in IUD users was due to the “consistent presence of three types of bias: use of an inappropriate comparison group (women using contraceptives that lower the risk of PID), systematic overdiagnosis of salpingitis among IUD users, and inability to control confounding factors (such as number of sexual partners)” (Grimes, 2000). It is now thought that PID is associated not necessarily with IUD use, but rather presence of STIs, especially upon IUD insertion. It is already well known that C. trachomatis and N. gonorrhoea are common causes of PID; however, the concern in question is whether insertion of an IUS or IUD in the presence of an STI increases the risk of PID development. If this is true, is the adolescent population, which is a group with statistically higher STI rates, more at risk for PID when an IUS is inserted? Is the IUS or IUD an appropriate method of contraception in adolescents, especially those with high risk of STIs?
Grimes (2000) notes that “if an IUD increases a woman’s risk of upper-genital-tract infection and if her exposure to infection remains constant, then her risk of PID should remain raised throughout the duration of her IUD use.” A study by Farley, Rosenberg, Rowe, Chen, and Meirik (1992) suggests that the risk of PID is higher immediately after insertion and more associated with the risk of STI and insertion process rather than the presence of the IUD itself. The study reviewed data from twelve randomized studies comparing two or more copper, inert, or hormonal IUDs and one non-randomized pilot study. In order to be included in the studies participants were required to have had at least one pregnancy of twenty weeks duration or, in most studies, one live birth. Exclusion criteria included STI in the past six months, history of PID, as well as genital tract malformations or malignancies. Data collection began in 1975 and included 22,908 women volunteering for IUD contraception at family planning centers in Europe, Asia, China, Americas and Africa. Most studies lasted two to three years and included various IUD types. PID was diagnosed by oral temperature ≥ 38°C, lower abdominal tenderness with guarding, and a pelvic examination revealing cervical motion tenderness, adnexal tenderness, or palpable adnexal mass. Results revealed 81 cases of PID out of 22,908 insertions representing 0.35% of the participants. The incidence of PID was found to be highest immediately after IUD insertion with decreased, constant rates up to eight years thereafter. Analysis of the date showed “the immediate post insertion risk is high up to 20 days, but then drops to a lower rate thereafter.” More specifically, a rate ratio of 6.36 times greater PID incidence was discovered within the first 20 days after insertion compared with after. When stratified by location, the PID rate was highest in Africa; “nearly six times higher than that in Asia and slightly less than three times higher than in Europe.” No cases of PID were found in China. When stratified by age, women in the 15-24 year age group were discovered to have the
highest PID rate with others having half of the risk. When stratified by parity, an inverse relationship between parity and PID incidence was found as “risk decreased with increased number of live births.” The researchers established that the most important factors affecting PID risk included the number of days post insertion, age, and region with the single most significant factor being the number of days after insertion “consistent with the demonstration of brief, transient microbiological contamination of the uterine cavity following IUD insertion.” This study indicates that PID risk does not increase with continued IUD use, but rather is associated with time of insertion. The researchers suggest that increased rates with younger age and lower parity number may be due to differences in lifestyle that may create greater risks of STIs. Regions with known higher STI rates such as Africa were found to have higher PID incidence than those areas with lower STI rates such as China. With analysis of the data, the researchers suggest that “IUD users selected for low risk of sexually transmissible disease do not have excess PID,” and that while “there is a higher risk immediately after insertion…exposure to sexually transmissible disease…is the major determinant of PID.” Limitations to this study include lack of information regarding confounding variables such as a participants’ number of sexual partners or the type and frequency of sexual activity. Also, the studies investigated relied on clinical diagnosis of PID (Farley, Rosenberg, Rowe, Chen, & Meirik, 1992).

This study suggests that the presence of STI upon insertion of an IUD may be the major contributor to PID rather than the presence of the IUD itself, as the risk of PID is high immediately after insertion and significantly declines thereafter even with the IUD still in place. The question is: does insertion of an IUD or IUS increase the risk of PID in women with an STI? If this is the case, then concern about IUS use in the adolescent population, who overall have a higher STI incidence, may be a warranted concern. The problem that presents, as described by
Grimes (2000) and Mohllajee, Curtis, and Peterson (2006), is that studies directly examining this question do not exist. In order to examine this directly, studies would need to compare this risk of PID in women with an STI upon insertion of an IUS or IUD to that of women with an STI not receiving an IUS. Instead, the evidence available is indirect from studies in which PID incidence is compared between women having an IUS or IUD inserted with concurrent STI as opposed to without concurrent STI. A one-month, prospective study by Faundes et al. (1998) in a family planning clinic in Brazil compares women with inadvertent insertion of an IUD in the presence of Chlamydia infection to insertion into women without infection. A total of 407 women were screened for “the diagnosis of Chlamydia or Neisseria infection based on history of multiple sexual partners, purulent cervical secretions, hyperemia, and bleeding of the cervix at touch or pelvic pain during bimanual vaginal exam.” Specimens were also collected to test for Chlamydia and Neisseria at the time of IUD insertion. The researchers note that the family planning clinic attempted to minimize insertion into women at risk of STIs by “radically restricting insertion in nulliparous women and excluding those who have had multiple sexual partners, those with history of PID after their last delivery, and those who have signs or symptoms suggestive of endocervicitis or upper genital tract infection.” Results showed positive Chlamydia tests in 6.7% of the study population and no positive tests for gonorrhea. Regarding those testing positive for Chlamydia, women older than 29 years of age were found to have significantly greater incidence than those less than 29 years. There was also a significant trend of increased incidence of Chlamydia with greater number of years with current sexual partner. No significant correlation was found with age at first intercourse, number of lifetime sexual partners or use of condoms with sexual activity. There was also no significant difference in vulvovaginal symptoms. Characteristics that could be indicative of infection on speculum exam
such as pain during pelvic exam, hyperemia, or foul-smelling fluid, and purulent cervical mucus were elevated in those with Chlamydia infection, but not statistically significant. It is noted that 19 of 327 women that had an IUD inserted were later found to have a positive Chlamydia test at the time of insertion. Of the 19, two women returned to the clinic with lower abdominal pain. One was clinically diagnosed with PID and had the IUD removed, while the other, with no fever and only mild pain on pelvic exam, was treated with 200mg/day doxycycline for 10 days with complete recovery. The other 17 Chlamydia-positive women showed no signs or symptoms of PID, but were treated with antibiotics. No other cases of PID were found among the rest of the study participants. Analysis of the data revealed a rate of PID in those with cervical infection of 1/19 or 2/19 if the second patient is considered positive for PID (Faundes, et al., 1998). In a systematic review by Mohllajee et al. (2006), further analysis of the data determined the PID incidence to be 5.2% in women with cervical infection at time of IUD insertion or 10.1% if the second case of suspected PID is considered (Mohllajee, Curtis, & Peterson, 2006). Limitations of the study include the short one-month follow-up and the lack of specific criteria for PID diagnosis (Faundes, et al., 1998).

Another prospective study by Skjeldstad, Halvorsen, Kahn, Nordbo, and Saake (1996) involving general practice settings in Norway examined the prevalence of Chlamydia infection at IUD insertion and evaluated “its effect on cause related termination during the first 90 days of use.” A total of 957 parous women between 18 and 45 years of age were screened for Chlamydia infection and had a serum sample for C reactive protein at time of insertion with results available more than a week after time of insertion. Chlamydia was found in five women or 0.5% of the participants by laboratory testing. The incidence of Chlamydia infection did not vary significantly in terms of age, marital status, parity or population factors. Reasons for IUD
removal within 90 days of follow up included expulsion, pain, bleeding, partial expulsion or insertion problems. It was found that one woman positive for Chlamydia at time of IUD insertion had a partial expulsion while the other four were treated with antibiotics within two weeks of insertion and experienced no complications. No women had the IUD removed due to PID. The researchers note that while no cases of PID were identified, “it is possible that in the absence of screening and treatment, some of the five test-positive women might have experienced problems such as PID.” Limitations of this study include lack of explanation of criteria regarding PID diagnosis, and lack of information about screening procedures such as clinical signs and symptoms of Chlamydia infection (Skjeldestad, Halvorsen, Kahn, Nordbo, & Saake, 1996).

A randomized study in Sweden by Pap-Akeson, Solheim, Thorbert, and Akerlund (1992) revealing information comparing PID rates in women with and without Chlamydia infection at the time of IUD insertion attempted to compare rates of genital tract infection development with position of IUD threads, either normal position or placed inside of the uterine cavity. This study involved 445 women between 20 and 47 years of age with all but four participants being parous. Exclusion criteria included history of previous salpingitis or ectopic pregnancy, ongoing pregnancy, symptoms or signs of genital infection and irregular bleeding. Participants received a gynecological exam and a sample for a Chlamydia test was taken at time of insertion, with results available after IUD insertion. At follow up visits, an exam was performed with clinical evidence of infection defined as a foul-smelling discharge with our without tenderness of the uterus or adnexa. Results revealed six cases of asymptomatic Chlamydia in the “threads up” group and seven cases in the “threads down” group who were treated with tetracyclines and experienced no signs or symptoms on infection (Pap-Akeson, Solheim, Thorbert, & Akerlund,
1992). Review of the study by Mohllajee et al. (2006) determined a 2.9% Chlamydia infection rate among participants at time of insertion (13/445). After antibiotic treatment, the women found to have infection at insertion had no complications or signs and symptoms of infection throughout the rest of the study. Women with no infection at the time of insertion were discovered to have three cases of salpingitis and six cases of endometritis representing 0.7% and 1.4% respectively and totaling 2.1% of the infection-negative group. It is also of note that more infections were found in the “threads down” group. Limitations of this study include lack of diagnostic criteria for salpingitis and endometritis (Mohllajee, et al., 2006).

Another study indirectly comparing the incidence of PID among women with and without a cervical infection at time of IUD insertion is that by Walsh et al. (1994) involving 447 potential IUD users at multiple clinical sites in California. The objective of the study was to determine if the use of prophylactic antibiotics given prior to IUD insertion would significantly decrease the number of IUD removals due to medical complications such as PID. A woman’s eligibility to receive the IUD was determined by clinicians at the involved clinical sites. A total of 98% of women were parous and 100% reported no current exposure to multiple partners. Women received an endocervical culture for gonorrhea and Chlamydia, some on the day of insertion and others prior to the day of insertion so that results were available before insertion. Participants included 221 women who were randomly assigned to take two 100mg capsules of doxycycline one hour prior to IUD insertion, whereas 226 received two placebo pills an hour prior to insertion. Of the 272 women screened for STIs at the time of insertion, six were found to have Chlamydia while one was positive for gonorrhea. None were found to develop PID, however, the participant positive for gonorrhea had the IUD removed. IUD removal rates for reasons including bleeding, cramping, painful intercourse and upper genital tract infection were found to
total 3.7% and 4.4% in the antibiotic and placebo group, respectively. It was noted that three or more women in each group had one or more symptoms of upper genital tract infection, but only one in each group met PID criteria according to the Infectious Disease Society for Obstetrics and Gynecology in the U.S. (Walsh, et al., 1994). Analysis of this data by Mohllajee et al. (2006) determined that six of 272 or 2.2% of women screened at the time of IUD insertion were found to have Chlamydia while one of 272 or 0.4% were discovered to have gonorrhea. Women with cervical infection at insertion were found to have no signs or symptoms of PID throughout the three month follow up. Women with no cervical infection at insertion revealed one confirmed case of PID of the 201 participants in the antibiotic group as well as one verified case of PID of the 200 participants in the placebo group. With these groups combined, the rate of PID in the infection-negative group was found to be 0.05%. Limitations of the study include the fact that STI screening information was only available in 61% of the study population (those screened at the time of insertion). Also, no discussion was made about whether the women positive for STIs at insertion were treated with antibiotics (Mohllajee, et al., 2006).

A double blind, randomized study by Sinei et al. (1990) adds information to the question at hand. The objective of the study was to determine whether to administration of doxycycline at the time of IUD insertion would provide a protective effect on the incidence of PID development. A total of 1813 women between 20 and 44 years of age requesting an IUD in Nairobi, Kenya received either a Lippes loop, Copper T, Nova T, or Multiload IUD with 904 randomly assigned to the prophylactic antibiotics group and 909 assigned to the placebo group. Exclusion criteria included history of ectopic pregnancy, pregnancy within the last 42 days, leiomyomata of the uterus, active PID, cervical or endometrial malignancy, among others. Each woman had an endometrial specimen taken for culture for gonorrhea and Chlamydia at time of
insertion. Follow up between four and six weeks of insertion included clinical assessment for PID by standards of the Infections Disease Society for Obstetrics and Gynecology in the U.S. Results revealed a 1.3% rate of PID in the antibiotic group compared to 1.9% of the placebo group with negligible change when adjusting for confounding variables such as education, parity, and age. It was found that women positive for Chlamydia showed little protective effect from PID by prophylactic doxycycline whereas those positive for gonorrhea showed substantial protective effect (Sinei, et al., 1990). Tailored analysis of the question at hand by Mohllajee et al. (2006) reports overall STI rates of 0.66% of participants positive for both Chlamydia and gonorrhea, 2.8% positive for gonorrhea only, and 11.2% positive for Chlamydia only. When considering the placebo group only, 3 of 27 women (11.1%) with gonorrhea only and 2 of 90 women (2.2%) with Chlamydia only developed PID. In the placebo group with no STI at insertion, 9 of 670 (1.3%) developed PID. When considering the placebo and antibiotic groups combined, 3 of 46 women with gonorrhea and 4 of 186 women with Chlamydia developed PID whereas 15 of 1339 women with no STI at insertion developed PID. Limitations to this study include the short, one month follow up time and the lack of information regarding clinical screening for signs and symptoms of STIs prior to IUD insertion (Mohllajee, et al., 2006).

A study by Morrison, Sekadde-Kigondu, Miller, Weiner, and Sinei (1999) in Nairobi, Kenya also provided evidence comparing the incidence of PID in women with and without STIs requesting an IUD. The original purpose of the study was to “evaluate the use of risk assessment algorithms to predict STD and subsequent IUD-related complications among IUD candidates.” The algorithms evaluated included “an STD risk assessment tool developed specifically for use in family planning settings; …CDC guidelines for the prevention and management of chlamydial infections; and…a data-derived tool with variable selection based on modeling of cervical
infections among study population.” Potential participants received a short interview, physical exam, Pap smear and blood specimen for HIV resulting in 1686 women fitting local IUD eligibility criteria, not considered to be high STI risk, and showing no evidence of current PID or cervicitis. These women were fitted with a Copper T 380A IUD. A total of 615 women, including 156 with HIV, were then selected for the study’s one month follow up. At the one month follow up visit, participants then received a pelvic exam and specimens were collected for testing of gonorrhea and Chlamydia. Results showed that of the 580 women that actually participated in the study follow up, 32 were found to have a cervical infection representing 5.5% of the participants, with 5% attributed to Chlamydia and 0.5% to gonorrhea. Of the study participants overall, three were found to develop PID as defined by the U.S. Infectious Disease Society of Obstetrics and Gynecology. Of the 32 women with a cervical infection, six had some sort of IUD-related complication with one developing PID, representing 3.1% of that population. This is compared with the two cases of PID in the group without cervical infection (0.4%). Limitations of this study include the one month lapse in time between IUD insertion and specimen collection for Chlamydia and gonorrhea. One is unable to determine whether STIs were present at the time of insertion, or acquired within the month following. On a side note, the study determined that the family planning risk algorithm including information such as age, marital status, number of sexual partners, STI symptoms, and partner with possible STI detected 75% of the cervical infections by identifying 54% of the participants as high risk of STI. The CDC risk assessment algorithm addressing information such as age, presence of cervical discharge, number of sexual partners, and condom use only identified 44% of the cervical infections by identifying 29% of participants as high risk. The weighted data-derived algorithm addressing information including age, marital status, parity, and ethnicity local to the area of
study detected 91% of the cervical infection by identifying women 47% of participants as high risk, though this algorithm was created by the researchers and has not yet received external validation. The researchers suggest that the STI risk assessment algorithms studied have use in identifying a woman’s risk of STI with those considered low risk recommended for IUD use while those of high risk either counseled against IUD or monitored closely post insertion for development of complications (Morrison, Sekadde-Kigondu, Miller, Weiner, & Sinei, 1999).

A systematic review of the previous six studies by Mohllajee et al. (2006) reaffirms the problem that when determining “whether women who have sexually transmitted infection and who are therefore at risk of developing pelvic inflammatory disease further increase the risk of PID with insertion and use of IUDs,” no direct studies exist to provide information or answers. The authors note that “none of the studies that examined women with STIs compared the risk of PID between those with insertion or use of an IUD and those who had not received an IUD.” Instead, as mentioned previously, indirect evidence was found in studies comparing the incidence of PID in women with and without an STI at the time of copper IUD insertion. Upon review and analysis of the data from the previously discussed studies, it was determined that “rates of diagnosed PID ranged from 0% to 5% among women with STIs at IUD insertion and 0% to 2% for those without STIS at IUD insertion.” It is noted that with the exception of one, “all of the studies observed a greater rate of PID among women with STIs (combining gonorrhea and chlamydial infection) at IUD insertion than women with no STI at insertion, with crude relative risks ranging from 1.63 to 46.35.” It is mentioned that the Sinei et al. (1990) study which included the largest number of subjects and highest follow-up rates had a relative risk of 2.69. With Chlamydia and gonorrhea being the major causes of PID, the authors determine that these increased rates are to be expected, but stress that due to the use of indirect, rather than
direct evidence, it cannot be determined “whether this increase in risk is the same or greater than
the risk for PID among women who do not undergo IUD insertion.” While increased risk was
discovered, the authors note that incidence of PID development was found to be low regardless
of the presence or absence of STI at IUD insertion and stress that of the six studies reviewed,
only two produced statistically significant differences between the two groups. Mohllajee et al.
(2006) describes limitations to these reviewed studies; namely that the studies provided only
indirect evidence for the topic in question. The authors also note that the studies were low in
quality overall due to the varied STI screening techniques as well as PID diagnostic criteria.
Information is limited by the small number of cases of STIs and PID “which can be explained by
the current practice of screening for STIs before inserting an IUD and the low prevalence of STIs
and PID in populations desiring IUD insertion,” (Mohllajee, et al., 2006).

The previously mentioned studies and systematic review demonstrate that those with an
STI at IUD insertion have an increased, yet still small incidence of subsequent PID compared to
those without STI at IUD insertion. For the purposes of this paper, the question becomes: are
adolescents at increased risk of PID development with IUS or IUD use, as this population is
generally considered high risk for STIs due general sexual practices, number of sexual partners,
and often unreliable use of barrier methods? The difficulty with the studies discussed previously
is that they most often included older women who were married or in a monogamous sexual
relationship, had a history of childbirth, few sexual partners in the past, and no history of STI or
PID, thus considered low risk for STIs and historically “good candidates” for IUD contraception.
Certain sexual behaviors in adolescents may include the decreased likelihood to be in
monogamous relationships and “the tendency to stop using condoms once a more reliable form
of birth control is implemented,” which may contribute to the increased risk and rate of STIs
(McNaught, 2006). In fact, the Centers for Disease Control and Prevention’s Sexually Transmitted Disease Surveillance reports that “compared to older adults, sexually-active adolescents 15 to 19 years of age and young adults 20 to 24 years of age are at higher risk for acquiring STDs for a combination of behavioral, biological, and cultural reasons,” (Centers for Disease Control and Prevention, 2009). The Centers for Disease Control and Prevention’s Youth Risk Behavior Surveillance report additionally notes that “nationwide, 13.8% of [high school] students have had sexual intercourse with four or more persons during their life” with prevalence reaching as high as 38.6% in certain ethnic or racial populations. Overall current sexual activity was recorded in 34.2% of students nationwide with rates reaching 53.1% among 12th grade females (Centers for Disease Control and Prevention, 2010). These reports show the character and possible consequences of adolescent behaviors which increase their risk for STIs and thus may cause some to consider the population historically “bad candidates” for IUD use.

A study by Campbell, Cropsey, and Matthews (2007) may provide insight about IUS or IUD use and subsequent PID risk in populations at high risk for STIs. The purpose of the study was to “examine the acceptability and impact of IUD use in an urban community that is located in a region that is noted to have the highest risk rates of STDs in the United States, according to the 2005 Centers for Disease Control Sexually Transmitted Disease Surveillance Report.” A retrospective chart review was performed discovering 194 women who had a copper-T IUD or LNG-IUS inserted between January 2000 and December 2005. The mean age of insertion was 31.6 years with 32.5% of the participants having a history of STI and 32% with a history of other gynecological infections including Chlamydia, gonorrhea, trichomoniasis, HPV, herpes simplex, and syphilis. Less than 1% of the participants had a history of PID. The average parity was 2.9 and 42.3% of participants were unmarried. Upon chart review, 5.4% of women were discovered
to have a clinically diagnosed STI and 19.4% a clinically diagnosed gynecological infection after insertion, with 2.2% of these being PID. Of the women with a history of STI before insertion, 11.9% reported STI after insertion compared with 2.4% of women with no prior STI history. This was found to be statistically significant. In regard to PID, as diagnosed in this study by the 2006 Centers for Disease Control and Prevention diagnostic criteria, women with prior STIs were not more likely to develop PID than those without prior STIs (1.7% compared to 2.4%). The researchers also note that women with prior STIs were not more likely to have the IUD/IUS removed early. The researchers comment that this study “demonstrates a high rate of acceptability and low rate of complications in a cohort of women who would not have been considered ‘good candidates’ for IUD/IUS insertion: one-third of the patients had a history of a STD; one-third of the patients had a history of other gynecological infections, such as bacterial vaginosis; and almost one half of the patients were unmarried.” They then remark that due to these results, “a history of STDs, PID, or participation in nonmonogamous relationships should not be considered exclusion criteria for IUD/IUS.” Limitations of this study include the retrospective chart review format and lack of control over standardized clinical procedure with insertion because use of antibiotics, counseling, or initial follow up time post insertion varied between clinic sites. Also, for the purposes of this paper, there were still factors, such as average age of participants, which was not comparable to adolescents. However, this study did provide information about women with IUD/IUS insertion who are considered as higher STI risk, which is the case for the adolescent population in general (Campbell, Cropsey, & Matthews, 2007).

Another study that may give insight into PID risk in adolescents with IUD use is a double-blind, randomized, prospective study by Luukkanen, Nygren, and Pyorala (1979) involving clinics in Denmark, Finland, and Sweden. The purpose of the study was to determine
the effectiveness and safety of two copper IUDs in a comparison between nulliparous and parous women. Participants gave a medical history, had a pelvic examination prior to IUD insertion, and then were to return for pelvic exams at three months and one year follow up. Of the participants, one-quarter were nulliparous. When complications were stratified by age, the age group under 25 years was found to have the greatest rates of IUD removal due to infection, which was diagnosed by palpation, elevated temperature, increased sedimentation rate, and in some cases, laparoscopy. In regard to parity, nulliparous and primiparous women had the highest rates of removal due to infection. There were very rare instances of infection in women over 25 years of age or those with more than one child. The researchers suggest that since infection rates were equally high in nulliparous and primiparous women, the correlation of pelvic infection is more likely associated with age than parity. They also suggest that the higher rate of removal due to infection in the age group of women less than 25 years old may reflect sexual behaviors in this group. Limitations of this study include lack of description of the screening process in potential participants, lack of a control group, and lack of distinction of STI status at IUD insertion (Luukkainen, Nielsen, Nygren, & Pyorala, 1979).

Shelton (2001) provides evidence of the risk of PID with IUD use in higher STI areas in a calculation of clinical PID risk attributable to an IUD using evidence and data from previous studies in Africa. It was determined that “somewhat high-end assumptions yield an estimate of full clinical PID risk due to IUD use of 0.15%, or less than one in 600,” in a population where prevalence of gonorrhea and Chlamydia is considered high at 10%. “With overall gonorrhea and chlamydia prevalence of 20%, the risk would be 0.3%, but would only be 0.075% for a prevalence of 5%.” The author notes potential problems with the risk estimate in that only symptomatic PID was addressed, “the relation between IUDs and PID might extend beyond
gonorrhea or Chlamydia” to include other gynecological infections, and the studies from which data was taken had high quality of care, therefore may not be able to generalize to other situations. The author also discusses that the studies from which data was taken had short follow up periods, but also notes that the highest risk of PID occurs within the first weeks to months after insertion. It is stated that in the presence of these potential problems, “even if the estimate is off by six-fold, the risk of PID is below 1% in a high STI setting (Shelton, 2001).

A similar model by Stanback and Shelton (2008) using studies in West Africa determined the risk of PID attributable to IUD as 0.075% in a population with an STI rate of 5%. The authors used the same model as the previous study which had the identical potential problems listed previously. They note, however, that “in clinical terms, even with large parameter changes such as a 10-fold increase in STI prevalence from 5% to 50%, the PID risk attributable to the IUD remains less that 1%,” (Stanback & Shelton, 2008).

In addition to these studies, current committee opinions lend their suggestions about intrauterine systems in women in general and the adolescent population more specifically. The American College of Obstetricians and Gynecologists (ACOG) 2005 practice bulletin on the intrauterine device describes contraindications for the method of contraception including PID currently or within the last three months, current sexually transmitted diseases, and purulent cervicitis, among others. Recommendations for appropriate candidates include “nulligravid and multiparous women at low risk of STDs who desire long-term reversible contraception.” It is noted that “contraceptive counseling should include information about risk factors for STDs and PID,” (American College of Obstetricians and Gynecologists, 2005). When considering the adolescent population specifically, the ACOG committee opinion about intrauterine devices and adolescents notes similar contradictions including PID that is current or within the last three
months as well as current STIs or purulent cervicitis. The committee notes that “the IUD is a highly effective method of contraception that is underused in the United States. Because adolescents contribute disproportionately to the epidemic of unintended pregnancy in this country, top tier methods of contraception, including IUDs and implants, should be considered as first-line choices for both nulliparous and parous adolescents,” (American College of Obstetricians and Gynecologists, 2007). The World Health Organization rates the levonorgestrel IUS as a category 2 method of contraception for those between the age of menarche to less than 20 years of age, meaning that “the advantages of using the method generally outweigh the theoretical or proven risks,” (World Health Organization, 2009). For those with current STIs, a category 4 is given for initiation of a LNG-IUS, meaning the use of such a method lends to an unacceptable health risk. A category 2, however, is given for continuation of the method, meaning a woman with a current STI that already has an IUD in place. Evidence states that “there is no evidence regarding whether IUD insertion among women with STIs increases the risk of PID compared with no IUD insertion. Among women who have an IUD inserted, the absolute risk of subsequent PID was low among women with STI at the time of insertion but greater than among women with no STI at the time of IUD insertion,” (World Health Organization, 2009). In regards to increased risk of STIs, the WHO gives a category 2/3 for initiation of LNG-IUS stating that “if a woman has a very high individual likelihood for exposure to gonorrhea or chlamydial infection, the condition is a category 3,” meaning “the theoretic or proven risks usually outweigh the advantages of using the method,” (World Health Organization, 2009). Due to the cautionary STI rates among the adolescent population and risk of infection as well as future fertility concerns, the American Academy of Pediatricians takes a
more conservative approach to adolescents and IUS/IUD use recommending that an IUD be reserved for parous women actively protecting themselves against STIs (Blythe & Diaz, 2007).
Pelvic Inflammatory Disease Discussion

Use of the Mirena LNG-IUS and other IUDs for contraception in the adolescent population has been a topic of controversy and hesitation by health care providers, especially in the United States, for several reasons. One potential reason is the concern of PID risk in IUS and IUD use, especially in the presence of STIs such as Chlamydia and gonorrhea. Considering that current adolescent STI rates are greater than any other age group, and that general adolescent sexual behaviors may increase STI risk, concern is raised that this population may be at increased risk of PID with IUS use. Concern continues in that if left untreated, PID could potentially lead to complications such as tubal infertility. It is this worry that may contribute to clinician hesitation to more widely use the IUS as a method of contraception in the adolescent population.

The problem with investigating such a topic is the lack of information available, both in terms of the amount of research involving the adolescent population as well as the Mirena LNG-IUS, due to the fact that it is a relatively newer contraceptive option. Studies involving mostly copper IUDs as well as those using adult women as participants were available for review. Also, in order to get a sense of understanding about PID risk in adolescent IUD or IUS users, studies involving adult women with similar STI risk factors, and those stratifying results by age had to be utilized. These studies demonstrated an increased, yet still relatively small PID risk with IUD or IUS insertion in women with a current STI compared to those without. This illustrates that the concern for IUS use in the adolescent patient may be warranted due to the higher risk of STIs in adolescents as a population overall. Problems with the data from the studies demonstrating small increased PID risk in IUD or IUS users with STIs at time of insertion is that they provided indirect evidence from older, parous, married or sexually monogamous participants with most
often with no history of STIs or PID. Also, the number of STI and PID cases within these studies was small, due to prior patient screening, therefore potentially underestimating or skewing the PID risk, making it hard to apply when considering IUS use in adolescents, who have higher STI rates and overall risk.

The study determining PID risk in a population considered “high STI risk” involved some participants with similar lifestyle factors that may be comparable to adolescents in terms of higher STI risk such as being unmarried or having a history of STI. This study showed no increased PID risk in women using an IUD with previous STIs compared to those without previous STIs. However, the studies stratifying IUD users by age generated data suggesting that younger users had increased rates of PID and IUD removal due to infection, possibly indicating that the sexual habits and behaviors of that age group in general may be associated.

While it is evident that further study and investigation needs to be completed in the area of IUS use in adolescents, based on the existing, available data reviewed in this paper, this person agrees with the current committee opinions in that the IUS and IUD are viable contraceptive options in a population with high unintended pregnancy rates, such as adolescents. However, it is this person’s opinion that there should be some limitations. Due to the small, yet still increased risk of PID in those with an STI at IUS/IUD insertion, it appears that, as the WHO category rating and ACOG as well as American Academy of Pediatricians committee opinions suggest, IUD/IUS use in adolescents should be reserved for those with low STI risk. This low risk would likely include adolescents with a monogamous sexual partner, strict barrier method use, and no current or history of STIs or other unsafe sexual behaviors. Those considered high risk, such as adolescents with multiple sexual partners, inconsistent barrier method contraceptive use and current or history of STIs or other unsafe sexual behaviors would likely benefit from
other long-term, reversible contraceptive options such as Depo Provera or Implanon. A key informant from Planned Parenthood in Toledo, Ohio states that their current practice denies Mirena LNG-IUSs placement in adolescents due to the overall increased risk of STIs, and thus potential PID. This current practice was contributed to common trends in adolescent sexual behaviors such as multiple partners and inconsistent barrier use.

When determining an adolescent patient’s STI risk and thus potential candidacy for an IUS, it is important to screen for sexual behaviors and practices such as number of sexual partners, both past and current, barrier use, and history of STIs. Also, if possible, it would be of benefit if bacteriological lab tests could be performed prior to IUS insertion to rule out current STIs such as Chlamydia or gonorrhea to even further decrease the potential risk of PID. It may also be beneficial to follow up with the patient soon after IUS insertion, to continue promoting the importance of barrier method use and general safe sex practices, remind of potential signs and symptoms of infection to watch for, and identify any early complications as the greatest risk of PID occurs within the first 20 days of insertion. Whether an adolescent’s STI risk is considered high or low upon screening, it is important for clinicians to provide effective and reasonable, yet safe contraceptive options for those seeking it. For adolescents, this may mean the Mirena LNG-IUS or others which may include Depo Provera or Implanon.
Implanon

Early Discontinuation Literature Review

Available in the United States since 2006, Implanon is a single rod subdermal implant system containing 68 milligrams of etonogestrel, the active metabolite of the progestin desogestrel, which provides contraceptive protection for up to three years. The etonogestrel initially releases at a rate of 60-70 micrograms per day which decreases to 35-45 by the end of the first year of use, 30-40 by the end of year two, and 25-30 by the end of year three. Like other progestin-only contraceptives, Implanon provides pregnancy prevention by suppressing ovulation, altering endometrial thickness, and increasing cervical mucus viscosity (Schering-Plough, 2009). Implanon is similar to the six-rod subdermal implant system Norplant, which contains a total of 216 milligrams of the progestin levonorgestrel, providing up to five years of contraceptive protection. Norplant production was discontinued in the United States in 2002 due to limited component supplies following a recall of implants thought to have contained lower levonorgestrel release levels (U.S. Food and Drug Administration, 2002).

In the adolescent population, concern with the use of Implanon as a form of contraception appears to lie with early termination of use, likely due to adverse effects such as irregular menstrual bleeding patterns. The aim of this analysis is to determine if early discontinuation of Implanon due to adverse effects is a large problem, especially in the adolescent population, and based on conclusions, establish if it is worthwhile contraceptive option in this age group.

The first few studies investigating the efficacy and acceptability of Implanon include adolescents within their participant population. A study by Lewis, Doherty, Hickey, and Skinner (2010) compared the tolerability, bleeding patterns, and incidence of repeat pregnancy in 12-18 year old postpartum mothers using Implanon versus combined oral contraceptive pills (COCP),
DMPA, barrier methods or no form of contraception. The two year study involved 137 adolescent females categorized into groups based on their contraceptive preference. Of the 137, 73 participants chose Implanon with 40 choosing COCP or DMPA and 24 using barriers or no method. Regarding the Implanon users, the most common bleeding patterns included spotting followed by no bleeding, and then irregular bleeding. Participant complaints about Implanon were also recorded and included irregular bleeding followed by spotting. In terms of early discontinuation, 52% of Implanon users had their implant removed by the completion of the two year study with 39% doing so due to abnormal uterine bleeding. When comparing Implanon acceptability and incidence of repeat pregnancy to that of other contraceptive forms, Implanon users continued their method significantly longer than other methods, with a mean duration of 18.7 months compared to 11.9 of the COCP/DMPA users. Of the 48 participants who had conceived by the end of the study, 27% had used Implanon compared to 40% of COCP/DMPA users and 50% of those using barriers or no methods of contraception. It is also noted that the average time until repeat pregnancy was significantly longer in those using Implanon, at 23.8 months compared to 18.1 months for COCP/DMPA users and 17.6 months for barrier methods/no contraception. Limitations to this study include the non-randomization of contraceptive methods as participants were allowed to choose their own method of contraception. It was determined that those choosing Implanon were more likely to be living with the birthfather of their first child, and less likely to be living with their own parents. It is also noted that those participants who were planning a second pregnancy by six weeks postpartum were less likely to have chosen Implanon as their contraceptive method. This likely had an effect on the Implanon’s efficacy and duration of use compared to other contraceptive methods (Lewis, Doherty, Hickey, & Skinner, 2010).
A three-year prospective, longitudinal study by Flores, Balderas, Bonilla, and Vazquez-Estrada (2005) also evaluated efficacy, adverse effects, and continuation rates of Implanon in multiple health centers throughout Mexico. A total of 417 women 15-49 years of age were implanted with Implanon and followed at one week, as well as one, three, and six months at which point a gynecological examination was performed as well as an assessment of side effects and menstrual patterns. Menstrual bleeding patterns were assessed by the WHO recommendations and definitions. Upon analysis, 22.9, 20.3, and 13.7% of participants experienced amenorrhea over years one, two, and three, respectively, whereas prolonged bleeding occurred in 19.7, 18.9, and 15.8%. Additionally, 4.9, 5.3, and 3.7% noted infrequent bleeding while 2.9, 0.8, and 0.8 experienced frequent bleeding in years one, two, and three, respectively. The researchers report that 44% of all participants noted side effects at three months post Implanon insertion which decreased to 16.5% of participants by 36 months. In terms of continuation, 78.2% had Implanon in place at 12 months whereas 66.7% and 61.4% were still continuing the method at 24 and 36 months, respectively. Of those who discontinued before the completion of the study, 21.1% did so due to menstrual disturbances, with prolonged bleeding making up more than half and amenorrhea accounting for 29%. Other reasons for discontinuation included the desire to become pregnant (8.1%), missed follow-up visits (4.6%), headache (2.8%), weight gain (2.6%), and mood changes (1.5%). Of the women who continued Implanon throughout the full study and attended the three month follow up visit, 62.2% chose to continue contraceptive use, with one-quarter of these opting to have a second Implanon inserted. Limitations to this study include the lack of any comparison group. Also, while adolescents were included within this study, results were not stratified by age, therefore it cannot be
determined if discontinuation rates or reasons for discontinuation varied in any way based on age (Flores, Balderas, Bonilla, & Vazquez-Estrada, 2005).

In a three year study by Agrawal and Robinson (2005) involving a family planning and reproductive health care center in Luton, United Kingdom, the demographic profile of Implanon users was identified along with continuation rates and reasons for removal. Of a population of 106 women age 15-43 years having an Implanon placed, 20 participants were lost to follow up. Considering the remaining 86 participants, 60 (69.8%) had the implant in place at the end of one year whereas 38 (44.1%) had it in place at the end of two years. At the end of three years, 26 subjects (30.2%) were still using Implanon. Of these 26, 16 women had the implant replaced with a second. Regarding early implant removal, bleeding irregularity was the most common cause which accounted for 40%. Other reasons for removal included planning for pregnancy (15%), mood changes (10%), weight gain (10%), no longer needing contraception (6.7%), and amenorrhea (3.3%). Limitations to this study include the small subject population, as well as the large loss to followup at nearly 20%. This study also lacked a comparison group of any kind. Additionally, continuation rates in this study were much lower than that of others to which the researchers contribute the fact that this study involved a real-life clinical setting, whereas the comparable studies involve actual clinical trials (Agrawal & Robinson, 2005).

A year-long Australian study by Weisberg and Fraser (2005) also investigated the experiences and acceptability of Implanon. A total of 651 women 15-50 years of age were implanted with an Implanon and then asked to fill out a self-administered questionnaire immediately after insertion and then at three and six months as well as one year. Questionnaire information included bleeding patterns, side effects, removal time and reason for removal. Upon analysis of the data, 68% chose Implanon due to its convenience, 67% for long duration, 59%
liked that there was “nothing to remember,” and 50% for its high efficacy. In terms of bleeding patterns, amenorrhea and infrequent bleeding were the most common patterns experienced while frequent and prolonged bleeding were less common. Other side effects included mood swings (10%), increased acne (7%), decreased libido (4%), weight gain (3%), and breast tenderness (3%). Regarding early removal, 164 of 475 questionnaire responders had the implant removed before the end of the one year study. Of these, 41 were within the first three months, 48 between months three and six, and 75 between six months and one year. The most common cause of early removal was unwanted side effects at 88%, with the majority being bleeding disturbances. The researchers note that younger participants better tolerated the varied bleeding patterns than older subjects, and as a whole, waited longer before bleeding-related implant removal.

Limitations to this study include the lack of comparison group and low survey response rate following Implanon insertion, which totaled only 58% at one year. Also, due to the self-administered questionnaire method of the study, responses regarding side effects, bleeding patterns and reasons for removal were subjective and self-reported (Weisberg & Fraser, 2005).

A retrospective, clinic-based chart review by Thamkhantho, Jivasak-Apimas, Angsuwathana, Chiravacharadej, and Intawong (2008) at the Siriraj Family Planning Clinic in Bangkok evaluated the demographic profile of Implanon users. Menstrual effects, discontinuation rates and reasons for removal were also investigated throughout the one year period. A total of 163 women between 14 and 40 years of age had an Implanon inserted. Of these participants, 20% were 19 years old or younger while 70% were between 20 and 34 years of age. Regarding menstrual patterns, 40.4% of the 89 women who attended the one year follow up visit reported a regular menstrual cycle. This was defined as having had bleeding for a few days each month. Moreover, 30.5% reported an irregular cycle, considered as normal menses for
a few months followed by amenorrhea, while 23.6% noted “no cycle,” and 5.6% reported prolonged bleeding between 10-15 days each month. During the first year of Implanon use, a total of 58 complaints occurred from 89 participants. Of these complaints, 20 were of prolonged bleeding and 9 of amenorrhea. Others included vertigo (11), weight loss (2), weight gain (2), and dysmenorrhea (8). One woman was reported to have the device removed due to pain, leaving 88 women or 54% continuation rate for the first year. Limitations to this study include the small population and poor one year follow up. Other limitations include the self-reported menstrual diary which few participants completed and returned at the end of their Implanon duration making it difficult to accurately analyze and report bleeding patterns. Additionally, the study notes only one actual implant removal. For those who did not attend the one year follow up, it cannot be determined whether or not they discontinued the method, making actual assessment of discontinuation rates impossible (Thamkhantho, Jivasak-Apimas, Angsuwathana, Chiravacharadej, & Intawong, 2008).

An additional retrospective chart review by Smith and Reuter (2002) aimed to assess the rates and factors associated with early Implanon removal at three community contraception and sexual health services in the United Kingdom. A total of 190 charts were reviewed on women 13-51 years of age who had been fitted with Implanon at one of the three clinics. Of the 190 participants, 105 answered questions about their reasoning for choosing Implanon of which 22% were happy past Norplant users, 20% wanted a method with no personal intervention, and 13% wished for a long-term method. Other reasons included effectiveness, friend recommendation, and need for a hidden method. Regarding continuation rates, at six months, 97 subjects had their implant in place while 22 had it removed, leaving 71 participants with an unknown status. This created a six month continuation rate of 88% assuming none of the 71 unknown status
participants had their implant removed. Survival analysis estimated a continuation rate of 84%. Of those with their implant in place at six months, 40 participants had their implants in place at one year while 21 had it removed, leaving 34 unaccounted for. Assuming none of the participants with an unknown status had their implant removed, the one year continuation rate was calculated as 78%, whereas survival analysis determined a rate of 67%. By the end of the study, a known total 43 implants had been removed. The main reason for discontinuation was bleeding problems at 34% followed by mood swings (24%), headaches (17%), weight gain (12%), and wish to become pregnant (10%). Analysis of removal rates according to participant age revealed an 8% decrease in risk of removal for every year increase in age, demonstrating that younger users were more likely to have their implants removed at an earlier time when compared to older users. Limitations for this study include the retrospective chart review design, lack of comparison group and small population size which included a large number of participants unaccounted for. This large loss to follow up may have had an effect on continuation rates (Smith & Reuter, 2002).

The previously reviewed studies involved adolescents within their subject populations, however, these are few in number, therefore studies involving only adult women may provide additional information about early discontinuation of Implanon and reasons for removal. One such study includes that by Yildizbas, Sahin, Kolusari, Zeteroglu, and Kamaci (2007) in Turkey involving 41 women 18-40 years of age which aimed to assess side effects following Implanon insertion. Follow up visits occurred at three and six months post-insertion at which point side effects were reported. Also, participants were asked to keep a menstrual diary throughout the duration of the study. Before implant insertion, all 41 participants reported a normal menstrual cycle whereas only three participants (7.3%) considered their cycle as normal at the end of six
month study. The most common bleeding patterns included amenorrhea (34.1%) and prolonged bleeding (29.3%) followed by irregular bleeding (17.9%) and frequent bleeding (7.3%) with infrequent bleeding being the least common pattern (4.9%). Other reported side effects included headaches, dizziness, nausea, depression, acne, and breast pain, with all but headache increasing significantly after six months post-insertion. Concerning discontinuation, 8 of 41 women removed their implant before the completion of the study, accounting for 19.58% of subjects. The most common reason for early removal was abnormal bleeding patterns, occurring in six women, whereas depression and weight gain each accounted for one discontinuation. Limitations to this study include the very small participant population as well as the extremely short study duration (Yildizbas, Sahin, Kolusari, Zeteroglu, & Kamaci, 2007).

An additional four year study by Kiriwat, Patanayindee, Koetsawang, Korver and Bennink (1998) took place at two hospitals in Bangkok, Thailand and was performed to determine the efficacy and acceptability of Implanon in 100 women 18-40 years of age. Upon implant insertion, participants were instructed to keep a daily menstrual bleeding diary which was then assessed by the WHO recommendations of analysis. Upon examination of bleeding patterns, it is noted that bleeding and spotting occurred more often and for longer duration during the first 90 day reference period, which reduced to 10 bleeding days among two bleeding-spotting episodes per reference period for the remainder of the study. Amenorrhea was initially reported as 29-39% of participants, but decreased to 20% and finally 10% throughout the course of the study. Infrequent bleeding took the opposite trend beginning between 24-38% and increasing to 39-56%. Frequent bleeding was rare at less than 7%, whereas prolonged bleeding ranged from 7-15% throughout the study. Other adverse effects included headache (7%), dizziness (6%), weight gain (4%), breast pain (4%), and acne (3%). Regarding early
discontinuation, 24% did so before the end of the study, of which 7% of participants attributed it to abnormal bleeding patterns. Of these, frequent bleeding, amenorrhea, and spotting each accounted for 1%. In addition, 5% discontinued due to other adverse effects. The remaining 12% discontinued due to other reasons such as wanting to become pregnant. Discontinuation rates were calculated to be 13.4, 25.3, and 28.0% at years two, three, and four, respectively. Limitations to this study include the small participant population and the lack of a comparison group of any sort (Kiriwat, Patanayindee, Koetsawang, Korver, & Bennink, 1998).

A similar, non-comparative, multicenter study in China was performed by Zheng, Zheng, Qian, Sang, and Kaper (1999). The study duration was two years with an option additional two year extension and involved 200 women 20-35 years of age. Following insertion, participants were instructed to keep a daily menstrual bleeding diary which was then assessed by WHO recommendation guidelines. After analysis of collected data, it was determined that the median number of bleeding-spotting days was 18-21 with a median of two bleeding-spotting episodes per 90 day reference period for the first two years and three bleeding-spotting episodes per 90 day reference period for the third and fourth years. Prolonged bleeding decreased from 69 to 26% by the end of the study, while amenorrhea ranged from 9-15% within the first two years followed by 2-8% during the subsequent two years. Frequent bleeding occurred in less than 5% of the participants while infrequent bleeding varied from 4-13%. Other adverse effects included headache, mood swings, acne, abdominal pain, and weight gain among others. Regarding early discontinuation, 26 women (13%) discontinued Implanon during the first two years. Half of those who discontinued did so due to bleeding. Three women discontinued due to amenorrhea, eight due to medical reasons and two women no longer needed contraception. Specifically regarding discontinuation attributed to bleeding, 8% of total study participants did so by year
two, 12% by year three, and 13% by year four. Cumulative continuation rates were 87, 79, and 74% at two, three, and four years, respectively. Limitations to this study include the small participant population and lack of comparison group (Zheng, Zheng, Qian, Sang, & Kaper, 1999).

A systematic review of 11 clinical trials by Blumenthal, Gemzell-Danielsson, and Marinthcheva-Petrova (2008) also determined safety and tolerability of Implanon. A total of 942 women 18-40 years of age participated in the 11 trials, of which all but one of the trials were of two years duration. With each trial, participants were required visit the clinic every three months throughout the duration of the trial to document adverse events. Upon analysis of the data, the most common side effects experienced were headaches occurring in 24.7% of subjects, vaginitis (14.4%), weight gain (13.4%), acne (13.1%), and breast pain (12.8%). Less frequently reported effects included emotional lability (5.7%), abdominal pain (5.2%), and decreased libido (2.3%).

Regarding adverse effects, 56 subjects reported 77 effects categorized as “serious” including gastrointestinal disorders, ovarian cysts, teratomas, asthma, fever, and headaches. In terms of discontinuation, 308 of the 942 participants (32.7%) had the implant removed before the end of the study. The most common reasons for discontinuation were combined adverse events (13.9%) including emotional lability, weight, acne, headache, and depression. Bleeding irregularities accounted for 10.4% of early discontinuations. It is noted that discontinuations due to adverse effects and bleeding irregularities decrease from two years and onward while plan for pregnancy became a main reason for removal during year three. Cumulative discontinuation rates were calculated for be 18.0, 30.3, and 36.4% for years one, two, and three, respectively. Limitations to this systematic review include the lack of investigation and assessment of bleeding irregularities as an adverse event, but rather was only included in discontinuation analysis. Also
the studies did not involve any comparison groups (Blumenthal, Gemzell-Danielsson, & Marintcheva-Petrova, 2008).

A three year Irish study by Riney, O'Shea, and Forde (2009) also investigated the acceptability and adverse effects of Implanon. A total of 75 women age 18–43 years were fitted with Implanon and then administered a telephone questionnaire at completion of the study. Of all participants, 53% experienced at least one adverse effect including local irritation of the implant site (17%), weight gain (8%), emotional effects (8%), dysmenorrhea (4%), and headaches (3%). By the end of the study, 21 subjects (28%) had Implanon removed and of these, 29% did so due to irregular bleeding, while 19% of removals were due to mood disorder such as irritability or low mood, and 14% due to weight gain. It is noted that younger participants appeared to tolerate abnormal bleeding patterns longer than older subjects before discontinuation. Of the 54 subjects who continued Implanon for the entire study, 55% had the implant replaced with a second, while 45% did not. Also noted in the study was the amount counseling participants received before implant insertion with 56% reporting being very well advised, 33% well advised, and 9% moderately advised. There was no analysis, however, of correlation between amount of counseling and method discontinuation. Other limitations include the small subject population as well as the lack of investigation and assessment of bleeding irregularities as an adverse event, but rather only included in discontinuation analysis. Also the study did not involve any comparison groups (Riney, O'Shea, & Forde, 2009).

All of the studies investigated thus far recognize irregular bleeding as a common side effect and one of the most frequent reasons for early discontinuation among users. Two studies investigate further by focusing specifically on uterine bleeding patterns in Implanon use. One study by Affandi (1998) involved an integrated analysis of 13 trials, which included six
noncomparative studies and seven comparing Implanon to Norplant. A total of 1716 women were fitted with Implanon compared to 689 Norplant users 18-40 years of age throughout Europe, North and South American and Southeast Asia. Follow up occurred over two years during which menstrual patterns were analyzed based on a 90 day reference period by the definitions and recommendations of the WHO. Bleeding pattern data was evaluated by comparing the patterns of those who completed the full two year study to those who discontinued the method early. This was to eliminate any bias in patterns between study discontinuers and completers. Among Implanon users, discontinuers were reported to have nearly twice as many bleeding and bleeding-spotting days than study completers, while frequent and prolonged bleeding-spotting was three times as prevalent. It was also found that amenorrhea was five times more common in the study completers. When comparing Implanon to Norplant, it was noted that Implanon users had significantly less bleeding-spotting days and bleeding-spotting episodes. Also, Implanon users were significantly more likely to have amenorrhea than Norplant users at 17.9-24.8% versus 2.0-7.0%, respectively. Implanon users, however, had higher incidences of infrequent, frequent, and prolonged bleeding, though not significantly. Those studies involving a third year noted that amenorrhea declined from an average of 13% during the first two years to 8.9% during year three, and frequent bleeding declined from 3.6% to 1.4%. Infrequent and prolonged bleeding trends did not seem to change. The researchers also noted that while individual bleeding patterns were not predictable, shifts from one bleeding pattern to another within an individual subject was rare. Regarding discontinuation, the researchers reported significant differences between Europe and Canada compared to Southeast Asia and Chile. The average discontinuation rate due to bleeding irregularities was 23% for Europe and Canada compared to 1.8% in Southeast Asia and Chile. The most common bleeding pattern leading to
discontinuation was frequent, irregular bleeding accounting for more than half of bleeding-related discontinuations at 13% in Europe/Canada. Prolonged bleeding accounted for 3.8% and 0.5% of discontinuations in Europe/Canada and Southeast Asia/Chile, respectively. Heavy flow accounted for 0.4 and 0.2%, spotting for 3.7 and 0.4%, and other bleeding patterns for 0.3 and 0.0% in Europe/Canada and Southeast Asia/Chile, respectively. Amenorrhea, while very prevalent, was rarely a reason for discontinuation at 1.8 and 0.3% (Affandi, 1998).

An additional study by Mansour, Korver, Marintcheva-Petrova, and Fraser (2008) investigated Implanon’s effects on bleeding patterns in an integrated analysis of 11 clinical trials. The trials were performed in the United States, Thailand, Singapore, Austria, Germany, Finland, Hungary, the Netherlands, Russia, and Malaysia, with most including at least two years of follow up. A total of 923 women 18-40 years of age were asked to complete daily menstrual bleeding diaries and attend follow up appointments every three months. Bleeding patterns were analyzed and defined by the WHO recommendations. Overall, infrequent bleeding and amenorrhea occurred in 33.6% and 22.2% of subjects, respectively. Prolonged bleeding was reported in 17.7% of participants while frequent bleeding was less prevent, found in 6.7% of subjects. Like the previous study, the data from early discontinuers and study completers were also evaluated separately to eliminate bias and effects on discontinuation rates. Those who discontinued before study completion had more bleeding-spotting days per 90 day reference period than study completers. Also, amenorrhea was rare, whereas frequent and prolonged bleeding was much more significant in discontinuers. By the end of the trials, 32.9% of the subjects discontinued Implanon, of which 11.3% did so because of bleeding pattern irregularities. Amenorrhea and heavy menstrual flow was responsible for little discontinuation at 0.8 and 0.9%, respectively. Prolonged and frequent, irregular bleeding accounted for a great amount of discontinuation at 3.4
and 4.2%, respectively. Like the previous study, location of the trial affected discontinuation rates due to bleeding with 13.1% reported in the United States, 13.6% in Europe/Chile, and 5.1% in Southeast Asia. It is also noted that discontinuation rates were highest during the first year following Implanon insertion and then decreased thereafter (Mansour, Korver, Marintcheva-Petrova, & Fraser, 2008).

The WHO provides a category 1 rating for levonorgestrel and etonogestrel implants in all women including those from menarche to less than 18 years of age meaning that no restriction is placed on use of the contraceptive (World Health Organization, 2009).
**Early Discontinuation Discussion**

Adverse effects and interrupted menstrual bleeding patterns are common with Implanon use, as with other progestin-only contraceptives. These adverse effects include headaches, weight gain, mood lability, acne, and dysmenorrhea, among others, while bleeding irregularities range from amenorrhea and infrequent bleeding to frequent and prolonged bleeding. It is evident from analysis of the previous studies that these effects are often a complaint of Implanon users and may lead to early method discontinuation. The most common reason for early implant removal is attributed to bleeding pattern irregularities in a majority of studies. Bleeding-related trends that appeared during this analysis of Implanon studies include the idea that some bleeding patterns are considered more favorable to patients than others. In a majority of studies, amenorrhea and infrequent bleeding were more prevalent in study participants than other bleeding irregularities, however, accounted for far less early bleeding-related discontinuations. On the other hand, frequent and prolonged bleeding were far less common than other bleeding patterns, but often accounted for a much larger percentage of bleeding-related implant removals. This suggests that patterns such as amenorrhea and infrequent bleeding are considered far more acceptable for Implanon users as a whole than frequent and prolonged bleeding patterns.

Another visible trend in most studies was that discontinuations due to bleeding patterns as well as other adverse effects occurred at higher rates at the beginning of use, such as within the first year, than later on during the studies. An additional trend that presented itself in several studies is that the type of bleeding disturbance is unpredictable in the individual Implanon user and that pattern may vary in severity throughout method continuation, however, varying between different patterns is rare for an individual to experience.
Few studies analyzed bleeding-related discontinuations with age as a variable, but those which did revealed conflicting results. One study noted a greater likelihood of early bleeding-related implant removal with younger participant age, even reporting an 8% smaller rate of discontinuation for each year older in subject age. Two other studies, however, noted that younger Implanon users were more likely to tolerate interrupted menstrual bleeding patterns for greater periods of time before opting for method discontinuations than older women. Because there were so few studies analyzing age as a factor in early Implanon removal, it would take much more research to determine if age actually has an influence on toleration of adverse effects as well as method discontinuation. This is important because it points out that health care providers should not automatically assume that adolescents will discontinue Implanon early merely because of age, and therefore not consider it as a viable contraception option for this age group.

Whatever the case may be, the purpose of this analysis was to determine if early discontinuation of Implanon due to adverse effects is a large problem, especially in the adolescent population, and to determine if this method is worth its use in this age group. Upon review of the data, early discontinuation due to adverse effects, particularly menstrual bleeding-related problems, is a rather considerable problem in Implanon users, including the adolescent population. Problems with early termination of the method, especially in adolescents, include the risk of unwanted pregnancy and potential misuse of resources due to the initial high cost of Implanon. However, it is this person’s opinion that this method is still of very beneficial use in this age group as it provides long-term, user-independent pregnancy protection.

One subject discussed in a large majority of studies previously analyzed is the need for pre-insertion and continued patient counseling throughout method use. Recommendations for
Implanon user counseling include describing the advantages and limitations of the method and determining the potential user’s motivation for two to three years of contraceptive protection. Other recommendations include providing a thorough discussion about possible adverse events, especially bleeding pattern disturbances and unpredictability which can include amenorrhea and infrequent bleeding which are more tolerable, as well as frequent and prolonged bleeding which more often lead to discontinuation. Providing education about the potential for adverse effects, and understanding the individual patient’s acceptance and tolerability of such effects, especially those which are menstrual bleeding related, will aid the provider in determining if Implanon is a proper contraceptive option. This increased knowledge may lead to more realistic expectations of the method possibly leading to longer method continuation and decreased likelihood of monetary waste and early discontinuation which could potentially lead to unwanted pregnancy, as well as the physical, emotional, and social aspects that accompany it.
Questions Clinicians Should Consider

The following are questions that clinicians should seek answers for when considering long-term, reversible, progestogenic contraception for the adolescent patient. These questions, while not all pertaining specifically to this clinical review, were compiled during reading and researching throughout this review process and may provide benefit for clinicians.

- Is she currently sexually active?
- Number of sexual partners in the past and currently?
- Does she engage in high-risk sexual behaviors (unprotected sex, multiple sexual partners)?
- History of STI and current status?
- For what time period is contraceptive protection desired?
  - Months? Years?
- Previously used contraceptive methods if any?
  - Dissatisfaction with previous contraceptive methods/reason for discontinuation?
- Is she currently pregnant?
- Parous or nulliparous?
  - If parous, what is parity number?
  - Currently breastfeeding?
- Any current medical conditions?
  - Sickle-cell anemia
  - Anorexia/eating disorders
  - Thromboembolic disorders
  - History of or current breast cancer
  - Seizures
  - Increased fracture risk
- Any gynecological problems?
  - Menorrhagia
  - Dysmenorrhea
  - Anatomical uterine abnormalities
- Willing to have a pelvic exam?
- Using any current medications?
- Race/ethnicity?
- Alcohol or tobacco use?
- Does she intake sufficient levels of calcium/vitamin D?
- Does she prefer contraceptive method to be hidden/invisible to others?
- What is her financial/insurance situation?
- Able to afford the high initial cost of Mirena or Implanon?
- Willing to undergo injections?
- Able/willing to return every three months for another DMPA injection?
- Body habitus/weight status/BMI?
- Willing to tolerate potential weight gain in exchange for pregnancy protection?
- Willing to regularly check IUS/IUD threads for placement?
- Able to tolerate side effects such as changes in menstrual bleeding patterns?
Conclusion

The aim of this clinical review was to evaluate the validity of common hesitations and concerns that arise with use of long-term, reversible, progestogenic contraceptives such as Depo Provera, Mirena, and Implanon in the adolescent population. In the United States especially, it is often thought that these types of contraceptive methods are underutilized in adolescents as concluded by such professional organizations as the American College of Obstetricians and Gynecologists (American College of Obstetricians and Gynecologists, 2007). The underutilization of these methods may in large part be due to clinician and patient hesitations regarding potential complications and side effects of method use. The most common of these include the potential risk of weight gain and decreased bone mineral density with Depo Provera use, the possible increased expulsion rate and risk of pelvic inflammatory disease with Mirena, and the concern of early discontinuation of Implanon due to intolerability of adverse effects such as irregular menstrual bleeding. Review of relevant clinical articles and committee opinions determined that while clinician and patient concerns are valid to some extent, they do not warrant the underutilization of such methods in the adolescent population.

Regarding Depo Provera, review of the current literature and research confirms decreased bone mineral density with method use. Decrease is found to occur throughout entire duration of use with highest rates occurring within the first one to two years. It is understandable that this would cause clinicians concern of future fracture risk and osteoporosis later in life. Reviewed studies propose, however, that bone mineral density is partially if not fully recovered after method discontinuation, thus suggesting little if any increased future risk of osteoporosis or fracture. Research also determined some validation of the concern of weight gain with Depo Provera use. Evidence shows significant weight increases in Depo Provera users compared with
non-users with baseline obesity appearing to be a risk factor for increased weight gain with method use. Additionally, early weight gain with use was found to be a significant risk factor for continued weight gain throughout method duration. It was determined, however, that more research is needed to establish if other factors such as race are associated with increased risk of weight gain with Depo Provera contraception. While weight gain is a valid concern with Depo Provera, it should not deter clinicians from using it for contraception in the adolescent patient. Knowledge of risk factors can aid in the increased vigilance in following weight changes as well as the promotion of good diet and exercise habits for the Depo Provera user.

Regarding Mirena, a review of the current literature and research suggests that younger age and nulligravidity/nulliparity may be associated with slightly increased, though still very small rates of expulsion, likely due to smaller uterine sizes compared to older, parous users. While expulsion rates may be slightly increased, this should not cause clinicians hesitation for use in adolescents regardless of parity. In terms of potential increased risk of pelvic inflammatory disease, evidence shows that increased risk due to IUS/IUD use is limited to the first 20 days post-insertion. PID risk appears to be more associated with current STI upon IUS/IUD insertion than the actual device itself. It is of current committee opinion that while the increased risk is still small, those with higher risk of STIs, which may include adolescent patients, should be encouraged to avoid Mirena or other IUDs and rather use a different form of contraception. While Mirena is not contraindicated in adolescents, it should be reserved for those who are considered low risk for STIs such as individuals who have no history of STIs and are actively protecting themselves by the strict use of barrier methods and safe sex practices.

Concerning Implanon, early discontinuation due to side effects, especially irregular menstrual bleeding, is a valid concern for clinicians when considering use in the adolescent
population. Early discontinuation of the method lends to a poor use of health resources and causes the clinician and adolescent patient to find themselves in a repeat scenario of evaluation for the proper contraceptive option. This could also lead to lapses of time when the adolescent is not using a form of contraception, thus risking unwanted pregnancy with its stigma and multifactorial complications. While early discontinuation is a concern, it should not prevent clinicians from prescribing Implanon in the adolescent patient who appears to be a good candidate. What seems to remain important is adequate patient education regarding the potential side effect profile of Implanon, an understanding of a patient’s acceptance and tolerance of such problems, and proper follow up of the patient to track the presence and severity of these issues. For the Implanon patient experiencing side effects such as interrupted or irregular menstrual bleeding, providing information and assurance about side effect trends including the decrease in incidence with longer duration of the method may aid in preventing early discontinuation and thus decrease the potential situations where an adolescent may not be using contraception and thus be more at risk for unplanned pregnancy.

As stated several times previously, research involving long-term, reversible, progestogenic methods of contraception use in adolescents is sparse, and thus was supplemented with studies involving adult women and involving similar and off-the-market contraceptive methods such as Norplant and copper IUDs. While more adolescent-focused research is needed, current information and literature allows for common hesitations to at least be initially evaluated and to provide aid to clinicians when considering these methods in the adolescent population. As with research for any topic, often more questions arise than may be answered, and opinion may change as new information is added over time. However, based on the examination and evaluation of available literature, research studies, and committee opinions through this clinical
review, long-term, reversible, progestogenic contraceptives such as Depo Provera, Mirena, and Implanon should be considered viable methods of pregnancy prevention in the adolescent population. As with any form of contraceptive, there may be exceptions in individual adolescent patients where these methods may not be ideal, such as Mirena use in those with high STI risk. In general, however, Depo Provera, Mirena, and Implanon should be considered safe, reliable, and acceptable contraception for adolescents.

As with any medical setting or situation, it is important to consider the individual adolescent patient being evaluated for proper contraception options. Important information to consider includes the length of time contraception is needed, acceptance and tolerance of side effects, number of sexual partners, high risk sexual behaviors, use of prior contraception methods and reasons for discontinuation if applicable. It is also essential to determine what the adolescent patient is looking for in a contraceptive method including efficacy, ease of use, and amount of personal responsibility such as daily or intercourse dependent use. Other pertinent questions for clinicians to ask and consider are presented earlier in this clinical review and can be used as a tool when prescribing contraception for adolescents. It is this information that will aid the clinician in selecting the proper contraception option in the individual adolescent patient. Those looking for efficacious, intercourse independent methods requiring little user responsibility would likely benefit from a long-term, reversible, progestogenic contraceptive such as Depo Provera, Mirena and Implanon, and should be strongly considered in such patients.
References


Abstract

Objective: To provide analysis of risks and benefits of long-term, reversible, progestogenic contraceptive use in adolescents in order to address clinician hesitations in prescribing.

Methods: Articles were found using PubMed and Science/Social Science Citation Index databases along with reference lists of pertinent studies and review articles.

Results: Over eighty committee opinions, systematic reviews, and original research articles were utilized including cross-sectional and longitudinal studies, surveys and questionnaires. Depo Provera may cause weight gain, especially in obese adolescents. It also transiently decreases bone mineral density during use. Mirena does not demonstrate significantly higher expulsion rates in adolescent or nulliparous users and increased risk of pelvic inflammatory disease is more associated with existing STI upon insertion than actual Mirena use. Implanon side effects, especially irregular menstrual bleeding, may lead to early method discontinuation.

Conclusion: While some hesitations have validity, overall, long-term, reversible, progestogenic contraceptives are viable options for adolescents seeking contraceptive management.