Contraception: Hormonal contraceptive vaginal rings

Authors: Jennifer Kerns, MD, MPH, Philip D Darney, MD, MSc
Section Editor: Courtney A Schreiber, MD, MPH
Deputy Editor: Kristen Eckler, MD, FACOG

All topics are updated as new evidence becomes available and our peer review process is complete.

Literature review current through: Apr 2021. | **This topic last updated:** Aug 10, 2020.

INTRODUCTION

Combined (estrogen-progestin) hormonal contraception is available as an oral pill (ie, oral contraceptive or OC), transdermal patch, or vaginal ring and is highly effective when used consistently and correctly. Commonly available combined hormonal contraceptive rings include the etonogestrel/ethinyl estradiol ring (ENG/EE, commercial name NuvaRing, EluRyng) and the segesterone acetate/ethinyl estradiol ring (SA/EE, commercial name Annovera). The hormonal contraceptive vaginal rings offer the same benefits as the other estrogen-progestin combined methods but have the advantage that daily or weekly user compliance is not required. This topic will review the indications, contraindications, side effects, and use of hormonal contraceptive vaginal rings.

Related content on contraceptive counseling and method selection and estrogen-progestin combined contraceptives is presented separately:

- (See "Contraception: Counseling and selection".)
- (See "Combined estrogen-progestin contraception: Side effects and health concerns".)

DESCRIPTION AND STRUCTURE

Etonogestrel and ethinyl estradiol ring — The etonogestrel/ethinyl estradiol (ENG/EE, commercial names NuvaRing, EluRyng) ring is a flexible device measuring 54 mm in diameter and 4 mm in cross-section that is worn vaginally for three weeks and then removed (and discarded) for one week (picture 1) [1]. The outer ring is composed of both ethinyl estradiol (EE) and an

ethylene vinyl acetate copolymer that contains crystals of ENG, the 3-keto-metabolite of desogestrel. The device releases an average of 120 mcg/day of ENG and 15 mcg/day of EE over 21 days of use [1,2]. The device is latex-free.

There is an immediate increase in serum hormonal concentration after insertion with a slow decrease over the cycle [3]. The concentration of EE is lower with the ENG/EE vaginal ring compared with other combined hormonal contraceptives:

- In one study, the maximum serum concentration of EE was 30 percent lower than desogestrel-containing oral contraceptives (OCs; 34.7±17.5 ng/L versus 124.9±46.3 ng/L) and systemic exposure to EE was half that of desogestrel-containing OCs [2].

- In a randomized trial comparing a levonorgestrel-containing OC, transdermal patch, and ENG/EE vaginal ring, users of the ENG/EE vaginal ring experienced 3.4 times lower EE exposure than patch users and 2.1 times lower EE exposure than OC users [3]. Exposure to EE in the ENG ring, OC, and patch groups were 10.6±2.5 ng-h/mL, 21.9±2.9 ng-h/mL, and 35.8±5.5 ng-h/mL, respectively. These differences were not all proportional to differences in EE dose of the three contraceptives: 30 mcg/day for the OC, 20 mcg/day for the patch, and 15 mcg/day for the ENG ring.

Unlike OCs where the peak concentration of the progestin occurs daily, the ENG/EE vaginal ring reaches its peak ENG concentration once per cycle, within seven days of insertion. Systemic exposure to ENG (as determined by area-under-the-curve) is similar for the ENG vaginal ring and desogestrel-containing OCs [2].

Segesterone and ethinyl estradiol ring — The one-year reusable segesterone acetate/ethinyl estradiol (SA/EE, commercial name Annovera) ring is 56 mm in overall diameter and 8.4 mm in cross-sectional diameter [4]. The ring is worn for three weeks and removed for one week, and that pattern is repeated for a total of 13 cycles. This pattern of use results in regular withdrawal bleeding and an overall pooled unintended pregnancy rate (Pearl index) of 2.98 per 100 woman-years. The ring contains two internal channels: one channel with both SA and EE and the other channel with SA only. The device releases approximately 150 mcg/day of SA and 13 mcg/day of EE over the 21-day use period. The inactive ingredients include silicone elastomers, titanium dioxide, dibutyltin dilaurate, and silicone medical adhesive. The device is latex-free. The median T_{max} of both hormones is approximately 2 hours after vaginal insertion; concentrations become more constant approximately 96 hours after insertion. Other product advantages include that it does not require refrigeration for storage and that it is not orally active, which may appeal to lactating women. This one-year ring is approved by the US Food and Drug Administration and available for use.

CANDIDATES AND SPECIAL POPULATIONS

Candidates — Women who desire highly effective, reversible, noncoitally dependent contraception and who have no contraindications to taking estrogen or progestins are candidates for the vaginal ring. The United States Centers of Disease Control and Prevention (CDC) and the World Health Organization have published medical eligibility criteria for women with various medical conditions and personal characteristics who desire an estrogen-progestin contraceptive. The combined hormonal rings provide the same benefits of combined oral contraceptive (OC) pills, including contraception, regulation of bleeding, endometrial protection, and, in some women, reduction of dysmenorrhea and endometriosis-related pain. In addition, the ring is a good option for women who want the benefits of combined OCs but prefer to avoid a method that requires daily user compliance [5,6].

The noncontraceptive benefits, risks, and side effects of combined estrogen-progestin contraceptives are reviewed in detail separately:

- (See "Combined estrogen-progestin oral contraceptives: Patient selection, counseling, and use".)
- (See "Combined estrogen-progestin contraception: Side effects and health concerns".)

Contraindications — Women who should not use combined estrogen-progestin contraceptives, including vaginal contraceptive rings, include those with [1,4]:

- A high risk of arterial or venous thromboembolic disease, including women over age 35 who smoke
- Estrogen- or progestin-sensitive cancer, including breast cancer
- Liver tumors or disease, particularly with abnormal liver function tests
- Undiagnosed or abnormal uterine bleeding
- Likely or confirmed pregnancy
- Hepatitis C who are taking drug combinations containing ombitasvir/paritaprevir/ritonavir, with or without dasabuvir

Use in special populations — Information regarding estrogen-progestin contraceptive use in women with specific medical issues can be found through the United States Centers of Disease Control and Prevention (CDC) and the World Health Organization. Commonly encountered distinct populations include:

- **Adolescents** – Vaginal contraceptive rings are a good option for adolescents [7]. Use of a vaginal ring can be more private than OCs and the transdermal patch. Compared with the depot medroxyprogesterone acetate injection, another contraceptive method that is popular with adolescents, vaginal rings offer the benefits of a combined hormonal method: shorter, lighter, and less painful periods, no association with weight gain, and no adverse effect on bone mineral density. Contraception selection for adolescents is discussed in detail separately. (See "Contraception: Issues specific to adolescents".)

- **Obese women** – Theoretically, contraceptive efficacy of combined hormonal contraceptives may be lower in obese women. (See "Contraception: Counseling for females with obesity", section on 'Contraceptive ring'.)

  Data on use of the hormonal contraceptive rings in women with body mass index (BMI) ≥30 are sparse as the initial etonogestrel/ethinyl estradiol (ENG/EE) clinical trials did not include such women and the segesterone acetate/ethinyl estradiol (SA/EE) trials excluded this subpopulation after two women with BMI >29 developed venous thromboembolisms [1,4]. Thus, it is not known if the contraceptive efficacy of the hormonal rings is reduced in women with BMI ≥30. However, preliminary data do not indicate any increased risk or decreased efficacy.

  There are limited data on efficacy or venous thromboembolism risk in obese women who use contraceptive rings. Most studies of obese women assess the impact of combined oral hormonal contraception [8,9]. The United States Centers of Disease Control and Prevention (CDC) lists all combined estrogen-progestin contraceptives as Group 2 (advantages generally outweigh theoretical or proven risks) for obese women but does not provide subgroup recommendations by type of combined contraceptive or obesity class.

  More information on contraceptive selection for obese women can be found elsewhere. (See "Contraception: Counseling for females with obesity".)

- **Postpartum and lactating women** – Nonlactating postpartum women with no other contraindications to combined estrogen-progestin contraceptives can use the contraceptive vaginal ring, although initiation is delayed until 21 days postpartum or more to reduce the risk of thromboembolic events [10,11]. Although there are conflicting data on the impact of combined hormonal contraception on lactation, lactating women are generally advised to delay contraceptive vaginal ring insertion until 30 days postpartum. (See "Postpartum contraception: Counseling and methods".)

- **Postabortion** – For women with no other contraindications, combined hormonal contraceptives, including the contraceptive vaginal ring, can be started after first- or second-

trimester abortions [10,11]. While the ENG/EE and SA/EE manufacturers advise women who undergo second-trimester abortion to wait four weeks before initiating the contraceptive vaginal ring (because of increased risk of venous thromboembolism), the CDC supports initiating combined hormonal contraception within seven days of the procedure, including the same day [1,4,11]. (See "Contraception: Postabortion".)

- **Perimenopause** – Women over age 35 can use contraceptive vaginal rings, if they do not have additional risk factors for cardiovascular or thromboembolic disease (eg, hypertension, diabetes, dyslipidemia, and obesity) [4].

COUNSELING POINTS

In addition to discussing the contraceptive benefits with patients, we discuss the efficacy, side effects, potential complications, and noncontraceptive benefits below.

Efficacy — Combined hormone vaginal contraceptive rings are highly effective at preventing pregnancy when used consistently and correctly (figure 1). For the etonogestrel/ethinyl estradiol (ENG/EE) ring, the failure rate, defined as the number of pregnancies per 100 woman-years of exposure in the first year of use, is equivalent to that of oral contraceptives (OCs) and the patch (0.3 percent for perfect use and 9 percent for typical use) (table 1) [12,13]. For the segesterone acetate/ethinyl estradiol (SA/EE) ring, the unintended pregnancy rate is nearly 3 per 100 woman-years based on pooled data from over 2000 women including over 17,400 cycles [4]. Ovulation also appears to be suppressed with off-label five- and six-week ring use [14-16]. Typical use effectiveness is lower than that for methods that are less user-dependent (eg, intrauterine contraception and implants).

Studies specific to each ring type include:

- For the ENG/EE ring:
  - In a noncomparative study of 2322 women from Europe and North America, the efficacy of the ENG/EE vaginal ring was 99.1 percent [6]. Over half of the pregnancies (11/21) were attributable to compliance problems. North American women experienced more pregnancies than European women, perhaps because a greater percentage of North American women were new contraceptive users instead of switching from another method (59 versus 38 percent), and more North American women reported that they removed the ring during intercourse.
  - A randomized trial in college students found that those assigned to the ENG/EE vaginal ring reported more perfect use in the first two months compared with OC users, but

differences were not statistically significant in the third month [17].

- For the SA/EE ring, in a multicenter study that included over 2200 women, the unintended pregnancy rate was 2.98 (95% CI 2.13-4.06) per 100 women-years [18]. The ring was more than 97.5 percent effective in Kaplan-Meier analysis. More than one-half of the women completed up to 13 cycles. Of the 290 women followed after ring discontinuation, all had resumption of menses, or pregnancy as desired, within six months.

For both ring types, the principle mechanism of contraceptive action is inhibition of ovulation [4,14,15,19]. Other contributory mechanisms include thickening of cervical mucus, which prevents penetration of sperm into the upper genital tract, inhibition of sperm capacitation, and slowing of tubal motility [20]. (See "Combined estrogen-progestin oral contraceptives: Patient selection, counseling, and use", section on 'Mechanisms of action'.)

Side effects

- **Systemic** – Systemic side effects from the vaginal rings are generally similar to those of combined estrogen-progestin OCs [21-25]. Breast tenderness and nausea (estrogen-related side effects) are reported less often by vaginal ring users than OC users, a finding that is consistent across three trials comparing the varying ethinyl estradiol (EE) doses and different progestins [21-23]. No differences in headache [21-23] or weight gain [24,26,27] are seen across studies comparing ring users with OC users. Ring use is not associated with clinically significant metabolic effects (eg, changes in blood pressure, blood chemistries, lipid levels, carbohydrate metabolism, thyroid function, hematological indices) [20]. (See "Combined estrogen-progestin contraception: Side effects and health concerns".)

- **Local** – Ring users report more vaginitis, vaginal wetness, and leukorrhea compared with OC users [13,21,23-25]. In a meta-analysis of trials comparing contraceptive the ENG/EE vaginal ring with various estrogen-progestin contraceptive pills, the odds of vaginitis were approximately 2.5 times more likely (odds ratios [OR] 2.48 to 2.84) and the odds of leukorrhea were three to six times as likely (OR 3.21 to 6.42) for women using the contraceptive ring [13]. These symptoms did not result in discontinuation of the ring. Additionally, these symptoms do not require treatment.

  Although the contraceptive ring appears to alter vaginal discharge, contraceptive ring users to not appear to have an increased risk of acquiring vaginal or cervical infections, including human immunodeficiency virus and human papilloma virus, although supporting data are partly derived from studies of OCs and other vaginal rings [28-33].

- **Unscheduled bleeding** – The vaginal ring provides cycle control equivalent or superior to

OCs and the transdermal patch [24,34,35]. Compared with an extended cycle regimen of contraceptive pills, the traditional 28-day ENG/EE ring cycle has a lower number of unscheduled bleeding days but a higher total number of bleeding/spotting days. A study of women using a continuous or 364-day ring cycle reported a median of zero bleeding days and 10 spotting days during the first three months of extended use; by comparison, for women using a 28-day ring cycle, the median number of bleeding and spotting days was 7.5 and 8, respectively [36]. Acceptability of continuous use is high, even with unscheduled bleeding [36-38]. For women who are bothered by this bleeding but otherwise benefit from continuous use, instituting a four-day ring-free period can improve their symptoms [37]. (See "Evaluation and management of unscheduled bleeding in women using contraception", section on 'Estrogen-progestin contraceptives'.)

- **Mood** – Data on the impact of combined estrogen-progestin OCs, which are often used as a proxy for the estrogen-progestin vaginal rings, on mood disorders are conflicting [39-42]. Specific to the ENG/EE vaginal ring, a trial of 188 women comparing depressive symptoms in women using the contraceptive ring or a levonorgestrel-containing OC pill reported no differences in depressive symptoms for ring users at cycles 6 (OR 0.31, 95% CI 0.08-1.19) and 12 (OR 0.23, 95% CI 0.05-1.03) [13]. A different trial of 201 women initiating either the ENG/EE vaginal ring or a triphasic norgestimate-containing OC reported that ring users were more likely to report no change in mood while OC users were more likely to report worsening mood [22]. Given that the data do not support an association between mood and use of the contraceptive vaginal ring, universal counseling is not necessary. For patients who are concerned about mood changes, providers should use a patient-centered approach and counsel that mood could improve, decline, or stay the same after initiating use.

- **Bone mineral density** – There is no evidence that the rings have an adverse effect on bone mineral density, although data are limited. One randomized trial compared markers of bone formation and resorption as well as bone mineral density between ENG/EE ring users, patch users, and controls and reported no differences by method or compared with controls [43].

Serious complications — The combined hormonal vaginal rings carry the same risks as other combined hormonal methods. There are limited data specifically about the rings, and recommendations regarding safety come mostly from studies of OCs. The United States Centers for Disease Control and Prevention's Medical Eligibility Criteria for Contraceptive Use is a useful guide for evaluating the safety of contraceptive methods, including vaginal rings, for particular patients.

Cardiovascular and thromboembolic events — Use of combined hormonal (estrogen-progestin) contraceptives (CHCs), including pills, patch, and rings, increases the risk of

thromboembolic events over that of nonusers [1,4]. For comparison, the risk of having a venous thrombotic event (VTE), per 10,000 women, is 1 to 5 for non-CHC users and 3 to 12 for CHC users. However, the VTE risk does not appear to be higher for ring users compared with users of other combined estrogen-progestin OCs. Similar to combined OCs, cases of stroke, both arterial and venous, thrombotic and hemorrhagic, as well as myocardial infarction have been reported in contraceptive ring users [44-47].

Examples of representative studies for the ENG/EE ring include:

- A 15-year Danish historical cohort study evaluated data from national registries to determine the risk of arterial events, thrombotic stroke, and myocardial infarction in users and nonusers of hormonal contraception [44]. The cohort included the entire population of Danish women, aged 15 to 49 years, for the period 1995 through 2009. During over 38,000 person-years of ENG/EE contraceptive vaginal ring use, more thrombotic strokes occurred in users than nonusers (31.4 versus 24.2 per 100,000 person years) for an adjusted relative risk of 2.5 (95% CI 1.41-4.41). The number of myocardial infarctions in ENG/EE ring users was too low to provide reliable estimates of relative risk.

- A 2013 multicenter analysis from the United States and several European sites compared venous and arterial thromboembolism risk among new users of the ENG/EE ring and new users of combined OCs [48]. In this study, which included over 66,000 woman-years of contraceptive use, ring users were not at greater risk of VTE or arterial thromboembolism than users of combined OCs containing a variety of progestins and low dose EE (VTE incidence for ring and OC users: 8.3 and 9.2 per 10,000 women-years, respectively; arterial thromboembolism 2.2 and 2.8 per 10,000 woman-years, respectively).

- A 2013 cohort study of over 570,000 United States women initiating combined hormonal contraception reported no increase in venous or arterial thrombotic events among women initiating the ENG/EE contraceptive ring compared with women initiating one of four low-dose comparator combined OCs (relative hazard total mortality for ATE and VTE 0.96, 95% CI 0.29-3.14) [49].

- A 2017 systematic review of three studies comparing ENG/EE ring users with users of combined OCs containing levonorgestrel noted mixed outcomes; one cohort study reported an elevated rate ratio for VTE, while a case-control and different cohort study reported no difference in VTE risk [50].

The relative and absolute cardiovascular and thromboembolic risks of combined estrogen-progestin OC, including the impact of differing estrogen doses and progestin types, is reviewed in detail separately.

- (See "Combined estrogen-progestin contraception: Side effects and health concerns", section on 'Cardiovascular effects'.)

Toxic shock — Rare cases of toxic shock syndrome have been reported in ENG/EE contraceptive ring users [20]. No cases of toxic shock syndrome occurred during the clinical trials for the SA/EE ring [4]. Causation has not been proven and may have been related to concurrent tampon use. (See "Staphylococcal toxic shock syndrome" and "Invasive group A streptococcal infection and toxic shock syndrome: Epidemiology, clinical manifestations, and diagnosis".)

Noncontraceptive benefits — Estrogen-progestin contraceptives, including vaginal rings, have several noncontraceptive benefits (table 2). Details specific to the vaginal ring include:

- **Cycle control and bleeding reduction** – While cycle control is a benefit of all combined hormonal contraceptive methods, vaginal rings provide cycle control that is at least equivalent, and possibly superior, to OCs and the transdermal patch based on studies of the ENG/EE ring [24,34,35]. Several studies have reported that ENG/EE ring users are less likely than users of monophasic or triphasic OCs to experience breakthrough bleeding, especially in the first few months of use [23-25,35,51,52]. Prolonged or frequent bleeding [35] and early or late withdrawal bleeding [23] are also less likely among ring users. There were no differences in bleeding patterns between those starting or those switching to the ENG/EE ring [53]. An improvement in cycle control has also been demonstrated among women who switch from OC or transdermal patch to the ENG/EE vaginal ring [54].

  In addition, contraceptive ring users have reductions in bleeding volume and duration similar to that of OC users. A trial comparing the ENG/EE contraceptive ring with oral norethisterone in 95 women with idiopathic heavy menstrual bleeding reported a 2/3 reduction in bleeding volume and three day reduction in bleeding duration after three cycles of use [55].

- **Reduction of endometriosis pain** – The contraceptive ring appears to reduce endometriosis-related pain. A cohort study comparing the ENG/EE vaginal ring with the transdermal patch for treatment of persistent endometriosis pain reported that both treatments reduced dysmenorrhea [34]. Ring users were more satisfied with their treatment than patch users (72 versus 48 percent). (See "Endometriosis: Treatment of pelvic pain", section on 'Estrogen-progestin contraceptives'.)

- **Less impact on insulin resistance** – Woman at risk for, or diagnosed with, insulin resistance may benefit from the contraceptive ring compared with OCs. One prospective observational study comparing the contraceptive ring users with estrogen-progestin OC users reported the ring had no impact on insulin resistance while OC use increased insulin levels [56].

- **Improved psychosexual function** – Although there are conflicting data on the impact of the contraceptive ring on sexual function, the overall body of evidence suggests improved sexual functioning [23,57-59].

Acceptability

- **Satisfaction** – Most women find the vaginal ring a highly acceptable form of contraception because it is easy to use, remains effective if removal or reinsertion are not performed precisely on time, results in low systemic hormone levels, and is rapidly effective and reversible.

  Studies of the ENG/EE ring have reported high satisfaction rates (84 to 96 percent) and high likelihood of recommending the method to a friend (87 to 98 percent) [6,53,54]. Women like the method's ease of use, once-a-month administration, and low dose of hormones (vaginal hormone delivery increases bioavailability) [21,60]. Less than 3 percent of women report ring expulsion, feeling the ring, or coital problems [53]. Vaginal ring users are as satisfied, or more satisfied, than OC users [21,22]. Satisfaction with the SA/EE ring is similar to that of the ENG/EE ring.

- **Continuation** – Discontinuation of combined hormonal contraceptive methods is common. Studies of the ENG/EE ring reported that 28 to 35 percent of women discontinued the vaginal ring before one year, and most discontinuations occurred in the first three to four cycles. Although side effects are the most commonly reported reason for discontinuing a contraceptive method, they only accounted for 11 to 30 percent of the discontinuation among ENG/EE ring users [6,21,52-54,61].

  While one trial reported that ring users overall were less likely to discontinue the method than OC users (12 versus 22 percent) [23], another trial reported no difference in discontinuation rate by method [17]. A trial including 201 women comparing the vaginal ring with a norgestimate-containing OC reported that among women using the "quick start" method, ring users were less likely to discontinue than OC users (11 versus 16 percent) [22].

  As with all hormonal contraceptives, providing or prescribing up to a one-year supply of contraception enhances convenience and continuation of the method.

- **Adherence** – Adherence with the vaginal ring is similar to that with OCs. Women in ENG/EE clinical trials report adherence with recommended use of the vaginal ring (three weeks in, one week out) in approximately 80 to 90 percent of cycles [21,52]. Many women report altering use of the vaginal ring by prolonging the ring-free period (more than seven days) [6,51,53] and extending use up to five weeks to regulate their cycles [60]. For both the ENG/EE

and SA/EE rings, cultural factors may play a role, as one study showed that North American women were slightly less likely (80 versus 91 percent) than European women to use the ring as instructed (eg, failing to replace it within three hours after removal) [6].

ADMINISTRATION AND USE

Health screening and pregnancy exclusion — Ideally, blood pressure should be measured before initiation of combined hormonal contraceptives; physical examination and laboratory tests are not necessary [11]. However, in settings where access to health care is limited, it is reasonable to initiate use of the ring without blood pressure documentation. (See "Combined estrogen-progestin oral contraceptives: Patient selection, counseling, and use", section on 'Screening requirements'.)

Similar to oral contraceptives, contraceptive rings can be started anytime during the cycle once pregnancy has been reasonably excluded (table 3). The patient can start the medication on the same-day she is seen or delay start to the onset of the next menstrual period (algorithm 1). If the date of last menses was more than 7 days prior (etonogestrel/ethinyl estradiol [ENG/EE] ring), more than 5 days prior (segesterone acetate/ethinyl estradiol [SA/EE] ring) or is uncertain, we advise the patient to use a back-up method of contraception (eg, male or female condom) for the first seven days of ring use. Of note, the ENG/EE manufacturer advises using a back-up method if the ring is inserted any time other than the first day of menses [62], while the United States Centers for Disease Control and Prevention (CDC) recommends back-up if it is inserted >5 days from the beginning of menstrual bleeding [11]. However, there is some evidence that ring insertion initiated as many as 10 days after the beginning of the last menstrual period does not compromise ovulation inhibition [15].

Insertion and use — The vaginal ring requires a prescription, but does not need to be fitted. Both the ENG/EE and SA/EE rings are available in one size and are self-administered (picture 1). For women using a different contraceptive method, the approach to starting to the contraceptive ring is presented in the table (table 4).

- **Insertion** – To insert, the woman should choose a comfortable position (figure 2). The sides of the ring are pressed together, and then it is inserted into the vagina as high as possible for comfort and to prevent it from falling out (figure 3). The position of the ring does not affect contraceptive efficacy.

- **Duration of use and removal** – Both the ENG/EE and SA/EE rings are left in place for three weeks and then removed for a single ring-free week to allow withdrawal bleeding [1]. Women using the ENG/EE ring discard the ring. Women using the SA/EE ring remove it, wash it with

mild soap and water, dry it with a clean cloth, and store the ring in its case [4]. As the SA/EE ring is used repeatedly for thirteen total cycles, the manufacturer advises writing the initiation and anticipated discard dates on the case so the product is not used longer than intended.

During the three weeks of use, women should periodically check to ensure the ring is in place, although the optimal timing or frequency is not known [63]. To begin a new cycle for either ring type, a new ring should be inserted on the same day of the week that the old ring was removed the previous week (ie, if the ring was removed on a Monday, a new ring should be inserted on the following Monday). The ring should not be removed during intercourse.

- **In event of delayed removal** – If the ring has been in place more than 3 but ≤5 weeks, it is removed, and a new one is inserted after a one-week ring-free interval. Alternately, the patients can immediately insert a new ring without using a one-week ring-free interval, although she may have breakthrough bleeding (see the menstrual suppression bullet below). If the ring has been in place for >5 weeks, the old ring is removed, a new ring is inserted, **and** back-up contraception (eg, male or female condom) is advised until the new ring has been in place for seven days. The ring contains sufficient steroids to maintain stable blood hormone concentrations for a five-week period of time [15]. Thus, inhibition of ovulation is sufficiently maintained if a woman forgets to remove the ring after the usual three-week use period.

- **In event of delayed insertion** – The US Selected Practice Recommendations for Contraceptive Use provides an algorithm for counseling patients who delay insertion or reinsertion of the ring (algorithm 2) [11]. For women who have delayed insertion of a new ring or reinsertion of a current ring for less than 48 hours, they should reinsert the ring immediately and remove it at the regularly scheduled time. No additional contraception is required. Women who have delayed ring insertion or reinsertion for 48 hours or more should also immediately insert the ring as soon as possible **and** use a second method of contraception, such as condoms.

- **Continuous use for menstrual suppression** – Data supporting continuous ring use for menstrual suppression come from studies of the ENG/EE ring. Women who desire fewer days of withdrawal bleeding and are willing to tolerate some spotting can safely use an extended ring regimen whereby the prior ENG/EE ring is removed and a new ring is immediately inserted every three weeks, which omits the hormone-free week and resultant withdrawal bleeding for up to one year [36,38,64-66]. Extended use is effective and does not worsen bothersome side effects, except for unscheduled bleeding [36,38].

  Data supporting continuous use of the SA/EE ring are not yet available, but continuous use (ie, no time break between yearly ring removal and replacement) is clinically reasonable. As

with the ENG/EE ring, patients are counseled about possible increase in unscheduled bleeding. (See 'Side effects' above.)

- **Broken ring** – Rarely, the contraceptive ring may break at the weld joint [1]. Although the break does not impact the contraceptive effectiveness, it may make the ring more likely to slip out, which will reduce efficacy. In the event of a broken ring, the broken ring should be removed and new ring inserted.

Reinsertion after unintended removal or expulsion — Unplanned removal (eg, with removing a tampon) or expulsion (eg, during a bowel movement) of the contraceptive ring can occur. If it accidentally falls out, it may be rinsed with cool or warm (not hot) water and reinserted into the vagina. Instructions for reinsertion timing and need for back-up contraception vary by ring type.

- **For the ENG/EE ring** – If the ENG/EE ring is out of the vagina for less than three hours, no additional steps are needed [1]. If the ring remains out for more than three consecutive hours, subsequent steps depend on the week of the cycle that the ring is out [67]:

  - During the first two weeks of the cycle, the ring is reinserted as soon as possible [1]. Pregnancy may not be prevented if the ring is out for more than three hours during this time, so an additional form of contraception, such as condoms with spermicide, is used until the reinserted ring has been in place for seven continuous days. The ring should subsequently be removed according to the original schedule, after which the woman can expect to have her normal period.

  - During week 3 of the cycle, the woman discards the ring [1]. She then chooses one of two different restart options:

    - Option one – Insert a new ring and begin a new three-week cycle. Back-up contraception or abstinence is recommended until the new ring has been used continuously for seven days. The woman may not have a regular period until she reaches her next ring-free week, but she may have vaginal spotting or bleeding prior to that point.

    - Option two – This option is only used if the prior ring was in place for seven consecutive days. Leave the ring out for up to seven days. During this ring-free time the woman may have her period. By day seven, insert a new ring and begin a new cycle. Back-up contraception or abstinence is recommended until the new ring has been used continuously for seven days.

  In contrast to the above approach, the CDC takes a more liberal stance and states that back-up contraception is not needed if reinsertion of the current ring occurs in less than 48 hours (

algorithm 2) [11]. There is evidence that ovulation is inhibited when the ring has been in place for only three days [14]; however, there are no data about actual failure rates after only three days of use, so a back-up method is recommended for one week.

If the ring has been out of the vagina for an unknown amount of time, then pregnancy should be excluded prior to reinsertion of the ring (table 3) [63].

- **For the SA/EE ring** – If the SA/EE ring is expelled or removed for up to two hours, the ring is reinserted after being washed with mild soap and water and dried [4]. No additional contraception is needed. If the SA/EE ring is out of the vagina for two continuous hours or more, or more than two cumulative hours (multiple episodes that add up to two hours), then the ring is cleaned and reinserted, and back-up contraception (eg, male condoms) is used for an additional seven consecutive days.

Follow-up — A routine follow-up examination is unnecessary, but blood pressure should be checked yearly, if possible. The woman should contact her provider if she has concerns about the method, wants to discontinue contraception or switch to another method, or has changes in health status that might affect the appropriateness of use of an estrogen-progestin contraceptive [11].

Return of fertility — Most women resume ovulation and regular menstrual cycles within a month after stopping contraceptive rings [1]. A study of 45 women using the ENG/EE contraceptive ring reported that, after removal of the vaginal ring, the median time to ovulation was 19 days and earliest ovulation occurred after 13 days [68]. In the initial trials of the SA/EE ring, all 290 women who desired pregnancy or switched to a nonhormonal method resumed menses within six months of discontinuation [4]. Women who desire pregnancy can attempt to conceive whenever they are ready to do so.

Use with other vaginal devices and products — The contraceptive ring can interfere with other female barrier contraceptives [63,69]. For example, the diaphragm, cervical cap, or female condom should be not be used as back-up contraception with the contraceptive rings [1]. Tampons may be used during menses as they do not impact hormone absorption from the rings, which are typically not in place during the time frame of vaginal bleeding [1]. Water-based vaginal lubricants and spermicides are compatible with the combined contraceptive rings, but oil-based products (including silicone-based lubricants) are not [1,4].

DRUG INTERACTIONS

Systemic medications — Combined hormonal vaginal rings can interact with other systemic

medications to both increase and decrease each other's levels. Much of the available information is based upon combined oral contraceptive (OC) pills. (See "Combined estrogen-progestin oral contraceptives: Patient selection, counseling, and use", section on 'Drug interactions'.)

- **Reduced estrogen/progestin levels** – Information on medication interactions that may reduce contraceptive ring estrogen and progestin levels is mostly based on studies of OC pills. Drugs that increase liver microsomal enzyme activity may decrease systemic exposure to the estrogen and progestins in contraceptive vaginal rings, and thus potentially decrease contraceptive efficacy. Such medications include aprepitant, barbiturates, bosentan, carbamazepine, efavirenz, felbamate, griseofulvin, oxcarbazepine, phenytoin, rifampin, rifabutin, rufinamide, topiramate, and products containing St. John's wort [1,4]. In addition, reduced systemic estrogen and progestin levels have been noted with the HIV protease inhibitors nelfinavir, ritonavir, darunavir/ritonavir, (fos)amprenavir/ritonavir, lopinavir/ritonavir, and tipranavir/ritonavir as well as the Hepatitis C protease inhibitors boceprevir and telaprevir. The non-nucleoside reverse transcriptase inhibitor nevirapine may also reduce systemic hormone levels. We advise women who require these medications to use an additional form of contraception (ie, backup contraception such as male condoms) or consider an alternate contraceptive method. (See "Contraception: Counseling and selection".)

- **Altered levels of other medications** – Combined hormonal contraceptives (CHCs) can decrease plasma lamotrigine levels [10,11]. Women who require both medications are advised to have their lamotrigine levels monitored. CHCs are also avoided in women using Hepatitis C medications ombitasvir/paritaprevir/ritonavir, with or without dasabuvir, due to potential for ALT elevations [1].

- **Use with emergency contraception** – The additional use of combined estrogen-progestin emergency contraception is not advised during segesterone acetate/ethinyl estradiol (SA/EE) ring use (eg, in event of ring expulsion for >2 hours) [4] Guidance for the etonogestrel/ethinyl estradiol (ENG/EE) ring is not available. Both the SA/EE and ENG/EE rings can be started after emergency contraception is used. (See "Emergency contraception".)

Use with vaginal medications — Water-based vaginal drugs, such as for the treatment of vaginal candidiasis or bacterial vaginosis, are compatible with the vaginal contraceptive rings [1,4]. However, the oil-based miconazole suppositories have been associated with increased hormone levels [1,4]. Thus, particularly for women using the SA/EE ring, only water-based or oral therapies are advised.

NEW DEVELOPMENTS IN VAGINAL RINGS

- **Nestorone and ethinyl estradiol combined hormonal vaginal ring** – The Population Council is studying vaginal rings containing estrogen (ethinyl estradiol [EE] or 17-beta-estradiol [E2]) and Nestorone (NES), a potent 19-nor-testosterone derivative that is not orally active, but is an effective contraceptive when administered via implants, transdermal systems, and rings [70-73]. NES does not bind to androgen or estrogen receptors and thus can potentially minimize some hormone-related side effects, such as acne. Three studies of long-acting (13 cycles) rings containing NES/EE reported efficacy and acceptability similar to other short-acting contraceptives [71-73]. As EE induces production of hepatic proteins and clotting factors [74], an E2/NES ring was created with the goal of providing a novel contraceptive method that did not appear to increase thrombogenic risk (based on studies in postmenopausal women) [73].

- **Progesterone-releasing vaginal ring** – The Progering is a progesterone-releasing vaginal ring for nursing women. It is available in parts of South America and Africa [75]. Each ring releases 10 mg of progesterone daily and lasts for four months [75,76], although it is approved for only three months of use. A ring that releases a synthetic progestin (Nesterone) is under development.

  Progesterone-only rings function primarily by thickening cervical mucus to prevent sperm penetration but also inhibit ovulation and endometrial receptivity. Progesterone-only rings may be less effective over the long-term than rings containing both a progestin and an estrogen but are still highly effective among breastfeeding women since breastfeeding provides some protection from pregnancy [77]. Unscheduled bleeding, which is a common side effect of all progestin-only methods, is less likely to occur in breastfeeding women because of prolonged lactational amenorrhea [78].

  The progesterone vaginal ring contains 22.5 percent progesterone dispersed in silicone. The system delivers 10 mg/day of the physiological hormone progesterone, but due to its homogeneous design, serum levels decline during its three-month duration of use [79]. A Phase 3 trial demonstrated that it has high contraceptive efficacy (98.5 percent) and safety [79]. Despite its effectiveness and application for lactating women, the progesterone vaginal ring has not yet become popular [80].

RESOURCES FOR PATIENTS AND CLINICIANS

- bedsider.org – A free website developed by the National Campaign to Prevent Teen and Unplanned Pregnancy, a private nonprofit group.

- CHOICE Project – A free website sponsored by the Washington University School of Medicine

in St. Louis that provides resources on contraceptive options and training resources for clinicians.

- Center for Young Women's Health – A free website run by Boston Children's Hospital that addresses reproductive health needs of teens and young adults.
- SexualityandU.ca – An educational site run by the Society of Obstetricians and Gynaecologists of Canada that includes descriptions of various methods and a tool to help with selection of birth control.
- Planned Parenthood – A nonprofit organization dedicated to reproductive health with resources for patients and clinicians.
- ACOG Contraceptive FAQs – American College of Obstetricians and Gynecologists addresses frequently asked questions (FAQs) about contraception.
- United States Medical Eligibility Criteria for Contraceptive Use
- United States Selected Practice Recommendations for Contraceptive Use
- World Health Organization Medical Eligibility Criteria for Contraceptive Use

SOCIETY GUIDELINE LINKS

Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "Society guideline links: Contraception".)

INFORMATION FOR PATIENTS

UpToDate offers two types of patient education materials, "The Basics" and "Beyond the Basics." The Basics patient education pieces are written in plain language, at the 5th to 6th grade reading level, and they answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials. Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are written at the 10th to 12th grade reading level and are best for patients who want in-depth information and are comfortable with some medical jargon.

Here are the patient education articles that are relevant to this topic. We encourage you to print or e-mail these topics to your patients. (You can also locate patient education articles on a variety of subjects by searching on "patient info" and the keyword(s) of interest.)

- Basics topic (see "Patient education: Hormonal birth control (The Basics)")
- Beyond the Basics topic (see "Patient education: Hormonal methods of birth control (Beyond the Basics)")

SUMMARY AND RECOMMENDATIONS

- There are two contraceptive vaginal rings. The first consists of an outer ring composed of ethinyl estradiol (EE) and an ethylene vinyl acetate copolymer that contains crystals of etonogestrel (ENG), a metabolite of desogestrel (commercial names NuvaRing or EluRyng). The second vaginal ring contains segesterone acetate/ethinyl estradiol (SA/EE) and provides contraception for one year (commercial name Annovera). (See 'Description and structure' above.)
- Vaginal rings are a highly effective method of contraception when used consistently and correctly (figure 1). The failure rate, defined as the number of pregnancies per 100 woman-years of exposure in the first year of use, is equivalent to that of oral contraceptives (OCs) and the patch (0.3 percent for perfect use and 9 percent for typical use). The unintended pregnancy rate for the SA/EE ring appears to be closer to 3 percent. (See 'Efficacy' above.)
- Appropriate candidates for vaginal ring contraception are women desiring contraception with no contraindications to estrogen or progestin therapy. The Centers of Disease Control and Prevention and the World Health Organization have published medical eligibility criteria for women with various medical conditions and personal characteristics who desire an estrogen-progestin contraceptive. (See 'Candidates and special populations' above.)
- Systemic side effects from the vaginal rings are generally similar to those of combined estrogen-progestin OCs. In contrast to OC users, ring users report more local (vaginal) symptoms, including vaginitis, wetness, and leukorrhea. However, these symptoms do not require treatment and generally do not result in ring discontinuation. (See 'Side effects' above.)
- While the risk of cardiovascular and thrombotic events is increased in ring users compared with nonusers of combined hormonal contraception, the risk does not appear to be higher compared with users of other combined OCs. (See 'Cardiovascular and thromboembolic events' above.)
- Prior to starting the contraceptive vaginal ring, blood pressure should be measured and pregnancy should be excluded. Physical examination and laboratory tests are not necessary. (See 'Health screening and pregnancy exclusion' above.)

- The vaginal ring requires a prescription, but does not need to be fitted. Both rings are available in one size and is self-administered. (See 'Administration and use' above.)
    - For the ENG/EE ring, the ring is left in place for three weeks and then removed and discarded. No ring is in place for a single ring-free week. To begin a new cycle, a new ring is inserted on the same day of the week that the old ring was removed the previous week (ie, if the ring was removed on a Monday, a new ring should be inserted on the following Monday). The ring does not need to be removed during sexual intercourse, but may be removed for up to three hours without affecting contraceptive efficacy. (See 'Insertion and use' above.)
    - For the SA/EE ring, the ring is also worn for three weeks and then removed for one ring-free week. However, the ring is not discarded but is washed and stored in its case for reinsertion for the next cycle [4]. As the SA/EE ring is used repeatedly for thirteen total cycles, the manufacturer advises writing the initiation and anticipated discard dates on the case so the product is not used longer than intended. (See 'Insertion and use' above.)
- Unplanned removal or expulsion of the contraceptive ring can occur. If it accidentally falls out, it may be rinsed with cool or warm (not hot) water and reinserted into the vagina. Subsequent steps, including need for back-up contraception, depend on the number of hours without the ring and the week of the cycle (for the ENG/EE ring only). (See 'Reinsertion after unintended removal or expulsion' above.)
- Fertility returns within approximately one month after discontinuing the ring. (See 'Return of fertility' above.)
- The contraceptive ring can interfere with other female barrier contraceptives (ie, diaphragm, cervical cap, and female condom) but not most vaginal medications. One exception is that the SA/EE ring should not be used with oil-based vaginal products or medications. Tampons may be used during menses as they do not impact absorption of hormones from the ring. (See 'Use with other vaginal devices and products' above.)

REFERENCES

1. Nuvaring [package insert]. Whitehouse Station, NJ. Merck and Co, Inc. 2001-2018. http://www.merck.com/product/usa/pi_circulars/n/nuvaring/nuvaring_pi.pdf (Accessed on May 17, 2018).
2. Timmer CJ, Mulders TM. Pharmacokinetics of etonogestrel and ethinylestradiol released from a combined contraceptive vaginal ring. Clin Pharmacokinet 2000; 39:233.

3. van den Heuvel MW, van Bragt AJ, Alnabawy AK, Kaptein MC. Comparison of ethinylestradiol pharmacokinetics in three hormonal contraceptive formulations: the vaginal ring, the transdermal patch and an oral contraceptive. Contraception 2005; 72:168.
4. Annovera [package insert]. New York, NY. Manufactured for Population Council. August 2018. www.accessdata.fda.gov/drugsatfda_docs/label/2018/209627s000lbl.pdf (Accessed on August 13, 2018).
5. Hatcher R, Trussell J, Stewart F. Contraceptive Technology, 18th ed, Ardent Media, Inc, New Yo rk 2004.
6. Dieben TO, Roumen FJ, Apter D. Efficacy, cycle control, and user acceptability of a novel combined contraceptive vaginal ring. Obstet Gynecol 2002; 100:585.
7. Gupta N, Corrado S, Goldstein M. Hormonal contraception for the adolescent. Pediatr Rev 2008; 29:386.
8. Horton LG, Simmons KB, Curtis KM. Combined hormonal contraceptive use among obese women and risk for cardiovascular events: A systematic review. Contraception 2016; 94:590.
9. Dragoman M, Curtis KM, Gaffield ME. Combined hormonal contraceptive use among women with known dyslipidemias: a systematic review of critical safety outcomes. Contraception 2016; 94:280.
10. Curtis KM, Tepper NK, Jatlaoui TC, et al. U.S. Medical Eligibility Criteria for Contraceptive Use, 2016. MMWR Recomm Rep 2016; 65:1.
11. Curtis KM, Jatlaoui TC, Tepper NK, et al. U.S. Selected Practice Recommendations for Contraceptive Use, 2016. MMWR Recomm Rep 2016; 65:1.
12. Trussell J. Contraceptive failure in the United States. Contraception 2011; 83:397.
13. Lopez LM, Grimes DA, Gallo MF, et al. Skin patch and vaginal ring versus combined oral contraceptives for contraception. Cochrane Database Syst Rev 2013; :CD003552.
14. Killick S. Complete and robust ovulation inhibition with NuvaRing. Eur J Contracept Reprod Health Care 2002; 7 Suppl 2:13.
15. Mulders TM, Dieben TO. Use of the novel combined contraceptive vaginal ring NuvaRing for ovulation inhibition. Fertil Steril 2001; 75:865.
16. Dragoman M, Petrie K, Torgal A, et al. Contraceptive vaginal ring effectiveness is maintained during 6 weeks of use: a prospective study of normal BMI and obese women. Contraception 2013; 87:432.
17. Gilliam ML, Neustadt A, Kozloski M, et al. Adherence and acceptability of the contraceptive ring compared with the pill among students: a randomized controlled trial. Obstet Gynecol 2010; 115:503.

18. Archer DF, Merkatz RB, Bahamondes L, et al. Efficacy of the 1-year (13-cycle) segesterone acetate and ethinylestradiol contraceptive vaginal system: results of two multicentre, open-label, single-arm, phase 3 trials. Lancet Glob Health 2019; 7:e1054.
19. Duijkers IJ, Klipping C, Verhoeven CH, Dieben TO. Ovarian function with the contraceptive vaginal ring or an oral contraceptive: a randomized study. Hum Reprod 2004; 19:2668.
20. Nanda K. Contraceptive patch and vaginal contraceptive ring. In: Contraceptive Technology, 19th edition, Hatcher RA, Trussell, J, Nelson, AL, et (Eds), Ardent Media, New York 2007. p.271.
21. Ahrendt HJ, Nisand I, Bastianelli C, et al. Efficacy, acceptability and tolerability of the combined contraceptive ring, NuvaRing, compared with an oral contraceptive containing 30 microg of ethinyl estradiol and 3 mg of drospirenone. Contraception 2006; 74:451.
22. Schafer JE, Osborne LM, Davis AR, Westhoff C. Acceptability and satisfaction using Quick Start with the contraceptive vaginal ring versus an oral contraceptive. Contraception 2006; 73:488.
23. Sabatini R, Cagiano R. Comparison profiles of cycle control, side effects and sexual satisfaction of three hormonal contraceptives. Contraception 2006; 74:220.
24. Bjarnadóttir RI, Tuppurainen M, Killick SR. Comparison of cycle control with a combined contraceptive vaginal ring and oral levonorgestrel/ethinyl estradiol. Am J Obstet Gynecol 2002; 186:389.
25. Veres S, Miller L, Burington B. A comparison between the vaginal ring and oral contraceptives. Obstet Gynecol 2004; 104:555.
26. Milsom I, Lete I, Bjertnaes A, et al. Effects on cycle control and bodyweight of the combined contraceptive ring, NuvaRing, versus an oral contraceptive containing 30 microg ethinyl estradiol and 3 mg drospirenone. Hum Reprod 2006; 21:2304.
27. O'Connell KJ, Osborne LM, Westhoff C. Measured and reported weight change for women using a vaginal contraceptive ring vs. a low-dose oral contraceptive. Contraception 2005; 72:323.
28. Polis CB, Phillips SJ, Curtis KM, et al. Hormonal contraceptive methods and risk of HIV acquisition in women: a systematic review of epidemiological evidence. Contraception 2014; 90:360.
29. Morrison CS, Chen PL, Kwok C, et al. Hormonal contraception and the risk of HIV acquisition: an individual participant data meta-analysis. PLoS Med 2015; 12:e1001778.
30. Ralph LJ, McCoy SI, Shiu K, Padian NS. Hormonal contraceptive use and women's risk of HIV acquisition: a meta-analysis of observational studies. Lancet Infect Dis 2015; 15:181.
31. Polis CB, Curtis KM, Hannaford PC, et al. An updated systematic review of epidemiological evidence on hormonal contraceptive methods and HIV acquisition in women. AIDS 2016; 30:2665.

32. Huang Y, Merkatz RB, Hillier SL, et al. Effects of a One Year Reusable Contraceptive Vaginal Ring on Vaginal Microflora and the Risk of Vaginal Infection: An Open-Label Prospective Evaluation. PLoS One 2015; 10:e0134460.
33. De Seta F, Restaino S, De Santo D, et al. Effects of hormonal contraception on vaginal flora. Contraception 2012; 86:526.
34. Vercellini P, Barbara G, Somigliana E, et al. Comparison of contraceptive ring and patch for the treatment of symptomatic endometriosis. Fertil Steril 2010; 93:2150.
35. Westhoff C, Osborne LM, Schafer JE, Morroni C. Bleeding patterns after immediate initiation of an oral compared with a vaginal hormonal contraceptive. Obstet Gynecol 2005; 106:89.
36. Miller L, Verhoeven CH, Hout Ji. Extended regimens of the contraceptive vaginal ring: a randomized trial. Obstet Gynecol 2005; 106:473.
37. Sulak PJ, Smith V, Coffee A, et al. Frequency and management of breakthrough bleeding with continuous use of the transvaginal contraceptive ring: a randomized controlled trial. Obstet Gynecol 2008; 112:563.
38. Barreiros FA, Guazzelli CA, Barbosa R, et al. Extended regimens of the contraceptive vaginal ring: evaluation of clinical aspects. Contraception 2010; 81:223.
39. Schaffir J, Worly BL, Gur TL. Combined hormonal contraception and its effects on mood: a critical review. Eur J Contracept Reprod Health Care 2016; 21:347.
40. Keyes KM, Cheslack-Postava K, Westhoff C, et al. Association of hormonal contraceptive use with reduced levels of depressive symptoms: a national study of sexually active women in the United States. Am J Epidemiol 2013; 178:1378.
41. Wiréhn AB, Foldemo A, Josefsson A, Lindberg M. Use of hormonal contraceptives in relation to antidepressant therapy: A nationwide population-based study. Eur J Contracept Reprod Health Care 2010; 15:41.
42. Skovlund CW, Mørch LS, Kessing LV, Lidegaard Ø. Association of Hormonal Contraception With Depression. JAMA Psychiatry 2016; 73:1154.
43. Massaro M, Di Carlo C, Gargano V, et al. Effects of the contraceptive patch and the vaginal ring on bone metabolism and bone mineral density: a prospective, controlled, randomized study. Contraception 2010; 81:209.
44. Lidegaard Ø, Løkkegaard E, Jensen A, et al. Thrombotic stroke and myocardial infarction with hormonal contraception. N Engl J Med 2012; 366:2257.
45. Selvan P, Piran P, Balucani C, et al. Stroke and Etonogestrel/Ethinyl Estradiol Ring (NuvaRing): Clinical, Radiological, and Prognostic Features. J Stroke Cerebrovasc Dis 2017; 26:608.
46. Kolacki C, Rocco V. The combined vaginal contraceptive ring, nuvaring, and cerebral venous

sinus thrombosis: a case report and review of the literature. J Emerg Med 2012; 42:413.

47. Vo TL, Cook RM, Rondina MT, Kaplan D. Cerebral venous sinus thrombosis in the setting of combined vaginal contraception. Blood Coagul Fibrinolysis 2014; 25:183.
48. Dinger J, Möhner S, Heinemann K. Cardiovascular risk associated with the use of an etonogestrel-containing vaginal ring. Obstet Gynecol 2013; 122:800.
49. Sidney S, Cheetham TC, Connell FA, et al. Recent combined hormonal contraceptives (CHCs) and the risk of thromboembolism and other cardiovascular events in new users. Contraception 2013; 87:93.
50. Tepper NK, Dragoman MV, Gaffield ME, Curtis KM. Nonoral combined hormonal contraceptives and thromboembolism: a systematic review. Contraception 2017; 95:130.
51. Oddsson K, Leifels-Fischer B, de Melo NR, et al. Efficacy and safety of a contraceptive vaginal ring (NuvaRing) compared with a combined oral contraceptive: a 1-year randomized trial. Contraception 2005; 71:176.
52. Oddsson K, Leifels-Fischer B, Wiel-Masson D, et al. Superior cycle control with a contraceptive vaginal ring compared with an oral contraceptive containing 30 microg ethinylestradiol and 150 microg levonorgestrel: a randomized trial. Hum Reprod 2005; 20:557.
53. Roumen FJ, Apter D, Mulders TM, Dieben TO. Efficacy, tolerability and acceptability of a novel contraceptive vaginal ring releasing etonogestrel and ethinyl oestradiol. Hum Reprod 2001; 16:469.
54. Merki-Feld GS, Hund M. Clinical experience with NuvaRing in daily practice in Switzerland: cycle control and acceptability among women of all reproductive ages. Eur J Contracept Reprod Health Care 2007; 12:240.
55. Abu Hashim H, Alsherbini W, Bazeed M. Contraceptive vaginal ring treatment of heavy menstrual bleeding: a randomized controlled trial with norethisterone. Contraception 2012; 85:246.
56. Cagnacci A, Ferrari S, Tirelli A, et al. Route of administration of contraceptives containing desogestrel/etonorgestrel and insulin sensitivity: a prospective randomized study. Contraception 2009; 80:34.
57. Guida M, Di Spiezio Sardo A, Bramante S, et al. Effects of two types of hormonal contraception--oral versus intravaginal--on the sexual life of women and their partners. Hum Reprod 2005; 20:1100.
58. Morotti E, Casadio P, Guasina F, et al. Weight gain, body image and sexual function in young patients treated with contraceptive vaginal ring. A prospective pilot study. Gynecol Endocrinol 2017; 33:660.
59. Guida M, Cibarelli F, Troisi J, et al. Sexual life impact evaluation of different hormonal

contraceptives on the basis of their methods of administration. Arch Gynecol Obstet 2014; 290:1239.

60. Roumen FJ, op ten Berg MM, Hoomans EH. The combined contraceptive vaginal ring (NuvaRing): first experience in daily clinical practice in The Netherlands. Eur J Contracept Reprod Health Care 2006; 11:14.
61. Stuart JE, Secura GM, Zhao Q, et al. Factors associated with 12-month discontinuation among contraceptive pill, patch, and ring users. Obstet Gynecol 2013; 121:330.
62. Nuva Ring Package Insert: Patient Information. Organon USA, Inc, 2008.
63. Nuvaring- etonogestrel and ethinyl estradiol insert, extended release. US Food and Drug Administration (FDA) approved product information. Revised May 30, 2017. US National Library of Medicine. https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=017343fb-86c4-45ab-9c47-52cc5b9f3a02 (Accessed on June 23, 2017).
64. Barreiros FA, Guazzelli CA, de Araújo FF, Barbosa R. Bleeding patterns of women using extended regimens of the contraceptive vaginal ring. Contraception 2007; 75:204.
65. Guazzelli CA, Barreiros FA, Barbosa R, et al. Extended regimens of the vaginal contraceptive ring: cycle control. Contraception 2009; 80:430.
66. Barreiros FA, Guazzelli CA, Barbosa R, et al. Extended regimens of the combined contraceptive vaginal ring containing etonogestrel and ethinyl estradiol: effects on lipid metabolism. Contraception 2011; 84:155.
67. Etonogestrel and ethinyl estradiol insert, extended release. US Food & Drug Administration (FDA) approved product information. Revised November, 2014. US National Library of Medicine. www.dailymed.nlm.nih.gov (Accessed on November 19, 2014).
68. Mulders TM, Dieben TO, Bennink HJ. Ovarian function with a novel combined contraceptive vaginal ring. Hum Reprod 2002; 17:2594.
69. Simmons KB, Kumar N, Plagianos M, et al. Effects of concurrent vaginal miconazole treatment on the absorption and exposure of Nestorone® (segesterone acetate) and ethinyl estradiol delivered from a contraceptive vaginal ring: a randomized, crossover drug-drug interaction study. Contraception 2018; 97:270.
70. Sivin I, Mishell DR Jr, Alvarez F, et al. Contraceptive vaginal rings releasing Nestorone and ethinylestradiol: a 1-year dose-finding trial. Contraception 2005; 71:122.
71. Fraser IS, Weisberg E, Brache V, et al. Serum Nestorone and ethinyl estradiol levels, and ovulation inhibition in women using three different dosage combinations of a Nestorone progestogen-ethinyl estradiol contraceptive vaginal ring on a bleeding-signaled regimen. Contraception 2005; 72:40.
72. Weisberg E, Brache V, Alvarez F, et al. Clinical performance and menstrual bleeding patterns

with three dosage combinations of a Nestorone progestogen/ethinyl estradiol contraceptive vaginal ring used on a bleeding-signaled regimen. Contraception 2005; 72:46.

73. Jensen JT, Edelman AB, Chen BA, et al. Continuous dosing of a novel contraceptive vaginal ring releasing Nestorone® and estradiol: pharmacokinetics from a dose-finding study. Contraception 2018; 97:422.
74. Archer DF, Thomas MA, Conard J, et al. Impact on hepatic estrogen-sensitive proteins by a 1-year contraceptive vaginal ring delivering Nestorone® and ethinyl estradiol. Contraception 2016; 93:58.
75. RamaRao S, Obare F, Ishaku S, et al. Do Women Find the Progesterone Vaginal Ring Acceptable? Findings from Kenya, Nigeria, and Senegal. Stud Fam Plann 2018; 49:71.
76. Massai R, Quinteros E, Reyes MV, et al. Extended use of a progesterone-releasing vaginal ring in nursing women: a phase II clinical trial. Contraception 2005; 72:352.
77. RamaRao S, Clark H, Merkatz R, et al. Progesterone vaginal ring: introducing a contraceptive to meet the needs of breastfeeding women. Contraception 2013; 88:591.
78. Nath A, Sitruk-Ware R. Progesterone vaginal ring for contraceptive use during lactation. Contraception 2010; 82:428.
79. Massai R, Miranda P, Valdés P, et al. Preregistration study on the safety and contraceptive efficacy of a progesterone-releasing vaginal ring in Chilean nursing women. Contraception 1999; 60:9.
80. Caucus on New and Underused Reproductive Technologies. Progesterone-only vaginal ring: a technical brief. In: Reproductive Health Supplies Coalition, 2009.

Topic 16682 Version 48.0

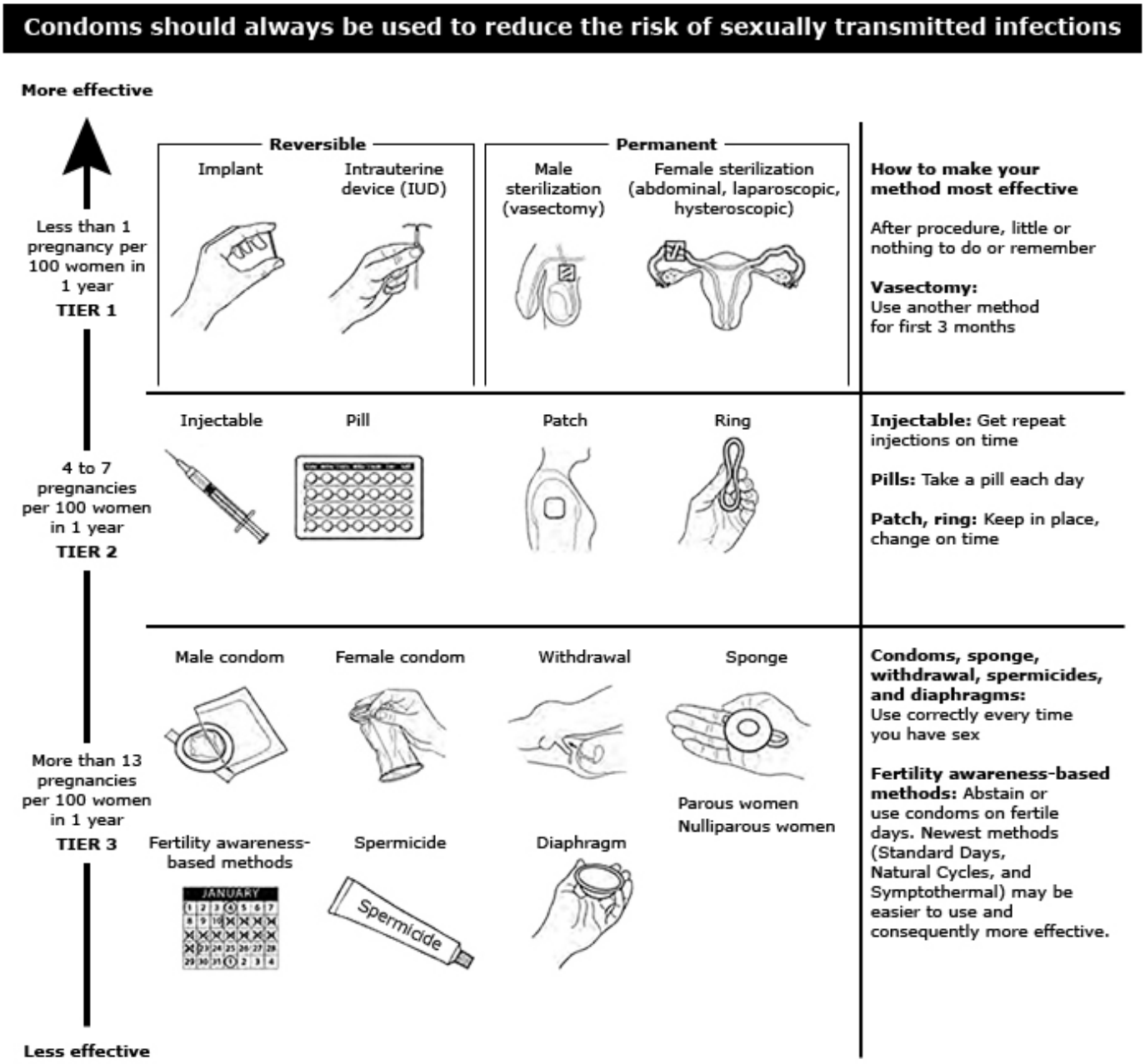
GRAPHICS

Contraceptive vaginal ring

NUVARING® image reproduced with permission of Merck Sharp & Dohme B.V., a subsidiary of Merck & Co., Inc., Kenilworth, New Jersey, U.S.A. All rights reserved.

Graphic 85785 Version 7.0

Comparison of effectiveness of contraceptive methods



Other methods of contraception:

- Lactational amenorrhea method – LAM is a highly effective, **temporary** method of contraception
- Emergency contraception – Emergency contraceptive pills or a copper IUD after unprotected intercourse substantially reduces risk of pregnancy

LNG: levonorgestrel.

Adapted from: U.S. Selected Practice Recommendations for Contraceptive Use, 2013: Adapted from the World Health Organization Selected Practice Recommendations for Contraceptive Use, 2nd Edition. MMWR Morb Mortal Wkly Rep 2013; 62:1.
Additional information from:

1. *Trussell J, Aiken ARA, Mickes E, Guthrie K. Efficacy, Safety, and Personal Considerations. In: Contraceptive Technology, 21st ed, Hatcher RA, Nelson AL, Trussell J, et al (Eds), Ayer Company Publishers, Inc., New York 2018.*

Graphic 57795 Version 9.0

Percentage of women experiencing unintended pregnancy during the first year of contraceptive use (typical and perfect use) and the percentage continuing use at the end of the first year: United States

Method	Percent of women experiencing an unintended pregnancy within the first year of use (%)		Percent of women continuing use at one year (%) [Δ]
	Typical use*	Perfect use [¶]	
No method [◊]	85	85	
Spermicides [§]	21	16	42
Female condom [¥]	21	5	41
Withdrawal	20	4	46
Diaphragm [‡]	17	16	57
Sponge	17	12	36
Parous women	27	20	
Nulliparous women	14	9	
Fertility awareness-based methods [†]	15		47
Ovulation method [†]	23	3	
TwoDay method [†]	14	4	
Standard Days method [†]	12	5	
Natural Cycles [†]	8	1	
Symptothermal method [†]	2	0.4	
Male condom [¥]	13	2	43
Combined and progestin-only pills	7	0.3	67
Evra patch	7	0.3	67
NuvaRing	7	0.3	67
Depo-Provera	4	0.2	56
Intrauterine contraceptives**			
ParaGard (copper T)	0.8	0.6	78
Mirena (52 mg LNG)	0.7	0.5	80
Skyla (13.5 mg LNG)	0.4	0.3	
Kyleena (19.5 mg LNG)	0.2	0.2	
Liletta (52 mg LNG)	0.1	0.1	
Nexplanon	0.1	0.1	89
Tubal occlusion	0.5	0.5	100
Vasectomy	0.15	0.1	100
Emergency contraceptives: Use of emergency contraceptive pills or placement of a copper intrauterine contraceptive after unprotected intercourse substantially reduces the risk of pregnancy.			
Lactational amenorrhea method: LAM is a highly effective, **temporary** method of contraception. [¶¶]			

Among *typical* couples who initiate use of a method (not necessarily for the first time), the percentage who experience an accidental pregnancy during the first year if they do not stop use for any reason other than pregnancy. Estimates of the probability of pregnancy during the first year of typical use for fertility awareness-based methods, withdrawal, the male condom, the pill, and Depo-Provera are taken from the 2006 to 2010 National Survey of Family Growth (NSFG) corrected for

under-reporting of abortion.

LNG: levonorgestrel; LAM: lactational amenorrhea method; FABM: fertility awareness-based methods; NSFG: National Survey of Family Growth; LH: luteinizing hormone.
* Data from United States populations.
¶ Among couples who initiate use of a method (not necessarily for the first time) and who use it perfectly (both consistently and correctly), the percentage who experience an accidental pregnancy during the first year if they do not stop use for any other reason.
Δ Among couples attempting to avoid pregnancy, the percentage who continue to use a method for 1 year.
◊ This estimate represents the percentage who would become pregnant within 1 year among women now relying on reversible methods of contraception if they abandoned contraception altogether.
§ 150 mg gel, 100 mg gel, 100 mg suppository, 100 mg film.
¥ Without spermicides.
‡ With spermicidal cream or jelly.
† Approximately 80% of segments of FABM use in the 2006 to 2010 NSFG were reported as calendar rhythm. Specific FABM methods are too uncommonly used in the United States to permit calculation of typical use failure rates for each using NSFG data; rates provided for individual methods are derived from clinical studies. The Ovulation and TwoDay methods are based on evaluation of cervical mucus. The Standard Days method avoids intercourse on cycle days 8 through 19. Natural Cycles is a fertility app that requires user input of basal body temperature (BBT) recordings and dates of menstruation and optional LH urinary test results. The Symptothermal method is a double-check method based on evaluation of cervical mucus to determine the first fertile day and evaluation of cervical mucus and temperature to determine the last fertile day.
** All of these estimates are low, below 1%, and we caution readers not to put any emphasis on the differences among these very small probabilities.
¶¶ However, to maintain effective protection against pregnancy, another method of contraception must be used as soon as menstruation resumes, the frequency or duration of breastfeeds is reduced, bottle feeds are introduced, or the baby reaches 6 months of age.

Graphic 120134 Version 3.0

Potential noncontraceptive benefits of cyclic estrogen-progestin contraceptives

• Reduction in dysmenorrhea
• Reduction in pelvic pain related to endometriosis
• Reduction of menorrhagia, with improvement in iron deficiency anemia related to blood loss
• Reduction in risk of ectopic pregnancy
• Reduction in symptoms associated with premenstrual syndrome and premenstrual dysphoric disorder
• Reduction in risk of benign breast disease
• Reduction in development of new ovarian cysts (true for higher dose estrogen pills only, which suppress ovulation), but no effect on existing ovarian cysts
• Reduction in ovarian cancer, including some hereditary forms, such as those associated with mutations in the *BRCA1* or *BRCA2* gene, presumably due to inhibition of ovarian stimulation
• Reduction in endometrial cancer, due to the progestin effect
• Reduction in colorectal cancer in current users
• Reduction in moderate acne
• Reduction in hirsutism
• More regular menstrual cycles

In addition, there may be a reduction in postmenopausal hip fracture risk for women who use estrogen-containing contraceptives in their 40s. Also, extended cycle or continuous estrogen-progestin contraception can reduce symptoms of menstrual migraine.

Graphic 82147 Version 3.0

Checklist used to assess the possibility of pregnancy

The provider can be reasonably certain that the patient is not pregnant if the patient has no symptoms or signs of pregnancy and meets ANY of the following criteria:
☐ The patient has not had intercourse since last normal menses.
☐ The patient has been correctly and consistently using a reliable method of contraception.
☐ The patient is within 7 days from the first day of menstrual bleeding.
☐ The patient is within 4 weeks postpartum (for nonlactating patients).
☐ The patient is within the first 7 days postabortion or miscarriage.
☐ The patient is fully or nearly fully breastfeeding, amenorrheic, and less than 6 months postpartum.

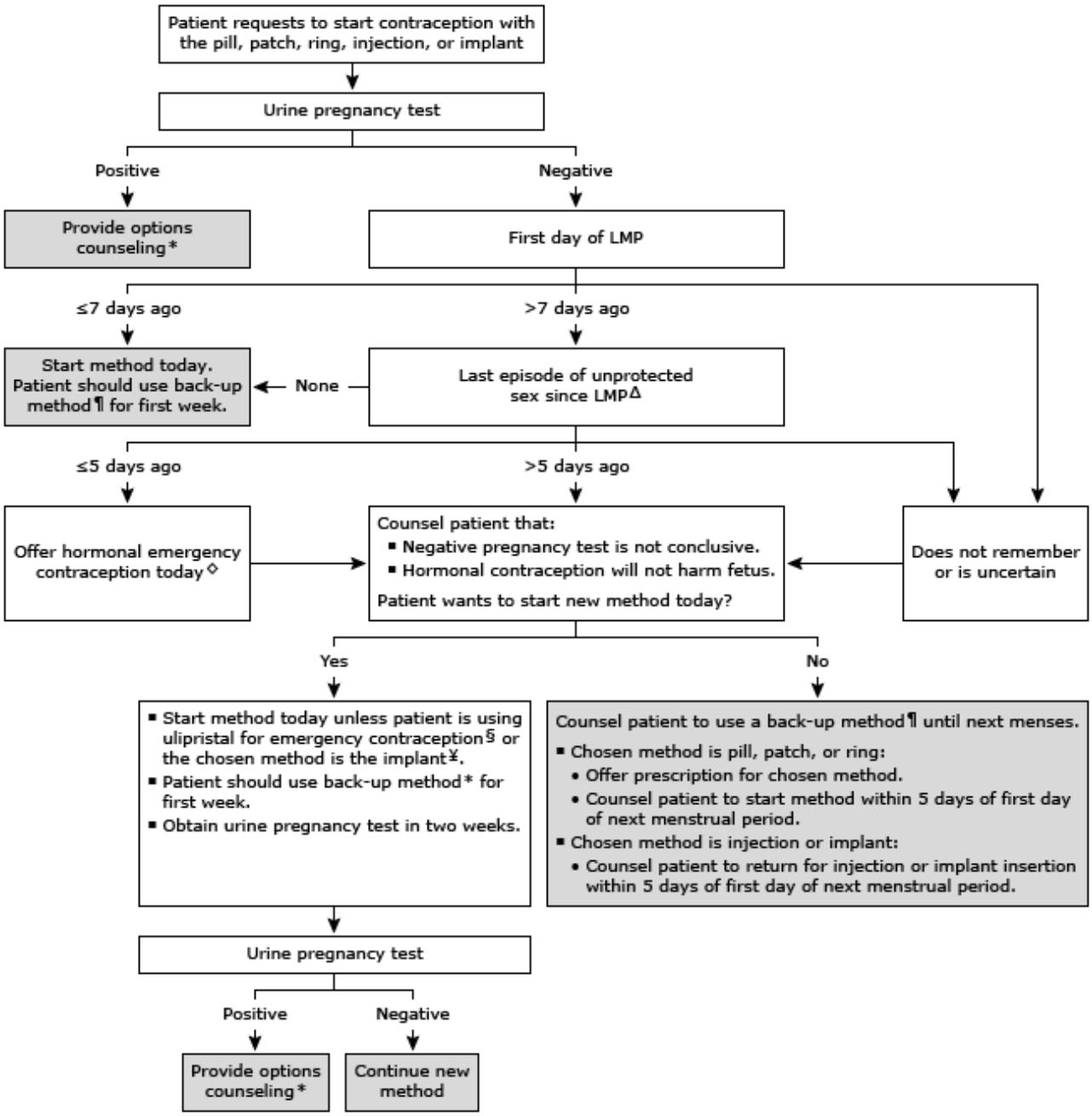
A systematic review of studies evaluating the performance of a pregnancy checklist compared with urine pregnancy test to rule out pregnancy concluded the negative predictive value of a checklist similar to the one above was 99 to 100%.

Data from:

1. *Tepper NK, Marchbanks PA, Curtis KM. Use of a checklist to rule out pregnancy: A systematic review. Contraception 2013; 87:661.*
2. *Curtis KM, Tepper NK, Jatlaoui TC, et al. United States Medical Eligibility Criteria for Contraceptive Use, 2016. MMWR Recomm Rep 2016; 65:1.*

Graphic 67567 Version 19.0

Quick-start (same-day start) approach to initiation of new birth control method: Pill, patch, ring, DMPA injection, implant



DMPA: depot medroxyprogesterone acetate; LMP: last menstrual period.

* Refer to UpToDate content on early pregnancy and pregnancy termination.

¶ Patient should use a barrier back-up method such as condoms for the first week after starting a new method.

Δ Unprotected sex includes episodes of sex in which a method of contraception was used but may not have been effective (eg, breakage of condom, multiple skipped pills).

◊ Refer to UpToDate content on emergency contraception.

§ For women using ulipristal for emergency contraception, progestin-containing contraception (ie, the pill, patch, ring, injection, and implant) should not be used for 5 days following ulipristal. For women taking levonorgestrel or combined estrogen-progestin emergency contraception, the new contraceptive method can be started after the emergency contraception. ◊

¥ If the patient would like the contraceptive implant, some providers prefer to offer a single injection of DMPA today and ask the patient to return for the implant within 5 days of the first day of her next menstrual period (to avoid the need for implant removal if the repeat urine pregnancy test is positive).

Adapted from: Quick Start Algorithm for Hormonal Contraception. RHEDI/The Center for Reproductive Health Education In Family Medicine, Montefiore Medical Center (Accessed on July 7, 2016).

Graphic 56863 Version 11.0

Switching between different methods of contraception

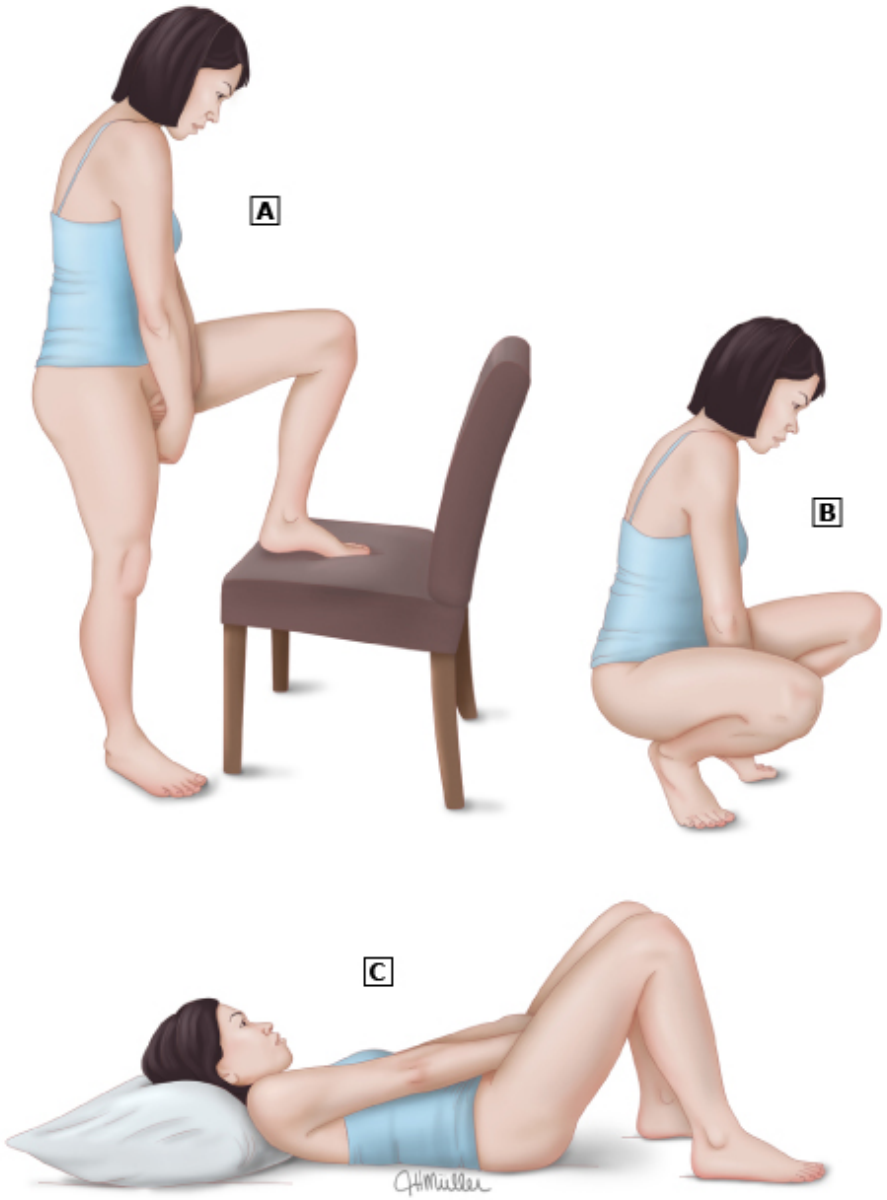
	Pill	Patch	Ring	Progestin shot ("Depo")	Progestin implant	Hormone IUD	Copper IUD
Pill	**No gap:** Take 1 st pill of new pack the day after taking any pill in old pack	Start patch **1 day before** stopping pill	**No gap:** Insert ring the day after taking any pill in pack	First shot **7 days before** stopping pill	Insert implant **4 days before** stopping pill	Insert hormone IUD **7 days before** stopping pill	Can insert copper IUD **up to 5 days after** stopping pill
Patch	Start pill **1 day before** stopping patch		**No gap:** Insert ring and remove patch on the same day	First shot **7 days before** stopping patch	Insert implant **4 days before** stopping patch	Insert hormone IUD **7 days before** stopping patch	Can insert copper IUD **up to 5 days after** stopping patch
Ring	Start pill **1 day before** stopping ring	Start patch **2 days before** stopping ring		First shot **7 days before** stopping ring	Insert implant **4 days before** stopping ring	Insert hormone IUD **7 days before** stopping ring	Can insert copper IUD **up to 5 days after** stopping ring
Progestin shot ("Depo")	Can take 1 st pill **up to 15 weeks after** the last shot	Can start patch **up to 15 weeks after** the last shot	Can insert ring **up to 15 weeks after** the last shot		Can insert implant **up to 15 weeks after** the last shot	Can insert hormone IUD **up to 15 weeks after** the last shot	Can insert copper IUD **up to 16 weeks after** the last shot
Progestin implant	Start pill **7 days before** implant is removed	Start patch **7 days before** implant is removed	Start ring **7 days before** implant is removed	First shot **7 days before** implant is removed		Insert hormone IUD **7 days before** implant is removed	Can insert copper IUD **up to 5 days after** implant is removed
Hormone IUD	Start pill **7 days before** IUD is removed	Start patch **7 days before** IUD is removed	Start ring **7 days before** IUD is removed	First shot **7 days before** IUD is removed	Insert implant **4 days before** IUD is removed		Can insert copper IUD **right after** hormone IUD is removed
Copper IUD	Start pill **7 days before** IUD is removed	Start patch **7 days before** IUD is removed	Start ring **7 days before** IUD is removed	First shot **7 days before** IUD is removed	Insert implant **4 days before** IUD is removed	Insert hormone IUD **right after** copper IUD is removed and use back-up method for **7 days**	

IUD: intrauterine device.

Reproduced with permission from: the Reproductive Health Access Project (http://www.reproductiveaccess.org). Accessed March 29th, 2011.

Graphic 77410 Version 5.0

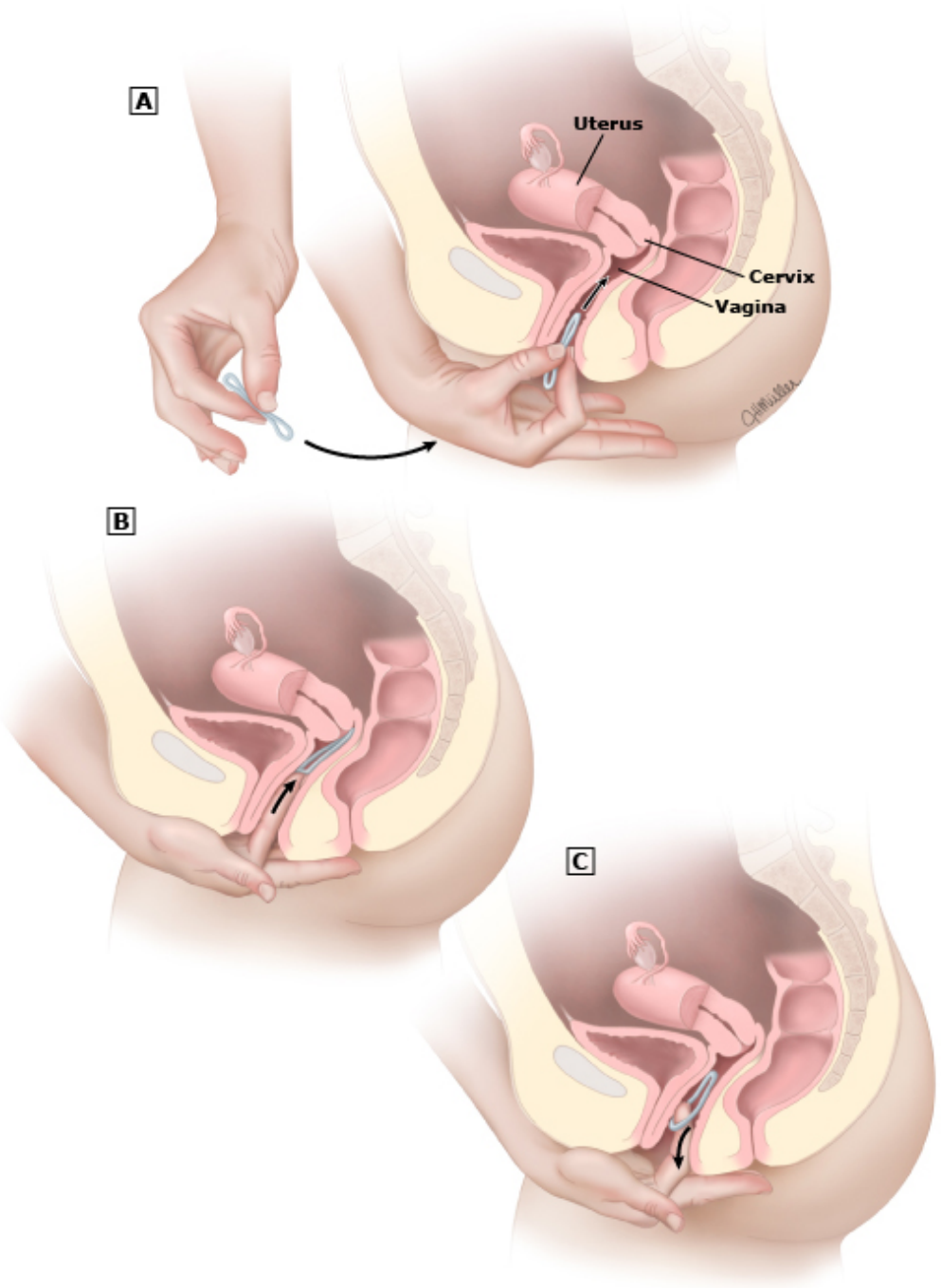
Positions for insertion of contraceptive devices



The woman should use the position that is most comfortable for her when inserting her diaphragm.

Graphic 85977 Version 1.0

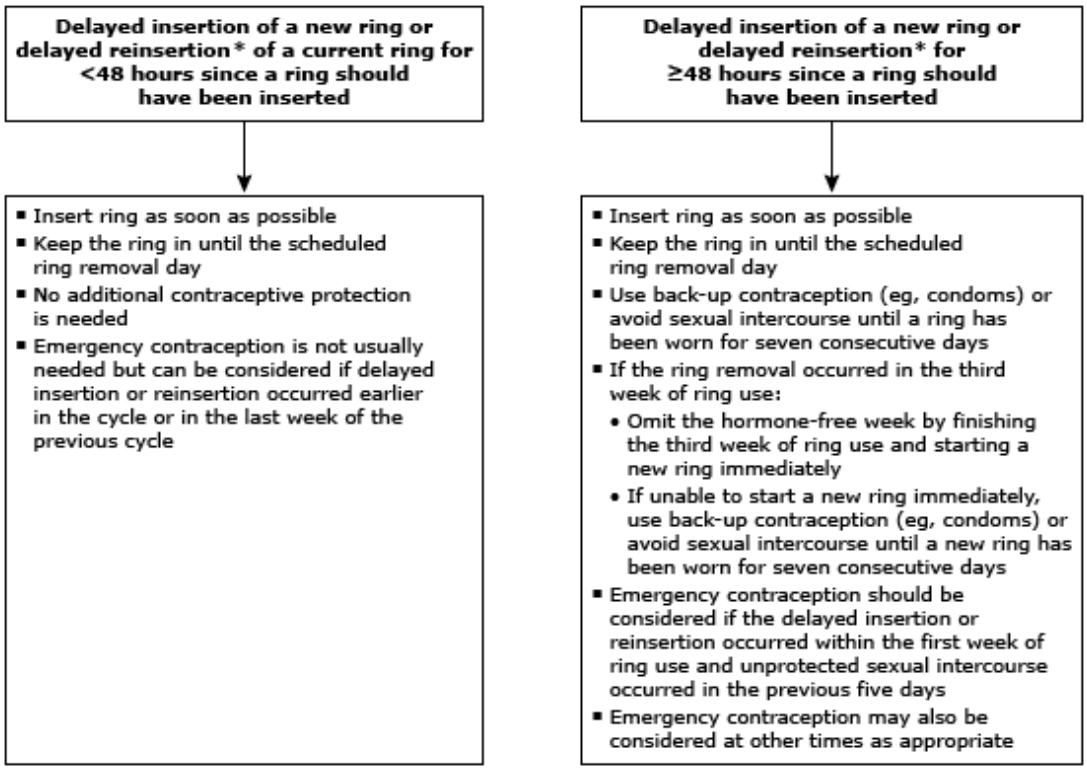
Insertion and removal of the contraceptive vaginal ring



A and B illustrate insertion of the contraceptive vaginal ring. C shows removal.

Graphic 85546 Version 1.0

Management of delayed insertion or reinsertion of the contraceptive vaginal ring



* If removal takes place but the woman is unsure of how long the ring has been removed, consider the ring to have been removed for ≥48 hours since a ring should have been inserted or reinserted.

Reproduced from: US Selected Practice Recommendations for Contraceptive Use, 2013: Adapted from the World Health Organization Selected Practice Recommendations for Contraceptive Use, 2nd Ed. MMWR Morb Mortal Wkly Rep 2013; 62:1.

Graphic 89824 Version 2.0

Contributor Disclosures

Jennifer Kerns, MD, MPH Nothing to disclose **Philip D Darney, MD, MSc** Grant/Research/Clinical Trial Support: Meds 360; Bayer [Intrauterine contraception]. Consultant/Advisory Boards: Merck [Implant contraception]; TherapeuticsMD [Contraceptive vaginal ring]. **Courtney A Schreiber, MD, MPH** Patent holder: Penn, Saul [Medical management of nonviable pregnancy]. Grant/Research/Clinical Trial Support: Bayer [Contraception]; Medicines360 [Contraception]; VeraCept [Contraception]. Consultant/Advisory Boards: Danco Pharmaceuticals [Early pregnancy loss]; Medicines360 [Consultant]. Other Financial Interest: American Board of Obstetrics and Gynecology. **Kristen Eckler, MD, FACOG** Nothing to disclose

Contributor disclosures are reviewed for conflicts of interest by the editorial group. When found, these are addressed by vetting through a multi-level review process, and through requirements for references to be provided to support the content. Appropriately referenced content is required of all authors and must conform to UpToDate standards of evidence.

Conflict of interest policy

→