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Literature from the Family Physicians  
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# When to suggest this OC alternative

Consider continuous use of the vaginal ring for women who want minimal bleeding and maximal protection.

## Practice changer

Recommend continuous or extended use of the transvaginal contraceptive ring to women who want fewer days of menstrual bleeding and have trouble remembering to, or prefer not to, take a daily pill. If breakthrough bleeding is troublesome, suggest a 4-day ring-free interval.<sup>1</sup>

### Strength of recommendation

**B:** Based on a single randomized controlled trial (RCT) with <80% follow up.

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;112:563-571.

## ILLUSTRATIVE CASE

**Case 1:** A healthy 25-year-old woman comes to see you because she's worried about getting pregnant. She's been on an extended-cycle oral contraceptive (OC) for several months and is happy to have her period only once every 3 months, but she frequently forgets to take her pill.

What can you offer that will give her the benefits of an extended-cycle OC, without the risk of pregnancy she incurs each time she misses a pill?

**Case 2:** You started a healthy 18-year-old on the transvaginal ring 6 months ago. After counseling, she opted for continuous cycling, so she inserts a new ring right after she removes the old one, on the same date each month. Although she likes the ring, she's disturbed by a recent increase in breakthrough bleeding. What can you recommend to decrease the bleeding?

Clinicians have long known that the traditional 21/7 OC cycle is not necessary for safety or efficacy. More recently, many women have been happy to learn that there is no physiologic reason to have a monthly period when they're using combination hormonal contraception. They're also happy to discover that fewer periods often mean fewer premenstrual mood swings, episodes of painful cramping, and instances of other troublesome symptoms.

## ■ The transvaginal ring is often overlooked

The US Food and Drug Administration (FDA) has approved 2 combination OCs for extended-cycle use and 1 for continuous use. But any monophasic OC can be used off-label for extended or continuous cycling to decrease bleeding frequency. So, too, can the transvaginal

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INSTANT POLL 

Which of the following best describes your current practice regarding the transvaginal contraceptive ring?

- I prescribe the ring based on the manufacturer's instructions (21/7 cycle) only.
- When I prescribe the ring, I discuss extended/continuous use with the patient.
- I have never prescribed the ring, but would consider doing so based on patient interest.
- I do not plan to prescribe the contraceptive ring.

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**FAST TRACK**

**The risk of venous thromboembolism associated with the ring is about the same as that of oral contraceptives—10 to 30 per 100,000 users.**

contraceptive ring (NuvaRing), an infrequently used contraceptive. (According to 1 study, just 5.7% of US women using contraception used either the ring or the patch.<sup>2</sup>) The ring has been studied for extended use,<sup>3</sup> but does not have FDA approval for longer-term regimens.

NuvaRing is a flexible, transparent device that contains the progestin etonogestrel and ethinyl estradiol. The manufacturer recommends a 21/7 cycle, inserting the ring in the vagina and leaving it in place for 3 weeks, removing it for 1 week, and then inserting a new ring.<sup>4</sup> The ring is well suited to women who have no contraindications to hormonal contraception but have difficulty remembering to take a pill every day—or simply prefer the convenience of less frequent dosing.

While the ring has been found to be effective and tolerable when used without a hormone-free interval—28-, 49-, 91- and 364-day dosing has been studied—breakthrough bleeding or spotting is a frequent side effect of extended-cycle hormonal contraception. In 1 study, 43% of women on a 49-day ring cycle experienced breakthrough bleeding, compared with 16% of those on a 28-day cycle.<sup>3</sup>

**High satisfaction, low risk**

Nonetheless, women who use the transvaginal ring often report high satisfaction. One study found that 61% of women were very satisfied with this method of contraception, compared with 34% of triphasic OC users ( $P<.003$ ).<sup>5</sup> The risk of pregnancy (1-2 pregnancies per 100 women-years of use, according to the manufacturer<sup>4</sup>) and the risk of venous thromboembolism (10-30 in 100,000 vs 4-11 in 100,000 nonpregnant women who are not using hormonal contraception) are comparable to that of women using OCs.<sup>6,7</sup> The risk of other severe side effects associated with the vaginal ring is comparable to that of OCs, as well.

**STUDY SUMMARY****■ An effective option that women used post-trial**

This RCT recruited women between the ages of 18 and 45 years who had been using combination hormonal contraceptives—OCs, the transdermal patch, or the transvaginal ring. All had been on a 21/7 cycle for at least 2 months. Exclusion criteria included a body mass index  $\geq 38$  kg/m<sup>2</sup>, smoking  $>10$  cigarettes per day, use of other estrogen- or phytoestrogen-containing products, and the presence of ovarian cysts  $>2.5$  cm or endometrial thickness  $>8$  mm. Women who wanted to get pregnant within a year were also excluded.

The study began with a baseline phase during which participants completed one 21/7 cycle with the ring for those using the ring prior to the study or two 21/7 cycles for those using the pill or patch prior to the study. Daily flow was assessed during this initial phase, using a scale of 0 to 4, with 4 being the heaviest. Women who completed this phase and wanted to continue using the ring (N=74) were then randomized into 2 groups (n=37) for the 6-month extended phase.

**Group 1** was assigned to use the contraceptive ring with no hormone-free days. Participants were instructed to replace the rings monthly, on the same calendar day of the month. **Group 2** also used the ring on a continuous basis with monthly replacement, but those who experienced breakthrough bleeding for more than 5 days were permitted to remove the ring for 4 days. Women in both groups kept a daily diary of ring usage, degree of menstrual flow, and symptomatology, including pelvic pain, headaches, and mood.

Most subjects were white (76%), nonsmokers (84%), and unmarried (68% in Group 1 and 57% in Group 2), with an average age of 28 to 29 years. Eight patients (22%) in Group 1 withdrew from the study prior to completing the 6-month extended phase, 4 of them because of side effects. Only 1 woman

withdrew from Group 2, because of plans for pregnancy. No one became pregnant while using the ring.

**Hormone-free interval reduced bleeding.** In Group 1, the average daily flow score was slightly reduced with continuous use (from 0.33 during the 21/7 baseline phase to 0.21 in the 6-month extended phase), but researchers reported no significant difference in flow-free days. On average, 85% of the days were flow-free in the 21/7 phase, vs 89% in the extended phase.

In Group 2, flow-free days increased, from 83% in the baseline phase to 95% in the extended phase, and average flow scores fell from 0.38 to 0.17.

Overall, the 65 participants who completed 6 months of continuous ring use had fewer bleeding days per month—1.8 days, on average, vs 3.3 days during the initial 21/7 phase, but more days of spotting per month (2.5 vs 1.8 days). There was no difference between Groups 1 and 2 in pelvic pain, headache, or mood scores, and no significant difference in headache or mood scores between the baseline and continuous phases of the trial. Pelvic pain scores were lower during the extended phase, however—0.18 vs 0.32 on a scale of 0 to 10.

**A high continuation rate.** After the 6-month extended phase, 57 of the 65 remaining participants chose to continue using the ring for contraception, on a continuous dosing basis—a continuation rate of 88%. But more than half of the women who chose to stick with the ring (57%) decided not to take advantage of the 4-day hormone-free interval to manage breakthrough bleeding or spotting, regardless of original group assignment.

#### WHAT'S NEW?

### ■ The ring moves further mainstream

Continuous or extended use of the transvaginal ring may be a new idea for many patients—and physicians. But the idea may catch on in light of this study's findings. Given the high rate of unwanted

pregnancy in the United States, many women may benefit from a contraceptive that is as safe and effective as an OC but doesn't involve a daily pill.

#### CAVEATS

### ■ Side effects, off-label concerns

In 2005, Oddsson et al found that women who used the ring reported more vaginitis and more leukorrhea than women who used OCs; conversely, they reported less nausea and less acne. Other side effects that are common to hormonal contraceptives, such as headache and weight gain, occurred at similar rates among women using the ring and OCs.<sup>6</sup>

However, the high proportion of patients who elected to keep using the ring at the end of the study by Sulak et al suggests that its side effects are acceptable.<sup>1</sup> As with all contraception, however, patient preference is a key consideration. The study population was highly motivated, particularly since women who had difficulty with this means of contraception dropped out after the baseline phase of the trial.

**Off-label use.** Pharmacokinetic research involving the contraceptive ring has shown that hormone levels required to protect against pregnancy persist for at least 35 days after it is placed in the vagina.<sup>8</sup> The manufacturer has data only to confirm contraceptive efficacy for up to 28 days and therefore does not recommend use beyond 4 weeks.<sup>4</sup>

This study highlights another off-label issue: Women in Group 2, who were allowed to remove the ring for 4 day-intervals to decrease breakthrough bleeding, were instructed to reinsert the same ring after 4 days and keep it in place until the next scheduled replacement date. But the manufacturer does not recommend reinsertion of a ring that has been out of the body for more than 3 hours. In my practice (KR), women are generally unwilling to store and replace a ring, preferring to place a new one after removal for more than a few hours.

#### FAST TRACK

**After the 6-month trial of extended use of the ring, 88% of the women continued to use it for contraception.**

CONTINUED

## Should she try continuous use?



Changing the ring on the same date each month may boost adherence for some women.

**Funding.** The research was funded by an unrestricted educational grant from Organon, Inc, the manufacturer of NuvaRing, which included salary support for 5 of the 6 authors. The published study gives no additional information about the involvement of the pharmaceutical company.

**Contraindications, drug interactions.** As with other combined hormonal contraceptives, women who have a history of venous thromboembolism, headaches with focal neurological symptoms, severe hypertension, breast or endometrial cancer, or liver disease, and smokers older than 35 years should not use the contraceptive ring.<sup>4</sup> In addition, women need to be aware that a number of medications—griseofulvin, rifampin, phenytoin, carbamazepine, and herbal products containing St. John's Wort, among others—may reduce the effectiveness of the contraceptive ring.<sup>4</sup>

### CHALLENGES TO IMPLEMENTATION

#### ■ Going off-label isn't for everyone

When it comes to choosing a contraceptive method, patient preference is paramount. Some women may not be com-

fortable inserting or removing the ring and should be counseled on other forms of contraception. Women who prefer to bleed every month should not use extended cycling. Similarly, some physicians may not be comfortable recommending an off-label use of the ring.

Those who are comfortable making the recommendation should be prepared to educate patients about this method of contraception and to discuss the benefits of extended or continuous use of the ring. For some women, the memory-triggering mechanism of changing the ring on the same date each month may boost adherence. For others, replacing the ring every 28 days may be acceptable—again, depending on patient preference. ■

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### References

1. 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;112:563-571.
2. Frost JJ, Singh S, Finer LB. US women's one-year contraceptive use patterns, 2004. *Perspect Sex Reprod Health.* 2007;39:48-55.
3. Miller L, Verhoeven C, Hout J. Extended regimens of the contraceptive vaginal ring: a randomized trial. *Obstet Gynecol.* 2005;106:473-482.
4. NuvaRing (etonogestrel/ethinyl estradiol vaginal ring) [prescribing information]. Roseland, NJ: Organon USA Inc; June 2008. Available at: <http://www.spfiles.com/pinuvaring.pdf>. Accessed March 10, 2009.
5. Schafer JE, Osborne LM, Davis AR, et al. Acceptability and satisfaction using Quick Start with the contraceptive vaginal ring versus an oral contraceptive. *Contraception.* 2006;73:488-492.
6. 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;71:176-182.
7. Wilks JF. Hormonal birth control and pregnancy: a comparative analysis of thromboembolic risk. *Ann Pharmacother.* 2003;37:912-916.
8. Timmer C, Mulders T. Pharmacokinetics of etonogestrel and ethinylestradiol released from a combined contraceptive vaginal ring. *Clin Pharmacokinet.* 2000;39:233-242.

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### FAST TRACK

**Women who use the ring report more vaginitis and more leukorrhea than women on OCs, but less nausea and acne.**