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## Hormonal Contraceptive Use Among Women of Older Reproductive Age: Considering Risks and Benefits

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### Abstract

As women approach menopause, fertility declines but pregnancy can still occur. Maternal and infant risks are increased among women of older reproductive age compared with younger women. A high proportion of pregnancies among women of older reproductive age are unintended and these pregnancies can also be associated with negative maternal and infant consequences. However, women and their healthcare providers may have concerns about risks associated with contraceptive use, particularly combined hormonal contraceptives, among women of older reproductive age who already may be at increased risk for conditions such as cardiovascular disease and breast cancer. Nonetheless, available evidence does not suggest that hormonal contraceptive use among women of older reproductive age substantially increases age-related risks of cardiovascular events or breast cancer. CDC recommends that contraception is still needed for women older than 44 years who have not reached menopause and wish to avoid pregnancy, and that based on age alone, all contraceptive methods are considered safe or generally safe for use by women of older reproductive age.

### Keywords

hormonal contraception; older reproductive ages; cardiovascular; breast cancer

### Introduction

Family planning is critical for women throughout the reproductive age spectrum, including during later years of fertility that may continue until menopause. Pregnancy among women of older reproductive age carries increased maternal and infant risks compared with women

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#### Disclaimer

The findings and conclusions in this article are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

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of younger age.<sup>1</sup> In addition, many pregnancies among this age group are unintended.<sup>2</sup> Therefore, access to contraception for women of older reproductive age who have not reached menopause and do not wish to become pregnant is essential.

While hormonal contraception may increase risk for certain conditions among women of all ages, such as cardiovascular disease or breast cancer, whether or not those risks are further increased among women of older reproductive age is unclear. Family planning considerations for these older women of reproductive age should balance any risks related to contraception with risks related to pregnancy. This report examines benefits and risks of contraceptive use among women of older reproductive age and describes recommendations from CDC for safe use of contraception by these women; discussion of contraceptive methods used for hormone replacement therapy is not included in this article.

## Benefits of Contraception for Pregnancy Prevention Among Women of Older Reproductive Age

Women can continue to be fertile until menopause. Spontaneous pregnancies have been documented as late as age 57 years.<sup>3</sup> Studies examining populations that do not use fertility control estimate 2%–15% probability of live birth among women aged 45–49 years.<sup>4–7</sup> Menopause is defined retrospectively after 12 months of amenorrhea and occurs on average at age 51 years in North America.<sup>8,9</sup> Menopause is a clinical diagnosis, and hormonal testing to assess menopausal status is difficult to interpret and not recommended.<sup>8</sup> Therefore, women should be assumed to still be fertile until menopause.

Pregnancies among women of older reproductive age are increasing in the United States. Among women aged 40–44 years, pregnancy rates increased 70% between 1990 (11.4 pregnancies per 1,000 women) and 2010 (19.4 pregnancies per 1,000 women).<sup>10</sup> The live birth rate among women aged 45–49 years quadrupled in the United States between 1990 (0.2 births per 1,000 women) and 2015 (0.8 births per 1,000 women).<sup>11</sup> In 2015, there were over 750 births in the United States to women aged 50–54 years.<sup>11</sup> While many of these pregnancies are likely intended, an estimated 48% of pregnancies among women aged 40–44 years are unintended,<sup>2</sup> although the proportion unintended among women aged >44 years is not known.

Pregnancies among women of older reproductive age have a higher rate of obstetrical risks compared with younger women. There is also an increased prevalence of medical conditions with increasing age, such as hypertension and diabetes, impacting pregnancy outcomes. The risk of pregnancy-related mortality in the United States is almost five times higher among women aged 40 years (66 deaths per 100,000 live births) than among women aged 25–29 years (14 deaths per 100,000 live births).<sup>12</sup> In addition, risks of obstetric complications are higher among women aged 44 years compared with younger women, and include pregnancy-induced hypertension (relative risk 2.8), cesarean delivery (relative risk 4.1), and gestational diabetes (relative risk 14.2).<sup>1</sup> Pregnancy loss can be as high as 52% in women aged 40 years and the risk of chromosomal abnormalities as high as 1 in 65 at age 40 years and 1 in 2 at age 45 years.<sup>13</sup> Finally, some studies have found unintended pregnancies themselves to be associated with an increased risk of certain negative consequences for

mother and baby, including delayed prenatal care, increased low birthweight, and decreased breastfeeding.<sup>14</sup>

## Risks of Contraception Among Women of Older Reproductive Age

Despite clear benefits for women of older reproductive age to prevent unintended pregnancy, women and their healthcare providers may be concerned about whether hormonal contraception might further increase age-related risks of certain conditions. This commentary focuses on risk of cardiovascular events and breast cancer among women using hormonal contraception, prevalent conditions for which risk increases with age and for which there is concern about increased risk with some methods of contraception.

### Cardiovascular risks

The risk of cardiovascular events, including myocardial infarction (MI), stroke, and venous thromboembolism (VTE), among women increases with age.<sup>15,16</sup> The prevalence of cardiovascular disease (coronary heart disease, heart failure, stroke, and hypertension) increases from 10% among women aged 20–39 years to 36% among women aged 40–59 years.<sup>15</sup> The prevalence of stroke increases from 0.7% among women aged 20–39 years to 2.2% among women aged 40–59 years.<sup>15</sup> Estimates of VTE incidence range from 2/10,000 to 5/10,000 among women aged 20–24 years and from 6/10,000 to 10/10,000 among women aged 45–49 years.<sup>16,17</sup>

Use of hormonal contraception, specifically combined hormonal contraceptives (CHCs) (which contain estrogen plus progestin), is also associated with increased risk of MI, stroke, and VTE compared with nonuse.<sup>18,19</sup> Estimates from meta-analyses show an increased relative risk of about 1.6 for MI, 2.0 for ischemic stroke, and 3.0 for VTE for combined oral contraceptive (COC) users compared with nonusers.<sup>18,19</sup> Use of most progestin-only contraceptives (including levonorgestrel intrauterine devices [LNG-IUDs], implants, and progestin-only pills [POPs]) has not been found to increase risk of cardiovascular events, while a few studies have found an increased risk of VTE with use of depot medroxyprogesterone acetate (DMPA).<sup>20</sup> Given the independent risks of age and CHCs on cardiovascular events, there is theoretical concern about the magnitude of absolute risk for cardiovascular events among women of older reproductive age who use CHCs.

There are few studies specifically examining risks associated with hormonal contraceptive use compared with nonuse among women of older reproductive age. Limited evidence suggests that the association between hormonal contraceptive use and MI does not increase with age. A U.S. hospital-based case-control study found that among women aged 45–49 years, the rate ratio for MI was 5.9 for current oral contraceptive (OC) use compared with nonuse.<sup>21</sup> However, the rate ratio for MI was elevated among all age groups when comparing OC use to nonuse, and no trend was detected to suggest that risk of MI associated with OC use increased as age increased.

A population-based case-control study from the Netherlands found no statistically significant difference in the odds of MI between OC users and nonusers among women aged 45–49 years (odds ratio [OR] 1.7, 95% confidence interval [CI] 0.8–3.3).<sup>22</sup>

A registry-based cohort study from Denmark found that the incidence of VTE increased with increasing age among both COC users and nonusers.<sup>16</sup> The incidence among current COC users increased from 4.2/10,000 women-years (WY) among women aged 15–19 years to 20.8/10,000 WY among women aged 45–49 years; VTE incidence among nonusers rose from 0.7/10,000 WY among women aged 15–19 years to 5.8/10,000 WY among women aged 45–49 years. The study did not provide stratum-specific relative risk estimates showing the association between COC use and VTE incidence by age group.

Overall, the evidence on cardiovascular events among hormonal contraceptive users of older reproductive age is limited by the small number of studies, lack of specificity on OC type, and lack of validated measures of OC use.<sup>21,22</sup> While there is clear evidence that risk of cardiovascular events increases with age and with CHC use, the limited available evidence does not suggest joint effects on the risk of MI. Although risk of VTE is elevated among women of older reproductive age using COCs, the absolute risk remains low overall, and is lower than the risk during pregnancy and the postpartum period.<sup>23</sup> No evidence is available comparing the risk of stroke or VTE associated with CHC use among older versus younger women of reproductive age, or for any of the cardiovascular events among women of older reproductive age using progestin-only contraceptives.

### Breast cancer

Similar to cardiovascular disease, the risk of breast cancer increases as women age. The risk of developing invasive breast cancer among U.S. women is 1 in 52 for ages <50 years, 1 in 44 for ages 50–59 years, and 1 in 29 for ages 60–69 years.<sup>24</sup> A 2013 meta-analysis found that ever use of OCs was associated with a slightly increased risk of breast cancer (OR 1.08, 95% CI 1.00–1.17,  $p < 0.001$ ), but was no longer significantly associated when including only U.S.-based studies (OR 1.03, 95% CI 0.93–1.14).<sup>25</sup> More recent use of OCs (within 5 years), compared with nonuse, was associated with a small but statistically significant increased risk of breast cancer, while remote use was not.<sup>25</sup> A systematic review of progestin-only contraceptives did not find an increased risk of breast cancer compared with nonuse.<sup>26</sup>

To assess whether risk of breast cancer is elevated if a woman uses hormonal contraception at older ages, several studies have examined hormonal contraceptive use among women in their 40s and subsequent risk of developing breast cancer. These studies found that relative risks for breast cancer among women who had used OCs during older ages were not statistically significantly increased compared with nonusers.<sup>27–34</sup> Studies that have examined DMPA use found no statistically significant association between use during older ages and breast cancer.<sup>34,35</sup> Two studies examining LNG-IUD use among older women found conflicting results, with one finding no association with breast cancer,<sup>36</sup> while the other found a statistically significantly increased risk of breast cancer during ages 50–54 years but not ages 45–49 years among women who had used the LNG-IUD during their 40s.<sup>37</sup>

The evidence on hormonal contraceptive use at older reproductive ages and risk of breast cancer is limited by lack of specificity on COC type, which may have included formulations with higher estrogen doses no longer regularly used in the United States,<sup>31,32</sup> use of

hospitalized controls,<sup>32–34</sup> and lack of validated measures of OC use.<sup>27,29–34,36</sup> Nonetheless, these studies suggest that there is no substantial interaction between age and hormonal contraception on the risk of breast cancer.

## CDC's Contraceptive Recommendations

CDC publishes evidence-based contraceptive recommendations to assist healthcare providers when counseling women about contraceptive use. In addition to safety, women may also consider factors such as effectiveness, accessibility, cost, ease of use, and side effects when making choices about which method to use. The U.S. Medical Eligibility Criteria for Contraceptive Use (U.S. MEC) provides recommendations on the safety of contraceptive methods for women with certain characteristics or medical conditions, and includes recommendations for women of older reproductive ages (Table 1).<sup>38</sup> According to the U.S. MEC, all hormonal contraceptive methods are considered safe or generally safe for use by women of older age, including LNG-IUDs, implants, DMPA, POPs, and CHCs. Copper IUDs are also considered safe for use by women of older age. Barrier methods, including condoms, spermicides, diaphragms, and cervical caps, are also considered safe, however, these methods are more user-dependent and therefore are less effective for pregnancy prevention with typical use.<sup>38,39</sup> Condoms are recommended for prevention of sexually transmitted diseases, including HIV.<sup>38</sup>

The U.S. Selected Practice Recommendations for Contraceptive Use (U.S. SPR) provides recommendations for common yet complex issues in contraceptive management.<sup>40</sup> The U.S. SPR recommends that contraception is still needed for women aged >44 years if they want to avoid pregnancy (Table 2). Together, these recommendations suggest that women of older reproductive age who wish to avoid pregnancy continue to need contraceptive protection and that all contraceptive methods can be considered based on a woman's age alone. Whether a woman has other medical conditions, such as hypertension or diabetes, should be considered in decision-making regarding safe contraceptive use. The full recommendations are available at: [www.cdc.gov/reproductivehealth/contraception/contraception\\_guidance.htm](http://www.cdc.gov/reproductivehealth/contraception/contraception_guidance.htm).

## Recommendations from Selected Professional Organizations

Several professional organizations also recommend that contraception be considered during the perimenopausal period (Table 2). The American College of Obstetricians and Gynecologists states that healthy, nonsmoking women can continue CHC use until age 50–55 years.<sup>9</sup> The North American Menopause Society also states that no contraceptive methods are contraindicated based on age alone, except OCs among heavy smokers, age >35 years, and recommends that women of older reproductive age who do not desire pregnancy should use effective contraception until 1 year after the final menstrual period.<sup>8</sup> The American Society for Reproductive Medicine also recommends that women continue contraception until 12 months after their last menstrual period if they do not desire pregnancy.<sup>41</sup>

## Conclusions

Although fertility declines as women approach menopause, consideration of contraception is still important for women of older reproductive age who wish to avoid pregnancy. While additional, adequately powered studies are needed to specifically examine women of older reproductive age, the limited, available evidence does not suggest that hormonal contraceptive use among women of older reproductive age substantially increases age-related risks of cardiovascular events or breast cancer. CDC recommends that all methods are considered safe or generally safe for use by women of older reproductive age, but additional considerations may be needed if women have medical conditions, such as hypertension or diabetes. Women of older reproductive age should be counseled about risks and benefits of contraceptive use and should not be denied access to any method of contraception based on age alone.

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U.S. Medical Eligibility Criteria for Contraceptive Use Classifications for Safety of Contraceptive Methods by Women of Older Ages

**Table 1.**

Condition	CopperIUD	LNG-IUD	Implants	DMPA	POP	CHC
Age	1 ( < 20 years of age)	1 ( < 20 years)	1 (>45 years)	2 (>45 years)	1 (>45 years)	2 ( < 40 years)

1 = A condition for which there is no restriction for the use of the contraceptive method; 2 = A condition for which the advantages of using the method generally outweigh the theoretical or proven risks; 3 = A condition for which the theoretical or proven risk usually outweighs the advantages of using the method; and 4 = A condition that represents an unacceptable health risk if the contraceptive method is used. Curtis et al.<sup>38</sup>

CHC, combined hormonal contraceptive; DMPA, depot medroxyprogesterone acetate; LNG-IUD, levonorgestrel intrauterine device; POP, progestin-only pill.

**Table 2.**

## Selected Recommendations for Contraceptive Use Among Women of Older Reproductive Age Who Do Not Desire Pregnancy

Organization	Recommendation*
American College of Obstetricians and Gynecologists <sup>9</sup>	Appropriate to continue CHCs until age 50–55 years
American Society for Reproductive Medicine <sup>41</sup>	Use until 12 months after last menstrual period if the woman wants to avoid pregnancy
CDC <sup>40</sup>	Still needed age >44 years if the woman wants to avoid pregnancy
North American Menopause Society <sup>8</sup>	Use until 1 year after last menstrual period if the woman wants to avoid pregnancy

\* Additional considerations may be needed if a woman has certain medical conditions.