

✓ Increased Risk of Triple-Negative Breast Cancer

Triple negative breast cancers are those that lack receptors for estrogen, progesterone and human growth factor on the tumor tissue. They constitute about 10-17% of all breast cancers and are most commonly found in younger women. They are harder to treat than other breast cancers and have a higher mortality rate. This study examined the risk factors associated with triple negative cancer cases in women age 45 and under living in the Seattle -Puget Sound area. Oral contraceptive use for 1 year or more was associated with a 2.5 fold (150%) increased risk of triple negative Breast cancer compared to women without breast cancer living in the same area. For women 40 and under this risk was even higher; 4.2 fold increase (320%).

- Dolle, Jessica M., et. al., "Risk Factors for Triple-Negative Breast Cancer in Women Under the Age of 45 Years," *Cancer Epidemiol Biomarkers Prev* 2009; 18(4), April 2009.

✓ Overall 19% Increased Risk of Premenopausal Breast Cancer

A group of physicians conducted a meta-analysis of all breast cancer studies published between 1980 and 2005. Meta-analysis is a statistical technique that allows pooling of studies that have common outcome measures in order to get a more precise estimate of risk or benefit. Of the 37 worldwide studies that met the criteria for inclusion in this analysis, 29 showed that oral contraceptive use in younger women (those under 50 years old) increased the risk of breast cancer, while only 8 showed a decreased risk. The combined analysis showed overall risk of breast cancer is increased 19% by use of oral contraceptives. The risk for breast cancer increased 44% among women who started using oral contraceptives before their first full term pregnancy, and 52% for women who used oral contraceptives 4 years or longer before their first full term pregnancy.

- Kahlenborn, Chris, M.D., et. al., "Oral Contraceptive Use as a Risk Factor for Premenopausal Breast Cancer: A Meta-analysis," *Mayo Clin Proc*, October 2006; 81(10), 1290-1302.

✓ Five-fold Increased Risk of Deep Vein Thrombosis

This large survey of Dutch women under age 50 examined the risk of Deep Vein Thrombosis (DVT, or spontaneous blood clots in the leg or arms) in women using oral contraceptives compared to age-matched women not using oral contraceptives. Women using oral contraceptives had a 5 fold (400%) increased risk of DVT compared to women not using OCs. The study was large enough to examine the effect of specific progestins used in various oral contraceptive formulations since newer progestins have been developed with the goal of making them safer. Levonogestrel (the oldest, most commonly used progestin in OCs) was associated with a 4-fold (300%) increased risk, while newer second and third generation progestins had even higher increased risks.

- Vlieg, A van Hylckama, et. al., "The venous thrombotic risk of oral contraceptives, effects of oestrogen dose and progestogen type: results of the MEGA case-control study," *BMJ*, 2009; 339:b2921.

✓ **30-130% Increased Risk of Stroke or Heart Attack**

This very large Danish study examined women aged 15-49 over a 15-year period and evaluated the relative risk of stroke or heart attack in women using hormonal contraception compared to those not using hormonal contraception. While rare overall, as young healthy women don't often have strokes and heart attacks, the relative risk of either increased between 1.3 and 2.3 fold (30-130% increased risk) for women using hormonal contraceptives that contained 30-40ug estrogen per dose (the most common dose used) compared to those not using. Higher estrogen doses increased the risk slightly and lower doses decreased the risk slightly. The progestin used within combined hormonal formations had relatively little effect on the relative risk.

- Lidegaard, Ojvind, M.D., et. al., "Thrombotic Strike and Myocardial Infarction with Hormonal Contraception," *N Engl J Med*, 2012; 366:2257-66.