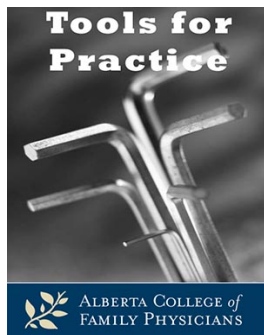


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**Reviewed: July 28, 2016**  
**Evidence Updated: New evidence**  
**Bottom Line: Modified, no major change**  
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## **What Is the Risk of VTE with Various Hormonal Contraceptives?**

**Clinical Question: How does the risk of venous thromboembolism (VTE) risk compare between hormonal contraceptives?**

**Bottom-line: Due to limits in the evidence, there is uncertainty whether the risks of VTE vary with different hormonal contraceptives. If they do, the increased risk appears to be about one extra VTE a year per 1,250 women.**

### **Evidence:**

- There are no long-term randomized controlled trials, which leaves cohort and case-control studies as best evidence.
  - Studies that found different VTE risk between hormonal contraceptives:
    - Combined oral contraceptives (COCs): 3<sup>rd</sup> generation progestins (desogestrel, drospirenone, gestodene, norgestimate, cyproterone) increase VTE risk (about 1.5-2x) over 1<sup>st</sup> or 2<sup>nd</sup> generation progestins (levonorgestrel or norethisterone).<sup>1-4</sup>
    - Transdermal estrogen and vaginal ring increase VTE risk (about 2x) over combined oral contraceptive (COC) with levonorgestrel.<sup>5</sup>
    - Levonorgestrel intra-uterine device (IUD) or progestin-only pills have same VTE risk as non-users.<sup>5</sup>
    - Lower-dose estrogen reduces VTE risk.<sup>2</sup>
  - Other studies found no increased VTE risk with drospirenone,<sup>6</sup> transdermal patch,<sup>1</sup> or vaginal ring.<sup>7</sup>
  - If these differences are real, the absolute VTE risk per 10,000 woman-years (or 1,000 women over 10 years) may be approximately:
    - 2-3 for non-users or women using progestin-only pills or progestin IUD.<sup>1</sup>
    - 7-9 for use of COC with levonorgestrel or norethisterone.<sup>1-3</sup>
    - 10-15 for use of COC with 3<sup>rd</sup> generation progestin, transdermal patch, or vaginal ring.<sup>1,3,5</sup>
    - 29 for pregnancy (for comparison).<sup>1</sup>

**Context:**

- Society of Obstetricians and Gynecologists of Canada (SOGC)<sup>8</sup> have previously stated evidence regarding risk of VTE with different progestins is inconclusive due to mixed results and high risk of bias.
- To keep the risk differences in perspective, 1,000-1,250 women would need to switch from higher- to lower-risk of COC to prevent one VTE per year.<sup>1,3</sup>
- Even the largest studies using confirmed VTE<sup>3-5</sup> were retrospective and had potential confounding, leaving uncertainty if increased risk is real.
- Other factors influencing VTE risk are age (45-49 about 6x risk age 15-19),<sup>3,9</sup> obesity (BMI  $\geq 35$  about 4x risk of BMI 20-25),<sup>3,10</sup> and smoking (about 2x risk).<sup>3,10</sup>

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