Risk of venous thromboembolism with non-or-oral hormonal contraception

An observational study suggests that women using the transdermal contraceptive patch or combined hormonal vaginal ring appear to have about twice the risk of venous thromboembolism compared with women using combined oral contraceptives containing levonorgestrel.

Overview: Hormonal contraception is highly effective and acceptably safe. However, all combined hormonal contraceptives (CHCs) are associated with a very small and rare risk of venous thromboembolism (VTE), compared with no use. The risk of VTE among users of combined oral contraceptives (COCs) is 9–10/10,000 woman-years (that is, 9–10 VTEs would occur if 10,000 women on COCs were followed for 1 year), compared with 4–5/10,000 woman-years among non-users. The absolute risk of VTE with COCs is considerably lower than the risk during pregnancy, which is 29/10,000 woman-years (The Faculty of Sexual and Reproductive Healthcare [FSRH] Combined hormonal contraception, 2011).

The risk of VTE is greatest in the first few months of starting treatment and varies slightly according to the dose of oestrogen and the type of progestogen. The risk is slightly higher in women taking COCs that contain drospirenone, desogestrel or gestodene compared with those taking levonorgestrel (The Medicines and Healthcare products Regulatory Agency [MHRA] Hormonal contraceptives, 2012).

See the NHS Evidence topic page on contraception for a general overview of the topic.

Current advice: The MHRA advises that levonorgestrel-containing COCs have the lowest thrombotic risk and are the safest CHCs for a woman who wants to start or switch contraception. However, any prescribing decision should also take into account each woman’s personal risk factors and any contraindications, including her experience with other contraceptive formulations. All CHCs should be prescribed with caution to obese women (BMI>30 kg/m2), or those with a higher baseline risk of VTE for other reasons. The MHRA advises that levonorgestrel-containing COCs have the lowest thrombotic risk and are the safest option for women who want to start or switch CHC (MHRA Hormonal contraceptives, 2012).

The Faculty of Sexual and Reproductive Healthcare advises that health professionals prescribing CHCs should be guided by the individual’s own personal preference, risk of VTE, any contraindications, possible non-contraceptive benefits and experience with other contraceptive formulations. When counselling women it is important to emphasise that, although use of some CHCs may be associated with a higher risk of VTE than others, the risk of VTE is small and lower than that associated with pregnancy. When prescribed appropriately the benefits of using CHC outweigh the risks of VTE (FSRH Combined hormonal contraception, 2011).

New evidence: The relationship between COCs and VTE is well established but there is little information on the risks associated with non-or-oral hormonal contraceptives; the combined hormonal contraceptive patch or vaginal ring, or the progestogen-only implant or levonorgestrel-containing intrauterine device. This retrospective observational study used four national data registries in Denmark to assess the risk of VTE in women using non-or-oral hormonal contraceptives (Lidegaard et al. 2012).

The study found that women using a transdermal contraceptive patch or vaginal ring had about twice the risk of VTE, compared with women using COCs containing levonorgestrel. The risk of VTE was significantly smaller in women using a levonorgestrel-containing intrauterine device compared with those taking levonorgestrel-
containing COCs. There was no significant difference in the risk of VTE between women using a subcutaneous implant and those taking levonorgestrel-containing COCs.

A single observational study, such as this one, can show only association not causation, and observational studies are prone to confounding. Limitations of this study include the reliance on clinical diagnoses entered on routine datasets, incomplete adjustment for possible confounding factors (for example, BMI or family history) and relatively small periods of exposure to some products (for example, patch, implants). Although the study provides new information on the risk of VTE associated with non-oral hormonal contraceptives, some of the analyses are underpowered and therefore the risk estimates are imprecise.

Although the study suggests that use of the contraceptive patch and vaginal ring carries a higher risk of VTE compared with levonorgestrel-containing COCs, the absolute risk remains very small and is lower than that associated with pregnancy. If thrombosis is the only consideration, then these preparations should not be considered first choice, although they may be appropriate for selected women who are starting or switching contraception.

**Commentary:** "Although the study has some weaknesses, the information it provides is valuable because there is little information available about the risks associated with non-oral hormonal contraceptives.

"Some of the results are reassuring. For example, the risk estimates for levonorgestrel-containing pills are within expectations, as are the declining risk estimates with time among COC users. However, many of the risk estimates for non-oral products are based on small numbers and therefore have wide confidence intervals (especially when examining confirmed thrombotic events only), emphasising the need to interpret them cautiously. The analysis for the combined patch was particularly underpowered and so does not provide clear information about whether this preparation carries a risk that is different to COCs. The analyses for implants were also based on a small period of observation, with a risk estimate that was statistically significant when all events were considered but not when only confirmed thrombotic events were analysed.

"Even if these risk estimates do represent the truth, they are well within the ranges seen for some frequently used combined oral contraceptives (those with desogestrel, gestodene or drospirenone). This suggests that many women and prescribers are willing to accept a very small higher thrombotic risk from these preparations. Contraceptive choices are always going to involve a careful balancing of many factors, including risk of different health outcomes, ease of use, convenience, aesthetic considerations and availability." – Professor Phil Hannaford. NHS Grampian Chair of Primary Care and Vice Principal of Research and Knowledge Exchange.

**About this article:** This article appeared in the August 2012 issue of the Eyes on Evidence newsletter. This free monthly newsletter from NICE Evidence outlines interesting new evidence and what it means for current practice. They do not constitute formal NICE guidance. The opinions of contributors do not necessarily reflect the views of NICE.

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