



Royal Institute of Technology,
Stockholm, Sweden

Correspondence to: T Johansson
therese.johansson@igp.uu.se

Cite this as: *BMJ* 2025;388:r237
<http://doi.org/10.1136/bmj.r237>

Arterial thrombosis in users of contemporary hormonal contraception

Increased relative risk of stroke and myocardial infarction, but absolute risk is low

Therese Johansson *Postdoctoral researcher*

Approximately 80% of women worldwide have used hormonal contraception at some point in their lives.¹ This high number underscores its crucial role in enabling family planning and addressing health conditions such as heavy menstrual bleeding and endometriosis. However, these benefits must be weighed against potential risks, including the risk of thrombotic events. Most previous research has focused on the risk of venous thromboembolism,²⁻⁵ which was noted as early as 1961 when the first contraceptive pill was introduced to the market.⁶ Since then, new drugs have been developed with pills containing a lower dose of oestrogen, combined with newer types of progestins, as well as new delivery options such as patches, vaginal rings, and intrauterine devices systems.⁷ These advancements seek to minimise the risk of thrombotic side effects while offering more personalised and convenient methods of contraception to address the varied needs of women. Nonetheless, the risk of arterial thromboses, such as myocardial infarction and ischaemic stroke, is less clear.

A significant limitation in assessing the risk of arterial thromboses among users of hormonal contraception is the absence of rigorous data. These diseases are rare, especially among young women, who represent the primary demographic using hormonal contraception. Hundreds of thousands of women need to be studied to provide robust findings. This population size is rare in clinical trials; therefore, the Nordic health registers offer an excellent basis to investigate the side effects of contemporary hormonal contraception.⁸

In a linked study (doi:10.1136/bmj-2024-082801),⁹ Yonis and colleagues report results using the Danish health registers to assess the risk of contemporary hormonal contraceptives, including the combined oestrogen-progestin pill, intrauterine system, vaginal ring, patch, progestin-only pills, subcutaneous implant, and intramuscular injections on the risk of myocardial infarction and ischaemic stroke. The study's primary strength lies in including all Danish women aged 15 to 49 years, encompassing more than two million women and a follow-up period of 22 million person years. The national prescriptions register allowed for detailed tracking of hormonal contraceptive use with daily updates, including specific formulations and delivery methods, while the patient register provided documentation of incident ischaemic stroke and myocardial infarction diagnoses.

Among the 2 025 691 women followed up in the study, 4730 had ischaemic strokes, and 2072 had a myocardial infarction. The most commonly used hormonal contraceptive, the combined

oestrogen-progestin pills, was associated with a twofold increase in the risk of ischaemic stroke and myocardial infarction, which translates to one additional ischaemic stroke for every 4760 women using the combined pill for one year, and one additional myocardial infarction for every 10 000 women per year of use. Risk estimates showed slight variation by oestrogen dose but suggested similar effects across various types of progestins in the pill. Progestin-only contraceptives, including pills and implants, carried a slightly elevated risk, though lower than the combined pills. Non-oral combined contraceptives, such as the vaginal ring and patch, had higher associated risks, with the vaginal ring increasing ischaemic stroke risk 2.4-fold and myocardial infarction risk 3.8-fold, while the patch increased ischaemic stroke risk 3.4-fold.

The levonorgestrel releasing intrauterine system was the only hormonal contraceptive not linked to an increased risk, making this option safer for cardiovascular health.

The study by Yonis and colleagues expanded existing findings by showing that the progestin-only pills and the non-oral combined contraceptives also increase the risk of arterial thromboses.¹⁰⁻¹² This study also showed that the intrauterine system, which has increased in popularity in the last few years, does not confer an increased risk of arterial thromboses. It is important to note that the absolute risk remains low. Nonetheless, these side effects are serious and given that approximately 248 million women use hormonal contraceptives daily,¹ the results carry important implications. Contraceptive counselling requires a careful assessment of individual risk factors, such as pre-existing cardiovascular risk factors, including hypertension, obesity, or smoking.

The study's findings highlight the need for targeted public health interventions at a population level. Educational campaigns should focus on increasing awareness of the potential risks associated with various contraceptive methods, thereby enabling women to make informed choices. These initiatives should be supported by training for healthcare providers to ensure consistent and evidence based counselling.

The study further underscores disparities in access and equity. In the Nordic countries, hormonal contraceptives are subsidised, ensuring affordability and accessibility, with free contraceptive counselling available to facilitate informed decision making.¹³⁻¹⁴ This provision stands in stark contrast to many countries worldwide, where financial and informational barriers restrict access to contraception.¹⁵ Policy makers should prioritise making safer alternatives, such as the levonorgestrel

releasing intrauterine system for women with cardiovascular risk factors, both affordable and accessible, particularly in low resource settings where cardiovascular risks are frequently underdiagnosed and untreated.

Provenance and peer review: Commissioned; not externally peer reviewed

Competing interests: The BMJ has judged that there are no disqualifying financial ties to commercial companies. The authors declare the following other interests: none. Further details of The BMJ policy on financial interests is here: <https://www.bmj.com/sites/default/files/attachments/resources/2016/03/16-current-bmj-education-coi-form.pdf>

- 1 United Nations Department of Economic and Social Affairs, Population Division. World Family Planning 2022: Meeting the changing needs for family planning: Contraceptive use by age and method. 2022
- 2 Lidegaard Ø, Løkkegaard E, Svendsen AL, Agger C. Hormonal contraception and risk of venous thromboembolism: national follow-up study. *BMJ* 2009;339:. doi: 10.1136/bmj.b2890. pmid: 19679613
- 3 Lidegaard Ø, Edström B, Kreiner S. Oral contraceptives and venous thromboembolism: a five-year national case-control study. *Contraception* 2002;65:-96. doi: 10.1016/S0010-7824(01)00307-9 pmid: 11929640
- 4 Lo Faro V, Johansson T, Johansson Å. The risk of venous thromboembolism in oral contraceptive users: the role of genetic factors-a prospective cohort study of 240 000 women in the UK Biobank. *Am J Obstet Gynecol* 2024;230:360.e1-13. doi: 10.1016/j.ajog.2023.09.012. pmid: 37734636
- 5 Meaidi A, Mascolo A, Sessa M, et al. Venous thromboembolism with use of hormonal contraception and non-steroidal anti-inflammatory drugs: nationwide cohort study. *BMJ* 2023;382:e074450. doi: 10.1136/bmj-2022-074450. pmid: 37673431
- 6 Barritt DW, Jordan SC. Clinical features of pulmonary embolism. *Lancet* 1961;1:-32. doi: 10.1016/S0140-6736(61)92891-4. pmid: 13687311
- 7 Christin-Maitre S. History of oral contraceptive drugs and their use worldwide. *Best Pract Res Clin Endocrinol Metab* 2013;27:-12. doi: 10.1016/j.beem.2012.11.004. pmid: 23384741
- 8 Laugesen K, Ludvigsson JF, Schmidt M, et al. Nordic health registry-based research: a review of health care systems and key registries. *Clin Epidemiol* 2021;13:-54. doi: 10.2147/CLEP.S314959. pmid: 34321928
- 9 Yonis H, Løkkegaard E, Kragholm K, et al. Stroke and myocardial infarction with contemporary hormonal contraception: real-world, nationwide, prospective cohort study. *BMJ* 2025;388:e082801.
- 10 Rosendaal FR, Helmerhorst FM, Vandenbroucke JP. Female hormones and thrombosis. *Arterioscler Thromb Vasc Biol* 2002;22:-10. doi: 10.1161/hq0202.102318. pmid: 11834517
- 11 Roach REJ, Helmerhorst FM, Lijfering WM, Stijnen T, Algra A, Dekkers OM. Combined oral contraceptives: the risk of myocardial infarction and ischemic stroke. *Cochrane Database Syst Rev* 2015;2015:CD011054. doi: 10.1002/14651858.CD011054.pub2. pmid: 26310586
- 12 Johansson T, Fowler P, Ek WE, et al. Oral contraceptives, hormone replacement therapy, and stroke risk. *Stroke* 2022;53:. doi: 10.1161/STROKEAHA.121.038659.
- 13 Lindh I, Skjeldestad FE, Gemzell-Danielsson K, et al. Contraceptive use in the Nordic countries. *Acta Obstet Gynecol Scand* 2017;96:-28. doi: 10.1111/aogs.13055. pmid: 27861709
- 14 Lindgren H, Bogren M, Osika Friberg I, Berg M, Hök G, Erlandsson K. The midwife's role in achieving the Sustainable Development Goals: protect and invest together - the Swedish example. *Glob Health Action* 2022;15:2051222. doi: 10.1080/16549716.2022.2051222. pmid: 35522127
- 15 Dehlendorf C, Krajewski C, Borrero S. Contraceptive counseling: best practices to ensure quality communication and enable effective contraceptive use. *Clin Obstet Gynecol* 2014;57:-73. doi: 10.1097/GRF.000000000000059. pmid: 25264697