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Re: Use of combined oral contraceptives and risk of venous thromboembolism: nested case-control studies using the QResearch and CPRD databases.

Rapid Response Letter in the BMJ 17 July 2018

Citation: Vinogradova Y, Coupland C, Hippisley-Cox. Re: Use of combined oral contraceptives and risk of venous thromboembolism: nested case-control studies using the QResearch and CPRD databases. BMJ 2015;350: h2135 [Rapid Response letter published online on 17 July 2018]
https://www.bmj.com/content/350/bmj.h2135/rapid-responses

The study was run separately on two large primary care databases and the results were combined using meta-analysis techniques. Overall, there was good consistency in the results between the two databases. Because of the large number of comparisons in our study, the value for statistical significance was set at the 1% level. For the combined analysis we had 72 pairs of odds ratios, and the only significant heterogeneity discovered was for use of norgestimate compared with no use of combined oral contraceptives.

The findings for norgestimate were of particular interest because of its historical position between second and third generation combined oral contraceptives. Although the results for the direct comparisons between norgestimate and levonorgestrel had different directions of association with VTE risk in the two databases, with a reduced odds ratio in favour of norgestimate) in CPRD (adjusted odds ratio 0.879, 95% confidence interval 0.688 to 1.123, p-value 0.302) and an increased odds ratio in QResearch (adjusted odds ratio 1.252, 95% CI 0.996 to 1.573, p-value 0.054), neither of the findings were statistically significant. Results for these direct comparisons of norgestimate with levonorgestrel were not significantly heterogeneous between the databases (the p-value for this heterogeneity test was 0.038). The most reliable odds ratio is therefore the combined odds ratio from the fixed effect model (combined odds ratio 1.06, 95% CI 0.90 to 1.26, p-value 0.480), which is very similar to that from the random effect model (combined odds ratio 1.08, 95% CI 0.89 to 1.30, p-value 0.443).

We concluded, therefore, that this study had not produced evidence that the risk of VTE associated with norgestimate is significantly different from levonorgestrel.

Competing interests: No competing interests