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Epidemiology of Oral Contraceptives and Cardiovascular Disease

To the Editor: Chasan-Taber and Stampfer (1) present the "recency of market introduction" as a potential source of bias in evaluating the risk for venous thrombosis associated with new oral contraceptives containing desogestrel or gestodene. The argument is that women receiving these pills started using them more recently, those receiving older contraceptives had been using them for a longer time, and the risk for thrombosis is higher in the early periods of use. The straightforward solution is to compare "like with like": women who are receiving different brands for similar time periods. This analysis was done by Jick and colleagues (2), who found that in the first 6 months of use, women receiving desogestrel and gestodene contraceptives have a sixfold to ninefold greater risk for venous thrombosis relative to women receiving levonorgestrel contraceptives. In several other studies, separate analyses showed that relative risk was increased rather than decreased in the first period of use (3). The correct interpretation of these findings is that the excess risk of desogestrel and gestodene contraceptives cannot be explained by "recency of introduction bias" because the effect does not disappear upon stratification. The higher excess risk in the first period of use indicates effect modification and supports the decision of the British and German authorities to caution against first-time prescription of these pills to young women.

Chasan-Taber and Stampfer misquote our paper: In the Leiden Thrombophilia Study, we did find the highest risk in the youngest users (4), in line with the data reported above. Because of the complexity of the issue, the World Health Organization convened an international group of independent scientists in November 1997. The main conclusions of their report, one of which is that contraceptives containing desogestrel or gestodene carry a risk for thrombosis beyond that of contraceptives containing levonorgestrel, have recently become available (5).

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In response: Vandenbroucke and colleagues state that we present the "recency of market introduction" as a potential source of bias in evaluating the risk for venous thromboembolism associated with oral contraceptives containing the new progestogens. They misconstrued our argument as stating that the risk for thrombosis is "higher in the early periods" of use and then declines over time. We instead suggest that clinicians prescribe newly introduced drugs to a population different from the population receiving more established drugs. Thus, the relative risk for venous thromboembolism in users of new drugs may be elevated because the population to whom new drugs are prescribed has a higher baseline risk. The excess risk observed by Bloemenkamp and colleagues (1) in younger women (a population in which most new users will be found) further supports this argument.

With banner headlines carrying the government's warning, there can be little doubt that many women either switched formulations or discontinued use of oral contraceptives, leading to increased rates of unplanned pregnancies and abortion. The British Pregnancy Advisory Service, which provides nearly 20% of abortions in the United Kingdom, reported a 10% increase in the number of abortions performed after the government's warning. Of women surveyed, 40% reported discontinuing oral contraceptive use immediately after the warning (2). A decrease in rates of thromboembolic disease after this sensational announcement has not been shown. A more moderate approach may have been better.

We agree that the evidence does suggest, although not confirm, an increased risk for thromboembolic disease associated with use of the newest progestogens. This apparent increase in risk cannot be dismissed as a result of bias, but neither has it been confirmed. The strength of the evidence and the appropriateness of response appear to be our area of disagreement.

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