Oral contraceptives and the risk of breast cancer in BRCA1 and BRCA2 mutation carriers. Narod SA, Dube MP, Klijn J, et al. *J Natl Cancer Inst* 2002; **94**(23): 1773–1779. (Reviewed in National Electronic Library for Health, NHS Centre for Reviews and Dissemination, University of York, York, UK)

Contraceptive advice for the woman with a strong family history of breast and ovarian cancer is a difficult area. Some of these women carry known genetic mutations (BRCA1 and BRCA2) predisposing to breast and ovarian cancer. It remains unclear whether contraceptive steroids further increase their cancer risks. A recent international case-control study looked at the risks of breast cancer among 2622 women with these mutations. It was found that women with the BRCA1 gene mutation had a slightly higher risk of early-onset breast cancer if they had ever used oral contraception. The increased risk related particularly to women who had used oral contraception for more than 5 years, or at a younger age, or before 1975. Women with the BRCA2 gene mutation appeared not to increase their breast cancer risk by using oral contraception, however far fewer of these women were studied.

This well-designed study adds to our knowledge in this difficult area but frustratingly did not look specifically at the oestrogen/progestogen content of oral contraceptives used by the women.

Any evidence of increased breast cancer risk must be weighed against growing evidence that combined oral contraception helps protect against ovarian cancer in these high-risk women.

Reviewed by **Kate Weaver,** MB ChB, BSc
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Young women's accounts of factors influencing their use and non-use of emergency contraception: in-depth interview study. Free C, Lee RM, Ogden J. *BMJ* 2002; **325**: 1393–1396

This study specifically included young women living in deprived areas of London with high teenage pregnancy rates. Thirty sexually active women were interviewed.

The main barriers to use of emergency contraception (EC) were an anticipation of being criticised, or not believing that they were personally vulnerable to pregnancy. Some subjects revealed a lack of knowledge about how they could have accessed EC. Twenty of those interviewed were classed as 'White British', 10 were in further education (college or university) and 14 of those interviewed were between the ages of 20 and 25 years, so their accounts may not be typical of younger, more vulnerable women. As in many qualitative studies, results are difficult to generalise.

We already know that professional efforts to increase knowledge about and access to EC have had limited success amongst teenagers. The conclusions from this study may be that a shift in cultural attitudes is needed, both to make teenagers feel they are unlikely to be criticised for seeking EC, and that pregnancy is a real possibility that they wish to postpone.

Reviewed by **Gill Wakley**, MD, MFFP
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Five-year clinical experiences with Nova T® 380 copper IUD. Batár I, Kuukankorpi A, Siljander M, et al. *Contraception* 2002; **66**: 309–314

This paper is the report of an open, single-group, phase III clinical trial of 5 years' duration. Four hundred women were recruited to be monitored for 5 years using the Nova T® 380 copper IUD. The study was restricted to parous women between the ages of 18 and 44 years with a mean age of 31.4 years. The other criteria for exclusion would be as expected for any intrauterine device (IUD) fitting.

The study gave a Pearl Index of 0.4, which is comparable to other IUDs with a similar copper loading. The rate in the first year was 0.5 rising to 1.9 in the fifth year. The authors admit that it was not a comparative trial so other criteria, such as removal rates for bleeding etc., are not directly

comparable with other IUDs. Even though there was no direct comparison, the side effect profile was not dissimilar to that shown by similar studies with other IUDs.

This phase III trial did not include women who were nulliparous or under the age of 18 years. As with any other product, when used in clinical practice the pregnancy rates and removal rates will vary according to the population using the method. The initial results suggest that the product is similar to IUDs already in established use.

Reviewed by **Judy Murty**, DRCOG, MFFP
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Low dose mifepristone and two regimens of levonorgestrel for emergency contraception: a WHO multicentre randomised trial. von Hertzen H, Piaggio G, Ding J, et al. *Lancet* 2002; **360**(9348): 1803–1810

Levonorgestrel (LNG) taken in divided doses has replaced the Yuzpe regimen for emergency contraception (EC) where it is available. This World Health Organization (WHO) trial was designed to see if LNG can be given as a single dose, and to compare both regimens with single-dose mifepristone, used up to 5 days after unprotected intercourse.

In this triple-blind study, using a secure method or randomisation, 4136 women were allocated to 10 mg mifepristone, a single dose of 1.5 mg LNG or two doses of 0.75 mg LNG taken 12 hours apart. It was an international study with just over half the participants coming from China. The loss to follow-up rate was low at 1.5%.

The pregnancy rates were similar with the three treatments: 1.5% each for mifepristone and single-dose LNG and 1.8% with the two-dose LNG. The relative risk of pregnancy of single- versus two-dose levonorgestrel was 0.83 (95% CI 0.46–1.50). When restricted to women who had treatment within 1–3 days of intercourse, the same comparisons gave a similar result (relative risk 0.79, 95% CI 0.41–1.52, difference in risk of pregnancy –0.4%, 95% CI –1.3%–0.6%, calculated from data in the paper).

There was a significant rising trend in pregnancy rates, for all treatments combined, in the five successive days from the time of intercourse ($p = 0.02$), although the pregnancy rate with LNG was numerically higher following treatment delay of 1 day compared to a delay of 2 or 4 days. The authors estimated that around 60% of expected pregnancies were prevented with each of the regimens when treatment was started 4–5 days after intercourse. The side effect profiles with the three regimens were very similar, the only difference being less frequent bleeding after treatment, and a delay in menses, with mifepristone.

This is a well-designed trial minimising opportunities for systematic bias. Together with its large size, it allows a confidence in using the results in clinical practice. A single dose of LNG can replace the standard two-dose treatment, up to 3 days after intercourse, with no loss of efficacy and no change in side effects. The remarkably similarity of reported side effects with mifepristone and LNG with different pharmacodynamics suggests that a placebo arm may have had similar effects. The simplification of the treatment is welcome.

The efficacy of LNG used beyond 72 hours after intercourse is as uncertain as ever. Even in this large trial fewer than 500 women attended 4–5 days after treatment and the wide confidence intervals for pregnancies prevented include no effect. Estimates of pregnancies prevented, however, have very limited validity as the method used to calculate 'expected pregnancies' is derived from different women in different circumstances and based on crude estimates of day of ovulation. Ultimately, the real efficacy can only be answered by a placebo-controlled randomised trial at a coitus-to-treatment interval where there is uncertainty about efficacy, and an intrauterine device (IUD) is inappropriate.

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