

## Intrauterine Devices Might Prevent More Than Pregnancy

### Non contraceptive benefit of the Intrauterine Devices

Castellsagué X et al. Intrauterine device use, cervical infection with human papillomavirus, and risk of cervical cancer: A pooled analysis of 26 epidemiological studies. *Lancet Oncol* 2011 Oct; 12:1023

*Meta-analysis shows that IUDs provide protection against cervical cancer.*

Studies show that contraceptive methods such as oral contraceptives and condom use can affect the risk of cervical cancer. Intrauterine device (IUD) use has been shown to reduce the risk of endometrial cancer, but little is known about its relation with cervical cancer. Because intrauterine devices (IUDs) pass through the cervix, there is always the concern that its use might affect risk for cervical cancer

A pooled analysis of data from two large studies by the International Agency for Research on Cancer and Institut Català d'Oncologia research programme on HPV and cervical cancer was carried out. One study included data from ten case—control studies of cervical cancer done in eight countries, and the other included data from 16 HPV prevalence surveys of women from the general population in 14 countries. 2205 women with cervical cancer and 2214 matched control women without cervical cancer were included from the case—control studies. The other study included 15 272 healthy women from the HPV surveys

After adjusting for relevant covariates, including cervical HPV DNA and number of previous Papanicolaou smears, **a strong and consistent inverse association was found between ever use of IUDs and cervical cancer** (odds ratio 0.55, 95% CI 0.42—0.70;  $p < 0.0001$ ). A protective association was noted for squamous-cell carcinoma (OR 0.56, 0.43—0.72;  $p < 0.0001$ ), adenocarcinoma and adenosquamous carcinoma (OR 0.46, 0.22—0.97;  $p = 0.035$ ), but not among HPV-positive women (OR 0.68, 0.44—1.06;  $p = 0.11$ ). No association was found between IUD use and detection of cervical HPV DNA among women without cervical cancer.

*Put simply, women who reported previous IUD use had half the risk of developing cervical cancer compared with women with no history of IUD use.*

The authors state that the associations found in our study strongly suggest that IUD use does not modify the likelihood of prevalent HPV infection, but

might affect the likelihood of HPV progression to cervical cancer. Thus, IUD use could possibly be regarded as a protective cofactor in cervical carcinogenesis. One putative mechanisms by which IUDs might exert this protective effect is through the induction of a reactive, chronic, low-grade, sterile inflammatory response in the endometrium, endocervical canal, and cervix that could modify, via changes in the local mucosal immune status, the course of HPV infections.

*Put simply cellular immunity triggered by the device might be one of several mechanisms that could explain the findings.*

Although types of IUDs were not specified in this analysis, in the countries where these studies were conducted, few women used hormone-releasing IUDs; thus, future work should be aimed at examining whether levonorgestrel-releasing IUDs could protect against cervical cancer.

Can we identify women at risk of pregnancy despite using emergency contraception? Data from randomized trials of ulipristal acetate and levonorgestrel

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Emergency contraception (EC) can prevent pregnancy after unprotected intercourse—but it does not always work.

Data from a meta-analysis of two randomized controlled trials comparing the efficacy of ulipristal acetate (UPA) with levonorgestrel( in both trials, LNG 1.5 mg orally was compared with UPA either 30 mg )were analyzed to identify factors associated with EC failure.

Women who had intercourse the day before estimated day of ovulation had a fourfold increased risk of pregnancy (OR, 4.42; 95% CI, 2.33–8.20;  $p < .0001$ ) compared with women having sex outside the fertile window. For both methods, women who had unprotected intercourse after using EC were more likely to get pregnant than those who did not (OR, 4.64; 95% CI, 2.22–8.96;  $p = .0002$ ).

The risk of pregnancy was more than threefold greater for obese women compared with women with normal body mass index (OR, 3.60; 95% confidence interval CI, 1.96–6.53;  $p < .0001$ ), whichever EC was taken. However, for obese women, the risk was greater for those taking levonorgestrel (OR,

4.41; 95% CI, 2.05–9.44,  $p=.0002$ ) than for UPA users (OR, 2.62; 95% CI, 0.89–7.00; ns).

The results are important to clinicians as they suggest those women **with BMI of 25 kg/m<sup>2</sup> and over, as well as those who have intercourse at the most fertile time of the cycle and those who have further acts of intercourse in the same cycle, are all at increased risk failure of EC.**

Overweight women are easily identified, and can be told that they may be at increased risk of EC failure and that they use UPA or an IUD rather than LNG.

It is much more difficult to ascertain pregnancy risk in relation to the timing of intercourse in the cycle. We might be reluctant to advise a woman that her risk is low or negligible but, we lose nothing by telling someone that the risk of pregnancy might be rather high and that she might be advised to have an IUD (if acceptable and accessible).

Effectiveness of emergency contraception is estimated by calculating the number of pregnancies that might have occurred without use of the intervention. These calculations are difficult and the effectiveness of emergency contraception has tended to be overestimated.

The contraceptive efficacy of emergency contraceptive pills containing levonorgestrel (LNG-EC) has been estimated in most previous studies by judging the day of ovulation from presumptive menstrual cycle data, thus providing poorly reliable estimates. The assumption that all luteal phases last for 14 days, contributed to the erroneous results

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levonorgestrel given before or after ovulation  
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In another study published recently\*, a more rigorous methodology was used to ascertain expected ovulation, in relation to LNG administration for EC. The efficacy of LNG-EC was determined in 393 cycles by dating ovulation on the basis of reliable hormonal and ovarian parameters validated by a database constructed in a separate study.

When the efficacy was determined separately for cycles in which LNG-EC was given before or after ovulation the findings were as follows: Among the 103 women who took LNG-EC before ovulation (days –5 to –1), 16 pregnancies were expected and no pregnancy occurred ( $p<.0001$ ). Among the 45 women who took LNG-EC on the day of ovulation (day 0) or thereafter, 8 pregnancies

occurred and 8.7 were expected ( $p=1.00$ ). These findings are incompatible with the inhibition of implantation by LNG-EC in women.

Authors conclusion: LNG-EC is highly effective for preventing unintended pregnancy when it is used before ovulation, but when used after ovulation, it is completely unable to prevent pregnancy because it has no effect on subsequent reproductive processes, including implantation of the embryo.

For all of us who look after women, the limitations of emergency contraception need to be understood .

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