

## JOURNAL REVIEWS

Qlaira if aggravation, exacerbation or new risks appear. No epidemiological studies on the effects of estradiol/estradiol valerate containing COCs exist. All of the following warnings and precautions are derived from clinical and epidemiological data of ethinylestradiol-containing COCs. Whether these warnings apply to Qlaira is unknown. Some studies suggest an association between COCs and an increased risk for venous and arterial thromboembolism. Risk for venous thrombosis associated with COCs increases with: age, family history of VTE, immobilisation, major surgery, any leg surgery, major trauma, obesity. There is an increased risk of VTE with any COC use compared to no COC use. The risk is highest in the first year of COC use but still much lower than that associated with pregnancy. VTE can be fatal. The risk of VTE during Qlaira use is currently unknown. Risk for arterial thrombosis or a cerebrovascular accident increases with: age, smoking, family history of arterial thromboembolism, obesity, dyslipoproteinaemia, hypertension, migraine, valvular heart disease, atrial fibrillation. Advise users to contact a doctor at first sign of possible thrombosis (e.g. chest or limb pain, breathlessness, numbness etc.). If thrombosis suspected or confirmed, stop COC use; consider increased risk during the puerperium. Diabetes, systemic lupus erythematosus (SLE), haemolytic uraemic syndrome (HUS), chronic inflammatory bowel disease and sickle cell disease are associated with increased risk of vascular events. Stop medication immediately if increase in frequency/severity of migraine, significant hypertension, or pregnancy occurs. Some studies suggest increased risk of cervical and breast cancer associated with COC use. Hepatic tumours have been reported with isolated cases of life-threatening haemorrhage. Possible increase in risk of pancreatitis if presence of family history of hypertriglyceridaemia. Certain conditions may occasionally occur or deteriorate: cholestatic jaundice and/or pruritus, gall stones, porphyria, SLE, HUS, Sydenham's chorea, herpes gestationis, otosclerosis-related hearing loss, depression, epilepsy, Crohn's disease, ulcerative colitis, chloasma. Stop COC use if recurrence of pregnancy or sex-steroid related jaundice or cholestasis – related pruritus occurs. Angioedema may be induced or exacerbated in women with hereditary angioedema. Acute or chronic disturbances in liver function may occur. If this happens stop COC use until markers of liver function return to normal. Chloasma may occur. If tendency to chloasma present, advise avoidance of sun/uv radiation. Contains not more than 50 mg lactose per tablet, which should be considered for patients with intolerance to certain sugars. Include personal and family medical history and physical examination as part of assessment prior to treatment. Blood pressure should be measured and a physical examination should be performed, guided by the contraindications and warnings. The frequency and nature of examinations should be based on established practice guidelines and adapted to the individual woman. Investigate bleeding irregularities that occur after regular cycles. Certain conditions, such as cardiac or renal dysfunction and diabetes during initial usage, require strict medical supervision. **Interactions:** Interaction with specific drugs will necessitate additional non-hormonal contraceptive measures. Qlaira may affect the metabolism of other medicines. Lab tests may be affected. The prescribing information of concomitant drugs should be consulted to identify potential interactions. **Pregnancy and lactation:** Qlaira should not be used during pregnancy or recommended during lactation. **Effects on ability to drive and use machines:** Qlaira has no influence on the ability to drive or use machines. **Undesirable effects:** Common - Headache (including tension headache), abdominal pain (including abdominal distension), acne, amenorrhoea, dysmenorrhoea, intracyclic bleeding (metrorrhagia), breast discomfort, weight increase. Serious side effects cf. CI/Warnings and Precautions – in addition hypertension, cervical dysplasia, migraine, uterine leiomyoma, genital hemorrhage, presumed ocular histoplasmosis syndrome, ruptured ovarian cyst. In addition to the above mentioned adverse reactions, erythema nodosum, erythema multiforme, breast discharge and hypersensitivity have occurred under treatment with ethinylestradiol-containing COCs (although these symptoms were not reported during the clinical studies performed with Qlaira, the possibility that they also occur under treatment cannot be ruled out). Other side effects - Prescribers should consult the SmPC in relation to other side effects. **Overdose:** There have been no reports of serious deleterious effects from overdose. Symptoms that may occur in case of taking an overdose of active tablets are: nausea, vomiting and, in young girls, slight vaginal bleeding. There are no antidotes and further treatment should be symptomatic. **Legal Category:** POM. **Package Quantities and Basic NHS Costs:** £25.18 per 3 x 28 tablets. **MA Number(s):** PL 00010/0576. **Further information available from:** Bayer Schering Pharma, Bayer plc, Bayer House, Strawberry Hill, Newbury, Berkshire RG14 1JA United Kingdom. Telephone: 01635 563000. **Date of preparation:** January 2009.

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**Adverse events should be reported.**  
Reporting forms and information can be found at [www.yellowcard.gov.uk](http://www.yellowcard.gov.uk).  
Adverse events should also be reported to Bayer Schering Pharma. Tel: 01635 563500, Fax: 01635 563703, Email: [phdsguk@bayer.co.uk](mailto:phdsguk@bayer.co.uk)

### Male circumcision for the prevention of HSV-2 and HPV infections and syphilis. Tobian AA, Serwadda D, Quinn TC, Kigozi G, Gravitt PE, Laeyendecker O, et al. *N Engl J Med* 2009; **360**: 1298–1309

Tobian and his team of researchers looked at data from two randomised controlled trials, to evaluate whether male circumcision in HIV-negative adolescents and adult men in Uganda would prevent acquisition of HSV-2, HPV and syphilis infection.

Previous clinical trials have shown protection against acquisition of HIV infection in circumcised males.<sup>1,2</sup> If circumcision could be shown to have further advantages in protecting against sexually transmitted infections (STIs) of even greater prevalence, this would add to support for circumcision as a beneficial public health intervention for males.

The trials in this study were carried out in parallel with a trial regarding male circumcision and HIV infection in Uganda. The research question in this case was clearly defined with regard to acquisition of HSV-2 or syphilis infection at baseline, 6, 12 and 24 months. A subgroup were evaluated for HPV infection at baseline and 24 months.

The authors did not describe how they randomised participants to intervention and control groups. There were no significant differences in the demographics of the two groups; however, there were some differences in sexual practices at baseline that could influence outcomes, namely significantly higher levels of condom use in the intervention group and higher alcohol use associated with sex in the control group. Results were adjusted to account for differences in sexual practice.

The method for selecting the small subgroup (609 of 3393 participants) for HPV testing was not described, although again the numbers appeared equally spread between the intervention and control groups.

In this study it was not possible to blind participants to which arm they were allocated; however, it was not described whether researchers carrying out follow-up questionnaires were blinded. Methodology for obtaining sexual behaviour data is not described, and may be significant for findings in such an intimate area.

Results relating to outcomes were clearly presented with robust statistical analysis. Acquisition of HSV-2, syphilis and HPV were described as hazard ratios and *p* values calculated both before and after adjustment for characteristics and practices. There was a significant reduction in HSV-2 and HPV infections, but no significant difference for syphilis infections. Confidence intervals were described and were supportive of the conclusions. The large number of participants lends further weight to the trial, although initial power calculations were not included in the report.

Overall, this is an important piece of research whose findings are significant in the debate surrounding effective interventions to combat the spread of STIs. The population involved here is one composed of young African heterosexual males, and we do not yet know if these findings can be extrapolated to Caucasian populations or to men having sex with men.

There is a postulated biological mechanism for the reduction in rates of HSV-2 and HPV infections in circumcised men involving

anatomical and cellular factors, therefore it is possible that this intervention will be more widely effective. This would, however, require further study.

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#### References

- 1 Bailey RC, Moses S, Parker CB, Agot K, Maclean I, Krieger JN, et al. Male circumcision for HIV prevention in young men in Kisumu, Kenya: a randomised controlled trial. *Lancet* 2007; **369**: 643–656.
- 2 Auvert B, Taljaard D, Lagarde E, Sobngwi-Tambekou J, Sitta R, Puren A. Randomised, controlled intervention trial of male circumcision for reduction of HIV infection risk: the ANRS 1265 trial. *PLoS Med* 2005; **2**(11): e298.

### Prevalence of child marriage and its effect on fertility and fertility-control outcomes of young women in India: a cross-sectional, observational study. Raj A, Saggurti N, Balaiah D, Silverman JG. *Lancet* 2009; **373**(9678): 1883–1889.

This very interesting and yet alarming article gives us an insight into the health consequences of the still prevalent child marriages in India. Defined as marriage before 18 years of age, child marriage has serious health consequences for national development and grave health consequences for both the young women and their children. India has maintained laws against child marriage since 1929. However, the legal age for marriage was increased from 12 to 18 years in 1978.

In this study, participants were selected from the India National Family Health Survey-3 (November 2005–August 2006). A nationally representative household-based sample was obtained and a uniform sampling design was used across all states. From a staggering sample of 124 385 women, a 95% response was obtained.

The results obtained are eye opening. More than two-fifths of women aged 20–24 years were married before the age of 18 years. Almost half of these women were married before 16 years, of which one-ninth were married before 13 years. Poor, less well-educated girls from the rural areas of Central or Eastern areas of the country were more vulnerable to this practice.

This practice is associated with poor contraceptive uptake and hence increased incidence of unwanted and terminated pregnancies. There is also increased incidence of repeat childbirth within 24 months. A marked association between child marriage and female sterilisation has been shown. Sterilisation reduces condom use in couples, thereby increasing risk of HIV and other sexually transmitted infections.

The recommendations from this study conclude that through government health care initiatives, India should establish reduction of child marriage as an essential element to build on the existing priorities of family planning, and maternal and child health. However, in drawing their conclusions, the authors admit that since their data were based on self-report, they are vulnerable to social desirability and recall biases.

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