**JOURNAL CLUB**


Although cervical cancer is now relatively uncommon in the UK, worldwide it is the second most common cause of cancer-related mortality in women. Persistent infection with oncogenic high-risk HPV viruses is the single most important factor in the development of pre-invasive and invasive cancer. Oncogenic types of HPV DNA are detected in virtually all cervical cancers and recognition of this crucial role has stimulated the investigation and development of HPV vaccines in both prophylactic and therapeutic settings. Such strategies could prevent cancer deaths, especially in developing countries where population screening is not feasible and therapeutic options can be limited. This paper presents an interim analysis of a large, double-blinded, multicentre randomised controlled trial. The aim of this trial is to determine if a HPV 16 virus-like particle (VLP) vaccine will prevent HPV 16 infection. A total of 2324 women, recruited from advertising at college campuses in the US, received three doses of either HPV 16 vaccine or placebo. The analysis presented is restricted to 1598 women with the eligible criteria of having no serological or DNA evidence of either current or previous HPV 16 infection at enrollment or 1 month after completing the vaccination regimen. Completion of the trial requires 4 years of follow-up post-vaccination and the median follow-up of this subgroup was 17.4 months. Of the women receiving the active vaccine, 99.7% seroconverted with mean antibody titre of 1510 mIU/mL compared with < 6 mIU/mL in the placebo arm. There were no serious adverse events reported and the most common side effect was pain at the injection site. One woman subsequently developed a persistent HPV 16 infection and nine women a HPV 16-positive cervical intraepithelial neoplasia (CIN) lesion. A total of 73 women had received placebo. This represents an incidence of persistent HPV 16 infection of 3.8 per 100 woman-years for the placebo arm and 0 per 100 woman-years in the vaccine arm. The data were also analyzed of HPV 16-negative CIN lesions which were equally distributed between the two arms. These early results on prophylactic HPV 16 vaccine are exciting and support the hypothesis that vaccination will prevent persistent HPV 16 infection. The vaccine appears to be safe and able to produce a significant serological response. HPV infection is extremely common and around 80% of women will have an HPV infection at some time before age 30. For the majority of women, these infections are transient and of no clinical significance and fewer than 10% of women with a persistent HPV infection will subsequently develop cervical cancer. This study has concentrated on HPV infection but it is fundamental to confirm whether preventing infection will impact on deaths from cervical cancer. The subjects in this study come from a high prevalence group. A public health vaccination programme will be directed by sexual behaviour and we need to know if the effect of vaccination on a population-based cohort. This is of particular importance in the developing world where such rigorous selection criteria and evaluation of HPV infection are not practical and the impact on cervical cancer, where screening is not an option, needs to be seen. This will require much larger population programmes with long-term follow-up. In addition, HPV vaccines are known to be highly specific and vaccinating against one subtype may produce less effect on cervical disease as other HPV infections replace the eliminated type. Effective vaccination against HPV has been anticipated for a number of years now and this demonstrates a highly significant impact on HPV 16 infection. The completion and final analysis of the trial will be as important as these early results and may produce essential data on the durability of protection offered by such a vaccination regime.

Reviewed by Maggie Cruikshank, MB ChB, MRCOG
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This small study questioned 186 university students on their understanding of the risks of venous thromboembolism (VTE) when taking the combined oral contraceptive (COC). One hundred and forty-five women in this group were taking the pill or had taken it in the past. The women were randomly divided into two groups. One group had the standard information about the COC and the other group had additional information about the risks of VTE following the statement of the Committee on Safety of Medicines (CSM) in 1999, where the previous advice of 1995 was withdrawn. Only about two thirds of each group could give the correct advice when asked in a questionnaire. The additional information made no difference. The authors are of the opinion that there is very little research done on how to put information cross to women regarding the risks of the pill, especially when information becomes sensationalised by unbalanced reporting in the press.

Reviewed by Judy Murty, DRCOG, MFFP
SCMO, Contraceptive and Sexual Health Services, Leeds, UK


This paper reviews a method of starting the pill at the first visit to the clinic. The authors describe it as the ‘Quick Start’ method. They consider that the traditional way of starting the pill on the first day of the menstrual cycle is to avoid an unexpected pregnancy occurring in the first packet of pills. It is now established that taking hormones in early pregnancy are not harmful to the fetus so it does not matter when the pill is started. The authors have used the Quick Start method of starting the combined oral contraceptive (COC) for several years in their clinics and it is offered to patients at the discretion of the provider. How they advised starting the pill was at the preference of the clinician. The study was not randomised. Two hundred and fifty women were recruited and 62 (25%) took the first pill at the clinic. The study reviewed the continuation rate of the method after one cycle. The authors believe that continuing with the COC was if the partner was aware (odds ratio (OR) 3.9; CI 1.9–8.3), this was followed by Quick Start (OR 2.8; CI 1.1–7.3). There were no differences in bleeding pattern when the Quick Start method was used. This study was not randomised and it depended on the clinician’s opinion whether the woman was offered Quick Start. In addition, the follow-up time was very short. So is the analysis reflecting the clinicians’ practice rather than the way the pill is started? The authors admit that a randomised trial is needed to see if there is a true effect. Does it help at all if the patient makes her own practice? The authors feel that it reduced the amount of counselling needed at the first visit as the women needed less information about how and when the pill is started. They do not forget the information. I am sure we all have instances in our own practice where young women have become pregnant after receiving the pills and before starting them. Maybe by getting them to start at the first visit will reduce the chance of pregnancy if they are not already at risk. Would it not be interesting to see when the women want to start the pill rather than when the clinician feels is the best time?

Reviewed by Judy Murty, DRCOG, MFFP
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US Government attacked on sexual health policies

In its role as Premier of the US Department of Health and Human Services, Dr. Donna Shalala, Secretary of the Department, has been attacked by the US Government attacked on sexual health policies. Shalala has been criticized for her position on sexual education. The information previously advised abstinence does not foster earlier sexual activity. The US Government attacked the American Civil Liberties Union for financially supporting Abstinence Education Programs which are part of the Bush administration’s ‘seemingly single-minded determination to strip women of reproductive rights and access to reproductive health services’. IPPF lost $18 million in US Government funding for Abstinence Programs. Younger adolescents who ‘pledge’ do delay first intercourse compared with those who choose not to pledge. However ‘pledging’ makes no difference to the sexual debut of 18-year-olds, evidence that ‘pledging’ is not likely to use contraception at first intercourse.

The International Planned Parenthood Federation (IPPF) General Director, Dr Steven Goodship, spoke recently of George Bush’s ‘seemingly single-minded determination to strip women of reproductive rights and access to reproductive health services’. IPPF lost $18 million in US Government funding for Abstinence Programs. Younger adolescents who ‘pledge’ do delay first intercourse compared with those who choose not to pledge. However ‘pledging’ makes no difference to the sexual debut of 18-year-olds, evidence that ‘pledging’ is not likely to use contraception at first intercourse.

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