
We are becoming accustomed to reading encouraging reports on the human papillomavirus (HPV) vaccine performance; from the initial observations where the monovalent HPV 16 vaccine prevented vaccine-type infection, to the high efficacy for quadrivalent vaccines demonstrated in the various clinical trials of the bivalent and quadrivalent vaccines. Justification for the introduction of costly HPV immunisation programmes has been predicated, heavily, on the reduction of high-grade cervical lesions (as a surrogate for cancer); however, there is clearly more to HPV-related disease and, indeed, cervical disease management than high-grade cervical lesions.

As a consequence, this article reports on a combined analysis of two quadrivalent vaccine prophylactic clinical trials (in women). Where efficacy for the reduction of low-grade lesions (including low-grade cervical and vulvo-vaginal lesions and genital warts) was assessed at each dose of vaccine, and where the bivalent and quadrivalent vaccines had high efficacy in per-protocol populations has been described previously. What is more interesting is that vaccine efficacy against any CIN 1 (irrespective of the HPV genotypes involving the lesion) was 30% (17–41%) in women who had received at least one dose of vaccine and who were HPV (vaccine type) negative at recruitment. It was also notable in this vaccine that both HPV 6 and 11 appeared to contribute to around 7–8% of CIN 1. Precise data on the burden of CIN 1 attributable to low-risk HPV types have been scarce, and may become an important consideration when considering the relative benefits of the quadrivalent and bivalent vaccines.

One limitation of this study (although acknowledged by the authors) is that the HPV-naive population were tested for (only) 14 types (i.e. vaccine types and 10 others). It is feasible that given that age of the recruits (16–26 years), other HPV types could have been present and responsible for low-grade lesions (known to harbour greater heterogeneity of infecting types compared with high-grade lesions). This said, ultimate HPV positivity would lead to an underestimation rather than overestimation of vaccine efficacy.

To conclude, these findings are positive: low-grade cervical abnormalities account for the majority of cervical abnormalities (in countries where cervical screening is offered) and their management can be challenging, hence the protracted and contentious debate on how to şiŋe them optimally. From a surveillance perspective, we have an opportunity to monitor the prevalence of low-grade lesions as an early metric of vaccine success.

Reviewed by Kate Cuschieri, PhD

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Reference

FICTION BOOK REVIEW


The novel opens in 1942 in a San Francisco torn apart by wartime activity and gives hints of earlier personal failures, before shifting back to Margaret’s formative years growing up in the Midwest during the 1880s. Although a popular device, it was irritating to know the ending before the rest of the story, which is otherwise told in chronological order, with the dates heading up each chapter. The historical events occurring in the background during sixty years are only lightly drawn. Like most of the events in Margaret’s life, they flow around her, increasing her bewilderment and helplessness.

The civil war provides the backdrop to Margaret’s early years. A self-contained child, she seems outwardly little affected by being taken to see a public hanging, although it becomes apparent (much) later that the memories were suppressed. Further traumatic events include the death of her two older brothers and the suicide of her father. Margaret is rejuvenated and released by the death of her husband, and moves with her daughter to her father’s farm. There the daughters are brought up to be wives and mothers. In a lengthy middle section of the novel, in which the younger daughters grow up and marry, Jane Smiley captures the rural unhurried life. Margaret reads classics, sews, takes long bicycle rides is a revelation; a glimpse into a freer, more to HPV-related disease and, indeed, cervical disease management than high-grade cervical lesions.

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Finally, at 27 and almost despairing, Margaret meekly types up Andrew's theories describing the change in Margaret when she eventually holds her son, her overwhelming absorption into being one with him, is excellent and moving. So, too, is her gradual realisation that the baby is seriously ill and the changes wrought by Rhesus incompatibility are minutely described. The reader is reminded of Margaret’s ability to contain her emotions, to remain passive and accepting of her fate despite her evident depression following the death of the child and Andrew's increasing eccentricity.

Margaret accepts Andrew's theories – she is increasingly sceptical of them but says nothing – and Andrew persists in refining and self-publishing his ideas in a fever of conviction that leaves no time for either of them to do much of anything else. If Andrew is guilty of megalomania and incuriosity about the woman he married, Margaret is guilty of battenning down and bearing, never saying anything to a man who needs a bit of reality. Both Andrew’s mother and Margaret’s leave hints about how marital life may help us to understand and empathise with the impossibility that Margaret might manage to prevent her husband, Andrew, from sliding from eccentricity into madness, give insights which, although from a previous age, are around us now in the many societies where women have no power. The moving descriptions of the emotional impacts of motherhood and the death of a baby may help us to understand and empathise with others.

Reviewed by Gill Wakley, MD, FFSRH

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Four year efficacy of prophylactic human papillomavirus quadrivalent vaccine against low grade cervical, vulvar, and vaginal intraepithelial neoplasia and anogenital warts: randomised controlled trial
Kate Cuschieri

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