JOURNAL REVIEW

Four year efficacy of prophylactic human papillomavirus quadrivalent vaccine against low grade cervical, vulvar, and vaginal intraepithelial neoplasia and anogenital warts: randomised controlled trial. FUTURE I/II Study Group, Dillner J, Kjaer SK, Wheeler CM, Sigurdsson K, Iversen OE, Hernandez-Avila M, et al. *BMJ* 2010; **341**: c3493

We are becoming accustomed to reading encouraging reports on human papillomavirus (HPV) vaccine performance; from the initial observations where the monovalent HPV 16 vaccine prevented vaccine-type infection, to the high prophylactic efficacy for disease 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 protocols (involving recruitment of over 17 000 women), where efficacy for the reduction of low-

grade lesions (including low-grade cervical and vulvo-vaginal lesions and genital warts) was assessed. The results are encouraging: vaccination led to a substantial reduction in the burden of all of these lesions (>95% in the per-protocol population). With respect to warts, the data are more reassuring than novel as high efficacy in per-protocol populations has been described previously.¹ What is more interesting is that vaccine efficacy against any CIN 1 (irrespective of the HPV type driving 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 that 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-‘naïve’ 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, under-reporting of 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 triage them optimally! Finally, 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

- 1 Garland SM, Steben M, Sings HL, James M, Lu S, Raikar R, et al. Natural history of genital warts: analysis of the placebo arm of 2 randomized phase III trials of a quadrivalent human papillomavirus (types 6, 11, 16, and 18) vaccine. *J Infect Dis* 2009; **199**: 805–814.

FICTION BOOK REVIEW

Private Life. Jane Smiley. London, UK: Faber & Faber, 2010. ISBN-13: 978-0-57125-874-1. Price: £12.99. Pages: 432 (paperback)

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 background 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. Her mother appears invigorated and released by the death of her husband, and moves with her daughters 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 walks, and makes jams and cordials. Her first bicycle ride is a revelation; a glimpse into a freer, faster, more dangerous life.

Finally, at 27 and almost despairing, Margaret marries Captain Andrew Early, 34, an astronomer who has returned to his home town under a cloud of scandal. Andrew is odd and aloof, but at least he's interesting, and he immediately bears her off to faraway California, where he has a position at a naval observatory near San Francisco.

These middle chapters describe the ways that Margaret's marriage shapes and circumscribes her life. It's a remarkable portrait not only of Margaret but of her husband, the sort of fellow who's convinced he's always getting the short end of the stick. Andrew is obsessed with his scientific theories that can't gain acceptance because a man named Albert Einstein has arrived on the scene who has the universe all wrong, but has managed to hoodwink everyone.

Conventionally, babies are to be produced. The expectation and disappointments of a miscarriage are well portrayed, but the section 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 meekly types up 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 up, 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 might be conducted otherwise – Margaret discovers letters in which Mrs Early chastised her son for the mistakes of pride and ego to which he is prone, and Mrs Mayfield's advice to her daughter as she leaves Missouri is that “a wife only has to do as she's told for the first year”. But Margaret has always been passive.

Margaret escapes the claustrophobic presence of her husband to visit a family of coots that live on the pond near her house. So taken is she with that happy brood that she asks Mr Kimura, a Japanese friend, to paint it for her. He does so, quickly and delicately, in a scroll that delights her. As she continues to visit the pond, to her dismay the chicks begin to disappear. When she goes home, heartsick, and studies Mr Kimura's painting, she sees what he saw all along: the green gold water, the golden hill above it, and then a stray chick, “larking about, swimming fast enough to make ripples”. Perched on a branch above is the outline of a menacing crow. This simile for her life begins to dawn on her – she doesn't see the perils until they have overtaken her – and the letters from her mother and her mother-in-law give her further insights.

Her life is contrasted with that of Dora, her unmarried sister-in-law, with independence conferred by having money of her own. However, exciting as Dora's life appears, she has her downfall. Excitement in Margaret's life is only hinted at, with the sexual and friendship relationship with the mysterious Cossack Pete.

The stultifying restrictions of a social order that insisted that marriage and childbearing were the only occupations for a woman, and 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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We hope that journal readers enjoyed reading *Private Life* and *Daughter of Dust: Growing Up an Outcast in the Desert of Sudan* (page 230), and also discovering whether their opinion of these books matched that of our guest reviewers. In the January 2011 issue, the fiction books under scrutiny will be *The Children's Book* by A S Byatt (624 pages, Vintage, 2009, ISBN-13: 978-0-09953-545-4, £7.99, paperback) and *The Shape of Her* by Rowan Somerfield (288 pages, Wiedenfield & Nicholson, 2010, ISBN-13: 978-0-29785-840-9, £12.99 paperback). We will also review another book that Journal readers might be interested in reading as follows: *Antigona and Me* by Kate Clanchy (273 pages, Picador, ISBN-13: 978-0-33044-933-5, £7.99, paperback).

We want to remind journal readers that if they would like to offer to review an appropriate fiction title of their own choosing then they should contact the Journal Editorial Office by e-mail (journal@fsrh.org) in the first instance with details of their nominated title