

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
Retired Professor of Primary Care Development and Freelance Writer, Abergavenny, UK

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

FICTION BOOK REVIEWS

Daughter of Dust: Growing Up an Outcast in the Desert of Sudan. Wendy Wallace. London, UK: Simon & Schuster UK Ltd, 2009. ISBN-13: 978-1-84737-530-8. Price: £12.99. Pages: 368 (paperback)

Wendy Wallace has spent many years in Sudan and tells Leila's story with fine attention to detail. She uses the story to explore the distress of exclusion from a deeply traditional society, the tensions between progressive and reactionary political forces and the cruelty, particularly of women to one another, in a world where women have no other power. The casual assumption of the men that they own females – even distant relatives – and can decide on their fate is contrasted with the caring nature of "Father Saif" who runs the orphanage where Leila spent most of her formative years and wants her to decide for herself about her future.

This is a story of a woman who has had the resilience to endure many vicissitudes. After abandonment, changes of orphanages, a glimpse of freedom in Jordan learning secretarial skills, temporary marital happiness and children, rejection by her husband and destitution, she goes on to establish an organisation to challenge the rejection of unwanted children – the "daughters of sin". The book provides a refreshing glimpse into a country often reported on in news bulletins. These events go on in the background in the book and sometimes influence how Leila has to behave, but the emphasis is on the small details of everyday life.

Leila's early life is so thoroughly recalled that it raises doubts: could anyone remember this much? The juxtaposition of Leila's beliefs and knowledge before and after an event which reveals injustice or betrayal is a clever device. It brings home her early ignorance about almost everything and the bewilderment of a child whose mother became unable to care for her and her sister. The lack of raw emotion I felt comes, perhaps, from an excess of pain – endurance rather than anger. The description of female circumcision captures well its almost universal acceptance – and even pride in it as a "purification ceremony".

Readers should not dismiss the events in this book as being those of a country far away with customs foreign to us. We will encounter many women from Sudan and other similar countries in our clinics and surgeries and we need to understand the background that leads them to be so accepting of their fate. Similarly, our own treatment of the excluded – the children who are rejected by our society for not having mothers who can care for them – is not something that lies comfortably with my own conscience. So many children who have been in care, or are from "careless" families, are damaged emotionally or physically. Many go on to survive in the adult world with drugs, prostitution and crime. Perhaps our society can learn something from the care Leila now champions.

Reviewed by **Gill Wakley**, MD, FFSRH
Retired Professor of Primary Care Development
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Daughter of Dust: Growing Up an Outcast in the Desert of Sudan. Wendy Wallace. London, UK: Simon & Schuster UK Ltd, 2009. ISBN-13: 978-1-84737-530-8. Price: £12.99. Pages: 368 (paperback)

Daughter of Dust: Growing Up an Outcast in the Desert of Sudan is one woman's account of her life growing up in Khartoum. Reflecting a culture where sex outside of marriage is forbidden, this narrative elegantly describes the resulting shame and alienation of the women whose children are born out of wedlock. The book highlights the unwanted pregnancies and courageous stories of the children who are subsequently abandoned, growing up in orphanages across Sudan.

Starting with her early life in the desert city, Leila believes that she is an outcast. Brought up in an orphanage from a very early age, Leila fights to find the truth of her heritage. She has no answer to the question of what terrible deeds have brought her to this loveless existence.

The first half of the book focuses on Leila's childhood years, where she is selected to move to a special children's home with Amal, her best friend. The story continues through her adolescence into adulthood, where she is later employed at the home as a secretary.

The story spans her marriage, the birth of her children and her ensuing happiness and heartbreak. Against the odds, she succeeds in founding a women's and children's charity for orphans, truly creating triumph from adversity.

This heart-warming book tells of a woman's struggle from birth to adulthood in an often cruel and judgemental society. Leila's courage and self-belief remain paramount throughout; she never falters in the idea that everyone 'belongs' somewhere. This is a brave novel that captures the essence of Leila's fight. At times parts of the story are difficult to follow, possibly due to the challenge of translation. However, the second half of the book has greater clarity.

Working in a clinic that provides a dedicated service for women who have undergone female genital mutilation (FGM), I had hoped that the narrative would discuss this subject in further depth. FGM is mentioned on the cover and associated advertising. I was disappointed to find that very little of the book is dedicated to this important topic – a missed opportunity perhaps?

Despite its limitations, the book provides an interesting insight into the life of a woman living on the outskirts of accepted society and culture of Sudan. As such, it makes a worthwhile and thought-provoking read.

Reviewed by **Katie Hopkins**, RGN, DipHe
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Editor's note

Katie Hopkins is a health adviser who works at the West London Centre for Sexual Health. Her specialist subject is female genital mutilation (FGM) and she offers a dedicated service for people with FGM. For support and advice please contact Katie on +44 (0) 208 846 1579 or alternatively e-mail her at cxh.healthadviser@chelwest.nhs.uk.

READERS' CONTRIBUTIONS INVITED ON 'A BETTER WAY OF WORKING'

The Journal publishes occasional 'A Better Way of Working' articles, the purpose of which is to disseminate service delivery suggestions likely to be of interest and relevance to the Journal's readership. Readers are invited to submit suggestions based on their own personal experience for consideration by the Journal Editor. Contributions normally should not exceed 1000 words and should be written in a standardised format responding to the following four questions (or similar): Why was change needed? How did you go about implementing change? What advice would you give to others who might be considering a similar course of action? How did you show that the change had occurred? All contributions should be submitted via the Journal's online submission system at <http://jfrhc.allentrack.net>.

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 or 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, amenorrhea, dysmenorrhea, 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.

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Adverse events should also be reported to Bayer Schering Pharma. Tel: 01635 563500, Fax: 01635 563703, Email: phdsuk@bayer.co.uk