# Women's Health Research Review

Making Education Easy

Issue 24 – 2017


## In this issue:



**Abbreviations used in this issue**

**FSRH** = Faculty of Sexual and Reproductive Healthcare
**HPV** = human papillomavirus
**IUD** = intrauterine device
**LARC** = long-acting reversible contraceptive

PHARMACY GUILD OF NEW ZEALAND

NZMA New Zealand Medical Association

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# Welcome to the latest issue of Women's Health Research Review.

This month we report sobering statistics for the treatment of gonorrhoea in NZ, a survey of the acceptability of self-collected HPV testing, and a report of the risk of ischaemic stroke associated with combined hormonal contraceptives in women with migraine. We also report safety outcomes for salpingectomy versus tubal occlusion for female sterilisation, retreatment rates after hysterectomy or laparoscopy for endometriosis, and the long-term effects of transobturator tape procedures in women with stress urinary incontinence.

We hope you find these and the other selected studies interesting, and welcome any feedback you may have.

Kind regards,


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## Treatment of gonorrhoea in Auckland, New Zealand: marked variation in prescriber adherence to treatment guidelines

**Authors:** Forster R et al.


**Summary:** This NZ study determined the proportion of patients with gonorrhoea who were treated according to NZ Sexual Health Society (NZSHS) guidelines. Treatment given to 706 adult patients with laboratory-proven gonorrhoea in Auckland during the first 6 months of 2015 was reviewed. Only 65% of episodes were treated according to current NZSHS guidelines. Guideline-compliant treatment was significantly more likely in patients who presented to a sexual health clinic (89%) than in those who presented to a general practice or community clinic (52%), or to a hospital (56%). 21% of patients who presented to a hospital and 8% of patients who presented to a general practice or community clinic were not treated with an antimicrobial regimen by the service that made the diagnosis.


**Comment (HR):** Rather sobering statistics here. Almost 10% of patients attending a general practice or other community provider and over 20% of patients attending a hospital service received no antimicrobial therapy from these services. Four recommendations for improving adherence to NZSHS guidelines are: (i) the inclusion of specific treatment advice, such as 'The treatment recommended for almost all patients with gonorrhoea is ceftriaxone 500mg IM PLUS azithromycin 1g PO stat. (For more information see: NZ Sexual Health Society Guidelines 2014)' on all community and hospital microbiology laboratory reports documenting the presence of *Neisseria gonorrhoeae* in a clinical specimen; (ii) increasing the ease of access to sexual health clinics for patients with sexual health problems; (iii) providing a link to the NZSHS treatment guidelines in the proposed electronic laboratory test ordering system; and (iv) ongoing education in primary and secondary care on the diagnosis and management of sexually transmitted infections.


***Reference: Intern Med J 2017;47(6):640-48***
Abstract


**Independent commentary provided by Associate Professor Helen Roberts**

Helen is Associate Professor Women's Health at the University of Auckland and involved with both undergraduate and postgraduate medical education in O&G.

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**Independent commentary provided by Dr Anil Sharma**

Anil works in gynaecology private practice from Ascot Central and Ascot Hospital. His key interests are in menstrual problems including fibroids, urogynaecology and endometriosis. **FOR FULL BIO CLICK HERE.**



## Clinician and patient acceptability of self-collected human papillomavirus testing for cervical cancer screening

**Authors:** Mao C et al.

**Summary:** This study evaluated clinicians' and patients' attitudes about home self-collected HPV testing for cervical cancer screening. 1,769 women who were participating in a randomised trial comparing home self-collected HPV testing to standard clinician-collected Pap screening were surveyed. 59.1% of them said they preferred self-collected HPV testing to clinician-collected tests, mostly because of convenience or time saving (82.7%), and for avoiding embarrassment or discomfort associated with pelvic examination (38.1%). Those who did not prefer self-collected HPV testing reported greater faith in clinician-collected samples (56.7%) or wanted a clinic visit so they could address other issues (42.4%). 118 physicians and midlevel providers also completed the survey. 78.0% of them reported that they would recommend a self-collected HPV test if it had high sensitivity and was cost-effective.

**Comment (HR):** This is interesting news, although in NZ when the new screening starts we will be changing from liquid- based cytology screening to primary HPV screening. The smear will be taken in the usual way and the liquid sample tested for the presence of HPV. Women who test positive for the high-risk HPV types (16 and 18) will be referred to colposcopy services. Women with other types of high-risk HPV will automatically have cytology performed on their samples to determine whether they are high or moderate risk for abnormal cell changes to help doctors make the best assessment and treatment decisions. The National Screening Unit website has a frequently asked questions area. This is what it says about women taking their own samples … "In the future it is possible that some women will be able to take their own sample for HPV testing. There are still questions to address regarding how self-sampling would work in New Zealand and how women would be supported for any follow up testing or treatment required. The Ministry of Health is funding further research about the acceptability and feasibility of self-sampling in New Zealand and is also investigating the effectiveness of different self-sampling devices. Any self-sample test needs to be as safe and effective as a sample collected by a smear taker". The new screening test was due to start next year in 2018. At present though it looks as if it might be late 2018 at the earliest, and may well be 2019.

***Reference: J Women's Health 2017;26(6):609-15***
Abstract

## IUD use among parous women and risk of uterine perforation

**Authors:** Heinemann K et al.

**Summary:** This analysis of data from the European Active Surveillance (EURAS) Study on Intrauterine Devices investigated whether delivery and lactation are risk factors for complete IUD perforations. Of 61,448 women enrolled in the study, there were 58 complete perforations (30 in lactating women). The incidence of IUD perforation (per 1000 insertions) was 4.5 for lactating women and 0.6 for nonlactating women. Time since delivery was also associated with IUD perforation risk.

**Comment (HR):** This reanalysis of the EURAS data looked only at complete perforations through the myometrium. The data were also analysed according to the time since delivery. Breastfeeding women <36 weeks since delivery had 3 times the risk of perforation than those >36 weeks post-delivery presumably due to the improvement in myometrial strength and thickness. The study does not comment on IUD insertion immediately post-delivery. The new 2017 FSRH guidelines urge District Health Boards to have enough staff trained to insert IUDs immediately post-delivery should a woman wish this. Interestingly, a Cochrane Review about intrauterine contraception soon after childbirth does not show an increase in perforation over the normal risk if performed within 10–30 minutes of placental delivery.

***Reference: Contraception 2017;95(6):605-7***
Abstract

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For more information, please go to www.medsafe.govt.nz

## Use of combined hormonal contraceptives among women with migraines and risk of ischemic stroke

**Authors:** Champaloux S et al.

**Summary:** This US study investigated the risk of ischaemic stroke in women with migraine taking combined hormonal contraceptives. 25,887 females aged 15–49 years who had a first-ever stroke in 2006–2012 were age-matched (1:4) with controls. Compared to females with neither migraine nor combined hormonal contraceptive use, odds ratios for ischaemic stroke were 6.1 in those with migraine with aura using combined hormonal contraceptives; 2.7 in those with migraine with aura not using combined hormonal contraceptives; 1.8 in those with migraine without aura using combined hormonal contraceptives; and 2.2 in those with migraine without aura not using combined hormonal contraceptives.

**Comment (HR):** Migraine with aura is a well-known contraindication to combined pill use and is UK Medical Eligibility Criteria for Contraceptive Use (UKMEC) 4 – do not use. Progestogen-only methods and IUDs are appropriate for women with this history. The last sentence of this research says it all "Accurately distinguishing migraine type and presence or absence of aura is critical for both future investigation and clinical decision making". So what is migraine with aura? Migraine accompanied by numbness or tingling affecting one arm is a relatively easy history to elicit .Unlike stroke the legs are not usually affected and there is no loss of power. However, the visual symptoms seem to be more confusing. Is it the presence of photophobia or the flashing lights or the fortification spectra or blurring of vision? It is none of these. The issue is well laid out in an article by Anne MacGregor who points out that the migraine headache usually follows aura and that there may be a gap of several hours. Visual aura is present in over 98% of auras. The classic description is a scotoma – an enlarging blank spot which increase in size. The edge of the scotoma may appear as zig zags or fortification spectra. The scotoma persists even with the eyes closed as it is emanating from the visual cortex. Visual aura symptoms are in one half of the visual fields of both eyes – homonymous hemianopia.

***Reference: Am J Obstet Gynecol 2017;216(5):489.e1-489.e7***
Abstract

## Implications of dispensing self-administered hormonal contraceptives in a 1-year supply

**Authors:** McMenamin S et al.

**Summary:** In 2016 the state of California passed legislation requiring health plans and insurers to cover a 12-month supply of self-administered hormonal contraceptives (e.g. contraceptive pill, patch or vaginal ring). This study assessed the implications of dispensing 12-months' supply at one time (estimated to occur in 38% of users) instead of smaller quantities. This change in dispensing patterns was estimated to result in 15,000 fewer unintended pregnancies, 2000 fewer miscarriages, and 7000 fewer abortions in California, decreasing total net health care expenditures by 0.03%.

**Comment (HR):** Previous research has shown a 30% reduction in the odds of unintended pregnancies with 12-month dispensing compared to 1- or 3-month dispensing. In this study, various assumptions were made in working out what the effect of this legislation might be. They say that the literature was reviewed to determine current utilisation of pills, patches and rings and unintended pregnancy rates among contraception users. The methodology does not clarify if use continuation was part of this review. We know now that LARCs are so much more effective because of their better use continuation; 80% at 1 year for LARCs and 68% at 1 year for the pill. A 12-month prescription of the pill initial supply may be problematic as the FSRH advises a follow-up visit 3 months after the first prescription of a combined hormonal method to allow blood pressure to be rechecked and assessment of any problems. However, after that yearly checks are all that are advised and a 12-month supply then could be a good idea.

***Reference: Contraception 2017;95(5):449-51***
Abstract

## Lifetime cancer risk and combined oral contraceptives

**Authors:** Iversen L et al.

**Summary:** This analysis of the Royal College of General Practitioners' Oral Contraception Study evaluated the lifetime cancer risks or benefits associated with the use of combined oral contraceptives. 46,022 women who were enrolled in the study in 1968 and 1969 were observed for up to 44 years. There were 4661 ever users with at least 1 cancer during 884,895 woman-years of observation and 2341 never users with at least 1 cancer during 388,505 woman-years of observation. Ever use of oral contraceptives was associated with reduced colorectal cancer (incidence rate ratio, 0.81), endometrial cancer (0.66), ovarian cancer (0.67), and lymphatic and hematopoietic cancer (0.74). An increased risk of lung cancer was seen only in ever users who smoked at baseline. The risk of breast and cervical cancer was increased in current and recent users but was lost within approximately 5 years of stopping the oral contraceptive, with no evidence of an increased risk of recurrence over time.

**Comment (HR):** This is the longest running study in the world on the health effects of the pill and it continues to provide ongoing information. The protection from colorectal and ovarian cancers may in fact persist for >35 years after stopping. It is interesting that the increased risk of breast cancer that was seen in current and recent users appeared to be lost within approximately 5 years of stopping oral contraception. These are the same findings as in the Oxford Family Planning Association Study and the Nurses Health Study. This is unlike combined hormone therapy use for menopausal women where the breast cancer risk persists after stopping. However, the incidence rate ratio for breast cancer increase was close to unity at 1.04 which translates into a very low attributable risk of 4.78/100,000 woman-years. Most of the pills used during this study will have been 50µg but, as the authors point out, we do have limited evidence to suggest similar effects from currently available products.

***Reference: Am J Obstet Gynecol 2017;216(6):580.e1-580.e9***
Abstract

## Safety outcomes of female sterilization by salpingectomy and tubal occlusion

**Authors:** Westberg J et al.

**Summary:** This study investigated the immediate and short-term safety of laparoscopic salpingectomy or tubal occlusion for female sterilisation. Outcomes for 149 procedures (81 salpingectomies and 68 tubal occlusions) at a single institution were reviewed. Salpingectomy and occlusion procedures had similar immediate (2.5% vs 2.9%) and short-term (4.9% vs 14.7%) complication rates. Surgical time was on average 6 min longer for salpingectomies than occlusion procedures (44 vs 38 min; p=0.018).

**Comment (AS):** Prophylactic removal of the fallopian tubes during other gynae operations has become popular. This is because of a 49% reduction in risk of ovarian cancer. Tubal occlusive methods of sterilisation also reduce ovarian cancer risks by 24–34%. This is a Californian retrospective cohort study looking at 81 salpingectomies vs 68 tubal occlusions. The immediate and short-term complication rates were not significantly different, although occlusion methods had more post-operative pain. Surgical time was around 6 minutes longer for salpingectomy and this operation required at least 3 keyhole ports (compared with 2 for occlusion). Despite a 3rd abdominal keyhole port being needed, pain was lower as occluding the tubes is painful. In our local scenario, costs are probably similar for both procedures. Also, the salpingectomy method avoids leaving Filshie clips behind (small silicon-lined titanium clamps), which whilst low risk, can migrate and (uncommonly) can cause problems including pain. The option of salpingectomies should be offered to women seeking permanent sterilisation but of course reversal of this operation is not possible unlike that for occlusion methods. Having said that, sterilisation should only be considered in the first place if the patient is certain that she doesn't want more children.

***Reference: Contraception 2017;95(5):505-8***
Abstract

## Retreatment rates among endometriosis patients undergoing hysterectomy or laparoscopy

**Authors:** Soliman A et al.

**Summary:** This US study determined the long-term retreatment rates after either hysterectomy or laparoscopy for endometriosis. 24,915 endometriosis patients who underwent hysterectomy and 37,308 who underwent laparoscopy were included. The estimated retreatment rates were 3.3%, 4.7%, and 5.4%, respectively, in the 2nd, 5th, and 8th year after hysterectomy, and 15.8%, 27.5%, and 35.2%, respectively, after laparoscopy. The hazard ratio for retreatment was 0.157 for women who underwent hysterectomy compared with laparoscopy.

**Comment (AS):** Endometriosis is a complex under-diagnosed chronic disease that leads to significant morbidity with dysmenorrhoea, dyspareunia, dyschezia, pelvic pain and subfertility. It also leads to an immense economic burden to society ($US69.4 billion in 2009 in the US). This US study looked retrospectively at women over 8 years (24,915 who underwent hysterectomy as treatment vs 37,308 who had laparoscopic surgery). Over the first year of follow-up, surgical retreatment rates were 2.6% vs 9.4%, respectively. Over 8 years of follow-up, surgical retreatment rates were 5.4% vs 35.2%, respectively. If one looked at all retreatment including medical treatments (nonsteroidal anti-inflammatory drugs, analgesics, combined oral contraceptive pill, hormones), then the 8-year retreatment rate was 76% (hysterectomy group) vs 90.8% (laparoscopy group). Only 43 of the hysterectomy group had a concurrent oophorectomy at index surgery. As endometriosis is an oestrogen-dependent disease this statistic is important in a more objective comparison with laparoscopy. This impressive, large retrospective study provides support to the surgical management of endometriosis including a hysterectomy if child-bearing is complete. Whilst more conservative surgery will be preferred by many women, the surgical retreatment rates for recurrent endometriosis will allow an informed discussion to take place.

***Reference: J Womens Health 2017;26(6):644-54***
Abstract



## Long-term outcomes of transobturator tapes in women with stress urinary incontinence

**Authors:** Karmakar D et al.

**Summary:** The E-TOT trial assessed long-term outcomes after surgery using transobturator tension-free vaginal tape for stress urinary incontinence. 341 women were randomised to receive either the 'inside-out' or the 'outside-in' procedure at a tertiary urogynaecology centre in the UK in 2005–2007. After a median follow-up period of 9.2 years, the adjusted response rate was 67.8%. In these women the overall patient-reported success rate was 71.6%, with a further 14% reporting 'improvement'. There was no significant difference between inside-out and outside-in groups. The success rate at 9 years was lower than that reported at 1 year (71.6% vs 80%; p=0.004), but similar to that at 3 years (73.1%). Eight percent of women needed further continence surgery, 4.5% reported tape extrusion/erosion, and 4.32% reported groin pain/discomfort.

**Comment (AS):** This study followed up 341 women with tension-free transobturator tapes (mid-urethral slings) for stress urinary incontinence for a median 9 years. There has been a relative paucity of longer term data for these obturator slings compared with retropubic ones. Mid-urethral slings are getting adverse publicity due to cases of complications with their use and their material similarity with the now withdrawn vaginal mesh which was used for different indications (prolapse repairs). A study like this is therefore timely. Of the 67.8% of the 341 patients that responded to a questionnaire, 71.6% reported success ('very much' and 'much' improved) with the sling and another 14% 'improved'. Approximately 8% of women had gone on to further continence surgery. The extrusion/tape erosion rate (where some of the material comes through the vaginal skin under which it is covered when placed) was 4.5%, and 4.3% reported groin pain with 1.4% requiring treatment for this. This paper helps to contextualise some of the current media reports. Women who have already trialled conservative management for stress urinary incontinence and wish to consider surgical management will be able to consider these figures as part of an informed consent process.

***Reference: BJOG 2017;124(6):973-981***
Abstract

## Efficacy and acceptability of long-term norethindrone acetate for the treatment of rectovaginal endometriosis

**Authors:** Morotti M et al.

**Summary:** This retrospective cohort study evaluated the efficacy of long-term norethindrone acetate in patients with rectovaginal endometriosis. 103 women with pain symptoms caused by rectovaginal endometriosis received norethindrone acetate alone (2.5–5 mg/day) for 5 years. 61 women completed the 5-year follow-up, with 16 women withdrawing because of adverse effects. Overall, 68.8% of women who completed the study were satisfied or very satisfied with treatment (40.8% of enrolled patients). The intensity of chronic pelvic pain and deep dyspareunia was significantly decreased after 5 years compared with baseline (p<0.001). Dyschezia improved after 1 year but remained stable between the first and second year.

**Comment (AS):** This Italian retrospective cohort study looked at 103 women with various pain symptoms due to rectovaginal endometriosis diagnosed clinically and then with magnetic resonance imaging and other imaging techniques (who declined surgery). Norethindrone acetate is known in NZ as norethisterone acetate and the dose used was 2.5–5mg per day (starting low and then increasing to 5mg if breakthrough bleeding after 30 days). Of the 61 women who completed the 5-year follow up, nearly 70% were satisfied or very satisfied overall which equates to 41% of the total number of women. There was improvement with symptoms of chronic pelvic pain, deep dyspareunia and dyschezia. After 5 years of treatment, a reduction in size of rectovaginal nodules was seen in 56%, stable size in 32%, but an increase in size in 12%. These women were highly motivated to undertake medical therapy as they had declined surgery (attendant risks). The withdrawal rate from side effects was 13%. However, a proven long-term, well tolerated, low cost therapy for women with rectovaginal endometriosis is to be welcomed in the arsenal of therapeutic options for this complex disease. Ongoing clinical follow-up is suggested as some of the patients showed increased nodule size and therefore disease progression.

***Reference: Eur J Obstet Gynecol Reprod Biol 2017;213:4-10***
Abstract