Women's Health Research Review

Making Education Easy

Issue 22 – 2017

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Abbreviations used in this issue

BMI = body mass index
ENG = etonogestrel
IUD = intrauterine device
LARC = long-acting reversible contraceptive
NICE = National Institute for Health and Care Excellence
POP-SS = Pelvic Organ Prolapse Symptom Score
RCOG = Royal College of Obstetricians and Gynaecologists

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

This month we report that a lot of NZ women continue to use contraceptives with a high practical failure rate (condoms and the contraceptive pill). They should instead be encouraged to use LARCs, although there are still some access problems that need to be addressed. This NZ research is followed by 3 studies of the etonogestrel contraceptive implant (use after pregnancy, breakthrough bleeding, and potential for extended use), and an interesting analysis of contraception in women with chronic disease. Auckland researchers report that obese women with abnormal uterine bleeding have a higher risk of endometrial hyperplasia or cancer, and UK investigators report that as many as 12% of women who undergo vaginal prolapse repair with synthetic mesh will have a mesh-related complication within the first 2 years.

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

Kind regards,

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Prevalence of contraceptive use in New Zealand women

Authors: Chesang J et al.

Summary: This study estimated the prevalence of contraceptive use among NZ women. 904 women aged 35–69 years were randomly selected from the electoral roll in 2013–2015 and sent a postal questionnaire to gather information on contraceptive use, socio-demographic characteristics and risk factors for ovarian cancer. Current and ever-use of contraceptives were compared with data collected in 1988. Response rate to the questionnaire was 47%. Oral contraceptives had the highest prevalence of ever-use among women aged 35–69 years (89%), followed by condom use (54%) and vasectomy (44%). Compared with 1988, there was an increase in ever-use of condoms (64% vs 24%), vasectomy (40% vs 26%) and oral contraceptives (89% vs 75%) in women aged 35–54 years, but lower use of tubal ligation (8% vs 22%).

Comment (HR): The response rate in this new study was smaller than that in the 1988 study and it is disappointing that so many NZ women still use condoms and the contraceptive pill. These methods have high practical failure rates. Condoms are tier 3 contraceptives (practical failure rate is 18 pregnancies per 100 women per year) and the pill is tier 2 (practical failure rate of 6–12 pregnancies per 100 women per year). In contrast, male and female sterilisation, IUD and implant are all tier 1 (<1 pregnancy per 100 women per year). The UK NICE guidelines remind us that LARCs should be offered to all women and are more cost-effective even at 1 year of use compared with pill use. Some of the problem with access here in NZ may well be getting training for GPs for LARC insertion and then getting funding support for women so that they can afford to access these procedures.

Reference: NZ Med J 2016;129(1444):58-67

Abstract

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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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The Royal Australian and New Zealand College of Obstetricians and Gynaecologists (RANZCOG) Fellows may claim 1 PD point per hour in the 'Self-Education' component of any of the three domain for any self-educational O&G activities completed (including reading of relevant Research Reviews).

Home or office etonogestrel implant insertion after pregnancy

Authors: Uhm S et al.

Summary: This study evaluated whether home visits for contraceptive implant insertion improve the postpartum uptake compared to clinic insertion. 40 women within 10 weeks of a birth or dilation and curettage (D&C) were randomised to home or standard office insertion. 37 of the women were postpartum and 3 were post-D&C. Most of the women stated a preference for a home visit for their implant insertion at the time of enrollment. Postpartum appointment attendance rates were similar between home and office visits (53% and 50%, respectively). Implant uptake tended to be better in women randomised to home insertion visits (63% vs 33%).

Comment (HR): Yes, home insertion is certainly a choice as long as one is prepared for the rare reactions to local etc. However what we are really striving for is immediate insertion before leaving hospital. The new guidelines are out from the Faculty of Sexual and Reproductive Health of RCOG in the UK – Contraception after Pregnancy. The main points are:

- Maternity services (including services providing antenatal, intrapartum and postpartum care) should give women opportunities to discuss their fertility intentions, contraception and preconception planning.
- Effective contraception after childbirth should be initiated by both breastfeeding and non-breastfeeding women as soon as possible, as sexual activity and ovulation may resume very soon afterwards.
- Maternity service providers should ensure that all women after pregnancy have access to the full range of contraceptives, including the most effective LARC methods, to start immediately after childbirth. This should not be limited to those women with conditions that may pose a significant health risk during pregnancy and vulnerable groups (including young people) at risk of a short interpregnancy interval (IPI) or an unintended pregnancy.
- Women should be advised that intrauterine contraception (IUC) and progestogen-only implant (IMP) can be inserted immediately after delivery.
- Clinicians should be aware that insertion of IMP soon after childbirth is convenient and highly acceptable to women. This has been associated with high continuation rates and a reduced risk of unintended pregnancy.
- Clinicians should be aware that insertion of IUC at the time of either vaginal or caesarean delivery is convenient and highly acceptable to women. This has been associated with high continuation rates and a reduced risk of unintended pregnancy.

Our next task is working out how we get these guidelines into action for NZ women!

Reference: Contraception 2016;94(5):567-71
Abstract

Tamoxifen for the treatment of breakthrough bleeding with the etonogestrel implant

Authors: Simmons K et al.

Summary: This double-blind study evaluated whether a short course of tamoxifen reduces bleeding/spotting days in etonogestrel (ENG) implant users. 56 women using an ENG implant who had frequent or prolonged bleeding or spotting were randomised to tamoxifen 10mg or placebo twice daily for 7 days, to be started after 3 consecutive days of bleeding/spotting. Treatment was repeated as needed up to three times in 180 days. Tamoxifen recipients reported 5 fewer days of bleeding/spotting over 30 days (p=0.05), and 15.2 more continuous bleeding-free days (p=0.02) than placebo recipients after first use of study drug. Conclusions could not be drawn after 30 days due to a higher-than-expected dropout rate.

Comment (HR): OK, another option. Irregular bleeding is one of the most common side effects of implant use and Jadelle® has the same problem – about 1 in 7 women have their implant removed for this reason. At insertion I always urge women to seek help with bleeding problems as soon as they can and not put up with them. Most of us would add a combined pill on top giving continuous hormones for a few months. If this is successful in stopping the bleeding but it returns on stopping then it can be continued for the duration of implant use. There seems to be a window of opportunity to address bleeding problems as soon as possible as women will often seek removal if not offered support.

Reference: Contraception 2017;95(2):198-204
Abstract

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Extended use up to 5 years of the etonogestrel-releasing subdermal contraceptive implant: comparison to levonorgestrel-releasing subdermal implant

Authors: Ali M et al.

Summary: This study evaluated whether the 3-year one-rod etonogestrel (ENG)-releasing subdermal contraceptive implant is effective during extended use up to 5 years. For the first 3 years, the study was an open-label, multicentre randomised trial comparing the 3-year ENG implant to the 5-year levonorgestrel (LNG)-releasing implant. After 3 years, a subset of 390 ENG participants consented to extended use (more than 200 women used the ENG implant for at least 5 years). No pregnancies occurred during the additional 2 years of follow-up in the ENG or LNG implant group. The overall 5-year Kaplan–Meier cumulative pregnancy rates for ENG and LNG implants were 0.6 and 0.8 per 100 women-years, respectively. Complaints of bleeding changes were similar, although ENG-users were more likely than LNG-users to experience heavy bleeding ($p<0.05$).

Comment (HR): Along with the information that IUDs can give contraception for longer than registered (e.g. 12 years for Copper T 380, up from 10 years), here is a study showing longer efficacy for the etonogestrel implant. We have Jadelle® in NZ (a 2-rod LNG implant) which at this point is used for 5 years. There has been some discussion regarding shorter durations of efficacy for obese women. However, a 2016 Cochrane Review did not show any statistical difference in pregnancy rates for the 2-rod implant in overweight or obese women.

Reference: Hum Reprod 2016;31(11):2491-98
Abstract

Pooled analysis of the effects of conjugated estrogens/bazedoxifene on vasomotor symptoms in the Selective Estrogens, Menopause, and Response to Therapy trials

Authors: Archer D et al.

Summary: This post hoc pooled analysis of the Selective Estrogens, Menopause, And Response to Therapy (SMART)-1 and SMART-2 trials examined the effects of conjugated estrogens/bazedoxifene on hot flashes (HF). Data from the 2 studies were pooled for nonhysterectomised postmenopausal women with moderate/severe HF given conjugated estrogens/bazedoxifene 0.45mg/20mg, 0.625mg/20mg, or placebo for 12 weeks. The pooled analysis included 403 participants. At 12 weeks, both combinations of conjugated estrogens/bazedoxifene significantly decreased moderate/severe HF frequency versus placebo, significantly reduced adjusted average daily HF severity score versus placebo, significantly increased the percentage of women who had a ≥50% or ≥75% reduction from baseline in daily frequency of moderate/severe HFs, and increased the percentage with ≥50% or ≥75% reductions in average daily HF severity score versus placebo. Conjugated estrogens/bazedoxifene therapy was more effective than placebo irrespective of time since menopause.

Comment (HR): This product is not yet registered in NZ. The hope will be that the addition of the selective estrogen receptor modulator to estrogen as opposed to progestogen will have better outcomes in regard to breast cancer – where it is the addition of progestogen that appears to confer the breast cancer risk. We will need to see the data regarding this in the years to come along with other outcome measures of endometrial cancer, stroke, venous thromboembolism (VTE) etc. I am not sure what the price is likely to be in NZ but this product is unlikely to be funded. In NZ, along with the funded option of oral Progynova® and Provera®, we now have transdermal Estradot® funded. Observational studies show that transdermal delivery of estrogen has lower VTE and stroke risk.

Reference: J Womens Health (Larchmt) 2016;25(11):1102-11
Abstract

Chronic diseases and use of contraception among women at risk of unintended pregnancy

Authors: Phillips-Bell G et al.

Summary: This study evaluated contraceptive use in women with chronic disease. Data from 2008–2010 were analysed from the Florida Behavioral Risk Factor Surveillance System for 4473 women aged 18–44 years who were at risk of unintended pregnancy. 87% of them were using any method of contraception (22.5% were using less effective methods and 64.5% were using effective/highly effective methods). Women with cardiovascular disease were more likely than those without cardiovascular disease to use any contraception, less effective contraception, and effective/highly effective contraception. Women with diabetes were more likely to use less effective methods than women without diabetes. No significant associations were observed in women with asthma.

Comment (HR): Well this is good to see and they are certainly doing better than we are in NZ. The 2015 study by Jane McDonald "Contraception post severe maternal morbidity: a retrospective audit" showed that we need to improve our support for these women. The study was a secondary analysis of severe acute maternal morbidity (SAMM) cases audited for preventability of SAMM in four District Health Board areas (covering a third of annual births in NZ) during a 17-month period. Of the 98 SAMM cases, 84 (85.7%) left hospital without contraception. The summary suggested that these figures indicate substandard care. And some suggestions were to have dedicated contraceptive nurses/midwives who could: a) give accurate information; b) offer immediate postpartum implant or prescription for other forms of contraception; c) teach junior medical staff; and d) be readily available to give contraceptive advice or access for women of reproductive age with severe comorbidities seeing non-obstetric specialists. Just like the recommendations from the UK Faculty regarding contraception after pregnancy that we discussed on page 2, the UK Medical Eligibility 2016 document also gives the same advice … "Women with conditions that may pose a significant health risk during pregnancy should be advised to consider using the most effective LARC methods, which provide a highly reliable and effective method of contraception (failure rate <1 pregnancy per 100 women in a year). The sole use of barrier methods and user-dependent methods of contraception (e.g. oral contraception) may not be the most appropriate choice for these women given their relatively higher typical-use failure rates".

Reference: J Womens Health (Larchmt) 2016;25(12):1262-69
Abstract

Body mass index trumps age in decision for endometrial biopsy

Authors: Wise M et al.

Summary: This retrospective cohort study investigated the influence of BMI on the risk of endometrial hyperplasia or cancer in premenopausal women with abnormal uterine bleeding. Data for 916 premenopausal women who had an endometrial biopsy for abnormal uterine bleeding in 2008–2014 were reviewed. Almost 5% of participants had complex endometrial hyperplasia or cancer. After adjusting for confounding factors, women with BMI ≥30 kg/m^2 were 4 times more likely to develop complex hyperplasia or cancer. Other risk factors were nulliparity (adjusted odds ratio, 3.08) and anaemia (adjusted odds ratio, 2.23).

Comment (AS): This Auckland retrospective cohort study of 916 premenopausal women with abnormal uterine bleeding showed that 5% had complex endometrial hyperplasia or endometrial cancer. Those with a BMI >30 kg/m^2 were four times more likely to develop these conditions than women with a BMI <30. Nulliparity conferred a 3-fold risk and anaemia a 2.23-fold risk for these conditions. A BMI >30 kg/m^2 should raise a red flag in women with abnormal uterine bleeding and lead to the performance of an endometrial biopsy.

Reference: Am J Obstet Gynecol 2016;215(5):598.e1-8
Abstract

Mesh, graft, or standard repair for women having primary transvaginal anterior or posterior compartment prolapse surgery

Authors: Glazener C et al., for the PROSPECT Study Group

Summary: The PROSPECT trials compared the use of synthetic mesh inlays, biological grafts, and standard repair in women undergoing vaginal prolapse repair at 35 secondary and tertiary referral hospitals in the UK. 1348 women undergoing primary transvaginal anterior or posterior compartment prolapse surgery were randomised to 1 of 2 trials that compared standard (native tissue) repair alone with standard repair augmented with either synthetic mesh (the mesh trial) or biological graft (the graft trial). The primary outcomes, measured at 1 and 2 years, were participant-reported prolapse symptoms and condition-specific quality-of-life scores. Mean POP-SS and mean prolapse-related quality of life scores did not differ significantly between treatment groups at 1 and 2 years. Serious adverse events occurred with similar frequencies in all groups in the first year of follow-up. The incidence of mesh complications over 2 years in women exposed to synthetic mesh was 12%.

Comment (AS): On the basis that up to 30% of non-mesh (native tissue) repairs for vaginal wall prolapse failed, and utilising the evidence that mesh for abdominal hernias was effective, the use of vaginal mesh for vaginal repairs became widespread. This multicentre, randomised controlled trial from the UK showed that mesh did not significantly improve women's outcomes in terms of quality of life, effectiveness or adverse effects. However 12% of women with synthetic mesh had a mesh-related complication. The use of mesh for vaginal prolapse surgery has become very uncommon since the adverse publicity related to complications and withdrawal of commercially available mesh kits.

Reference: Lancet 2017;389(10067):381-92
Abstract

Independent commentary provided by Dr Anil Sharma

Anil has a background in medical education with interests in clinical practice, teaching and informed consent. **FOR FULL BIO CLICK HERE.**

Pelvic floor muscle training for secondary prevention of pelvic organ prolapse (PREVPROL)

Authors: Hagen S et al.

Summary: The PREVPROL study assessed whether pelvic floor muscle training helps in the secondary prevention of pelvic organ prolapse. The randomised controlled trial was conducted at three centres in NZ and the UK. 414 women of any age who had stage 1–3 prolapse but had not sought treatment were randomised 1:1 to either an intervention group (one-to-one pelvic floor muscle training at 5 physiotherapy appointments over 16 weeks, plus Pilates-based pelvic floor muscle training classes, and a DVD for home use) or a control group (prolapse lifestyle advice leaflet). The primary outcome was self-reported prolapse symptoms at 2 years. At baseline, 97% of the women had prolapse above or at the level of the hymen. The mean symptom score was maintained over the 2-year period in the control group, but decreased in the intervention group. At 2 years, the mean POP-SS score was 4.2 in the control group and 3.2 in the intervention group (p=0.004).

Comment (AS): This randomised controlled trial (NZ and UK) included women with stage 1 to 3 prolapse who hadn't sought treatment thus far. One group was assigned to five one-to-one pelvic physio sessions AND Pilates pelvic floor muscle classes AND a DVD for pelvic exercises for home use. The other group were given a prolapse lifestyle advice leaflet. The results showed a small but probably important reduction in prolapse symptoms. Symptoms such as 'something coming down the vagina' and need to 'push to empty the bladder' tended to decrease over time in the exercise group. It is therefore likely worthwhile referring women with symptomatic prolapse to pelvic floor physiotherapy services. Gynaecologists should also be considering these interventions in most cases where surgery for prolapse is being planned to improve success rates.

Reference: Lancet 2017;389(10067):393-402
Abstract

The effectiveness of the levonorgestrel intrauterine system in obese women with heavy menstrual bleeding

Authors: Shaw V et al.

Summary: This NZ study evaluated the effectiveness of the levonorgestrel intrauterine system (LNG-IUS) in obese women with heavy menstrual bleeding. 20 women with heavy menstrual bleeding who agreed to treatment with the LNG-IUS and had a BMI >30 kg/m^2 completed two validated tools (Menstrual Impact Questionnaire and the Pictorial Bleeding Assessment Chart) at recruitment, and at 6 and 12 months' follow-up. Three LNG-IUS were removed due to infection and pain; these women were subsequently booked for a hysterectomy. The LNG-IUS decreased menstrual loss by an estimated 19.7% per month (p<0.001), translating to 73.2% per period of 6 months and 92.8% per period of 12 months. Quality of life measures improved significantly in 14 women but only 12 women were satisfied with the treatment.

Comment (AS): This prospective study at Middlemore Hospital looked at 20 women with heavy menstrual bleeding with a BMI >30 who had treatment with the LNG-IUS (Mirena®). By 6 months' follow-up 2 women had removal due to pain in 1 case and infection in another. Another woman expelled the device. One was lost to follow-up. Of the remaining 16 women, another was lost to follow-up and another had removal due to pain later. This represents a removal percentage of 22.2%. The overall success rate of the device with satisfied users was 67%, which was 12 of the 14 who had a good therapeutic trial without mishap. Whilst a relatively small study, this is similar to my clinical experience with the device for heavy menstrual bleeding for obese women. The success or satisfaction rates seem low but given the higher risk of morbidity and mortality with hysterectomy for women with significantly raised BMI, both this device and endometrial ablation remain efficacious options. Careful patient selection with assessment including sonography would increase the success rate.

Reference: Aust NZ J Obstet Gynaecol 2016;56(6):619-23
Abstract