Women's Health Research Review

RESEARCH REVIEW 10 YEARS
MAKING EDUCATION EASY SINCE 2006

Making Education Easy

Issue 21 – 2016

In this issue:

Abbreviations used in this issue
BPAC = Best Practice Advocacy Centre
HPV = human papillomavirus
IUD = intrauterine device
LARC = long-acting reversible contraceptive
NSU = National Screening Unit
SIS = saline infusion sonohysterography
TVUS = transvaginal ultrasonography
WHI = Women's Health Initiative

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

This month we report a large French cohort study of the safety of combined oral contraceptives, plus a meta-analysis of the use of plant-based therapies for menopausal symptoms. Trends in the global incidence of abortion over the last 25 years are discussed, and an interesting article reports the acceptability and feasibility of HPV self-sampling for cervical cancer screening. A local study of prescribing trends for uncomplicated cystitis finds considerable variation from current guidelines, and we finish with positive results for prophylactic tranexamic acid in women undergoing hysterectomy.

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

We're also delighted to announce that 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 domains for reading relevant Research Reviews.

Kind regards,

Associate Professor Helen Roberts
helenroberts@researchreview.co.nz

Dr Anil Sharma
anilsharma@researchreview.co.nz

Low dose oestrogen combined oral contraception and risk of pulmonary embolism, stroke, and myocardial infarction in five million French women

Authors: Weill A et al.

Summary: This cohort study investigated the dose-related risk of pulmonary embolism, ischaemic stroke and myocardial infarction (MI) in women taking combined oral contraceptives. Data from the French national health insurance database were linked with hospital discharge data for the period July 2010 to September 2012. 4,945,088 women aged 15–49 years with ≥1 reimbursement for oral contraceptives and no previous cancer, pulmonary embolism, ischaemic stroke, or MI were included. 1800 cases of pulmonary embolism, 1046 ischaemic strokes, and 407 MIs were observed. After adjustment for progestogen and risk factors, the relative risks for women using low dose estrogen (20µg vs 30–40µg) were 0.75 for pulmonary embolism, 0.82 for ischaemic stroke, and 0.56 for MI. After adjustment for estrogen dose and risk factors, desogestrel and gestodene were associated with higher relative risks for pulmonary embolism (2.16 and 1.63, respectively) compared with levonorgestrel. Levonorgestrel + estrogen 20µg was associated with a lower risk of each of the 3 serious events compared with levonorgestrel + estrogen 30–40µg.

Comment (HR): The pulmonary embolism findings agree pretty much with a lot of other research although we don't have a lot of previous data re different pills and stroke and MI. The lowest risk for all 3 of these outcomes was with a 20µg estrogen pill with levonorgestrel – this is Ava 20® which is funded in NZ at $5 script charge for 6 months. It may cause more breakthrough bleeding though compared to Ava 30® (also funded at $5 for 6 months). As expected the study showed that the risk of pulmonary embolism, MI and stroke increases with age; so perhaps a 20µg pill may be particularly useful for these women. Use of the combined pill for women aged 35–50 years is fine as long as they are non-smoking and do not have risk factors for cardiovascular disease.

Reference: BMJ 2016;353:i2002
Abstract

CLICK HERE to read previous issues of Women's Health Research Review

Use of plant-based therapies and menopausal symptoms

Authors: Franco O et al.

Summary: This systematic review and meta-analysis determined the effect of plant-based therapies on menopausal symptoms. A search of the electronic databases Ovid MEDLINE, EMBASE, and Cochrane Central identified 62 randomised clinical studies of plant-based therapies on hot flushes, night sweats, and vaginal dryness in a total of 6653 menopausal women. Meta-analysis of the data showed that use of phytoestrogens decreased the number of daily hot flushes and the vaginal dryness score, but not the number of night sweats. Individual phytoestrogen interventions such as dietary and supplemental soy isoflavones were associated with improvement in daily hot flushes and vaginal dryness score. Several herbal remedies (but not Chinese medicinal herbs) decreased the frequency of vasomotor symptoms.

Comment (HR): In this meta-analysis phytoestrogens were found to be helpful for hot flushes and vaginal dryness but not night sweats. The 2013 Cochrane Review on phytoestrogens specifically found that supplements with at least 15mg of genistein per day were effective. Interestingly, although red clover did not help flushes, one study showed an improvement in night sweats. There was initial data from some new herbal remedies but we probably need to wait for further data regarding these. This analysis did not find black cohosh useful for menopausal symptoms nor any Chinese herbal remedies. Some women may be keen not to use hormone therapy for hot flushes and night sweats but it is still the most effective treatment for these symptoms and we need to remember that the subgroup analysis from the WHI trial showed low risks for women in the age group 50–59 years.

Reference: JAMA 2016;315(23):2554-63
Abstract

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).

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.

FOR FULL BIO CLICK HERE.

Abortion incidence between 1990 and 2014: global, regional, and subregional levels and trends

Authors: Sedgh G et al.

Summary: This report determined regional and global trends in abortion incidence between 1990 and 2014. Abortion data were requested from government agencies, and data were compiled from international sources and nationally representative studies. Worldwide, approximately 35 abortions occurred annually per 1000 women aged 15–44 years in 2010–2014. This was 5 points less than the 40 per 1000 reported in 1990–1994. Because of population growth, the annual number of abortions worldwide increased from 50.4 million in 1990–1994 to 56.3 million in 2010–2014. The annual abortion rate declined from 46 to 27 per 1000 women in the developed world and from 39 to 37 per 1000 women in the developing world. 25% of pregnancies ended in abortion in 2010–2014. Globally, 73% of abortions were obtained by married women and 27% by unmarried women in 2010–2014. Abortion rates did not vary between countries grouped according to the legality of abortion.

Comment (HR): Worldwide the number of abortions are decreasing and this paper reports 35 per 1000 women from 2010–2014. The NZ Abortion Supervisory Committee report for 2015 also showed a decrease in the number of abortions from 18.2 to 14.4 per 1000 women in the same time period. They put this down to the increasing use of LARCs e.g. IUD and Jadelle® and these methods are now considered Tier 1 contraception (<1 pregnancy per 100 women in 1 year) as opposed to Depo Provera® or the pill which are Tier 2 (6–12 pregnancies per 100 women in 1 year). At the Epsom Day Unit in Auckland both of these methods can be inserted for free at the time of abortion. However, LARCs may be less available in developing countries.

Reference: Lancet 2016;388(10041):258-67
Abstract

Regional variation in postabortion initiation of long-acting reversible contraception in New Zealand

Authors: Rose S & Garrett S

Summary: This study investigated whether the immediate post-abortion initiation of LARC varies regionally in NZ. Post-abortion LARC initiation ranged from 32% to 61.4% across the 16 regions of NZ. Implant use varied from 6.8–32.7% and IUD use varied from 21.4–54.7%. Regional variation in LARC uptake was most marked for women aged <20 years (20.3–70.9%). The ratio of IUD to implant users ranged from 0.7–4.1 across regions, with IUDs being prescribed twice as frequently as implants nationwide.

Comment (HR): This study collected data from part of the Abortion Supervisory Committee form filled out by certifying consultants at the time of abortion. For reasons of confidentiality the data were only available at regional not clinic level. However 8 of the 16 regions have only one service provider. The overall uptake of IUDs was 34% of women throughout NZ at the time of abortion. However only 22% of women aged <20 years had an IUD which may reflect that providers and women themselves still have the mistaken opinion that this method is not a choice for young women. Comparing regions with the highest and lowest LARC insertions, IUD differed by 2.5 times and implant by 5 times. The highest IUD insertions were in Northland (54.7% of women) and the lowest in Marlborough and Otago (21.4% of women). For implants, the highest uptake was Southland (32.7%) and Marlborough (32.5%) and the lowest Taranaki (6.8%). The study conclusion was that the findings point to the need for immediate review of post-abortive LARC provision In NZ with implementation of training and policy changes.

Reference: Aust NZ J Obstet Gynaecol 2016;56(3):315-22
Abstract

Acceptability and feasibility of human papilloma virus self-sampling for cervical cancer screening

Authors: Kumar I et al.

Summary: This study examined the acceptability and feasibility of HPV self-sampling among patients and clinic staff in two clinics in Miami. 180 Haitian and Latina women aged 30–65 years with no Pap smear in the past 3 years were offered HPV self-sampling or traditional Pap smear screening. 67% of the women selected HPV self-sampling. Among those who selected traditional screening, 22% were not screened 5 months post-recruitment. More than 80% of the women agreed that HPV self-sampling was faster, more private, easy to use, and they would prefer to use it again. 80% of clinic staff agreed that they would be willing to incorporate HPV self-sampling into practice.

Comment (HR): Good to hear that HPV self-sampling was acceptable and feasible for both women and clinicians. At present in NZ the NSU has a consultation document on its website "Clinical Guidelines for National Cervical Screening Programme". This discusses screening with HPV testing for cervical cancer prevention. The plan is to implement in 2018 and will mean a move from 3-yearly cytology screening to 5 yearly HPV screening. The two face-to-face consultation meetings in Christchurch and Auckland were held earlier in October but the consultation document is a 6-week public process which started September 16th. It is hoped the finalised guidelines will be available at the end of this year. The new 9-valent HPV vaccine should be in the vaccination schedule in 2017 – the current vaccine only protects against 4 types of HPV. Although it has not been decided yet the document on the website suggests that self-sampling may be an option for NZ women.

Reference: J Womens Health 2016;25(9):944-51
Abstract

Cognitive effects of estradiol after menopause: a randomized trial of the timing hypothesis

Authors: Henderson V et al.

Summary: This study tested the hypothesis that the effect of estrogen-containing hormone therapy on cognitive abilities differs between early and late postmenopausal women. 567 healthy women within 6 years of menopause or 10+ years after menopause were randomised to oral 17β-estradiol 1 mg/day or placebo. Women with a uterus received cyclic micronised progesterone vaginal gel or placebo. After a mean treatment duration of 57 months, differences in verbal memory score between estradiol and placebo groups did not differ between early and late postmenopausal women. Differences between treatment groups were not significant for executive functions or global cognition.

Comment (HR): There is still the hope with the timing hypothesis that if estrogen is given early enough in the menopause it may help cognitive outcomes. The evidence from this randomised study shows that this is not the case. These findings agree with those from the ELITE study (which used conjugated estrogens and transdermal estradiol) and follow-up analysis of WHI. The latter found no residual cognitive effect of conjugated estrogens given to women aged 50–55 years who were examined 7 years after the study was terminated. The authors of this study point out that it lacked power to exclude small treatment effects in participant subgroups. Also it was not designed to assess short-term cognitive effects of estradiol or effects on risks of mild cognitive impairment or Alzheimer disease.

Reference: Neurology 2016;87(7):699-708
Abstract

Does the addition of saline infusion sonohysterography to transvaginal ultrasonography prevent unnecessary hysteroscopy in premenopausal women with abnormal uterine bleeding?

Authors: Short J et al.

Summary: This observational study investigated whether TVUS followed by saline infusion sonohysterography (SIS) prevents unnecessary hysteroscopy in premenopausal women with abnormal uterine bleeding. Outcomes for 65 women with abnormal uterine bleeding who underwent TVUS followed by SIS were reviewed. TVUS indicated that all 65 women had a focal endometrial abnormality but SIS showed no evidence of a focal endometrial abnormality in 8 women. The SIS scan was not completed in 8 women because of technical difficulties, and they were referred for hysteroscopy. Of the 45 women who had a hysteroscopy, 12 showed no evidence of a focal endometrial abnormality, 23 had a polypectomy and/or insertion of a Mirena®, and 10 were referred for a subsequent hysterectomy or laparoscopy within 1 year. The number of patients that needed to be investigated by SIS to avoid one hysteroscopy was 65/8 or 8.125. The cost of SIS per hysteroscopy avoided was calculated to be $NZ3347.50.

Comment (AS): This is a relatively small observational study (65 premenopausal women with abnormal uterine bleeding) where all the women had a sonographic diagnosis of endometrial polyp or submucosal fibroid. The number of patients that needed to have SIS to avoid one hysteroscopy was 8.125 which in this study led to an overall higher cost for SIS. Other factors obviously need to be considered as well, including the relative invasiveness and pain/risks of the procedure and any anaesthetic. Other considerations include the ability to undertake both biopsies and therapeutic procedures during hysteroscopy (e.g. resection of fibroids). Currently and not least with the newer simpler outpatient hysteroscopy procedures that are becoming available, I believe that saline infusion ultrasonography has a quite limited role in current practice.

Reference: Aust NZ J Obstet Gynaecol 2016; 56(4):432-5
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.

RESEARCH REVIEW™
Making Education Easy — Since 2006

Treatment of uncomplicated cystitis: analysis of prescribing in New Zealand

Authors: Gauld N et al.

Summary: This study described prescribing trends for women with suspected urinary tract infection (UTI) in NZ. Women who attended a pharmacy for prescribed treatment for a UTI were asked to complete a questionnaire. The analysis focused on prescribing for women with symptoms of uncomplicated cystitis. Valid questionnaires were received from 789 women attending 139 pharmacies. Analysis of the questionnaires indicated that 17% of women had symptoms of cystitis without complicating features. Most prescribing was for a first-line agent (59% for trimethoprim and 14% for nitrofurantoin), but norfloxacin was also common (21%). Women with self-reported antibiotic use for suspected cystitis in the past 6 months were more likely to be prescribed norfloxacin than those with no such history. Many prescriptions were not consistent with NZ treatment guidelines.

Comment (AS): This observational questionnaire study with 789 (female) completed surveys at 139 pharmacies finds considerable variance from BPAC guidelines (2011 and 2013) for empirical prescribing in cases of uncomplicated suspected cystitis. There is room for considerable improvement in antibiotic prescription regimens as norfloxacin was prescribed in 21%. Furthermore most prescriptions were for longer periods than advised by the guidelines. Current advice is for the use of trimethoprim 300mg once daily for 3 days or nitrofurantoin 50mg 4 times daily, with norfloxacin as second-line. For pregnant women, trimethoprim (except first trimester) or nitrofurantoin (except from week 36) are used at the same dosages but for 7 days instead and norfloxacin is avoided.

Reference: NZ Med J 2016;129(1437):55-63
Abstract

An altered perception of normal: understanding causes for treatment delay in women with symptomatic uterine fibroids

Authors: Ghant M et al.

Summary: This study examined factors contributing to treatment delay in women with symptomatic uterine fibroids. 60 women with symptomatic or recently treated uterine fibroids completed an in-depth interview. The mean age of participants was 43 years; 61.7% were African American, 25.0% were Caucasian, 8.3% were Hispanic, and 5.0% were Asian. Many women reported having a delayed diagnosis for their uterine fibroids despite having severe symptoms. Reasons for them delaying seeking treatment included the perception that their symptoms were "normal," they had a low knowledge of fibroids, they did not feel at risk for fibroids, they used avoidance-based coping strategies, and/or they dissociated themselves from their fibroids.

Comment (AS): Given that 65% of all women have uterine fibroids by the age of 50, it is remarkable that women's knowledge about them is so poor. This study showed that 48% of women with symptomatic fibroids that were subsequently treated had no idea what they were until diagnosed. This study was small but offers a fascinating documentation of women's reasons for not seeking help expeditiously for their symptomatic fibroids. A belief that their abnormal symptoms were normal and simply having no idea what they were are 2 reasons given. Other reasons included avoidance-based coping strategies ('I will just suck it up') and dissociation strategies ('it's not me it's the alien'). Being busy in their lives also figured highly. One thing that is clear is a lack of knowledge and education about fibroids. It would be good to compare men's reasons for avoidance of seeking help for ailments.

Reference: J Womens Health 2016;25(8):846-52
Abstract

Anti-hemorrhagic effect of prophylactic tranexamic acid in benign hysterectomy

Authors: Topsoee M et al.

Summary: This study investigated the antihaemorrhagic effect of prophylactic tranexamic acid in women undergoing elective benign hysterectomy. 332 women were randomised to receive either 1g intravenous tranexamic acid or placebo at the start of surgery. Intraoperative total blood loss was reduced in the tranexamic acid group compared with the placebo group when estimated both subjectively by the surgeon (p=0.006) and objectively by weight (p=0.004). The incidence of blood loss ≥500ml was also reduced (6 vs 21 women; p=0.003), as was the use of open-label tranexamic acid (7 vs 18 women; p=0.024), and the risk of reoperation due to postoperative haemorrhage (2 vs 9 women; p=0.034). This corresponded to an absolute risk reduction of 4.2% and number needed to treat of 24. No thromboembolic events were reported in either group.

Comment (AS): This study was of great interest to me. The use of a single intravenous dose of 1g of tranexamic acid versus placebo reduced intraoperative blood loss by 25% and also the chance of reoperation due to bleeding (the number needed to treat to avoid one reoperation was 24). There was no incidence of thromboembolism in any group. This study also serves as a timely reminder that tranexamic acid (Cyklokapron®) is of evidence-based use in the management of heavy abnormal uterine bleeding whilst considering investigation of it.

Reference: Am J Obstet Gynecol 2016;215(1):72.e1-8
Abstract