Advances in Women’s Health: Hot Topics in the Last Year

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Hot Topics in Women’s Health
- Not cancer screening, osteoporosis, menopause
- Human Papilloma Virus
- Contraception
- Dysfunctional Uterine Bleeding
- Breast Cancer Risk and Prevention

Case 1: Maria’s HPV vaccine
- 20 year old college student
- Received 2 doses of the HPV vaccines years ago
- Never got the third dose
- Virgin in high school
- Three lifetime partners
- Using condoms
- Has never had a pap

Which do you think is most important for Maria?

A. HPV #3
B. Pap #1
C. Chlamydia screen
D. Birth control discussion
Is Less More with HPV Vaccine?

- Over 7000 women in Costa Rica studied in a RCT of bivalent HPV vaccine
- 83%--3 doses; 11%--2 doses; 6%--1 dose
- Efficacy was not diminished
  - 81%--3 doses; 84%--2 doses; 100%--1 dose
- ↓doses may save money, time, resources
- Also consider disparities in HPV and paps
- Goal is to ↓cervical cancer in ↑est risk

Kreimer AR, JNCI 2011 Goldie S J, JNCI 2011

New Pap Guidelines

- Agreement between ACS, ACOG, and USPSTF
  - ACS and USPSTF drafts in 2011, ACOG in 2009
- Start at 21 and screen every 3 years
- HPV testing has no role in adolescents
- HPV testing should be done in women 21-30 ONLY if pap shows ASCUS
- Stop screening at age 65 (if well-screened, ↓ risk)
- After hysterectomy, D/C pap if no cancer or dysplasia

Feldman NEJM 2011

Chlamydia Screening--USPSTF

- Screen in all sexually active women under 25
- Grade A Recommendation
- Nucleic acid amplification tests (NAATs) have high specificity--vaginal swab or urine
- In low-prevalence populations (<5%), more likely to be false positive than true positive
- Population prevalence is 5% in women <25

USPSTF, Annals of IM, 2007
Cervical cancer risk and IUD use

- Pooled analysis of 26 studies
- Adjusted for cervical HPV DNA and number of prior paps
- Strong inverse association between IUD use and cervical cancer (OR 0.55)
- IUD ↓ uterine cancer and may trigger cellular immunity to ↓ cervical cancer

Casstellsaque, Lancet Oncol 2011

Maria wants OCP instead of IUD….

What’s new on OCP’s?

- No evidence of increased risk of breast cancer
- Levonorgestrel-containing OC’s are among the safest of the safe
- Some health care providers have fixed ideas about monthly cycles and medical amenorrhea
- Women who were given 12 packs of OCP’s were less apt to have an unplanned pregnancy (OR = 0.70) or abortion (OR = 0.54) compared with those given 3 packs or less

Lu Y, CEBP 2011
Lidegaard, BMJ 2011
Jick SS, BMJ 2011
Foster D, Ob Gyn 2011

3 months later, Maria is pregnant

- She wasn’t 100% adherent with OCP
- She got a UTI and was concerned that antibiotics would decrease efficacy of OCP
- Changed to condoms, but it broke last month and she didn’t know about “morning after” pill

Despite over-the-counter availability of EC, few women receive counseling; however EC use is ↑

Toh S, Contraception 2011

Preventing unintended pregnancy
New Evidence

- Counseling for emergency contraception
  - Over-the-counter since 8/2006
  - National Survey of Family Growth, > 7000 US ♀
  - 3% of ♀ received EC counseling in last year
  - 10% of those surveyed reported ever using EC
  - Most got EC OTC and used it only once

- Texting for contraception
  - RCT of 962 women
  - Continuation at 6 months- 64% text, 54% control p = .005

Kavanaugh ML Fertil Steril 2011
Castano ObGyn 2012
Which of the following are true?

A. Rates of unintended pregnancy in the US have not significantly changed in a decade
B. The proportion of unintended pregnancies ending in abortion has ↓ slightly
C. IUD use in the US has ↑ slowly
D. Emergency contraception use in the US has ↑ slightly
E. All of the above are true

If Maria chooses to terminate, is she at risk for mental disorders?

- First-trimester induced abortion was studied in multiple Danish registries (n = 84,620)
- Psychiatric contact was study outcome and childbirth was comparison group
- In the 9 months before or 12 months after abortion, no evidence of ↑ psychiatric contact
- Psychiatric contact ↑ after childbirth (p < 0.001) for 6-9 months; RR = 3.8 in first postpartum month

Maria’s Case Conclusion

- Maria chose to terminate her pregnancy and wanted to change to longer-acting birth control
- She got a depo-provera (D-MPA) injection in clinic and will return every 3 months for these
- In 2004, FDA “black box” notification regarding bone loss and cautioning against long-term use (>2 years)
- New data suggests that benefits of D-MPA over 2 years outweigh bone loss risks

Case 2: Sarah’s Bothersome Menorrhagia

- 44 year old G2P2
- Heavier and more frequent menses
- Cycles every 22-24 days
- Last cycle was on time
- But her bleeding lasted 3 days > usual and she’s still spotting.
What would you do next?

A. Transvaginal ultrasound
B. Endometrial biopsy
C. Progestin-containing medication
D. Hematocrit
E. Pregnancy Test

Sarah’s Menorrhagia

- Sarah is not pregnant
- She has a 3 cm posterior fiboid
- Her hematocrit is 34%
- Her symptoms are interfering with her life
- She has no desire for more children
- What are her options?
  - Medications (PO and SQ)
  - IUD
  - Other procedures: Ablation, Embolization, Surgery

Which do you recommend?

A. Progestin-containing PO medication
B. Transexamic Acid (SQ injection)
C. Uterine Artery Embolization
D. Surgery (Myoectomy/Hysterectomy)
E. Progestin-containing IUD

Transexamic Acid for Menorrhagia

- Inhibits activation of plasminogen, increasing clot formation
- Injectable approved in 1986; oral used safely in Europe for 40 yrs and approved in US in 2009
- RCT (n = 196) for 5 days/month had ↓ blood loss q month x 6 and ↓ social and physical limitations with menses
- Could provide short-term relief, but prior study of levonorgestrel IUD had more long-term efficacy

Lukes AS, Ob Gyn 2010
RCT of Embolization vs. Surgery and Cost-Effectiveness

- RCT (n = 157) began in 2000 in UK
- Uterine artery embolization (n = 106) vs. surgery (n = 42 hysterectomies + 9 myomectomies)
- 5 year outcomes were QoL, recommend procedure, adverse events, and re-intervention
- AE in UAE -- 19%; AE in surgery -- 25% (NS)
- Re-intervention in UAE – 32%; in surgery – 4%*
- UAE had cost benefit at 1 year, but this was negated by 5 years

Moss JG, BJOG 2011
Roberts TE, BMJ 2011
Munfo MG, Menopause 2011

Advances in Hysterectomy and New Data on Oophrectomy

- Minimally invasive laparoscopic hysterectomy had no difference in safety, lower morbidity, shorter hospital stays, and decreased costs.
- Oophrectomy was not associated with long-term adverse events
- Both were observational studies, difficult to study these questions with RCT

Jonsdottir GM, Ob Gyn 2011
Jacoby VT, Archives 2011

What did Sarah chose?

- Progestin-containing IUD provides birth control and ↓ menorrhagia
- Recommended for 5 years for birth control efficacy—up to 7 years for menorrhagia
- Efficacy comparable to tubal ligation (0.1% failure/year)

Worldwide Use of IUD

<table>
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<tr>
<td>Asia</td>
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<tr>
<td>North America</td>
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Population Reference Bureau 2002
Sarah and mammography

- She’s 44 and now that her menorrhagia is under control, she’d like to discuss mammography
- No prior mammogram
- Normal clinical breast exam
- No family history of breast cancer
- No significant breast cancer risk factors
- No strong opinions about mammos in the 40’s
- Her community mammography center has digital and computer-aided mammography

What do you recommend for Sarah regarding mammography?

A. Annual mammography
B. Mammography every 2 years
C. Wait til 50 years old
D. Have a personalized discussion about pros/cons

Digital mammography and computer-aided detection

- Observational studies of community practice
  - 70% of mammography machines in US are digital
  - Overall detection rates are similar with digital and film mammography
  - Digital mammography had better sensitivity when breast tissue was dense
- Multicenter study results suggest that computer-assisted detection lowers specificity with little potential to improve breast cancer outcomes.

Ivana’s Breast Cancer Prevention

- Ivana tested positive for a BRCA2 family mutation
- What lifestyle changes can she make to lower risk?
- What is the latest on risk-reduction medications?
**HBOC: Earlier onset with each generation?**
- Younger ages with diagnoses of breast cancer
- Lifestyle related?
- Screen related?
- Similar to Iceland data in BRCA2 founder mutations

*Litton Cancer 2011*

**Lifestyle advice for Ivana?**
- She is 25, doesn’t smoke, and exercises 3 days/week
- BMI is 23
- She drinks wine most nights, about 2 glasses 7 nights a week
- She is sexually active, has never been pregnant, and always uses condoms

**Which lifestyle change would most ↓ breast cancer risk?**
A. ↑ exercise to 6-7 days a week for at least 30 min
B. ↓ alcohol to 0-1/week
C. ↓ 10 pounds
D. Start OCP

**Even moderate alcohol ↑ risk**
- Low levels of alcohol consumption are associated with moderately elevated risk
- In the general population, benefits of alcohol should also be considered
- New model predicts the effects of modifying alcohol consumption, physical activity, and body-mass index.
- Predicting risk is risky business, differences in framing absolute and relative risk

*Petracci E, JNCI 2011
Chen WY, JAMA 2011*
Alcohol and breast cancer risk

Exercise and risk of breast cancer

- Overall 25-30% decreased risk
- Greatest in thinner women
- Lifetime exercise matters
- Modest amounts: 1-3 hours brisk walking/week

If Ivana was interested in “chemoprevention”

Would you recommend….

A. Tamoxifen
B. Raloxifen
C. Exemestane
D. None of the above

New data on exemestane

- RCT of 4560 postmenopausal women, either
  - > 60; 5 year risk > 1.66; prior neoplasia
- During mean follow up of 3 years, invasive breast cancer diagnosed in 11 exemestane recipients and 32 placebo recipients
  - Annual incidence 0.19% vs. 0.55%*
  - NNT of about 100 to prevent 1 case during 3 years
- Hot flashes and joint pain main side effects


Goss PE, NEJM 2011
Ivana’s Case Conclusion

- Ivana will decrease her alcohol intake and increase her exercise
- She will focus on lifestyle changes in her 20’s and early 30’s
- She will consider oophrectomy after having children
- She will consider chemoprevention in her 30’s or 40’s

Hot Topics in Women’s Health

- HPV vaccine may be effective without all 3 doses, but this deserved dedicated study
- Long-term contraceptives are most effective; IUD use in the US is slowly increasing
- Multiple options and new data exists for menorrhagia
- Reducing the risk of breast cancer can involve lifestyle, “chemoprevention,” and surgery—match intervention to risk
- Mammography in the 40’s is still a hot topic!