Controversial Topics in Women’s Health

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39th Annual CAPA Conference
Palm Springs, CA – October 10, 2015

Conflicts of Interest Disclosure

Anita L. Nelson, MD

| Grants/Research | Bayer, Agile, Merck, ContraMed |
| Honoraria/Speakers Bureau | Actavis, Agile, Aspen Pharma, Bayer, Merck |
| Consultant/Advisory Board | Actavis, Agile, Bayer, ContraMed, Female Health, Merck, MicroCHIPS Biotech, PharmaNest |

Learning Objectives

At the conclusion of this presentation, the participant will be able to:

- Current controversies about value of mammographic screening recommendations.
- New approaches to reduce risks of gynecologic cancers.
- New treatments for acute heavy menstrual bleeding.
- Need for immediate postpartum contraception.
Nelson: Controversial Topics in Women’s Health

GYN Carcinoma Incidence in U.S. Women, 2015

<table>
<thead>
<tr>
<th>Carcinoma</th>
<th>New Cases</th>
<th>Deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ovarian</td>
<td>21,290</td>
<td>14,180</td>
</tr>
<tr>
<td>Uterine corpus</td>
<td>54,870</td>
<td>10,170</td>
</tr>
<tr>
<td>Uterine cervix</td>
<td>12,900</td>
<td>4,100</td>
</tr>
<tr>
<td>Vulvar</td>
<td>5,150</td>
<td>1,080</td>
</tr>
<tr>
<td>Vaginal &amp; other</td>
<td>4,070</td>
<td>910</td>
</tr>
<tr>
<td>Breast</td>
<td>231,840</td>
<td>40,290</td>
</tr>
</tbody>
</table>


Overestimation of Breast Cancer Risk

- USA Today/Gallop Poll on Nov. 24, 2009 of women following release of US Preventative Services Task Force recommendations
  - 40% of women estimated that a 40 year old’s chance of developing breast cancer in the next decade is 20-50%
  - Real risk is 1.4%

Risk Factors for Breast Cancer

- For premenopausal and postmenopausal women
  - Age
  - Breast density
  - Family history of breast cancer
  - Prior breast procedure or chest irradiation
- Additional factors only for postmenopausal women
  - Race, ethnicity
  - BMI
  - Natural menopause
  - Hormone therapy > 5 years
  - Prior false positive mammogram

Atypical Hyperplasia

- 1 million breast biopsies done in US annually: benign
- 10% have atypical hyperplasia
- Has some, but not all features of cancer
- “Premalignant” lesion
- Cannot use standard prediction models
- 30% of women will develop cancer in 25 years of follow-up
- Younger age at diagnosis, higher the risk
- Usually not included as MRI candidates
- Chemoprevention measures rarely taken


Breast Cancer Screening Recommendations: General Population

<table>
<thead>
<tr>
<th>Mammography</th>
<th>CBE</th>
<th>SBE</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACOG</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥ 40 Q yr</td>
<td>20-39</td>
<td>? High risk</td>
</tr>
<tr>
<td>Q 1-3 yr</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ACS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥ 40 Q yr</td>
<td>Same as ACOG</td>
<td>Optimal ≥ 20 yr</td>
</tr>
<tr>
<td>NCCN</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥ 40 Q yr</td>
<td>Same as ACOG</td>
<td>Recommended</td>
</tr>
<tr>
<td>NCI</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥ 40 Q 1-2 yr</td>
<td>Recommended</td>
<td>Not recommended</td>
</tr>
<tr>
<td>USPSTF</td>
<td>50-74 Q 2 yr</td>
<td>Insufficient evidence</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Not recommended</td>
</tr>
</tbody>
</table>


Shanghai SBE Trial

- Initial instruction, 1 year & 3 year reinforcement lessons
- SBE practice under medical supervision every 6 months for 5 years
- Ongoing reminders to practice monthly
- 1989-91 instructions followed for morbidity to 2000

<table>
<thead>
<tr>
<th></th>
<th>BSE</th>
<th>Control</th>
<th>RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>132,979</td>
<td>133,085</td>
<td></td>
</tr>
<tr>
<td>Cancer deaths</td>
<td>135</td>
<td>131</td>
<td>1.04 (0.82-1.33)</td>
</tr>
<tr>
<td>Benign lesions</td>
<td>2,387</td>
<td>1,296</td>
<td></td>
</tr>
</tbody>
</table>

Cochran Update: Mammograms Efficacy

- In randomized trials mammography reduced breast cancer mortality by 15%
- Absolute risk reduction of 0.05% per woman
- For every 2,000 women invited for screening for 10 years
  - One would have life prolonged
  - 10 healthy women will be treated unnecessarily


Benefits and Harms of Annual Mammographic Screening 10,000 50Y-Old Women for 10Y

- 3,568 will have normal mammogram results for all 10Y
- 302 will be diagnosed as having breast cancer
  - 173 will survive breast cancer regardless of screening
  - 10 deaths will be averted
  - 57 over-diagnoses
  - 6,130 will have at least 1 false-positive
- 940 will have an unnecessary biopsy


Trade-Offs in General Population

<table>
<thead>
<tr>
<th>Ages</th>
<th>Mammograms /1000 women</th>
<th>% Mortality reduction</th>
<th>Cancer deaths averted /1000 women</th>
<th>Life Years Gained /1000 women</th>
<th>False-Positive Results /1000 women</th>
<th>Unnecessary biopsies /1000 women</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biennial screening</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>40-69</td>
<td>13,865</td>
<td>16</td>
<td>6.1</td>
<td>120</td>
<td>1,250</td>
<td>88</td>
</tr>
<tr>
<td>50-69</td>
<td>8,944</td>
<td>15</td>
<td>5.4</td>
<td>99</td>
<td>780</td>
<td>55</td>
</tr>
<tr>
<td>Annual screening</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>40-69</td>
<td>27,583</td>
<td>22</td>
<td>8.3</td>
<td>164</td>
<td>2,250</td>
<td>158</td>
</tr>
<tr>
<td>50-69</td>
<td>17,759</td>
<td>20</td>
<td>7.3</td>
<td>132</td>
<td>1,350</td>
<td>95</td>
</tr>
</tbody>
</table>

USPSTF 2009 Recommendations: General Population Breast Cancer Screening

- Recommends against
  - Breast self-examination
  - Mammography before age 50
- Recommends mammography
  - Every other year from age 50-74
- States evidence insufficient regarding
  - Mammography after age 74
  - Clinical breast examination women over 40
  - Use of digital mammography or MRI in place of film mammography

**USPSTF. Ann Intern Med. 2009;151(10):716-726.**

USPSTF 2009 Recommendations: General Population Breast Cancer Screening

- Later initiation (age 50)
  - Low prevalence of disease in 40-49 year olds
  - Increases positive predictive value
    - 49% false positives over 10 years
  - Decreases number of women to test
- Less frequent screening
  - 81% of mortality reduction maintained
  - 50% reduction in false positive results


Over-Diagnosis of Breast Cancer with Mammography

- Mammographic screening rates rose from 1980 to 2008 from 30 to 70%

<table>
<thead>
<tr>
<th>Cancer</th>
<th>1970-78*</th>
<th>2006-08*</th>
<th>Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early breast</td>
<td>112</td>
<td>234</td>
<td>122</td>
</tr>
<tr>
<td>Late stage</td>
<td>102</td>
<td>94</td>
<td>8</td>
</tr>
</tbody>
</table>

* Cases per 100,000 women

Breast Cancer Mortality Reductions: Is It Mammography or Better Treatments?

- Since introduction of mammography for women ≥ 40 years breast cancer mortality in that age group decreased by 28%
- Concurrent breast cancer mortality for women under 40 who did not have mammographic screening declined by 42%
  - Attributed to better therapy not screening


Latest Analysis Benefits and Risks of Mammography

- Mammogram screening associated with reduction in breast cancer mortality
  - 19% overall
  - 15% for women in 40’s
  - 32% for women in 60’s
- For women in 40’s or 50’s undergoing 10 years of annual mammography:
  - Cumulative risk of false positive 61%
  - 19% cancers diagnosed would never have become clinically apparent
- Net benefit depends on baseline breast cancer risk


Mammography Costs 2010

- Assuming 85% seek testing
- USPSTF criteria
  - $3.5 billion
- Actual costs for screening 70% following current “melange”
  - $7.8 billion
- If 85% had been tested using current “melange”
  - 10.1 billion
- Includes costs of imaging, recalls, biopsies, etc.

Swiss Medical Board

- Mammographic screening does not reduce overall death rate from disease
- Modest reduction in mortality rate from breast cancer is offset by its harms
  - Overdiagnoses leading to unnecessary biopsy and harmful treatment
- Recommendation
  - Switzerland should STOP introducing new mammography screening programs and phase out existing ones
  - All systematic screening programs should be replaced with screening information and asking women to make choices.


New Proposal From USPSTF

- Women age 40-50 who are worried may be offered mammography every 2 years if they believe that the benefits of screening outweigh the risks for them.

Breast Density Reporting Laws

- 21 states have various laws regarding follow-up needed for women with mammographic “dense breasts”
  - Dense breasts > 50% fibroglandular tissue
  - 40-50% of all women
- Require that clinician inform women that she has this and educate her about:
  - Increased risk of breast cancer
  - Supplemental screening for early breast cancer
- Some states require physicians to offer supplemental: whole-breast ultrasonography, independent of her other risk factors

What Should We Be Doing?

- Personalize screening
  - Stop screening women with no benefit
    - 48% of primary care physicians said they would recommend breast cancer screening for women diagnosed with terminal lung cancer
  - Calculate patient's individual breast cancer risk
    - Use estimate to determine screening frequency and modality
  - Provide chemoprevention or other interventions when appropriate


Risk Estimation: High Risk Women

- Known or likely carrier of *BRCA* mutation or other more rare high-risk genetic syndrome and women who had radiation to chest for Hodgkin’s disease
- “Likely carrier” = first degree related is carrier
  - ≥ 20% lifetime risk of breast cancer
- Models to use with high risk women to calculate risk
  - Claus model of early onset
  - Tyrer model
  - BOAD/CEA model for breast and ovary
  - All available at
    - http://caonline.amcancersoc.org/cgi/data/57/2/75/DC1.1


Use of Gail Model and Breast Cancer Preventive Therapy

- Survey 2012, 316 MD's in IM, CM, GYN
  - 55% response rate
- Gail model used 40%
  - 37% IM
  - 33% FM
  - 60% GYN
- Recommended or prescribed chemoprevention:
  - 13%
  - 9% IM
  - 8% FM
  - 30% GYN
- Among prescribers, most ≤ 5 times

### Screening for High Risk Women

- **Candidates:** BRCA1, BRCA2 mutation
  - Lifetime risk ≥ 20% (BRCAPRO, BODACEA, Claus)
  - Thoracic irradiation history
  - Atypical hyperplasia, LCIS, DCIS
- **SBE**
- **Semiannual CBE**
- **Annual mammography**
- **Annual Breast MRI**
  - *Not for DCIS and perhaps not LCIS*

References:

### Prevention of Breast Cancer: Moderate Risk Women

- **2 FDA approved products:** Tamoxifen, Raloxifene
- **2 million US women could potentially benefit from treatment**
  - 4% of women at high risk for breast cancer used
  - 0.08% of all US women age 40-79
- **Numbers topping 120,000 in 2000**
  - Dropped to 60,000 in 2005
- **Concerns:** Rare but serious effects
  - VTE, endometrial cancer
  - Tamoxifen only

References:

### Raloxifene: FDA-Approved Treatment to Reduce the Risk of Invasive Breast Cancer in Postmenopausal Women

- **FDA approval restricted to postmenopausal women**
  - With osteoporosis
  - With high risk for invasive breast cancer
    - Gail model 5-year risk ≥ 1.66%
    - ≥ 1 first degree relative with breast cancer
    - Biopsy proven LCIS or atypical hyperplasia
  - Not indicated for
    - Reduction of risk of recurrent breast cancer
    - Reduction of noninvasive breast cancer
    - Reduction in BRCA1/BRCA2 mutations

References:
Breast Cancer Risk Reduction Therapies

- Chemoprevention benefits outweigh risks
- Caucasian women in 50’s
  - Gail score ≥ 3%
- Afro-American women in 50’s
  - Gail score ≥ 6%*
- Premenopausal women with menses – tamoxifen
- Postmenopausal women with osteoporosis – raloxifene

* VTE risks higher


Potential Breast Cancer Risk Reduction Agents

- SERMS for osteoporosis and breast cancer prevention
  - Lasofoxifene
  - Bazedoxifene ± conjugated estrogens
  - Ospemifene
- Aromatase inhibitors (off-label use being recommended)
  - Exemestane
  - Anastrozole


Considerations for Medical Risk Reduction Measures

- Intact uterus – raloxifene or aromatase inhibitor
- DVT risk – aromatase inhibitor
- Dry vagina – tamoxifen
- Joint pain – tamoxifen or raloxifene
- Osteoporosis – tamoxifen or raloxifene
Endometrial Carcinoma

- US women lifetime risk: 1 in 38
  - Most common gynecologic cancer
  - 4th most common cancer
  - 2015: 54,870 new cases; 10,170 deaths\(^1\)
- 3 of most important risk factors\(^2\)
  - Obesity
  - Endometrial hyperplasia
  - Lynch syndrome (2-5%)\(^3\)


Types of Uterine Corpus Carcinoma

- Endometrial carcinoma
  - Starts as focal disease in endometrial layer
  - May be missed on biopsy if still early stage
  - Depth of invasion into myometrium important prognostic feature
- Myometrial sarcoma
  - Considerably more lethal
  - Does not involve endometrial layer until later
  - May have normal biopsy initially
  - Different subtypes
### Endometrial Cancer Screening

<table>
<thead>
<tr>
<th>American Cancer Society Guidelines</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Average risk</td>
<td>No screening recommended</td>
</tr>
<tr>
<td>Increased risk</td>
<td>No screening recommended</td>
</tr>
<tr>
<td>High-risk (HNPCC)</td>
<td>Annual endometrial biopsy starting at age 35 + prophylactic hysterectomy and oophorectomy after childbearing complete</td>
</tr>
</tbody>
</table>


### Endometrial Biopsy: Reevaluation

- Blind endometrial biopsy not sensitive to detecting focal intrauterine pathology:
  - Misses polyps and fibroids
- Endometrial hyperplasia and carcinoma start as focal lesions:
  - Post menopausal women with bleeding
    - 4.5% polyps are malignant polyps
Endometrial Hyperplasia Therapies

<table>
<thead>
<tr>
<th>Endometrial Hyperplasia</th>
<th>% of Women Who Normalized</th>
<th>Oral Progestins</th>
<th>LNG - IUS</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Simple</td>
<td>84 (77-100)</td>
<td>96 (76-100)</td>
<td>0.41</td>
<td></td>
</tr>
<tr>
<td>Complex</td>
<td>66 (58-74)</td>
<td>92 (65-100)</td>
<td>&lt; 0.01</td>
<td></td>
</tr>
<tr>
<td>Atypical</td>
<td>69 (58-83)</td>
<td>90 (62-100)</td>
<td>&lt;0.04</td>
<td></td>
</tr>
</tbody>
</table>


Ovarian Cancer: US Statistics

- 2015: 24,290 new cases; 14,180 deaths
- Lifetime risk 1.4% (1 in 71); death risk (1 in 95)
- Prevalence low 40/100,000 women >50
- 2/3’s cases diagnosed after 55
- 90% of cases sporadic
- Risk triples if 1st degree relative has breast or ovarian cancer
- BRCA1 mutation: 39-46% lifetime risk
- BRCA2 mutation: 12-20% lifetime risk

High Grade Serous Ovarian Carcinoma: New Insights

- Comprises ≥ 90% of advanced stage ovarian carcinoma
  - Rarely detected in stage 1 (< 1%)
  - Shorter duration of symptoms
- Fallopian tube in situ lesions may be present for 4 years
  - Once spread beyond tube, disease progression very rapid
- Screening must target detecting tubal lesions


US Preventive Service Task Force

- Recommends against routine ovarian cancer screening
- Only 2 methods available: CA-125, ultrasound
  - “A high percentage of women who undergo screening experience false-positive test results and consequently may be subjected to unnecessary harms, such as major surgery.”
- Panel considers only risks and benefits of screening, not costs


Available Screening Tools

- Pelvic examination
  - Detects 1 cancer in 10,000 asymptomatic women
- Serum CA125
  - Detects only 50% of ovarian cancer confined to ovary
    - High false positive rates
- Ultrasound
  - Expensive
  - High false positive rates

Simple Ovarian Cysts: Women > 55 Years

- 15,535 mostly postmenopausal women
- Annual transvaginal ultrasounds x 4 years
- 14.1% had simple cysts detected
  - 55-59: 10%
  - >60: 15%
- New cysts: 8% per year
- At time of second ultrasound:
  - 54% retained simple cyst
  - 32% no cyst seen
- Presence of simple cyst not associated with increased risk of later invasive ovarian cancer


Need to Identify High Risk Women

- Genetic counseling increases accuracy of risk perception
  - Decreases intention for genetic testing among unlikely carriers
  - Decreases cancer-related worry, anxiety and depression
- No trials evaluated effectiveness of intensive screening
  - Mastectomy decreased breast cancer 85-100%
  - BSO decreased: breast cancer 37-100%
    ovarian cancer 69-100%
  - all-cause mortality 55-100%


United Kingdom Collaborative Trial of Ovarian Cancer Screening Early Results

- Holds best (and currently only) hope
- Studying changes in annual CA-125 levels over time in algorithm with US as second line test (MMS) vs. annual ultrasound (USS) vs. placebo
- Abnormal screens → repeat tests
  - Surgery for persistent abnormalities
- Mortality data will be available 2015

Ovarian Carcinoma Risk Reduction *BRCA* Mutation Carrier

- Salpingectomy age 40 with delayed oophorectomy at age 50:
  - Highest quality-adjusted life expectancy
  - Cost per year life saved
    - *BRCA1* $37,805/year
    - *BRCA2* $89,680/year


U.S. Incidence of Cervical Cancer

- In US in 2015, 12,900 new cases and 4,100 deaths
- 70% reduction due to Pap smear screening
- Cervical cancer is disease of economically disadvantaged—elderly, minorities and low socioeconomic status
- Types of cervical carcinoma: squamous 85%; adenocarcinoma 15%

Natural Course of HPV Infection
## Screening Recommendations

<table>
<thead>
<tr>
<th>Age/Condition</th>
<th>Screening</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 21</td>
<td>No Screening</td>
</tr>
<tr>
<td>21 – 29</td>
<td>Cytology alone Q3 years</td>
</tr>
<tr>
<td>30 – 65</td>
<td>HPV and cytology “co-testing” Q 5 years OR</td>
</tr>
<tr>
<td>&gt; 65</td>
<td>Cytology alone Q 3 years</td>
</tr>
<tr>
<td>After hysterectomy</td>
<td>No screening if no prior ≥ CIN 2 in prior 20 years</td>
</tr>
</tbody>
</table>


## Primary High-Risk HPV Testing for Cervical Cancer Screening: Interim Guidelines

- Persistent HR-HPV risk for cervical dysplasia and cancer
- HR-HPV test approved by FDA for
  - Triage of ASC-US
  - Co-testing
  - Primary HR-HPV screening for women ≥ 25 years

Nelson: Controversial Topics in Women’s Health

**HPV Screening Algorithm**

```
HPV Screening Algorithm

Type 16/18 Positive
  → Cervical Biopsy

Primary HPV Screening
  → 12 other hHPV → Cytology
  → Follow up in 12 months

Negative
  → Routine Screening
```


**Alternative Screening Methods**

- High risk HPV testing of urine sample
  - Concordance with cervical cytology 80%
  - Sensitivity for HSIL 100%
  - Specificity for HSIL 80%
  - Positive predictive value 91%
- Blind vaginal swabs for HR-HPV
  - Acceptable yield of endocervical cells
- Self swabbing for cytology and HR-HPV samples


**Future Developments: Cervical Adenocarcinoma**

- HPV 16, 18 account for:
  - 70% squamous cell carcinoma
  - 80% adenocarcinoma
- HPV test-based screening may be more effective than cytology-based screening for adenocarcinoma
  - HPV 77.8% vs. PAP 17.4%
  - HPV adenocarcinoma detected earlier by HPV-tests

9-Valent Vaccine Trial

- 9-valent (9vHPV) vs 4-valent (qHPV) trial (3 injections at baseline, months 2 and 6)
  - 14,209 young women (16-26 years old) followed 54 months
- 9-valent reduced incidence of high grade cervical, vulvar and vaginal disease due to HPV 31,33,45,52, and 58
  - 96.7% in per protocol population (0.1 vs 1.6/1,000 person-years)
  - All cases occurred in women who were HPV-infected prior to vaccination

9-Valent Vaccine Trial con’t

- Rate of high grade cervical, vulvar or vaginal disease caused by any HPV in modified ITT population 14/1,000 person years in both groups
- Antibody to HPV 6,11,16,18 were same in non-inferiority trial
- Potential qHPV → 9vHPV:
  - Prevent 70% → 90% cervical cancer


Treatment CIN 2-3
Topical Imiquimod: 16 Week Trial

- Randomized, double-blind, placebo-controlled phase 2 trial self applied vaginal imiquimod vs. placebo:

<table>
<thead>
<tr>
<th></th>
<th>Imiquimod</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reduced to ≤ CIN 1</td>
<td>73%</td>
<td>39%</td>
</tr>
<tr>
<td>Complete remission</td>
<td>47%</td>
<td>14%</td>
</tr>
<tr>
<td>HPV clearance</td>
<td>60%</td>
<td>14%</td>
</tr>
<tr>
<td>Complete remission HPV-16</td>
<td>47%</td>
<td>0</td>
</tr>
<tr>
<td>Microinvasive</td>
<td>0</td>
<td>5%</td>
</tr>
<tr>
<td>Erythema</td>
<td>37%</td>
<td></td>
</tr>
<tr>
<td>Erosion</td>
<td>30%</td>
<td></td>
</tr>
<tr>
<td>Severe edema</td>
<td>13%</td>
<td></td>
</tr>
</tbody>
</table>

New Technologies Impacting on Traditional Testing Recommendations

- NAATs (Nucleic Acid Amplification Tests)
  - Able to detect single copy (for maybe 2)
  - Now able to change testing used for
    - Gonorrhea
    - Chlamydia
    - Trichomonosis
    - Cervical dysplasia

Routine Testing Recommendations

- 17 year old sexually active asymptomatic woman needs tests for which?
  - Chlamydia
  - Gonorrhea
  - Syphilis
  - High Risk HPV
  - HIV
  - Cervical cytology
  - Trichomoniasis
  - Herpes simplex II

Chlamydia Testing

- Rank in order of sensitivity
  - Cervical swab
  - Urine specimen
  - Vaginal swab – patient collected
  - Vaginal swab – clinician collected
How Often Do Women **Need** Screening Pelvic Examination?

- Annually
- Every 2 years
- Undefined, maybe never?

**Pelvic Exam: Future Predictions**

- Pelvic examinations will not be routinely performed as screening test
  - Insensitive for detecting pelvic masses
  - Other routine screening tests will not require traditional pelvic examination
    - Vaginal swabs for GC/CT/HR-HPV
  - Pelvic examination will become almost exclusively diagnostic test

**Random Questions**

- Do we ever need to culture for Neisseria gonorrhea?
- Is a test of cure needed in 3 months for any STD?
- What are the California state regulations about patient delivered partner therapy?
Heavy Menstrual Bleeding: Factors Influencing Therapies

- Age of patient
- Severity of symptoms
- Presence of associated pelvic pathology
- Fertility plans

**NOTE:** Most therapies recommended are off-label

- The only drugs that are FDA-approved for the treatments of heavy bleeding are cyclic MPA, LNG-IUS20mg, tranexamic acid, E₂/V/DNG oral contraceptive

High Dose Progestin Treatments for Acute Uterine Bleeding (n=40)

MPA 20mg given orally 3 times a day for 7 days, then once daily for 21 days

**vs.**

35 mcg EE/1 mg NETA given orally 3 times a day for 7 days, then 20 mcg EE/1 mg NETA once daily for 21 days

<table>
<thead>
<tr>
<th></th>
<th>MPA</th>
<th>COC</th>
</tr>
</thead>
<tbody>
<tr>
<td>No surgery</td>
<td>100%</td>
<td>95%</td>
</tr>
<tr>
<td>Cessation of bleeding</td>
<td>76%</td>
<td>88%</td>
</tr>
<tr>
<td>Days to Cessation</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Patient satisfaction (0-4)*</td>
<td>3</td>
<td>3</td>
</tr>
</tbody>
</table>

* 0 = unsatisfied


Good News: MediCal Covers

- Immediate postpartum placement of IUDs
  - Placement at time of elective c/Section has lower expulsion rates
- Postpartum (before she goes home) placement of contraceptive implants
  - Will not adversely impact on breastfeeding success
- Sad news:
  - High risk women often don't return for postpartum follow-up care
  - ≥ 40% of women requesting postpartum tubal ligation do not get it.