Timing of Induction of Labor: Myths, Facts, and Misunderstandings?

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Financial Relationships

- No financial disclosures related to this talk
- Medical Advisor to:
  - Celmatix
  - Mindchild
- Bob's Red Mill

Outline

- **Gestational age at term**
- **'Elective' IOL varying GA**
  - **Early Term**
  - **Late Term**
  - **Full Term**
- **Induction of labor**
  - **Outcomes**
  - **Cesarean**

Definitions

- **Early Term 37 0/7 to 38 6/7**
- **Full Term 39 0/7 to 40 6/7**
- **Late Term 41 0/7 to 41 6/7**
- **Postterm 42 0/7 and beyond**

Outcomes by Gestational Age

Caughey AB, Musci TJ. Obstet Gynecol, 2004;103:57-62

Neonatal Morbidity by GA

Neonatal Outcomes

	37 weeks	38 weeks	39 weeks	40 weeks	41 weeks
5-minute Apgar <7	1.01 %	0.69 %	0.61 %	0.70 %	0.93 %
5-minute Apgar <4	0.19 %	0.13 %	0.11 %	0.12 %	0.14 %
Meconium stained amniotic fluid	2.27 %	3.24 %	5.20 %	7.39 %	10.33 %
Meconium aspiration	0.07 %	0.08 %	0.12 %	0.19 %	0.27 %
Hyaline membrane dz	0.45 %	0.19 %	0.14 %	0.14 %	0.18 %
Mech vent >30min	0.57 %	0.32 %	0.28 %	0.29 %	0.38 %

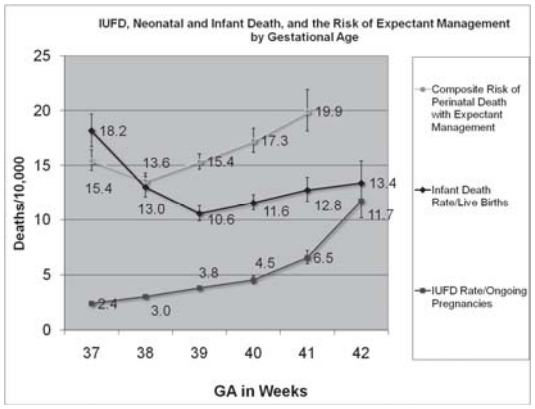
Cheng YW, et al. AJOG, 2008

Elective CDs: NICU by GA

Outcome	Wk 37 (N=834)	Wk 38 (N=3909)	Wk 39 (N=6512)	Wk 40 (N=1385)	Wk 41 (N=505)	Wk ≥42 (N=113)	P for Trend†
			number/total number (percent)				
Any adverse outcome or death	128/834 (15.3)	430/3909 (11.0)	524/6512 (8.0)	101/1385 (7.3)	57/505 (11.3)	22/113 (19.5)	<0.001
Adverse respiratory outcome							
Respiratory distress syndrome	31/833 (3.7)	75/3904 (1.9)	58/6510 (0.9)	13/1381 (0.9)	4/504 (0.8)	2/113 (1.8)	<0.001
Transient tachypnea of the newborn	40/833 (4.8)	153/3904 (3.9)	178/6508 (2.7)	34/1381 (2.5)	24/504 (4.8)	7/113 (6.2)	<0.001
Respiratory distress syndrome or transient tachypnea of the newborn	68/833 (8.2)	213/3904 (5.5)	221/6510 (3.4)	42/1381 (3.0)	26/504 (5.2)	9/113 (8.0)	<0.001
Admission to the NICU	107/833 (12.8)	316/3905 (8.1)	382/6510 (5.9)	66/1381 (4.8)	40/504 (7.9)	16/113 (14.2)	<0.001

Tita A et al. NEJM, 2009

IUFD/Infant Death Rates - Compare



Rosenstein MR, et al. Obstet Gynecol, 2012

Elective IOL – What?

- **Common Medical Indications for IOL**
  - **Preeclampsia / Gest HTN**
  - **Diabetes Mellitus (A1GDM?)**
  - **Postterm (41 wks vs. 42 wks)**
  - **Intrauterine Growth Restriction**
  - **Nonreassuring fetal testing**

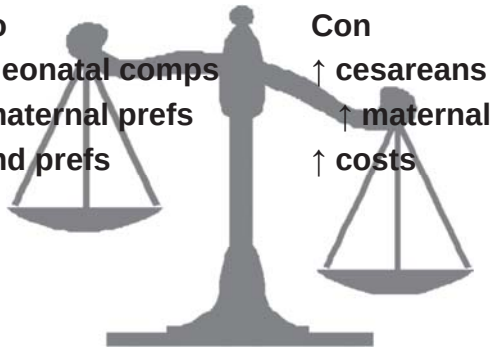
Elective IOL – What?

- **Not a medical indication for IOL**
  - **Impending macrosomia**
  - **Increased risk for developing:**
    - **Preeclampsia**
    - **IUGR (e.g. EFW 19%ile)**
  - **Favorable cervix**

Elective IOL – Why does it matter?

- **Indicated IOL**
  - **Risks and benefits have been considered**
  - **IOL vs. Expectant Mgmt**
- **Elective IOL**
  - **Risks and benefits should be considered**
  - **IOL vs. Expectant Mgmt**

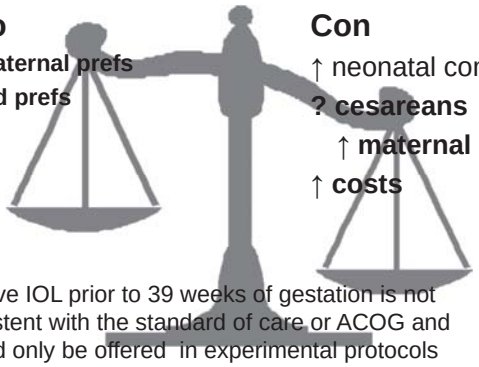
Elective IOL



Pro
? neonatal comps
↑ maternal prefs
↑ md prefs

Con
↑ cesareans
↑ maternal comps
↑ costs

Elective IOL – early term



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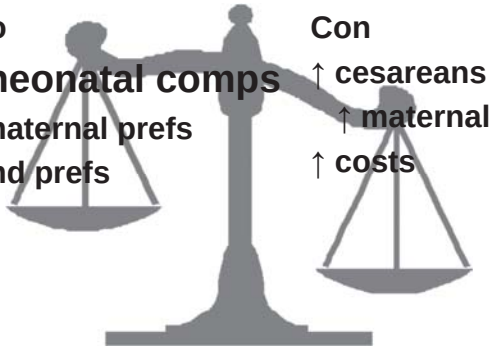
? cesareans
↑ maternal comps
↑ costs

Elective IOL prior to 39 weeks of gestation is not consistent with the standard of care or ACOG and should only be offered in experimental protocols with written informed consent

IOL – Early Term

- **IOL – When to deliver?**
  - **Preeclampsia / Gest Htn**
  - **Chronic Htn**
  - **Diabetes Mellitus (A1GDM?)**
  - **Intrauterine Growth Restriction**
    - **10%ile, 5%ile, 3%ile, changes on Doppler**
  - **Nonreassuring fetal testing**
  - **Cholestasis**
  - **Previa / accreta**
  - **Twins (Di-di vs. Mo-di)**

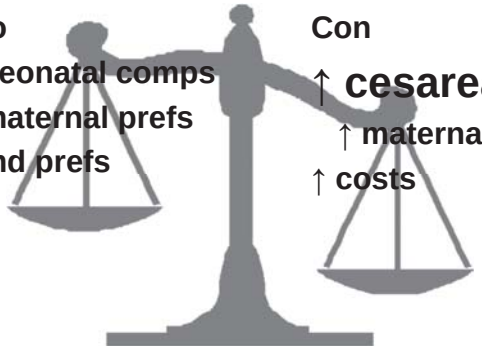
Elective IOL – late term



Pro
↓ neonatal comps
↑ maternal prefs
↑ md prefs

Con
↑ cesareans
↑ maternal comps
↑ costs

Elective IOL – late term



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↑ md prefs

Con
↑ cesareans
↑ maternal comps
↑ costs

Elective IOL - CS

- **Does IOL increase cesarean delivery?**

- **Cohort and case-control data**
  - **IOL increases cesareans**
- **Prospective RCTs**
  - **41 weeks GA – decreases cesareans**
  - **<41 weeks GA – ?**

Induction of Labor

- Comparison of IOL vs. ANT
  - (Hannah et al., NEJM, 1992
- 1701 IOL @ 41 wks vs. 1706 ANT @ 41 wks
  - C/S higher in ANT group (24.5% vs. 21.2%)
  - C/S for FD higher as well (8.3 % vs. 5.7%)
  - Higher rate of meconium in ANT group
  - No difference noted in neonatal morbidity

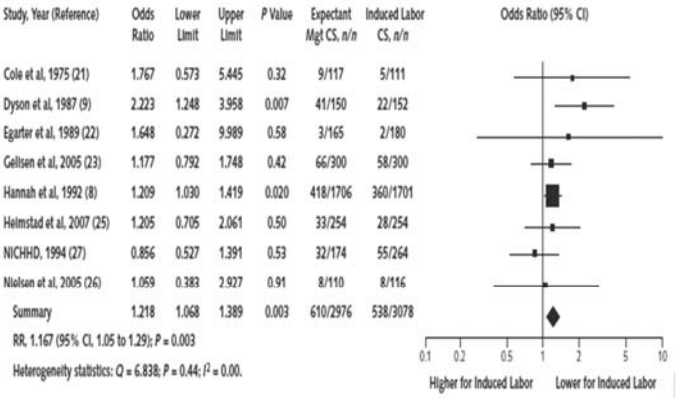
Induction of Labor

- IOL vs. Expt Mgmt 41 wks and beyond
  - Sanchez-Ramos et al, OB Gyn, 2003
  - Meta-analysis, 16 prospective RCTs
- Mode of delivery

	IOL	Expt Mgmt	OR 95% CI
•	CS - 20.1%	CS – 22.0%	0.78 – 0.99
•	Mec – 22%	Mec – 27%	0.49 – 0.88
•	PMR – 0.09%	PMR – 0.33%	0.14 – 1.18

PMR = perinatal mortality rate

Elective IOL at 41 wks or less

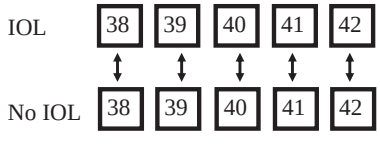


Caughey AB, et al. Ann Int Med, 2009;151:252-63.

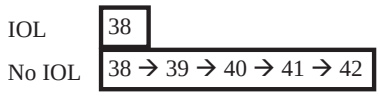
Induction of Labor - CS

- Retrospective studies - more CS with IOL
- Prospective studies – fewer CS or no diff
- What are the groups being compared?
- IOL at 39 weeks vs.
  Spont labor at 39 weeks
- However, in RCT:
  - IOL at 39 weeks GA vs.
  - Patients beyond 39 weeks GA

Induction of Labor < 41 wks GA



A. Comparison by week of gestation



B. Comparison of IOL and Expectant Management

Caughey et al, AJOG 2006;195:700-5

Elective IOL - CS

Elective IOL vs. Expt. Mgmt - Cesarean Delivery

Gestational Age Group (wk)	Model	Cesarean Delivery
All deliveries		
37	305,099	0.44 (0.34–0.57)
38	245,006	0.43 (0.38–0.50
39	150,730	0.46 (0.41–0.52)
40	58,845	0.57 (0.50–0.65)
Nulliparous		
37	143,982	0.66 (0.49–0.89)
38	118,283	0.74 (0.63–0.87)
39	75,828	0.75 (0.67–0.83)
40	30,837	0.77 (0.67–0.88)

Darney B, et al. OBG. 2013

IOL at term

- **ARRIVE Trial**
- **6106 women randomized to IOL vs. Expt Mgmt. at 39 to 39 4/7 wks GA**

Maternal	IOL	Expt Mgmt		
Cesarean delivery	569 (18.6)	673 (22.2)	0.84	0.76 – 0.93
Preeclampsia/gestational hypertension	277 (9.1)	427 (14.1)	0.64	0.56 – 0.74
Chorioamnionitis	407 (13.3)	429 (14.1)	0.94	0.83 – 1.07
3rd/4th * laceration	103 (3.4)	89 (2.9)	1.15	0.87 – 1.52
Post-partum hemorrhage	142 (4.6)	137 (4.5)	1.03	0.82 – 1.29
Intensive care unit	4 (0.1)	8 (0.3)	0.50	0.13 – 1.55

Grobman W, et al., NEJM 2018

IOL at term

- **ARRIVE Trial**

	IOL	EM	RR	95% CI
Perinatal				
Perinatal composite	133 (4.4)	164 (5.4)	0.81	0.64 – 1.01
Perinatal death	2 (0.1)	3 (0.1)	0.66	0.12 – 3.33
Respiratory support (intubation, CPAP or high-flow nasal cannula for ventilation or CPR) within first 72 hours	91 (3.0)	127 (4.2)	0.71	0.55 – 0.93
Apgar ≤ 3 at 5 minutes	12 (0.4)	18 (0.6)	0.66	0.32 – 1.37
Hypoxic ischemic encephalopathy	13 (0.4)	19 (0.6)	0.68	0.34 – 1.37
Seizures	11 (0.4)	4 (0.1)	2.73	0.91 – 8.12
Infection (confirmed sepsis or pneumonia)	13 (0.4)	14 (0.5)	0.92	0.43 – 1.96
Meconium aspiration syndrome	17 (0.6)	26 (0.9)	0.65	0.35 – 1.19
Birth trauma	14 (0.5)	18 (0.6)	0.77	0.38 – 1.55
Intracranial or subgaleal hemorrhage	9 (0.3)	7 (0.2)	1.28	0.48 – 3.42
Hypotension requiring pressor support	3 (0.1)	5 (0.2)	0.60	0.13 – 2.27

Grobman W, et al. AJOG, NEJM 2018

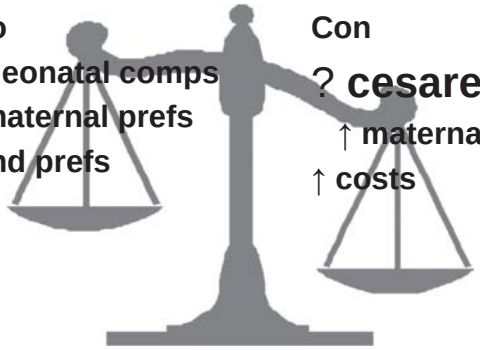
Elective IOL – full term

Pro

? neonatal comps

↑ maternal prefs

↑ md prefs



Con

? cesareans

↑ maternal comps

↑ costs

Elective IOL - CS

- **Prospective RCT at 41 wks – lower CS**
- **Prospective RCTs < 41 wks – lower CS**
- **Multiple retrospective studies – higher CS**
- **Appropriate retrospective studies – lower/no diff in CS**
- **Research protocols vs. Actual practice**

IOL - patience

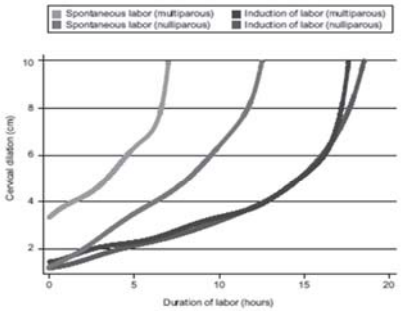


Fig. 1. Average labor curves stratified by parity and type of labor onset.
Harper. Normal Labor in Induction. Obstet Gynecol 2012.

Is 39 the new 41?

- **Why Not**
  - **The proportion impacted is dramatically different**
  - **The risk from 39 to 40 differs from 41 to 42**
  - **ARRIVE is great, but we have many more 41 RCTs**
  - **Need to understand global clinical/economic impact**
- **Maybe**
  - **Cesarean data is convincing, at least in right settings**
  - **Also prevents hypertensive complications**
  - **Might be cost effective**

Summary – Should Every Woman Be Induced at 39 weeks?

- Early Term (37-38 wks GA)
  - Currently, a bad idea without indication
- 41 wks GA (some call this postterm)
  - ACOG recommends
  - Improved outcomes
- Full Term (39-40 wks GA)
  - Not a violation of SOC
  - Evidence is evolving
  - Depends on environment
  - Economic Impact

Thank You

Elective IOL - CS

Elective IOL vs. Expt. Mgmt - Perinatal Mortality

Gestation week of IOL	No with outcome/Total No in group (%)		Univariate analysis
	Expectant management	Elective IOL	Odds ratio (99% CI)
Primary analysis: comparator delivery beyond gestation of IOL			
37	2829/1 213 639 (0.23)	4/4429 (0.90)	0.39 (0.11 to 1.40)
38	2190/1 073 170 (0.20)	9/11 384 (0.08)	0.39 (0.16 to 0.92)
39	1 521/810 720 (0.19)	9/16 344 (0.06)	0.29 (0.12 to 0.69)
40	627/350 643 (0.18)	37/44 764 (0.08)	0.46 (0.30 to 0.71)
41	127/58 028 (0.22)	50/76 028 (0.07)	0.30 (0.20 to 0.46)

Stock S. BMJ. May, 2012

Case #3

- 27 yo G1P0 at 39 1/7 requesting IOL
  - Unfavorable cervix
- Expt Mgmt & ANT vs. IOL
  - Neonatal outcomes
  - Maternal outcomes
  - Cesarean Delivery
- What are the R/B/A

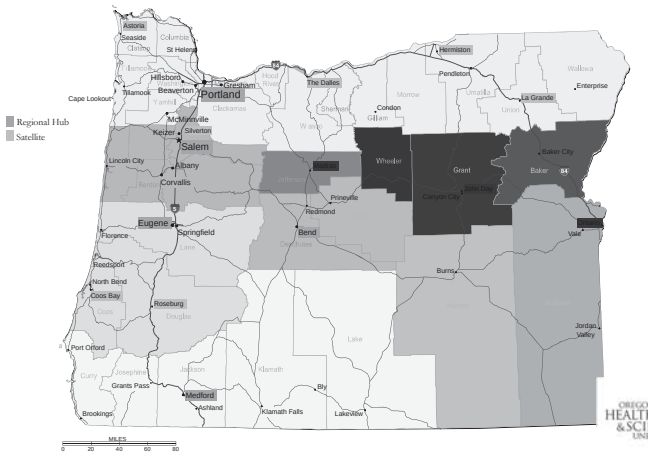
Back to Case #3

- 27 yo G1P0 at 39 1/7 requesting IOL w an unfavorable cervix.
- Plan:
  - A) IOL now
  - B) IOL at 40 wks
  - C) IOL at 41 wks
  - D) IOL at 42 wks

Elective IOL – Hard Stop

- Why?
- Right thing to do medically.
- IOL costly
- Need to do geographically
  - Facilitates providers to “just say no”

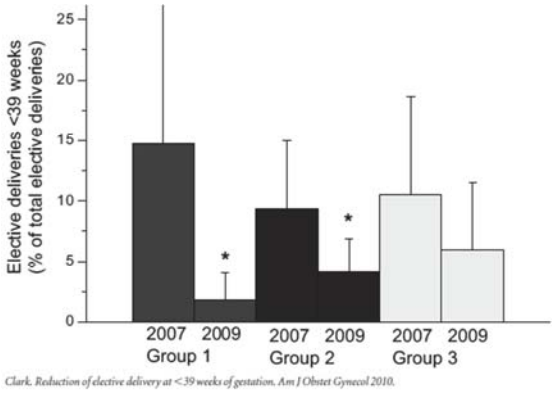
Elective IOL – Hard Stop



Prevention of Early Term Births

- HCA - Clark S, et al. – 2010
- Three approaches
  - Hard stop – not allowed
  - Soft Stop – MDs agreed not to do
  - Education

Prevention of <39 weeks

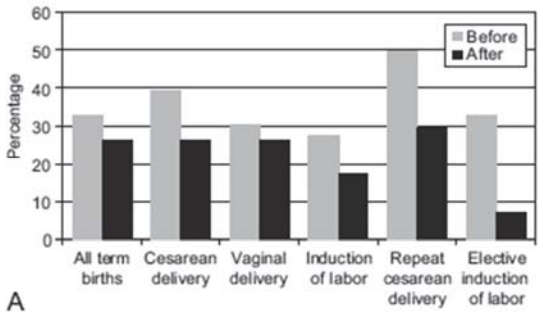


Clark. Reduction of elective delivery at <39 weeks of gestation. Am J Obstet Gynecol 2010.

Clark et al, Am J Obstet Gynecol, 2010

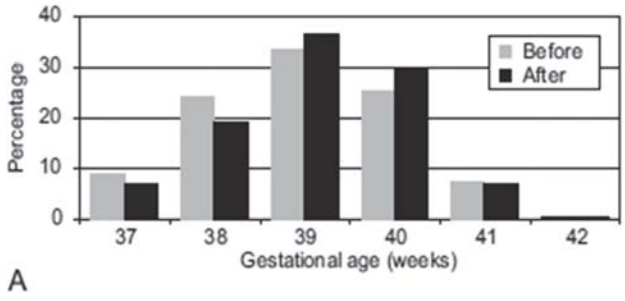
Elective IOL – Hard Stop

Term births at 37 or 38 weeks’ gestation



Ehrenthal et al, Obstet Gynecol, 2011

Elective IOL – Hard Stop



Ehrenthal et al, Obstet Gynecol, 2011

Elective IOL – Hard Stop

Table 3. Crude and Adjusted Odds of Neonatal Intensive Care Unit Admission and Macrosomia Overall and Stratified by Race and Ethnicity for All Live Births After (2008 and 2009) When Compared With Before (2005 and 2006) Implementation of Guidelines

Outcome	Characteristic (n)	Crude OR	95% CI	Adjusted OR	95% CI
NICU admission*					
Overall	24,028	0.91	0.84–1.00	0.92	0.84–1.01
White	13,927	0.89	0.79–1.00	0.88	0.78–1.00
African American	5,602	0.97	0.82–1.16	1.02	0.85–1.23
Hispanic	2,832	0.90	0.70–1.16	0.95	0.72–1.26
Macrosomia†					
Overall	24,028	1.06	0.97–1.15	1.11	1.01–1.22
White	13,927	1.16	1.05–1.29	1.17	1.05–1.31
African American	5,602	1.24	0.97–1.58	1.22	0.93–1.58
Hispanic	2,832	0.73	0.56–0.96	0.75	0.57–0.99

Ehrenthal et al, Obstet Gynecol, 2011

Elective IOL – Hard Stop

Table 4. Stillbirths, Stillbirth Rate, and Relative Risk of Stillbirth by Gestational Age Group After (2008 and 2009) When Compared With Before (2005 and 2006) Implementation of Guidelines

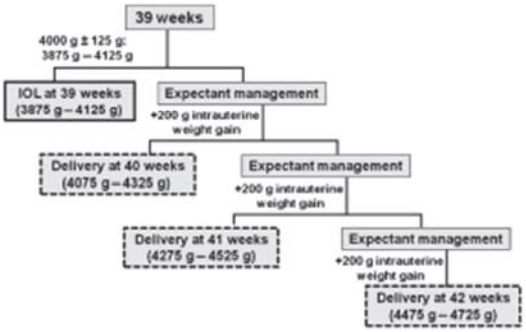
	Before			After				
Gestational Age (wk)	Stillbirths	Ongoing Pregnancies	Rate*	Stillbirths	Ongoing Pregnancies	Rate*	Relative Risk (95% CI)	P
Early term							3.67 (1.02–13.15)	.032
37	3	12,022	0.249	6	12,028	0.498		
38	0	10,939	—	5	11,153	0.448		
Full term							0.91 (0.23–3.64)	.896
39	2	4,018	0.249	2	4,406	0.226		
40	1	3,079	0.248	1	3,550	0.225		
41	1	944	1.06	1	885	1.29		

Ehrenthal et al, Obstet Gynecol, 2011

Case #3 – What are R&B?

- 27 yo G1P0 at 39 1/7 requesting IOL
  - LGA
- Based on past evidence:
  - IOL at 40 weeks GA as compared to ANT
    - No difference in cesarean rate
    - No difference in neonatal outcomes

IOL for Macrosomia



Cheng et al, BJOG, 2012

IOL for Macrosomia

Table 2. Frequency and adjusted odds ratio of caesarean delivery and neonatal outcome by gestational age at delivery in women with neonates with birthweight 4000 ± 125 g at time of induction compared with delivery at a later gestational age (expectant management), assuming an intrauterine weight gain of 200 g/week

4000 ± 125 g	Caesarean delivery (%)	aOR*	95% CI
39 weeks of gestation			
Induction (n = 10 381)	35.2	Referent	1.17–1.33
Expectant (n = 32 042)	40.9	1.25	
40 weeks of gestation			
Induction (n = 10 119)	36.1	Referent	1.23–1.40
Expectant (n = 14 245)	42.6	1.31	
41 weeks of gestation			
Induction (n = 5722)	38.9	Referent	1.06–1.28
Expectant (n = 3509)	41.8	1.16	

Cheng et al, BJOG, 2012

2 Induction of labor or expectant management for large-for-dates fetuses: a randomized controlled trial

Michel Boulvain[1], Marie-Victoire Senat[2], Patrick Rozenberg[3], Olivier Irion[1]
[1]University Hospitals of Geneva, Gynecology and Obstetrics, Geneva, Switzerland, [2]Bicetre Hospital, Gynecology and Obstetrics, Le Kremlin-Bicetre, France, [3]CHI Poissy-Saint-Germain-en-Laye, Gynecology and Obstetrics, Poissy, France

OBJECTIVE: To compare induction of labor with expectant management for large for dates fetuses to prevent macrosomia at birth, shoulder dystocia and the associated neonatal morbidity.
STUDY DESIGN: We conducted a randomized controlled trial in collaboration with 20 teaching hospitals, members of the GROG group, in France, Switzerland and Belgium. We included 817 women with a fetus with an estimated weight above the 95th percentile at 37 to 38 weeks of gestation. Women with diabetes treated v history of cesarean section or shoulder dystocia The screening was first performed clinically (esti the 90th percentile), then a sonography was perfo eligible if the sonographic estimated weight was centile. Women were randomized to induction of (n=407) or expectant management (n=410). Th measure was neonatal trauma, including significa (defined as resolved by maneuvers other than Mcl the clavicle and brachial plexus injury, or perinat
RESULTS: Baseline characteristics were similar bet ference in mean birthweight of nearly 300 gr b obtained (3831 gr versus 4112 gr). The risk of n reduced with induction of labor (n=9, 2.2%), cor management (n=27, 6.6%) (RR: 0.34; 95%CI: 0.1 lihood of a spontaneous vaginal delivery was high- 1.00 to 1.29) in the induction of labor group. T section was not increased after induction of labor the induction and expectant groups, respectively). Other neonatal morbidities were similar between groups, with no recorded cases of wet lung, brachial plexus palsy and perinatal death.
CONCLUSION: Induction of labor in case of suspected large for dates fetus is associated with a lower risk of trauma at birth. This intervention does not result in an increased risk of cesarean section and improve the likelihood of a spontaneous vaginal delivery.

RESULTS: Baseline characteristics were similar between groups. A difference in mean birthweight of nearly 300 gr between groups was obtained (3831 gr versus 4112 gr). The risk of neonatal trauma was reduced with induction of labor (n=9, 2.2%), compared to expectant management (n=27, 6.6%) (RR: 0.34; 95%CI: 0.16 to 0.71). The likelihood of a spontaneous vaginal delivery was higher (RR 1.14; 95%CI: 1.00 to 1.29) in the induction of labor group. The risk of cesarean section was not increased after induction of labor (28.0% vs 31.7% in the induction and expectant groups, respectively). Other neonatal morbidities were similar between groups, with no recorded cases of wet lung, brachial plexus palsy and perinatal death.

Case Presentations

- 1 – 32 yo G3P2 at 38 0/7 requesting IOL
  - Normal Pregnancy
- 2 - 34 yo G2P1 at 41 2/7 declining IOL
  - Normal ANT
- 3 - 27 yo G1P0 at 39 1/7 requesting IOL
  - Unfavorable cervix

Case #1

- 32 yo G3P2 at 38 0/7 requesting IOL
  - Normal pregnancy
- Elective IOL prior to 39 weeks of gestation is not consistent with the standard of care or ACOG and should only be offered in experimental protocols with written informed consent

Elective IOL – Hard Stop

the Atlantic

POLITICS | BUSINESS | ENTERTAINMENT | INTERNATIONAL

Why Hospitals in Portland Are Banning Early Births

AUG 12 2011, 10:38 AM ET

Induced labor and c-sections are all the rage among patients and doctors alike. They're also more expensive and dangerous than the alternative.

Hospitals take 'hard stop' on early elective C-sections, inductions

Oregon is the latest state where some hospitals are refusing to do the procedures before 39 weeks of pregnancy

Case #2

- 34 yo G2P1 at 41 2/7 declining IOL
  - Normal ANT
- Expt Mgmt & ANT vs. IOL
  - Neonatal outcomes
  - Maternal outcomes
  - Cesarean Delivery
- What is the pt's understanding of R/B/A

Induction of Labor

- Even w/ unfavorable cvx, @ 41 wks IOL:
  - Lower cesarean delivery rate
  - Lower meconium-stained fluid
  - Lower perinatal mortality rate (small diff)

Back to Case #2

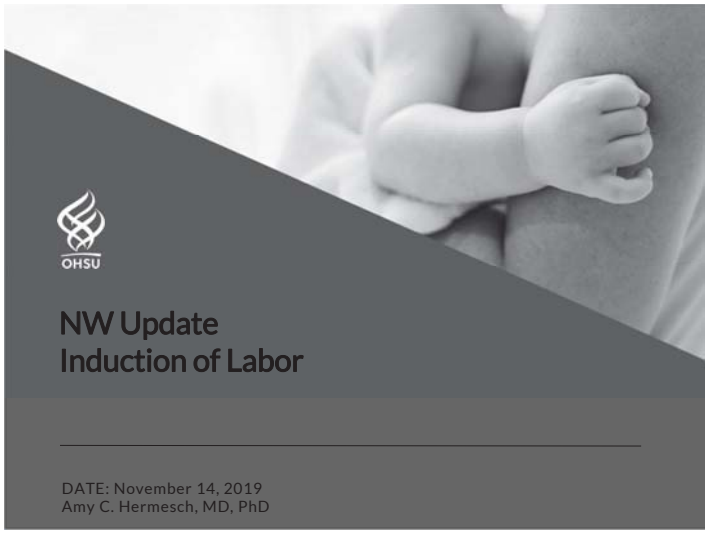
- 34 yo G2P1 at 41 2/7 declining IOL
- Biggest concern is that her pregnancies are supposed to go longer
- Another concern is labor pain similar to first IOL
- Plan:
  - Extensive counseling re: R&B
  - Strip membranes
  - ANTC at 41 4/7 – strip again
  - Plan IOL at 42 0/7

IOL < 41 wks GA

- **Cochrane DB – Gülmezoglu AM et al, 2006**
- **IOL < 41 weeks had lower CS rate**
- **RR 0.58; 95% CI 0.34 to 0.99**

Questions?
Contact me

OHSU Physician Advice & Referral Service
- 503-494-4567
- 800-245-6478 (toll-free)



NW Update
Induction of Labor

DATE: November 14, 2019
Amy C. Hermesch, MD, PhD

Financial Disclosures

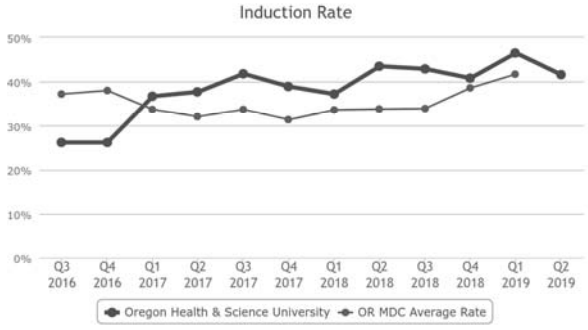
- None

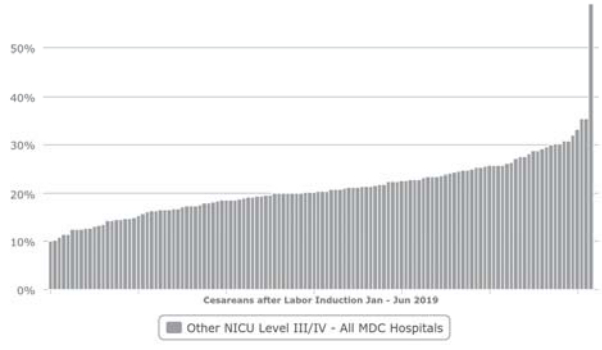
Outline

- IOL as a Quality Project
- Guideline development
- Limited evidence review
- Summary

Choosing a quality project

- Externally mandated measures/required reporting?
- High volume of patients impacted?
- High cost of disease process or potential for significant cost reduction?
- Variability in practice pattern?
- Quality of patient safety concern?
- Potential for improved patient or provider satisfaction?
- Is there evidence to guide practice?



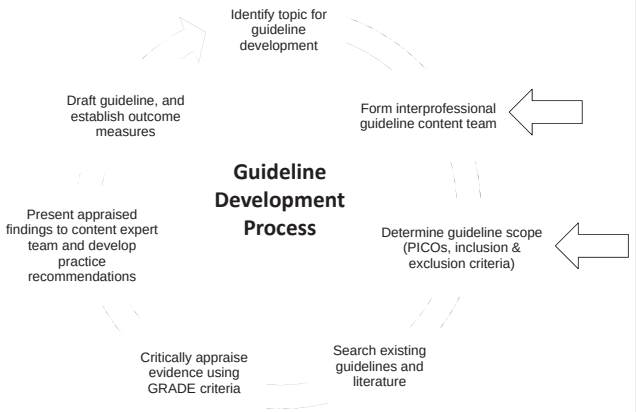


Oregon Maternal Data Center (OMDC)

OHSU Office of Clinical Integration and Evidence-Based Practice

- Promoting best practice and reducing undesirable practice variation.
- Supports clinical decision making
- Develops infrastructure that supports delivery of value based care, shifting focus from volume of services delivered to the patient-centered outcomes achieved.

Step 1: Facilitated Guideline Development



OHSU Health System
Office of Clinical Integration and Evidence-Based Practice
Induction of Labor Guideline Evidence Summary

November 2019

Date started: December 2018
Date completed: November 2019

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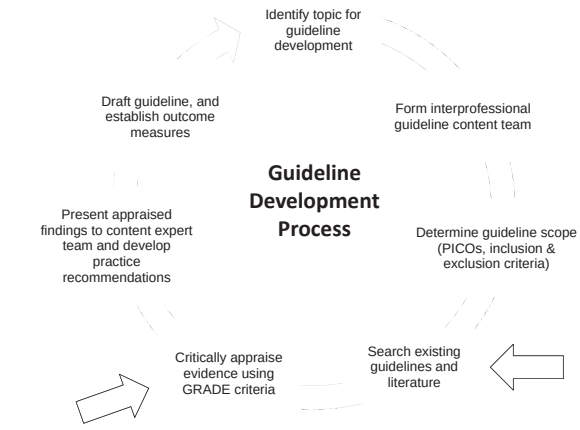
IOL Guideline Content/Scope Determined by Content Expert Team:

- Outcomes:
  - Efficacy
  - Length of time from start of IOL to delivery
  - Maternal outcomes including CD rate
  - Neonatal outcomes
- Guideline Content Overview:
  - Pharmacologic, non-pharmacologic (membrane sweeping, breast stim, etc), mechanical and combination methods. Dosing? Route?
  - Setting of cervical ripening
  - Optimal oxytocin protocol after ripening
  - Optimal route and dose of nutrition and hydration during IOL
  - What are patients views and experiences during IOL?
  - What are the effects of staffing models during IOL?
  - Early vs late administration of epidural anesthesia?
  - When is cesarean delivery for failed IOL indicated?

Step 1: Facilitated Guideline Development



Existing National and Local Guidelines

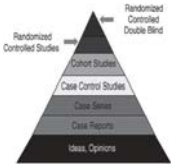
External Guideline	Organization and Author	Last Update
National and International Guidelines		
ACOG Practice Bulletin on the Induction of Labor	The American College of Obstetricians and Gynecologists	2009
Practice Guidelines for Obstetric Anesthesia	American Society of Anesthesiologists Task Force on Obstetric Anesthesia and the Society for Obstetric Anesthesia and Perinatology	2015
Clinical Practice Guideline: Planning for Labor and Vaginal Birth After Cesarean	American Academy of Family Physicians	2014
Clinical Guideline: Induction of Labor	National Institute for Health and Clinical Excellence (NICE) United Kingdom	2013
Polish Gynecological Society recommendations for labor induction	Polish Gynecological Society	2017
Internal Guideline		
OB Cervical Ripening and Induction/ Augmentation of Labor	OHSU	2018

The seven published clinical guidelines were evaluated for this review using the **University of Pennsylvania's Center for Evidence-Based Practice Trustworthy Guideline rating scale.** The scale is based on the Institute of Medicine's "Standards for Developing Trustworthy Clinical Practice Guidelines" (IOM), as well as a review of the AGREE Enterprise and Guidelines International Network domains.

Guideline Issuer and Date	ACOG 2009	ASA 2015	AAFP 2014	NICE 2013	PGS 2017	OHSU 2018
1. Transparency	B	A	A	A	C	C
2. Conflict of interest	NR	A	A	A	NR	NR
3. Development group	NR	A	A	A	C	NR
4. Systematic Review	B	A	A	A	B	B
5. Supporting evidence	B	A	A	A	A	C
6. Recommendations	A	B	A	A	A	C
7. External Review	NR	NR	NR	A	NR	NR
8. Currency and updates	B	A	A	A	A	A

See appendix B for full description of the Trustworthy Guideline grading system.

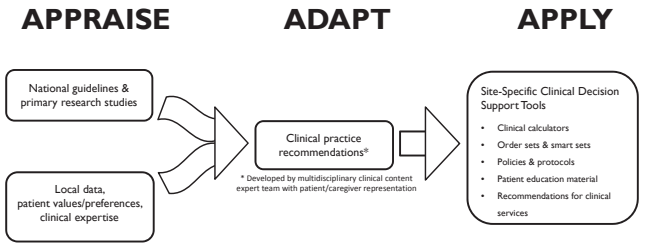
GRADE



GRADE (Grading of Recommendations Assessment, Development and Evaluation): common, sensible and transparent approach to grading quality (or certainty) of evidence and strength of recommendations. Many international organizations have provided input into the development of the GRADE approach which is now considered the standard in guideline development.

Recommendation	
STRONG	Desirable effects clearly outweigh undesirable effects or vice versa
WEAK	Desirable effects closely balanced with undesirable effects
Quality	**Type of Evidence**
High	Further research is very unlikely to change our confidence in the estimate of effect.
Moderate	Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low	Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very Low	Any estimate of effect is very uncertain.

Step 1: Facilitated Guideline Development



Cervical Ripening

- The "sour apple" of IOL
- Pharmacologic, mechanical, alternative and combination methods.
- Setting? PGE1 vs PGE2? Which route? Which dose?

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GUIDELINE FOR INDUCTION OF LABOR

Outpatient

- In low risk patients, outpatient cervical ripening with Foley Catheter may be considered. – **Conditional Recommendation, Low Quality Evidence** [9, 10]

Methods for Cervical Ripening:

- It is reasonable to offer membrane sweeping for cervical ripening, with the timing and frequency at the discretion of the provider and patient. – **Strong Recommendation, High Quality Evidence** [11]
- Evidence was inconclusive for cervical ripening with castor oil or acupuncture. If patient is interested in these methods, risk/benefit discussion with provider should include dialogue of inconclusive evidence. – **Conditional Recommendation, Moderate Quality Evidence** [12, 13]
- Sexual intercourse should not be routinely recommended solely for the purpose of cervical ripening. Inform patient that in the evidence, sexual intercourse was not effective for this purpose. – **Conditional Recommendation, Moderate Quality Evidence** [14-16]

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GUIDELINE FOR INDUCTION OF LABOR

Inpatient

Monitoring:

- For inpatient cervical ripening, fetal wellbeing should be assessed according to the pharmacologic agent used (see Table 1). **–Consensus Statement**

Methods for Cervical Ripening:

- Shared decision making should be used when choosing the method for cervical ripening. **– Strong Recommendation, Very low Quality Evidence** [17, 18]
- For inpatient cervical ripening, breast stimulation with a breast pump may be considered. **–Conditional Recommendation, Low Quality Evidence** [19, 20]

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- Preferred Options (see Table 1 for more details) includes:
  - Misoprostol
    - Vaginal administration, 25µ misoprostol every four hours – **Strong Recommendation, Moderate Quality Evidence**[24] or
    - Oral administration, 50µ misoprostol every four hours – **Strong Recommendation, Low Quality Evidence**[25, 27] or
    - Oral misoprostol stepwise regimen of 50µ then 100µ after four hours followed by another 100µ after four hours – **Strong Recommendation, Very Low Quality Evidence** [28, 29]

    OR
  - Foley catheter alone filled with 60mL of saline – **Strong Recommendation, Low Quality Evidence** [30-33]

    OR
  - Foley catheter combined with any of the above misoprostol options – **Strong Recommendation. Moderate Quality Evidence** [33-37]
- Alternative Options (see Table 1 for more details) includes:
  - Dinoprostone 10mg vaginal insert – **Conditional Recommendation, Moderate Quality Evidence** [22, 38, 39]

    OR
  - Cook© Catheter used per the manufacturer's instructions – **Conditional Recommendation, Moderate Quality Evidence** [24, 40]

    OR
  - Foley catheter filled with 60mL saline with concurrent oxytocin, dosage TBD – **Conditional Recommendation, Very Low Quality Evidence** [41-43]
- Amniotomy, Oxytocin alone, Laminaria tent, and extra-amniotic saline infusion were not included in this evidence appraisal and can be used at the discretion of the clinician. **Consensus Statement**

Cervical ripening

- Cost
  - Misoprostol (PGE1, Cytotec): $0.50 per 100 mcg tablet
  - Dinoprostone (PGE2, Cervidil): $353 per insert
- Compared to PGE2, misoprostol is associated with:
  - Less common oxytocin augmentation
  - Less epidural analgesia use
  - Higher vaginal delivery rate within 24 hrs
  - Some studies show reduced risk of CD, some show no difference
  - Berghella V. Obstetric Evidence Based Guidelines, 3rd Edition
- Combination methods (misoprostol + foley)
  - Shorter mean duration from admit to delivery
  - *Al-Ibraheemi et al. Obstet Gynecol 2018. Jan; 131 (1): 23-29.*
  - *Carbone JF et al. Obstet Gynecology 2013. Feb 121: 247-52.*

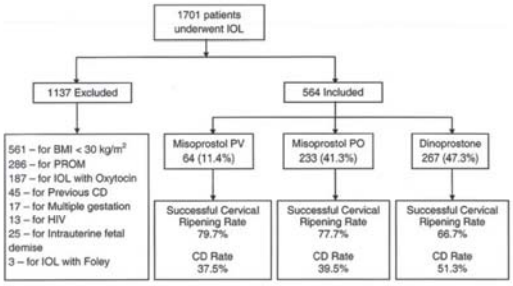

Fig. 1 Patient distribution. BMI, body mass index; CD, cesarean delivery; HIV, human immunodeficiency virus; IOL, induction of labor; PO, oral; PROM, premature rupture of membranes; PV, vaginal.

Suidan et al. Am J. Perinatol 2015; 32: 187-192.

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GUIDELINE FOR INDUCTION OF LABOR

Table 1. Cervical Ripening Options

Initial section	Dose, timing, and route	Monitoring	Special Considerations	Contraindications
Preferred Methods				
Misoprostol	Option 1: Vaginal: 25 µ every 4 hours. Max 6 doses Option 2: Oral: 50 µ every 4 hours. Max 6 doses Option 3: Oral Stepwise: begin with 50 µ, then continue with 100 µ every 4 hours. Max 4 total doses	Uterine activity and FHR monitored for **at least 3 hours** after administration depending on contraction patterns.	May consider stepwise dosing for patients with a BMI ≥40[44] or if patient is not responding to 50 µ every 4 hours	Patients with a uterine scar Fetal loss <28 weeks More than 5 painful contractions in 10 min
Foley Catheter plus misoprostol	FC: Saline information below, leave in up to 24h **Misor**: Option 1, 2 or 3 above for dosing	Uterine activity and FHR monitored for at least 3 hours after administration	-May consider step dosing for patients with a BMI ≥30[30] or if patient is not responding to 50 µ every 4 hours -Caution when used with low lying placenta	Uterine scar
Foley Catheter	Fill to 60 mL with saline and leave in for up to 24h	Electronic fetal monitoring for at least 30 min post placement	Caution when used with low lying placenta	
Alternative Methods				
Dinoprostone	Insert: 10 mg	Uterine activity and FHR monitored continuously while in place and at least for 15 min after removal	May be less effective in patients with a BMI ≥30[24,45]	Patients with a parity ≥5 Uterine scar More than 5 painful contractions in 10 min
Cook© Catheter	Use per manufacturer's instructions (Appendix A)	Electronic fetal monitoring for at least 30 min post placement	Caution when used with low lying placenta	Use per manufacturer's instructions (Appendix A)
Foley Catheter plus oxytocin	FC: Fill to 60 mL with saline **Oxytocin**: TBD	Continuous	-Use caution when patient has prolonged QT syndrome -Caution when used with low lying placenta	

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GUIDELINE FOR INDUCTION OF LABOR

Induction of Labor Phase 2: Active Labor

Oxytocin:

- Once the cervix is ripened, it is reasonable to use either a lower dose oxytocin protocol (start at 2mU/min and increase by 2 mu/min q 30 min) or higher dose oxytocin protocol (start at 4 mu/min and increase by 4 mu/min every 30 minutes) for induction of labor. – **Strong Recommendation, Moderate Quality Evidence** [44, 45]

Oxytocin Infusion

- ACOG Practice Bulletin No. 107: Induction of Labor. 2009 Aug; 114(2 Pt 1): 386-97.
  - Low or high dose oxytocin regimens are appropriate for women in whom IOL is indicated.

Table 2. Labor Stimulation with Oxytocin: Examples of Low- and High-Dose Oxytocin

Regimen	Starting Dose	Incremental Increase (mU/min)	Dosage Interval (min)
Low-Dose	0.5–2	1–2	15–40
High-Dose	6	3–6*	15–40

*The incremental increase is reduced to 3 mU/min in presence of hyperstimulation and reduced to 1 mU/min with recurrent hyperstimulation.

- Budden, A., L.J.Y. Chen, and A. Henry, *High-dose versus low-dose oxytocin regimens for induction of labour at term.* Cochrane Database of Systematic Reviews, 2014(10): p. CD009701.
  - 8 trials
  - 2023 women
  - No difference in CD rates. Higher rates of "hyperstimulation." **No difference in maternal or neonatal outcomes.**
- Zhang, J., et al., *Oxytocin regimen for labor augmentation, labor progression, and perinatal outcomes.* Obstet Gynecol, 2011. **118**(2 Pt 1): p. 249-56.
  - Secondary analysis Consortium of Safe Labor
  - 15,054 women, six hospitals
  - **Starting 4 mu/min and increment 4 mu/min associated with shorter duration of 1st stage (compared with lower dose regimens)**
  - No difference in CD rate or perinatal outcomes

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GUIDELINE FOR INDUCTION OF LABOR

Induction of Labor: Additional Considerations

Nutrition and Hydration:

- Low risk patients can have unrestricted oral intake of fluid during induction of labor. – **Strong Recommendation, Moderate Quality Evidence**[166]
- It is reasonable to offer intravenous D5NS at the rate of 250mL/h during active labor in women undergoing induction of labor, may improve outcomes such as shortened duration of labor and reduction in the incidence of cesarean delivery.-**Conditional Recommendation, Moderate Quality Evidence** [166]

Epidural analgesia:

- Provide patients in early labor (i.e., <5 cm dilation) the option of neuraxial analgesia on an individualized basis – **Conditional Recommendation, Moderate Quality Evidence**
- Do not withhold neuraxial analgesia on the basis of achieving an arbitrary cervical dilation – **Strong Recommendation, Moderate Quality Evidence**

Continuous labor support:

Continuous support during labor may improve outcomes for women and infants, defined as support from nurse, midwife, doula, childbirth educator, family member, friend or spouse/partner. Outcome include increased spontaneous vaginal birth, shorter duration of labor, and decreased caesarean birth, instrumental vaginal birth, use of any analgesia, use of regional analgesia, low five-minute Apgar score and negative feelings about childbirth experiences. – **Conditional Recommendation, Low Quality Evidence** [47]

Hydration

- Ehsanipoor, R.M., et al., *Intravenous fluid rate for reduction of cesarean delivery rate in nulliparous women: a systematic review and meta-analysis. [Review].* 2017. **1**(7): p. 804-811.
  - 7 trials
  - 1215 women
  - Women who received IV fluids at 250 cc/hr (vs 125 cc/hr) had significantly shorter length of labor, lower CD rates and no difference in pulmonary edema
- Fong et al, *A randomized, double-blinded, controlled trial of the effects of fluid rate and/or presence of dextrose in IV fluids on the labor course of nulliparas.* AJOG. 2017 Aug;217(2):208.
  - Prospective RCT
  - 274 women, spontaneous labor.
  - Comparison: NS 250 cc/hr vs D5NS 250 cc/hr vs D5NS 125 cc/hr
  - No difference in length of labor or CD rates
- Pare et al, *Reduction of total labor length through the addition of parenteral dextrose solution in IOL in nulliparous: results of DEXTRANS prospective randomized controlled trial.* AJOG. 2017 May; 216 (5):508.
  - Prospective RCT
  - 193 women, induction of labor
  - Comparison: NS 250 cc/hr vs D5NS 250 cc/hr (started with oxytocin)
  - Length of labor significantly shorter with D5NS 250 cc/hr (median 76 min), no difference in neonatal or maternal outcomes.

Hydration

- Bottom Line: Hydration is important. Volume and type of fluid matter.
- PO vs IV
- Barriers to adequate hydration
  - Nausea or frequent vomiting
  - Availability of hydration/nutrition options in hospital
  - Maternal exhaustion
  - Long induction of labor
  - High risk aspiration, needing emergent CD
  - Labor is distracting! Cannot rely on patients feeling "thirsty."

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GUIDELINE FOR INDUCTION OF LABOR

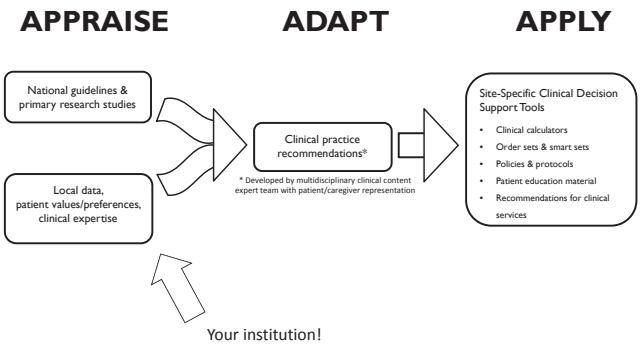
Failed Induction Definition

If the maternal and fetal status allow, cesarean deliveries for failed induction of labor in the latent phase can be avoided by allowing longer durations of the latent phase (up to 24 hours or longer) and requiring that oxytocin be administered for at least 15 hours *after membrane rupture* before deeming the induction a failure. – **Strong Recommendation, Moderate Quality Evidence** [2, 48, 49]

- Caughey, A.B., et al., *Safe prevention of the primary cesarean delivery.* Am J Obstet Gynecol, 2014. **210**(3): p. 179-93.
- Rouse, D.J., et al., *Failed labor induction: toward an objective diagnosis.* Obstet Gynecol, 2011. **117**(2 Pt 1): p. 267-72.
- Grobman, W.A., et al., *Defining failed induction of labor.* American Journal of Obstetrics & Gynecology, 2018. **218**(1): p. 122.e1-122.e8.

Conclusions

- Misoprostol , combination methods best choice
- Oxytocin regimen required to achieve adequate contractions may need to be individualized. Need options available to clinicians.
- Hydration is important.
- Use standardized definition for failed IOL.



https://oregonperinatalcollaborative.org/initiative/iol/

Cervical Ripening

- Chen, W., et al., *A systematic review and network meta-analysis comparing the use of Foley catheters, misoprostol, and dinoprostone for cervical ripening in the induction of labour. [Review].* 2016. **1**(3): p. 346-54.
- Lin, M.G., et al., *Misoprostol for labor induction in women with term premature rupture of membranes: a meta-analysis.* 2005. **1**(3): p. 593-601.
- Dallenbach, P., et al., *Oral misoprostol or vaginal dinoprostone for labor induction: a randomized controlled trial.* 2003. **1**(1): p. 162-7.
- Colon, I., et al., *Prospective randomized clinical trial of inpatient cervical ripening with stepwise oral misoprostol vs vaginal misoprostol.* 2005. **1**(3): p. 747-52.
- Fisher, S.A., V.P. Mackenzie, and G.A. Davies, *Oral versus vaginal misoprostol for induction of labor: a double-blind randomized controlled trial.* 2001. **1**(4): p. 906-10.

Cervical Ripening: Alternative Methods

- Boulvain, M., C. Stan, and O. Irion, *Membrane sweeping for induction of labour.* Cochrane Database of Systematic Reviews, 2005(1): p. CD000451.
  - 19 RCTs, 2389 women
  - Membrane sweeping versus expectant managment
  - Increased likelihood of spontaneous labor in 48 hrs
  - NNTT 8 women

What makes a good quality project?

- **Clinically relevant outcome measures**
  - Cesarean Delivery Rate
  - Chorioamnionitis
  - Patient Satisfaction
  - Neonatal Outcomes
  - Length of labor

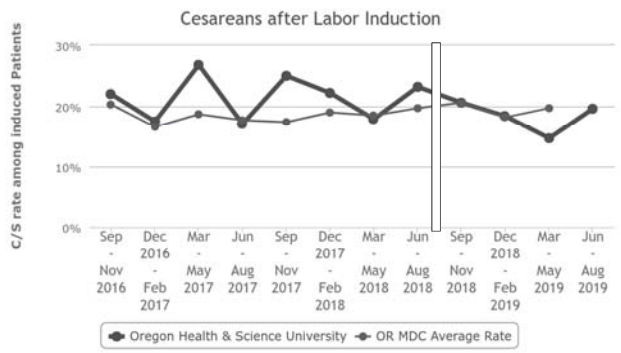
What makes a good quality project?

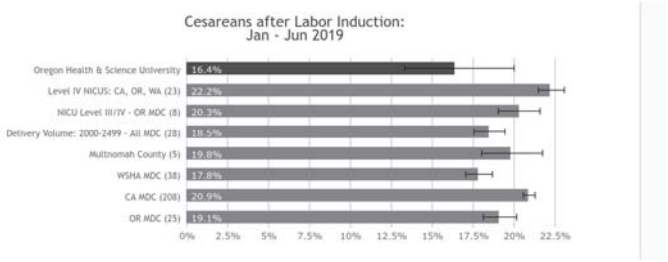
- **Variability in practice patterns**
  - Cervical ripening
    - Mechanical and pharmacologic options
    - Different doses
    - Different routes of administration
  - Oxytocin
    - Management in labor
    - Different titration regiments
  - Other management strategies
    - IV fluids: how much (if any) what type
    - Continuous labor support
  - Definition of failed induction?
    - When to stop….

Example IOL Guideline

Induction of labor: Evidence-based changes

- Change from buccal to oral misoprostol
- Cervidil taken off formulary
- Higher dose oxytocin protocol available
- Oxytocin checklist





Speed Dating…..

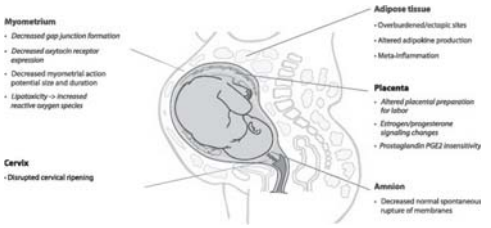
- Which outcomes do you currently track related to IOL?
- Very briefly describe your hospitals primary cervical ripening method (dose and route) and oxytocin protocol.
- How does your institution assess hydration status for actively laboring women? What type of IV fluids are used? NS? LR? D5NS or D5LR? What type of PO hydration options are easily available to women on your labor unit?
- Have you made any recent changes to your IOL protocol? Why?
- What is something your institutions does really well? Why?
- What is something you would like to see improve at your institution?
- What do you need to support your hospital to improve outcomes of women who undergo IOL?

Can misoprostol be used for IUGR, oligohydramnios and post-dates pregnancies?

- Prospective and observation data suggest no difference in cesarean delivery rates or neonatal outcomes between misoprostol and Cervidil:
- Oligohydramnios:
  - *Kawakita et al. Am J Perinatol 2017. Jan 34 (2): 204-210.*
- IUGR, post-dates pregnancy:
  - ***Rozenberg P et al. 2004 Jul; 191 (1): 247-53. *RCT***
  - *Foeller ME et al. Am J Perinatol. 2015. Dec 32(14): 1311-7.*
  - *Rossi RM et al. J Mat Fet Neo Med. 2018 May 27:1-6.*

Oxytocin Utilization

- Obesity is associated with higher oxytocin requirement
- Higher volume of distribution, dilutional effect
- Physiologic mechanisms may mediate response



Carlson NS el al. Reprod Biol Endocrinol. 2015.

Oxytocin Utilization

- Generally, one oxytocin protocol per institution
  - Starting dose, interval dose, maximum dose
- Should we consider a more patient specific approach?
- Area needing high quality research: Which oxytocin regiment is best for which patient?
  - Low CD rates, low chorioamnionitis rates, optimal time to delivery.

III. Oxytocin Dosing

1. Low Dose Protocol: Patients being induced or augmented without the indications below for protocol 2

a) Starting rate: 1-2 mu/min

b) Rate of increase: Increase by 2 mu/min every 30 minutes until target contraction pattern is reached

c) 20 mu/min unless patient is re-evaluated by the by the provider and an order to exceed is given

d) Maximum is 40 mu/min

e) Smaller more frequent incremental doses may be considered

2. Intermediate Dose Protocol: Patients with current magnesium sulfate infusion, BMI> 35, chorio, or provider discretion

a) Starting rate: 4 mu/min

b) Rate of increase: Go up 4 mu/min every 30 minutes until target contraction pattern is reached

c) 20 mu/min unless patient is re-evaluated by the by the provider and an order to exceed is given

d) Absolute maximum is 40 mu/min

Obstet Gynecol. 2011 Aug;118(2 Pt 1):249-56. doi: 10.1097/AOG.0b013e3182220192.

Oxytocin Research

Overview: past, present & future discovery

November **, 2019 - Elise Erickson PhD, CNM

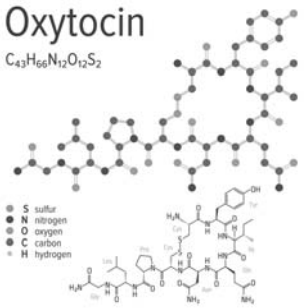
Disclosures

- No conflicts

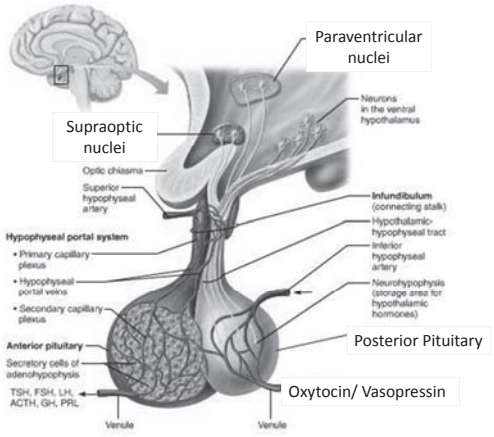
Overview

- Briefly review physiology
- Oxytocin system variation/ regulation
- Oxytocin discovery on the horizon

Physiology and Pharmacology



Hypothalamic Neuroendocrine Peptide



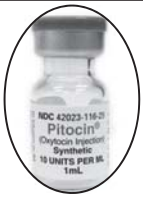
Endogenous/Exogenous Oxytocin

Sir Henry Dale

- 1906: pituitary extracts
- 1911: clinical use

Vincent du Vigneaud

- 1953: Synthesized peptide sequence, structure
- 1955: Nobel prize
- First peptide ever synthesized

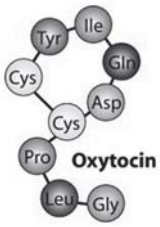


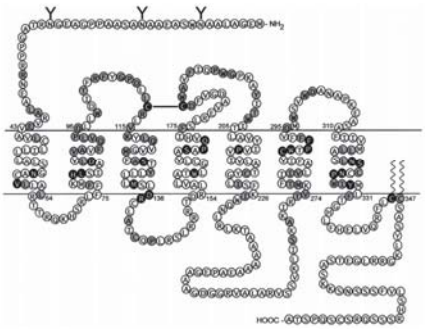
Present Use

- ~25% induced
- 30-57% (?) augmented
- AMTSL
- 2nd trimester termination/ miscarriage management

1906 1911 1955 2019

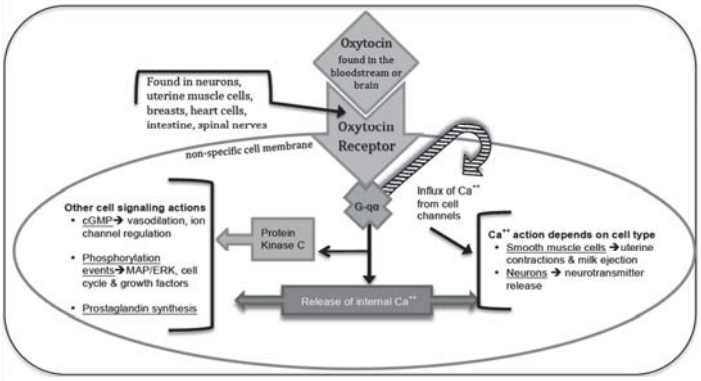
Oxytocin / OXTR- structure





Gimpl, G., & Fahrenholz, F. (2001).

Oxytocin Receptor (OXTR) Function



Bell, Erickson, Carter (2014) Journal of Midwifery and Women's Health

Where are oxytocin receptors found ?

- **Kidney/Adrenal**
- **Blood vessels**
- **Heart**
- **Platelets**
- **Breast**
- **Myometrium**
- **Placenta**
- **Bone**
- **Ovary**
- **Testicles**
- **Prostate**
- **Smooth muscle intestine**
- **Cancer cells**
- **Adipose cells**

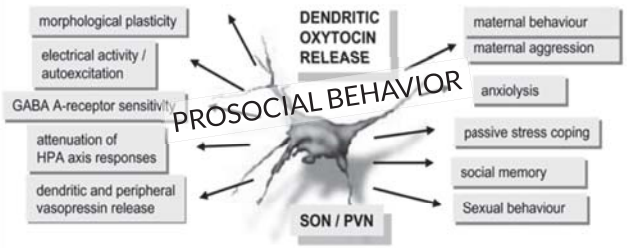
Yang, H.-P., Wang, L., Han, L., & Wang, S. C. (2013). Nonsocial Functions of Hypothalamic Oxytocin. *ISRN Neuroscience*.
Japundzic-Zigon, N. (2013). Vasopressin and Oxytocin in Control of the Cardiovascular System. *Current Neuropharmacology*.

Peripheral oxytocin action

- Uterine muscle contraction
- Myoepithelium of breast—milk ejection
- Prostaglandin production (decidua of placenta)
- Decreased heart rate, blood pressure, temperature
- Decreased cortisol
- Suppression pro-inflammatory cytokines
- Increased glucose uptake & insulin secretion
- Cell growth (anti-proliferative)
- Inhibits growth of adipose cells

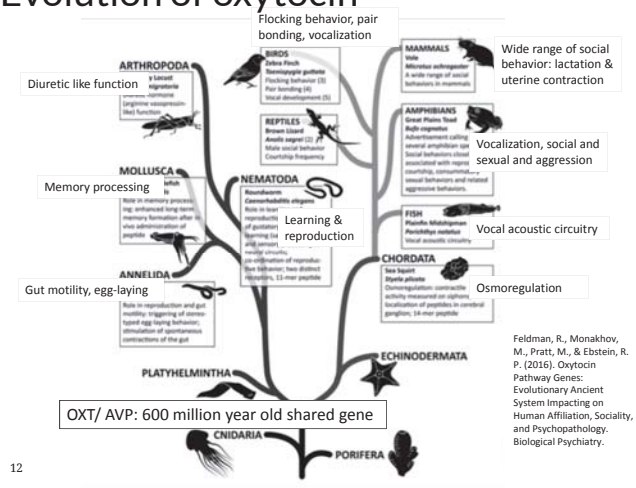
Yang, H.-P., Wang, L., Han, L., & Wang, S. C. (2013). Nonsocial Functions of Hypothalamic Oxytocin. *ISRN Neuroscience*.

- HPA (CRH->Cortisol)
- Dopaminergic pathways (limbic/cortex)
- Serotonin neurons
- Vagus nerve (afferent & efferent)



Neumann, I. D. (2007). Stimuli and consequences of dendritic release of oxytocin within the brain. Biochemical Society Transactions, 35(Pt 5), 1252–1257.

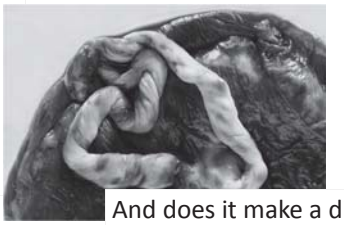
Evolution of oxytocin



Feldman, R., Monakhov, M., Pratt, M., & Ebstein, R. P. (2016). Oxytocin Pathway Genes: Evolutionary Ancient System Impacting on Human Affiliation, Sociality, and Psychopathology. Biological Psychiatry.

Regulation and Variation

How does endogenous oxytocin function vary between individuals?



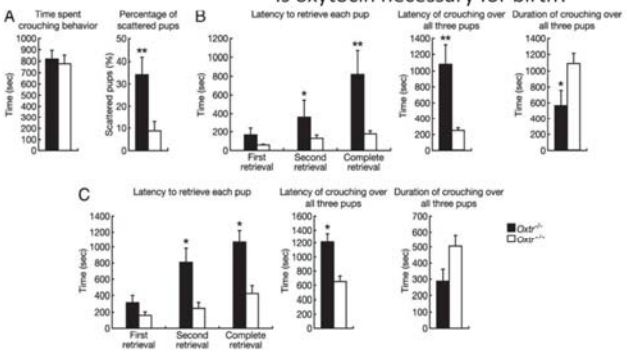
And does it make a difference during the perinatal period?

OXT/OXTR variation in human perinatal experience?

- When labor starts?
- How long labor lasts?
- Response to exogenous oxytocin during or after labor?
- Lactation variation?
- Neurotransmitter Pro-social OXT: Mood/ Parenting Behaviors?

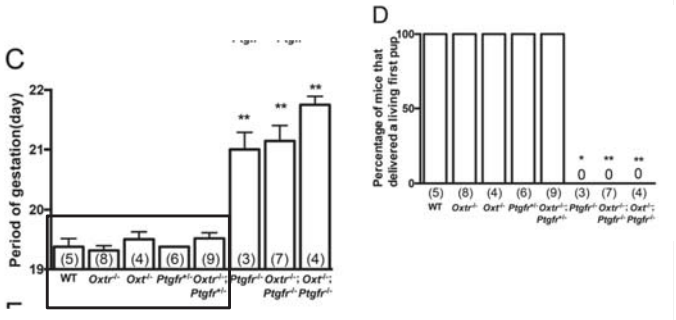
Knockout Mice

Is oxytocin necessary for birth?



Takayanagi, Y., Yoshida, M., Bielsky, I. F., Ross, H. E., Kawamata, M., Onaka, T., et al. (2005). Pervasive social deficits, but normal parturition, in oxytocin receptor-deficient mice. Proceedings of the National Academy of Sciences, 102(44), 16096–16101.

Prostaglandin & Oxytocin Knockouts



Yoshida, M., Takayanagi, Y., Ichino-yamashita, A., Sato, K., Sugimoto, Y., Kimura, T., ... Online, F. (2019). Functional hierarchy of uterotonics required for successful parturition in mice. *Endocrinology*.

Questioning the role of pituitary oxytocin in parturition: spontaneous onset of labor in women with panhypopituitarism – a case series

Shiri Shinar *, Ariel Many, Sharon Maslovitz
Lis Maternity Hospital, Obstetrics and Gynecology, Sourasky Medical Center, Sackler School of Medicine, Tel Aviv University, Israel

4 cases
4 had spontaneous labor
2 needed oxytocin augmentation in active phase
2 had Cesarean, 1 had instrument assisted birth
4 had PPH (one delayed PPH)
4 had no milk production

Human Reproduction Update, Vol.22, No.5 pp. 535–560, 2016
Advanced Access publication on June 30, 2016 doi:10.1093/humupd/dmw022

human reproduction update | GRAND THEME REVIEW

Novel concepts on pregnancy clocks and alarms: redundancy and synergy in human parturition

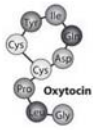
Ramkumar Menon[1,*], Elizabeth A. Bonney[2], Jennifer Condon[3], Sam Mesiano[4], and Robert N. Taylor[5]

"…the need to ensure successful pregnancy likely produced a redundancy of pathways to ensure reliable uterine emptying and expulsion of the fetus."

Pharmacokinetics of OXT/OXTR

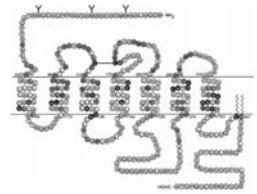
Peptide
- Half life
- *Degradation

- Onset of action within 3 to 5 minutes
- Half-life studies: 3-6 minutes vs. 10 to 15 minutes (in blood, longer in CSF/brain)
- Steady state 30 to 60 minutes
- Degraded/inactivated by "oxytocinase"
  - Zinc-dependent aminopeptidase
  - PLAP (placental leucine aminopeptidase)



20

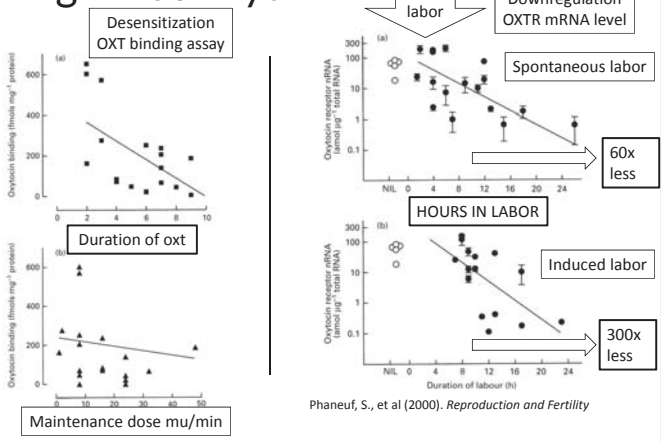
Receptor Pharmacology



Receptor
- Upregulation (gestational age, hormone)
- Desensitization
- Degradation *(via internalization)*
- Down-regulation

21

Exogenous oxytocin



Phaneuf, S., et al (2000). *Reproduction and Fertility*

22

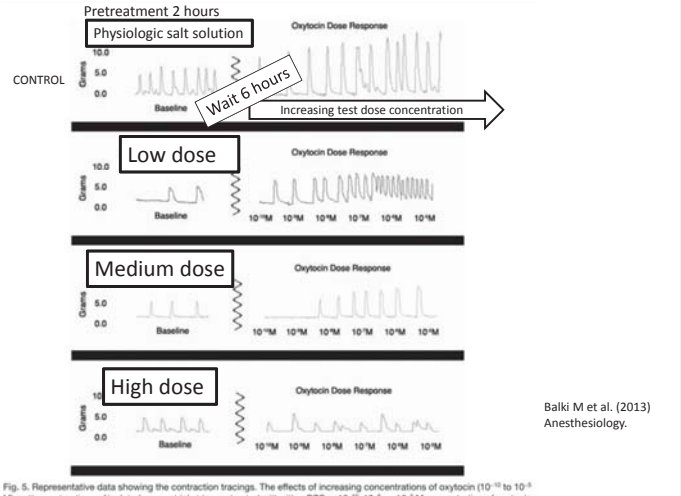


Fig. 5. Representative data showing the contraction tracings. The effects of increasing concentrations of oxytocin (10^{-12} to 10^{-5} M) on the contractions of isolated myometrial strips pretreated with either PSS or 10^{-12}, 10^{-8}, or 10^{-5} M concentration of oxytocin for 2 h are shown. PSS = physiological salt solution.

Balki M et al. (2013) Anesthesiology.

Oxytocin & Obesity

- Lower levels of oxytocin in circulation
- Lower levels post-menopause
  → Estrogen promotes upregulation of OXTR
- Less likely to start labor spontaneously
- Require higher doses of oxytocin during labor augmentation
- BMI >30, more likely to need to go over 20mu/min

24

Maestrini (2018) European Journal of Obesity
Carlson (2015) Reproductive Biology & Endocrinology
Adams et al (2019) Am. J Perinatology

Are associations between differences in oxytocin function and other conditions a consequence of the condition?

Or does oxytocin dysregulation/dysfunction contribute to the development of the condition?

J. Ernie Blevins, Ph.D.

Research Associate Professor, Medicine
University of Washington

Biography | Contact | Research & Clinical Interests

Research Interests:

- Brain pathways regulating leptin signaling from the hypothalamus to the brainstem linked to the control of food intake
- Neuroanatomical techniques-for mapping neural circuits (oxytocin, corticotropin releasing hormone) involved with mediating the effects of leptin on food intake and energy expenditure
- Role of hindbrain oxytocin receptor signaling in the pathogenesis underlying diet-induced obesity
- Role of brown adipose tissue thermogenesis in mediating oxytocin-elicited weight loss in diet-induced obese rodents and nonhuman primates

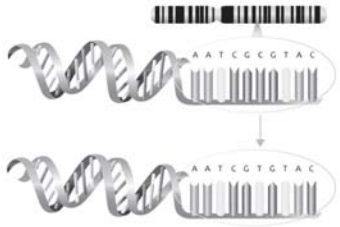
26

Genotype Variation

JAMA Pediatrics | Original Investigation (2017)

Socioeconomic Disparities in Childhood Obesity Risk: Association With an Oxytocin Receptor Polymorphism

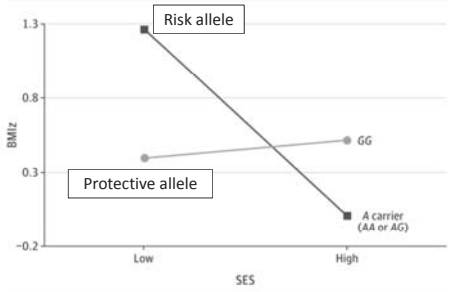
Nicole R. Bush, PhD; Amber L. Allison, PhD; Alison L. Miller, PhD; Julianna Deardorff, PhD; Nancy E. Adler, PhD; W. Thomas Boyce, MD



Single Nucleotide Polymorphism (SNP)

27

Figure 1. Socioeconomic Status (SES) and Oxytocin Polymorphism Interaction Predicting Standardized Body Mass Index *z* Score (BMIz)



Children with an *A* allele in low SES families had the highest BMIz, while those in high SES families had the lowest BMIz. *GG* children were unaffected by their SES environment.

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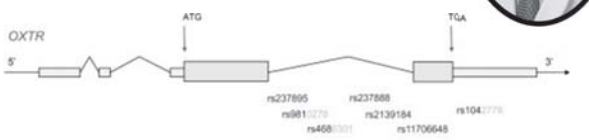
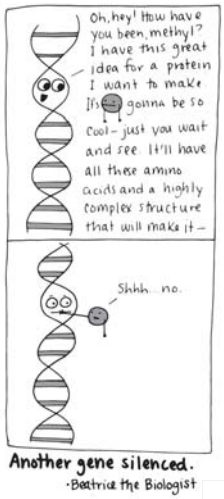
Labor & Genotype



Total Dose | Oxytocin max infusion rate | Duration of induced labor | Cesarean birth

Grotegut, C. A., Ngan, E., Garrett, M. E., Miranda, M. L., Ashley-Koch, A. E., & Swamy, G. K. (2017). American Journal of Obstetrics and Gynecology

29



Epigenetic Regulation

- DNA methylation
  - ⇨ less OXTR gene
  - Postpartum depression
  - Preterm delivery

http://www.beatricebiologist.com/

OXT production: Perinatal Mood

- Stuebe, A. M., Grewen, K., & Meltzer-Brody, S. (2013). *Journal of Women's Health*, *22*(4), 352–361.

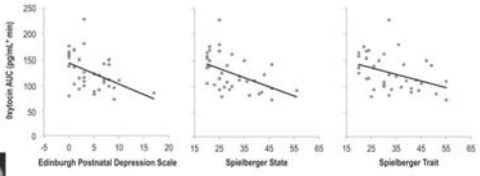


FIG. 2. Correlation between maternal mood at 8 weeks postpartum and oxytocin area under the curve during breastfeeding ($n = 39$). Spearman R: EPDS, $R = -0.48$, $p < 0.01$; STAI-State, $R = -0.53$, $p < 0.01$; STAI-Trait, $R = -0.44$, $p < 0.01$.

PROJECT™
www.NewMomHealth.com

Dr. Alison Stuebe
University of North Carolina

Oxytocin, mood, lactation

- Association between suboptimal lactation outcomes and perinatal depression

JOURNAL OF WOMEN'S HEALTH
Volume 21, Number 3, 2012
© Mary Ann Liebert, Inc.
DOI: 10.1089/jwh.2011.3083

Failed Lactation and Perinatal Depression: Common Problems with Shared Neuroendocrine Mechanisms?

Alison M. Stuebe, M.D., M.Sc.[1,2] Karen Grewen, Ph.D.[3] Cort A. Pedersen, M.D.[3] Cathi Propper, Ph.D.[4] and Samantha Meltzer-Brody, M.D., M.P.H.[3]

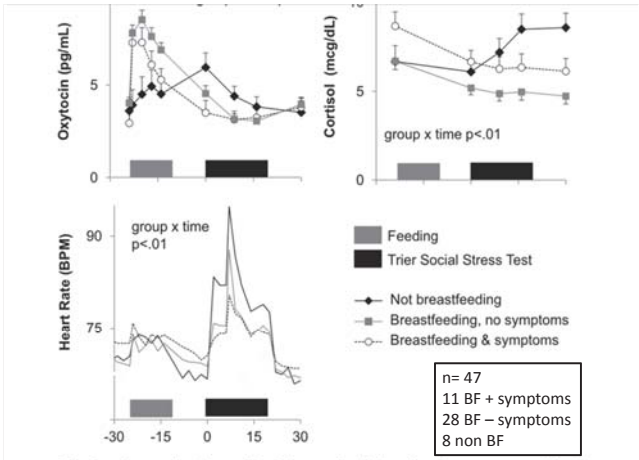


Fig. 3 Neuroendocrine profile during study visit by affective symptoms and feeding.

Cox, E. Q., Stuebe, A., Pearson, B., Grewen, K., Rubinow, D., & Meltzer-Brody, S. (2015). Psychoneuroendocrinology, 55, 164–172.

Association of peripartum synthetic oxytocin administration and depressive and anxiety disorders within the first postpartum year

Aimee R. Kroll-Desrosiers, M.S.[1*] | Benjamin C. Nephew, Ph.D.[2*] | Jessica A. Babb, Ph.D.[3] | Yurima Guilarte-Walker, M.S.[4] | Tiffany A. Moore Simas, M.D., M.P.H, M.Ed.[5] | Kristina M. Deligiannidis, M.D.[6,7]

N=46,732 singleton births (9,648 oxytocin, 21%)
Diagnosis of postpartum mood disorder or medication

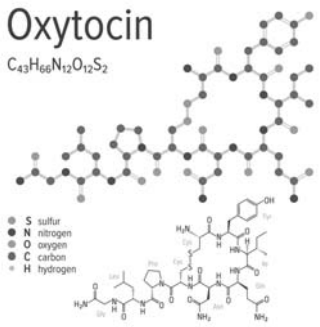
History of mood disorder/meds
→ 36% more likely to have PP diagnosis

No prior history of mood disorder/meds
→ 32% more likely have PP diagnosis

Kroll-Desrosiers AR et al. *Depress Anxiety*. 2017;34(2):137-146.

1) Is synthetic oxytocin a contributing factor in development of PPD or 2) a symptom of OXT/OXTR dysfunction?

Future of Oxytocin Research



Future Oxytocin Therapeutics

- Atosiban: oxytocin receptor antagonist
  - Preterm labor?
- Carbetocin: longer-lasting agonist (40 min half life)
  - Postpartum Hemorrhage?
- Intranasal Oxytocin: (central vs. peripheral debate)
  - Obesity/ blood glucose regulation
  - Cardiovascular protection during ischemia
  - Social behaviors/ mood symptoms

OHSU

SCIENTIFIC AMERICAN

Oxytocin Nasal Spray May Boost Social Skills in Children with Autism

Study suggests a biomarker for treatment with the "love hormone"

By Jessica Wright, Spectrum on July 11, 2017

READ THIS NEXT

MIND
New Oxytocin Neuroscience Counters "Cuddle Hormone" Claims
June 25, 2015 — Helen Shen and Nature magazine

MIND
Be Mine Forever: Oxytocin May Help Build Long-Lasting Love
February 12, 2013 — Luciana Gravante

THE SCIENCES
Fact or Fiction?: Oxytocin Is the "Love Hormone"
September 8, 2014 — Gary Stix

Oxytocin Receptor Expression In Pregnancy: When Does It Turn On?

- ❑ Dr. Jessica Reid- Family Planning Fellow
  - samples myometrium throughout late 2nd trimester to term
  - determine at what GA OXTR expression increases
  - inform clinical management of post-abortion hemorrhage

Oregon birch

Higher DNAm = Lower OXTR
→ less uterine tone

- Postpartum Hemorrhage
- More exogenous oxytocin

Secondary outcomes
- Postpartum Mood
- Suboptimal Lactation

Summary

- OXT/OXTR genes are pleiotropic
- OXT works as a neurotransmitter in addition to having many peripheral functions
- Clinicians interact with oxytocin system variation
- New research and therapies on the horizon may one day influence care during the childbearing process as we broaden our view of oxytocin as more than a uterotonic.

References

- Ottenhausen, M., Bodhinayake, I., Banu, M. A., Stieg, P. E., & Schwartz, T. H. (2015). Vincent du Vigneaud: following the sulfur trail to the discovery of the hormones of the posterior pituitary gland at Cornell Medical College. *Journal of Neurosurgery*, 1–5.
- Martin, J. A., Hamilton, B. E., Osterman, M. J. K., Driscoll, A. K., & Drake, P. (2018). Births: Final for 2017. *National Vital Statistics Reports*, *67*(8), 1–49. Gimpl, G., & Fahrenholz, F. (2001). The oxytocin receptor system: structure, function, and regulation. *Physiol Rev*, *81*(2), 629–683.
- Bell, A. F., Erickson, E. N., & Carter, C. S. (2014). Beyond labor: The role of natural and synthetic oxytocin in the transition to motherhood. *Journal of Midwifery and Women's Health*, *59*(1), 35–42.
- Lee, H. J., Macbeth, A. H., Pagani, J. H., & Scott Young, W. (2009). Oxytocin: The great facilitator of life. *Progress in Neurobiology*, Vol. 88, pp. 127–151.
- Yang, H.-P., Wang, L., Han, L., & Wang, S. C. (2013). Nonsocial Functions of Hypothalamic Oxytocin. *ISRN Neuroscience*.
- Feldman, R., Monakhov, M., Pratt, M., & Ebstein, R. P. (2016). Oxytocin Pathway Genes: Evolutionary Ancient System Impacting on Human Affiliation, Sociality, and Psychopathology. *Biological Psychiatry*.
- Bell AF, Carter CS, Steer CD, et al. Interaction between oxytocin receptor DNA methylation and genotype is associated with risk of postpartum depression in women without depression in pregnancy. Front Genet. 2015;6(38):1161–10..
- Kimmel M, Clive M, Gispen F, et al. Oxytocin receptor DNA methylation in postpartum depression. Psychoneuroendocrinology.
- Reiner I, Van Ijzendoorn MH, Bakermans-Kranenburg MJ, Bleich S, Beutel M, Frieling H. Methylation of the oxytocin receptor gene in clinically depressed patients compared to controls: The role of OXTR rs53576 genotype. J Psychiatr Res. 2015;65:9-15..
- Behnia F, Parets SE, Kechichian T, et al. Fetal DNA methylation of autism spectrum disorders candidate genes: association with spontaneous preterm birth. Am J Obstet Gynecol. 2015;212(4):533.e1-.e9..
- Rijlaarsdam J, van Ijzendoorn MH, Verhulst FC, et al. Prenatal stress exposure, oxytocin receptor gene (OXTR) methylation, and child autistic traits: The moderating role of OXTR rs53576 genotype. Autism Res. 2017;10(3):430-438..
- Elagoz Yuksel M, Yuceturk B, Karatas OF, Ozen M, Dogangun B. The altered promoter methylation of oxytocin receptor gene in autism. J Neurogenet. 2016;30(3-4):280-284..
- Jack A, Connelly JJ, Morris JP. DNA methylation of the oxytocin receptor gene predicts neural response to ambiguous social stimuli. Frontiers in Human Neuroscience. 2012;6..
- Kim J, Pitlick MM, Christine PJ, et al. Genome-wide analysis of DNA methylation in human amnion. ScientificWorldJournal. 2013;2013(4):678156–11..
- Mitsuya K, Singh N, Sooranna SR, Johnson MR, Myatt L. Epigenetics of Human Myometrium: DNA Methylation of Genes Encoding Contraction-Associated Proteins in Term and Preterm Labor1. Biol Reprod. 2014;90(5):590-598.
- van Vliet, E. O. G., Nijman, T. A. J., Schuit, E., Heida, K. Y., Opmeer, B. C., Kok, M., … Oudijk, M. A. (2016). Nifedipine versus atosiban for threatened preterm birth (APOSTEL III): a multicentre, randomised controlled trial. *The Lancet*, *387*(10033), 2117–2124.
- Jin, B., Du, Y., Zhang, F., Zhang, K., Wang, L., & Cui, L. (2016). Carbetocin for the prevention of postpartum hemorrhage: a systematic review and meta-analysis of randomized controlled trials. *The Journal of Maternal-Fetal & Neonatal Medicine*, *29*(3), 400–407.
- Parker, K. J., Oztan, O., Libove, R. A., Sumiyoshi, R. D., Jackson, L. P., Karhson, D. S., … Hardan, A. Y. (2017). Intranasal oxytocin treatment for social deficits and biomarkers of response in children with autism. *Proceedings of the National Academy of Sciences of the United States of America*, *114*(30), 8119–8124.

Thank You

ericksel@ohsu.edu

Improved access to medication abortion in Oregon using telemedicine

DATE: Nov 14, 2019 PRESENTED BY: Maureen Baldwin, MD MPH
Pacific NW Update, Portland, OR

Objectives

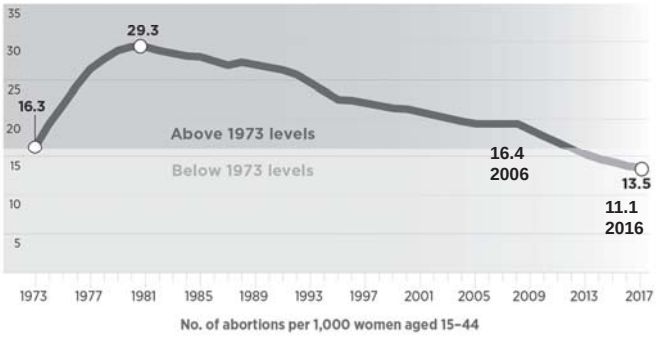
- Review the epidemiology of FDA-approved medication abortion in Oregon
- Understand barriers to abortion access, particularly in rural Oregon
- Compare strategies for medical abortion via telemedicine: The TelAbortion Project
- Review a model for implementation of direct to patient telemedicine medical abortion in Oregon

Disclosures

- Merck Pharmaceuticals – trainer
- Bayer Healthcare – trainer, medical advisory committee
- Medicines360 – research site co-investigator
- National Hemophilia Foundation – medical advisory committee

TRENDS IN ABORTION

The U.S. abortion rate reached a historic low in 2017.

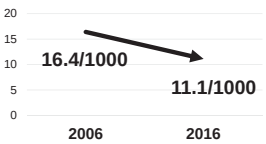


No. of abortions per 1,000 women aged 15–44

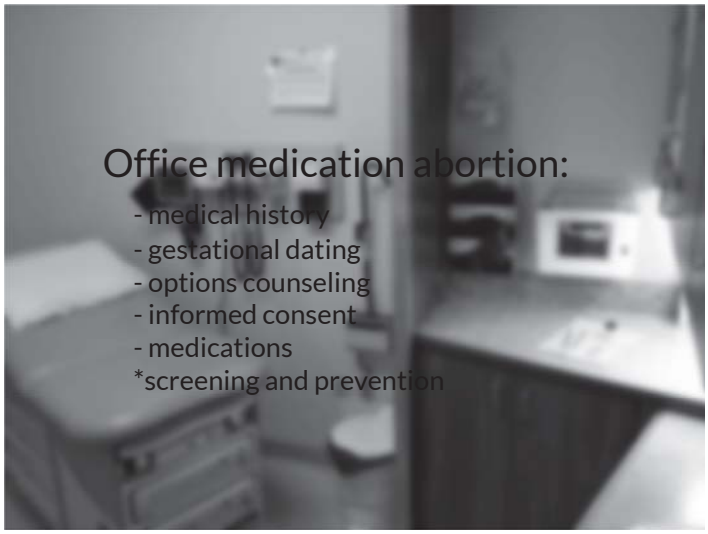
www.guttmacher.org

Oregon abortion rates

33% decline in a decade



8,900 abortions per year
→ half at Planned Parenthood clinics
→ 65% use medication abortion



Office medication abortion:

- medical history
- gestational dating
- options counseling
- informed consent
- medications

*screening and prevention

Medication abortion <10 weeks

- Two medication regimen:
  - Mifepristone
  - Misoprostol taken 1-2 days later
  - Most pass the pregnancy in 4-6 hours
- Follow-up to ensure completed abortion
  - Self-evaluation +
    - Repeat ultrasound (1-2 weeks)
    - Serial blood tests (before and 1-2 weeks)
    - Negative pregnancy test (3-4 weeks)

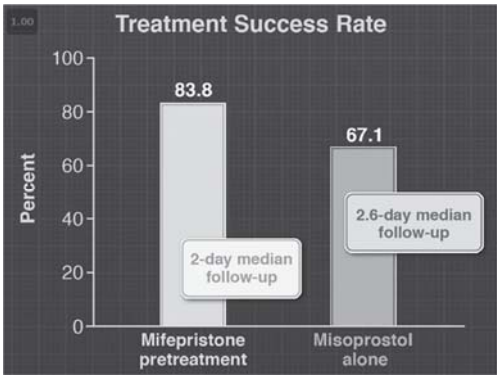
Best practices – combined regimen

The NEW ENGLAND JOURNAL of MEDICINE
ESTABLISHED IN 1812 JUNE 7, 2018 VOL. 378 NO. 23

Mifepristone Pretreatment for the Medical Management of Early Pregnancy Loss

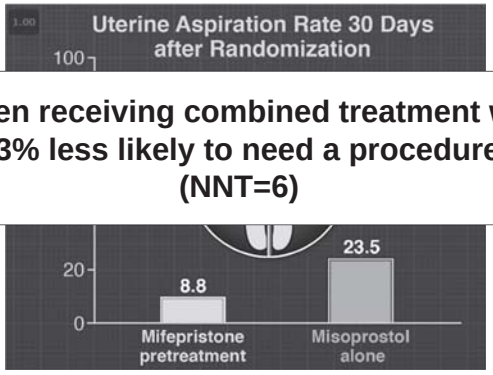
Courtney A. Schreiber, M.D., M.P.H., Mitchell D. Creinin, M.D., Jessica Atrio, M.D., Sarita Sonalkar, M.D., M.P.H., Sarah J. Ratcliffe, Ph.D., and Kurt T. Barnhart, M.D., M.S.C.E.

Medication management of EPL - RCT



Schreiber et al. NEJM 2018

Addition of mifepristone improves outcomes



Women receiving combined treatment were 63% less likely to need a procedure (NNT=6)

Safe and effective

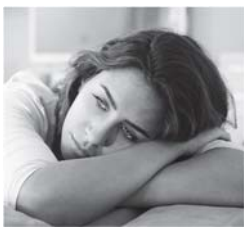
Planned Parenthood® Care. No matter what.

- Review of 2927 medical abortions <7 weeks
  - Serious adverse outcomes in 0.6%
    - Infection in 17
    - Hemorrhage in 2
  - ED visits in 1.3%
  - Ongoing pregnancy in <1%
  - Aspiration procedure in <3%

Baldwin MK, Bednarek PH, Russo J. 2017 NAAFP conference poster

What am I going to do?

- 26 year old with 2 kids under 5
- Lives in Astoria
- Just started a new job
- 6 weeks pregnant
- Seeking abortion



How soon can it happen?

- Where can I go that's safe?
- How far away?
- How much time does it take?
- How long do I need to be off work?
- How much childcare will I need?
- How much does it cost?
- Will it be private?

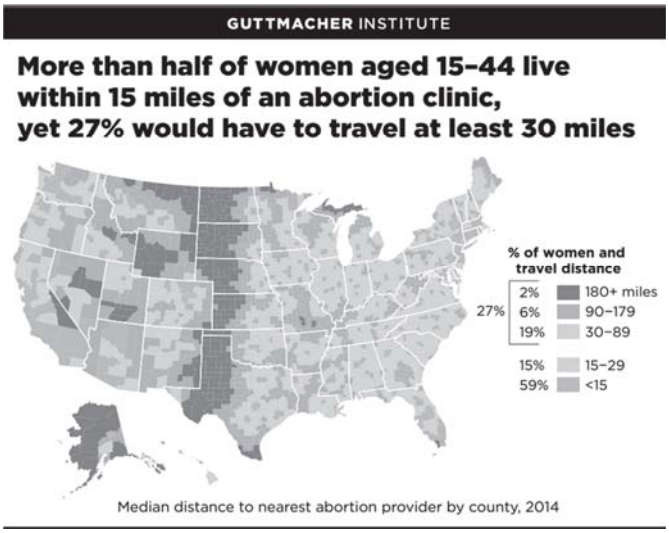
How much does it cost?

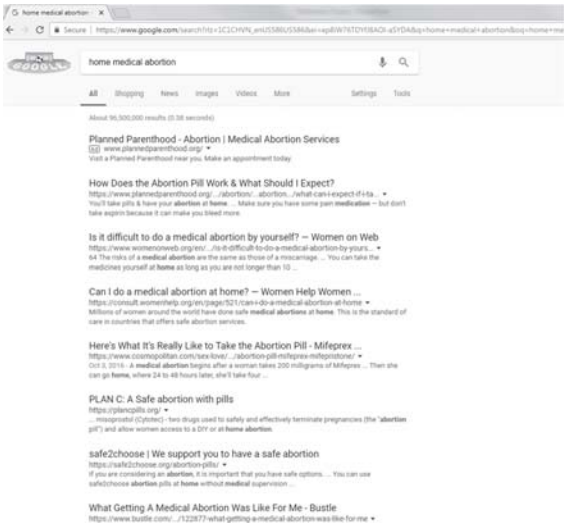
- Medicaid: free
- Private insurance: variable
- Planned Parenthood: $475
- OHSU out of pocket: $514
  → In-hospital ~$10,000

Where can I go?

97 miles to Portland from Astoria
$ tank of gas
$ full day of childcare

→ 30% of Oregon women live in a county without an abortion provider

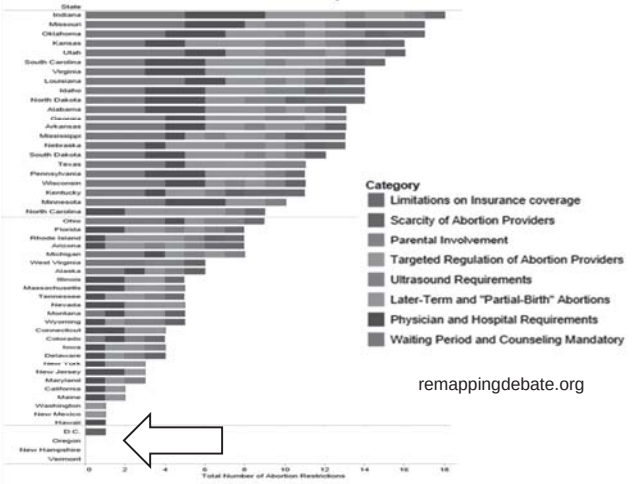




Health system barriers

- Trained providers
- Health system restrictions
  - Ethical and Religious Directives (ERDS)
- FDA restrictions
  - Risk Evaluation and Mitigation Strategy (REMS)
  - mifepristone not in pharmacies

Abortion restrictions by state



remappingdebate.org

FDA restrictions

NDA 020687 MIFEPREX® (mifepristone) Tablets, 200 mg

Antiprogestational Synthetic Steroid

Danco Laboratories, LLC
PO Box 4816
New York, NY 10185

RISK EVALUATION AND MITIGATION STRATEGY (REMS)

I. GOAL

The goal of the Mifeprex REMS is to mitigate the risk of serious complications associated with Mifeprex by:

a) Requiring healthcare providers who prescribe Mifeprex to be certified in the Mifeprex REMS Program.

b) Ensuring that Mifeprex is only dispensed in certain healthcare settings by or under the supervision of a certified prescriber.

c) Informing patients about the risk of serious complications associated with Mifeprex

FDA restrictions

2. Mifeprex must be dispensed to patients only in certain healthcare settings, specifically clinics, medical offices, and hospitals, by or under the supervision of a certified prescriber.

   a. Danco Laboratories must:

      i. Ensure that Mifeprex is available to be dispensed to patients only in clinics, medical offices and hospitals by or under the supervision of a certified prescriber.

      ii. Ensure that Mifeprex is not distributed to or dispensed through retail pharmacies or other settings not described above.

Mifeprex prescribers:

- Review prescribing information
- Complete Prescriber Agreement Form
  - Have the following qualifications:
    - Ability to assess the duration of pregnancy accurately
    - Ability to diagnose ectopic pregnancies
    - Ability to provide surgical intervention in cases of incomplete abortion or severe bleeding, or to have made plans to provide such care through others, and ability to assure patient access to medical facilities equipped to provide blood transfusions and resuscitation, if necessary
    - Will follow the guidelines for use of Mifeprex

FDA protocol for medical abortion

Prior version 2011-2016
- Pregnancy up to 49 days
- Mifepristone 600 mg
- Mifepristone *administered*
- Misoprostol taken in office
- Follow-up in clinic

Current since March 2016
- Pregnancy up to 70 days
- Mifepristone 200 mg
- Mifepristone *dispensed*
- Misoprostol taken at home
- Follow-up as preferred

→ FDA exemption filed (an IND) to be able to use medication off-label for research

Telemedicine in OR/WA

- Synchronous two-way interactive video conferencing
- Visit occurs/originates where the patient is located
  - Site to site
  - Direct to patient
- Insurance coverage = office visits

Center for Connected Health Policy
The National Telehealth Policy Resource Center

http://cchpca.org

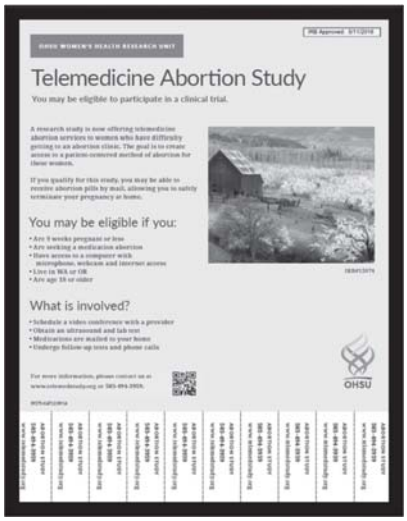
ER2

www.telabortion.org

OHSU

Slide 25

ER2 Switched out the website to our new one.
Elizabeth Raymond, 10/22/2019



OHSU

www.telabortion.org

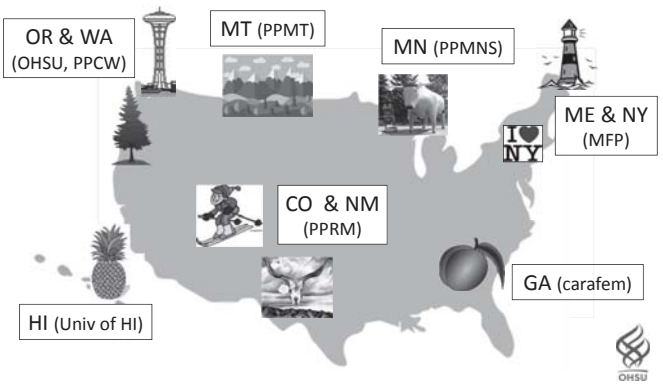
OHSU

Visit flow

OHSU

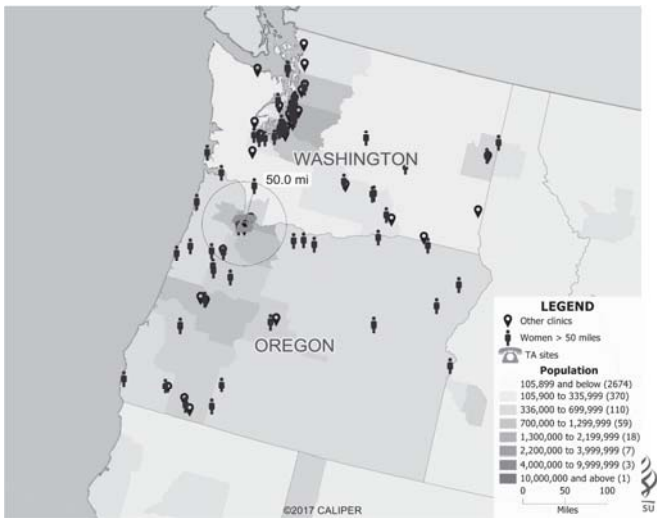
ER4

States and Partners

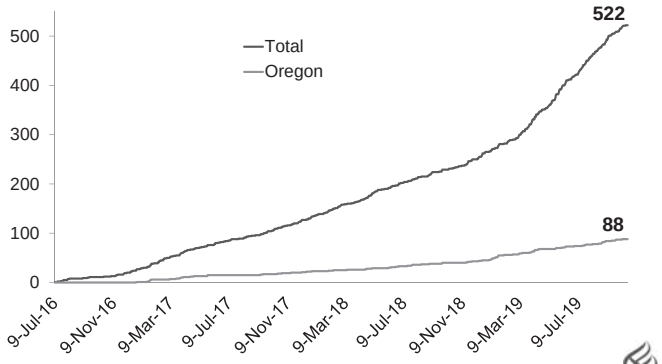


Slide 30

ER4 Replaced the map.
Elizabeth Raymond, 10/22/2019

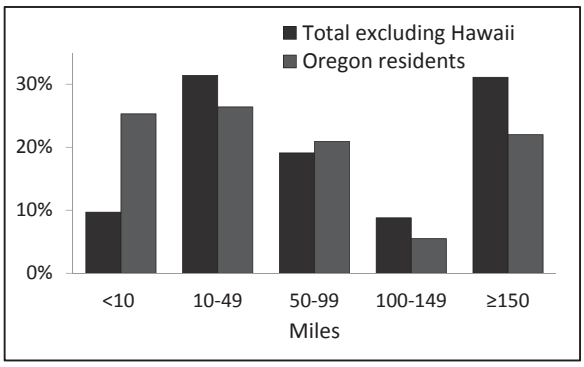


Abortions Provided



Through October 20 2019

Distance from Home to Site



Abortion Outcome

522 packages sent

- Lost or still being followed: 22%
- Changed mind about abortion: 2%
- Completed abortion: 76%

Complete medical abortion: 95%

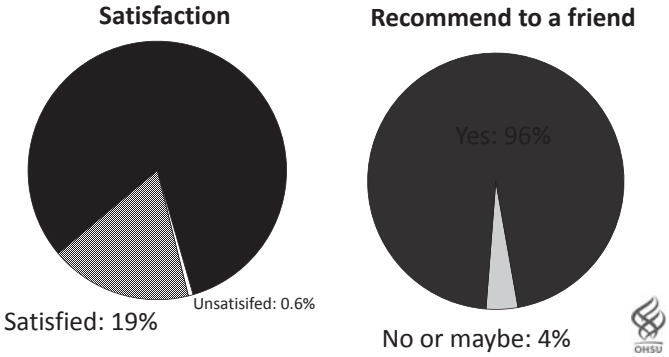
Aspiration: 5%

Complications

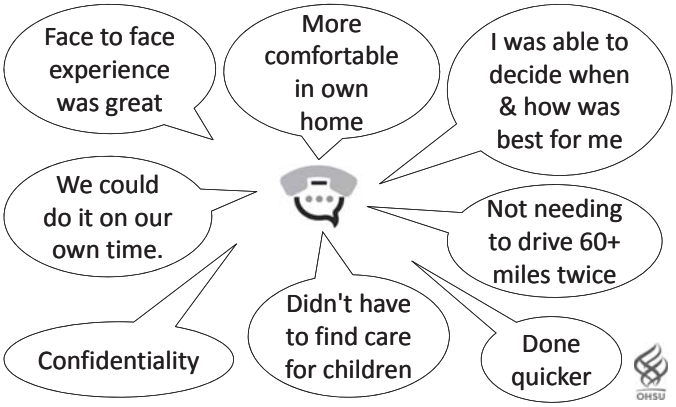
444 patients with follow-up

- No related significant complications
- 2 hospitalizations, neither related to telemedicine
- 37 ED visits (8%), mostly for bleeding/cramping
  - All but 8 lived ≥50 miles from study site

Acceptability N=343



Quotes from OR



Implementation outcomes

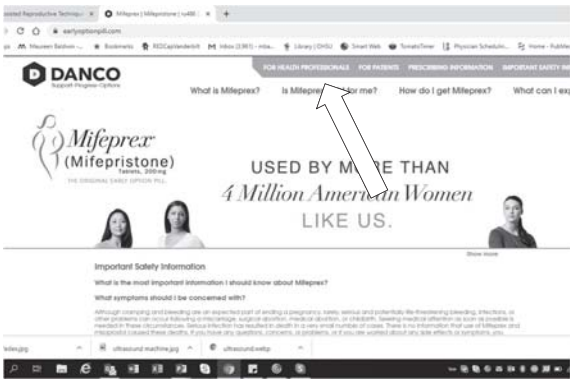
ADVANTAGES

Privacy
Patient choice
Convenience
Efficiency
Equivalent

CHALLENGES

Billing and coding
Multiple components
Multiple communications
Dis-coordinated medical systems
Lost opportunities for screening and prevention

www.earlyoptionpill.com



Thank you!!!

schaum@ohsu.edu

www.telabortion.org

TelAbortion
Safe. Effective. Private. Convenient.

OHSU Physician Advice & Referral Service
- 503-494-4567
- 800-245-6478 (toll-free)

Telemedicine to Evaluate and Manage Perinatal Risk

11.14.19

Leonardo Pereira MD, MCR, Associate Professor

Director, Division of Maternal-Fetal Medicine

Oregon Health & Science University

pereiral@ohsu.edu

Disclosures

No financial conflicts of interest

Coping with just turning 50 and having a 21 y.o. daughter

Bias towards the Philadelphia Eagles

Telemedicine in MFM Overview

Current utilities

Advantages

Challenges

Future directions

Telemedicine in Perinatology

Well suited for telemedicine

High frequency of consultative services

High frequency of ultrasound services

Telemedicine Current Utilities

MFM consultation

Genetic counseling

Fetal ultrasound

Prenatal visits

Diabetes management

Postpartum visits

Telemedicine Current Utilities

Arkansas ANGELS program since 2003

Coordinated state wide telehealth with live ultrasound and consultation

Complex case management

Virtual neonatal rounds - telenursery

Implementation of OB psychiatric care

24/7 RN call center

Telemedicine Current Utilities

Arkansas ANGELS program

Successes:

Higher rate of delivery of high risk neonates at tertiary center

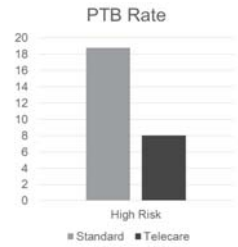
Reduced infant mortality

Coordinated care for fetal anomalies

Telemedicine Current Utilities

Georgia 2011: Private MFM and SW Georgia Public Health District partnership to provide telemedicine consults to 500 high risk-risk women in a centering program:

Reduced PTB from 18 to 8% during 18 month study period



Telemedicine Current Utilities

At OHSU:

Ultrasounds

Genetic Counseling

Educational conferences: OPNN (Oregon Perinatal and Neonatal Network)

Telemedicine Current Utilities

Genetic Counseling:

Patient satisfaction has been good (surveys)

Concerns about assessing non-verbal communication for difficult conversations

Decreased travel and cost to patients

Decreased cost to practices / health systems

Telemedicine Current Utilities

GDM management:

No data that TM improves outcomes over standard care

Patient perceived increase in how closely monitored they are)

Reduced travel and unscheduled visits

Telemedicine Current Utilities

OB outcomes meta-analysis: Lannsens et al 2017

Some data indicates cost savings

Some improved outcomes:

reduced unscheduled visits GDM
increased GA at delivery
decreased LBW and NICU admission rates
quality of evidence is low (bias)

Telemedicine Current Utilities

Telemedicine Accuracy for fetal sonography

All scans 2010-2012 showed similar accuracy; anomaly prevalence 5.7%

2368 TM scans; 3145 live in person scans
TM : sensitivity 57%, specificity 98%
LIVE: sensitivity 77%, specificity 91%
TM exams completed in 1 visit 82%

Rabie NZ et al, JUM 2017

Telemedicine Advantages

Financial benefit to patients – transportation costs, missed time off work

Patient's family may be present more easily

Provide specialty services remotely where they are not locally available

Telemedicine Advantages

Providers/Health Care System benefits from reduced cost and time of providers traveling to satellites

Local health care providers/systems increased charges and revenue

Improved educational opportunities for local providers: OPNN example

Telemedicine Advantages

Patient engagement is higher

Patient satisfaction is higher

Uncertainties:

Impact on health outcomes

Impact on costs

Telemedicine Challenges

Need high speed T1 optic fiber network for high speed image transfer

Sonographer limitations: experience, NT certification, ECHO, Dopplers

Equipment limitations

Telemedicine Challenges

Reimbursement

In U.S. health insurance companies may not reimburse services or reimburse them at a lower rate

Variable, determined at the state level but increasing in general

Most reimburse real time care; less commonly store and forward or remote patient monitoring (RPM)

Telemedicine Challenges

Licensure:

Medical licensure in Oregon allows you to bill Medicaid for telehealth services in several states: Idaho, Montana, Utah, Washington and Wyoming

Medical licensure in Washington allows you to bill Medicaid for telehealth services in Alaska, Idaho, Montana, Oregon, Utah and Wyoming

Telemedicine Challenges

Medicaid Reimbursement Policies

2014: 32 states had guidelines on telemedicine

2018: 49 states had guidelines on telemedicine (MASS)

3 guidelines specific to perinatal care

AJOG, EM Okoroh et al 2016
CCHP 50 state report 2018; cchpca.org

Telemedicine Challenges

Store and forward as opposed to live in time interactions

Teleradiology is reimbursed and not considered store and forward

Store and forward examples:
Fax reports, Derm pictures, dental exam pictures – 11 states currently reimburse this (Washington, California, and Nevada do)

physician to physician email consults – only Connecticut reimburses at present time

Telemedicine Challenges

Remote Patient monitoring (RPM)

Only reimbursed in 20 states:

Washington and Utah

Usually only for specific chronic conditions: COPD, asthma, diabetes CHF

Telemedicine Challenges

Limited (but increasing) data on outcomes

Some publications showing telemedicine outcomes inferior to person to person care

More recent publications show equivalent outcomes

Telemedicine Future Directions

Virtual prenatal care: limited data, similar pregnancy outcomes, high satisfaction among middle-high income patients who already have children

Pflugeisen BM. Am JMCN 2016
Pflugeisen BM, MCH 2017

Fetal Heart Rate Monitoring: private companies developing tech for FHR

Telemedicine Future Directions

HOTEL study: multicentered Dutch RCT

416 patients > 26 weeks singletons

Wireless CTG and automated BP monitoring

Randomized to in hospital management versus remote monitoring from home

van den Heuvel JFM, BMJ Open 2019

Telemedicine Future Directions

HOTEL study: multicentered Dutch RCT

Inclusions: preeclampsia, IUGR, PPROM, prior stillbirth, decreased fetal movements

Primary outcome is composite adverse perinatal outcome

Secondary outcomes: safety satisfaction, cost effectiveness

van den Heuvel JFM, BMJ Open 2019

Questions?
Contact me

OHSU Physician Advice & Referral Service
- 503-494-4567
- 800-245-6478 (toll-free)

Autism, Gender, and Health: A Guide for Ob/Gyn and Women's Health Providers

Christina Nicolaidis, MD, MPH
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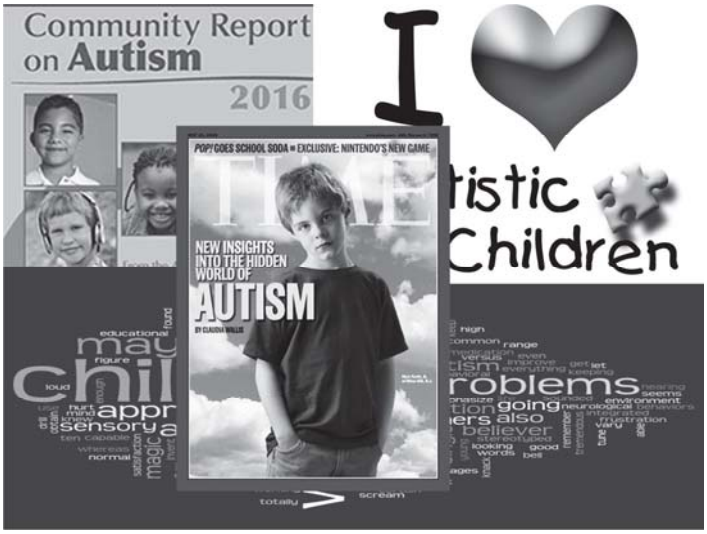
Associate Professor, School of Medicine, Oregon Health & Science University
Co-Director, Academic Autism Spectrum Partnership in Research and Education (www.AASPIRE.org)
Editor-in-Chief, *Autism in Adulthood*

AASPIRE

Disclosures

- I have no conflicts of interest to disclose.
- Funding for this work has come from the National Institute of Health
  - **NIMH: R34MH092503, R34MH092503, R21MH112038**
  - **NICHD: R21HD078830**
  - The Oregon Clinical and Translational Research Institute (OCTRI), grant number UL1 RR024140 from the National Center for Research Resources (NCRR), a component of the National Institutes of Health (NIH), and NIH Roadmap for Medical Research



Today's Agenda

- Autism Basics
- Autism and Gender
- Health Care for Autistic Adults
- Sexual Health and Pregnancy

AASPIRE

- Academic Autism Spectrum Partnership in Research and Education (www.aaspire.org)
- Co-Founded in 2006 with Dora Raymaker
- Autistic adults, academics, family members, disability services and healthcare providers
- Community Based Participatory Research
  - Autistic adults serve as equal partners throughout all phases of our research projects.

Nicolaidis et al, *PCHP*, 2011

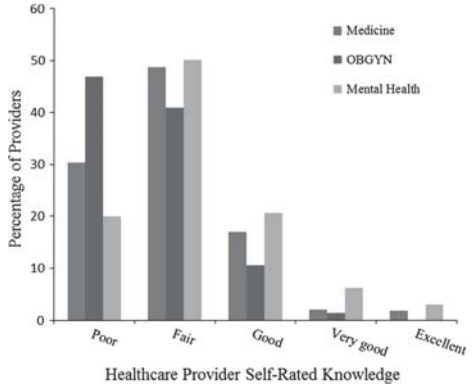
Frameworks and Language

- Neurodiversity paradigm
  - Diversity in neurodevelopment to be valued in the same way that we value other forms of human diversity
  - Social model of disability
  - Focus on supports and accommodations instead of cures
- Ongoing language debate
  - Preference among self-advocates for identity-first (e.g. autistic adult) vs. person-first (e.g. adult with autism)
  - Similar to Deaf community

Nicolaidis 2012; Gernsbacher, 2017; Kapp et al, 2013; Kenny et al 2016; Sinclair, 1999

Autism Basics

Provider Knowledge and Training



Kaiser survey of 922 healthcare providers for adults

Zerbo et al, *JADD*, 2015

Prevalence of Autism

- Dramatic rise of diagnosed prevalence over time
- CDC: 1 in 59 children identified with an ASD
- Population-based study: 1% of adults met criteria for ASD
- Fewer adults have been formally diagnosed.
- Majority of increase in prevalence is likely due to changes in diagnostic criteria and how they are applied.
- Continued under-diagnosis in females and people of color

Baio, 2018; Brugha 2009; Hill 2015; Liptak 2008; Dean 2017

History of ASD

- First described in 1940's (but likely always existed)
- First included in DSM in 1980
  - Not even a dx when baby-boomers were kids
- "Asperger's Disorder" added in 1995; heightened awareness through late 90's and early 2000's.
  - Most Gen-X'ers not diagnosed in childhood
  - Millennials with dx now entering adulthood
- DSM-5 unified diagnoses of autistic disorder, Asperger's disorder, and PDD-NOS into "Autism Spectrum Disorder"

DSM-5 Criteria for ASD	
A. Persistent deficits in social communication and social interaction across multiple contexts. (3 of 3)	1. Deficits in social-emotional reciprocity
	2. Deficits in nonverbal communicative behaviors used for social interaction
	3. Deficits in developing, maintaining, and understanding relationships
B. Restricted, repetitive patterns of behavior, interests, or activities (2 of 4)	1. Stereotyped or repetitive motor movements, use of objects, or speech
	2. Insistence on sameness, inflexible adherence to routines, or ritualized patterns of verbal or nonverbal behavior
	3. Highly restricted, fixated interests that are abnormal in intensity or focus
	4. Hyper- or hyporeactivity to sensory input or unusual interest in sensory aspects of the environment
C. Symptoms must be present in the early developmental period (but may not become fully manifest until social demands exceed limited capacities, or may be masked by learned strategies in later life)	
D. Symptoms cause clinically significant impairment in social, occupational, or other important areas of current functioning.	
E. These disturbances are not better explained by intellectual disability or global developmental delay. Intellectual disability and autism spectrum disorder frequently co-occur; to make comorbid diagnoses of autism spectrum disorder and intellectual disability, social communication should be below that expected for general developmental level.	

A Few Caveats…

- Do not to rely on stereotypes.
- Fallacy of the linear spectrum
  - Skills and challenges fall along spectra on multiple axes.
  - Within each axis, skills and challenges can change depending on environmental stimuli, supports, and stressors.
  - Skills and challenges can change over time.
- Autistic traits can be both strengths and challenges.
- Autistic people do not always shy from social interactions and some maintain strong friendships.

Associated Conditions

- Epilepsy
- Gastroesophageal reflux disease (GERD), constipation, dysphagia
- Feeding and nutrition problems
- Metabolic syndrome
- Anxiety, depression, sleep disturbances, and suicidality
- Post-traumatic stress symptoms (including those associated with childhood treatments)
- Higher risk of experiencing violence and abuse victimization
- Reduced life expectancy

Croen 2015; Woolfenden 2012; Hivikoski 2016; Nicolaidis 2014; Kupferstein 2018.

Behavior Change

- Common medical problems can present in unusual ways.
- Illness often presents as a change from baseline behavior or function.
  - Patients who present to psychiatry frequently have undiagnosed or under-treated medical problems.
- Short-term use of risperidone or aripiprazole can be effective in treating irritability, hyperactivity, and stereotypies in autistic children, **but the risks and side effects often outweigh the benefits**. No long-term data.
- Some data on non-pharmacologic approaches (mindfulness, CBT, exercise, improved communication).

Nicolaidis et al, *Med Clin N Am*, 2014

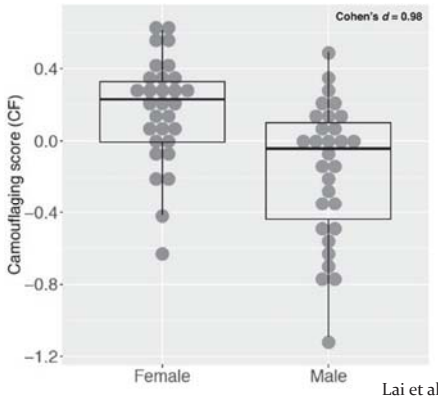
Autism and Gender

Sex Differences in Prevalence

- "4:1 ratio of males to females"
  - Biological difference?
  - Skewed diagnostic criteria
  - Under-diagnosis
- Clues to under-diagnosis
  - More severe impairments in girls with diagnosis
  - Later age at diagnosis
- Recent increase of CDC prevalence estimates from 1 in 68 to 1 in 59 largely attributed to increasing diagnosis in girls and children of color

Hill 2015; Bageer 2012,

Camouflaging



Lai et al, *Autism*, 2017

Gender Identity

- Strikingly high number of non-cis-gendered autistic adults in autistic self-advocacy community
- Small, but growing literature confirming association
  - Higher rates of gender dysphoria amongst autistic children and adults
  - Higher rates of autistic traits or diagnoses amongst patients seeking treatment for gender dysphoria
- Biology vs gender as a social construct?
  - "I don't feel like a particular gender I'm not even sure what a gender should feel like"

Gliden et al, *Sex Med Rev*, 2016; Kourti et al, *Autism in Adulthood*, 2018

Clinical Implications for Ob/Gyn

- High likelihood that many of your patients are not formally diagnosed
  - Potential benefits (and costs) to adult diagnoses
- Patients may be camouflaging traits, (but possibly to the detriment of their health); may not be able to do so under stress (e.g. illness, hospitalization, surgery).
- Patients identified as girls at birth may not identify as women by adolescence or adulthood, but may still need ob/gyn care – great sensitivity needed to both autism and trans issues to provide quality care.

Health Care for Autistic Adults

Healthcare Disparities

- Online survey comparing autistic adults (N=209) to non-autistic adults (N=228) with and without other disabilities.
- Greater unmet healthcare needs
  - Physical health needs (aOR 1.9)
  - Mental health needs (aOR 2.2)
  - Prescription medication needs (aOR 2.8)
- Greater Emergency Department use (aOR 2.1)
- Lower use of Pap Smears (aOR 0.5)
- Lower satisfaction with patient-provider communication and healthcare self-efficacy

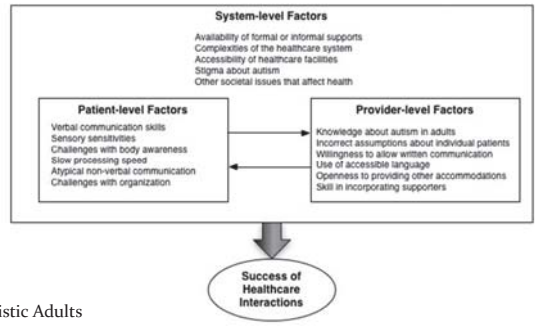
Nicolaidis et al, *JGIM* 2013

Barriers to Healthcare

- Autistic people and people with other disabilities experience many more barriers than people without disabilities.
- Autistic group reported more barriers to healthcare than people with other disabilities, plus different pattern.
- Top barriers:
  - Fear or anxiety (35%)
  - Can't process information fast enough in real-time (32%)
  - Concern about cost (30%)
  - Facilities cause sensory issues (30%)
  - Difficulty communicating with providers (29)

Raymaker et al, *Autism*, 2017

Healthcare Experiences



39 Autistic Adults
16 Supporters

Nicolaidis et al, *JGIM* 2015

Sensory Sensitivities

"The lights in the office are very bright and that is exacerbated by the white walls. Sometimes the waiting rooms are crowded and I cannot filter out the background of people talking or shuffling magazines. I feel disoriented by being led down long hallways to different rooms … I am not able to bring up my concerns because it is all I can manage to figure out what the doctor is saying so I can respond to his questions. But he refills my usual meds and I go on my way."

Sensory Sensitivities

- Use natural light, turn off fluorescent lights, make the lighting dim.
- Try to see the patient in a quiet room.
- Only have one person talk at a time and try not to talk to the patient while there are other noises.
- Avoid unnecessarily touching the patient (for example, to express concern).
- Warn the patient before you touch him or her.

Challenges with Body Awareness

"Like when they ask if pain is shooting or stabbing or burning, it's like, I don't know, it just feels funny."

"The problem is it is difficult for me to isolate specific sources of pain and identify duration and intensity. It's sort of like the equivalent to white noise."

- Consider the possibility that differences in body awareness may be affecting how a patient recognizes or describes a symptom, or how a patient responds to illness.
- In some cases, you may need to do additional testing or imaging as information from the history and physical may be limited.

Providers' Incorrect Assumptions

- "I have used my Alphasmart [portable communication device] when my speech is too slow or difficult to understand for medical appointments. Some of the doctors have been really great, but others have acted really condescending when I used it, also immediately assuming I couldn't be alone, had to have had parents there too … So I try to go without, even when my speech is in a poorer shape."
- "Usually when I demonstrate a large vocabulary or some fundamentals, my needs especially around communication are then ignored. My choice is then to pretend to be less intelligent and accept their infantilism, or to be confused, frustrated, and stressed out."

Communication and Openness to Accommodations

- "I prefer and find it easier to communicate in text … But with every doctor I speak to, they wave away the note-card and look at me to ask the same question I have just answered and interpret my confusion as my being non-compliant with the medicine. I wish health care providers would read the notes I make for them."

Communication

- Check your assumptions.
- Use preferred communication mode
- Be very concrete and specific.
- Avoid open-ended, broad questions.
- Do not force patient to make eye contact; it may be uncomfortable or hinder effective communication.

Need for Consistency

- Enable the patient or supporters to get pictures of the office and/or staff.
- Explain, in detail, what is likely to happen during the visit.
- Write down a list of topics and point out when there is a change of topic.
- Show the patient equipment before using it. If possible, do a "trial run" of difficult exams or procedures.

Difficulty with Planning, Organization, and Sequencing

"I wish they understood how easy it is to get confused with all the administrative hoops a patient has to jump through to get help. It sounds pathetic at my age, but I need someone to hold my hand. I don't know what I am doing. But nobody understands that I need that, and there is definitely nobody willing to do it."

- Write out detailed step-by-step instructions.
- Have office staff help with care coordination.
- Provide detailed information about how to communicate with office staff between visits.

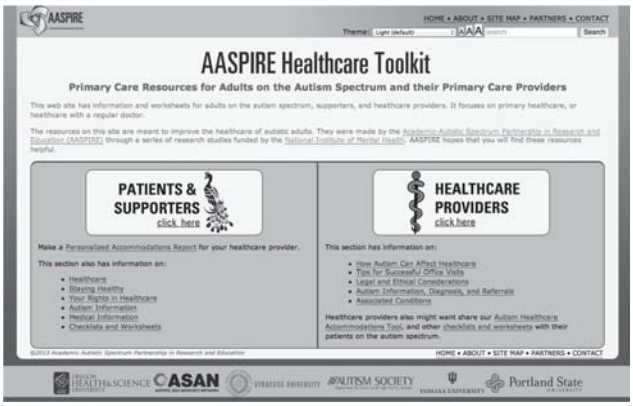
Patient Autonomy

- "Just because I might need more information to understand things, it doesn't mean they can or should just talk to me like a child or leave me without knowledge of my own health. My body is my body, and my experiences and wishes about my body are MINE TO MAKE!"

Very Heterogeneous Condition

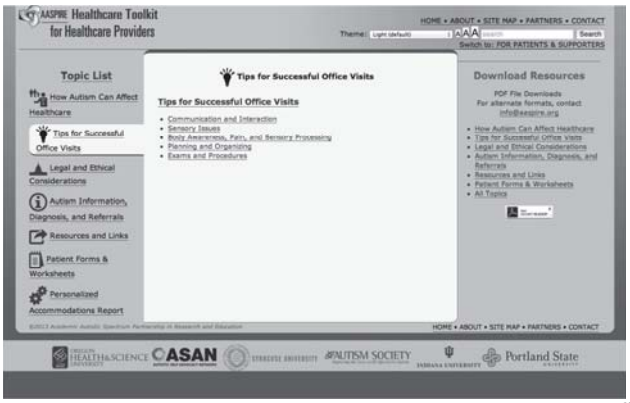
"When you have met one autistic person, you have met one autistic person"

Need for individualized tools!



www.autismandhealth.org

Provider and Staff Strategies



Autism Healthcare Accommodations Tool (AHAT)

- Fill out a survey
- Computer uses answers to create a personalized and healthcare provider-friendly report of accommodations

Sample Provider Report

Patient: Dora Raymaker

IV. Recommendations to Assist with Shared Decision Making

- Allow her extra time for making decisions (might involve communicating decision at a later time).
- Be very blunt and give concrete examples of what would happen if a recommendation was or wasn't followed.
- Give a trusted person detailed information about health conditions and choices.
- Allow time for her to discuss choices with a trusted person.

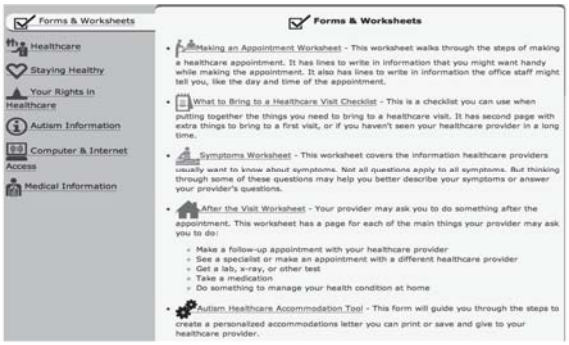
V. Recommendations to Help Ms. Raymaker Comply with Recommendations

- Write out your impressions and the plan for next steps or treatments.
- Write out detailed step-by-step instructions.
- Show pictures as much as possible.
- Show her what to do while she is still in the office.
- Have staff help with scheduling follow-up visits, referrals, or tests.

(just part of the full report)

Patient and Supporter Information

Forms and Worksheets



AASPIRE Toolkit Evaluation

- Mixed-methods, single arm, 1-month pre-post intervention study design in real-life setting.
- 170 autistic participants; 41 PCPs
- 95-97% found it easy to understand, important, & useful.
- Significant changes between pre- and post-test in
  - Number of barriers to healthcare
  - Healthcare self-efficacy
  - Patient Provider communication
- Strong qualitative themes around toolkit utility
  - Means to clarify and communicate needs
  - Validation of experience and empowerment re self-advocacy
  - Improved self-efficacy; better able to prepare for visits
  - Examples of changes in provider behaviors

Nicolaidis et el, *JGIM* 2016

Next Steps

- Current NIMH-funded project integrating toolkit into 3 health systems (6 intervention and 6 control clinics)
- New collaboration in UK to adapt toolkit and disseminate it throughout National Health Service
- New collaboration in Australia to adapt toolkit to inpatient and emergency medicine settings

Reproductive Health

Autism and Sexual Health

- Societal de-sexualization of people with disabilities
- Most studies of sexual behavior in autism use parent report!
- Greater discomfort amongst parents communicating about sex with autistic adolescents
- Small literature assessing sexual health directly among autistic adolescents and adults
  - Lower knowledge
  - Greater concerns
  - Higher rates of experiencing sexual abuse

Holmes et al, *JADD*, 2014; Mehzabin and Stokes, *RASD*, 2011; Brown-Lavoie et al, *JADD*, 2014

Pregnancy, Disability, and Women's Decisions

- NICHD-funded qualitative study with 51 women (34 with intellectual disability and 17 on the autism spectrum)
- Community Advisory Board of autistic women and women with intellectual disabilities

Significant Impact of Social Determinants of Health

- Many participants described struggles with abusive partners, past trauma, poverty, substance use, the legal system, health complications, and other social determinants of health.

"It was largely domestic violence and I didn't think I could take care of a baby on my--I didn't have the financial resources, I didn't know how I was gonna make it, you know, I couldn't keep a job down, I lost my job while I was pregnant and, you know, I didn't know what I was gonna do."

Isolation

- Being apart from a strong social support network
- Motherhood and/or disability as isolating
- Most women only received support or had discussions about pregnancy decisions from only a small number of close family members
- Many women felt the need to keep their decision-making private

Isolation

- *"I kept [my decision-making] to myself. I figured the less I say to [others] the less I have to hear."*
- *"I just felt really like alone and depressed all the time. I couldn't really talk to nobody.... I didn't really have the supports--I had the supports of finding stuff that I needed sometimes, but the supports of talkin' to somebody about what's goin' on and how I'm feeling, you know..."*

Discrimination

- Many stories of ableism, racism, sexism
- Some feared their children would be discriminated against if they had a disability
- Social expectation that women become mothers can either be normalizing (if they choose to have children) or something they are discriminated against for (if they chose not to have children)

"[I'd be worried if my child had a disability] 'cause how other people act to people with disabilities.... They discriminate....Like when I'm out and about sometimes discriminate against me...I don't wanna bring a kid up in this world because this world [scoffs] they don't, they don't--this world don't have boundaries...on how they treat people."

Ableism Within Healthcare

"...just the language and all of the paperwork and questionnaires around genetic testing is like incredibly offensive, I mean they refer to everything as birth defects rather than developmental disabilities.... It's like the entire infrastructure is set up to discourage women from carrying pregnancies to term if there's any possibility that the child will have a disability. And that there's this, that there's this implicit bias in the language and in all conversations about pregnancy that is all about fear of disability and, um, you know disability as like the ultimate tragedy that we're working together to avoid. I was just much more aware of that climate. Especially because you know I'm 42 so obviously there's like a lot more genetic testing and stuff that's recommended when you're pregnant at this age and I'm autistic and I have a child who's autistic and I have physical disabilities and some of those are genetic and like there's a very, very high chance that this child will have some disability or another. And I don't fuckin' care [laughs] like you know that's not, that's not important to me.

Independence and Resilience

- Some women were put under a lot of pressure to have a child, to abort a child, or to otherwise do what others wanted them to
- However, most described making their own decisions, even when others disapproved
- Women often had a sense of pride about their self-sufficiency in their decisions and their lives

"I was extremely stubborn and when I make a decision and I want something I'm not gonna let somebody stand in my way... I was not going to have an abortion and nobody was going to tell me what to do. So regardless of how anybody in my household, the people I lived with, or anybody felt about it, it did not matter to me...you can not tell me what to do with my body."

Not So Different

- Women described motivations for their decisions to become or not become pregnant that weren't qualitatively different from any women's motivations – desire for family, biological age, positive (or negative) experiences with children and babysitting, coping with grief after a miscarriage, not wanting to pass along trauma they experienced to a child, etc.

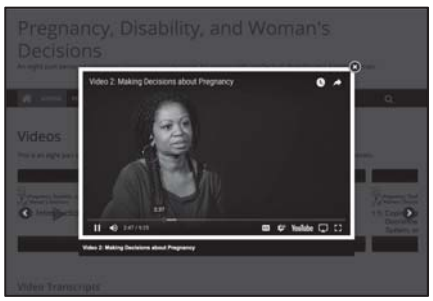
Resource Needs

- Most women had no trouble finding prenatal care or providers
- Most women knew where to look for resources such as WIC
- Many women mentioned needs in:
  - Accessible pregnancy and motherhood training programs
  - Interactions with women like them around pregnancy and motherhood
  - Knowing what the reality of pregnancy and motherhood is like
  - Accessible education on birth control and family planning

Resource Development

- Talked with CAB about interview findings and their own experiences
- Collectively decided to make videos related to key findings
- Scripted and created in collaboration between, co-investigators, CAB, and participants from the research study
- https://pregnancyanddisability.org
- Proposal under review to develop and test pregnancy decision aid

Video Series



1. Introduction
2. Making Decisions About Pregnancy
3. Talking with Others About Pregnancy
4. Managing Pregnancy
5. Coping with Discrimination, the Legal System, or Mistreatment
6. Health and Pregnancy
7. Motherhood and Looking Back
8. About This Series

Take Home Points

If you only remember 3 things…

- Try to understand and meet your patients' accommodation and support needs.
  - Our toolkit may help - www.autismandhealth.org
- Actively engage autistic patients in discussions about sex, contraception, and pregnancy choices.
- Recognize that your autistic patients may be experiencing significant isolation and discrimination.
  - Avoid ableist language and concepts
  - Offer resources at www.pregnancyanddisability.org

Many Thanks to…

- The AASPIRE Team (www.aaspire.org)
  - Dora Raymaker, PhD, Katie McDonald, Phd, E. Ashkenazy, Mel Baggs, Jane Rake, Steven Kapp, PhD, Tobi Rates, JD, Joelle Smith, Andee Joyce, Morrigan Hunter, Micheal Weiner, MD, MPH, Clarissa Kripke, MD, Mirah Scharer, Alannah Mitchell, Gavin Schneider, Kelly Zhen
- The Pregnancy Decisions Project Team (www.pregnancyanddisability.org)
  - Mary Oschwald, PhD, Dora Raymaker, PhD, Mary Ann McCammon, DNSc, Michelle Berlin, MD, Andee Joyce, Annie Wallington, E. Ashkenazy, Phoenix Lomis, Sherri Osburn, and Sonja Sizemore, Khaki Marino, PhD

Project Nurture

Pacific NW Update in Ob/Gyn and Women's Health 11/14/19

Amanda Risser MD MPH, Sr. Medical Director of Substance Use Disorder Services

CENTRAL CITY CONCERN
HOMES HEALTH JOBS

PROJECTNURTURE

Collaborative care between perinatal services and substance use disorder services
Supported by Affordable Care Act Transformation Funds

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Model Components:

- Pregnancy care, care for mother and infant after birth
- Receipt of MSR (buprenorphine or methadone)
- RN case management
- Professional doula support (Peer Recovery Mentor)
- Teaching and mentorship.

Important features

- Care for woman and child to one year after the birth
- Group care model
- Integration and innovation in systems (physical health, mental health, substance use treatment, hospitals)
- Collaboration with Social Services

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Some OHSU/CODA data

- > 53 women and their babies.
- > 50% of the patients required residential treatment.
- More than half of the patients were concurrently using methamphetamines.
- 25% were using marijuana.
- 88% were using tobacco.
- 50% of their babies required treatment for neonatal opioid withdrawal syndrome.

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More OHSU/CODA data

- Postpartum Contraception:
  - 6% tubal ligation
  - 15% injection
  - **17% implant (in hospital!)**
  - **26% IUD!**
- Parenting!
  - 76% of our patients go home with their babies.
  - 70% are short and long term caregivers.
  - 18% experience temporary relinquishment of their babies.
  - These benefits were seen county-wide.
  - This is the main source of system cost savings for this model.

CENTRAL CITY CONCERN
HOMES HEALTH JOBS

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Breastfeeding?

- 70% breastfed within 24 hours
- 44% breastfeeding 3 months postpartum
- LOTS of trouble with infant weight gain and breastfeeding.
- Patients need a great deal of support through this time.
- Breastfeeding has been something we've been especially challenged by.

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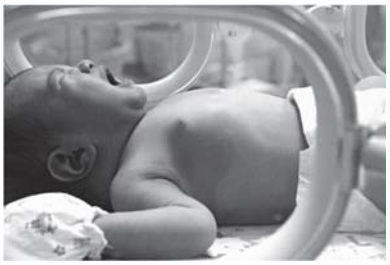
Other Outcomes: System Innovation

- Most project nurture collaboratives changed their systems of care:
  - OHSU- re wrote the neonatal opioid withdrawal protocols
  - Providence- introduced buprenorphine prescribing into a resistant system
  - Legacy- developed a protocol for universal substance use disorder screening
- These activities changed the region of care: evidence that county-wide, project nurture activities changed the way that care was delivered and changed outcomes of care.

System Innovation: changing approach to Neonatal Opioid Withdrawal (NOW)



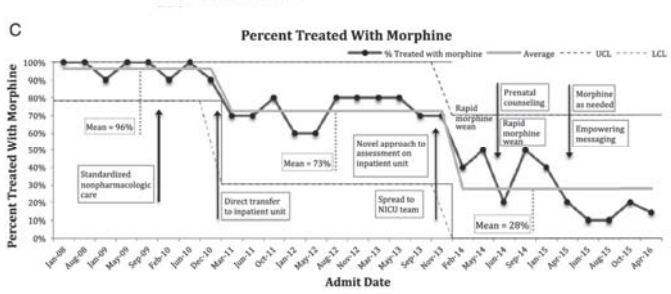
- NICU admission
  - Separating mom and baby
- High levels of exposure to pharmacologic treatment
- Finnegan "NAS Scores"
  - Poor inter-observer reliability
  - Just One Sneeze
  - Disruptive neurologic stress test
- Long taper up & down
  - 17 days LOS overall
  - 23 days LOS for those treated

LOS = Length of Stay NICU = Neonatal Intensive Care Unit
NAS = Neonatal Abstinence Syndrome

(Jansoon, 2017) (McQueen, 2016)

Grossman Yale Study 2017: Eat Sleep Console

- PDSA Cycles:



LOS = Length of Stay NICU = Neonatal Intensive Care Unit
LCL = lower control limit UCL = upper control limit

OHSU Doernbecher Baseline Data

From Sept 2015 - Feb 2017
Before the policy, slowly starting to room in

"Exposed"		"Diagnosed"	
P04.49 Newborn affected by maternal use of drugs of addiction	43 Infants Admitted 7.7 Average LOS 5.3 Average NICU LOS	**P96.1** Neonatal Abstinence Syndrome (AKA NOW)	49 Infants Admitted 18.8 Average LOS 7.2 Average NICU LOS

LOS = Length of Stay NICU = Neonatal Intensive Care Unit

Goals of Policy Change

1. **Focus on comfort**
   = Less Pharmacologic Management
2. **Prioritize Rooming In**
   = No more NICU
3. **Focus on Infant Function AKA Eat-Sleep-Console**
   = No More Finnegan Scoring
4. **Less Pharmacologic Management**
   = Morphine starts as PRN (as needed)

NICU = Neonatal Intensive Care Unit

Comfort is first line treatment for NOW

- Tend to all crying with consoling (swaddle, non-nutritive sucking, rocking, holding)
- Frequent skin to skin or cuddling by birth mother, family or volunteers
- Minimize interruptions, avoid waking for cares, bundle care
- Quiet any noises, dim bright lights
- Ensure optimal feeding
- Skin care with all diaper changes

Rooming in is prioritized:

- Rooming-in on MBU → Doernbecher Inpatient Pediatrics once mom discharged
- No more NICU admissions for NOW
- Participation of parents, family or caregivers
- Provide education and support to parents
- Volunteers

Infants on morphine do not require post-dose monitoring at low doses (<0.12mg/kg/dose)

NICU = Neonatal Intensive Care Unit

No more Finnegan: Eat-Sleep-Console (ESC)

EAT - SLEEP - CONSOLE		
EAT	**Poor eating due to NOW?**	
	NO Eating well or feeding problems not due to NOW	8 - 12 feeds per day with effective latch and milk transfer by breast or at expected volume for age by bottle when showing feeding cues
	YES Poor eating due to NOW	Unable to coordinate feed within 10 mins of showing hunger cues due to NOW symptoms such as fussiness, tremor, or excessive suck
SLEEP	**Sleeping less than 1 hour (after a feeding) due to NOW?**	
	NO Sleeping well or sleep problems not due to NOW	Able to sleep for more than 1 hour at a time
	YES Poor sleeping due to NOW	Unable to sleep for more than 1 hour due to NOW symptoms such as fussiness, restlessness, increased startle, or tremors
CONSOLE	**Unable to console within 10 minutes due to NOW?**	
	NO Consolable or difficulty consoling not due to NOW	Able to be consoled within 10 mins with self-soothing, rocking, skin to skin, swaddle, non-nutritive sucking, feeding, or other consoling
	YES Difficulty consoling due to NOW	Unable to be consoled within 10 mins with caregivers effectively providing non-pharmacologic management for NOW

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Our results: Pre and Post intervention

- No significant change in LOS: our LOS already relatively short
- Decrease in infants given morphine: 40% to 20%
- VERY SIGNIFICANT decrease in amount of morphine given to infants:
  - 20.08 to 0.87 mg/kg/infant (95.6% reduction)

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Other developments:

- Project Nurture specifically called out in the governor's budget.
- Other programs emerging: Kaiser, Women's Healthcare Associates.
- Expanded access to withdrawal management services (Hooper).
- With Oregon statute revision around access to treatment services that provide medically supported recovery: some increased access to best practices for women (but still far far from meeting the need especially for women taking methadone).

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DEPRESSION SCREENING UPDATES

Wendy N Davis, PhD

Postpartum Support International

Pacific NW Update in ObGyn and Women's Health

Thursday Nov 14, 2019

POSTPARTUM SUPPORT INTERNATIONAL

Toll-free Helpline 800-944-4PPD
Support in English & Spanish

Free Telephone Chat with an Expert
Online Support Groups
Provider Consultation

www.postpartum.net
1-800-944-4PPD
1-800-944-4773

Portland Area Support

Baby Blues Connection

1-800-557-8375

info@babybluesconnectiong.org

www.babybluesconntion.org

"You Can't Tell by Looking"

"I finally told my husband that he and my daughter would be better off without me—that I was not a good mother or wife. I felt like things were never going to get better—that I would never feel happy again. The only way out was to die."

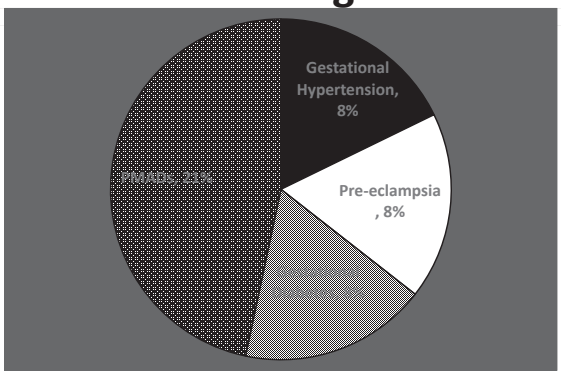
…"I am going to act as though everything is fine and I am terrified of what lies ahead."

Why Should We Screen?

- "You can't tell by looking"
- High prevalence rate
- Effective screening and treatments available
- Increases rate of detection
- Satisfies WHO criteria for population-based screening
- Reduces relative risk of continued depression at 3-5 months by 18-59%
- Risks of untreated PMADs are well documented

(Learman, 2018; Gjerdingern & Yawn, 2007)

Does prevalence warrant screening?



Wisner et al, 2013; Nhibi.nih.g

Barriers to Implementation

- Survey of more than 200 physicians
- Top barriers to screening
  - Time constraints
  - Inadequate training
  - Lack of knowledge of the diagnostic criteria
- Personal experience (through friend, family, or self) associated with increased screening

J Psychosom Obstet Gynaecol. 2011;32(1):27-34.

PMAD Study of 10,000 women

- **21% had postpartum depression**
- **26.5% -** before pregnancy with more chronic pattern
- **33.4% -** onset in pregnancy
- **40.1% -** onset postpartum

Wisner KL, Sit DKY, McShea MC, et al. *JAMA Psychiatry March 2013*

PMAD Study of 10,000 women

Of those who had symptoms…

- **68.5% - unipolar depression**
- **66% - comorbid anxiety disorders**
- **22.6% - diagnosed with bipolar disorder**
- **19.3% - endorsed thoughts of harming themselves**

Wisner KL, Sit DKY, McShea MC, et al. *JAMA Psychiatry March 2013*

Prevention

We know:

- Who is at risk
- How to screen
- How to refer
- Where to refer
- Reliable treatment methods

Screening Recommendations

The U.S. Preventive Services Task Force (USPSTF) recommends screening for depression among adolescents and adults, including pregnant and postpartum women. The American College of

Obstetricians and Gynecologists (ACOG) recommends that clinicians screen patients at least once during pregnancy or the postpartum period for depression and anxiety symptoms using a standardized, validated tool.

The USPSTF and ACOG also recommend that screening be implemented with adequate systems in place to ensure accurate diagnosis, effective treatment and appropriate follow-up.

ACOG Redesigns Postpartum Care

- 2018 - **Fourth Trimester** Guidelines
- ACOG Published committee opinion calling for health care providers to assist women in navigating the transition from pre- to postpartum care.
- Women should have ongoing contact, starting in first three weeks postpartum.
- Follow-up visits as needed, and a comprehensive postpartum visit at 12 weeks.

Obstet Gynecol. 2018;131(5):e140-e150.

American Medical Association

- 2017: New polices promoting implementation of a routine protocol for depression screening of perinatal women.
- *"As attention is turned toward the newborn, the health and wellbeing of the mother can, unfortunately, take a back seat, even as preventable physical and mental issues pose dangers. We need to recognize that dangers of post-partum depression and recognize that pregnancy-related deaths have been increasing,"* Albert J. Osbahr III, MD

Maternal Mental Health Safety Bundle

The Council on Patient Safety in Women's Health Care
https://safehealthcareforeverywoman.org

1. **Readiness** (Every Clinical Care Setting)
2. **Recognition & Prevention** (Every Woman)
3. **Response** (Every Case)
4. **Reporting/Systems Learning** (Every Clinical Care Setting)

Proposed New Measures for HEDIS® 2020

NCQA proposed two new perinatal depression measures for HEDIS 2020 commercial and Medicaid health plan reporting:

- Prenatal Depression Screening and Follow-Up (PND)
- Postpartum Depression Screening and Follow-Up (PPD)

https://blog.ncqa.org/depression-measure-mothers/

Timing Recommended

1. First prenatal visit
2. At least once in second trimester
3. At least once in third trimester
4. Two-week postpartum visit
5. Six-week postpartum visit
6. Repeated screening at 6 and/or 12 months in OB and primary care settings

http://www.postpartum.net/learn-more/screening/

Evidence Based Screening Tools

The most well researched and validated perinatal measures:

- Edinburgh Postnatal Depression Scale (EPDS)
- Patient Health Questionnaire (PHQ) 9

Margaret Spinelli, Pec Indman, John Cox, Wendy Davis, and Birdie Gunyon-Meyer at the 2010 PSI-Marce Meeting

Culturally Sensitive Interventions and Informed Interactions

- Interpret screening cautiously
- Use educational programs, incorporating appropriate descriptions and language
- Recognize impact of discrimination and racism
- Provide culturally informed care

Screening Tool Tips

- Make standard practice for all families.
- Routinely give with other papers and forms for Mother to fill out.
- Should have a written introduction on screening tool or be verbally explained prior to giving to mother.
- Score, review, and document in standard place on office/hospital forms/electronic document.
- Have referral plan and/or list available for referrals

Edinburgh Postnatal Depression Scale (EDPS)

- Ten item self report
- Score of > 10 is considered positive
- Cut off score varies by population/culture

Cox and Holden (1994) Perinatal Psychiatry: Use and Misuse of the Edinburgh Postnatal Depression Scale. London: Gaskell

January 2014 : Perinatal Mental Health:The EPDS Manual,(2nd edition), Cox, Holden,Henshaw

Edinburgh Postnatal Depression Scale (EDPS)

- Most thoroughly validated
- Cost effective - free to copy if original authors cited
- Designed for Perinatal use
- Validated with many cultures
- Validated with teens, dads
- Validated for telephone
- Easy to administer and score
- Available in ~ 60 languages

Sample Lead In Statement for Screening

- *Please be as open and honest as possible when answering these questions.*
- *It is not easy being a new mother and it is OK to feel unhappy at times. As you have recently had a new baby, we would like to know how you are feeling.*
- *Please state the answer which comes closest to how you have felt during the past seven days, not just how you are feeling today.*

Adapted from Registered Nurses Association of Ontario Nursing Best Practices Guidelines

Name _____ Baby's EDC or Birthdate _____

Today's Date _____

Please circle the answer that best describes how you have felt over the past 7 days.

1. I have been able to laugh and see the funny side of things.
0 As much as I always could
1 Not quite so much now
2 Not so much now
3 Not at all

2. I have looked forward with enjoyment to things.
0 As much as I ever did
1 Somewhat less than I used to
2 A lot less than I used to
3 Hardly at all

3. I have blamed myself unnecessarily when things went wrong.
0 No, not at all
1 Hardly ever
2 Yes, sometimes
3 Yes, very often

4. I have been anxious or worried for no good reason.
3 Yes, often
2 Yes, sometimes
1 No, not much
0 No, not at all

5. I have felt scared or panicky for no good reason.
3 Yes, often
2 Yes, sometimes
1 No, not much
0 No, not at all

6. Things have been too much for me.
3 Yes, most of the time I haven't been able to cope at all
2 Yes, sometimes I haven't been coping as well as usual
1 No, most of the time I have coped well
0 No, I have been coping as well as ever

7. I have been so unhappy that I have had difficulty sleeping.
3 Yes, most of the time
2 Yes, sometimes
1 Not very often
0 No, not at all

8. I have felt sad or miserable.
3 Yes, most of the time
2 Yes, quite often
1 Not very often
0 No, not at all

9. I have been so unhappy that I have been crying.
3 Yes, most of the time
2 Yes, quite often
1 Only occasionally
0 No, never

10. The thought of harming myself has occurred to me.
3 Yes, quite often
2 Sometimes
1 Hardly ever
0 Never

Severity Ranges for the EPDS

- None or minimal depression (0–6)
- Mild depression (7–13) Cutoffs may vary between 10-12
- Moderate depression (14–19)
- Severe depression (19–30)

McCabe-Beane et al, 2016

PHQ -9

- Nine item self report questionnaire
- Easy to score and linked with DSM diagnostic criteria
- Can asses and track treatment response
- Useful for broad range of patients -- developed for Family Practitioners

PHQ 9

Patient Name ***Date***

1. Over the last 2 weeks, how often have you been bothered by any of the following problems? Read each item carefully, and circle your response.

Not at all 0 | Several days 1 | More than half the days 2 | Nearly every day 3

1. Little interest or pleasure in doing things
2. Feeling down, depressed, or hopeless
3. Trouble falling asleep, staying asleep, or sleeping too much
4. Feeling tired or having little energy
5. Poor appetite or overeating
6. Feeling bad about yourself, feeling that you are a failure, or feeling that you have let yourself or your family down
7. Trouble concentrating on things such as reading the newspaper or watching television.
8. Moving or speaking so slowly that other people could have noticed. Or being so fidgety or restless that you have been moving around a lot more than usual
9. Thinking that you would be better off dead or that you want to hurt yourself in some way

Totals

2. If you checked off any problem on this questionnaire so far, how difficult have these problems made it for you to do your work, take care of things at home, or get along with other people?

Not Difficult At All 1 | Somewhat Difficult 2 | Very Difficult 3 | Extremely Difficult 0

PHQ-2

PHQ 2 - Short version

Over the past 2 weeks, how often have you been bothered by any of the following problems?

Little interest or pleasure in doing things
0=Not at all
1=Several days
2=More than half the days
3=Nearly every day

Feeling down, depressed, or hopeless
0=Not at all
1=Several days
2=More than half the days
3=Nearly every day

Total point score:_____

PHQ-4

Over the past 2 weeks have you been bothered by these problems?	Not at all	Several days	More days than not	Nearly every day
Feeling nervous, anxious, or on edge	0	1	2	3
Not being able to stop or control worrying	0	1	2	3
Feeling down, depressed, or hopeless	0	1	2	3
Little interest or pleasure in doing things	0	1	2	3

The thought of harming myself has occurred to me (circle one) No Yes

Screening for BP Spectrum

- **www.psycheducation.org - Jim Phelps, MD**
- **Mood Disorders Questionnaire (MDQ)** is a screen for Bipolar I. Now copyrighted by its lead author
- **Primary Care Mood Check - Phelps**
  - More comprehensive screening tool
  - Will remain in the public sector (not copywritten)
  - Integrates the Bipolar Spectrum Diagnostic Scale, which has higher specificity than MDQ

Suicide Risk Question

- **Question #10 on EPDS or PHQ: "The thought of harming myself has occurred to me."**
- **If she answers with anything other than 0, provider must follow up to address threat of harm.**
- **Do not avoid questions that are uncomfortable.**
- **Assess, Refer, and Follow Up**

Steps after Screening

A positive score from a screening tool indicates a need for further assessment and referral

Essential for the provider to facilitate continuity of screening, assessment, referral, and treatment

WHAT'S YOUR ALGORITHM?

Screening > Assessment > Refer >Tx

Locate Screening Tools

- **EPDS:** www.fresno.ucsf.edu/pediatrics/downloads/edinburghscale.pdf
- **PHQs, GAD-7, and translations:** http://www.phqscreeners.com/
- **PHQ 2:** http://health.utah.gov/rhp/pdf/PHQ-9%20two%20question.pdf
- **PHQ 4:** www.psychiatrictimes.com/all/editorial/psychiatrictimes/pdfs/scale-PHQ4.pdf
- **MDQ:** www.integration.samhsa.gov/images/res/MDQ.pdf
- **PCMC:** https://psycheducation.org/primary-care-provider-resource-center/moodcheck/

No cost to the caller

First national perinatal psychiatric consultation line

Provided for medical professionals

Providers call to make appointment with a PSI perinatal psychiatric expert

PRIMARY CARE TRAINING

PSI Frontline Provider Training (webinar)

www.postpartum.net/professionals/trainings-events/frontline-provider-trainings/

ACOG WEBINAR

www.acog.org/Womens-Health/Depression-and-Postpartum-Depression

MCPAP FOR MOMS – Toolkits and Algorithms
https://www.mcpapformoms.org/

Contact Information

Wendy Davis, PhD
503-277-3925 call or text
wdavis@postpartum.net

Postpartum Support International
800-944-4773 helpline
503-894-9453 office
www.postpartum.net

Help Map www.postpartum.net/get-help/locations/

Postpartum Salpingectomy for Permanent Contraception and Cancer Risk Reduction

PNW Update in Ob/Gyn and Women's Health

DATE: November 14, 2019
PRESENTED BY: JESSICA REID, MD; Instructor and Family Planning Fellow

Disclosures

- None

Objectives

- Review methods of permanent contraception and fallopian tube etiology of ovarian cancer
- Understand current recommendations and practice patterns
- Discuss literature regarding safety, feasibility, and cost-effectiveness of postpartum salpingectomy

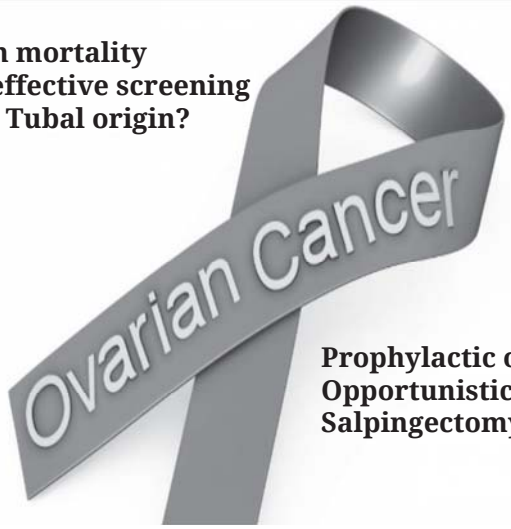
Pop Quiz! True or False

- A salpingectomy is the removal of the mid-section of the fallopian tube.
- Salpingectomy should be discussed with all women undergoing a tubal ligation.

Female Permanent Contraception

- 2nd most common US contraceptive method
- Surgical technique
  - Variable
  - Hysteroscopic – no longer available
- Timing
  - Interval
  - Postpartum

- **High mortality**
- **No effective screening**
- **70% Tubal origin?**



Prophylactic or Opportunistic Salpingectomy

2013 **2015** **2019**

Society of Gynecologic Oncologists (SGO):

Consider salpingectomy at time of hysterectomy or other pelvic surgery to reduce ovarian cancer risk.

2013 **2015** **2019**

ACOG COMMITTEE OPINION

Number 774 (Replaces Committee Opinion Number 620, January 2015)

Committee on Gynecologic Practice

This Committee Opinion was developed by the American College of Obstetricians and Gynecologists' Committee on Gynecologic Practice in collaboration with committee member Lubna Chohan, MD, and committee liaison Debra L. Richardson, MD.

Opportunistic Salpingectomy as a Strategy for Epithelial Ovarian Cancer Prevention

2013 **2015** **2019**

Society of Gynecologic Oncologists (SGO):

Consider salpingectomy at time of hysterectomy or other pelvic surgery to reduce ovarian cancer risk.

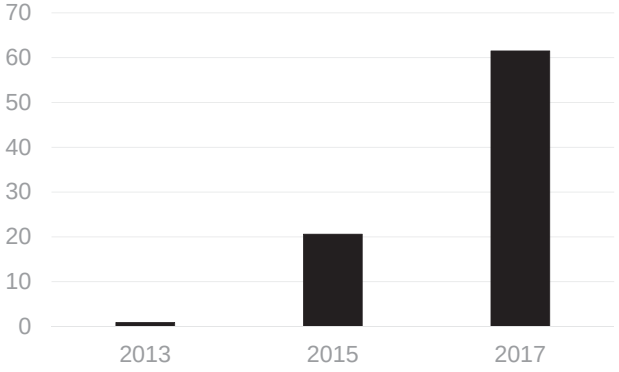
American College of Obstetricians and Gynecologists (ACOG):

"Although data are limited, postpartum salpingectomy and salpingectomy at the time of cesarean delivery appear **feasible and safe**."

"The risks and benefits of salpingectomy should be discussed with patients who desire permanent sterilization."

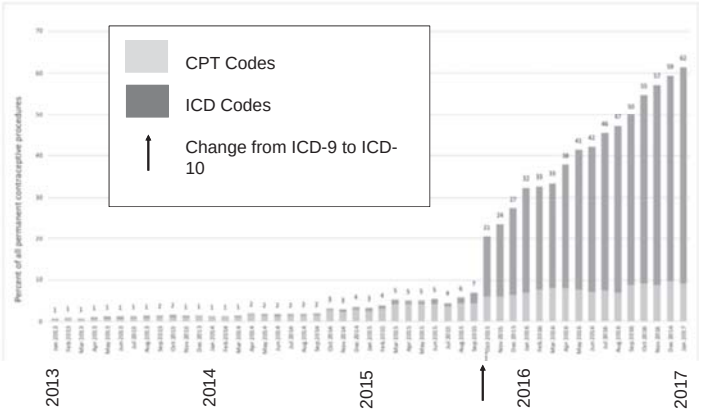
Technique: remove fimbriated ends and any fimbrial attachments to the ovary.

Salpingectomy Rates Pre/Post ACOG Guidelines



Polen-De et al. Contraception. 2019.

Salpingectomy Rates by CPT and ICD Codes



Polen-De et al. Contraception. 2019.

Original Research

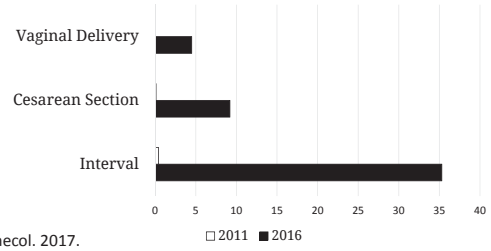
Salpingectomy for Sterilization

Change in Practice in a Large Integrated Health Care System, 2011–2016

C. Bethan Powell, MD, Amy Alabaster, MPH, Sarah Simmons, MD, Christine Garcia, MD, MPH, Maria Martin, MD, Sally McBride-Allen, BS, and Ramey D. Littell, MD

- Northern California Kaiser Database including >10,000 procedures

Increased Rate of Salpingectomy from 2011-2016



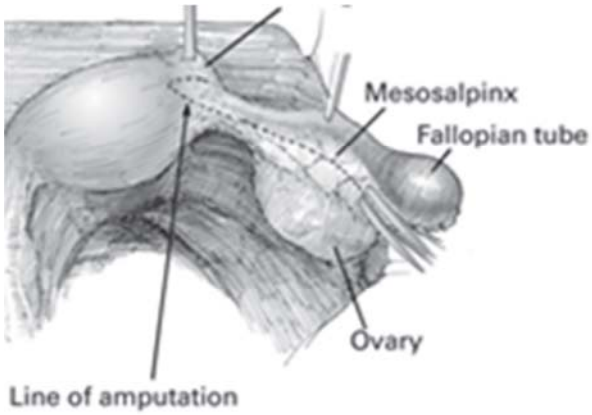
Powell et al. Obstet Gynecol. 2017.

Is it feasible?

- Randomized control trial
- Population:
  - Women undergoing C-section
    - Standard BTL: Partial salpingectomy
    - Complete bilateral salpingectomy
- Primary Outcome
  - Mean total operative time
  - Completion rate

Subramaniam A et al. Obstet Gynecol. 2018.

Salpingectomy Technique



Primary Outcomes:

- Mean total operative time: salpingectomy 15 min longer
- Completion: salpingectomy less successful 68% vs 95%

Secondary Outcomes:

- Mean tubal operative time: salpingectomy 12 min longer
- Median EBL for tubal procedure: higher in salpingectomy group 10cc [5-25] vs. 5cc [5-10]
- No adverse outcomes in either group

	BTL	Salpingectomy
Delivery BMI	39.4 +/- 7.4	38.8 +/- 10.0
H/o abdominal or pelvic surgery	5%	8%
# of prior cesareans	2.0 +/- 1.0	2.0 +/- 0.8
Cesarean type		
Primary	18%	3%
→ Repeat	83%	98%
Skin incision		
→ Vertical	8%	18%
Pfannenstiel	93%	83%

Of those where salpingectomy was assigned, but not completed:
- Higher BMI (46 vs 36)
- Longer time from skin to tubal start (18 minutes)

Surgeon Satisfaction & Attitudes

	BTL	Salpingectomy
Satisfied with feasibility	92%	62%
Satisfied with safety	97%	53%

Conclusions

- 15 minutes extra operative time
- Safe
- 2/3rds successful completion
- Similar findings in other studies

If we think salpingectomy is a safe and feasible alternative…

- Do the benefits outweigh the risks?
- Is it cost effective?

Original Research

OBSTETRICS

Cost-effectiveness of opportunistic salpingectomy vs tubal ligation at the time of cesarean delivery

Kartik K. Venkatesh, MD, PhD; Leslie H. Clark, MD; David M. Stamilio, MD, MSCE

- Theoretic cohort of women undergoing cesarean delivery who desired permanent contraception
  - Bilateral tubal ligation
  - Bilateral opportunistic salpingectomy
  - Postpartum LARC (baseline reference group)
- Examined clinical outcomes and cost-effectiveness

Venkatesh KK et al. Am J Obstet Gynecol. 2019.

Assumptions

Operative complications:

- Absolute baseline risk 6.9%
  - BTL: + 10 minutes = 7.6%
  - Salpingectomy: + 20 minutes = 8.3%

Pregnancy outcomes (unintended / ectopic):

- BTL: 0.45% risk pregnancy / 20% ectopic
- Salpingectomy: 0.38% risk pregnancy / 10% ectopic

Ovarian cancer:

- Absolute baseline risk 1.28%
  - BTL: 34% risk reduction
  - Salpingectomy: 64% risk reduction

TABLE 2

Clinical outcomes in study population of pregnant women seeking permanent sterilization at time of cesarean delivery

Strategy	No. of ovarian cancer cases	No. of ovarian cancer deaths over 10 y	No. of surgery complications	No. of intrauterine pregnancies	No. of ectopic pregnancies
Cesarean delivery with salpingectomy	507 ⇩ 422	302 ⇩ 252	9130 ⇧ 770	376 ⇩ 20	42 ⇩ 57
Cesarean delivery with tubal ligation	929	554	8360	396	99
Cesarean delivery with LARC	1051	625	7700	517	583

Assuming study population of 110,000 pregnant women desiring permanent sterilization at time of cesarean delivery.

LARC, long-acting reversible contraception.

Venkatesh et al. Cost-effectiveness of salpingectomy vs tubal ligation at cesarean. Am J Obstet Gynecol 2019.

Cost Effectiveness

- BTL procedure is cost-saving $64
- Both BTL and salpingectomy have favorable cost effectiveness ratios.
- Salpingectomy is more cost effective for outcomes of contraception and ovarian cancer risk reduction.

Is there a preferred strategy?

- 49% chance that BTL is the preferred strategy
- If salpingectomy complication risk is > 2% higher than BTL

OR

- If cancer risk reduction of salpingectomy is <52%

THEN

- Bilateral tubal ligation is the preferred strategy.

Conclusions

- BTL and Salpingectomy are both cost-effective strategies for permanent contraception and ovarian cancer risk reduction.
- Risks and benefits of salpingectomy with cesarean delivery need to be better defined before a preferred strategy can be determined.

Summary

- No evidence of short-term (peri-operative) risk or long-term risk with salpingectomy.
- Salpingectomy appears to be safe and feasible at time of cesarean section, though operative time may be increased.
- Limited data exists regarding salpingectomy the time of post-partum tubal (after vaginal delivery).
- Benefits include contraceptive efficacy and ovarian cancer risk reduction.
- Appears to be cost-effective
- Some questions still remain…

Considering postpartum salpingectomy in your practice?

- Discuss options during prenatal care
  - Benefits of BTL and salpingectomy: contraception and ovarian cancer risk
  - Risks: increased operative time, regret, inability to complete procedure
- Consider patient specific risks/surgical difficulty
- Develop a standardized technique and consider implementing a training plan
- Choose method based on intraoperative findings

Questions?

Jessica Reid MD
Instructor OB/GYN & Family Planning Fellow
reidje@ohsu.edu

OHSU Section of Family Planning
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  - Outpatient clinic sessions M-Th
  - 3 outpatient moderate sedation clinics + OR time
  - Multi-disciplinary (Heme+Gyn) clinics for Women & Girls with heavy menstrual bleeding
  - Center of Experience in Deep Implant Removals

CPT Codes:

- **<u>At time of cesarean section:</u>**
  - **58611**: ligation or transection of fallopian tube(s) done at the time of cesarean delivery or intra-abdominal surgery.
  - **58700:** Salpingectomy, complete or partial, unilateral or bilateral (separate procedure)
- **<u>At time of laparoscopy:</u>**
  - **58670:** laparoscopy surgical; with fulguration of oviducts (With or without transection). This was developed specifically for reporting a laparoscopic elective sterilization.
  - **58661:** laparoscopy surgical with removal of adnexal structures. This should be used when a disease process is involved (adnexal mass, paratubal cyst, etc).

Should we be routinely performing salpingectomy during cesarean deliveries?

"Ultimately, the value of salpingectomy requires more study to accurately balance the risks including complications, cost, surgical time, lack of reversibility, and potential effect on ovarian reserve against the benefits, including a higher rate of sterilization, lower reoperation rates, and, most importantly, the comparative reduction in ovarian cancer offered by salpingectomy over tubal occlusion."

Powell et al. Obstet Gynecol. 2017.

References

- ACOG Committee Opinion #774: Opportunisitic Salpingectomy as a Strategy for Epithelial Ovarian Cancer Prevention; April 2019.
- Chene G, Rahimi K, Mes-Masson A, Provencher D. Surgical implications of the potential new tubal pathway for ovarian carcinogenesis. Journal of minimally invasive gynecology. 2013;20:153-9.
- Danis RB, Della Badia CR, Richard S. Postpartum Permanent Sterilization: Could Bilateral Salpingectomy Replace Bilateral Tubal Ligation? J Min Invasive Gyn 2016; 23(6) 928-932).
- Deshpande NA et al. relationship between body mass index and operative time in women receiving immediate postpartum tubal ligation. Contraception 2019; 100:106-110.
- Dilley SE, Havrilesky LJ, Bakkum-Gamez J, Cohn DE, Straughn Jr JM, Caughey AB, et al. Cost-effectiveness of opportunistic salpingectomy for ovarian cancer prevention. Gynecol Oncol. 2017;146:373-9.
- Ganer Herman H, Gluck O, Keidar R, Kerner R, Kovo M, Levran D, et al. Ovarian reserve following cesarean section with salpingectomy vs tubal ligation: A randomized trial. Am J Obstet Gynecol. 2017;217:472.e1,472.e6.
- Garcia C, Moskowitz OM, Chisholm CA, Duska LR, Warren AL, Lyons GR, et al. Salpingectomy compared with tubal ligation at cesarean delivery: A randomized controlled trial. Obstet Gynecol. 2018;132:29-34.
- Guttmacher Fact Sheet: Contraceptive Use in the United States, July 2018. https://www.guttmacher.org/fact-sheet/contraceptive-use-united-states

References

- Kurman RJ, Shih I. Molecular pathogenesis and extraovarian origin of epithelial ovarian cancer—shifting the paradigm. Hum Pathol. 2011;42:918-31.
- Medeiros F, Muto MG, Lee Y, Elvin JA, Callahan MJ, Feltmate C, et al. The tubal fimbria is a preferred site for early adenocarcinoma in women with familial ovarian cancer syndrome. Am J Surg Pathol. 2006;30:230-6.
- Polen-De C, et al. Nationwide salpingectomy rates for an indication of permanent contraception before and after published practice guidelines. Contraception 2019; 100:111-115.
- Powell C et al. Salpingectomy for Sterilization: Change in Practice in a Large Integrated Health Care System, 2011-2016. 2017 Obstet Gynecol. 130(5):961-967.
- Siegel RL, Miller KD, Jemal A. Cancer statistics, 2015. CA: a cancer journal for clinicians. 2015;65:5-29.
- Subramaniam A, et al. Feasibility of Complete Salpingectomy Compared with Standard Postpartum tubal Ligation at Cesarean Delivery A Randomized Controlled Trial. Obstet Gynecol 2018; 132(1):20-27.
- Subramaniam A, Einerson BD, Blanchard CT, Erickson BK, Szychowski J, Leath III CA, et al. The cost-effectiveness of opportunistic salpingectomy versus standard tubal ligation at the time of cesarean delivery for ovarian cancer risk reduction. Gynecol Oncol. 2019;152:127-32
- Venkatesh KK, Clark LH, Stamillo DM. Cost-effectiveness of opportunistic salpingectomy vs tubal ligation at the time of cesarean delivery. Am J Obstet Gynecol 2019;220:106e1-10.

Questions?
Contact me

OHSU Physician Advice & Referral Service
- •503-494-4567
- •800-245-6478 (toll-free)

Opioid Treatment Options & Hot Topics:
Approaches to Perinatal Substance Use Disorder

Pacific NW Update in Ob/Gyn and Women's Health 11/14/19

Amanda Risser MD MPH, Sr. Medical Director of Substance Use Disorder Services

CENTRAL CITY CONCERN
HOMES HEALTH JOBS

Perinatal Opiate Treatment Options and Hot Topics:

- Scope of issue in Oregon
- Methamphetamines
- Treatment options
- Benefits of treatment
- Withdrawal: risky?
- Syndemic: syphilis, HIV, HCV
- HCV treatment

Oregon: worse prevalence, worse access to treatment

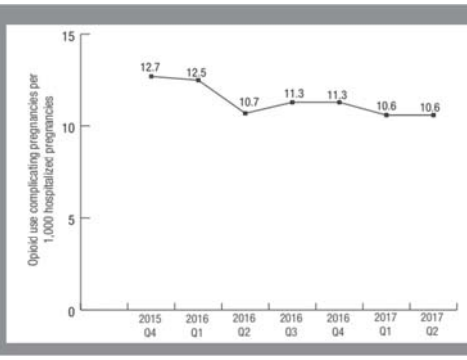
Substance Use Disorders in Oregon – Prevention, Treatment & Recovery

Oregon Substance Use Disorder Research Committee
November 2017

Oregonians suffer more from SUD of almost every substance than the national average and most other states. Almost one of every 10 adults in Oregon depends upon or abuses illicit drugs or alcohol, as well as one of every 15 Oregon youth.[8] However, only 11 percent of adult Oregonians with SUD received treatment, worse than the national average of 14 percent.[9]

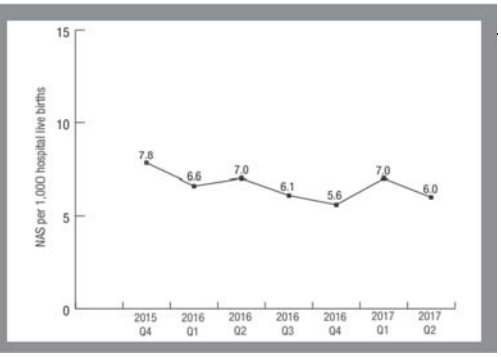
Opioid Use Complicating Pregnancies by Quarter, Oregon

Data Source: Oregon Hospital Discharge Data. Opioid use complicating pregnancy includes opioid abuse, dependence, and use. This includes ICD10CM codes: Any O code + F11.1, F11.2, or F11.9.



Neonatal Abstinence Syndrome by Quarter, Oregon

Data Source: Oregon Hospital Discharge Data, Oregon Center for Health Statistics. NAS includes ICD10CM code: P96.1.

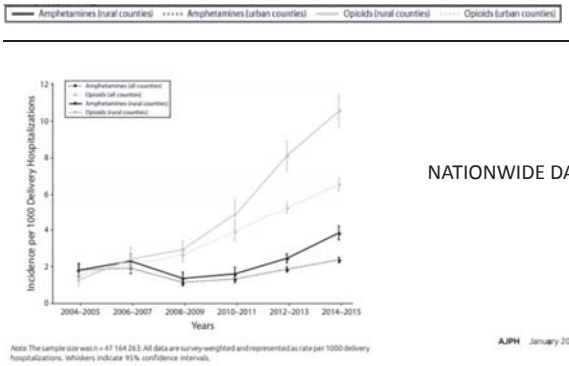


Dramatic REGIONAL variation in use patterns:

Amphetamine- and Opioid-Affected Births: Incidence, Outcomes, and Costs, United States, 2004–2015

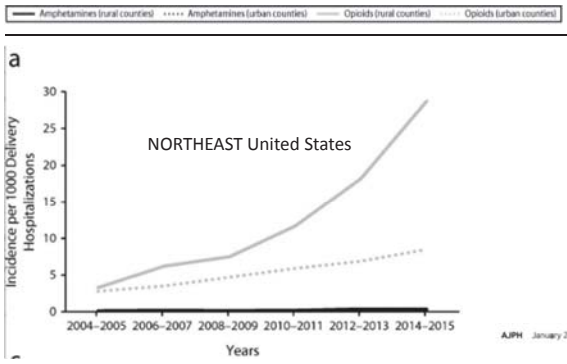
Lindsay K. Admon, MD, MS, Gavin Bart, MD, PhD, Katy B. Kozhimannil, PhD, MPA, Caroline R. Richardson, MD, Vanessa K. Dalton, MD, MPH, and Tyler N. A. Winkelman, MD, MS.

AJPH January 2019, Vol 109, No. 1



NATIONWIDE DATA

AJPH January 2019, Vol 109, No. 1



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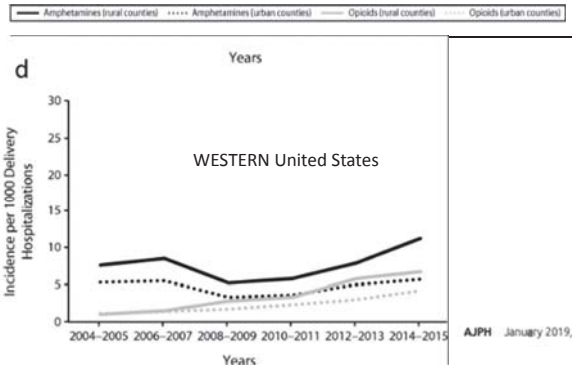
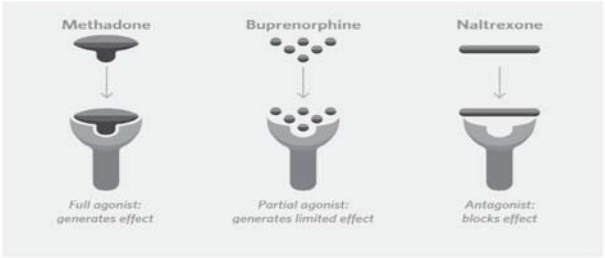


AJPH January 2019, Vol 109, No. 1

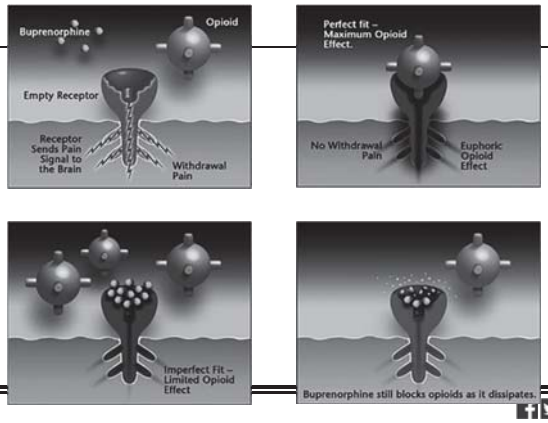
Treatment is Effective: some perspective

Perinatal intervention	Outcome		
Antenatal Steroids	Prevention of RDS Prevention of need for surfactant Prevention of IVH	NNT 11 NNT 9 NNT 9	NNH 8 (high sugar)
Aspirin	Prevention of preeclampsia: high risk patients	NNT 50	
Progesterone	Prevention of preterm birth before 34 wks w prior h/o spontaneous preterm birth	NNT 22-80 NNT 7-9.1	NNH 63-167
Alcohol Use Disorder	Acamprosate Total Abstinence Naltrexone Total Abstinence Naltrexone Zero Heavy Drink	NNT 12 NNT 20 NNT 12	
Buprenorphine	Retention in Treatment (proxy for decreased use)	NNT 2-4	

Pharmacotherapy for Opiate Use Disorder:



Two common formulations-
Suboxone: buprenorphine/naloxone
Subutex: buprenorphine



Benefits of Pharmacotherapy for OUD in pregnancy:

- Less likely to die.
- Less likely to be incarcerated.
- Less likely to have injection associated infectious diseases (HIV, HCV, HBV, cellulitis, endocarditis).
- Less likely to have small and/or early babies.
- More likely to be employed and stably housed.
- Less likely to have psychiatric symptoms.
- More stable family and social life.
- More likely to obtain abstinence.

Opiate withdrawal in pregnancy?

Detoxification from opiate drugs during pregnancy

Jennifer Bell, MD; Craig V. Towers, MD; Mark D. Hennessy, MD; Callie Heitzman, RN; Barbara Smith; Katie Chattin

BACKGROUND: The current recommendation regarding the management of a pregnant patient with opioid dependence is not to perform detoxification during pregnancy because of a potential risk for preterm labor, fetal distress, or fetal demise.
OBJECTIVE: The objective of the study was to evaluate the safety of full opiate detoxification during pregnancy in a large number of patients through 4 different methods and analyze the rate of newborn treatment of neonatal abstinence syndrome for each method.
STUDY DESIGN: This was a retrospective analysis of data collected prospectively during ongoing prenatal care of opiate-addicted pregnant women. Data were analyzed for pregnancy complications including fetal demise and preterm labor of opiate-addicted pregnant women who underwent detoxification during pregnancy through 4 different methods: acute detoxification of incarcerated patients; inpatient detoxification with intense outpatient follow-up management; inpatient detoxification without intense outpatient follow-up management; and slow outpatient buprenorphine detoxification. The rates of newborns treated for neonatal abstinence syndrome were also assessed for each group.
RESULTS: Over 5.5 years, 301 opiate-addicted pregnant patients were fully detoxified during pregnancy with no adverse fetal outcomes related to detoxification identified. There were 94 patients who delivered newborns treated for neonatal abstinence syndrome (31%). There was an 18.5% rate of neonatal abstinence syndrome in the 108 acutely detoxified while incarcerated, a 17.4% rate of neonatal abstinence syndrome in the 23 who had inpatient detoxification with intense outpatient follow-up management, a 17.2% rate of neonatal abstinence syndrome in the 93 who went through slow outpatient buprenorphine detoxification, but a 70.1% rate of neonatal abstinence syndrome in the 77 who had inpatient detoxification without intense outpatient follow-up management.
CONCLUSION: With these data and other published studies, more than 600 patients have been reported to detoxify from opiates during pregnancy with no report of fetal harm related to the process. These data highly suggest that detoxification of opiate-addicted pregnant patients is not harmful. The rate of neonatal abstinence syndrome is high but primarily when no continued long-term follow-up occurs. Once a patient is drug free, intense behavioral health follow-up is needed for continued success.

Key words: decreasing neonatal abstinence syndrome, opiate detoxification, substance abuse in pregnancy

Bell J, Towers CV, Hennessy MD, et al. Detoxification from opiate drugs during pregnancy. Am J Obstet Gynecol 2016;215:374.e1-6.

Detox: harmful to fetus?

- Based on two case-reports from the 70s.
- Subsequent studies have called this into question.
- This fear of harm has guided treatment for decades.
- There are other reasons to feel an urgency around treatment of withdrawal symptoms than fetal harm.

Bell J, Towers CV, Hennessy MD, et al. Detoxification from opiate drugs during pregnancy. Am J Obstet Gynecol 2016;215:374.e1-6.

Retrospective Analysis, comparison between 4 groups:

- Group 1: incarcerated patients, involuntary acute detox w/o MAT
- Group 2: inpatient detox with buprenorphine with intensive behavioral treatment
- Group 3: inpatient detox with buprenorphine without intensive behavioral treatment
- Group 4: outpatient SLOW taper/detox over 8-16 weeks.

Bell J, Towers CV, Hennessy MD, et al. Detoxification from opiate drugs during pregnancy. Am J Obstet Gynecol 2016;215:374.e1-6.

NAS rate and relapse rate:

Group	1 jail	2 detox + BH	3 detox - BH	4 slow taper
Rate of NAS N (%)	20 (18.5%)	4 (17.4%)	54 (70.1%)	16 (17.2%)
Rate of Relapse N (%)	25 (23.1%)	4 (17.4%)	57 (74%)	21 (22.5%)

Bell J, Towers CV, Hennessy MD, et al. Detoxification from opiate drugs during pregnancy. Am J Obstet Gynecol 2016;215:374.e1-6.

Fetal/Pregnancy Outcomes

"With our 301 study patients and the patients reported in these 5 follow-up studies, more than 600 patients have undergone detoxification during pregnancy, with no report of intrauterine fetal demise or preterm delivery related to the process."

Bell J, Towers CV, Hennessy MD, et al. Detoxification from opiate drugs during pregnancy. Am J Obstet Gynecol 2016;215:374.e1-6.

The article leads to revised ACOG guidance:

"If a woman does not accept treatment with an opioid agonist, or treatment is unavailable, medically supervised withdrawal can be considered under the care of a physician experienced in perinatal addiction treatment and with informed consent; however, to be successful, it often requires prolonged inpatient care and intensive outpatient behavioral health follow up."

- (ACOG committee opinion August 2017)

Context is important:

- 2014: Tennessee passed a "fetal assault law", women whose babies were diagnosed with NOW were incarcerated.
- Women were very motivated to minimize risk of NOW for their infants.
- Also- group 1 was incarcerated and had no choice because of the lack of access to MSR while incarcerated.
- While the law saw its "sunset" in 2016 this was the context in which the retrospective data was accumulating.
- Women received intensive BH treatment which isn't sustainable.

Bell J, Towers CV, Hennessy MD, et al. Detoxification from opiate drugs during pregnancy. Am J Obstet Gynecol 2016;215:374.e1-6.

"Our idea is to get the girls off drugs before delivery, then equip them to be better moms," Thomas said. "We could save the state lots of money, and save the babies the anguish of withdrawal for six weeks."

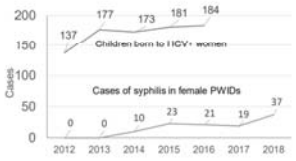
(one of the authors quoted in NBC news))

CD summary

SEX, DRUGS, AND INFECTIOUS DISEASES — THE NEW SYNDEMIC

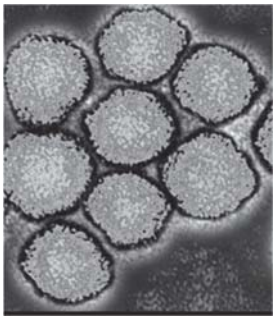
- Syndemic: two or more epidemics occurring simultaneously that interact and exacerbate the burden of disease.
- Ten congenital syphilis cases in Oregon in 2018: up from a very low incidence prior.
- All driven by injection drug use (esp meth) and behaviors which are co-occurring (condomless sex, transactional sex, sex w mult partners).

Figure 1. Impact of opioid epidemic and injection drug use on women and infants, Oregon, 2012–2018



Refer your patients to LOW BARRIER HCV tx:

- While interventions to prevent vertical transmission of HCV are not backed by strong evidence, general approach is:
  - Avoid FSE unless benefits > risks
  - Avoid AROM, work to minimize length of time that membranes ruptured
- Until 2019, Medicaid patients couldn't receive medications for HCV treatment unless they were: sober, had liver damage.
- This excluded reproductive age women!
- Now: no sobriety or liver damage requirements for prior authorizations to get treatment! Get your patients to a place that will treat them! **Or TREAT THEM YOURSELF!**



Cognitive Behavioral Therapy for Depression

Teni Davoudian, PhD, ABPP
Clinical Psychologist
Assistant Professor of Psychiatry

November, 14, 2019

Depression in Ob/Gyn Settings

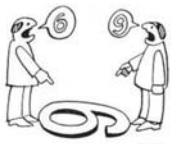
- Women are twice as likely as men to develop depression (Albert, 2015)
- Several gynecological conditions are associated with depressive symptoms:
  - Premature ovarian insufficiency (Schmidt et al., 2016)
  - Polycystic ovarian syndrome (Deeks, Gibson-Helm, & Teede, 2010)
  - Stillbirth (Hogue et al., 2015)
  - Endometriosis (Chen et al., 2016)
- 11% of ob/gyn visits – depression is chief complaint (Crimele et al, 2013)
  - Additional 30% of ob/gyn visits – pt mentions psychological distress (depressed mood, anxiety, stress)

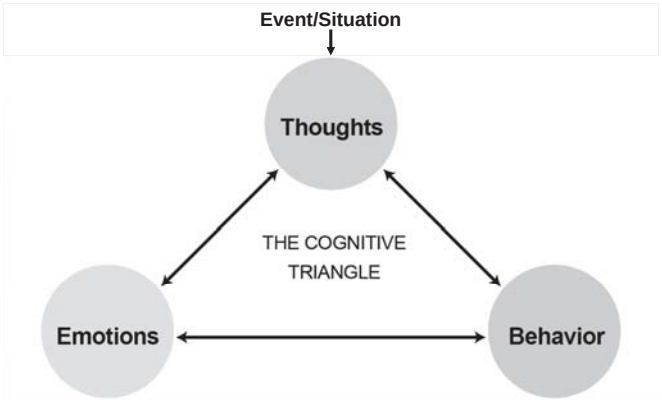
CBT: Treatment Outcome Research

- CBT reduces depressive symptoms and/or increases quality of life and/or improves medical treatment outcomes:
  - Perimenopause (Green et al., 2013)
  - Infertility (Domar et al., 2000)
  - Pregnancy and postpartum (Sokol, 2015)
  - COPD (Fritzche, Clamor, & von Leupolt, 2011)
  - Cancer (Hart et al., 2012)
  - Chronic pain (Edhe, Dillworth, & Turner, 2014)
  - Irritable bowel syndrome (Li et al, 2014)

Theoretical Underpinnings of CBT

- "People are not disturbed by things but by the view they take of them." –Epictetus
- Psychopathology is (partially) the result of faulty information processing
- Cognitions, emotions, and behaviors are interrelated
- Cognitions are modifiable



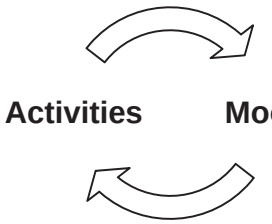


Structure of CBT

- Short-term psychotherapy (approximately 6-12 sessions)
  - Booster sessions may be needed
- Psychoeducation
- Goal-oriented
- Home practice
  - Homework facilitates generalization and maintenance of skills learned during therapy session
- Mechanisms of action:
  - Behavioral activation ⇦
  - Cognitive Restructuring

Behavioral Activation

- Increases patient activity (re-introduction to abandoned activities or introduction to new activities)
- Improves self-efficacy and increases exposure to reinforcing situations



Behavioral Activation

- Questions to ask patient:
  - What do you miss doing?
  - What did you used to do?
  - What did you want to try but never had the chance to?
  - Who do you enjoy spending time with?
- If pt cannot come up with an answer, provide list of pleasurable activities



Cognitive Distortions

- Inaccurate, inflated, irrational thoughts or beliefs that distort our perceptions of reality
- Negative views of the self, world, or future
- Distorted automatic thoughts
  - Cognitions that come to mind involuntarily and effortlessly
  - Create feelings of failure, inadequacy, and disempowerment
- In order to reframe/restructure distorted cognitions, we must first identify them as such

Cognitive Restructuring

- Dispute cognitive distortions
- Thoughts are not facts
- Evidence for and against thoughts
  - What is the evidence that this thought is true?
- Pros and cons of holding onto thoughts
  - What are the emotional costs of holding on to this thought?
- Helps us to slow down and develop alternative/balanced thought

Cognitive Restructuring

- What type of cognitive error is the statement below?
  - "Now that I have a baby, I never sleep"
- How can it be restructured?

Introducing CBT to Patients

1. Present cognitive triangle (thoughts, emotions, behaviors are interrelated)
2. Describe goal of CBT: develop balanced thinking and establish helpful behaviors
3. Decide whether to start with cognitions or behaviors

Cognitive Route	Behavioral Route
• Cognitive distortions form • Thought log	• List of pleasurable activities • Activity scheduling calendar

CBT Training for Physicians

- CBT-trained physicians incorporated some CBT techniques into practice 6 months after training (Wieber & Griever, 2005)
- Main barriers for physicians:
  - Lack of time
  - Limited confidence in methods
  - Interruptions
  - Pt preferences for pharmacotherapy
- Beck Institute for Cognitive Behavior Therapy offers on-site and off-site training programs to teach CBT skills.

Self-Administered CBT for Patients

- Apps
  - Cognitive Diary CBT Self-Help
  - CBT Thought Record Diary
  - What's Up
    - Pilot studies suggest effectiveness of internet-based/computerized CBT for depression (Khatri et al., 2014)

- Books
  - Feeling Good: The New Mood Therapy
    by David Burns, MD
  - Mind Over Mood: Change How You Feel By Changing How You Think
    by Dennis Greenberger, PhD and Christine Padesky, PhD

Final Thoughts

- Medical providers play an integral role in managing depression
- CBT is an accessible modality of psychotherapy in medical settings
- CBT can be utilized while waiting for antidepressants to take effect
- CBT may not be appropriate for pts with:
  - Thought disorders
  - Limited intellectual functioning (consider behavioral focus)
- Psychodynamic, interpersonal therapy, acceptance commitment therapy are as effective as CBT (Beltman et al., 2010; Cujipers et al., 2010; Tolin, 2010)

References

Albert, P. R. (2015). Why is depression more prevalent in women?. *Journal of psychiatry & neuroscience: JPN*, *40*(4), 219.

Butler, A. C., Chapman, J. E., Forman, E. M., & Beck, A. T. (2006). The empirical status of cognitive-behavioral therapy: a review of meta-analyses. *Clinical psychology review*, *26*(1), 17-31.

Cerimele, J. M., Vanderlip, E. R., Croicu, C. A., Melville, J. L., Russo, J., Reed, S. D., & Katon, W. (2013). Presenting symptoms of women with depression in an obstetrics and gynecology setting. *Obstetrics and gynecology*, *122*(2 0 1), 313.

Chen, L. C., Hsu, J. W., Huang, K. L., Bai, Y. M., Su, T. P., Li, C. T., ... & Chen, M. H. (2016). Risk of developing major depression and anxiety disorders among women with endometriosis: A longitudinal follow-up study. *Journal of affective disorders*, *190*, 282-285.

Deeks, A. A., Gibson-Helm, M. E., & Teede, H. J. (2010). Anxiety and depression in polycystic ovary syndrome: a comprehensive investigation. *Fertility and sterility*, *93*(7), 2421-2423.

Domar, A. D., Clapp, D., Slawsby, E., Kessel, B., Orav, J., & Freizinger, M. (2000). The impact of group psychological interventions on distress in infertile women. *Health Psychology*, *19*(6), 568.

Ehde, D. M., Dillworth, T. M., & Turner, J. A. (2014). Cognitive-behavioral therapy for individuals with chronic pain: efficacy, innovations, and directions for research. *American Psychologist*, *69*(2), 153

Fritzsche, A., Clamor, A., & von Leupoldt, A. (2011). Effects of medical and psychological treatment of depression in patients with COPD–a review. *Respiratory medicine*, *105*(10), 1422-1433.

Green, S. M., Haber, E., McCabe, R. E., & Soares, C. N. (2013). Cognitive–behavioral group treatment for menopausal symptoms: A pilot study. *Archives of women's mental health*, *16*, 325-332.

Gullikkson, M., Burell, G., Vessby, B., Lundin, L., Toss, H., & Svärdsudd, K. (2011). Randomized controlled trial of cognitive behavioral therapy vs standard treatment to prevent recurrent cardiovascular events in patients with coronary heart disease: Secondary Prevention in Uppsala Primary Health Care project (SUPRIM). *Archives of internal medicine*, *171*(2), 134-140

Hart, S. L., Hoyt, M. A., Diefenbach, M., Anderson, D. R., Kilbourn, K. M., Craft, L. L., ... & Spring, B. (2012). Meta-analysis of efficacy of interventions for elevated depressive symptoms in adults diagnosed with cancer. *Journal of the National Cancer Institute*, *104*(13), 990-1004.

Hofmann, S. G., Asnaani, A., Vonk, I. J., Sawyer, A. T., & Fang, A. (2012). The efficacy of cognitive behavioral therapy: A review of meta-analyses. *Cognitive therapy and research*, *36*(5), 427-440.

Hogue, C. J., Parker, C. B., Willinger, M., Temple, J. R., Bann, C. M., Silver, R. M., ... & Reddy, U. M. (2015). The Association of Stillbirth with Depressive Symptoms 6–36 Months Post-Delivery. *Paediatric and perinatal epidemiology*, *29*(2), 131-143.

Khatri, N., Marziali, E., Tchernikov, I., & Shepherd, N. (2014). Comparing telehealth-based and clinic-based group cognitive behavioral therapy for adults with depression and anxiety: a pilot study. *Clinical interventions in aging*, *9*, 765

Li, L., Xiong, L., Zhang, S., Yu, Q., & Chen, M. (2014). Cognitive–behavioral therapy for irritable bowel syndrome: A meta-analysis. *Journal of psychosomatic research*, *77*(1), 1-12.

Sharry, J., Davidson, R., McLoughlin, O., & Doherty, G. (2013). A service-based evaluation of a therapist-supported online cognitive behavioral therapy program for depression. *Journal of medical Internet research*, *15*(6), e121.

Li, L., Xiong, L., Zhang, S., Yu, Q., & Chen, M. (2014). Cognitive–behavioral therapy for irritable bowel syndrome: A meta-analysis. *Journal of psychosomatic research*, *77*(1), 1-12.

Sharry, J., Davidson, R., McLoughlin, O., & Doherty, G. (2013). A service-based evaluation of a therapist-supported online cognitive behavioral therapy program for depression. *Journal of medical Internet research*, *15*(6), e121.

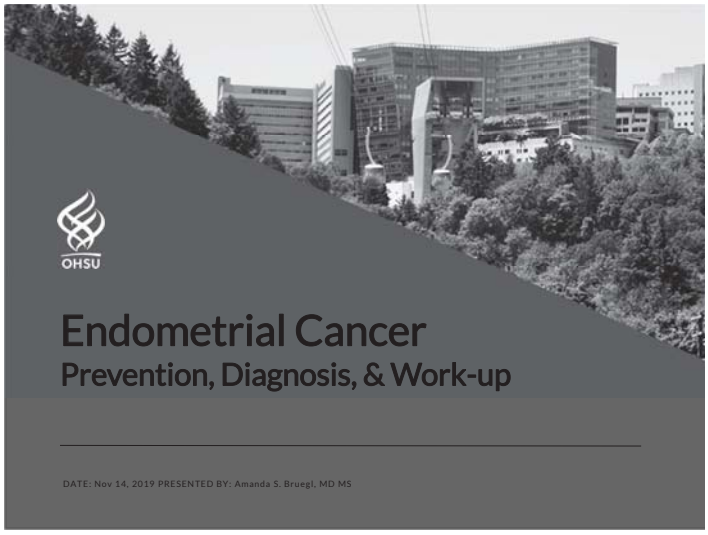
Schmidt, P. J., Cardoso, G. M., Ross, J. L., Haq, N., Rubinow, D. R., & Bondy, C. A. (2006). Shyness, social anxiety, and impaired self-esteem in Turner syndrome and premature ovarian failure. *Jama*, *295*(12), 1373-1378.

Sockol, L. E. (2015). A systematic review of the efficacy of cognitive behavioral therapy for treating and preventing perinatal depression. *Journal of Affective Disorders*, *177*, 7-21.

Questions?
Contact me

OHSU Physician Advice & Referral Service
- 503-494-4567
- 800-245-6478 (toll-free)

Thank You



Endometrial Cancer
Prevention, Diagnosis, & Work-up

DATE: Nov 14, 2019 PRESENTED BY: Amanda S. Bruegl, MD MS

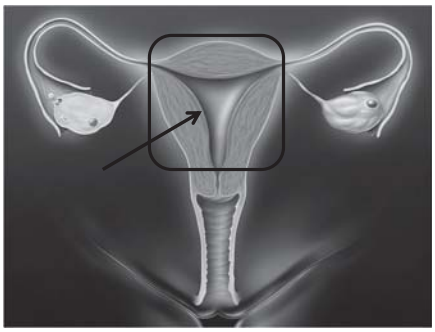
Disclosures:

- None

Objectives

- Understand epidemiology and risk factors of endometrial cancer
- Discuss prevention strategies in high risk patients
- Discuss clinical assessment of abnormal uterine bleeding in premenopausal and postmenopausal women
- Discuss work-up strategy while awaiting referral to gynecologic oncologist

Uterine vs Endometrial Cancer



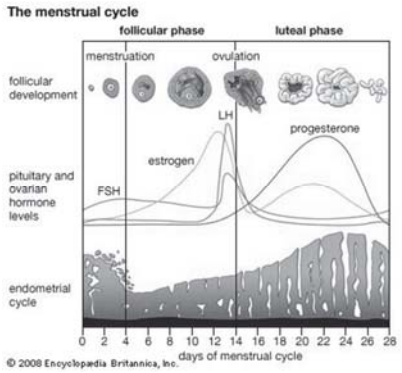
www.medscape.com

Epidemiology and Risk Factors

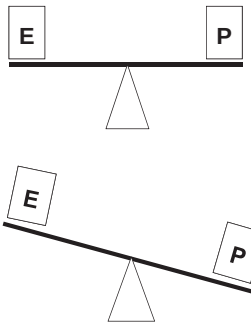
Basic epidemiology of endometrial cancer

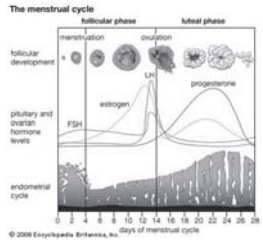
- Endometrial cancer is most common gynecologic malignancy in developed nations
- 4th most common malignancy among women in both the U.S. and Canada
- 70% of women will be diagnosed with Stage I disease
- Mean age of diagnosis is 63

Normal Bleeding Pattern in Cycling Women



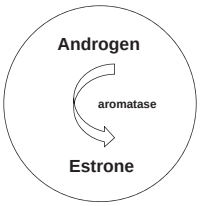
Risk Factor: Unopposed Estrogen





***** Unopposed estrogen can crease risk for endometrial cancer 10-20X**

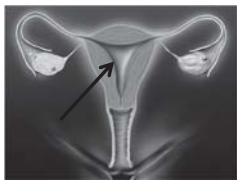
Risk Factor: Obesity



↓ Sex Hormone Binding Globulin

↑ Insulin

↑ Bioavailable Estrogen



Risk Factor: Tamoxifen

Tamoxifen → Breast Tissue: Anti-Estrogen

Tamoxifen → Endometrial Tissue: Pro-Estrogen

Tamoxifen results in a 3-fold increase in risk for EC

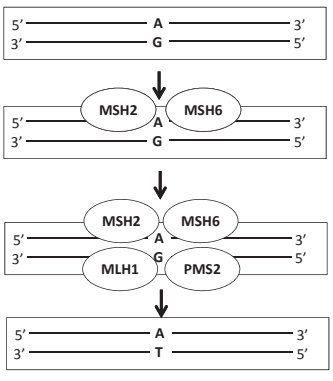
Development of EC can occur *after* discontinuation of Tamoxifen

RISK Factor: Hereditary Risk

Lynch Syndrome (HNPCC)

- **Autosomal-dominant hereditary cancer syndrome**
- **Characterized by an increased prevalence of endometrial and colorectal cancer**
- **Germline mutations in the DNA mismatch repair (MMR) genes constitute the genetic basis for Lynch Syndrome**

DNA MMR System



Risk Factor: Hereditary Risk

Lynch Syndrome (HNPCC)

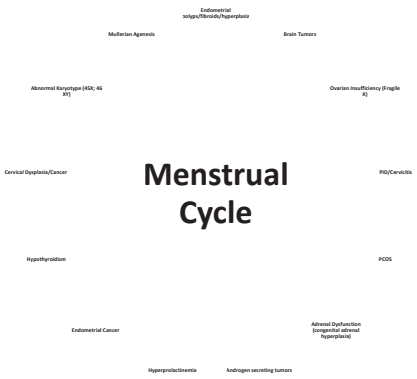
- **Colonoscopy at age 20-25 every 1-2 y, or 2-5 yrs prior to earliest colon cancer if before age 25**
- **Consider upper endoscopy every 3-5 y at age 30-35. Consider testing/treating H. pylori**
- **Consider annual urinalysis starting age 30-35 (if MSH2 mutation or FH of urothelial ca)**
- **Consider annual physical/neurological exam starting age 25-30**
- **CA125 and US at clinician's discretion***
- **Consider EMB q1-2 years starting age 30**
- **Risk-reducing hyst, BSO ~age 40**

Risk Factor: Other

Risk Factor	Relative Risk
Increasing Age	2-3
Residency in North America or Northern Europe	3-18
Higher level of education or income	1.5-2
White Ethnicity/Race	2
Nulliparity	3
History of Infertility	2-3
Menstrual Irregularities	1.5
Unopposed Estrogen	10-20
Tamoxifen Use	2-3
Obesity	2-5
Diabetes, HTN, Gallbladder disease, thyroid disease	1.3-3
Lynch Syndrome	22-50% lifetime risk

ACOG/SGO Practice Bulletin No 149, April 2015

Prevention



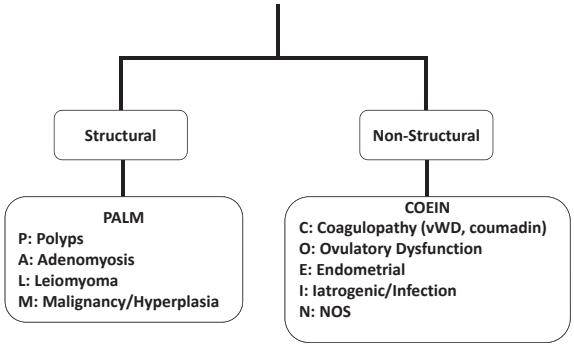
Assessment of cycles at well-woman visits

- Timing, intermenstrual bleeding, duration, presence of clots
- Contraception?
- Any changes in bleeding pattern?
- Bleeding, of any volume, after menopause?

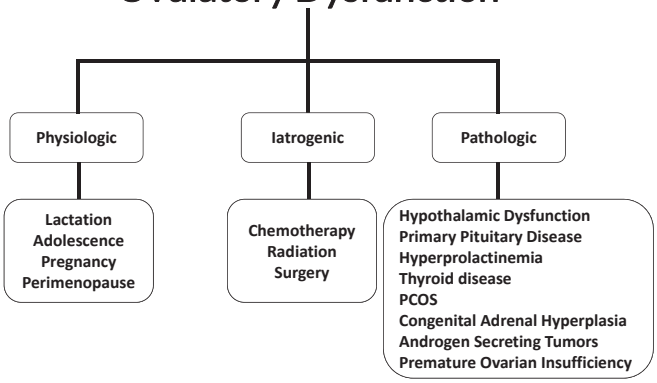
The Menstrual Years: Normal Menstruation

Normal Menstrual Cycles in the mature HPO Axis	
Cycle interval	**21-35 days**
Menstrual flow length	**5 days or less**
Menstrual product use	**3-6 pads/tampons per day**

Abnormal Uterine Bleeding



Abnormal Uterine Bleeding – Ovulatory Dysfunction



Ovulatory Dysfunction and Abnormal Uterine Bleeding – Regulating Cycles

Age Range	Options to Regulate
13-18	OCPs
19-39	OCPs, Progesterone containing IUD, Weight loss and Exercise
40-menopause	Cyclic progesterone, progesterone containing IUD, OCPs

ACOG practice bulletin on Bleeding due to Anovulation

Evaluation of Abnormal Bleeding

Abnormal Uterine Bleeding – When to Biopsy

- **Endometrial biopsy if:**
  - **Age 45 or older**
  - **Age 35 with RF for EC**
  - **Not responding to hormonal regulation**
  - **<u>Any point</u> after menopause**

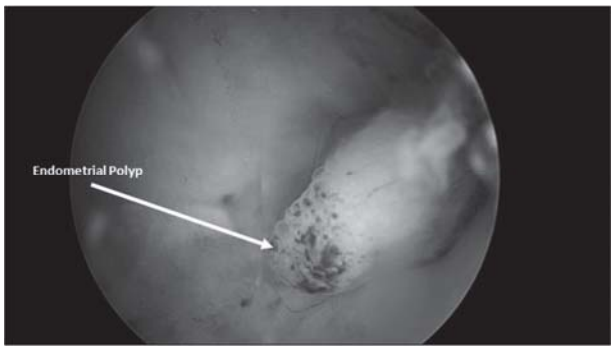
Age Range	EC Risk
13-19	0.2/100,000
20-34	1.6%
35-44	6.2%
40-menopause	13-24/100,000

ACOG practice bulletein on Bleeding due to Anovulation

Abnormal Uterine Bleeding – What is in a biopsy?

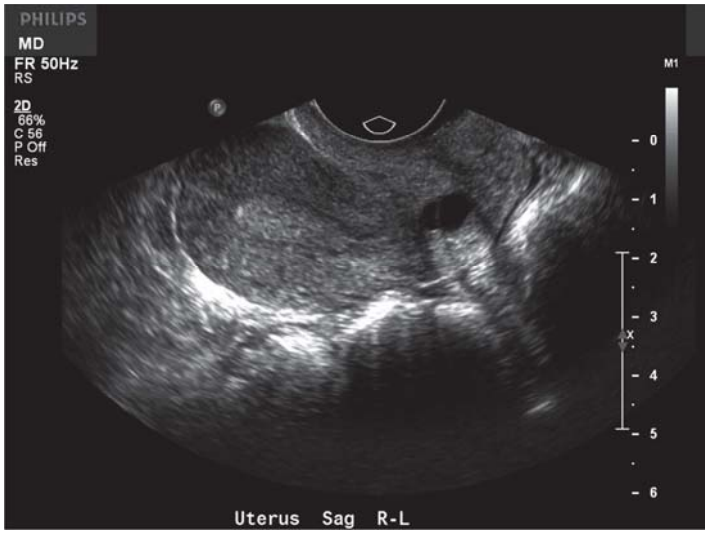
- **EMB samples ~ 4% of the endometrial cavity**
- **Sensitivity for detecting abnormalities**
  - **EMB: 68%**
  - **Hysteroscopy, D&C: 78%**

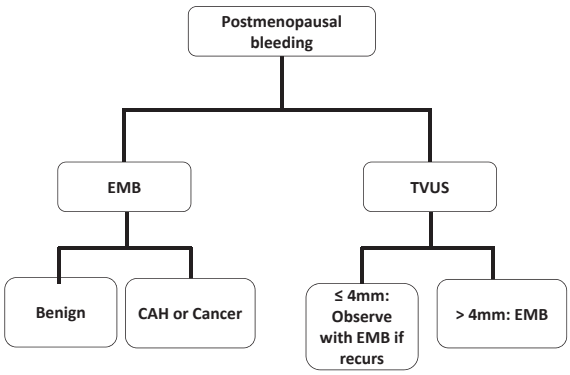
Hysteroscopy



Abnormal Uterine Bleeding – How often to biopsy?

- **Persistent or recurrent bleeding needs to be evaluated**
- **TVUS as an adjunctive tool**
  - **Premenopausal**
    - **Proliferative Phase: EMS = 4-8 mm**
    - **Secretory Phase: EMS = 8-14 mm**
  - **Postmenopausal**
    - **EMS ≤ 4 mm**





I Diagnosed Cancer…. Now What?

Reassuring Facts to Share with Patients with Grade 1 EMB

Stage	Distribution	5 yr Survival
I (Uterus)	73%	86%
II (Cervix)	12%	66%
III (Pelvis and Lymph Nodes)	12%	44%
IV (Upper abdomen/Lungs)	3%	16%

- **Many women require no treatment after surgery, others will have radiation to pelvis or vaginal cuff to decrease risk of recurrence**

What if it's not reassuring?

- If EMB shows clear cell, uterine serous, or grade 3 endometrioid histology
  - More aggressive histology that can be associated with advanced disease or higher risk of recurrence
- Symptoms or imaging suggestive of advanced disease
  - Changes in bowel/bladder habits
  - Pelvic pressure
  - Early satiety

How can I help move things forward for my patient?

- Referral to gynecologic oncologist
- Preoperative risk assessment (EKG, labs, etc)
- If high risk (high grade biopsy, serous, clear cell): obtain CT C/A/P with IV and po contrast
- If serous, add CA125 to labs

Endometrial Cancer: An Opportunity to Improve Wellness

- Most women do not die of endometrial cancer but of the comorbidities that often coincide with the disease

BMI	Risk of Death
24-30	2.53
35-40	2.77
> 40	6.25

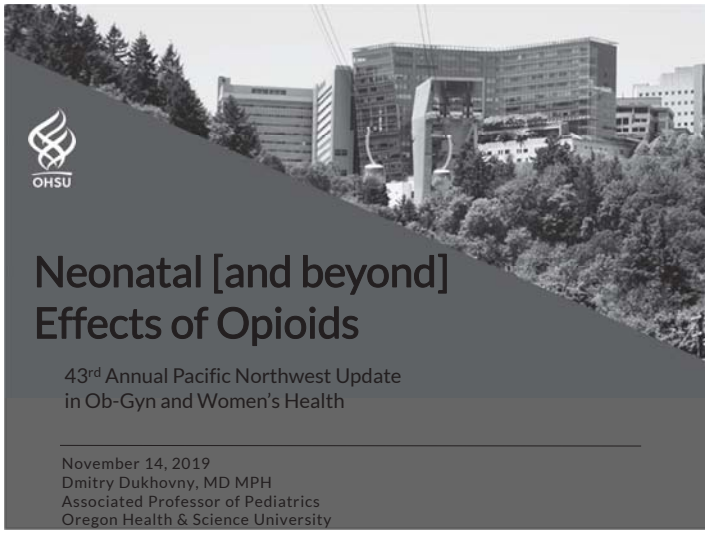
- Only 42% of women with endometrial cancer were aware of how weight related to diagnosis and post treatment prognosis

Take Home Messages

Questions? Contact me

OHSU Physician Advice & Referral Service
•503-494-4567
•800-245-6478 (toll-free)

Thank You



Neonatal [and beyond] Effects of Opioids

43rd Annual Pacific Northwest Update in Ob-Gyn and Women's Health

November 14, 2019
Dmitry Dukhovny, MD MPH
Associated Professor of Pediatrics
Oregon Health & Science University

Disclosures

- No relevant disclosures or conflict of interest

Objectives

- Incidence
- Neonatal Effects of Opioids
- Management of neonates (and their families)

Neonatal Opioid/Opiate Exposure

- Different terminology:
  - Neonatal Abstinence Syndrome (NAS)
  - Neonatal Opioid Withdrawal (NOW)
- Neonates are born "dependent" not "addicted" to opioid/opiates

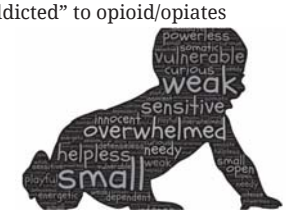


Image from https://www.vumc.org/nas/what-neonatal-abstinence-syndrome, accessed 10/22/2019

JAMA Network

From: **Neonatal Abstinence Syndrome and Associated Health Care Expenditures: United States, 2000-2009**

Patrick SW et al. JAMA. 2012;307(18):1934-1940. doi:10.1001/jama.2012.3951

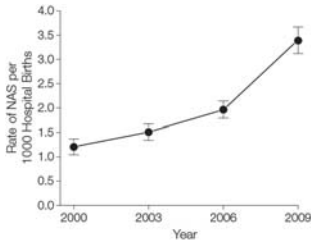


Figure Legend:

NAS indicates neonatal abstinence syndrome. Error bars indicate 95% CI. P for trend < .001 over the study period. The unweighted sample sizes for rates of NAS and for all other US hospital births are 2920 and 784 191 in 2000; 3761 and 890 582 in 2003; 5200 and 1 000 203 in 2006; and 9674 and 1 113 123 in 2009; respectively.

JAMA Network

From: **Neonatal Abstinence Syndrome and Associated Health Care Expenditures: United States, 2000-2009**

Patrick SW et al. JAMA. 2012;307(18):1934-1940. doi:10.1001/jama.2012.3951

Table 3. Mean Hospital Charges and Length of Stay for Neonatal Abstinence Syndrome vs All Other US Births

	Mean (95% CI)				*P* for Trend
	2000	2003	2006	2009	
Neonatal Abstinence Syndrome					
Unweighted sample, No.	2920	3761	5200	9674	
Length of stay, d	15.8 (14.2-17.3)	15.9 (14.5-17.3)	15.3 (14.6-16.0)	16.4 (15.8-17.1)	.06
Hospital charges, 2009 US $	39 400 (33 400-45 400)	47 900 (40 800-55 100)	44 600 (40 400-48 900)	53 400 (49 000-57 700)	<.001
All Other US Births					
Unweighted sample, No.	784 191	890 582	1 000 203	1 113 123	
Length of stay, d	3.1 (3.0-3.1)	3.2 (3.1-3.2)	3.2 (3.2-3.3)	3.3 (3.3-3.4)	<.001
Hospital charges, 2009 US $	6600 (5800-7300)	7300 (6900-7600)	8200 (7800-8600)	9500 (9000-9900)	<.001

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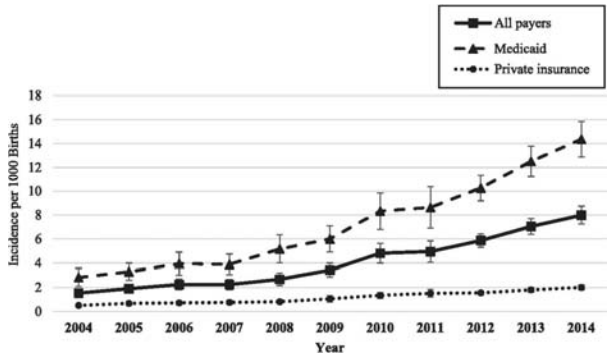
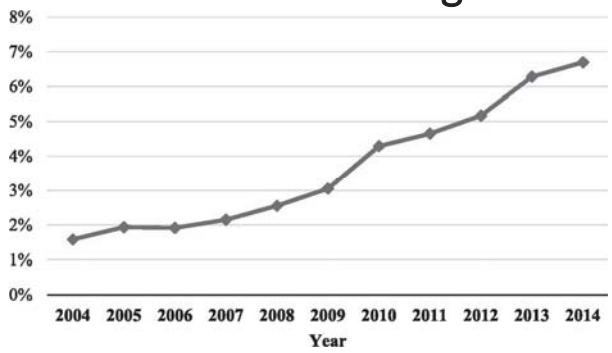
Incidence of NAS by primary payer



Tyler N.A. Winkelman et al. Pediatrics 2018;141:e20173520

PEDIATRICS

Proportion of birth-related hospital costs due to NAS among infants

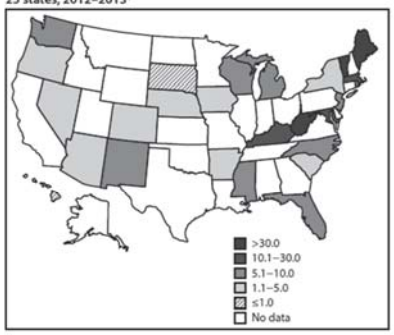


Tyler N.A. Winkelman et al. Pediatrics 2018;141:e20173520

PEDIATRICS

Incidence of NAS

FIGURE. Neonatal abstinence syndrome (NAS) incidence rate* — 25 states, 2012–2013†



Source: State Inpatient Databases, Healthcare Cost and Utilization Project.
* NAS cases per 1,000 hospital births.
† Incidence rates reported are for 2013, except for four states (Maine, Maryland, Massachusetts, and Rhode Island) for which 2013 data were not available; 2012 data are reported for these states.

Figure from Ko et al. MMWR 2016 Aug 12; 65 (31)

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9

JAMA Network

From: **Association Among County-Level Economic Factors, Clinician Supply, Metropolitan or Rural Location, and Neonatal Abstinence Syndrome**

Patrick S\

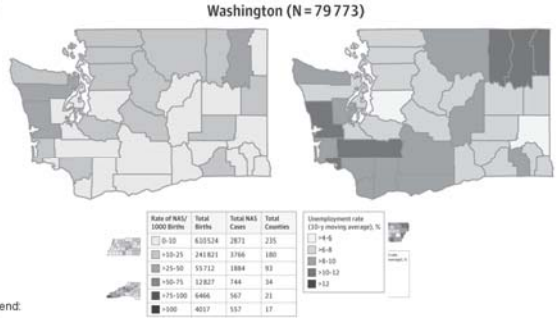

Figure Legend:

County Variation in Neonatal Abstinence Syndrome (NAS) per 1000 Hospital Births and 10-Year Moving Average Unemployment Rate for 2015Data are from an analysis of the Healthcare Cost and Utilization Project's State Inpatient Databases, the Tennessee All-Payer Database, and the Health Resources and Services Administration Area Health Resources Files.

[a]Data from New York are from 2014, which is the most recent year available.

Neonatal (and beyond) Effects of Opiates and Opioids

11

Neonatal Signs and Symptoms

- Neurologic Excitability
- Gastrointestinal dysfunction
- Other systemic signs

12

Hudak et al. "Neonatal Drug Withdrawal". Pediatrics 2012.

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Neurologic Excitability

- Increased muscle tone
- Tremors
- Difficult to console
- High Pitch Cry
- Hyperactive DTRs
- Exaggerated moro reflex
- Frequent yawning and sneezing
- Seizures (rare – some studies site 2-11%)

GI Dysfunction

- Vomiting, diarrhea
- Poor/uncoordinated feeding
  - –Poor weight gain/failure to thrive
  - –Dehydration
  - –Increased caloric demand

Systemic Signs

- Temperature instability/fever
- Increased sweating
- Nasal stuffiness
- Tachypnea

Timing and Types of Symptoms Vary

- Type of opiate/opioid
- Last use
- Placental transfer
- Maternal metabolism
- Poly-substance use (including alcohol and nicotine)

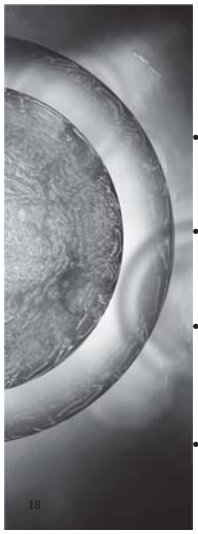
Poly-substance use

TABLE 2 Maternal Nonnarcotic Drugs That Cause Neonatal Psychomotor Behavior Consistent With Withdrawal

Drug	Signs	Onset of Signs	Duration of Signs*	Ref. No.
Alcohol	Hyperactivity, crying, irritability, poor suck, tremors, seizures; onset of signs at birth, poor sleeping pattern, hyperphagia, diaphoresis	3–12 h	18 mo	14,15
Barbiturates	Irritability, severe tremors, hyperacusis, excessive crying, vasomotor instability, diarrhea, restlessness, increased tone, hyperphagia, vomiting, disturbed sleep; onset first 24 h of life or as late as 10–14 d of age	1–14 d	4-6 mo with prescription	12,13
Caffeine	Jitteriness, vomiting, bradycardia, tachypnea	At birth	1-7 d	161
Chlordiazepoxide	Irritability, tremors; signs may start at 21 d	Days–weeks	9 mo; 11/2 mo with prescription	11
Clomipramine	Hypothermia, cyanosis, tremors; onset 12 h of age		4 d with prescription	162
Diazepam	Hypotonia, poor suck, hypothermia, apnea, hypertonia, hyperreflexia, tremors, vomiting, hyperactivity, tachypnea (mother receiving multiple drug therapy)	Hours–weeks	8 mo; 10–66 d with prescription	10
Ethchlorvynol	Lethargy, jitteriness, hyperphagia, irritability, poor suck, hypotonia (mother receiving multiple drug therapy)		Possibly 10 d with prescription	163
Glutethimide	Increased tone, tremors, opisthotonos, high-pitched cry, hyperactivity, irritability, colic		6 mo	164
Hydroxyzine	Tremors, irritability, hyperactivity, jitteriness, shrill cry, myoclonic jerks, hypotonia, increased respiratory and heart rates, feeding problems, clonic movements (mother receiving multiple drug therapy)		5 wk with prescription	58
Meprobamate	Irritability, tremors, poor sleep patterns, abdominal pain		9 mo; 3 mo with prescription	165
SSRIs	Crying, irritability, tremors, poor suck, feeding difficulty, hypertonia, tachypnea, sleep disturbance, hypoglycemia, seizures	Hours–days	1–4 wk	31–33,35

* Prescription indicates the infant was treated with pharmacologic agents, and the natural course of the signs may have been shortened.

Table 2 from Hudak et al. "Neonatal Drug Withdrawal". Pediatrics 2012.



Withdrawal Onset (and Monitoring)

- 24-48 hours for short acting (e.g. heroin, oxycodone)
  - –Minimum observation 3 days (AAP)*
- Typically >48 hours for long acting (e.g. methadone, OxyContin)
  - –Minimum observation 5-7 days (AAP)*
- Can last up to 14 days (although typically 5-7 days)
  - –Both instances after the typical discharge of a healthy newborn
- Preterm infants tend not to have as many signs and symptoms

*American Academy of Pediatrics (AAP)
Hudak et al. "Neonatal Drug Withdrawal". Pediatrics 2012.

Length of Stay

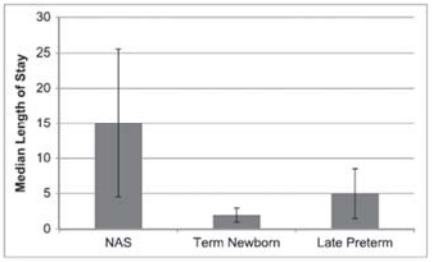


Figure 1 from Patrick SW et al. Hospital Pediatrics 2015

Readmission – 30 day and 1 year

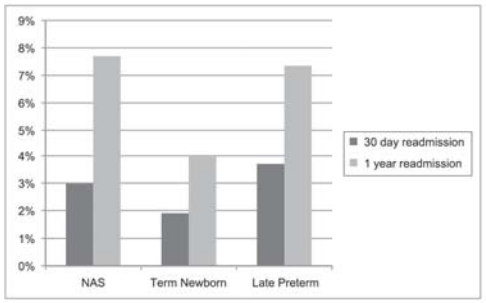


Figure 2 from Patrick SW et al. Hospital Pediatrics 2015

30 day readmission risk factors

	OR (95% CI)	P
Infant characteristics		
Female	0.75 (0.73–0.78)	<.001
Low birth weight	1.13 (1.04–1.23)	.004
Uncomplicated term	REF	
Late preterm	2.26 (2.09–2.45)	<.001
NAS	2.49 (1.75–3.55)	<.001
Clinical comorbidities		
Respiratory diagnoses	1.00 (0.89–1.15)	.981
Sepsis	1.19 (1.02–1.39)	.03
Feeding problems	1.38 (1.20–1.59)	<.001
Seizure	5.01 (3.02–8.33)	<.001
Health care utilization		
Private insurance	REF	
Medicaid	1.50 (1.45–1.56)	<.001
Uninsured	1.10 (1.02–1.18)	.01
Other	1.61 (1.46–1.79)	<.001
Length of birth hospitalization, d	0.94 (0.92–0.96)	<.001

Table 2 from Patrick SW et al. Hospital Pediatrics 2015

Long term implications of in-utero opiate/opioid exposure

- Multi-factorial (social determinants of health)
- Inconsistent data, but some suggestions of neurodevelopmental implications from the in utero exposure
- Visual impairment (nystagmus) [1]
- Hepatitis C follow up (where applicable)
- Impact on school performance[2]

[1]McGlone et al. British Journal of Ophthalmol 2014
[2]Oei et al. Pediatrics 2017

School Performance

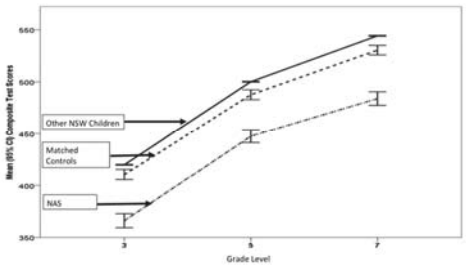


Figure 2 from Oei et al. Pediatrics 2017

Management of newborns with in-utero exposure to opiates/opioids

Supportive Care

- Non-pharmacologic management
- Environmental stressors
- Social stressors
- Maternal care
- Breastfeeding support
- Rooming in with the mother

Assessment for withdrawal

- Finnegan Scale
- Eat, Sleep, Console (ESC)

Pharmacologic management

- 1st line medication
  - –Morphine
  - –Methadone
  - –Buprenorphine
  - –Clonidine
- Adjunct Treatment
  - –Clonidine
  - –Phenobarbital

Keys to Neonatal Management

- Multidisciplinary approach
- Start antenatal when possible
- Standardize
- Standardize
- Standardize

Standardization of Care and reduced LOS

- Withdrawal assessment ("scoring")[1]
  - –3 day reduction in LOS
- Weaning of medications[2]
  - –10 day reduction in LOS
  - –14 day reduction in treatment with opioid
- Transition to ESC from Finnegan[3]
  - –6.5 day reduction in LOS

[1]Vermont Oxford Network - Patrick SW et al. Pediatrics 2016
[2]Ohio Perinatal Quality Collaborative – Hall et al. Pediatrics 2014
[3]Boston Medical Center – Wachman et al. Journal of Perinatology 2018

Reduction in Pharmacologic Treatment

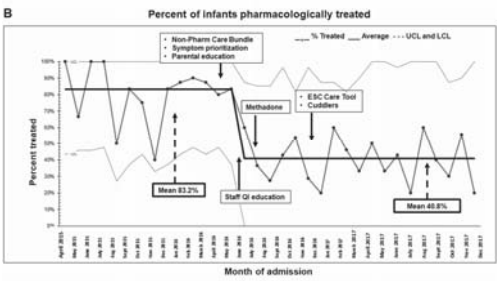


Figure 1B from Wachman et al. Journal of Perinatology 2018

Oregon Resources

- 2017-2018 Oregon Pregnancy and Opioids Workgroup Recommendations
  - –Multidisciplinary group
  - –14 recommendations
    - Primary prevention
    - Secondary prevention
    - System and policy recommendations

Accessed 10-28-2019
https://www.oregon.gov/oha/PH/PREVENTIONWELLNESS/SUBSTANCEUSE/OPIOIDS/Documents/Oregon-Pregnancy-and-Opioids-Recommendations.pdf

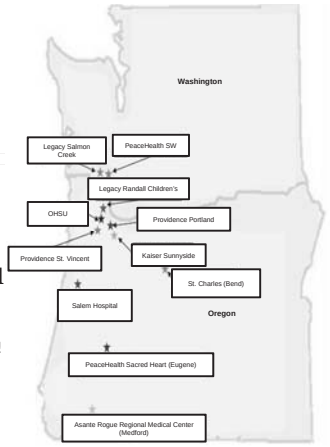
OR – Neonatal Specific

- R11 – Encourage breastfeeding for women with opioid use disorder (including medication assisted treatment)
- R12 – Closely monitor an infant born to a mother who used opioids during pregnancy.
  - –Manage care with a standardized protocol for assessment and treatment of infants at risk for NAS

Accessed 10-28-2019
https://www.oregon.gov/oha/PH/PREVENTIONWELLNESS/SUBSTANCEUSE/OPIOIDS/Documents/Oregon-Pregnancy-and-Opioids-Recommendations.pdf

NWIPA
Northwest Neonatal Improvement Priority Alliance

- ***N***orth***w***est Neonatal ***I***mprovement ***P***riority ***A***lliance (NW IPA)
- 11 level III+ NICUs in Oregon and Southwest Washington
  - Neonatologists, Advanced Practitioners, Nurses, Families, Pharmacists, and more!
  - Goal: Improving the quality and safety of medical care for all newborn infants and their families throughout the region



http://www.oregon-pip.org/projects/NWIPA.html

Summary

- In utero substance exposure of neonates is a rising problem (incidence and cost)
- Short term and long term implications of in utero exposure to opiates/opioids
- Breastfeeding/provision of breastmilk is RARELY contraindicated and should be supported
- Standardization of care leads to less pharmacologic treatment and shorter LOS
- Multidisciplinary approach that does not start and end with the birth hospitalization

Questions?
Contact me

OHSU Physician Advice & Referral Service
- 503-494-4567
- 800-245-6478 (toll-free)

At Pacific NW Update in Women's Health
- Thursday: Lunch Roundtable Host

Thank You

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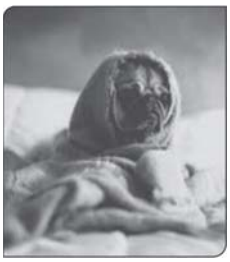
MINDFULNESS FOR DEPRESSION

CATHERINE POLAN ORZECH M.A. LMFT

MAJOR DEPRESSIVE DISORDER DSM-5

- Depressed mood most of the day, nearly every day – sad, empty, hopeless
- Diminished pleasure in all or almost all activities
- Significant weight loss or gain
- Insomnia or hypersomnia
- Psychomotor agitation or retardation
- Fatigue or loss of energy
- Feeling worthless
- Difficulty concentrating or indecisiveness
- Recurrent thoughts of death

DEPRESSION LOOKS LIKE…



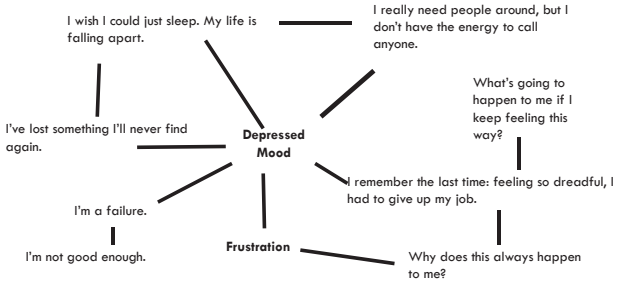
• "…Jane would often wake very early in the morning, unable to sleep, with a heavy feeling in her body and thoughts going round and round, impossible to switch off. She'd sometimes get up to make a cup of tea, sitting in the kitchen with a blanket around her shoulders, viewing whatever tidbits she could find on her phone, or trying to answer emails that had come through during the night. At last, exhausted, she'd go back to bed, only to find that the thoughts carried on, going round and round, but now a new voice: "this is terrible. You'll be too tired to think straight today. Why is this happening? Why can't you ever pull yourself together? What's wrong with you?"

UNHAPPINESS ITSELF IS NOT THE PROBLEM

Stage 1 = Unhappiness arises

Stage 2 = The unhappy mood brings up negative thinking patterns, feelings and memories for the past – this makes us more unhappy.

Stage 3 = We try to get rid of the unhappiness in ways that actually keep it going and just make things worse.



I AM DEPRESSED

PHYSIOLOGY OF SELF-COMPASSION AND SELF-CRITICISM (GILBERT, 2009)

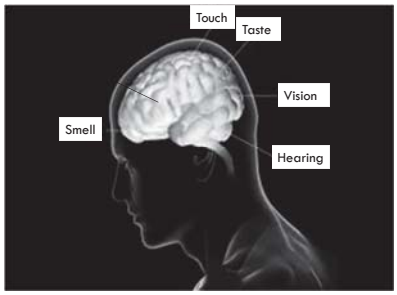
When we criticize ourselves we're tapping into the body's threat-defense system – amygdala gets triggered, we release cortisol and adrenaline, and get ready to fight, flee or freeze.

When the "threat" is to our self-concept – we feel inadequate or weak we end up attacking the problem – Ourselves!

This threat response causes even more stress and is related to conditions like anxiety and depression.

SELF-CRITICISM AND STRESS

WHAT IS MINDFULNESS?



RESOURCES FOR DEVELOPING MINDFULNESS

- The Head Space App
- The Mindfulness App
- The Mindful Self-Compassion Workbook (Kristin Neff & Chris Germer)
- Courses
  - Mindfulness-Based Stress Reduction (in-person) OHSU's March Wellness Center and in the community
  - Mindfulness-Based Cognitive Therapy (online) https://www.mindfulnessstudies.com/personal/mbct-online
  - Mindful Self-Compassion (online) https://centerformsc.org/lomsc

REFERENCES

- Teasedale, J., Williams, M., Segal, Z. (2014) *The mindful way workbook: an 8-week program to free yourself from depression and emotional distress*. New York: Guilford Press.
- Gilbert, P. (2009). *The compassionate mind: A new approach to life's challenges*. Oakland, CA: New Harbinger

Questions?
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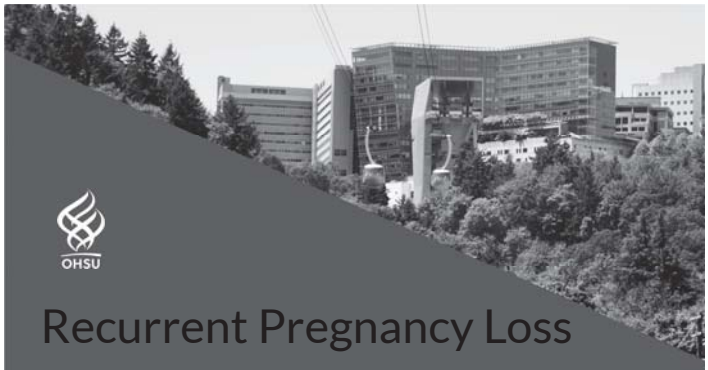


Recurrent Pregnancy Loss

Sacha Krieg MD, PhD
Assistant Professor OB/GYN
Division of Reproductive Endocrinology and Infertility
Oregon Health Sciences University

Overview

- Defining RPL
- Causes
- Treatment options
- Special considerations

Miscarriage

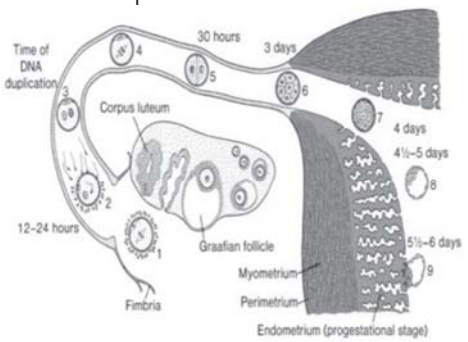
- Spontaneous pregnancy loss is common
  - 15% of all pregnancies
  - Increases with age
    - at age 40, ~40%
- Recurrent pregnancy loss (RPL) impacts 1-5% of all couples
  - Defined as 2 or more consecutive losses (ASRM)
    - With confirmed fetal pole or pathological diagnosis
    - <20 weeks of pregnancy
    - Risk of subsequent loss similar for 2 or 3 losses
      - 30% risk
    - Evaluation recommended after 2 losses

Recurrent pregnancy loss

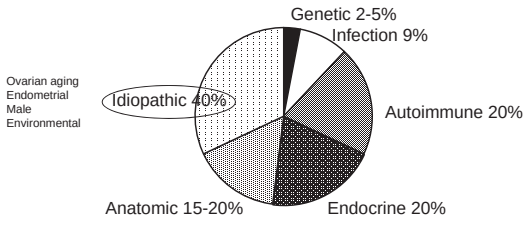
- Two or more consecutive, *clinical* losses
- What about biochemical pregnancies??
  - Pregnancy of unknown location
    - Could be ectopic as well
  - Evaluation in this instance is controversial
    - Poor prognostic factor for future live birth rate
    - Recent study by Kolte et al. suggests that eval may be beneficial

Kolte et al. Hum Reprod 29(5):931-937

Ovulation to Implantation



Causes of RPL

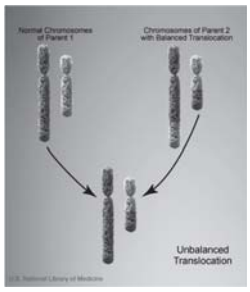


Evaluation of RPL

- Parental Karyotypes
- Antiphospholipid antibodies
- Endocrine
  - TSH, anti-thyroid antibodies
  - Glucose testing, ovarian reserve, PRL
- HSG or hysteroscopy w/laparoscopy
- Fetal karyotype if currently undergoing a loss
- Cultures if strong suspicion for endometritis/cervicitis

Genetic causes of RPL

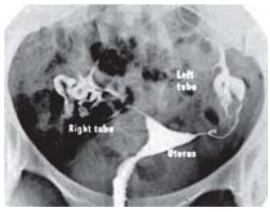
- Comprise 2-5% of cases
- Most commonly-- balanced or Robertsonian translocations (13, 14, 15, 21 and 22).
- Inversion, insertions and mosaicism
- Treatment
  - Expectant management
  - PGD
  - Donor Gametes



Stephenson and Sierra 2006 Human Reprod. 21(4):1076

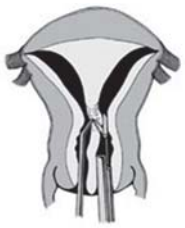
Diagnosis of Uterine anomalies

- HSG
- Hysteroscopy
  - With concurrent laparoscopy
- MRI
  - Evaluate collecting system also
- 3D US w/saline infusion sonography



Anatomic contributions to RPL

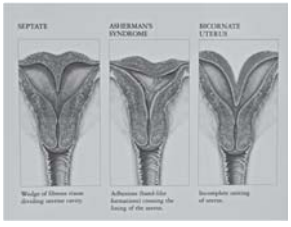
- Septate uterus
  - Most common abnormality
  - Readily treatable with resection
  - Live birth rate after resection ~85%
- Leiomyomas
  - More controversial
  - Submucosal and Myomectomy for transmural >5cm has a benefit
  - Live birth rate as high as 93%
- Other mullerian anomalies
  - Smaller increase in RPL
- Cervical insufficiency



Jurkovic et al. 1995 Ultrasound Ob&Gyn
Dabirashrafi et al. 1995 Am J OB/Gyn
Bajekal and Li 2000 Human Reprod updates

Mullerian anomalies

- Most studies are small case series
- Septate uteri
  - 44% loss rate
- Arcuate
  - 25.7% loss rate
- Bicornuate
  - 36% loss rate



Antiphospholipid antibody syndrome

- Antiphospholipid antibodies
- Impact trophoblastic invasion
- Diverse population of antibodies

Antiphospholipid antibody syndrome

- Antiphospholipid Ab syndrome linked to RPL
- Criteria for APLAS (1 clinical and 1 laboratory criteria:
  - Clinical:
    - 1 or more thrombotic events
    - 3 consecutive losses without other causes
    - 1 fetal demise >10wks gestation
    - 1preterm birth due to severe pree or placental insufficiency (<34wks)
  - Laboratory (repeated 2 times at least 12 wks apart)
    - ACA levels (IgG or IgM) in medium-high range
    - Plasma levels of lupus anticoagulant
    - Anti-β 2 glycoprotein antibodies in medium-high range (>40)
  - Treatment with bASA and Heparin results in pregnancy rate of 70-75%

ACOG practice bulletin No 118

APLAS continued

- bASA and Heparin
  - Therapeutic low-molecular weight heparin
- Steroids have been shown to have no benefit
- RR of first trimester sAB-0.46 with treatment

Endocrine causes of RPL

- Hypothyroidism
  - Anti-thyroid antibody testing more controversial
- Poorly controlled DM
- Hyperprolactinemia
- Luteal phase defect
  - No evidence to support testing

Marai et al. Am J Reprod Immunol. 2004 51(3):235-40.
Kutteh et al. 1999 Fertil Steril 71: 843
Hirahara F et al.1998 Fertil Steril.70:246–252.

Thyroid disease and RPL

- Untreated hypothyroidism assoc. w/RPL
  - Treat to a TSH<2.5
  - Increase by 30% in pregnancy
  - Subclinical hypothyroidism assoc. w/sAB
- Role of anti-thyroid antibodies is less clear
- Untreated hyperthyroidism assoc. w/sAB and infertility

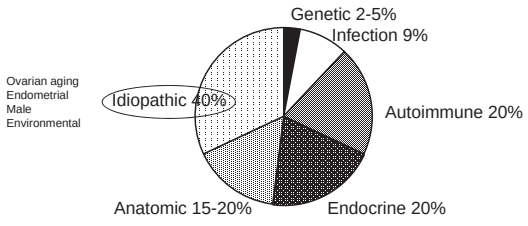
Vaquero et al. Am J Reprod Immunol 43:204-208
Negro et al. Best prac Endo and Metab 25(6):927-43

Chronic Endometritis

- Persistent inflammation of the endometrium—often asymptomatic
- Testing
  - EMB with pathology for presence of plasma cells and CD138 IHC
- Addition of CD138 increases sensitivity
- Incidence of 7% to 57.8% in the RPL population [1-3]
- An increase in LBR has been noted after treatment
  - 7% to 56% after treatment with doxycycline($p<0.001$)[1]
  - 17.5% to 78.4% after treatment targeted to pathogen ($p<0.001$)[2]
- Studies are limited in size
- As of yet, not a recommended part of RPL eval by ASRM or ACOG

1. McQueen et al. F&S 2014 101(4):1026-1030
2. Cicinelli et al. Reprod Sci 2014 21(5):640-647
3. McQueen et al. F&S 2015 104(4):927-931

Causes of RPL



Idiopathic RPL

- Possible Etiologies:
  - Ovarian
    - After the age of 35: 78% of losses are *de novo* aneuploidies
  - Male factor
  - Endometrial
- Treatment:
  - Progesterone, bASA may be of benefit
  - Supportive care
  - PGTa
    - Somewhat controversial

Oates-Whitehead et al. Cochrane Database Syst Rev. 16(2):2008
Lathi et al. 2009 F&S in press

Aneuploidy and RPL

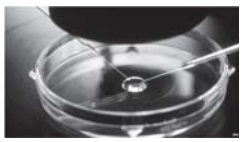
- Over the age of 35, chromosomal abnormalities are found in 78% of POC[1]
  - RPL patients undergoing miscarriage
- In larger studies using all age groups[2,3]
  - 70% of losses <6wks are aneuploid
  - 50% of loss 6-10wks are aneuploid

1. Marquard et al. 2010 F&S 94(4):1473-1477
2. Hassold et al. 1985 Human Genetics
3. Ohno et al. 1991 Obstet Gynecol

Is PGTa useful for Idiopathic Recurrent Pregnancy Loss?

- Comprehensive Chromosomal Screening
  - Allows for screening of all chromosomes as opposed to PGS w/FISH
- Several modalities available
  - SNP
  - aCGH
  - NGS
- More evidence is supporting the use of PGTa for older RPL patients

IVF with preimplantation genetic screening for RPL



- Requires an IVF cycle
- Testing for all chromosomes
- Has the potential to address a common cause of miscarriage
- This benefit appears to be the greatest in patients over the age of 37
  - Controversial as longer time to live birth and need for RCT
  - This benefit does not quite reach statistical significance in most studies

Kushnir et al. 2016 F&S

Progesterone supplementation

- Progesterone or HCG supplementation
  - HCG associated w/OHSS
    - 500 IU QOD
  - Can also consider clomid
- Vaginal preparations have 30x greater endometrial conc.
  - 200-600mg/day
  - Micronized, gel and tablets
- Im progesterone
  - 50mg/day
- Oral
  - Prometrium
  - Assoc. w/poorer pregnancy and increased sAB rates
    - IVF pts.

Luteal Progesterone

- 2 recent RCTs comparing vaginal progesterone either 3 days after +OPK or immediately after US documented ovulation
- Stephenson et al. F&S 2017 n=59
  - Vaginal progesterone 100-200mg BID pv, 3 days after LH surge
  - OR 2.1 for Live birth
- Ismail et al. J of Maternal-fetal and neonatal medicine 2017 n=700
  - 400mg progesterone pessaries vs placebo pessaries
  - 91.6% vs 77.4% LBR ($p<0.05$)
  - The progesterone group also had a lower rate of preterm delivery

Stephenson et al. 2017 F&S
Ismail et al. 2017 J of Maternal-Fetal and neonatal medicine

Supportive care

- Recurrent Pregnancy Loss associated with:
  - Depression
  - Anxiety
  - Decreased self esteem
- Grief process follows any sAB
- Increased marital discord
- Increase in sexual dysfunction
- Antenatal counseling and psychological support increases live birth rates
- 20% of women suffer from postpartum depression after a miscarriage

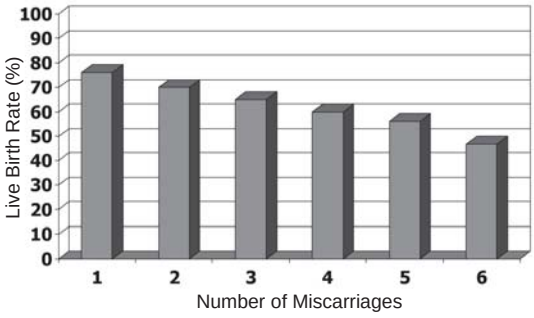
Stray-Pederson 1984
Serrano 2006
Klock et al. Psychosomatics 38(5):503-507

Treatment outcomes

- With appropriate treatment the probability of a successful pregnancy is as high as 90%

OHSU

Probability of live birth for patients with unknown etiology



*average age 34

Brigham et al. 1999 Human Reprod. 14(11):2868-2871

OHSU

Conclusions

- Recurrent Pregnancy Loss is a treatable condition
- Begin evaluation for recurrent pregnancy loss after 2 consecutive losses
- Considering karyotyping products of conception after 1st loss
- With appropriate treatment and supportive care a high live birth rate may be expected

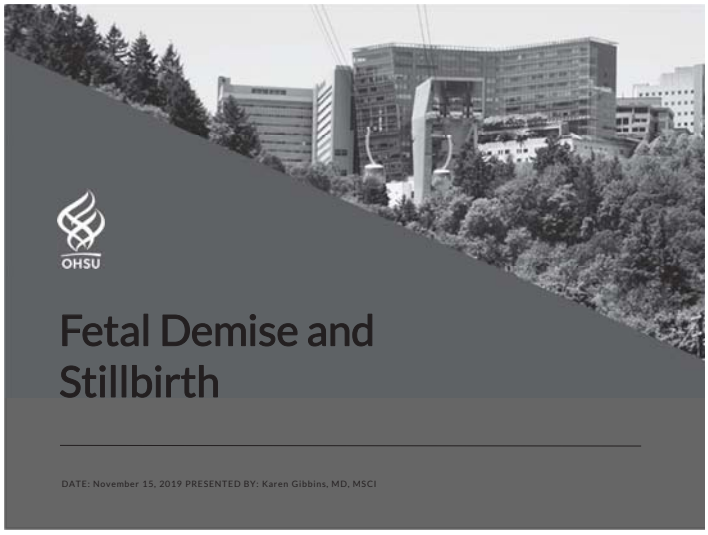
OHSU

Questions…?

University Fertility Consultants
OHSU
3303 SW Bond Ave CHH
503-418-3700

OHSU Physician Consult
& Referral Service
(503) 494-4567
(800) 245-6478 toll-free

OHSU



Fetal Demise and Stillbirth

DATE: November 15, 2019 PRESENTED BY: Karen Gibbins, MD, MSCI

Disclosures

2

Objectives

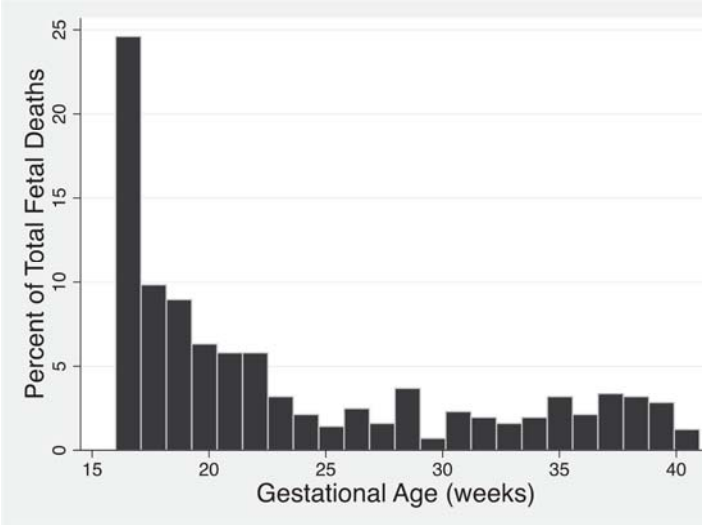
- To give a pragmatic outline of the following:
  - Incidence, risk factors, and causes of stillbirth
  - Initial workup
  - Basic bereavement care
  - The next pregnancy

3

Stillbirth in the U.S. - definitions

- 6 per 1000 or 1 in 160 deliveries – not changing
  - 25,000 annually
  - Oregon: 185 in 2017 or
    - 4.2 per 1000 live births
    - Neonatal death rate: 3.6 per 1000 births
- Defined as fetal death at 20 weeks or greater, or a weight of 350 grams or more if GA unknown (50th %ile for 20 weeks)
- Terminations are excluded
- Arbitrary cutoff of 20 weeks

4



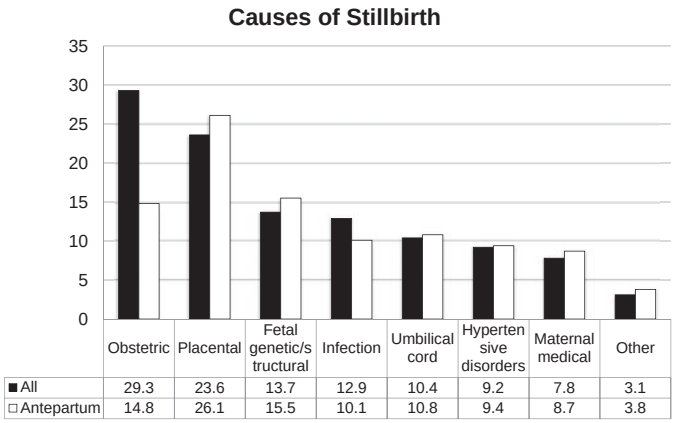
Risk Factors (aOR)

Modifiable		Nonmodifiable	
Chronic HTN	1.19 (NS)	Previous loss	2.8
Diabetes	2.5	Previous stillbirth	6.41
Drug addiction	2.08	AMA 35-39	1.19
Tobacco	1.57	AMA 40+	2.41
Obesity	1.72	Non-Hispanic Black race	2.12
Multifetal	4.59	Nulliparity	1.49

6

Causes

- SCRN: 95% of all stillbirths in 5 geographic catchment areas
- Full workup and INCODE assignment in 512 stillbirths



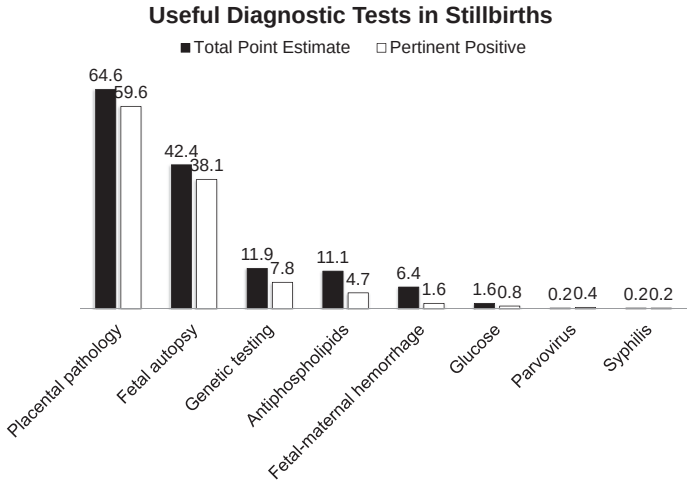
	Obstetric	Placental	Fetal genetic/structural	Infection	Umbilical cord	Hypertensive disorders	Maternal medical	Other
■ All	29.3	23.6	13.7	12.9	10.4	9.2	7.8	3.1
□ Antepartum	14.8	26.1	15.5	10.1	10.8	9.4	8.7	3.8

Causes

- FGR: risk of stillbirth with EFW <5th%ile is 2.5% without monitoring
- Cord events:
  - nuchal cord at 30% of normal births
  - Need e/o obstruction or circulatory compromise
  - exclude other causes

Workup

- Shotgun versus targeted approach
- ACOG: autopsy, karyotype, placental examination, CBC, Kleihauer Betke, parvovirus IgG/IgM, RPR/FTA, lupus anticoagulant, anticardiolipin antibodies, TSH, thrombophilia panel, parental karyotype, indirect Coombs, HgbA1c, toxicology, further genetic testing



Targeted Testing

- If FGR:
  - placental pathology 88.7%
  - fetal autopsy 79.2%
  - antiphospholipids 32.1%
  - genetic testing 26.4% (most had known anomalies)
- If hypertensive disorders:
  - Placental pathology 90%
  - fetal autopsy 50%
  - antiphospholipids 28%

Targeted Testing (cont.)

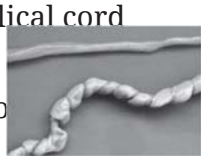
- If suspected fetal anomalies:
  - fetal autopsy 90.3%
  - genetic testing 87.1%
  - placental pathology 41.9%
- Preterm labor/chorio/PPROM
  - Placental pathology 80.5%
  - fetal autopsy 44.2%
  - genetic testing 5.2%
  - fetal-maternal hemorrhage 5.2%

Barriers to autopsy

- Fewer than 50% of stillbirths receive autopsy
- Patient and provider misconceptions
- Cost
- Provider counseling improves uptake
- Partial autopsy: radiographs, external examination, limited incision
- MRI on horizon

Document

- Visual appearance – any dysmorphology, maceration, size
- Describe placenta and umbilical cord
- Give chronology
- This is your gift to future pro



Delivery and Bereavement

- Mementos, photographs, videos
  - offer to store
- Mixed data on PTSD and holding
- Cuddle Cot
- Encourage parenting

Mode of Delivery

- D&E: option based on fetal size, provider expertise
- IOL:
  - mifepristone 200mg
  - misprostol vs oxytocin
  - 20% need for additional procedure
- Cesarean only in rare circumstances

Postpartum

- Notify your staff
- Eliminate the waiting room
- EPDS?
- Mental health referral

The next pregnancy…

- Recurrence risk – depends on the cause
- Preconception visit
- Establish mental health care
- Modify the modifiable
- Minimal intervention: baby aspirin, LMWH for APS
- Genetic screening, early anatomy ultrasound
- Antepartum surveillance
- Fetal movement monitoring
- Timing of delivery

Pregnancy after loss

- Frequent visits
- Communicate history to staff
- Confirm mental health care
- Language matters
  - use baby's name
  - don't say "at least"
- Avoidance of triggers
  - doctor and hospital switching is common
  - ask about rooms to avoid
  - check heartbeat first!
- Dates and anniversaries

Delivery after loss

- Delivery room trauma/triggers
- MOD can be complicated
- New layers of grief – high risk for PPD/anxiety

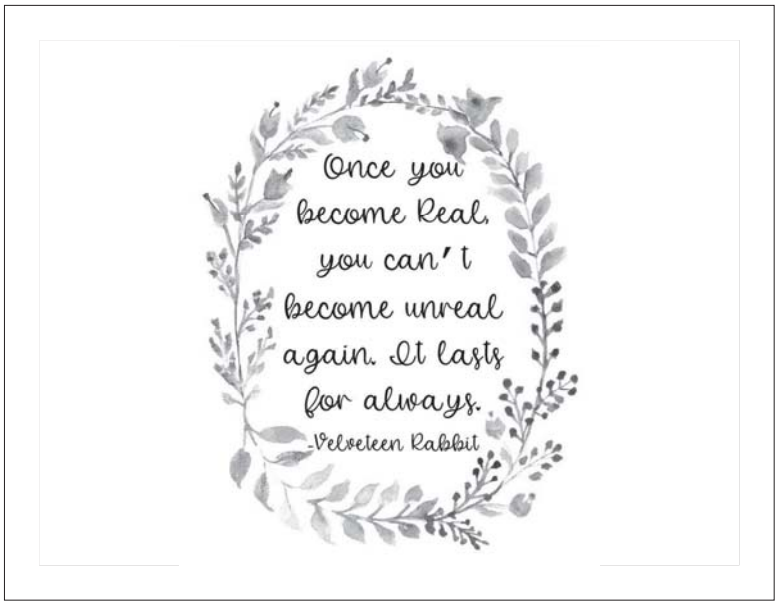
Conclusions

- Uncommon but not rare
- Cause matters
- Placental pathology and autopsy are important
- Small gestures make a big difference

References

- Autry, A. M., Hayes, E. C., Jacobson, G. F., & Kirby, R. S. (2002). A comparison of medical induction and dilation and evacuation for second-trimester abortion. *American Journal of Obstetrics and Gynecology*, *187*(2), 393–397.
- Crane, J. M. G., Keough, M., Murphy, P., Burrage, L., & Hutchens, D. (2011). Effects of environmental tobacco smoke on perinatal outcomes : a retrospective cohort study, 865–871.
- Dudley, D. J., Goldenberg, R., Conway, D., & Silver, R. M. (2010). A New System for Determining the Causes of Stillbirth, *116*(2), 254–260.
- Mills, T., Ricklesford, C., Cooke, A., Heazell, A., Whitworth, M., & Lavender, T. (2014). Parents' experiences and expectations of care in pregnancy after stillbirth or neonatal death: a metasynthesis. *BJOG: An International Journal of Obstetrics & Gynaecology*, *121*(8), 943–950.
- Page, J. M., Christiansen-Lindquist, L., Thorsten, V., Parker, C. B., Reddy, U. M., Dudley, D. J., … Silver, R. M. (2017). Diagnostic tests for evaluation of stillbirth: Results from the stillbirth collaborative research network. *Obstetrics and Gynecology*, *129*(4), 699–706
- Silver, R., Siassakos, D., & Dudley, D. (2018). Pregnancy after stillbirth: anxiety and a whole lot more. *BJOG: An International Journal of Obstetrics & Gynaecology*, *125*(2), 211–211. Stillbirth Collaborative Research Network Writing Group (2011). Causes of death among stillbirths. *JAMA*, 306(22): 2459-2468.

Thank You


Once you become Real, you can't become unreal again. It lasts for always.
-Velveteen Rabbit

Psychological Aftermaths of Pregnancy Loss

Teni Davoudian, PhD, ABPP
Clinical Psychologist
Assistant Professor in Psychiatry & Ob/Gyn
November 15, 2019

Grief

- Grief has physical, emotional, spiritual, and social components
- Non-linear process
  - States rather than stages of grief
- Anger is component of grief

> Grief is a force of energy that cannot be controlled or predicted. It comes and goes on its own schedule. Grief does not obey your plans, or your wishes. Grief will do whatever it wants to you, whenever it wants to. In that regard, Grief has a lot in common with Love.
>
> –ELIZABETH GILBERT

Pregnancy Loss Grief

- Facilitates bond with deceased as a coping strategy
- "Prospective" grieving for the life and relationship projected into the future (versus retrospective grieving)
- Peaks at 6 months
- Women also grieving:
  - Loss of confidence in one's body
  - Loss of confidence in medicine
  - Loss of control

Grief vs. Major Depression

	Grief	Major Depression
Course	• Decreases over time • Waves of grief (triggered by thoughts/reminders of the deceased)	• Persistent depressed mood
Emotional Spectrum	• Normal to experience positive emotions and laughter while grieving • Fluctuating ability to feel pleasure	• Pervasive unhappiness • Misery
Cognitive Processes	• Thoughts and memories of deceased	• Self-critical thoughts • Negative ruminations
Self-Esteem	• Mostly preserved through grief process • Some concerns about "failing" the deceased	• Lowered self-esteem • Self-loathing • Worthlessness
Suicidal Ideation	• If SI occurs, it is in the context of reuniting with the deceased	• Focused on ending one's life due to feelings of worthlessness and perceived inability to cope with depression

Comorbid Psych Dx

- Major Depressive Disorder
  - RPL: 5x more likely to develop moderate/severe depression (Kolte, 2015)
- Generalized anxiety disorder
  - RPL: Increased severity of generalized anxiety (Fertl et al, 2009)
- PTSD (Englehard, 2004)
- Guilt, self-blame, and isolation (Bardos et al., 2015)
- No validated psych screenings specific to pregnancy loss

Public Perceptions of Miscarriage

- Majority believe that miscarriage occurs <5% of pregnancies (Bardos et al., 2015)
- Believed causes of miscarriage:
  - 95% genetic abnormalities
  - 76% stressful event
  - 64% lifting heavy object
  - 31% past abortion
  - 28% previous use of IUD
  - 21% getting into an argument
- Possible psychological results of misconceptions:
  - Feelings of isolation and guilt among women who experience miscarriage(s)

Public Perceptions of Miscarriage

- Emotional reactions of women with history of miscarriage(s): (Bardos et al., 2015)
  - 47% felt guilty
  - 41% reported that they had done something wrong
  - 41% felt alone
  - 28% felt ashamed
  - 19% blamed self even when cause of miscarriage found

Pregnancy Loss & Relationships

- Gap in literature regarding experiences of same-sex couples, transgender individuals, single parents by choice
- Discordant/incongruent grief among men and women in heterosexual relationships (Serrano & Lima, 2006)
- Sexuality following pregnancy loss: (Zhang et al., 2016)
  - Women: lowered libido
  - Men: decreased sexual satisfaction, increased erectile dysfunction
- Higher risk of relationship dissolution for up to 3 years after loss (Gold, Sen, & Hayward, 2010)

Other Stakeholders

- Surviving sibling(s) grieve: (Calister, 2006)
  - Loss of their expected sibling
  - Loss of the parents as they knew them prior to the loss
- Supporting grieving children:
  - Recognize and acknowledge the child's grief
  - Read children's books about death (Erlandsson et al., 2010)
  - Allow children to witness some of parent's grief (Erlandsson et al., 2010)

IUFD & Stillbirth

- Elevated anxiety and depression for 2 years following IUFD (Cacciatore et al., 2008)
- Higher risk of relationship dissolution for up to 9-10 years after IUFD (Gold, Sen, & Hayward, 2010)
- IUFD has no major impact on women's QoL or risk of experiencing depression 18 years after loss (Gravensteen et al., 2012)
- Interventions that may mitigate long-term psychopathology: (Gravensteen et al., 2012)
  - Postpartum consultation with the obstetrician or midwife
  - Meeting with a psychologist/psychiatrist
  - Follow-up from PCP
  - Consultation with a religious counsellor

Supporting Patients

- Following a loss, patients desire: (Evans, 2012; Koert et al., 2018; Munsters et al., 2011)
  - Inclusion of partner in consultations and treatments
  - Reliable and accurate information about miscarriages
  - Attention to both physical and psychological aspects of miscarriage
  - Access to psychological treatment
  - Practical advice about lifestyle and diet
  - Written information

Supporting Patients

- Mimic patient's vocabulary regarding fetus
- Ask open ended questions
- Depending on gestational age, inquire about patient's intent or interest in memorializing the fetus
- If appropriate, remind patient that she is not to be blamed
  - Women who receive reassurance from their providers following a loss report less guilt and self-blame (Corbett-Owen & Kruger, 2001)
- Avoid comments that may trivialize the patient's loss
- Who are you trying to comfort? The patient(s) or yourself?

Patient Care Factors to Consider

- Setting (Covington, 2009)
  - Privacy? Patient dressed?
- Perception of patient(s)
  - Assess her/his/their understanding of the loss
- Invite emotional reactions
  - "Would you like to talk about how you're feeling right now?"
- Provide plan for next steps
  - What happens next? Which medical providers will be there?

Resources

Books:

- Conquering Infertility: Dr. Alice Domar's Mind/Body Guide to Enhancing Fertility and Coping with Infertility
  By Alice Domar, PhD
- Not Broken: An Approachable Guide to Miscarriage and Recurrent Pregnancy Loss
  By Lora Shahine
- Loved Baby: 31 Devotions Helping You Grieve and Cherish Your Child after Pregnancy Loss
  By Sarah Philpott, PhD

Support Groups:

- Resolve Support Group
- Brief Encounters

References

- Abboud, L., & Liamputtong, P. (2005). When pregnancy fails: coping strategies, support networks and experiences with health care of ethnic women and their partners. *Journal of Reproductive and Infant Psychology*, *23*(1), 3-18.
- Armstrong, D. (2001). Exploring fathers' experiences of pregnancy after a prior perinatal loss. *MCN: The American Journal of Maternal/Child Nursing*, *26*(3), 147-153.
- Bardos, J., Hercz, D., Friedenthal, J., Missmer, S. A., & Williams, Z. (2015). A national survey on public perceptions of miscarriage. *Obstetrics and gynecology*, *125*(6), 1313.
- Cacciatore, J., Rådestad, I., & Frederik Frøen, J. (2008). Effects of contact with stillborn babies on maternal anxiety and depression. *Birth*, *35*(4), 313-320.
- Callister, L. C. (2006). Perinatal loss: A family perspective. *Journal of Perinatal and Neonatal Nursing, 20*(3), 227-234.
- Corbet-Owen, C., & Kruger, L. M. (2001). The health system and emotional care: Validating the many meanings of spontaneous pregnancy loss. *Families, Systems, & Health*, *19*(4), 411.
- Covington, S. N. (2009). Pregnancy Loss: A Protocol to Help Patients COPE. *Topics in Obstetrics & Gynecology*, *29*(9), 1-7.

References

- Due, C., Chiarolli, S., & Riggs, D. W. (2017). The impact of pregnancy loss on men's health and wellbeing: a systematic review. *BMC Pregnancy and Childbirth*, *17*(1), 380.
- Engelhard, I. M. (2004). Miscarriage as a traumatic event. *Clinical obstetrics and gynecology*, *47*(3), 547-551.
- Erlandsson, K., Avelin, P., Saflund, K., Wredling, R., & Radestad, I. (2010). Siblings' farewell to a stillborn sister or brother and parents' support to their older children: a questionnaire study from the parents' perspective. *Journal of Child Health Care, 14*(2), 151-160.
- Fertl, K. I., Bergner, A., Beyer, R., Klapp, B. F., & Rauchfuss, M. (2009). Levels and effects of different forms of anxiety during pregnancy after a prior miscarriage. *European Journal of Obstetrics & Gynecology and Reproductive Biology*, *142*(1), 23-29.
- Gameiro, S., van den Belt-Dusebout, A. W., Bleiker, E., Braat, D., van Leeuwen, F. E., & Verhaak, C. M. (2014). Do children make you happier? Sustained child-wish and mental health in women 11–17 years after fertility treatment. *Human Reproduction*, *29*(10), 2238-2246.
- Gissler, M., Hemminki, E., & Lonnqvist, J. (1996). Suicides after pregnancy in Finland, 1987–94: register linkage study. *Bmj*, *313*(7070), 1431-1434.
- Gravensteen, I. K., Helgadottir, L. B., Jacobsen, E. M., Sandset, P. M., & Ekeberg, Ø. (2012). Long-term impact of intrauterine fetal death on quality of life and depression: a case–control study. *BMC pregnancy and childbirth*, *12*(1), 43.

References

- Gold, K. J., Sen, A., & Hayward, R. A. (2010). Marriage and cohabitation outcomes after pregnancy loss. *Pediatrics*, *125*(5), e1202-e1207.
- He, L., Wang, T., Xu, H., Chen, C., Liu, Z., Kang, X., & Zhao, A. (2019). Prevalence of depression and anxiety in women with recurrent pregnancy loss and the associated risk factors. *Archives of gynecology and obstetrics*, 1-6.
- Kersting, A., Dölemeyer, R., Steinig, J., Walter, F., Kroker, K., Baust, K., & Wagner, B. (2013). Brief internet-based intervention reduces posttraumatic stress and prolonged grief in parents after the loss of a child during pregnancy: a randomized controlled trial. *Psychotherapy and Psychosomatics*, *82*(6), 372-381.
- Kolte, A. M., Olsen, L. R., Mikkelsen, E. M., Christiansen, O. B., & Nielsen, H. S. (2015). Depression and emotional stress is highly prevalent among women with recurrent pregnancy loss. *Human Reproduction*, *30*(4), 777-782.
- Koert, E., Malling, G. M. H., Sylvest, R., Krog, M. C., Kolte, A. M., Schmidt, L., & Nielsen, H. S. (2018). Recurrent pregnancy loss: couples' perspectives on their need for treatment, support and follow up. *Human Reproduction*, *34*(2), 291-296.
- Lok, I. H., & Neugebauer, R. (2007). Psychological morbidity following miscarriage. *Best Practice & Research Clinical Obstetrics & Gynaecology*, *21*(2), 229-247.
- Lok, I. H., Yip, A. S. K., Lee, D. T. S., Sahota, D., & Chung, T. K. H. (2010). A 1-year longitudinal study of psychological morbidity after miscarriage. *Fertility and sterility*, *93*(6), 1966-1975.

References

- Magee, P. L., MacLeod, A. K., Tata, P., & Regan, L. (2003). Psychological distress in recurrent miscarriage: the role of prospective thinking and role and goal investment. *Journal of Reproductive and Infant Psychology*, *21*(1), 35-47.
- Musters, A. M., Taminiau-Bloem, E. F., van den Boogaard, E., van der Veen, F., & Goddijn, M. (2011). Supportive care for women with unexplained recurrent miscarriage: patients' perspectives. *Human reproduction*, *26*(4), 873-877.
- O'Leary, J. M., & Gaziano, C. (2011). Sibling grief after perinatal loss. *Journal of Prenatal & Perinatal Psychology & Health*, *25*(3), 173.
- Ockhuijsen, H. D., Boivin, J., van den Hoogen, A., & Macklon, N. S. (2013). Coping after recurrent miscarriage: uncertainty and bracing for the worst. *J Fam Plann Reprod Health Care*, *39*(4), 250-256.
- Purandare, N., Ryan, G., Ciprike, V., Trevisan, J., Sheehan, J., & Geary, M. (2012). Grieving after early pregnancy loss--a common reality.) *Irish Medical Journal*, *105*.
- Saraiya M, Green CA, Berg CJ, Hopkins FW, Koonin LM, Atrash HK (1999) Spontaneous abortion – related deaths among women in the United States – 1981–1991. Obstet Gynecol 94:172–176
- Serrano, F., & Lima, M. L. (2006). Recurrent miscarriage: psychological and relational consequences for couples. *Psychology and Psychotherapy: Theory, Research and Practice*, *79*(4), 585-594

References

- Turton, P., Badenhorst, W., Hughes, P., Ward, J., Riches, S., & White, S. (2006). Psychological impact of stillbirth on fathers in the subsequent pregnancy and puerperium. *The British Journal of Psychiatry*, *188*(2), 165-172
- Wilson, R. E. (2001). Parents' support of their other children after a miscarriage or perinatal death. *Early Human Development, 61*(1), 55-65.
- Zhang, Y. X., Zhang, X. Q., Wang, Q. R., Yuan, Y. Q., Yang, J. G., Zhang, X. W., & Li, Q. (2016). Psychological burden, sexual satisfaction and erectile function in men whose partners experience recurrent pregnancy loss in China: a cross-sectional study. *Reproductive health*, *13*(1), 73.

Questions?
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Thank You

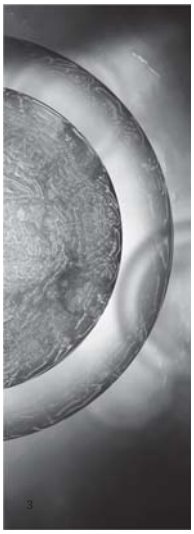
Updates in Cervical Cancer Screening and HPV Disease Prevention

Katie Au, MD
Assistant Professor
Obstetrics & Gynecology

DATE: NOVEMBER 15, 2019

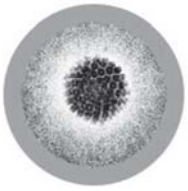
Disclosures/Conflict of Interest

- None



Objectives

- Describe the burden of HPV disease
- Review HPV vaccination practices
- Review pap test and cervical cancer screening guidelines
- Future directions



HPV
(Human papillomavirus)

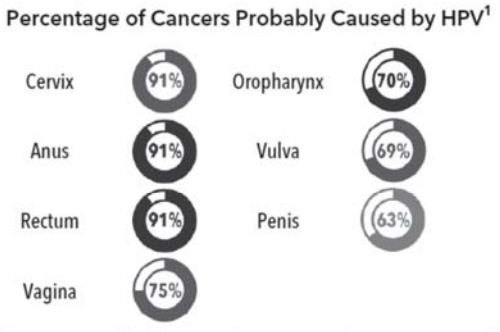
Understanding the Burden

HPV INFECTION & DISEASE

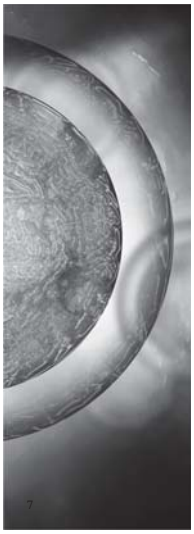
HPV Infection

- Most common STI: The CDC estimates >80% of sexually active men and women
- Most females and males will be infected with at least one type of mucosal HPV at some point in their lives
  - Estimated 79 million Americans currently infected
  - 14 million new infections/year in the US
  - HPV infection is most common in people in their teens and early 20s (likely soon after sexual debut)
- Most people will never know that they have been infected

Satterwhite et al. Sex Transm Dis. 2013



1 National Cancer Institute

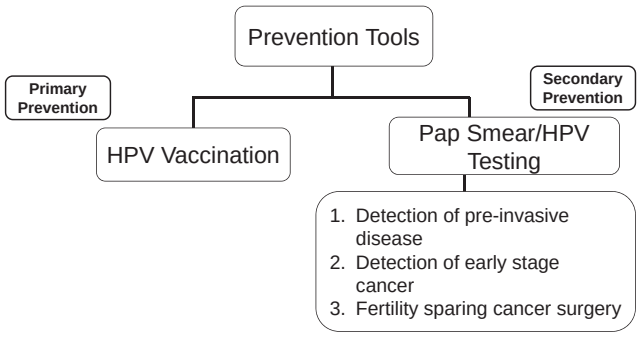


Cervical Cancer

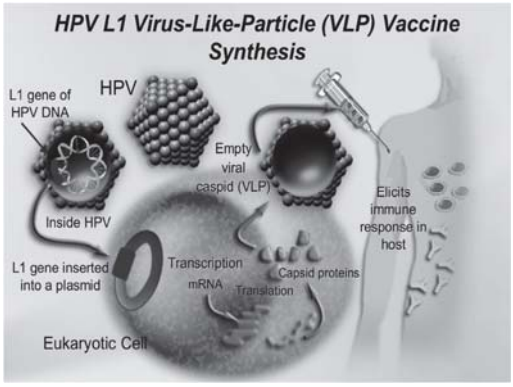
- Worldwide: ~500,000 new cases each year
  - Leading cause of cancer-related death in women in underdeveloped countries
- United States: ~11,000 new cases each year & ~4,000 deaths
  - ~110 new cases in Oregon annually
- >90% association with HPV
  - >60% associated with subtype 16

Cervical Cancer Is Preventable!

Cervical Cancer is Preventable!



Primary HPV Prevention



HPV Vaccines Currently Licensed in U.S.

	Bivalent 2vHPV (Cervarix)	**Quadrivalent 4vHPV** (Gardasil)	**9-Valent 9vHPV** (Gardasil 9)
Manufacturer	GlaxoSmithKline	Merck	Merck
HPV Types Included	**16, 18**	6, 11, **16, 18**	6, 11, **16, 18,** 31, 33, 45, 52, 58
Contraindications	Hypersensitivity to latex*	Hypersensitivity to yeast	Hypersensitivity to yeast
Dose Schedule	3 dose series: 0, 1, 6 months	3 dose series: 0, 2, 6 months	**Ages 15-45** 3 dose series: 0, 2, 6 months
UPDATED Dose Schedule			**Ages 9-14** ***2 dose series: 0, 6 months***

HPV Vaccine Recommendations

CDC recommends routine vaccination at age 11 or 12 years to prevent HPV cancers, *for both boys and girls*

- The vaccination series can be started at age 9 years
- Two doses of vaccine are recommended
- The second dose of the vaccine should be administered 6 to 12 months after the first dose.

Meites et al. MMWR. 2016.

"But what about adults ages 27 to 45?"

The New York Times

HPV Vaccine Expanded for People Ages 27 to 45

About 14 million women and men become infected with the human papillomavirus each year in the United States, according to the Centers for Disease Control and Prevention.
Keith Bedford/The Boston Globe, via Getty Images

By Denise Grady and Jan Hoffman

14

FDA, October 2018

"In 3,200 women ages 27 through 45, followed for an average of 3.5 years, Gardasil was 88 percent effective in the prevention of a combined endpoint of persistent infection, genital warts, vulvar and vaginal precancerous lesions, cervical precancerous lesions, and cervical cancer related to HPV types covered by the vaccine."

Number Needed to Vaccinate

	Anogenital Warts	CIN2 +	Cancer
Ages 9-26	40	450	3,260
Adults through age 45 y/o	120	800	6,500

15

CDC Centers for Disease Control and Prevention
CDC 24/7: Saving Lives, Protecting People™

A-Z Index
Search

Morbidity and Mortality Weekly Report (*MMWR*)

CDC

Human Papillomavirus Vaccination for Adults: Updated Recommendations of the Advisory Committee on Immunization Practices

Weekly / August 16, 2019 / 68(32);698–702

Elissa Meites, MD[1]; Peter G. Szilagyi, MD[2]; Harrell W. Chesson, PhD[3]; Elizabeth R. Unger, PhD, MD[4]; José R. Romero, MD[5]; Lauri E. Markowitz, MD[1] (View author affiliations)

View suggested citation

16

"Evidence suggests that although HPV vaccination is **safe for adults aged 27 through 45 years, population benefit would be minimal**; nevertheless, some adults who are not adequately vaccinated might be at risk for new HPV infection and might benefit from vaccination in this age range."

17

Should adults ages 27-45 be vaccinated?

- Vaccination is not recommended for everyone older than age 26 years.
- Most sexually active adults have already been exposed to HPV, although not necessarily all of the HPV types targeted by vaccination. At any age, having a new sex partner is a risk factor for getting a new HPV infection. People who are already in a long-term, mutually monogamous relationship are not likely to get a new HPV infection.
- HPV vaccination prevents new HPV infections but does not treat existing infections or diseases.

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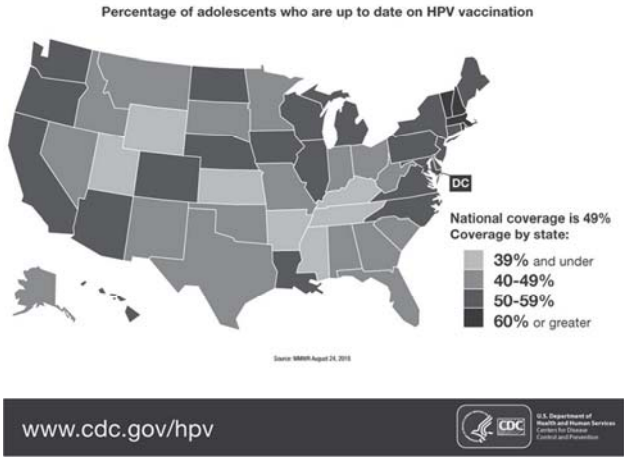
https://www.cdc.gov/hpv/hcp/schedules-recommendations.html

HPV vaccination provides the **most benefit** when given before a person is exposed to any HPV. That's why CDC **recommends HPV vaccination at ages 11-12**.



MMWR August 24, 2018

Monitoring Impact of HPV Vaccine Programs on HPV-Associated Outcomes

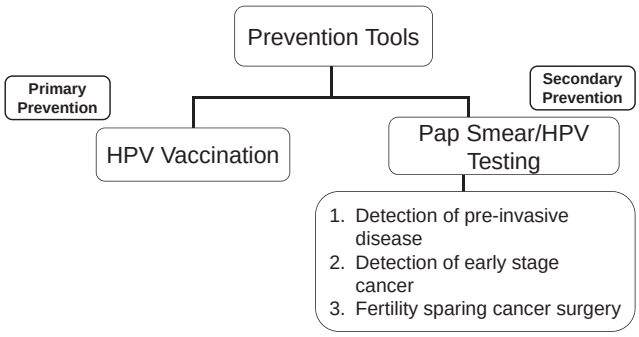
HPV VACCINE IMPACT

Objectives

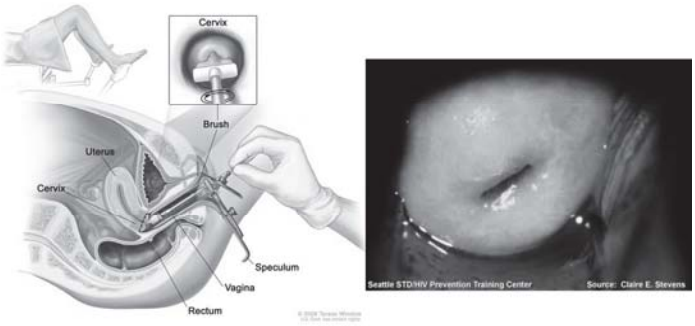
- Describe the burden of HPV disease
- Review HPV vaccination practices
- Review pap test and cervical cancer screening guidelines
- Future directions

Cervical Cancer Is Preventable!

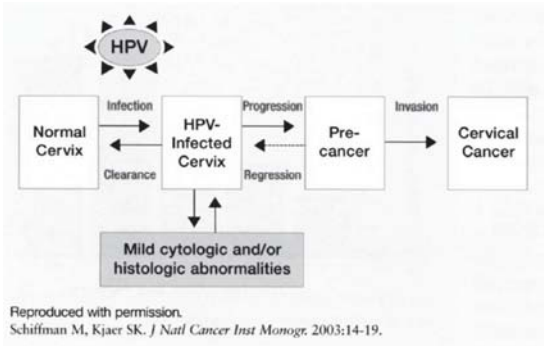
Cervical Cancer is Preventable!



Pap Smear Screening

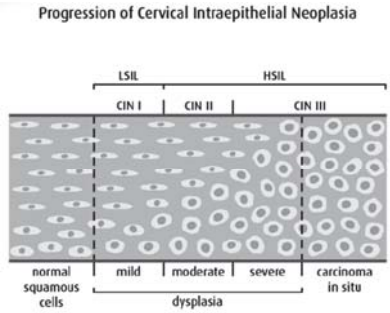


Rationale for screening



Reproduced with permission.
Schiffman M, Kjaer SK. *J Natl Cancer Inst Monogr.* 2003;14-19.

Cervical Dysplasia



Clinical Review & Education | August 21, 2018

JAMA | US Preventive Services Task Force | RECOMMENDATION STATEMENT

Screening for Cervical Cancer
US Preventive Services Task Force Recommendation Statement

US Preventive Services Task Force

IMPORTANCE The number of deaths from cervical cancer in the United States has decreased substantially since the implementation of widespread cervical cancer screening and has declined from 2.8 to 2.3 deaths per 100 000 women from 2000 to 2015.

OBJECTIVE To update the US Preventive Services Task Force (USPSTF) 2012 recommendation on screening for cervical cancer.

EVIDENCE REVIEW The USPSTF reviewed the evidence on screening for cervical cancer, with a focus on clinical trials and cohort studies that evaluated screening with high-risk human papillomavirus (hrHPV) testing alone or hrHPV and cytology together (cotesting) compared with cervical cytology alone. The USPSTF also commissioned a decision analysis model to evaluate the age at which to begin and end screening, the optimal interval for screening, the effectiveness of different screening strategies, and related benefits and harms of different screening strategies.

Editorial page 647
Author Audio Interview
Related articles pages 687, 706 and JAMA Patient Page page 732
CME Quiz at jamanetwork.com/learning and CME Questions page 715
Related article at jamainternalmedicine.com

Screening Guidelines

< 21	• No Screening
21-29	• Cytology q 3 years (reflex HPV only) *Grade A Recommendation*
30-65	• hrHPV and Cytology co-testing q 5 years OR • Cytology q 3 years OR • hrHPV testing q 5 years (USPSTF) *Grade A Recommendation*
> 65	• No Screening • UNLESS: hx of moderate or severe pre-cancer → screening for 20 years following diagnosis

Ages 30-65

- Cytology q3 years
- hr-HPV and cytology Co-test q 5 years
- hr-HPV alone q5 years
  - USPSTF update in 2018 !

2018 USPSTF Update Ages 30-65

- **CYTOLOGY ALONE q 3 years**, based on observational data and modeling studies
  - Lower sensitivity than primary hrHPV testing or cotesting
  - Lower false-positive rate and rate of additional testing
  - Compared to no screening, cytology q3y can **reduce the number of cervical cancer deaths from 8.34 to 0.76 deaths per 1000 women**

2018 USPSTF Update Ages 30-65

- **COTESTING q 5 years**, based on RCTs, prospective cohort studies, and modeling studies:
  - May detect slightly more cases of CIN than screening with hrHPV testing alone but with a significant increase in the number of tests and procedures
  - Highest false-positive rate
  - Compared to no screening, contesting q 5 years can **reduce the number of cervical cancer deaths from 8.34 to 0.30 deaths per 1000 women**

2018 USPSTF Update Ages 30-65

- **PRIMARY hrHPV TESTING q 5 years**, based on RCTs, one prospective study, and modeling studies:
  - Has adequate sensitivity
  - Compared with no screening, primary hrHPV screening q5y can **reduce the number of cervical cancer deaths from 8.34 to 0.29 deaths per 1000 women**

*"USPSTF now recommends **screening every 5 years with hrHPV testing alone** as an alternative to screening every 3 years with cytology alone among women aged 30 to 65 years. **These are the 2 preferred screening strategies…. Cotesting as an alternative strategy has demonstrated similar effectiveness**, although it may result in more tests and procedures compared with either cytology or hrHPV testing alone."*

Other Organizations

- AAFP: in agreement with USPSTF
- ACS/ASCCP: cotesting q 5 years or cytology q 3 years
- ASCCP/SGO interim update 2015: primary hrHPV screening starting at age 25 as an alternate to cytology alone or cotesting
- ACOG: cytology alone and cotesting still specifically recommended, but primary hrHPV screening in women 25 and older can be considered as an alternative

Screening Guidelines

< 21	• No Screening	
21-29	• Cytology q 3 years (reflex HPV only)	*Grade A Recommendation*
30-65	• hrHPV and Cytology co-testing q 5 years OR • Cytology q 3 years OR • hrHPV testing q 5 years (USPSTF)	*Grade A Recommendation*
> 65	• No Screening • UNLESS: hx of moderate or severe pre-cancer → screening for 20 years following diagnosis	

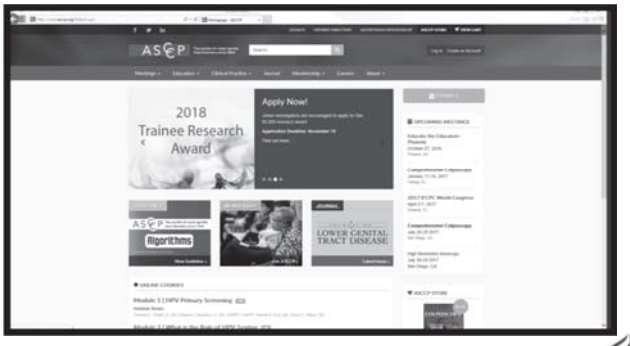
Future Directions

- ASCCP Guidelines 2020
- HPV self swabs?
- Improving HPV vaccination rates

ASCCP 2020

- Better incorporate a patient's prior history in addition to current results ("Risk-Based")
- Will use a computer-based risk matrix to estimate/calculate a patient's risk of CIN3 based on her current and prior results
- Focuses more on CIN3 as a pre-cancer and less on CIN2 (which has a higher chance of regression and is a less reproducible result)
- Should clarify who needs 1 yr vs 3 yr vs 5 yr follow-up

Visit www.asccp.org



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At Pacific NW Update in Women's Health
- Friday: Lunch Roundtable Host

Thank You

PACIFIC NW UPDATE IN OBGYN AND WOMEN'S HEALTH

HPV and Anal Neoplasia

Daniel Herzig, MD, FACS, FASCRS
Digestive Health Center and Knight Cancer Institute
November 15, 2019

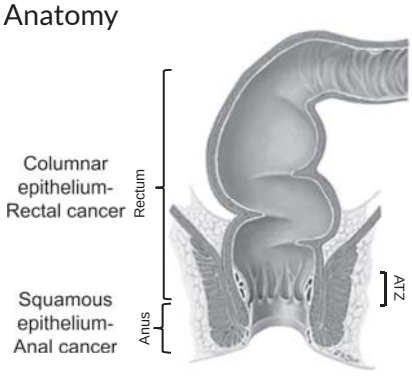
Disclosures

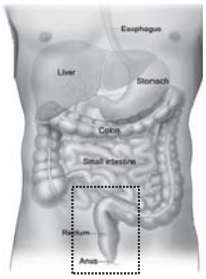
Nothing to disclose

Objectives

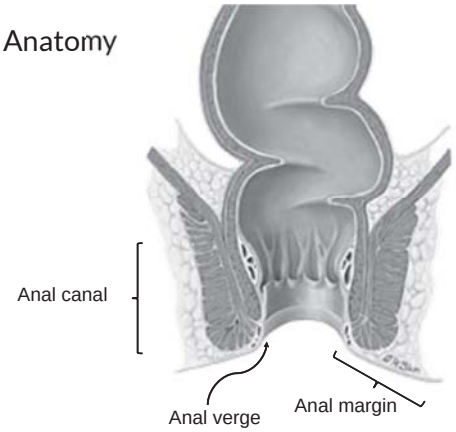
- Describe how HPV affects the anus
- Review the current trends in anal cancer and anal dysplasia epidemiology
- Evaluate current strategies for screening and prevention

Anatomy





Anatomy



DH1

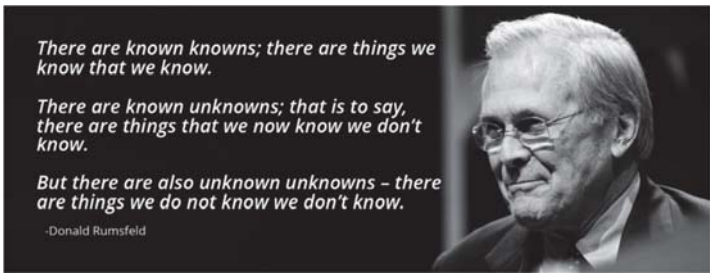
Anal Canal
- Uncommon
- HPV, HIV, immune
- Treatment is complex

Anal Margin
- Very uncommon
- Like SCC of the skin
- Easily treated with WLE

Squamous cell cancer

Anal canal cancer

Normal Cervix ⟷ (Infection / Clearance) HPV infected Cervix ⇢ (Progression / Regression) Pre-cancer → (Invasion) Cancer



Anal canal cancer

KNOWN KNOWNS	KNOWN UNKNOWNS
8,000 cases per year, 80% HPV related HIV, immunosuppression, increasing age, female gender, ARI are risk factors Terminology, staging and treatment	Is there an impending epidemic of anal cancer? Is anal dysplasia the precursor lesion? Can treatment of anal dysplasia prevent the progression to cancer?
UNKNOWN KNOWNS	**UNKNOWN UNKNOWNS**
You should be listening to someone else….	We'll find out later…

Known Knowns: Terminology

✓

Low -grade Squamous Intraepithelial Lesion (LSIL)
High-grade Squamous Intraepithelial Lesion (HSIL)

⊗

Anal Intraepithelial Neoplasia I (AIN1)
Anal Intraepithelial Neoplasia 2/3 (AIN2, AIN3)
Squamous cell carcinoma in situ

Darragh et al. *Arch Pathol Lab Med.* 2012;136:1266–1297.

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Known Knowns: staging and treatment

Staging
T: <2cm, 2-5 cm, >5 cm, adjacent organs
N: inguinal/internal iliac, external iliac
M: Metastases

Most present with early stage tumors

Treatment
Nigro protocol
radiation (54-59 Gy)
5-FU/mitomycin
5FU/cisplatin (2nd choice)
Trial:pembrolizumab

Cure rates 70-80%

Ajani et al. *JAMA.* 2008;299:1914–1921..

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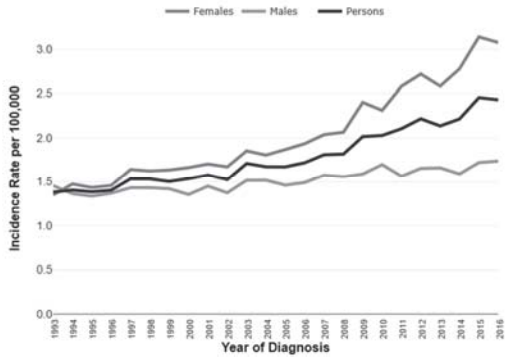
Known Unknowns: An Epidemic?



CancerResearchUK

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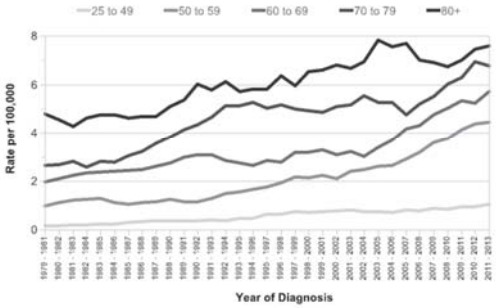
Known Unknowns: An Epidemic?



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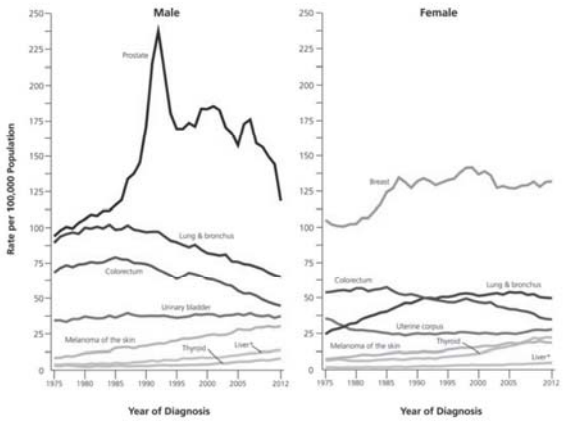
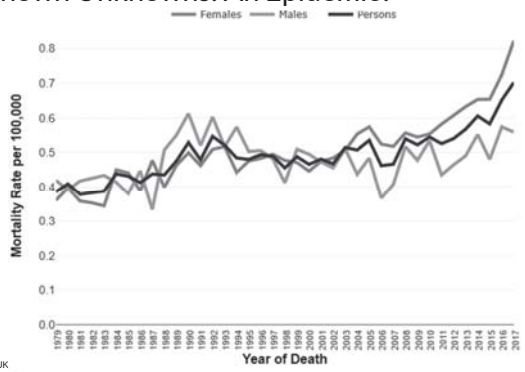


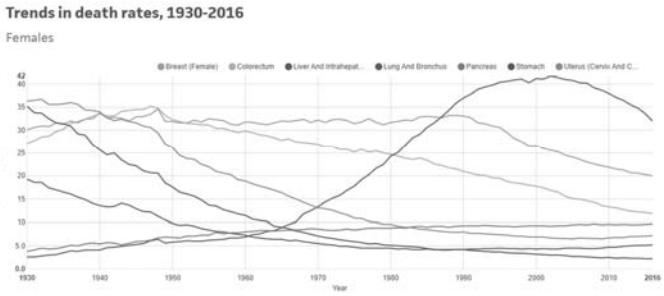
CDC/National Center for Health Statistics

Known Unknowns: An Epidemic?



CancerResearchUK

Known Unknowns: An Epidemic?



CDC/National Center for Health Statistics

Known Unknowns: Can we prevent anal cancer?

Rate of AIN3/HSIL in HIV pos MSM: 30%
Incidence of anal cancer in HIV pos MSM 45/100K
Incidence of anal cancer in HIV neg MSM 5.1/100K

Machalek et al. *Lancet Oncol.* 2012;13:487–500.

Known Unknowns: Screening for high risk individuals?

Anal Pap
HPV testing (p16 staining)

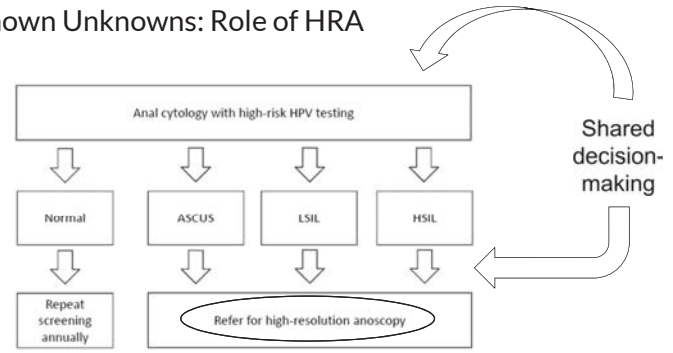
} Sensitivity ~60%, Specificity~40%

High resolution anoscopy (HRA)
Screening/Treatment

Stewart et al. *Dis Colon Rectum* 2018; 61: 755–77.

HRA Technique

Known Unknowns: Role of HRA



Ablation options

Topical : TCA, 5 FU, Imiquimod
Surgical: HRA or electrocautery
Vaccine: no effect

Wilkin et al. *Clin Infect Dis.* 2018;67:1339-1346
Stewart et al. *Dis Colon Rectum* 2018; 61: 755–77.

Known Unknowns: Can we prevent anal cancer?

4 studies with HRA-based intensive treatment:
~50% recurrence of HSIL
Cancer incidence up to 1% per year
- 1/377-633 per year HIV pos MSM
- 1/4000 per year HIV neg MSM

SEER database, 2000-2011
592 patients, HIV pos, AIN3
33 patients developed SCCA
- 1.2% at 1 yr
- 5.7% at 5 yrs

Median time 24 months
No difference based on treatment (or any)

Machalek et al. *Lancet Oncol.* 2012;13:487–500.
Arens et al. *Dis Colon Rectum* 2019;62:934-40.

Objectives

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Thank You

43rd Annual Pacific Northwest Update in Ob-Gyn and Women's Heath

Keynote Lecture

November 15, 2019 1:15-2:15

Menopause and Midlife Sexuality: a bit dry but a must have conversation

Cheryl B. Iglesia, MD
Director, Section of Female Pelvic Medicine and Reconstructive Surgery
MedStar Washington Hospital Center
Professor, ObGyn and Urology
Georgetown University School of Medicine

MedStar Washington Hospital Center

Learning Objectives

- Define vulvovaginal atrophy (VVA), and genitourinary syndrome (GSM) and the impact on post-menopausal dyspareunia
- Identify clinician-based & patient-based factors may inhibit the diagnosis of dyspareunia
- Describe clinician counseling approaches to facilitate a discussion about their symptoms
- Discuss the benefits and risks of innovative therapeutic interventions indicated for the management of menopause related dyspareunia including hormonal, non-hormonal and energy-based therapies

Yes… Even YOUR Mother has Sex: 60 is the New 40

Michelle *O*bama, 55

Brigitte Macron, 66

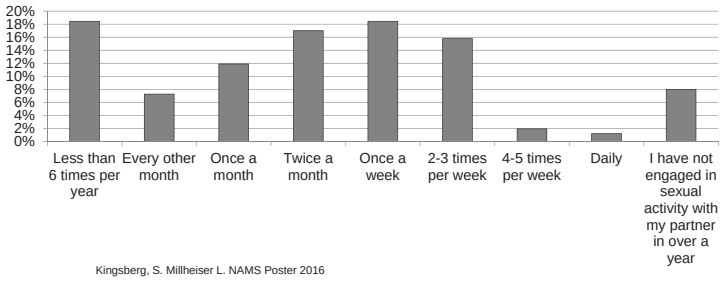
Diane Sawyer, 73

Correlates of Sexual Activity in Older Women: MIDUS II

- Not Sexually Active mean age 62.0 (11.8) n=771
- Sexually Active mean age 51.8 (10.9) n=1345
- **Romantic Partner Status best predictor of whether one was sexually active (regardless of age) even for women in their 70s and 80s**
- Sexually active women still sexually satisfied regardless of age or menopause status

Thomas, Hess, Thurston Ann Fam Med 2015, vol 13.

Postmenopausal women are still sexually active



Kingsberg, S. Millheiser L. NAMS Poster 2016

The Impact of Sexual Dysfunction on a Relationship

When sex is good

It adds 15-20% additional value to a relationship

When sex is bad/non-existent

It plays an inordinately powerful role draining the relationship of all positive value, about 50-70%!

Barry McCarthy 1997 JSMT

Two Most Prevalent Sexual Problems in Postmenopausal Women

- Dyspareunia Due to Genitourinary Syndrome of Menopause (GSM)
- Hypoactive Sexual Desire Disorder (HSDD)

Genitourinary Syndrome of Menopause (GSM)

- A collection of symptoms and signs associated with decreased estrogen and other sex steroids
  - Can involve changes to labia majora/minora, vestibule/introitus, clitoris, vagina, urethra, and bladder
  - Symptoms include, but are not limited to, dryness, pain with sex that may lead to subsequent sexual dysfunction, bladder and urethral symptoms, frequent urinary tract infections, burning, itching, and irritation that are bothersome or distressing.
- Symptomatic vulvovaginal atrophy (VVA) is one component of GSM
  - Treatment of symptomatic VVA may improve all components of GSM

Portman D, Gass M et al, Menopause 2014

Vulvar and Vaginal Atrophy (VVA)

•Affects up to 69% of postmenopausal women[1,2] and has a detrimental effect on quality of life and sexual function[3,4]

•Most women do not seek medical treatment for their VVA symptoms[3]

1. Cumming GP, et al. *Menopause Int* 2007;13:79-83. 2. Parish SJ, et al. *Int J Women's Health* 2013;5:437-447. 3. Nappi RE, Kokot-Kierepa M. *Maturitas* 2010;67:233-238.

50%
of postmenopausal women suffer from symptomatic GSM [1,2]
32 million women

1. North American Menopause Society. Menopause. 2013;20(9):888-902.
2. Wysocki S et al. *Clin Med Insights Reprod Health*. 2014;8:23-30

50%
of postmenopausal women suffer from symptomatic GSM [1,2]
32 million women

Only 50% (16 million) of women ever seek treatment [2,3]

OTC, over-the-counter.
1. North American Menopause Society. Menopause. 2013;20(9):888-902.
2. Wysocki S et al. *Clin Med Insights Reprod Health*. 2014;8:23-30
3. MacBride MB et al. *Mayo Clin Proc*. 2010;85:87-94.
4. TherapeuticsMD "EMPOWER" Survey, 2016

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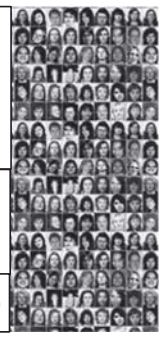
7% of Women Treated with Prescription Medication [5]



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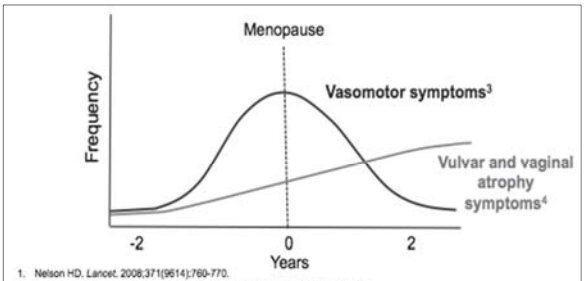
Unmet Need of Women
16 million (50%) Never treated

OTC, over-the-counter.
1. North American Menopause Society. Menopause. 2013;20(9):888-902.
2. Wysocki S et al. *Clin Med Insights Reprod Health*. 2014;8:23-30
3. MacBride MB et al. *Mayo Clin Proc*. 2010;85:87-94.
4. TherapeuticsMD "EMPOWER" Survey, 2016

Onset of Vasomotor Symptoms vs Vulvovaginal Symptoms



1. Nelson HD. *Lancet*. 2008;371(9614):760-770.
2. Bachmann GA, Nevadunsky NS. *Am Fam Physician*. 2000;61(10):3090-3096.
3. Kronenberg F. *Ann N Y Acad Sci*. 1990;592:52-86.
4. Dennerstein L et al. *Obstet Gynecol*. 2000;96(3):351-358.

U.S. Women Don't Realize VVA Symptoms Are Caused by Menopause

- When women in the survey were asked, in an unaided question, to name the cause of their VVA symptoms:
  - Only 24% of the women attributed their symptoms directly to Menopause
- Of the 76% citing another cause for their VVA symptoms, 33% responded they "Don't Know"

REVIVE, Real Women's Views of Treatment Options for Menopausal Vaginal Changes Survey Kingsberg S, et al. *J Sex Med*. 2013;10:1790-1799.

REVIVE, Real Women's Views of Treatment Options for Menopausal Vaginal Changes Survey Kingsberg S, et al. *J Sex Med*. 2013;10

Suffering in Silence

- Although quite common and bothersome, most women fail to get treatment (~ 93%)[1] due to:
  - Embarrassment[2]
  - Lack of knowledge about VVA[1]
  - Lack of knowledge of approved treatment options[1]
  - Negative attitudes regarding hormone therapy[3]
- Women who do seek treatment are often dissatisfied with the safety, convenience, and efficacy of current approved products.[1]

1. Kingsberg SA et al. *J Sex Med*. 2013;10:1790-1799.
2. Nappi et al. *Maturitas*. 2010;67:233-238.
3. Simon et al. *Menopause*. 2013;20:1043-1048.

Factors Contributing to Sub-Optimal Sexual Health Outcomes for Women

- **Social Stigma and Conversation Avoidance**
  - Female patients are often apprehensive to discuss sex and sexual health with healthcare professionals
  - Healthcare professionals may forego initiating conversation on sexual health
- **Low Awareness of Sexual Health Conditions**
  - Midlife women are often unaware or have misconceptions about conditions that may adversely impact their sexual life
- **Misperceptions about or Low Awareness of Available Treatments**
  - Claims about unproven treatments are prevalent, as are negative perceptions about effective treatments
- **Limited Clinician Training and Time**
  - Most HCPs receive little formal sexual health training
- **Cost, Coverage and Regulatory/Policy Issues**
  - High costs, limited insurance coverage, and/or regulatory issues may prevent uptake of effective treatments

Kingsberg SA, Schaffer J. Faught B, Pinkerton J. et al. Female Sexual Health: Barriers to Optimal Outcomes and a Roadmap for Improved Patient-Clinican Communications. JWH 2019

Key Barriers to Patient Treatment

- **Lack of awareness** by patients of symptoms relating to menopause[2]
- **Lack of discussion** regarding symptoms with HCPs[2]
- **Self-medication** with OTC lubricants/moisturizers and/or herbal medications[17]
- **Dissatisfaction with delivery systems** (e.g., messy creams)[18]
- Unwillingness to take FDA-approved estrogen therapies due to **"safety concerns"**[5]
- **Discontinuation** after initiation (typically 2-3 months)[18]

5. Wysocki S, Kingsberg S, Krychman M. *Clin Med Insights: Reprod Health* 2014:8 23-30.
17. Al Baghdadi O, Ewies AAA. *Climacteric* 2009;12 91-105
18. Portman D, Shulman L, Yeaw J, et al. *Menopause* 2015;22(11):1197-1203.

Consistent Findings Across Multiple Large Surveys of Women with VVA

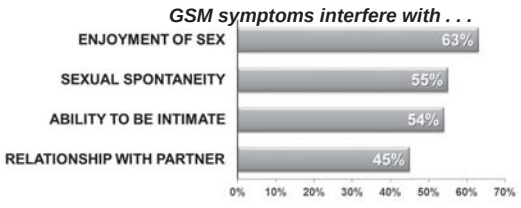
Name / Date	Country	Subjects	Method
VVA Focus Groups 2015	USA	38; with VVA symptoms; 49-74y	Focus Group
VIVA 2010	International / USA	3,520; postmenopausal; 55-65 y	Online survey
CLOSER 2011-12	Europe / N America	4,100; no menstruation for ≥12 mo; 55-65 y	Online survey
REVIVE 2012-14	USA / Europe	3,046/3768 postmenopausal; VVA symptoms; 45-75 y	Online survey
EMPOWER 2016	USA	1,858; with VVA symptoms; ≥45 y	Online survey

CLOSER: Clarifying Vaginal Atrophy's Impact on Sex and Relationship; EMPOWER: Women's EMPOWER survey, REVEAL: Revealing Vaginal Effects at Mid-Life; REVIVE: Real Women's Views of Treatment Options for Menopausal Vaginal Changes; USA: United States of America; VIVA: Vaginal Health: Insight, Views, & Attitudes; Presented at the North American Menopause Society Annual Meeting, October 9, 2015, Las Vegas NV.

2. Krychman M, Graham S, Bernick B, Mirkin S, Kingsberg SA. *J Sex Med*. 2017

Impact of GSM Symptoms on Sexual Function (REVIVE)

- Vaginal dryness (55%); dyspareunia (44%); vaginal irritation (37%)



REVIVE, Real Women's Views of Treatment Options for Menopausal Vaginal Changes Survey. Kingsberg S, et al. *J Sex Med*. 2013;10:1790-1799.

VVA Unmet Need (REVIVE)

- Women reported only 19% of HCPs addressed their sexual life
  - Only 13% raised the issue of VVA symptoms specifically during their checkup
  - 50% of patients think GSM is a natural—and perhaps unavoidable—consequence of aging
  - Others do not associate GSM with menopause
  - 40% of these women expected that their HCP would initiate discussion related to menopausal symptoms

Kingsberg S, Wysocki S, Magnus L, Krychman M. *J Sex Med, 2013.*

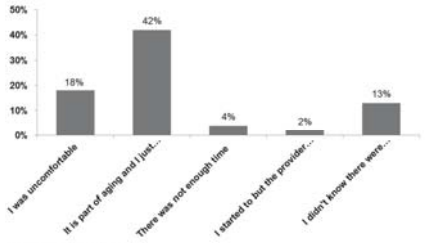
The Women's EMPOWER survey

Evaluated postmenopausal women's:

- Knowledge of condition, causation, and treatment options for VVA
- Motivation for seeking and continuing treatment
- Interaction with HCPs
- Perception of existing products

Kingsberg S, et al J Sex Med 2017 March 14(3)

The Women's EMPOWER survey: The Most Common Reasons Why Women Do Not Bring up Pain with Sex



- **Thought the symptoms are a part of aging**
- **Were uncomfortable**
- **Were not aware of treatments available**

Kingsberg S, et al J Sex Med 2017 March 14 (3)

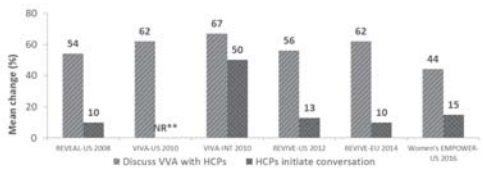
Barriers to Communication, Diagnosis and Treatment and Some Solutions

Physician Barriers to Addressing Sexual Health

- Perception it takes too long
- Consider other issues as higher priorities
- HCP embarrassment
- Inadequate knowledge/skills
- Fear of embarrassing patient
- Assume reimbursement is poor
- Few FDA approved treatments

- Korenman, SG, 1998; Brokeman, CPM et al, 1994; Eid JF et al, 2001; Baum, N et al, 1998

HCPs Are Reluctant to Initiate Dialogue With Their Patients regarding Symptoms of Vaginal Atrophy[2]*



- Data for individual studies can be found in specific references cited in Krychman, **NR = not reported

CLOSER: Clarifying Vaginal Atrophy's Impact on Sex and Relationship; EMPOWER: Women's EMPOWER survey; REVEAL: Revealing Vaginal Effects at Mid-Life; REVIVE: Real Women's Views of Treatment Options for Menopausal Vaginal Changes; USA: United States of America; VIVA: Vaginal Health: Insight, Views, & Attitudes; WVM: Women's Voices in Menopause

2. Krychman M, Graham S, Bernick B, Mirkin S, Kingsberg SA. *J Sex Med.* 2017 In Press.

Screening for VVA and Dysparuenia

- Normalize/universalize conversations about sexual health issues
- Start with open-ended **ubiquity-style question**
  - "Many women after menopause start to develop sexual problems such as pain with sex and/or dryness. What changes have you noticed?
  - Open, non-defensive body posture
  - Sit and maintain eye contact
  - Avoid nervous gestures

Sadovsky et al. J Sex Med. 2006;3:795-803.

Open-Ended Questions

- HCPs ask ≈1 question/min; >90% are closed-ended
- Actual time for patient to tell their story
  Max 150 seconds, most <60 seconds

Open-ended questions improve:

- assessment of functional impairment
- adherence
- patient satisfaction

Beckman & Frankel 1984; Marvel et al 1999; Rabinowitz et al, 2004.

Discomfort with Silence

On average, how quickly is a patient interrupted?

Allow Patients to Talk

Research shows *that, on average* ***patients are interrupted*** *by physicians every* ***12-23 seconds*** *during a consultation*

- Beckman & Frankel 1984
- Marvel et al 1999
- Rhoades et al 2001
- Langewitz 2002

The Power of Silence

Basic Screening for Sexual Function

Legitimize importance of assessing sexual function; normalize as part of usual history and physical

Are you currently involved in a relationship…sexual ?

YES

Have your partners included men, women or both?
What sexual concerns do you have?

NO

Do you have sexual concerns that you would like to discuss or that have contributed to lack of sexual behavior?

Adapted from Kingsberg S. Sex, Urol Clin N Am. 2000;34:497-506.

Office Based Counseling for Sexual Problems: Follow PLISSIT Model

Permission to talk about sexual issues, reassurance and empathy

Limited **I**nformation
e.g., education about genital anatomy or educational resources

Specific **S**uggestions
e.g., use of lubricants, altering position

Intensive **T**herapy
e.g., referral for psychotherapy/sex therapy

Annon, 1976

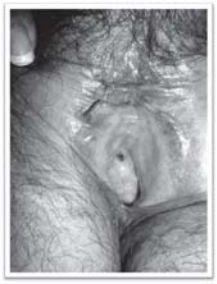
FIRST SUMMARY

- GSM and dyspareunia is common but underdiagnosed and undertreated
- Initiate the discussion with ALL of your patients
- Many safe and effective treatments

Beyond Sandpaper Sex…or Die Trying

GSM Symptoms

- Irritation
- Burning
- Itching
- Increased discharge or odor
- Dyspareunia
- **Vaginal and vulvar dryness**
- LUTS—dysuria, frequency, urgency



Bachmann G, et al. *Up to Date.* 2012; Grady D. *N Engl J Med.* 2006; Kingsberg S, et al. *Int J Women's Health*. 2009; Portman DJ et al JSM 2014

Gynecological Cancers and Breast Cancer

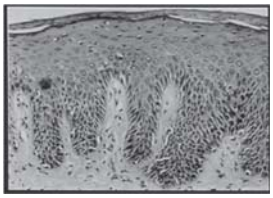
- **Vaginal atrophy** is often result of radiotherapy, chemotherapy and/or hormonal manipulation
- Majority of tumors are hormone-sensitive

Limited data on vaginal estrogens in women with hormone-sensitive cancers

Non-hormonal therapies preferred but often ineffective

Vaginal Consequences of Estrogen Deficiency

Vaginal Histology



Premenopause

Epithelium well-estrogenized,multi-layered with good blood supply, superficial cells rich in glycogen

Postmenopause

Estrogen-deficiency atrophy with marked thinning of epithelium, blood supply reduced, and loss of glycogen

Vaginal Maturation Index

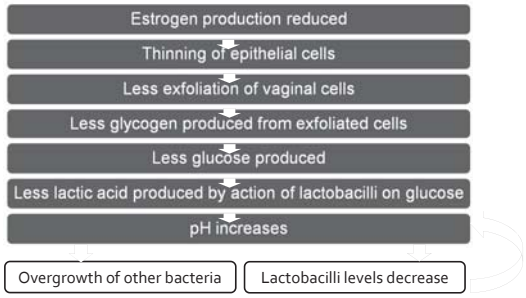
Postmenopausal vaginal epithelium:

- Superficial cells decreased
- Parabasal cells increased

	Premenopause		Postmenopause
Superficial cells	15%		1%
Intermediate cells	80%		60%
Parabasal cells	5%		39%

Freedman M. Menopause Manag. 2008;17:9-13. Reprinted with permission.

Mechanism of Vulvovaginal Atrophy

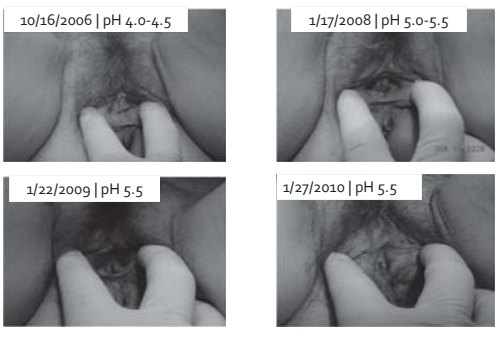


MacBride M, et al. *Mayo Clin Proc.* 2010; Krychman ML. *Medscape Ob/Gyn.* 2007.

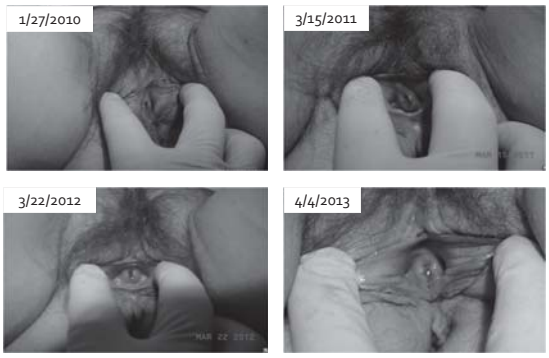
patient DS G2P2

- **Age 53** pH 4-4.5 E2=51
- **Age 55** pH 5-5.5 E2=17
- **Age 56** pH 5.5 amenorrheic 2yr

Courtesy Dr. M A Freedman



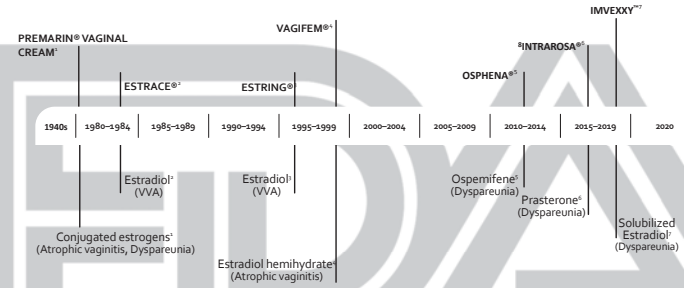
(Courtesy M Freedman)



FDA Approved Options Dyspareunia/Vulvovaginal Atrophy

- Local estrogen:
  - vaginal cream, vaginal ring, vaginal pill
- Ospemifene
- DHEA prasterone
- Solubized estradiol

FDA-Approved Treatment Options



PREMARIN, ESTRACE, ESTRING, VAGIFEM, OSPHENA and INTRAROSA are registered trademarks of their respective owners. IMVEXXY is a trademark of TherapeuticsMD, Inc.

VVA: vulvar and vaginal atrophy

1. Premarin (conjugated estrogens) prescribing information, Pfizer.
2. Estrace (estradiol) prescribing information, Allergan.
3. Estring (estradiol) prescribing information, Pfizer.
4. Vagifem (estradiol) prescribing information, Novo Nordisk Inc.
5. Osphena (ospemifene) prescribing information, Duchesnay USA, Inc.
6. Intrarosa (prasterone) prescribing information, AMAG Pharmaceuticals, Inc.
7. IMVEXXY (estradiol) prescribing information, TherapeuticsMD, Inc.

Conveying Risks and Warnings About Vaginal Estrogen Therapy

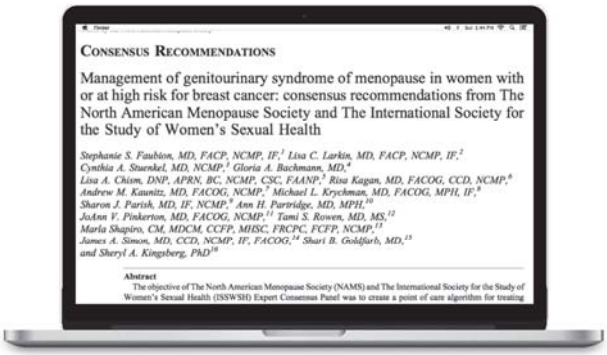
85%

Aware and concerned about safety issues with hormones

Low-dose vaginal estrogen therapy is safer than systemic therapy

Santoro N, et al. *J Sex Med.* 2009.; Grady D. N Engl J Med. *2006.;* Bachmann G, et al. *Up to Date.* 2012.

NAMS Guidelines 2018



CONSENSUS RECOMMENDATIONS

Management of genitourinary syndrome of menopause in women with or at high risk for breast cancer: consensus recommendations from The North American Menopause Society and The International Society for the Study of Women's Sexual Health

Stephanie S. Faubion, MD, FACP, NCMP, IF,[1] Lisa C. Larkin, MD, FACP, NCMP, IF,[2] Cynthia A. Stuenkel, MD, NCMP,[3] Gloria A. Bachmann, MD,[4] Lisa A. Chism, DNP, APRN, BC, NCMP, CSC, FAANP,[5] Risa Kagan, MD, FACOG, CCD, NCMP,[6] Andrew M. Kaunitz, MD, FACOG, NCMP,[7] Michael L. Krychman, MD, FACOG, MPH, IF,[8] Sharon J. Parish, MD, IF, NCMP,[9] Ann H. Partridge, MD, MPH,[10] JoAnn V. Pinkerton, MD, FACOG, NCMP,[11] Tami S. Rowen, MD, MS,[12] Marla Shapiro, CM, MDCM, CCFP, MHSC, FRCPC, FCFP, NCMP,[13] James A. Simon, MD, CCD, NCMP, IF, FACOG,[14] Shari B. Goldfarb, MD,[15] and Sheryl A. Kingsberg, PhD[16]

Abstract

The objective of The North American Menopause Society (NAMS) and The International Society for the Study of Women's Sexual Health (ISSWSH) Expert Consensus Panel was to create a point of care algorithm for treating

NAMS Guidelines

Individualize treatment based on symptoms, QoL and risk for recurrence

First Line Therapy

- **Moisturizers, lubricants, Pelvic floor PT, dilators**
- Local hormones if OK with oncologist
- Compounded vaginal estriol and testosterone **not recommended**
- Ospemifene **not studied** in women at hi risk for breast cancer

Women at high risk for breast cancer (BRCA etc)

- Local hormones reasonable for those who have failed non-hormone treatment
- Observational data suggest no increased risk of breast cancer

NAMS Guidelines for Breast Cancer Survivors

ER+ breast cancer on tamoxifen

- With severe symptoms, local hormone at low risk for recurrence

ER + breast cancer on AI

- Severe symptoms, may consider local hormones or switch to tamoxifen

Triple negative breast cancer

- Local hormone reasonable but data lacking

Women with metastatic disease

- QoL, intimacy, comfort may be priority
- Use of local hormone may be viewed differently in women with limited survival

Treatment	Product Name	Initial Dose	Maintenance Dose
Vaginal cream 17 Beta Estradiol Conjugated Estrogen	Estrace Premarin	0.5-1gm/d x 2 wk	0.5-1 gm 1-3x/wk
Vaginal Inserts Estradiol 17 Beta estradiol soft gel DHEAS prasterone	Vagifem/Yuvafem Imvexxy Intrarosa	10ug/d x 2 wk 4,10 or 25 ug/d x 2 wk 6.5 mg/d	1 twice/wk 1 twice/wk 1/d
Vaginal Ring	Estring	7.5ug/day	90 days
SERM Ospemifene	Osphena	60 mg/d	60 mg/d

Ospemifene and Dyspareunia Associated with GSM

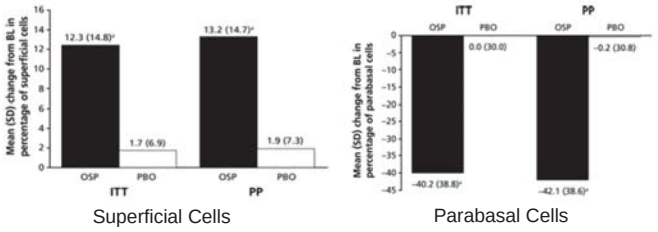
- Multicenter phase 3 randomized, double-blind 12-week efficacy and safety study
- 605 women 40-80 yrs (mean age 58) with self-reported most bothersome symptom MBS of dyspareunia
  - Ospemifene 60 mg po daily (n = 303) vs placebo (n = 303)

- Co-primary endpoints
  - pH, parabasal, superficial cells
  - Change in severity using VVA symptom questionnaire of MBS of dyspareunia

Portman DJ, Bachman GA, Simon JA. *Menopause* 2013;20(6):1-8.

Ospemifene and Dyspareunia Associated with VVA

Change in baseline to week 12



P< 0.0001 versus placebo for all

Portman DJ, Bachman GA, Simon JA. *Menopause* 2013;20(6):1-8.

Ospemifene and Dyspareunia Associated with VVA

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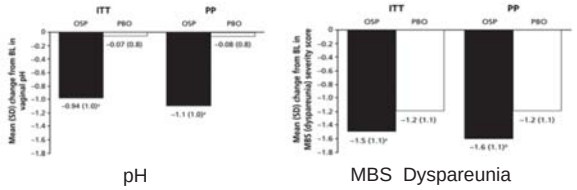
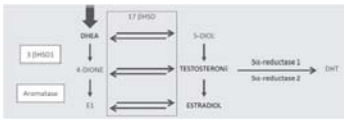


P< 0.0001 versus placebo for all

Portman DJ, Bachman GA, Simon JA. *Menopause* 2013;20(6):1-8.

INTRAROSA (prasterone) Vaginal Inserts: Putative Mechanism of Action

- The mechanism of action of INTRAROSA in postmenopausal women with vulvar and vaginal atrophy is not fully established[1]
- Prasterone is a synthetic form of the inactive endogenous steroid, DHEA
- Prasterone is converted in the body into active androgens and/or estrogens by steroidogenic enzymes such as hydroxysteroid dehydrogenases, 5α-reductases and aromatases[2]



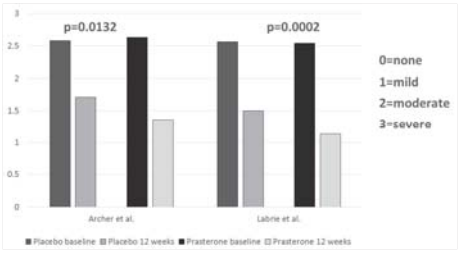
[1]INTRAROSA® Prescribing Information, AMAG Pharmaceuticals, February 2018.
[2]Labrie et al. Menopause 2016;23: 243-256.

Prasterone Efficacy: 2 Clinical Studies

	Archer et al. [1]	Labrie et al. [2]
# Patients	253	558
Age (mean, range), years	58.6 (40-75)	59.5 (40-80)
Study Length	12 weeks	12 weeks
Randomization	1:1:1 (0.25% prasterone: 0.5% prasterone: placebo)	2:1 (0.5% prasterone: placebo)
Intent-to-treat	All women receiving at least one dose of the study drug or placebo	
Co-primary endpoints (change from baseline to 12 weeks)	% Parabasal cells % Superficial cells Vaginal pH Change in dyspareunia score	

[1] Archer et al. Menopause 2015;22: 950-963.
[2] Labrie et al. Menopause 2016; 23: 243-256.

Significant Decreases in Dyspareunia with Prasterone Vaginal Inserts

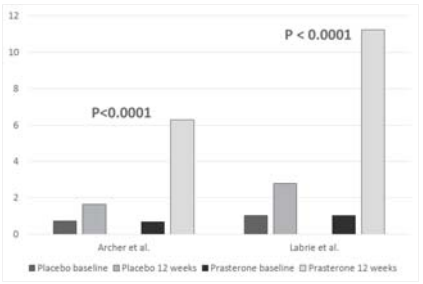


Difference from placebo: Prasterone (Week 12 mean – Baseline mean) – Placebo (Week 12 mean – Baseline mean). p-value calculation: analysis of covariance using treatment as the main factor and baseline value as the co-variate

[1] Archer et al. Menopause 2015;22: 950-963.
[2] Labrie et al. Menopause 2016; 23: 243-256.

Significant Increases in % Superficial Cells with Prasterone Vaginal Inserts

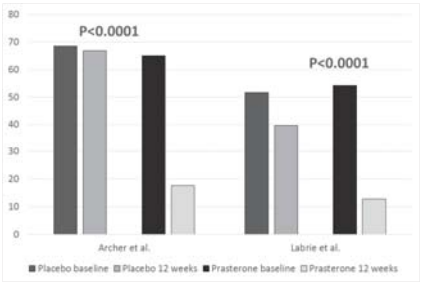
Difference from placebo: Prasterone (Week 12 mean – Baseline mean) – Placebo (Week 12 mean – Baseline mean). p-value calculation analysis of covariance using treatment as the main factor and baseline value as the co-variate



[1] Archer et al. Menopause 2015;22: 950-963.
[2] Labrie et al. Menopause 2016; 23: 243-256.

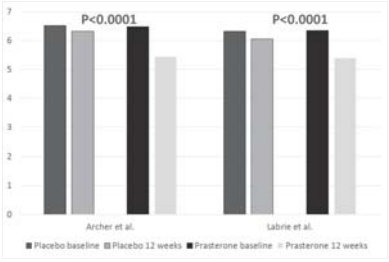
Significant Decreases in % Parabasal Cells with Prasterone Vaginal Inserts

Difference from placebo: Prasterone (Week 12 mean – Baseline mean) – Placebo (Week 12 mean – Baseline mean). p-value calculation analysis of covariance using treatment as the main factor and baseline value as the co-variate.



[1] Archer et al. Menopause 2015;22: 950-963.
[2] Labrie et al. Menopause 2016; 23: 243-256.

Significant Decreases in Vaginal pH with Prasterone Vaginal Inserts



[1] Archer et al. Menopause 2015;22: 950-963.
[2] Labrie et al. Menopause 2016; 23: 243-256.

Adverse Reactions

- 4 placebo-controlled, 12-week clinical trials (n=1,129), **vaginal discharge** was the most frequently reported adverse reaction (**5.71%** prasterone versus 3.66% in the placebo group)[1]
- In a 52-week non-comparative clinical trial (n=521), vaginal discharge was reported in 14.2% of women and **abnormal Pap smear in 2.1%**
  - 11 cases of abnormal Pap smear at 52 weeks included 1 case of low-grade squamous intraepithelial lesion (LSIL) and 10 cases of atypical cells of undetermined significance (ASCUS)
    - **5 HPV negative; 4 status unknown; 1 HPV positive[2]**

[1]INTRAROSA® Prescribing Information, AMAG Pharmaceuticals, February 2018.
[2]Data on File. ERC-230 Clinical Study Report. AMAG Pharmaceuticals 2017.

Provided as a courtesy by AMAG Pharmaceuticals, Inc. Please see full Prescribing Information.

Vaginal moisturizers: Research

- Replens has beneficial clinical effects
  - Symptomatic improvement
  - Clinical improvement
    - Dryness, pallor, mucosal thinning, petechiae and labial atrophy
- Vaginal cytology
  - Treatment with Replens increased mean cellular area, no change in maturation index
  - Replens lowers vaginal pH due to acidity and buffering capacity
  - Mean vaginal pH: **5.8-5.2 to 4.8-4.7** (12 weeks of therapy)

Bachmann GA. *Clin Pract Sex* 1991;7:1-8.
Fertil Steril 1994;61:178-80.

Hybrid Moisturizer/Lubricant

- **LUVENA**
- Prebiotics
- Lacto-peroxidase and lactoferrin
- Purportedly Inhibits candida and bacteria
- Works as both a moisturizer and a lubricant

Costantino D and Guaraldi C. *Minerva Ginecol* 2008;60(2):121-5.

Vulvar Soothing Creams—No Data

Neogyn vulvar soothing cream® (cutaneous lysate)

- >100 cytokines
- Growth factors
- Interferons and anti-inflammatory interleukins: IL-1RA, IL-4, and IL-10

**In clinical studies: improvement (vs placebo) in symptoms of vulvar pain and dyspareunia in vulvar pain patients*

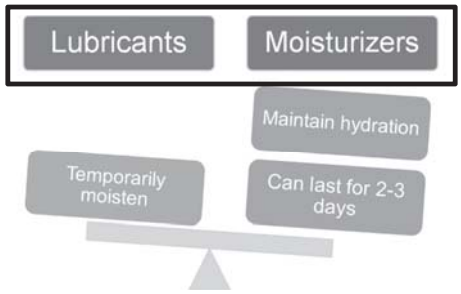
Vajuvenate

- Avocado butter, coconut oil, sunflower oil

Releveum with 4%lidocaine (Desert Harvest)

Donders G. *J Lower Genital Tract Dis* 2012;16:

Vaginal Atrophy Treatment: Non-hormonal Therapy



Marshall DD, et al. *OBG Management.* 2009; Bachmann G, et al. *Up to Date.* 2012.

Non-hormonal Therapy: Lubricants

– Local solutions that temporarily moisturize the vaginal epithelium

– Must be applied at time of intercourse

Marshall DD, et al. *OBG Management.* 2009; Bachmann G, et al. *Up to Date.* 2012; www.amazon.com; www.drugstore.com.

Avoid: Oil- and Petroleum-based Lubricants, Warming Gels, Menthols

Marshall DD, et al. *OBG* Management. 2009.

Non-hormonal Therapy: Moisturizers

– Gels or creams used regularly to maintain hydration of the vaginal epithelium for long-term relief of vaginal dryness

– Effects last two to three days

Marshall DD, et al. *OBG Management.* 2009; Bachmann G, et al. *Up to Date.* 2012; Lee YK, et al. *Obstet Gynecol.* 2011; www.amazon.com; www.drugstore.com.

TABLE Lubricants and moisturizers for treating GSM and VVA[*,6,7]

Treatment	Comments	Available products
Lubricants		
Water-based	Ingredients: deionized water, glycerin, propylene glycol; latex safe; rare irritation; dry out with extended sexual activity	Astroglide, Good Clean Love, K-Y Jelly, Natural, Organic, Pink, Sliquid, Sylk, Yes
Oil-based	Ingredients: avocado, olive, peanut, corn; latex safe; can be used with silicone products; staining; safe (unless peanut allergy); nonirritating	Coconut oil, vegetable oil, vitamin E oil
Silicone-based	Ingredients: silicone polymers; staining; typically nonirritating; long lasting; waterproof; should not be used with silicone dilators, sexual toys, or gynecologic products	Astroglide X, Oceanus Ultra Pure, Pink Silicone, Pjur Eros, Replens Silky Smooth, Silicone Premium JO, SKYN, Überlube, Wet Premium
Petroleum-based	Staining; ingredients: mineral oil, petroleum jelly, baby oil; irritating; not latex safe and not for use with cervical caps or intravaginal diaphragms	Rarely recommended
Fertility friendly	Minimize harm to sperm motility; designed for couples trying to conceive	Astroglide TTC, Conceive Plus, Pre-Seed, Yes Baby

ObGManagement April 2017

Moisturizers		
Vaginal moisturizers	For maintenance use 1 to 3 times weekly; can benefit women with dryness, chafing with ADL, and recurrent vaginal infections irrespective of sexual activity timing	Balance Active Menopause Vaginal Moisturizing Lubricant, Canesintima Intimate Moisturizer, Replens, Rephresh, Sylk Natural Intimate Moisturizer, Yes Vaginal Moisturizer
Hybrids	Properties of both water- and silicone-based products (combination of a vaginal lubricant and moisturizer); nonirritating; good option for women with allergies and sensitivities	Lubrigyn, Luvena

*Before using or recommending a product patients and their providers should check a product's pH, ingredients, and additives, and ensure the product is 510K FDA cleared.

Abbreviations: ADL, activities of daily living; FDA, US Food and Drug Administration; GSM, genitourinary syndrome of menopause; VVA, vulvovaginal atrophy.

Available Moisturizers

Product	Ingredients	Use	Price	Studies
Replens	Polycarbophil glycerin, mineral oil	Every 3 days	$17.5/14 app	Yes
LUVENA	Lactoperoxidase lactoferrin	2x/wk	$20/ 5 app	Yes
KY Liquibeads (ovules)	Dimethicone, gelatin, glycerin, dimethiconol	1-7d/wk		No
KY long lasting	Various polymers glycerin, mineral oil	2-3x/wk	$16/6 app	No
Emerita personal moisturizer	Aloe vera gel, calendula, vitamin E, ginseng, chamomile, allantoin	As needed	$16/4 oz	No
Moist again	Carbomer, aloe glycerin, chlorhexidine	As needed	$7/4 oz	No
Hyalofemme	Hyaluronic acid	7 days >2/wk	$17/30 gram	HA-yes
Pre-seed	Hydroxyethylcellulose, pluronic, arabinogalactan	As needed	$20/9 app	Yes

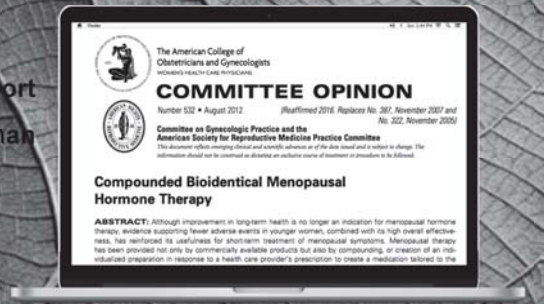
Not Effective, Not Recommended Therapies for Vaginal Atrophy

- Cooking oils
- Oral phytoestrogens
- Black cohosh
- Vaginal vitamin E
- Omega-3 supplements

Hill DA, et al. *Am Fam Physician.* 2010; Bachmann G, et al. *Up to Date.* 2012; Marshall DD, et al. *OBG Management.* 2009.

Bioidentical Hormones

No data to support they are safer than synthetic hormones


The American College of Obstetricians and Gynecologists
WOMEN'S HEALTH CARE PHYSICIANS

COMMITTEE OPINION

Number 532 • August 2012 (Reaffirmed 2016. Replaces No. 397, November 2007 and No. 322, November 2005)

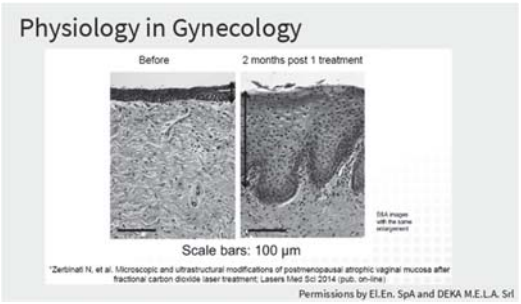
Committee on Gynecologic Practice and the American Society for Reproductive Medicine Practice Committee

Compounded Bioidentical Menopausal Hormone Therapy

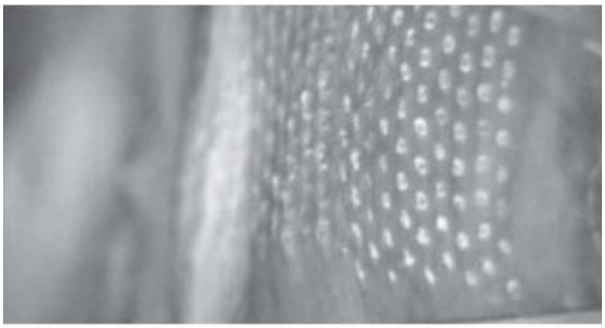
ABSTRACT: Although improvement in long-term health is no longer an indication for menopausal hormone therapy, evidence supporting fewer adverse events in younger women, combined with its high overall effectiveness, has reinforced its usefulness for short-term treatment of menopausal symptoms. Menopausal therapy has been provided not only by commercially available products but also by compounding, or creation of an individualized preparation in response to a health care provider's prescription to create a medication tailored to the

ACOG Committee on Gynecologic Practice. *Obstet Gynecol.* 2005; reaffirmed 2016.

Histologic Changes Fractional CO_2



Fractionated CO_2



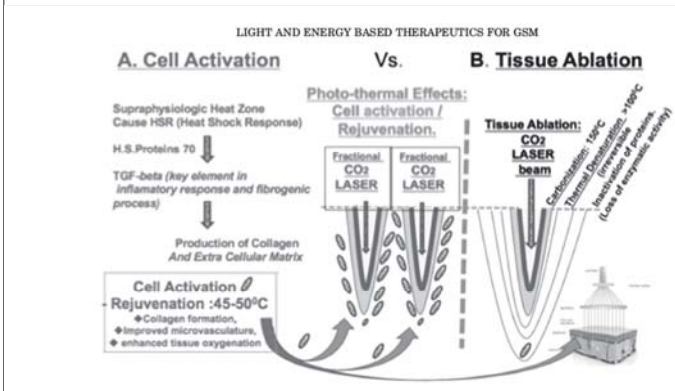
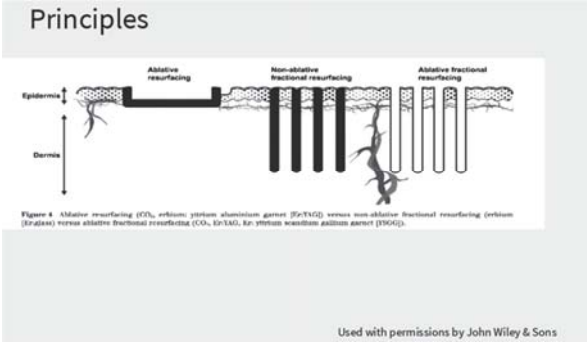
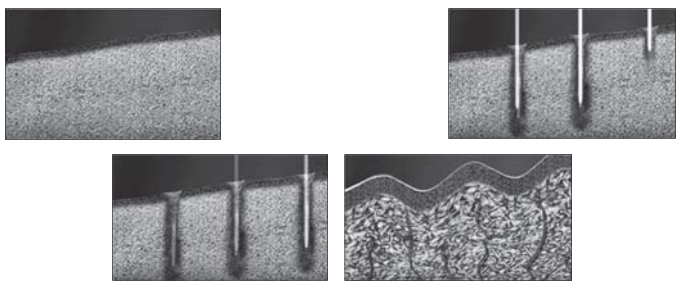


Fig. 6. (A) Fractional micro-ablation inducing cell activation and tissue rejuvenation at 45–50°C [42]. (B) Tissue ablation and thermal effects on adjacent layers (Courtesy: Tadir Y).

Ablative, Non-ablative, Fractional



Fractional Photothermolysis: Mucosa



FDA Clearance?

Incision, excision, ablation, vaporization and coagulation of body soft tissues in medical specialties, including aesthetic (dermatology & plastic surgery), podiatry, otolaryngology (ENT), **gynecology**, neurosurgery, orthopedics, geneal and thoracic surgery (including open and endoscopic), dental and oral surgery and genitourinary surgery.

FDA Notifications 30 July 2018

Venus Concept: **vaginal** health restoration

Cynosure: painful symptoms of **menopause and intimacy, penetrate vaginal wall** and stimulates cells

Alma: to improve v**aginal** irregularities, vaginal mucosa revitalization

Sciton DiVa: laser v**aginal** therapy

Thermiva: vaginal rejuvenation

InMode: Vaginal rejuvenation and urinary stress incontinence

SGS 2018 Systematic Review Group SRG

Fractional CO2 Laser

Outcome	No. Studies	Total N	Methodological Quality	Other Considerations	Evidence Quality	Effect	Outcome Importance
Vaginal Maturation Indices	1	22	1A (0)	0	Moderate	Equal	Moderate
Vaginal health index	6	319	1A, 5C (0)	0	Low	Favors laser	Moderate
Dryness	7	321	1A, 6C (-1)	0	Low	Improved	Critical
Burning	5	200	1A, 4C (-1)	0	Low	Improved	High
Dyspareunia	9	369	1A, 8C (-1)	0	Low	Improved	Critical
Dysuria	3	127	3C (-1)	-1	Low	Improved	Moderate
ICIQ - SF	1	161	1C (0)	0	Low	Improved	High
FSFI	3	128	1A, 2C (0)	-1	Low	Equal	High
Pain during insertion	2	76	2C (-1)	0	Low	Minimal	Moderate

Erbium Laser vs Estrogen

Outcome	No. Studies	Total N	Methodological Quality	Other Considerations	Evidence Quality	Effect	Outcome Importance
Dryness	2	112	1B , 1C (-1)	-2	Low	Equal	Critical
Dyspareunia	2	112	1B, 1C (-1)	-2	Low	Equal	Critical
Irritation	1	50	1B (-1)	-1	Low	Favors laser	High
Vaginal health index	1	62	1B (0)	0	Moderate	Favors laser	Moderate
Maturation value	1	50	1C (0)	-1	Moderate	Favors laser	Moderate
Vaginal pH	1	50	1C (0)	-1	Moderate	Favors laser	Moderate
ICIQ-SF	1	19	1B (0)	0	Moderate	Improved	High

Balance of Benefits and Harms

Erbium laser is not superior to local estrogen for vaginal dryness and dyspareunia

There are minimal comparative data for fractional CO2 laser

Menopause: The Journal of The North American Menopause Society
Vol. 25, No. 1, pp. 21-28
DOI: 10.1097/GME.0000000000000955
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Randomized, double-blind, placebo-controlled clinical trial for evaluating the efficacy of fractional CO_2 laser compared with topical estriol in the treatment of vaginal atrophy in postmenopausal women

Vera L. Cruz, MD,[1] Marcelo L. Steiner, MD, PhD,[2] Luciano M. Pompei, MD, PhD,[2] Rodolfo Strufaldi, MD, PhD,[2] Fernando L. Afonso Fonseca, PhD,[3] Lucila H. Simardi Santiago, MD, PhD,[4] Tali Wajsfeld, MD,[1] and Cesar E. Fernandes, MD, PhD[1,2]

Abstract

Objective: The aim of the study was to evaluate efficacy of fractional CO_2 vaginal laser treatment (Laser, L) and compare it to local estrogen therapy (Estriol, E) and the combination of both treatments (Laser + Estriol, LE) in the treatment of vulvovaginal atrophy (VVA).

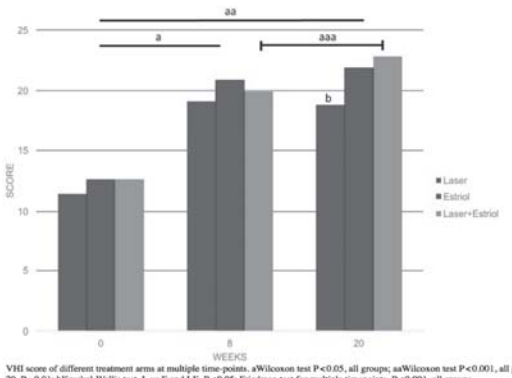
Methods: A total of 45 postmenopausal women meeting inclusion criteria were randomized in L, E, or LE groups. Assessments at baseline, 8 and 20 weeks, were conducted using Vaginal Health Index (VHI), Visual Analog Scale for VVA symptoms (dyspareunia, dryness, and burning), Female Sexual Function Index, and maturation value (MV) of Meisels.

Results: Forty-five women were included and 3 women were lost to follow-up. VHI average score was significantly higher at weeks 8 and 20 in all study arms. At week 20, the LE arm also showed incremental improvement of VHI score ($P = 0.01$). L and LE groups showed a significant improvement of dyspareunia, burning, and dryness, and the E arm only of dryness ($P < 0.001$). LE group presented significant improvement of total Female

TABLE **Comparison of VAS and FSFI scores by treatment group in a randomized trial (45 participants) by Cruz and colleagues**

VAS scores*	Laser	Estriol	Laser plus estriol	P=
Dyspareunia				
Baseline	4.9 (3.7)	3.2 (3.4)	6.5 (3.9)	.09
Week 20	0.7 (1.5)	0.2 (0.6)	0.9 (1.8)	.95
Dryness				
Baseline	8.0 (2.6)	5.6 (2.9)	7.9 (3.0)	.07
Week 20	1.4 (2.0)	0.5 (1.4)	0.3 (.07)	.35
Burning				
Baseline	3.9 (4.5)	0.9 (1.6)	4.9 (3.8)	.017[‡]
Week 20	0.5 (1.5)	0.1 (0.3)	0.4 (1.1)	.95
Total FSFI scores[b]				
Baseline	18.6 [16.4; 24.6]	23.6 [17.5; 29.8]	18.7 [7.2; 22.6] 23.6 [14.9; 28.6]	.21
Week 20	14.4 [7.8; 22.4]	25.4 [16.8; 29.3]		.10

*Items listed as mean (SD).
†Items listed as median [interquartile range].
‡P values of .05 were considered statistically significant.
§P<.06.
Abbreviations: FSFI, Female Sexual Function Index; VAS, visual analog scale.



VHI score of different treatment arms at multiple time-points. aWilcoxon test P<0.05, all groups; aaWilcoxon test P<0.001, all groups; aaaWilcoxon test, LE week 8 vs week 20, P=0.01; bKruskal-Wallis test, L vs E and LE, P<0.05; Friedman test for multiple timepoints, P<0.001, all groups.

The Vaginal Laser versus Vaginal Estrogen Therapy: The VeLVET Trial

MFR Paraiso[1], CA Ferrando[1], M Karram[2], ER Sokol[3], CR Rardin[4], CA Matthews[5], CB Iglesia[6]

Sections of Urogynecology and Reconstructive Pelvic Surgery

[1]Cleveland Clinic Cleveland, OH; [2]Christ Hospital, Cincinnati, OH; [3]Stanford University Hospital, Palo Alto, CA; [4]Women and Infants Hospital, Providence, RI; [5]Wake Forest, Winston-Salem, NC; [6]Medstar Washington Hospital Center, Washington DC

Foundation for Female Health Awareness

6 Month Outcome Data N=62

Outcome	Fractionated C02 laser N=33	Conjugated estrogen cream N=29	P value
Mean difference VAS score			
Dryness	-5.48 ± 2.68	-5.76 ± 2.48	0.67
Itching	-1.84 ± 3.01	-1.24 ± 2.96	0.45
Irritation	-3.29 ± 3.73	-3.49 ± 3.19	0.87
Dysuria	-1.4 ± 2.89	-2.11 ± 2.85	0.36
Mean difference VHI	0.9 ± 0.7	1.2 ± 0.9	0.07
Mean difference DIVA	-3.3 ± 3.2	-4.4 ± 3.1	0.18
Mean difference VMI^	3.9 ± 30.6	25 ± 22.6	0.04*
Mean difference FSFI	1.7 ± 6.7	4.9 ± 8.3	0.1
Mean difference UDI	-9.4 ± 15.7	-6.2 ± 12	0.37
% sexually active	45.5 (15)	48.3 (14)	0.82

*statistically significant at P ≤ 0.05
^remained statistically significant after controlling for confounding factors

6 Month FSFI Outcome Data N=62

	Fractionated C02 laser N=33	Conjugated estrogen cream N=29	p value
Mean difference FSFI Score1 Desire†	0.32±1.3	1.02±1.4	0.05*
Mean difference FSFI Score2 Arousal†	0.62±1.6	1.63±1.9	0.03*
Mean difference FSFI Score3 Lubrication	0.11±1.2	0.35±1.4	0.50
Mean difference FSFI Score4 Orgasm	0.37±1.3	0.9±1.6	0.17
Mean difference FSFI Score5 Satisfaction	0.88±2.1	1.7±1.7	0.50
Mean difference FSFI Score6 Pain	-0.59±2.8	-0.04±3.3	0.81

*statistically significant at P ≤ 0.05
^remained statistically significant after controlling for confounding factors
†no longer statistically significant after controlling for confounding factors

Results: Adverse Events

- 10 adverse events (AE) mild or moderate: vaginal bleeding, pain, breast tenderness, UTI, migraine, and abdominal cramping
- AEs did not differ between groups

VELVET TRIAL Conclusion

- At 6-months, fractionated Co2 vaginal laser and vaginal estrogen treatment resulted in similar improvement in GSM symptoms but lower FSFI arousal and desire scores in the laser arm
- Similar patient satisfaction in both groups
- No serious adverse events

FINAL SUMMARY

1. First line GSM
   Moisturizers, lubricants
   Pelvic PT, dilators
2. Vaginal Exercise-–with or without a partner
3. Local hormone therapy for those who failed non-hormonal tx
4. Ospemifene oral tablet
5. DHEAS
6. Involve treating oncologist for breast cancer pts
7. Compounded off-label testosterone/estriol not recommended

FINAL SUMMARY (continued)

8. Advertising Energy Based Therapy (EBT) for specific gynecologic conditions is PREMATURE
9. Early data suggests benefit for GSM but do need to discuss alternatives
10. Large scale comparative and sham trials needed

Alliance for Advancing Women's Health

www.advancingwomenshealth.org

"Attention is the most basic form of love."

Zen teacher John Tarrant

Thank you for your attention!

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@cheryliglesia

@cbiglesia

Initial Evaluation and Treatment of Infertility

In a Primary Care Setting

DATE: November 15, 2019
PRESENTED BY: Jamie Peregrine, MD, MS
Asst Professor, Reproductive Endocrinology and Infertility

Objectives

- Identify indications for seeking (in)fertility treatment
- Outline factors contributing to (in)fertility and their evaluation
- Interpret AMH results
- Contrast (in)fertility treatments by diagnosis

Infertility

- A disease defined by the failure to achieve a successful pregnancy after 12 months of appropriate, timed unprotected intercourse or therapeutic donor insemination

 ACOG Committee Opinion Number 781. Infertility Workup for the Women's Health Specialist. 2019.

Other reasons for (in)fertility evaluation/treatment

- Medical history/physical findings that justify
  - Anovulation/oligoovulation/amenorrhea
  - History/anticipated gonadotoxic exposure
- 6 months in women over 35
- Women over 40
- Need/desire for third-party reproduction
  - Donor egg/sperm/embryo
  - Gestational carrier
- Recurrent pregnancy loss
- Planned fertility preservation

Factors contributory to (in)fertility

- Male factor
- Tubal factor
- Uterine factor
- Ovulation
- Ovarian reserve

EVALUATION

- Male factor
- Tubal factor
- Uterine factor
- Ovulation
- Ovarian reserve
- Semen analysis
- Hysterosalpingogram
- Ultrasound/Exam
- History/Labs
- Ultrasound/Labs

 ACOG Committee Opinion Number 781. Infertility Workup for the Women's Health Specialist. 2019.

Histories

- Infertility duration/treatment
- OB/GYN
  - Menstrual
  - Pregnancy
  - Contraceptive
  - Coital/sexual
  - STI
  - Cervical
- Surgical/Medical/Medication
- Targeted ROS
- Family
- Exposure

Physical Exam

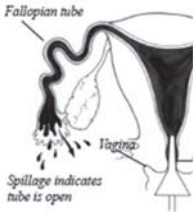
- Vitals
- Thyroid
- Breast
- Signs of androgen excess
- Pelvic

Semen Analysis

*Reference ranges vary by lab

WHO 2010, Kruger strict criteria

• Volume	1.5 mL
• Concentration	15 mil/mL
• Motility	40%
• Morphology	4%



Hysterosalpingogram

- Timing: not bleeding, pre-ovulatory
- Doxy 100 mg bid x 5 days if history of PID or hydrosalpinx

The American College of Obstetricians and Gynecologists

ACOG PRACTICE BULLETIN

Clinical Management Guidelines for Obstetrician–Gynecologists

NUMBER 195 • JUNE 2018 *(Replaces Practice Bulletin Number 104, May 2009, and Committee Opinion Number 571, September 2013)*

Committee on Practice Bulletins—Gynecology. This Practice Bulletin was developed by the Committee on Practice Bulletins—Gynecology with the assistance of David E. Soper, MD, and David Chelmow, MD.

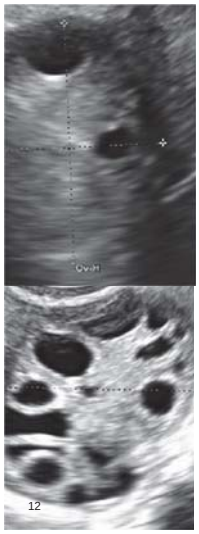
Prevention of Infection After Gynecologic Procedures

Ovulation

- Midluteal progesterone > 3 ng/ml
- Urinary LH
- Cervical mucus
- BBT
- Cycle length/ regularity/ molimina/ Mittelschmirtz

Oligo/An-

- TSH
- Prolactin
- Androgens
- Gonadotropins



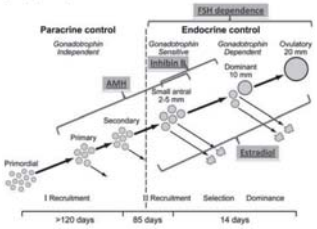
Ovarian reserve

- AMH >1 ng/mL
- FSH <10 IU/L, E2 < 60-80 pg/ml
- AFC >5-7
- Prior IVF #eggs retrieved >3

AMH as ovarian reserve marker

- Best single test – with limitations

DOES…	DOES NOT…
Modify anticipated age of menopause	Predict natural fertility/fecundability
Correlate with IVF oocyte yield/ response to gonadotropins	Reliably predict oocyte quality/ chromosome #
Vary by assay, birth control method	Show as much intracycle variance as FSH, AFC
Help set expectations	Mean someone shouldn't seek treatment



Broer et al. Clinical implications of anti-Mullerian hormone testing. Hum Reprod Update 2014.

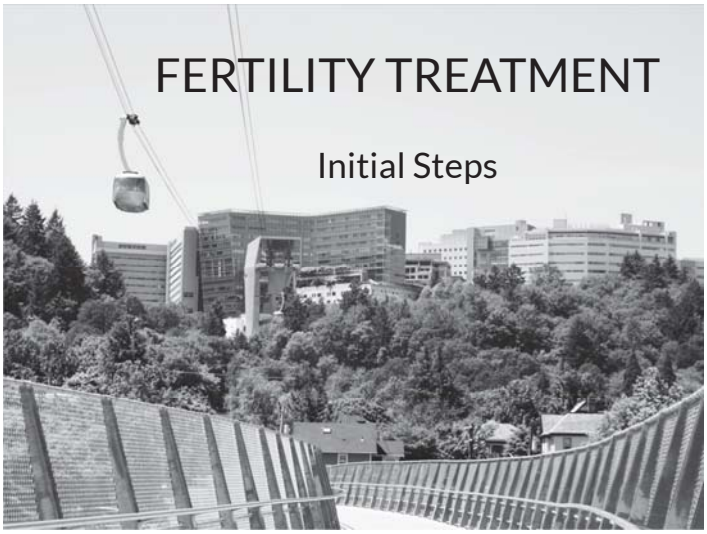
Choosing Wisely
An initiative of the ABIM Foundation

American Society for Reproductive Medicine
asrm

Ten Things Physicians and Patients Should Question

1. Routine diagnostic laparoscopy
2. Advanced sperm function tests
3. Postcoital test
4. Thrombophilia test
5. Immunological test
6. Karyotype screen
7. Prescribing testosterone to men
8. FSH to ID menopause
9. EMB for infertility
10. Prolactin w/o symptoms

http://www.choosingwisely.org/wp-content/uploads/2015/02/ASRM-Choosing-Wisely-List.pdf



Optimizing natural fertility

- Coital frequency/practices
  - Q1-2 days
  - Lubricants (mineral oil, canola oil, hydroxyethylcellulose-based)
- Fertile window
  - 3 days ending on day of ovulation
  - OPK testing limitations
- Diet/lifestyle

Optimizing natural fertility: a committee opinion. ASRM 2016. Fertil Steril 2017; 107:52-8.

Tubal surgery

- Fair evidence (in young women w/ no other significant fertility factors)
  - Tubal cannulation for proximal occlusion
  - Laparoscopic fimbrioplasty or neosalpingostomy for mild hydrosalpinges
- Good evidence
  - Removal of surgically irreparable hydrosalpinges to improve IVF rates

Role of tubal surgery in the era of ART: a committee opinion. ASRM 2015.

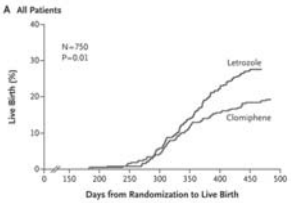
Other reproductive surgery

- In women w/ pelvic pain, visible endometriosis observed during surgery should be treated
- Limited evidence, hysteroscopic septum resection may improve outcomes when infertility or RPL present
- Fair evidence that myomectomy for cavity-distorting fibroids improves pregnancy and reduces EPL

Treatment of pelvic pain assoc with endometriosis: a committee opinion. ASRM 2014.
Uterine septum: a guideline. ASRM 2016.
Removal of myomas in asymptomatic patients to improve fertility and/or reduce miscarriage rate: a guideline. ASRM 2017

Ovulation induction

- Letrozole is first-line, off-label for OI in PCOS



- Hypogonadotropic hypogonadism should not respond to oral OI agents
- Bromocriptine or cabergoline until pregnancy for hyperprolactinemia

Legro RS et al. Letrozole versus clomiphene for infertility in the polycystic ovary syndrome. N Engl J Med. 2014;371(2):119-29.

Subclinical hypothyroid tx

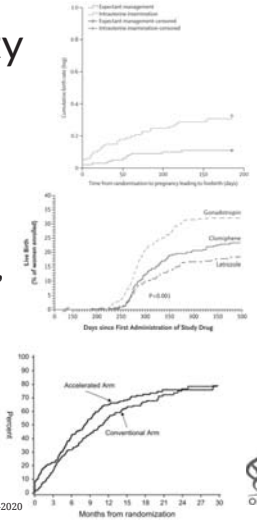
- TSH screening reasonable in infertility, diagnostic test for oligoovulation
- If >4.0 mIU/L (or >reference), treat to <2.5 mIU/L while trying to conceive
- Management of 2.5-4.0 mIU/L controversial, ASRM consider treatment, TPO Ab testing
- 2019 RCT found no difference in LB treating TPO+ women trying to conceive

Outcome		Levothyroxine Group	Placebo Group	Relative Risk or Mean Difference (95% CI)†
Primary outcome				
Live birth at ≥34 wk — no./total no. (%)		176/470 (37.4)	178/470 (37.9)	0.97 (0.83 to 1.14)
Thyrotropin concentration at baseline				0.59
≥2.5 mIU/liter	121/325	120/327		1.00 (0.83–1.22)
>2.5 mIU/liter	55/145	58/143		0.91 (0.69–1.20)

Subclinical hypothyroidism in the infertile female population: a guideline. ASRM 2015.
Dhillon-Smith et al. Levothyroxine in Women with Thyroid Peroxidase Antibodies before Conception. N Engl J Med. 2019;380(14):1316-25.

Unexplained infertility

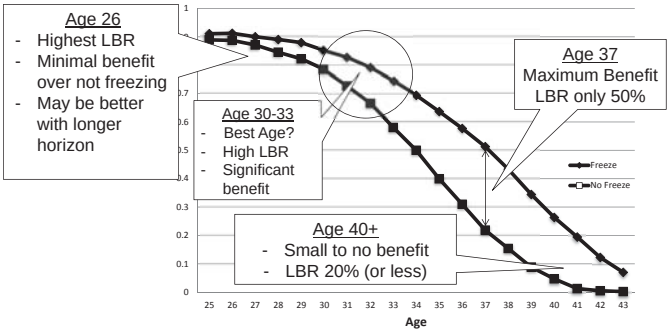
- IUI w/o OS and OS w/o IUI not more effective than expectant management
- Oral OS + IUI > expectant
  - CC 100 – IUI best studied, LTZ – IUI equivalent
- IVF as next step generally recommended over gonadotropin-IUI



Farquhar et al. TUI trial. Lancet 2018.
Diamond et al. AMIGOs trial. NEJM 2015.
Reindollar et al. FASTT trial. Fertil Steril 2010.
ASRM Guideline on Treatment of Unexplained Infertility expected 2019-2020

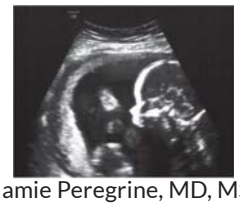
At what age should planned oocyte cryo be considered?

Assume: 7 years between potential egg freezing and attempting conception, WOULD use donor sperm if not married



Adapted from Mesen et al. Optimal timing for elective egg freezing. Fertil Steril 2015.

Thank You



Jamie Peregrine, MD, MS
peregrin@ohsu.edu
University Fertility Consultants: 503-418-3700
Direct office line: 503-418-8137
Cell/text: 949-413-0337

Cleaning Up the Mesh

Examining the History of Transvaginal Mesh Use in Urogynecology

DATE: NOVEMBER 15, 2019 PRESENTED BY: IAN FIELDS, MD

Disclosures

- none

Learning Objectives

1. Describe the evolution of transvaginal mesh use in urogynecology from its introduction in 1996 to present practice.
2. Understand recent Food and Drug Administration (FDA) warnings regarding transvaginal mesh and their implications on incontinence and prolapse repair surgeries.
3. Identify recent trends in mesh-augmented prolapse repair and anti-incontinence surgeries.

Let's Start With a Quiz

Turn on the TV

www.cbs.com

Turn to Google

Surgeons fear pelvic mesh lawsuits will spook patients
https://www.modernhealthcare.com › article › NEWS › surgeons-fear-pelv...
Jan 11, 2019 - Doctors who specialize in female **pelvic** medicine say lawsuits by four states over products used to treat **pelvic** floor disorders might scare ...

What does pelvic mesh do and why are women suing over it ...
https://www.theguardian.com › aug › vaginal-pelvic-mesh-explainer
Aug 31, 2017 - Urogynaecological **mesh** is used to treat stress incontinence and **pelvic** organ prolapse – and its use has triggered class actions in the US, UK ...

FDA Halts All Sales of Vaginal Mesh Products - WebMD
https://www.webmd.com › Women's Health › News
Apr 16, 2019 - The companies will have 10 days to submit plans to withdraw these products from the market, the FDA said. Most **pelvic mesh** products have ...

Transvaginal Mesh - UCLA Female Pelvic Medicine and ...
obgyn.ucla.edu › ... › Services
Transvaginal **Mesh** Removal and **Mesh** Related Complications.

F.D.A. Halts U.S. Sales of Pelvic Mesh, Citing Safety Concerns ...
https://www.nytimes.com › 2019/04/16 › health › vaginal-pelvic-mesh-fda

Go outside

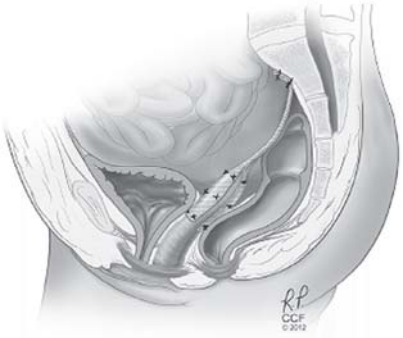
https://www.meshmedicaldevicenewsdesk.com/mesh-injured-speak-their-truth-to-urogynecologists/

History of Mesh in Surgery

- 1894 – silver coils
- 1900 – silver filigrees
- 1948 – tantalum gauze
- 1952 – stainless steel
- 1954 – Fortisan
- 1956 – polyester
- 1957 – polyvinyl
- 1958 - polypropylene

https://collection.cooperhewitt.org/objects/18679167/
www.gynsurgery.org/meshesh-pros-and-cons

Abdominal Sacrocolpopexy



https://www.researchgate.net/figure/Robotic-assisted-abdominal-sacrocolpopexy-RASC-mesh-secured-from-the-vagina-to-the_fig2_288022327

Abdominal Sacrocolpopexy

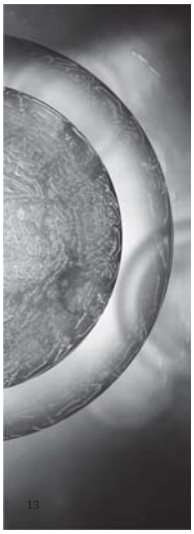
Transvaginal Mesh

FDA Medical Device Regulation

- **Class I**
  - Bandages, gloves, surgical instruments
  - Approval: Labeling, Good Manufacturing
- **Class II**
  - Catheters, wheelchairs, LSC trocars, mesh kits for SUI and POP
  - Approval: 510K process
- **Class III**
  - Cardiac pacemakers, interstim, urethral bulking
  - Approval: Premarket Approval Study

FDA 510(k) Process

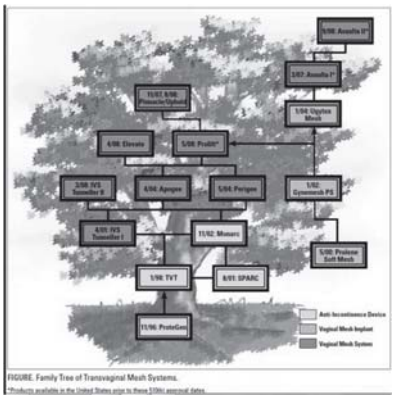
- No trials; no requirement of clinical safety or efficacy
- Allows the FDA to determine whether a device is equivalent to a device already placed on the market
  - Termed **predicate devices**
- Predicate devices – on the market prior to May 1976



It all begins in 1996

Boston Scientific

https://www.mpo-mag.com/contents/view_top30/2016-07-19/12-boston-scientific/



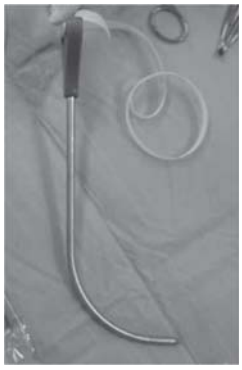
https://www.meshmedicaldevicenewsdesk.com/family-tree-of-meshes-from-the-female-patient-april-2009/

FDA Enforcement Report

Issued March 17, 1999

"Use of the ProteGen in the treatment of female urinary incontinence associated with a higher than expected rate of vaginal erosion and dehiscence, and appears not to function as intended"

Where we meshed up



The IVS Tunneler
Approved in April 2001 – treatment of POP

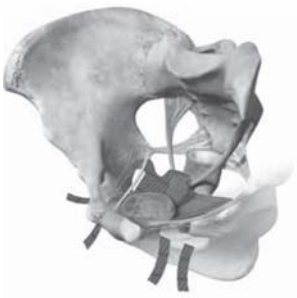
https://www.researchgate.net/figure/S-Tunneller-with-polypropylene-tape_fig2_8068891

Where we meshed up

The Perigee system

https://www.pinterest.com/pin/313281717822680570/

Where we meshed up



膣前壁

The ProLift system

https://www.meshmedicaldevicenewsdesk.com/mesigian-prolift-pelvic-mesh-trial-underway-in-philadelphia/

The Lawsuits Begin

FDA MAUDE Database

Manufacturer and User Facility Device Experience Database - (MAUDE)

www.fda.gov

FDA MAUDE Database

Rank	Adverse Events	# of MDRs	Percentile Rate
1	Erosion	528	35.1%
2	Pain	472	31.4%
3	Infection	253	16.8%
4	Bleeding	124	8.2%
5	Dyspareunia	108	7.2%
6	Organ Perforation	88	5.8%
7	Urinary Problems	80	5.3%
8	Neuro-muscular problems	38	2.5%
9	Vaginal scarring (41)/ Shrinkage (2)	43	2.8%
10	Recurrence, Prolapse	32	2.1%

www.fda.gov

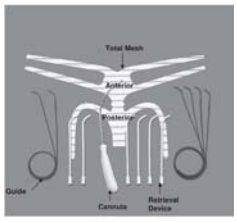
FDA Public Health Notification

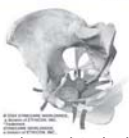
FDA Public Health Notification: Serious Complications Associated with Transvaginal Placement of Surgical Mesh in Repair of Pelvic Organ Prolapse and Stress Urinary Incontinence

Issued: October 20, 2008

http://www.amiform.com/web/documents-risques-op-coelio-vagi/fda-notification-about-vaginal-mesh.pdf

2010 – Prolift RCT Stopped





https://www.semanticscholar.org/paper/Vaginal-Mesh-Kits-for-Pelvic-Organ-Prolapse%2C-Friend-Moore-Miklos/608f625b30edfcfcfbc968a18539ad5baa9583e7

FDA Update – July 2011

UPDATE on Serious Complications Associated with Transvaginal Placement of Surgical Mesh for Pelvic Organ Prolapse: FDA Safety Communication

https://www.burgsimpson.com/wp-content/uploads/2018/03/FDA-safety-communication-pelvic-mesh.pdf

Obstetrics & Gynecology Device Panel – September 2011

www.fda.gov

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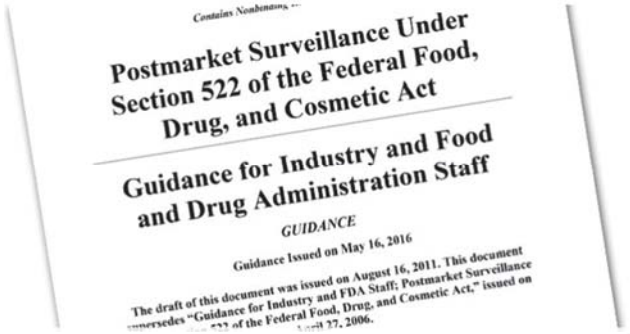
Postmarket Surveillance



Contains Nonbinding ...

Postmarket Surveillance Under Section 522 of the Federal Food, Drug, and Cosmetic Act

Guidance for Industry and Food and Drug Administration Staff

GUIDANCE

Guidance Issued on May 16, 2016

The draft of this document was issued on August 16, 2011. This document supersedes "Guidance for Industry and FDA Staff; Postmarket Surveillance ... 522 of the Federal Food, Drug, and Cosmetic Act," issued on ... 27, 2006.

www.fda.gov

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AUGS 2012 Guidelines

Guidelines for Providing Privileges and Credentials to Physicians for Transvaginal Placement of Surgical Mesh for Pelvic Organ Prolapse

American Urogynecologic Society's Guidelines Development Committee

www.augs.org

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Vaginal Placement of Synthetic Mesh for Pelvic Organ Prolapse

The American College of Obstetricians and Gynecologists
Women's Health Care Physicians

COMMITTEE OPINION

Number 513 • December 2011

Committee on Gynecologic Practice

This document reflects emerging clinical and scientific advances as of the date issued and is subject to change. The information should not be construed as dictating an exclusive course of treatment or procedure to be followed.

American Urogynecologic Society
Advancing Female Pelvic Medicine and Reconstructive Surgery

www.acog.org

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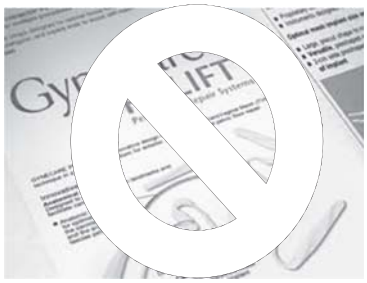
Gynecare Prolift Recalled



www.schmidtlaw.com

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FDA NEWS RELEASE

FDA strengthens requirements for surgical mesh for the transvaginal repair of pelvic organ prolapse to address safety risks

www.acog.org

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Outside the United States

Blog.storyhunter.com

Pelvic Floor Disorders Registry

Pelvic Floor Disorders Registry PFDR

The PFD Registry is supported in part by:

ACell ASTORA WOMEN'S HEALTH Boston Scientific Advancing science for life™ Coloplast

Blog.storyhunter.com

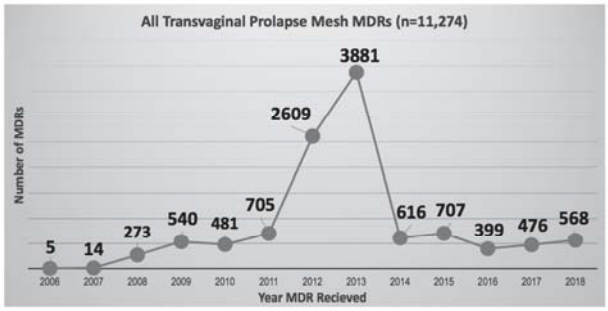
FDA NEWS RELEASE

FDA takes action to protect women's health, orders manufacturers of surgical mesh intended for transvaginal repair of pelvic organ prolapse to stop selling all devices

Boston Scientific Xenform

FDA, Coloplast, and Boston Scientific websites

Where Are We Now?



www.fda.gov

Top 10 Medical Device Reports

	Patient Problem	Count
1	Pain	3717
2	Erosion/Exposure	3509
3	Infection	1794
4	Injury	1701
5	Incontinence	814
6	Scar Tissue	761
7	Bleeding	475
8	Infection, Urinary Tract	371
9	Disability	339
10	Neurological Deficit/Dysfunction	272

www.fda.gov

AUGS Best Practice Statement

AUGS Best Practice Statement: Evaluation and Counseling of Patients With Pelvic Organ Prolapse

FEMALE PELVIC MEDICINE & RECONSTRUCTIVE SURGERY

ACOG Practice Bulletin

The American College of Obstetricians and Gynecologists
WOMEN'S HEALTH CARE PHYSICIANS

AUGS
Advancing Female Pelvic Medicine and Reconstructive Surgery

COMMITTEE OPINION

Number 694 • April 2017

Committee on Gynecologic Practice
American Urogynecologic Society

This Committee Opinion was developed by the American College of Obstetricians and Gynecologists' Committee on Gynecologic Practice and the American Urogynecologic Society.

This document reflects emerging clinical and scientific advances as of the date issued and is subject to change. The information should not be construed as dictating an exclusive course of treatment or procedure to be followed.

Management of Mesh and Graft Complications in Gynecologic Surgery

What About Slings?

AUGS
Advancing Female Pelvic Medicine and Reconstructive Surgery

SUFU
Society of Urodynamics, Female Pelvic Medicine & Urogenital Reconstruction

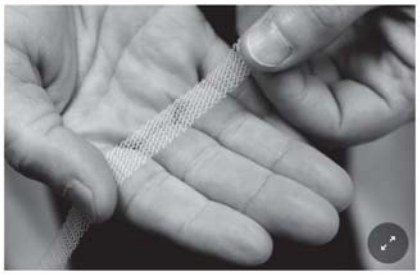
Position Statement

This Position Statement was developed by a joint task force between the American Urogynecologic Society (AUGS) and the Society for Urodynamics, Female Pelvic Medicine and Urogenital Reconstruction (SUFU). This document reflects clinical and scientific advances as of the date issued and is subject to change. The information should not be construed as dictating an exclusive course of treatment or procedure to be followed.

Mesh Midurethral Slings for Stress Urinary Incontinence

Beware!

Two Men Charged in Pelvic Mesh Removal Scheme



www.nytimes.com

Where Does Blame Lie?

- Industry?
  - Marketing before R&D
- Regulatory Bodies?
  - 510(k) process
- Physicians?
  - Efficacy unclear
- Academics?
  - Insufficient safety data

https://www.dougtedder.com/2015/02/26/dont-point-that-finger-at-me/

Take Home Point

- Transvaginal mesh kits now banned by the FDA.
- Polypropylene mesh midurethral sling remains the standard of care for surgical management of symptomatic stress urinary incontinence.
- Mesh placed abdominally for the treatment of pelvic organ prolapse (ie. Sacrocolpopexy) has not been restricted or banned by the FDA.

OHSU Physician Advice & Referral Service
- 503-494-4567
- 800-245-6478 (toll-free)

Thank You

Ethical Frameworks for *Doing* Shared Decision Making

A How-To Guide

DATE: November 15, 2019 PRESENTED BY: Michele Megregian, CNM

Objectives

- Describe the concept of shared decision making and how its definition and implementation have changed over time
- Be familiar with strategies for implementing optimal shared decision making in clinical practice
- Understand the relationship between evidence-based guidelines, new research findings, and shared decision making.

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 AUGUST 9, 2018 VOL. 379 NO. 6

Labor Induction versus Expectant Management in Low-Risk Nulliparous Women

"These results suggest that policies aimed at the avoidance of elective labor induction among low-risk nulliparous women at 39 weeks of gestation are unlikely to reduce the rate of cesarean delivery on a population level; the trial provides information that can be incorporated into discussions that rely on principles of shared decision making."

Society for Maternal-Fetal Medicine

July 2019

Shared decision-making when counseling women about elective IOL is critical.

SMFM Statement on Elective Induction of Labor in Low-Risk Nulliparous Women at Term: the ARRIVE Trial

Society of Maternal-Fetal (SMFM) Publications Committee

The American College of Nurse-Midwives strongly endorses the need for shared decision-making and equitable access to evidence-based information to use in discussions between childbearing families and their health care providers

ACNM Responds to Release of ARRIVE Trial Study Results: Acknowledges Quality of Study but Raises Concerns about Potential for Misapplying Results

FOR IMMEDIATE RELEASE: Thursday, August 9, 2018

Practice Advisory: Clinical guidance for integration of the findings of The ARRIVE Trial: Labor Induction versus Expectant Management in Low-Risk Nulliparous Women

ACOG The American College of Obstetricians and Gynecologists

…this recommendation may be conditional upon the values and preferences of the pregnant woman, the resources available (including personnel), and the setting in which the intervention will be implemented. A collaborative discussion with shared-decision making should take place with the pregnant woman.

Planned early delivery or expectant management for late preterm pre-eclampsia (PHOENIX): a randomised controlled trial

Chappell et al, 2019

"In conclusion, our trial supports offering initiation of delivery in women with late preterm pre-eclampsia. The trade-off of lower maternal morbidity and severe hypertension against higher neonatal unit admissions, albeit without additional respiratory or other morbidity, should be discussed with women with late preterm preeclampsia to allow shared decision making on timing of delivery."

Prevention of Group B Streptococcal Early-Onset Disease in Newborns ACOG CO #782 July 2019 *

"may be reasonable to offer … may consider discussing the option … as a shared decision making process in this clinical scenario"

ROUTE OF DELIVERY IN WOMEN WITH A LOW-LYING PLACENTA UpToDate®

The optimal route for delivery of pregnancies where the distance between the placental edge and internal os is 0 to 20 mm is debatable. The fetal head may tamponade the adjacent placenta, thus preventing hemorrhage.

"However, this is a shared decision…"

What do Women Say?

- Conversations **prenatally** about possible interventions
  - Decision Aids

- **Inclusion** in decision-making during labor
  - Staff training in communication and SDM techniques

Original Research ajog.org

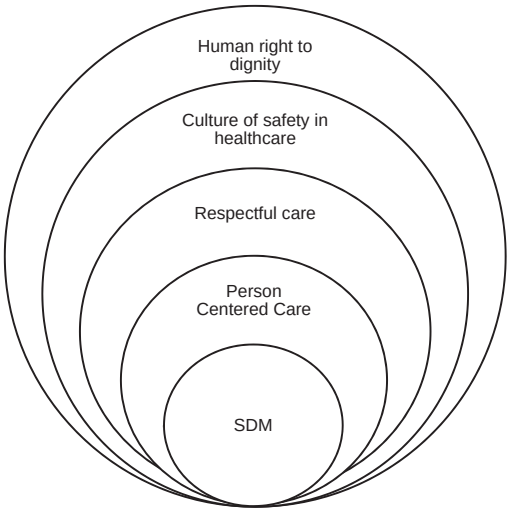
OBSTETRICS

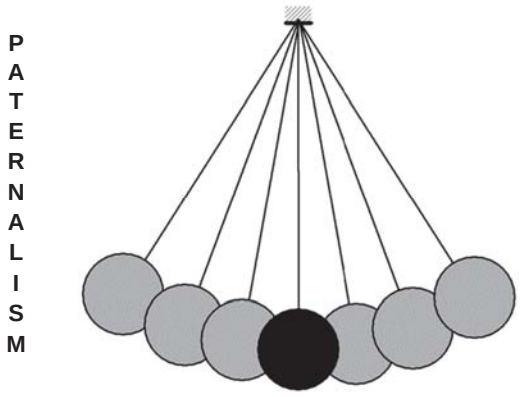
The maternal childbirth experience more than a decade after delivery

Carla M. Bossano, MD; Kelly M. Townsend, MS; Alexandra C. Walton, BS; Joan L. Blomquist, MD; Victoria L. Handa, MD, MHS

CONCLUSION: Maternal satisfaction with childbirth is influenced by mode of delivery. The birth experience leaves an impression on women more than a decade after delivery.

- **Debriefing**





Shared Decision Making

Clinically Appropriate Patient

Decision Aid

Preference Sensitive Condition

Decision Aids in Maternity Care

↓ Anxiety → **↓ Decisional Conflict** → **↑ Knowledge**

↑ Informed Choice → **↑ Satisfaction** → **? Final Choice / Outcome**

Preference Sensitive Condition

- More than one clinically appropriate intervention or strategy option exists
- Expectant management
- Each option has varying benefits and drawbacks
- Person's values and preferences should be critical in determining the chosen intervention.
- Evidence-based recommendations
- Risk perception & risk tolerance

Sharing … ?

Provider	Woman
Biases	Risk perception
Preferences	Risk tolerance
Expertise	Values / Goals

Legare et al 2013

Reasons to...			
Plan a repeat cesarean birth	How much does it matter to you?	**Plan a vaginal birth (VBAC)**	How much does it matter to you?
You can know the date your baby will be born	★★★★★	You have a greater chance of having a vaginal birth	★★★★★
You know what to expect from the surgery	★★★★★	You have a greater chance of having an easier recovery and a shorter stay in the hospital	★★★★★
You have a smaller chance of having a tear in the scar on your uterus	★★★★★	You have a smaller chance of problems after surgery, such as infection, blood clots, or hysterectomy	★★★★★
Your baby has a smaller chance of very rare but serious complications from uterine rupture	★★★★★	You have a greater chance of having uncomplicated pregnancies in the future (fewer placenta problems)	★★★★★
You have a greater chance of avoiding labour altogether	★★★★★	You have a greater chance of having your baby with you after the birth (less admission to the nursery)	★★★★★
	★★★★★		★★★★★
	★★★★★		★★★★★
TOTAL STARS:	Repeat Cesarean =		VBAC =

SDM in practice

SDM-Q9

- Validated questionnaire
- Measures involvement in decision making process from provider's perspective
- Preference Sensitive Condition

Driever et al 2019

Control Preferences Scale (CPS)

- Originally designed to assess patients' preferences in decision making (1997)
- Active Role (Patient)
  - Informative Role (Provider)
- Collaborative Role
  - Shared Decision Making
- Passive Role (Patient)
  - Paternalistic Role (Provider)

SDMQ-9 DOC

1. I made clear to my patient that a decision needs to be made.
2. I wanted to know exactly from my patient how he/she wants to be involved in making the decision.
3. I told my patient that there are different options for treating his/her medical condition.
4. I precisely explained the advantages and disadvantages of the treatment options to my patient.
5. I helped my patient understand all the information.
6. I asked my patient which treatment option he/she prefers.
7. My patient and I thoroughly weighed the different treatment options.
8. My patient and I selected a treatment option together.
9. My patient and I reached an agreement on how to proceed.

completely disagree ❑ strongly disagree ❑ somewhat disagree ❑ somewhat agree ❑ strongly agree ❑ completely agree ❑

*Adapted with permission; the SDM-Q-9 DOC is licensed under the Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License

I make it clear that a decision needs to be made						
Strongly Agree	Agree	Somewhat Agree	Neither	Somewhat Disagree	Disagree	Strongly Disagree
6 (30%)	7 (35%)	5 (25%)	1 (5%)	1 (5%)	0	0

I want to know exactly how my pt wants to be involved in DM						
Strongly Agree	Agree	Somewhat Agree	Neither	Somewhat Disagree	Disagree	Strongly Disagree
8 (40%)	7 (35%)	2 (10%)	2 (10%)	1 (5%)	0	0
I select a treatment option with my patients						
Strongly Agree	Agree	Somewhat Agree	Neither	Somewhat Disagree	Disagree	Strongly Disagree
11 (55%)	5 (25%)	1 (5%)	1 (5%)	2 (10%)	0	0

Control Preference Scale: Provider Preferred vs Usual Role

- Informative Role
  - The patient makes the final decision about …
  - The patient makes the final decision about … , but after considering my opinion.
- Shared Role
  - The patient and I share responsibility for making a final decision about …
- Paternalistic Role
  - I make the final decision about … , but after considering the patient's opinion.
  - I make the final decision about …

INDUCTION OF LABOR

	Preferred Role	Actual Role
Informative	10 (53%)	14 (74%)
Shared	9 (47%)	4 (21%)
Paternalistic	0 (0%)	1 (5%)

ASA PROPHYLAXIS

	Preferred Role	Actual Role
Informative	9 (47%)	10 (53%)
Shared	10 (53%)	6 (31%)
Paternalistic	0 (0%)	3 (16%)

ACTIVE MANAGEMENT TSL

	Preferred Role	Actual Role
Informative	7 (37%)	9 (47%)
Shared	7 (37%)	7 (37%)
Paternalistic	5 (26%)	3 (16%)

DOING SHARED DECISION MAKING

Team Talk
- Describe idea of choice & options
- Ask about goals

Options Talk
- Risk communication
- Self Efficacy

Decision Talk
- Make recommendations
- Check/clarify understanding

Elwyn et al BMJ 2017;359:j4891 doi.org/10.1136/bmj.j4891

Screening for Decisional Conflict

- **S**ure: do you feel sure about the best decision for you?
- **U**ninformed: do you know the benefits/risks of each option?
- **R**isk/Benefit Ratio: are you clear about which benefits or risks matter more to you?
- **E**ncourage: do you have enough support to make a decision?

Next Steps

- Reflection: What is your preferred role in decision making?
- Preferred Sensitive Conditions?
- Authors: if you recommend SDM, identify the key points
- Guideline influencers: Decision Aids!

References

- Begley, et al. Shared decision-making in maternity care: Acknowledging and overcoming epistemic defeaters. J Eval Clin Pract. 2019;1–8.
- Van der Weijden, et al. How can clinical practice guidelines be adapted to facilitate shared decision making? A qualitative key-informant study. BMJ Qual Saf 2013;22:855–863
- Légaré, et al. Interventions for increasing the use of shared decision making by healthcare professionals. Cochrane Database of Systematic Reviews 2018, Is 7
- Land, et al. Communication practices that encourage and constrain shared decision making in health-care encounters: Systematic review of conversation analytic research. Health Expectations. 2017;20:1228–1247
- Beach M, Sugarman J. Realizing Shared Decision-making in Practice. JAMA, 2019 322(9):811-812

References

- Moore, et al. Moving Toward Patient-Centered Care: Women's Decisions, Perceptions, and Experiences of the Induction of Labor Process. 2014 Birth 41:138-146
- Stevens, et al. Patient decision aids in routine maternity care: Benefits, barriers, and new opportunities. 2016 Women and Birth 29: 30–34
- Schwarz, et al. Women's perceptions of induction of labour outcomes: Results of an online-survey in Germany. Midwifery, 2016 35:3–10
- Driever, et al. Shared decision making: physicians' preferred role, usual role and their perception of its key components. PEC, 2019
- Degner, et al. The Control Preference Scale. Canadian Journal of Nursing Research, 1997 29(3):21-43

OHSU

Thank You

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Maternal Morbidity & Mortality

Taking Action on the State Level

DATE: MONTH 22, 2015 PRESENTED BY: RACHEL PILLIOD, MD

Disclosures

- CDC Cooperative agreement NU58DP006358
- AIM Participation

Learning Objectives

1. Describe the trends in maternal morbidity and mortality over the last 20 years and the growing disparities in health outcomes.
2. Understand the purpose of state based quality improvement efforts in perinatal care
3. Identify the current and planned statewide initiatives run by the Oregon Perinatal Collaborative

Why all the fuss… now?

- 19th Century – 7 deaths per 100 births
- 20th Century
  - Home to hospital
  - Aseptic technique
  - Antibiotics
  - Oxytocin
  - Transfusion medicine
  - Antihypertensive medications
- Improvements in Europe, US & Canada

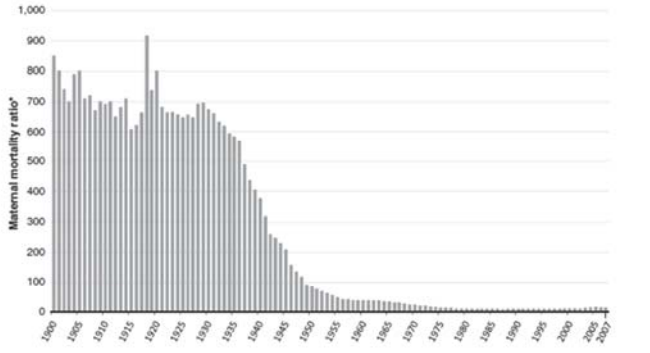
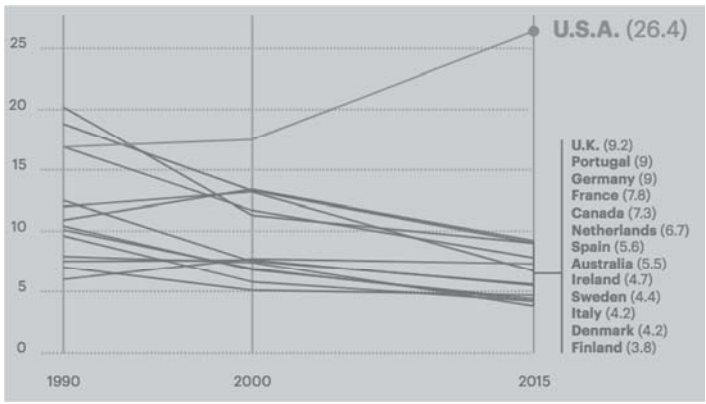


FIGURE 1. Maternal mortality in the United States: 1900 to 2007. *Number of maternal deaths per 100,000 live births per year. Data from the National Center for Health Statistics available at: http://wonder.cdc.gov.



Lancet, 2015 & graphics courtesy ProPublica

Pro-Publica & National Focus

- MFMU: 4/34 initiatives primarily target women, while 24 aimed at infants
- Title V Maternal Child Health Block Grants: 6% of grants in 2016 aimed at women, 78% for infants and children
- Medicaid Funding & Pregnancy Care
  - Eligibility thresholds
  - Documentation status & CHIP
  - Postpartum cut offs
- Joint Commission Perinatal Core Measures
  - 1/6 focused on maternal health (CS rates)

How do we know what we know?

- Pregnancy-Related Death (CDC) – the death of a woman while pregnant or within 1 year of pregnancy termination, regardless of the duration or site of the pregnancy, from any cause related to or aggravated by the pregnancy or its management, but not from accidental or incidental causes
- Pregnancy-Related Death (WHO) – the death of a woman while pregnant or within 42 days of termination of pregnancy, irrespective of cause of death

How do we know what we know?

- Pregnancy-Related Mortality Ratio (CDC) – an estimate of the number of pregnancy-related deaths for every 100,000 live births
- Maternal Mortality Ratio (WHO) – The number of maternal deaths per 100,000 live births

How do we know what we know?

- Current methods to identify maternal deaths are problematic...

National Center for Health Statistics

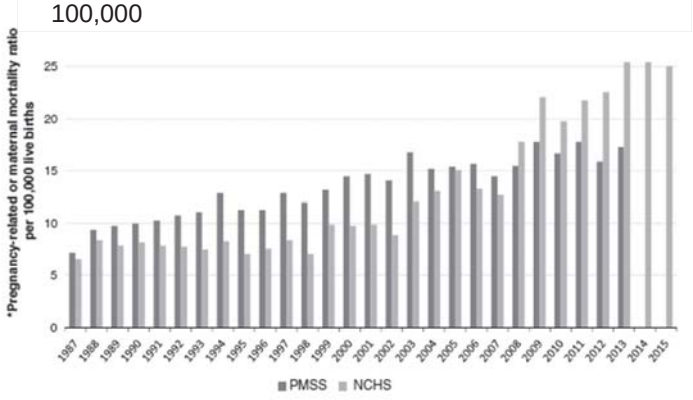
NVSS National Vital Statistics System

Mortality Data

Pregnancy Mortality Surveillance System

Creanga, Clin Obstet & Gynecol. 2018

- ~700 die annually in the US (PMSS data)
- Overall PRMR 16.7 pregnancy related deaths per 100,000



Petersen EE, et al. MMWR, 2019, *Creanga, Clin Obstet & Gynecol. 2018*

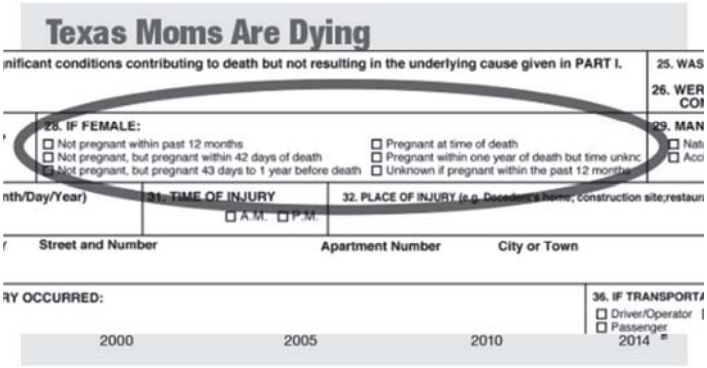
Can we believe the trend?

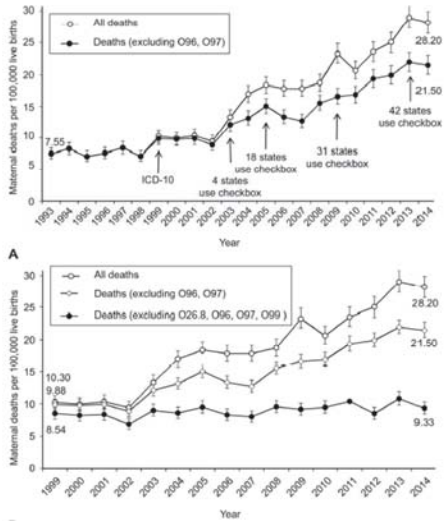
- We are more sick
- Socioeconomic factors
- CS rates
- Selection bias for CPD overcome by CS
- Disparities in care and outcomes

Improvement in ascertainment methods?
- 2003 Death Certificate Check Box
- ICD-9→ICD-10

Creanga, Clin Obstet & Gynecol. 2018

Why Texas Is the Most Dangerous U.S. State to Have a Baby





Joseph, Obstet Gynecol, 2018

Can we believe the trend?

- We are more sick
- Socioeconomic factors
- CS rates
- Selection bias for CPD overcome by CS
- Disparities in care and outcomes

Improvement in ascertainment methods?

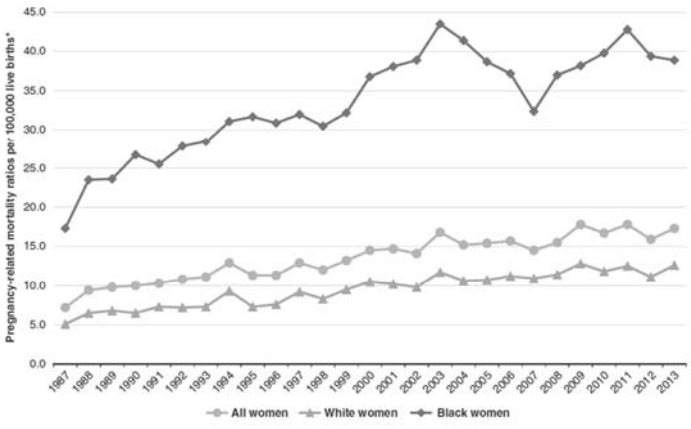
Despite uncertainty: risk of death during and shortly after pregnancy from pregnancy related causes has not declined in the US for more than 25 years

Causes of Maternal Death

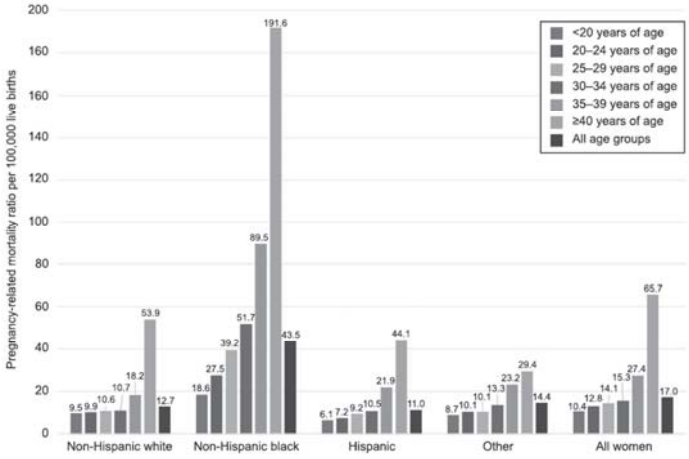
- Serious morbidity vs mortality
- The when matters (<42 days, within 1 year)
- The where matters
- The who matters: age, education, marital status, insurance status

Race || Ethnicity || Nativity

For Serena Williams, Childbirth Was a Harrowing Ordeal. She's Not Alone.



Creanga, Clin Obstet & Gynecol. 2018



Creanga, Obstet & Gynecol. 2017

Racial/Ethnic Disparities

- NH black women 3-4 times more likely to die from pregnancy related causes than NH white women
- Native Americans, Native Alaskans, Asians/Pacific Islanders, Latina women also face disparities
- Regional variation: 12 fold higher risk of pregnancy related death for NHB than NHW
- For every maternal death, 100 women suffer a severe obstetric morbidity, life threatening diagnosis or undergo a lifesaving procedure during hospitalization

Peterson, MMWR, 2019
Howell, Clin Obstet & Gynecol. 2018

Differences in leading cause of Death

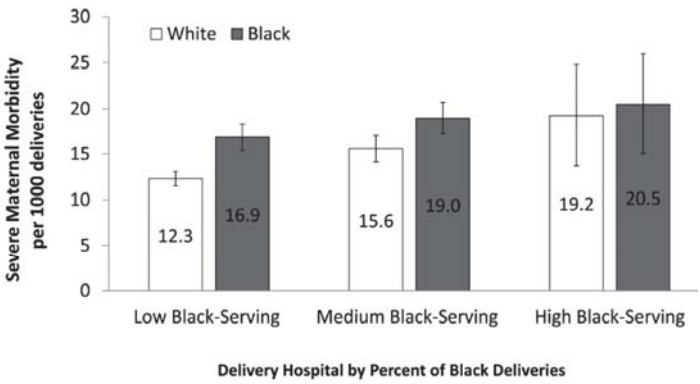
Non-Hispanic white	**Non-Hispanic black**
1. CV conditions(15.5%)	1. Cardiomyopathy (14.0%)
2. Hemorrhage (14.4%)	2. CV conditions (12.8%)
3. Infection (13.4%)	3. Pre-/eclampsia (11.6%)
4. Mental Health (11.3%)	4. Hemorrhage (10.5%)
5. Cardiomyopathy (10.3%)	5. Embolism (9.3%)

CDC, 9 MMRCs. 2018

Disparities in Maternal Mortality

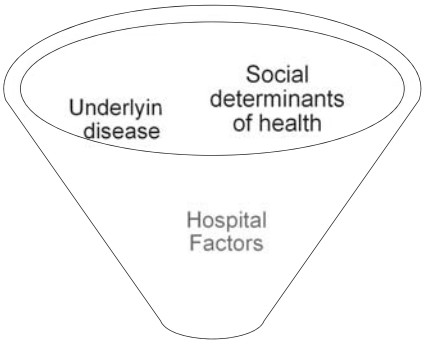
- NH black case fatality rate 2.4-3.3 times higher than that of NH white women for:
  - Preeclampsia
  - Eclampsia
  - Placental abruption
  - Placenta previa
  - Postpartum hemorrhage

Tucker, Am J Public Health. 2007



Howell, AJOG. 2016

Disparities in Maternal Mortality



Maternal Mortality

So what is being done?

- Fellowship Training
  - ICU, L&D, D&C Training
- CDC & HRSA Funding
- Public Awareness & Quality Metrics
- Maternal Levels of Care (LOCATe)
- Maternal Mortality Review Committees (MMRCs)
- Growth of Perinatal Quality Collaboratives (PQC)

The Joint Commission

Prepublication Requirements

• Issued August 21, 2019 •

New Standards for Perinatal Safety

APPLICABLE TO THE HOSPITAL ACCREDITATION PROGRAM

Effective July 1, 2020

Provision of Care, Treatment, and Services (PC) Chapter

PC.06.01.01

Reduce the likelihood of harm related to maternal hemorrhage.

Levels of Maternal Car

- Introduced by SMFM and ACOG in 2015
- Four designations for maternity care hospitals based on nursing, provider, and facility resources

Level I: Basic Care

Level II: Specialty Care

Level III: Subspecialty Care

Level IV: Regional Perinatal Care

- Hospital volume & Access to specialty providers are known to affect obstetric outcomes
- States are beginning to implement the levels of maternal care but limited data exists yet on their utility or ability to improve maternal care

Clapp; AJOG 2018

Weight	Conditions
5	Severe preeclampsia/eclampsia Chronic congestive heart failure
4	Congenital heart disease Pulmonary hypertension
3	Chronic ischemic heart disease Sickle cell disease Age >44
2	Cardiac valvular disease Systemic lupus erythematosus Human immunodeficiency virus Mild or unspecified preeclampsia Drug abuse Placenta previa Age 40-44
1	Chronic renal disease Pre-existing hypertension Previous cesarean delivery Gestational hypertension Alcohol abuse Asthma Pre-existing diabetes mellitus Age 35-39

Significant interaction between patient risk and hospital acuity --> patient outcomes

Risk ratio of experiencing SMM among high-risk patients was ***greater*** in low acuity hospitals compared to high acuity hospitals, supporting the concept of regionalization

Patient comorbidity risk	Hospital, adjusted risk ratio (95% confidence interval)	
	Low acuity	High acuity
Low	Reference	Reference
Intermediate	1.53 (1.33–1.77)	1.57 (1.49–1.65)
High	9.55 (6.83–13.35)	6.50 (5.95–7.09)

Clapp; AJOG 2018

Maternal Mortality Review

- 1930 -- New York Academy of Medicine & Philadelphia County Medical Society
- 1968 – 44 states + DC
- 2012 – 18 states + Philadelphia
- 2019 – 34 states + Philadelphia & NYC
  - *Planning: 10 states + Puerto Rico*

Slide courtesy Julie Zaharatos, CDC

Maternal Mortality Review

	CDC – National Center for Health Statistics (NCHS)	CDC – Pregnancy Mortality Surveillance System (PMSS)	Maternal Mortality Review Committees
Data Source	Death certificates	Death certificates linked to fetal death and birth certificates	Death certificates linked to fetal death and birth certificates, **medical records, social service records, autopsy, informant interviews…**
Time Frame	During pregnancy – 42 days	During pregnancy – 365 days	During pregnancy – 365 days
Source of Classification	ICD-10 codes	Medical epidemiologists (PMSS-MM)	**Multidisciplinary committees**
Terms	Maternal death	Pregnancy associated, (Associated and) Pregnancy related, (Associated but) Not pregnancy related	Pregnancy associated, (Associated and) Pregnancy related, (Associated but) Not pregnancy related
Measure	Maternal Mortality Rate - # of Maternal Deaths per 100,000 live births	Pregnancy Related Mortality Ratio - # of Pregnancy Related Deaths per 100,000 live births	Pregnancy Related Mortality Ratio - # of Pregnancy Related Deaths per 100,000 live births
Purpose	Show national trends and provide a basis for international comparison	Analyze clinical factors associated with deaths, publish information that may lead to prevention strategies	**Understand medical and non-medical contributors to deaths, prioritize interventions that effectively reduce maternal deaths**

Passive Surveillance *Active Surveillance*

Slide courtesy Julie Zaharatos, CDC

Maternal Mortality Review

- Authority to access data
- Confidentiality and protection of collected data, proceedings and activities
- Immunity for committee members
- Regular reporting and dissemination of findings
- Multidisciplinary committee with local input

Maternal Mortality Review

Slide courtesy Julie Zaharatos, CDC

Maternal Mortality Review

79th OREGON LEGISLATIVE ASSEMBLY--2018 Regular Session

Enrolled

House Bill 4133

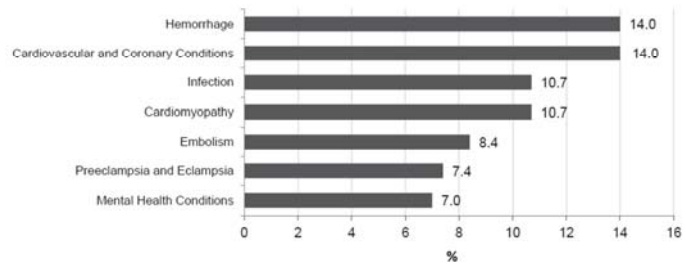
Sponsored by Representative KENY-GUYER, Senator STEINER HAYWARD, Representative BYNUM, Senator FREDERICK; Representatives ALONSO LEON, HAYDEN, HERNANDEZ, MALSTROM, MARSH, NOBLE, PARRISH, POWER, SALINAS, SANCHEZ, SMITH DB, Senators DEMBROW, JOHNSON, MONNES ANDERSON, ROBLAN (Presession filed.)

Maria I. Rodriguez, MD, MPH – Chair

17 Cases for review

MMRC -9 states

Figure 4. Leading Underlying Causes of Pregnancy-Related Deaths*

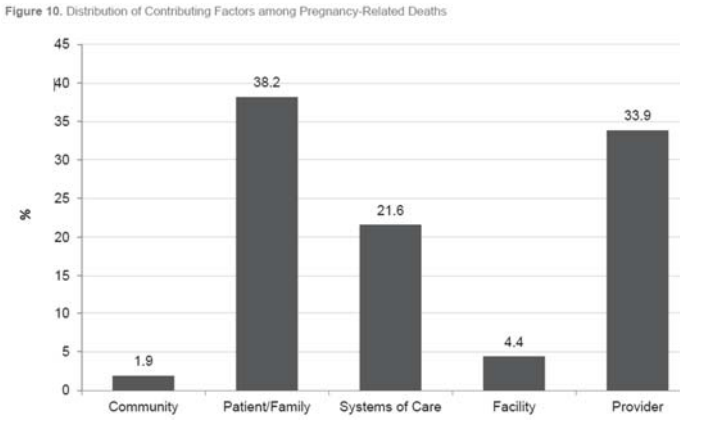


CDC, 9 MMRCs. 2018

MMRC – 9 States

Figure 9. Distribution of Preventability Among Pregnancy-Related Deaths, by Timing in Relation to Pregnancy

CDC, 9 MMRCs. 2018



CDC, 9 MMRCs. 201

The Birth of PQCs

Vermont Oxford Network

California Perinatal Quality Care Collaborative

CMQCC Sets the Standard

Maternal data center with 200 hospitals representing 90% of California births

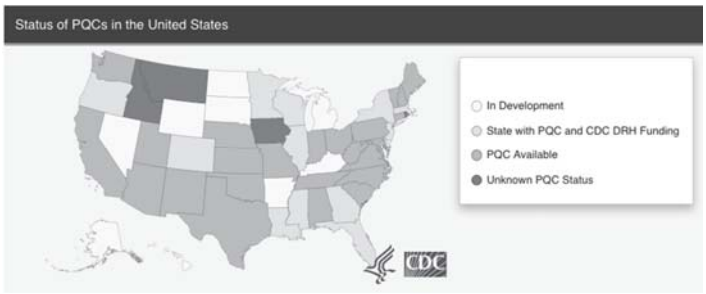
- QI improvement projects, toolkits
  - Hemorrhage
  - Venous thromboembolism
  - Severe hypertension
  - Reducing disparities
- Reduced Maternal Mortality Ratio by 55% from 16.9 in 2006 to 7.3 in 2013

Ozimek, Obstet Gynecol Clin N Am. 2018

COUNCIL ON PATIENT SAFETY IN WOMEN'S HEALTH CARE

safe health care for every woman

- Maternal Mental Health: Depression and Anxiety
- Maternal Venous Thromboembolism (+AIM)
- Obstetric Care for Women with Opioid Use Disorder (+AIM)
- Obstetric Hemorrhage (+AIM)
- Postpartum Care Basics for Maternal Safety
  - From Birth to the Comprehensive Postpartum Visit (+AIM)
  - Transition from Maternity to Well-Woman Care (+AIM)
- Prevention of Retained Vaginal Sponges After Birth
- Reduction of Peripartum Racial/Ethnic Disparities (+AIM)
- Safe Reduction of Primary Cesarean Birth (+AIM)
- Severe Hypertension in Pregnancy (+AIM)



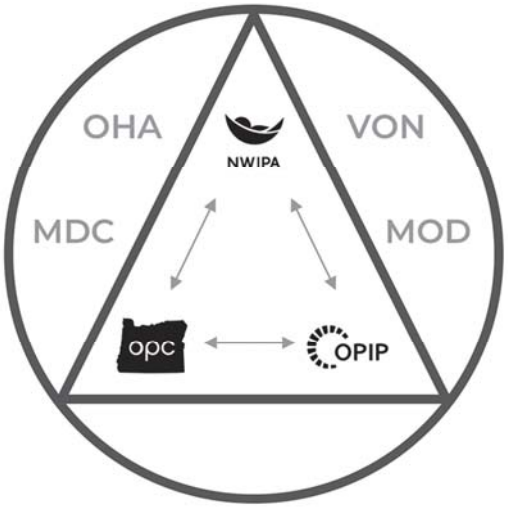
Success of California and other leading states

- 2017 Additional CDC Funding – 13 states: Colorado, Delaware, Florida, Georgia, Illinois, Louisiana, Massachusetts, Minnesota, Mississippi, New Jersey, New York, **Oregon**, Wisconsin
- National Network of Perinatal Collaboratives

OPC Vision

Everyone in Oregon will have access to and receive high-quality maternal and neonatal care to optimize health.

OPC Mission: We work together to advocate for improved maternal and childhood health outcomes through collaboration, implementation of evidence-based practices, and policy change throughout the state of Oregon.



Where

- ~700 die annually in the US (PMSS data)
- Overall PRMR 16.7 pregnancy related deaths per 100,000

ProPublica: Advice From Mothers Who Almost Died

Illian Kumagai/ProPublica, icons by Gregor Cresnar/Noun Project

"If you have a hemorrhage, don't clean up after yourself! Make sure the doctor is fully aware of how much blood you are losing. I had a very nice nurse who was helping to keep me clean and helping to change my (rapidly filling) pads. If the doctor had seen the pools of blood himself, rather than just being told about them, he might not have been so quick to dismiss me."

— Valerie Bradford, 30, survived hemorrhage in 2016

"While my doctor was amazing, **we live in a smaller town and they don't carry enough blood/platelets on hand for very emergent situations**. They have patients shipped to larger hospitals when they need more care. Had I been aware of that we would have decided to deliver at a larger hospital so in case something happened to me or our daughter we wouldn't be separated, which we were when I was life-flighted out."

— Kristina Landrus, 26, survived hemorrhage in 2013

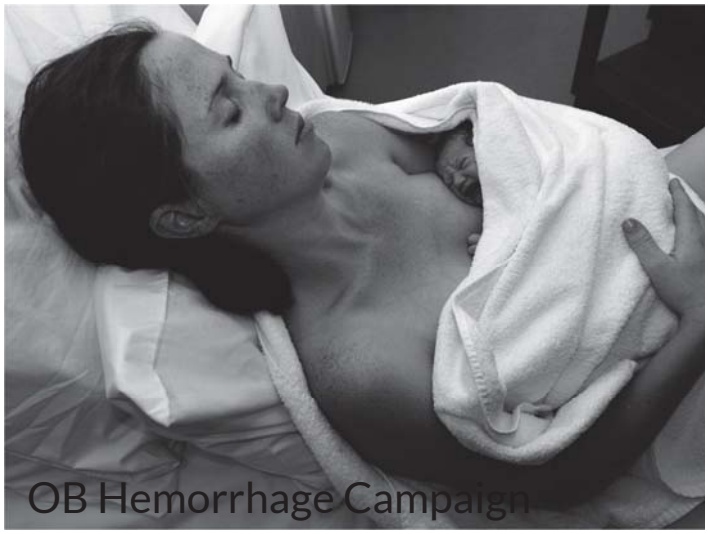
"Key pieces of information every woman should know before choosing a hospital are: What are their safety protocols for adverse maternal events? No one likes to think about this while pregnant, and providers will probably tell you that it's unlikely to happen. But it does happen and it's good to know that the hospital and providers have practiced for such scenarios and have protocols in place."

— Marianne Drexler, 39, survived hemorrhage and hysterectomy in 2014

Provider Fall Out – the 2nd Victims

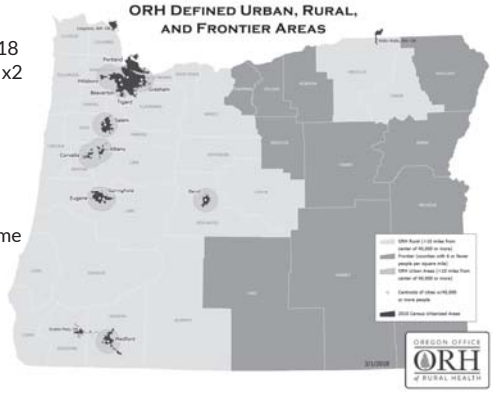
"No matter how much you fool yourself you are over something, and maybe even though I hadn't thought of it for months, I had that woman's name seared into my memory and as soon as I saw that name, my chest was up in my throat."

"I still think about it. Just randomly you forget and then something will happen and it just pops into your head. You go over it again, what could I have done differently, what could I have said, what should I have done?"



Oregon at a Glance
- ~42,600 births 2018
- Birthrate declined x2 years
- 2026 (deaths > births)

Unique Populations
- Community or Home Births
- Rural | Frontier | Critical Access



OB Hemorrhage Statewide Launch

September 2018 – Perinatal Summit (VTE, HTN, IOL, Hemorrhage)

March 2019 – Steering Group Convened

May 2019 – AIM State Application

June-August 2019 – Planning, materials, generating interest

July-August 2019 – Baseline survey

48 Hospitals w/OB Service Lines
- 22 responded
- 18 expressed interest
- 55% of births statewide

15 community birth providers
- Largely from independent practices, not birth center based facilities
- QI Experience
- Majority have policies which are followed most of the time (range 25-100%)
- Majority kept statistics, most referenced MANA stats.

Total Births		County
Adventist	777	Multnomah
Asante – Ashland	253	Jackson
Asante Rogue Regional Medical Center	1606	Jackson
Good Samaritan Regional Medical Center	940	Benton
Samaritan Albany General Hospital	536	Linn
Samaritan Lebanon Community Hospital	281	Linn
Samaritan North Lincoln Hospital	145	Lincoln
Samaritan Pacific Communities Hospital	164	Lincoln
Harney District Hospital	39	Harney
Kaiser Westside Medical Center	1527	Washington
Legacy Emanuel Medical Center	1826	Multnomah
Legacy Good Samaritan Medical Center	984	Multnomah
Legacy Meridian Park Medical Center	961	Clackamas
Legacy Mt Hood Medical Center	915	Multnomah
Legacy Silverton Medical Center	1346	Marion
Mercy Medical Center	857	Douglas
Providence Medford Medical Center	476	Jackson
Providence Portland Medical Center	2882	Multnomah
Providence Seaside Maternity Services	95	Clatsop
Salem Health	3386	Marion
Tuality Community Hospital	577	Washington
Willamette Valley Medical Center	427	Yamhill
Oregon Health & Science University	2291	Multnomah

OB Hemorrhage Statewide Launch

September 2018 – Perinatal Summit (VTE, HTN, IOL, Hemorrhage)

March 2019 – Steering Group Convened

May 2019 – AIM State Application

June-August 2019 – Planning, materials, generating interest

July-August 2019 – Baseline survey

September 2019 – Follow up, letter of commitment, speaking engagements

October 28-29th– Statewide kickoff & Team training

INITIATIVE LAUNCHED!

Key Elements of Participating

- ☐ Identify a multidisciplinary team at your hospital to actively champion bundle implementation
- ☐ Assure Zoom capability (Zoom allows users to meet virtually. Click on below link for a short tutorial
- ☐ Commit to attend at least 80% of the OB Hemorrhage sessions (at least one member of team on each session)
- ☐ Commit to present at least one patient or systems case per team (include amount of times / frequency participants will be expected to present once determined by the group)
- ☐ Meet monthly as a hospital team to review your progress and data
- ☐ Attend the OPC annual summit in Oregon City on Monday 10/28/19 (as many as possible from your team)
- ☐ Attend the OB Hemorrhage AIM half-day in Portland on Tuesday 10/29/19 (at least team lead)

opc Oregon Perinatal Collaborative

Obstetric Hemorrhage Initiative Toolkit

A Collaborative Quality Improvement Initiative with the Alliance for Innovation in Maternal Health and the Centers for Disease Control and Prevention

HRSA Maternal & Child Health | Alliance for Innovation on Maternal Health | March of Dimes | CDC

Readiness
- Domain 1: Hemorrhage Cart / Kit
- Domain 2: Medication Access
- Domain 3: Obstetric Emergency Response Team
- Domain 4: Massive Transfusion Protocols
- Domain 5: Education & Unit-Based Drills
- Educational Tools
- Simulation & Unit-Based Drills

Recognition & Prevention
- Domain 1: Hemorrhage Risk Assessment
- Domain 2: Quantification of Blood Loss
- Domain 3: Active Management of Third Stage of Labor

Response
- Domain 1: Emergency Plan
- Domain 2: Patient, Family & Staff Support

Reporting & Systems Learning
- Domain 1: Briefs, Huddles & Debriefs
- Domain 2: Severe Obstetric Hemorrhage Review
- Domain 3: Process, Structure & Outcome Measures

CHECKLIST:
One Time Only
Are these elements in place?
If already in place, have we reviewed them?

Quarterly: Education & Drill/Simulation Efforts

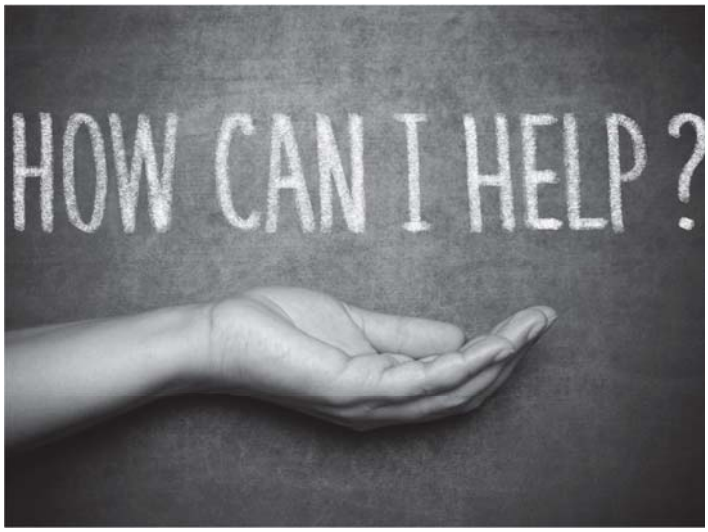
Monthly Case Review:
Is screening & QBL happening?
Are briefs & debriefs happening?
Any issues you are succeeding or struggling in?

Data Trend:
Comagine/OMDC

OB Hemorrhage Initiative

- 18 Structure Measures (Once)
- 5 Process Measures (Quarterly)
  - Unit Drills
  - Provider Education
  - Nursing Education
  - Risk Assessment
  - QBL
- 4 Outcome Measures (Monthly)
  - SMM
  - SMM, excluding transfusions
  - SMM among hemorrhage cases
  - SMM excluding transfusions among hemorrhage cases

Adventist	Multnomah
Asante – Ashland	Jackson
Asante Rogue Regional Medical Center	Jackson
Good Samaritan Regional Medical Center	Benton
Samaritan Albany General Hospital	Linn
Samaritan Lebanon Community Hospital	Linn
Samaritan North Lincoln Hospital	Lincoln
Samaritan Pacific Communities Hospital	Lincoln
Kaiser Sunnyside Medical Center	Clackamas
Kaiser Westside Medical Center	Washington
Legacy Emanuel Medical Center	Multnomah
Legacy Good Samaritan Medical Center	Multnomah
Legacy Meridian Park Medical Center	Clackamas
Legacy Mt Hood Medical Center	Multnomah
Legacy Silverton Medical Center	Marion
Oregon Health & Science University	Multnomah
Providence Portland Medical Center	Multnomah
Providence Seaside Maternity Services	Clatsop
Salem Health	Marion
Tuality Community Hospital	Washington



OB Hemorrhage

- Join!
- Thought leadership/cultural shift
- Refer your patients
- Spread the word
- Implicit bias training

Other Projects

- Opioid Use Disorder
- Family Well Being Assessment & Social Determinants of Health
- Rural Health & OB Ready Projects
- Maternal Levels of Care

www.oregonperinatalcollaborative.org

Thank you

opc

OHSU

ALLIANCE FOR INNOVATION ON MATERNAL HEALTH AIM

HRSA Maternal & Child Health

MARCH OF DIMES

Comagine Health

CDC Centers for Disease Control and Prevention

PROVIDENCE Health & Services Oregon and Southwest Washington

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Thank You