Excess Adiposity in Pregnant People: Implications for Physiology, Labor, & Birth

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ACNM WEBINAR

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Learning Objectives

1. Describe current estimates of excess adiposity in pregnancy within the U.S. population.

2. Understand the basic pathophysiology of excess adiposity during pregnancy, including its influence on cervical and uterine preparation for labor, uterine contractility during labor, and other structures essential for labor/birth.

3. Understand how excess adiposity during pregnancy affects pregnancy outcomes, including labor duration and birth.

4. Describe how excess maternal adiposity during pregnancy influences the course of labor induction, including strategies that the midwife can adapt to optimize outcomes in this population.

Acknowledgements

BMI = Adiposity?

BMI = Adiposity?

BMI has only limited usefulness as a predictor of lipotoxicity in pregnancy

Roughly 30% of 'normal weight' BMI = metabolic syndrome

Roughly 30% of 'obese' BMI = healthy metabolism

Discrepancy between BMI and adiposity is worst in Black females

Body fat percentage is probably a better measure than BMI (data coming…)

Use of the term obesity

Excess Adiposity in Pregnant People

Figure 1. Prepregnancy obesity, by maternal race and Hispanic origin: United States, 2016–2019

Non-Hispanic black[1]
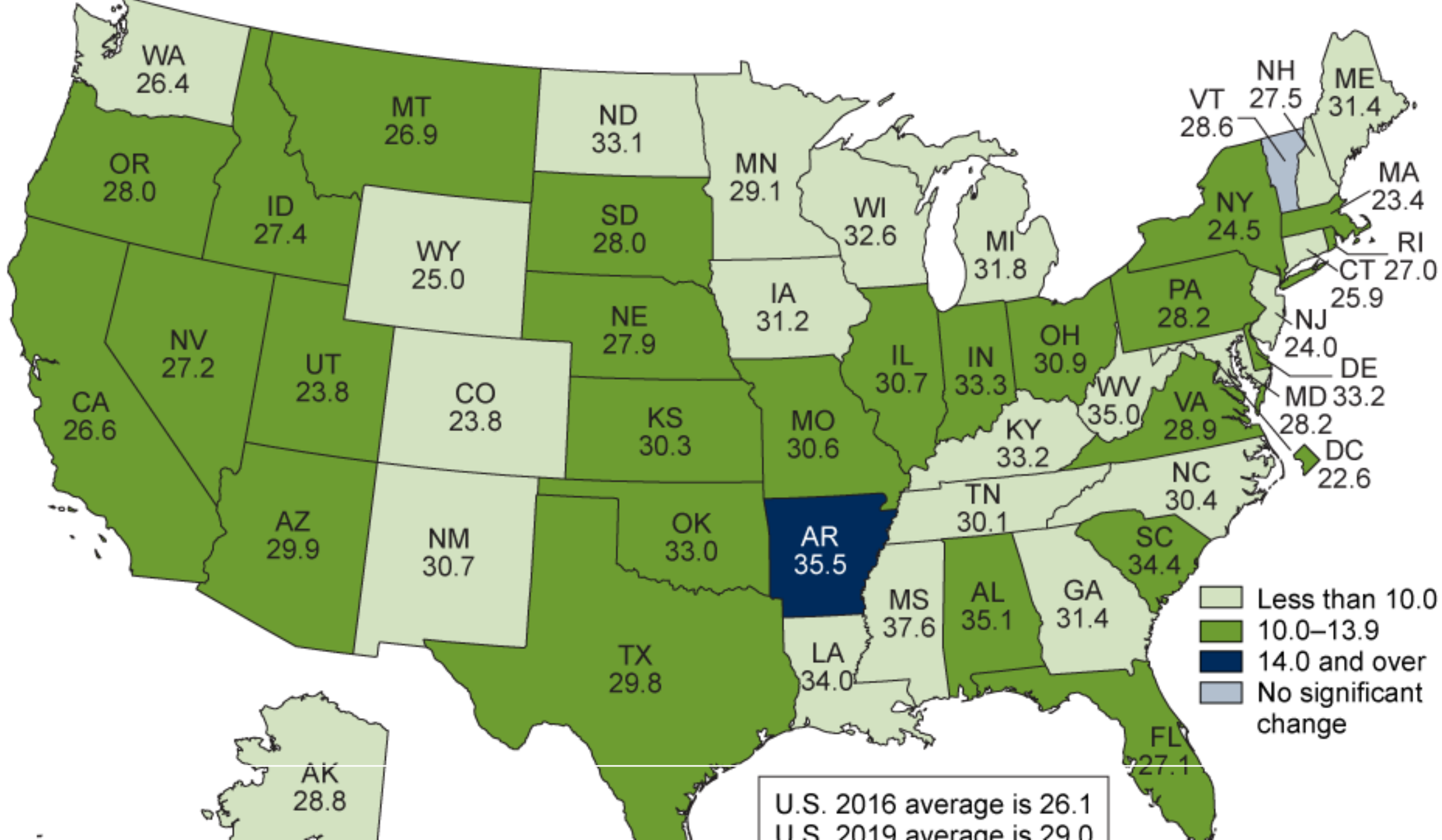
Hispanic[1]

Total[1]

Non-Hispanic white[1]
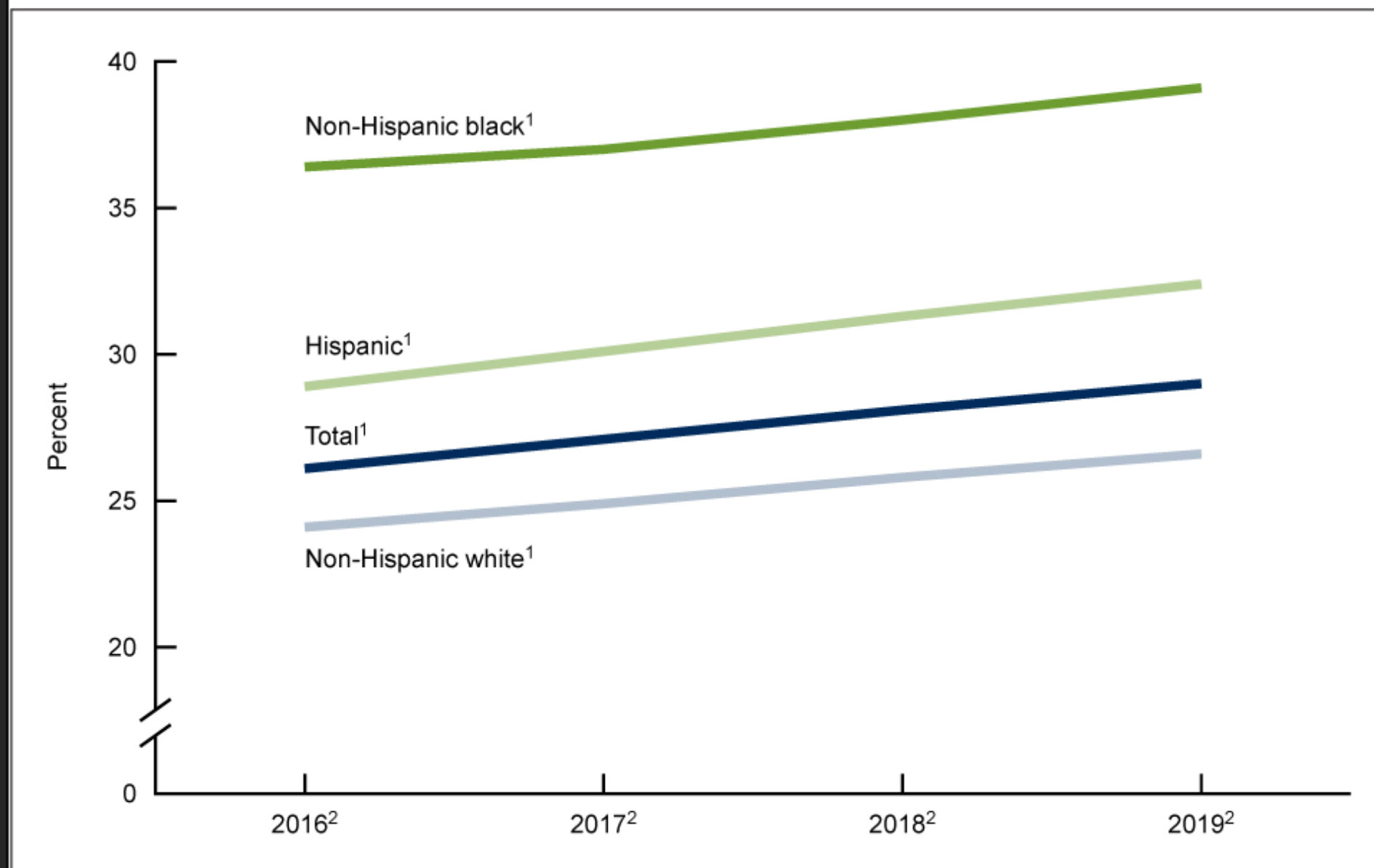
[1]Significant increasing trend from 2016 through 2019 ($p < 0.05$).
[2]Significant difference between all race and Hispanic-origin groups ($p < 0.05$).
NOTES: Obesity is a body mass index of 30.0 or higher. Total includes all race and Hispanic-origin groups. Access data table for Figure 1 at:
https://www.cdc.gov/nchs/data/databriefs/db392-tables-508.pdf#1.
SOURCE: National Center for Health Statistics, National Vital Statistics System, Natality file.

WA 26.4
MT 26.9
ND 33.1
MN 29.1
ME 31.4
VT 28.6
NH 27.5
OR 28.0
ID 27.4
SD 28.0
WI 32.6
NY 24.5
MA 23.4
RI 27.0
CT 25.9
WY 25.0
IA 31.2
MI 31.8
NV 27.2
NE 27.9
IL 30.7
IN 33.3
OH 30.9
PA 28.2
NJ 24.0
DE
MD 33.2
UT 23.8
CO 23.8
KS 30.3
MO 30.6
KY 33.2
WV 35.0
VA 28.9
DC 22.6
CA 26.6
AZ 29.9
NM 30.7
OK 33.0
AR 35.5
TN 30.1
NC 30.4
SC 34.4
TX 29.8
LA 34.0
MS 37.6
AL 35.1
GA 31.4
AK 28.8
FL 27.1

Legend:
- Less than 10.0
- 10.0–13.9
- 14.0 and over
- No significant change

U.S. 2016 average is 26.1
U.S. 2019 average is 29.0

The Problem:
Maternal Adiposity & Pregnancy Outcomes

Excess maternal adiposity during pregnancy is linked to a variety of adverse health outcomes:

- For the birthing person:

  Gestational Diabetes

  Hypertension

  Preeclampsia

  Labor dystocia

  Cesarean birth

- For the newborn:
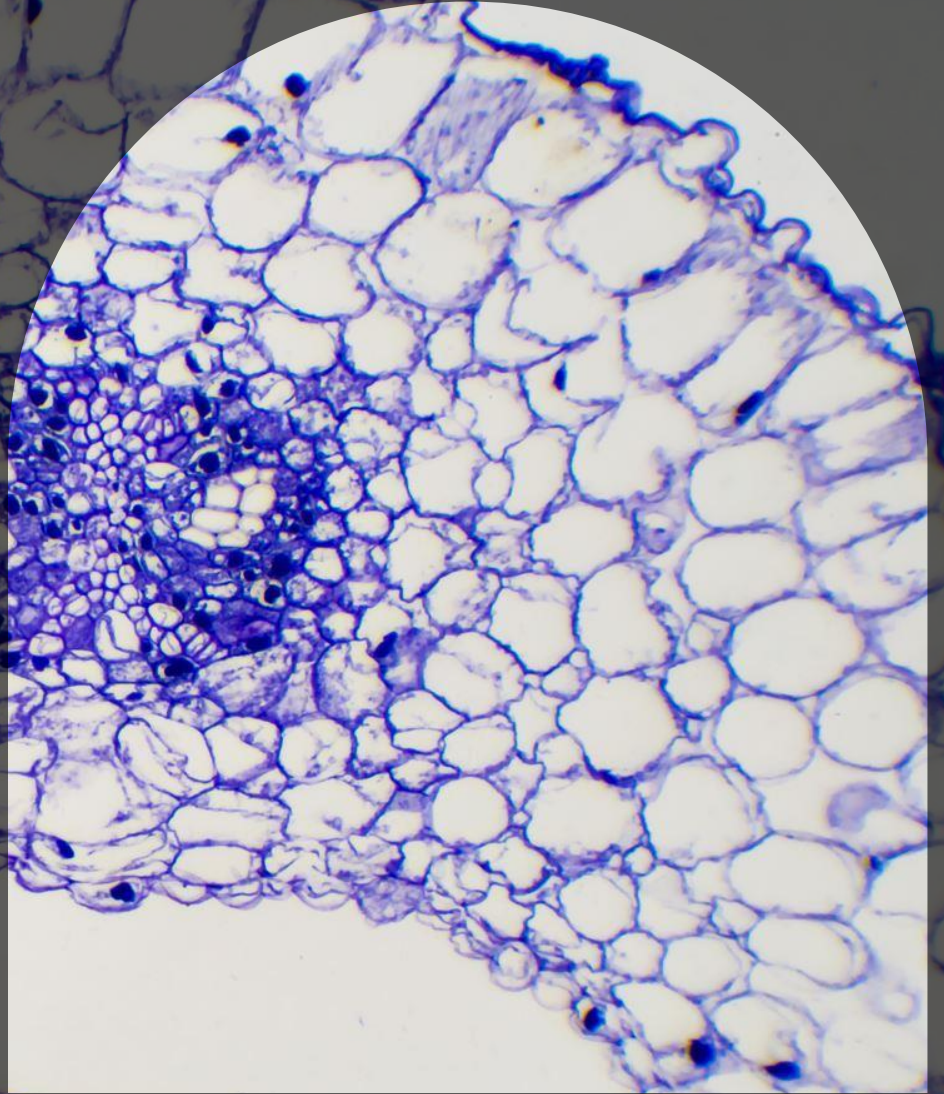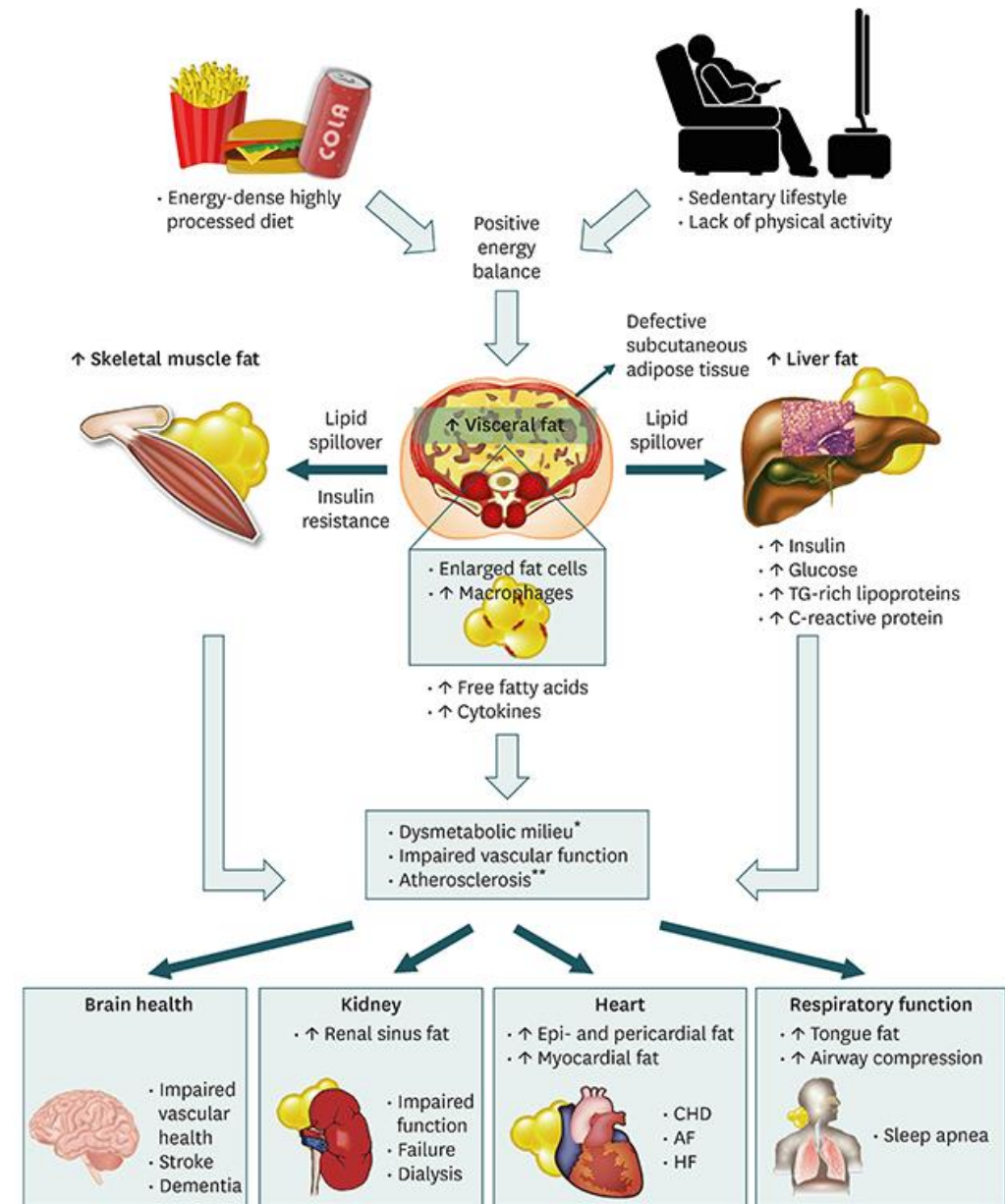
  Preterm birth

  Large size for gestational age

  Infant death

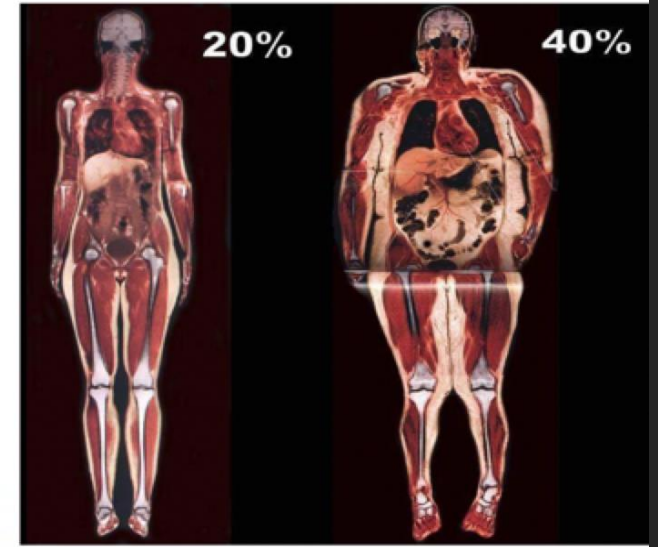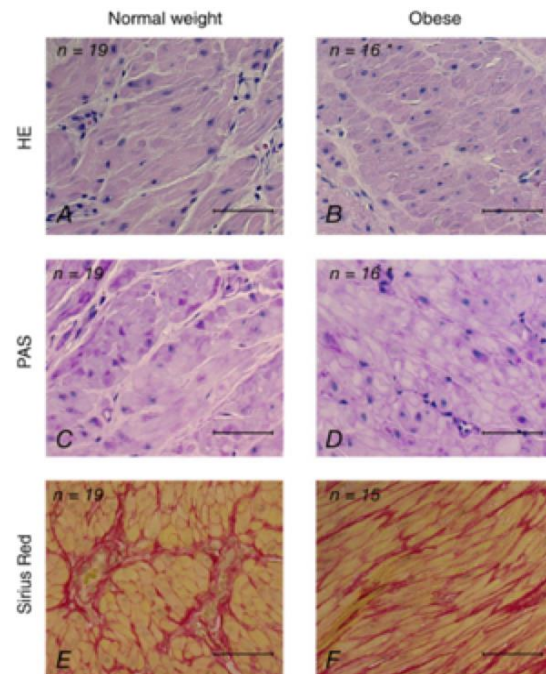# Physiology of Excess Adiposity in Pregnancy

Lipotoxicity

Interplay between "toxic" features of our lifestyle, accumulation of adipose tissue/lipids at undesired sites and production of a dysmetabolic milieu impairing vascular health and function of key target organs.
*Including type 2 diabetes.
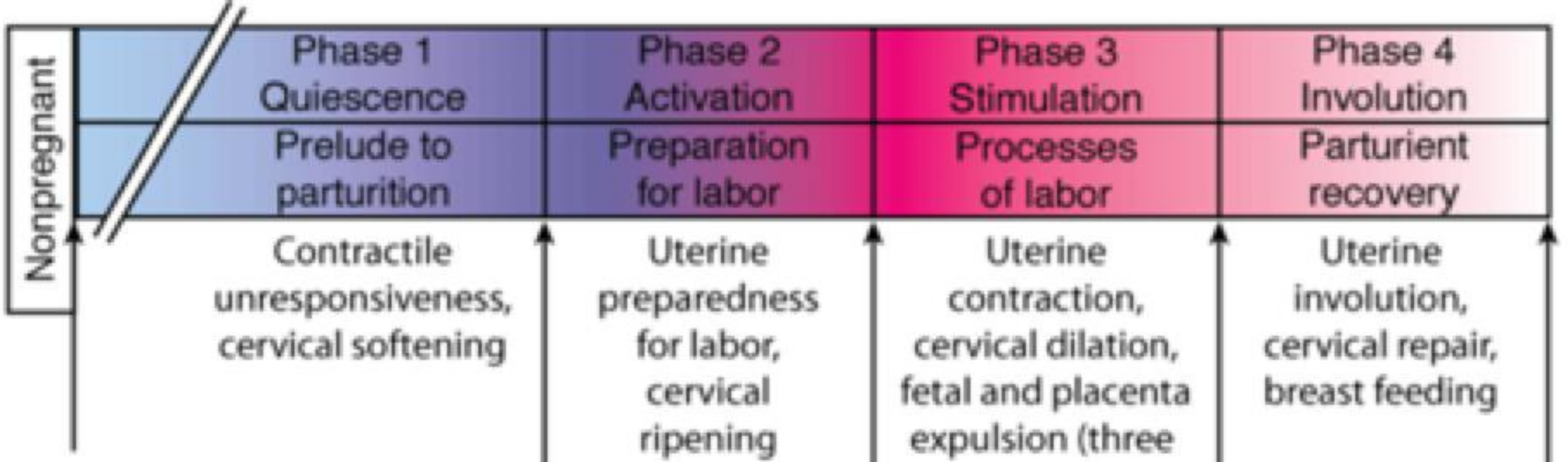**Some of the clinical outcomes are independent from the presence/absence of atherosclerosis.
AF = atrial fibrillation; CHD = coronary heart disease; HF = heart failure; TG = triglycerides.

Despres, J-P (2021) Cardiometab Syndr J.

Lipotoxicity: Cellular uptake of excess lipids results in ectopic fat deposits

20% 40%

Normal weight Obese

HE
n = 19 A
n = 16 B

PAS
n = 19 C
n = 16 D

Sirius Red
n = 19 E
n = 16 F

↑FFA

ECTOPIC FAT visceral

LEPTIN RESISTANCE
↑FFA storage
↓FFA oxidation
↑adipocyte formation

ECTOPIC FAT deposits laid down in organs throughout body

|	Phase 1 Quiescence	Phase 2 Activation	Phase 3 Stimulation	Phase 4 Involution
Nonpregnant	Prelude to parturition	Preparation for labor	Processes of labor	Parturient recovery
	Contractile unresponsiveness, cervical softening	Uterine preparedness for labor, cervical ripening	Uterine contraction, cervical dilation, fetal and placenta expulsion (three	Uterine involution, cervical repair, breast feeding

Parturition

- Source: Cunningham FG et al Williams Obstetrics, 24th ed
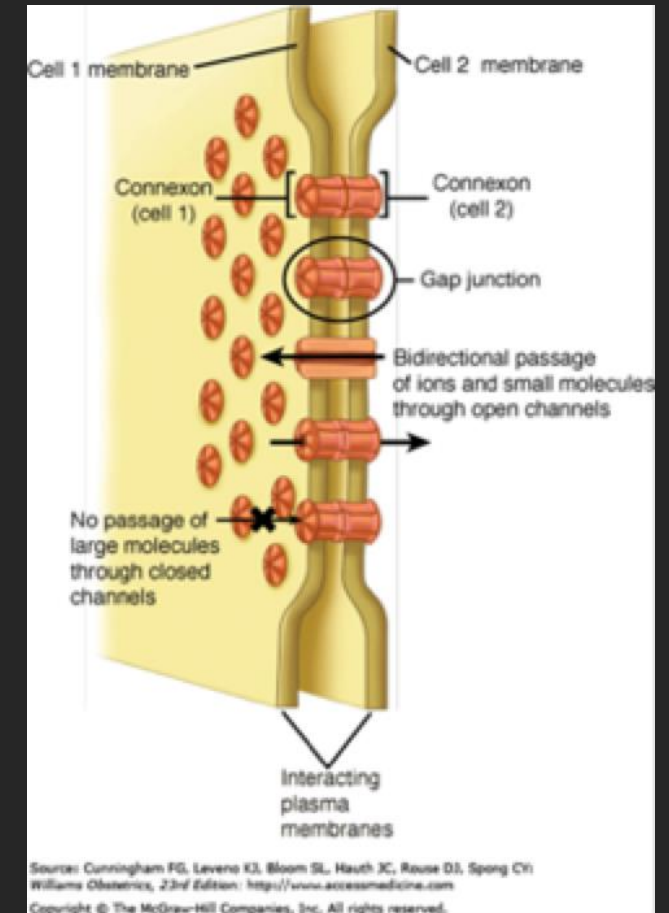
Phase 1: Prelude

- •95% of pregnancy

- •Myometrial quiescence

- •Cervical softening

  •*Most of phase 1: closed and firm*

  •*Barrier to protect from infection*

  •*Resist gravitational forces imposed by expanded uterus*

- •Weeks 28-32 weeks, structural changes to soften
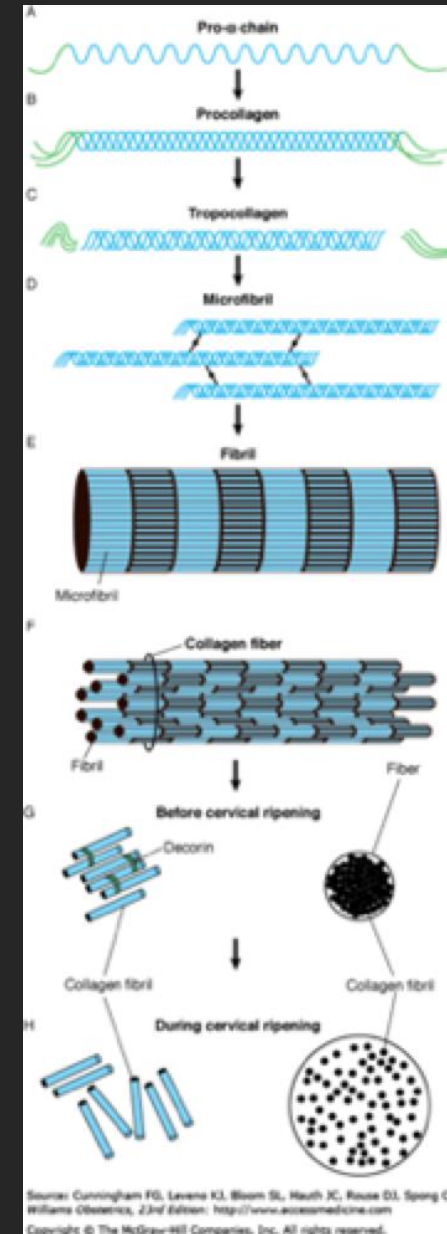
Phase 2: Myometrial Activation

- 6-8 weeks prior to spontaneous onset labor

- Preparation for labor
  - *Cervical Ripening*
  - *Uterine awakening*

- Contraction-associated proteins (CAPs) expressed
  - *Oxytocin receptors*
  - *Prostaglandin F receptor*
  - *Connexin 43 gap junction*

Cell 1 membrane — Cell 2 membrane

Connexon (cell 1) — Connexon (cell 2)

Gap junction

Bidirectional passage of ions and small molecules through open channels

No passage of large molecules through closed channels

Interacting plasma membranes

Phase 3: Stimulation

- Uterine contractions and progressive cervical change, ending in birth of the newborn & placenta

- Prostaglandins and oxytocin are the two major players in this stage
  - *As cervix dilates, decidual tissue exposed, releasing prostaglandins.*
  - *Uterine contractions synchronize*
  - *Myometrium increases in sensitivity to oxytocin*
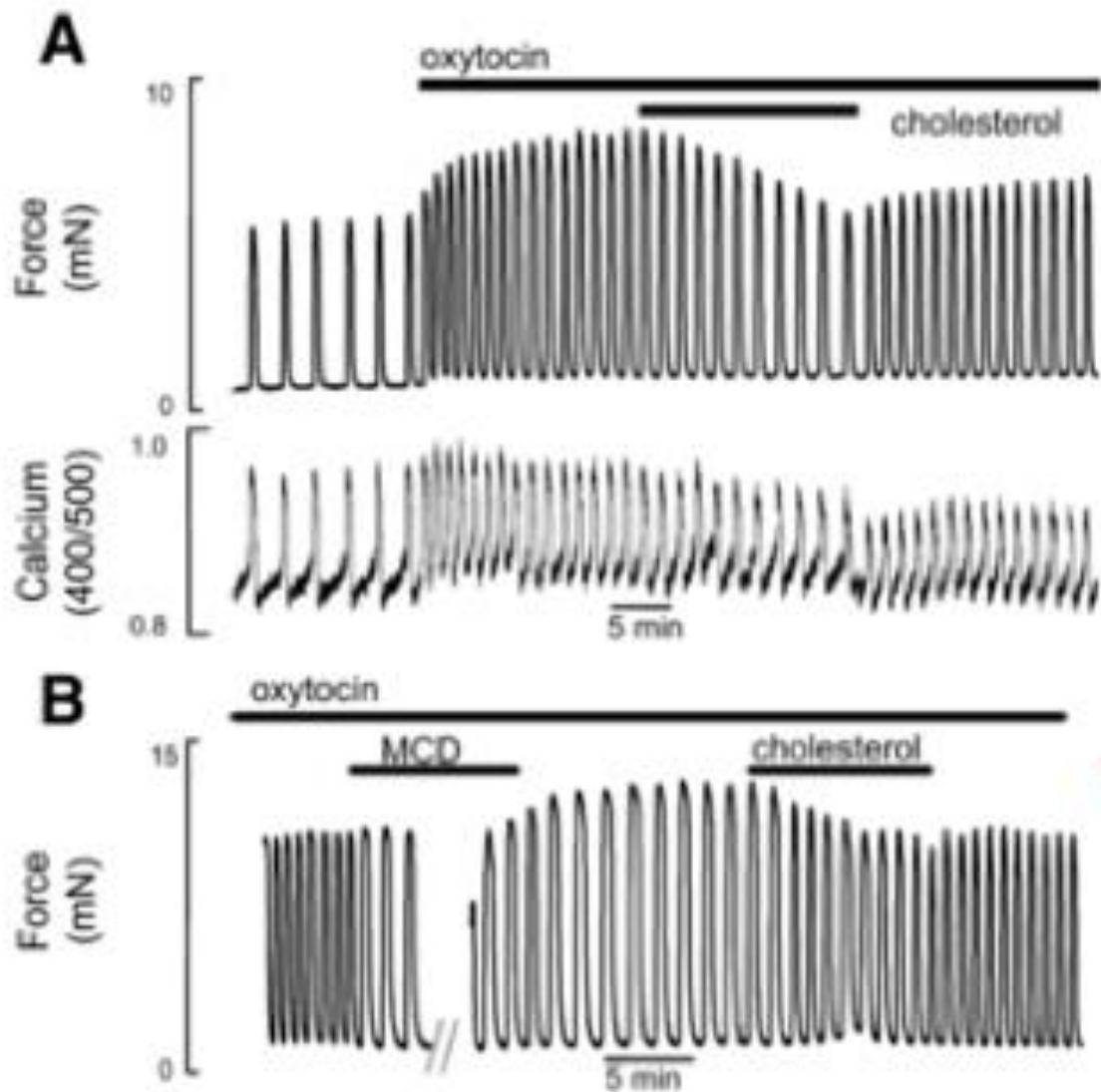

Amnion

Chorion

Cervix

Forebag

Decidual fragments
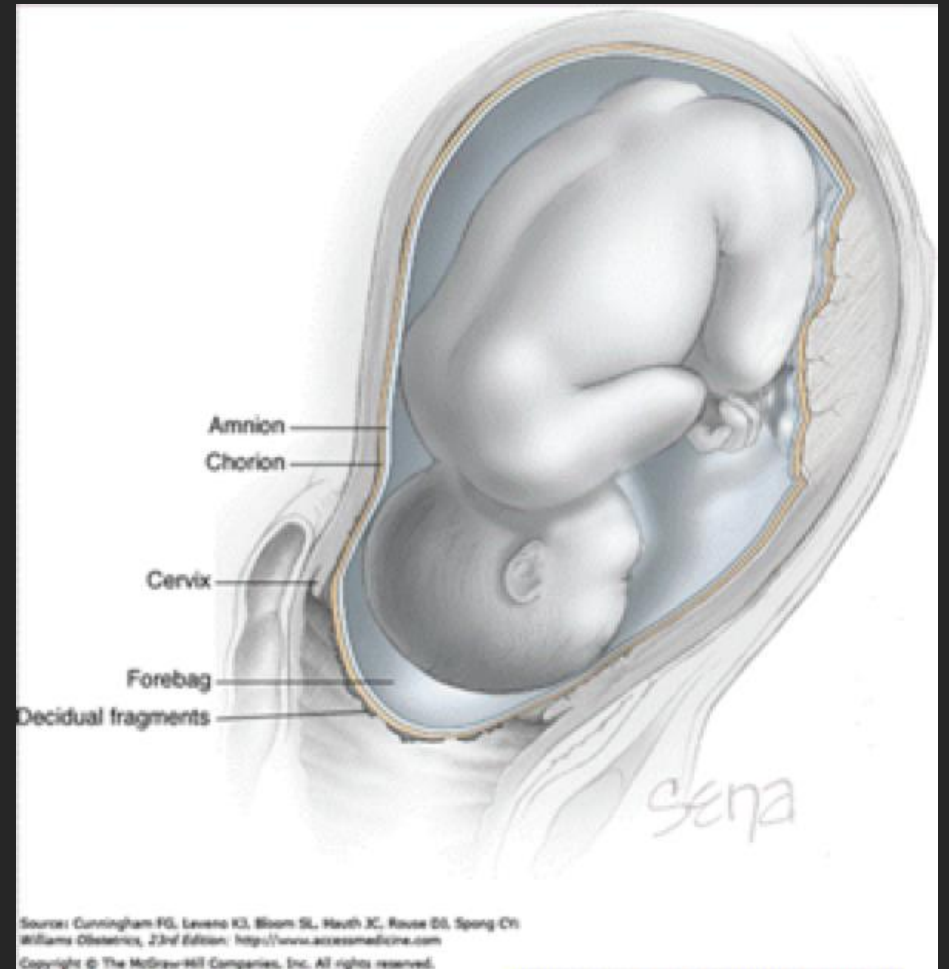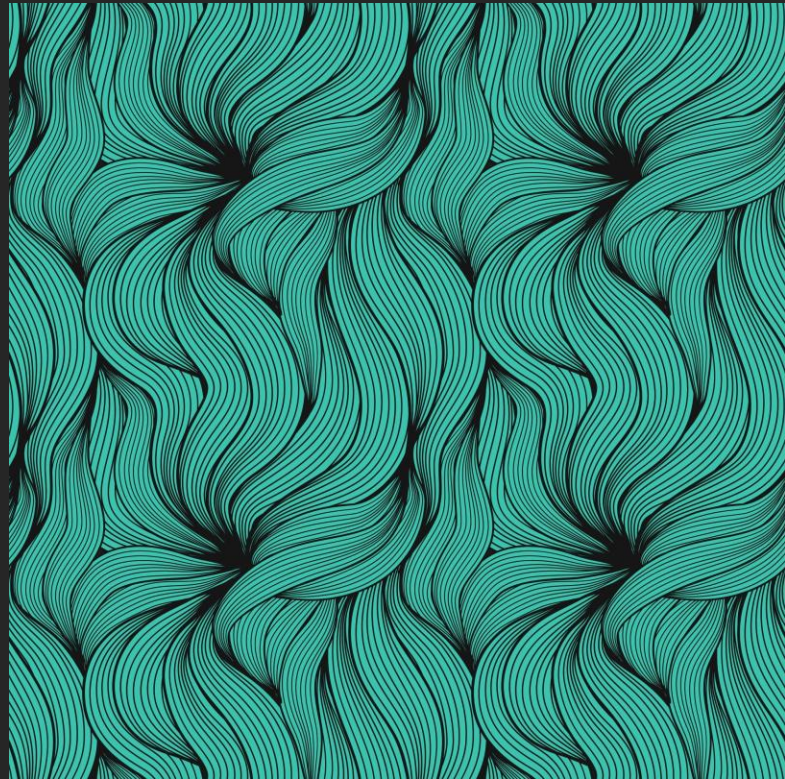
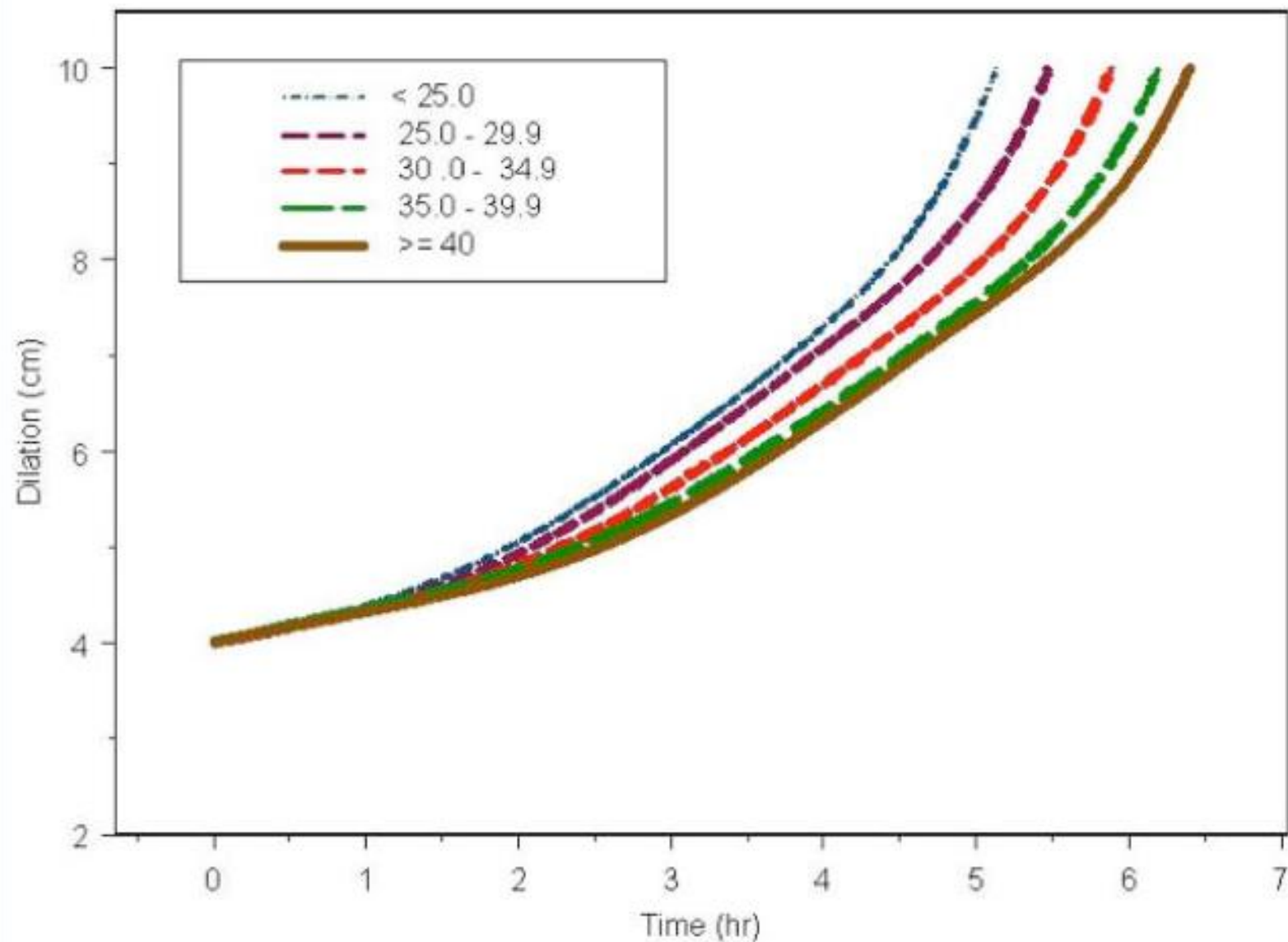# Excess Maternal Adiposity & Parturition

Decreased myometrial action potential size and duration

Labor Curves in Nulliparas by Body Mass Index Category

Kominiarek et al, 2011

MODEL 1
Decreased myometrial action
potential
size and duration

MODEL 2
Leptin disrupts cervical ripening
and preparation of amniotic
membrane for spontaneous
rupture.

Wendremaire et al, 2012

From Moynihan et al, 2006

Decreased myometrial action potential
size and duration

MODEL 2
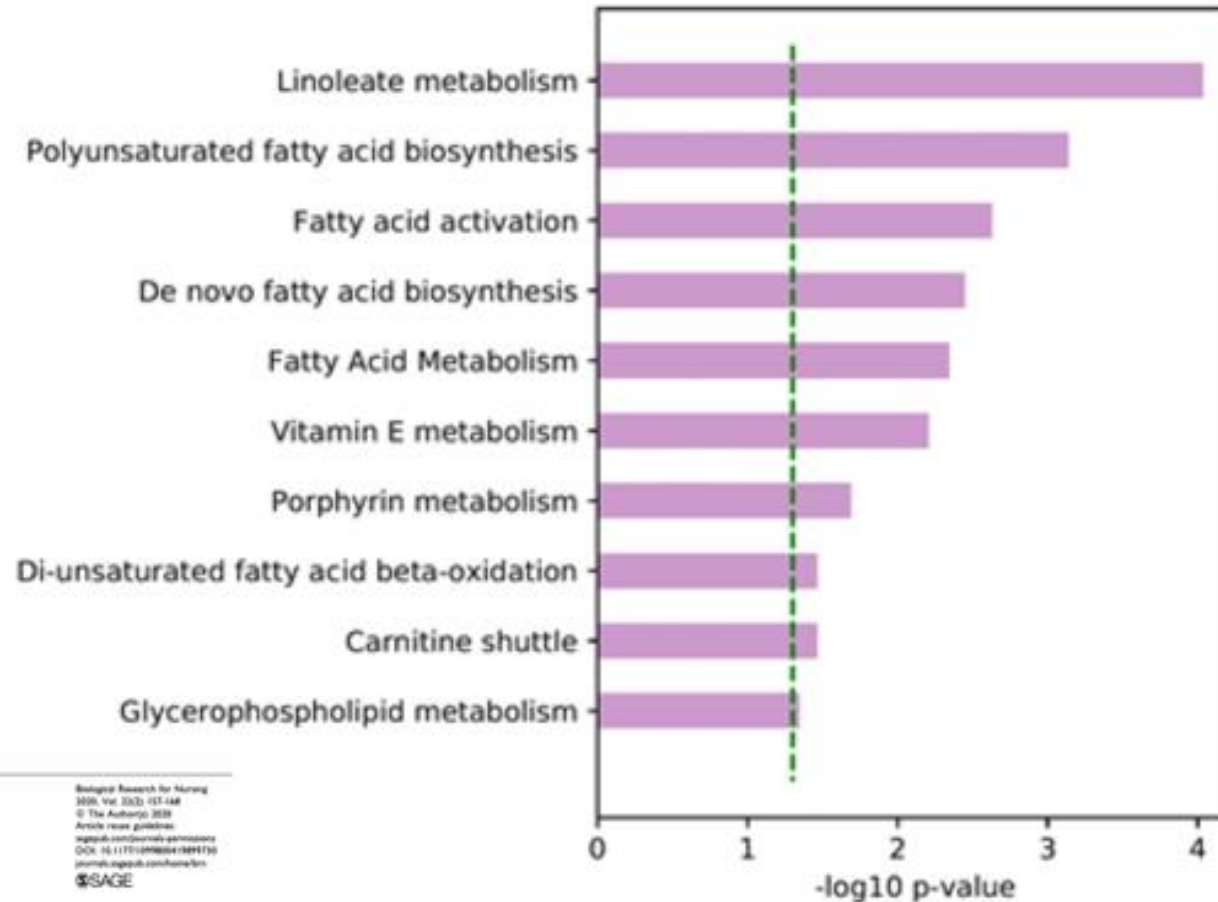Leptin disrupts cervical ripening and amniotic membrane weakening.

MODEL 3
Decreased oxytocin receptors

MODEL 4
Decreased Connexin-43 connections between myocytes.

Metabolomics Pathways: High-Oxytocin IOL

Linoleate metabolism
Polyunsaturated fatty acid biosynthesis
Fatty acid activation
De novo fatty acid biosynthesis
Fatty Acid Metabolism
Vitamin E metabolism
Porphyrin metabolism
Di-unsaturated fatty acid beta-oxidation
Carnitine shuttle
Glycerophospholipid metabolism

-log10 p-value

Nicole S. Carlson, PhD, CNM[1], Jennifer K. Frediani, PhD, RD, ACSM-CES[1],
Elizabeth J. Corwin, PhD, RN[1,2], Anne Dunlop, MD, MPH[1,3,4],
and Dean Jones, PhD[5]

Induction of Labor: The Process

Cervical Ripening

Active Dilation

0 1 2 3 4 5 6 7 8 9 10

Cervical Dilation

- *Prostaglandins*
- *Transcervical Catheters*

Synthetic Oxytocin Infusion
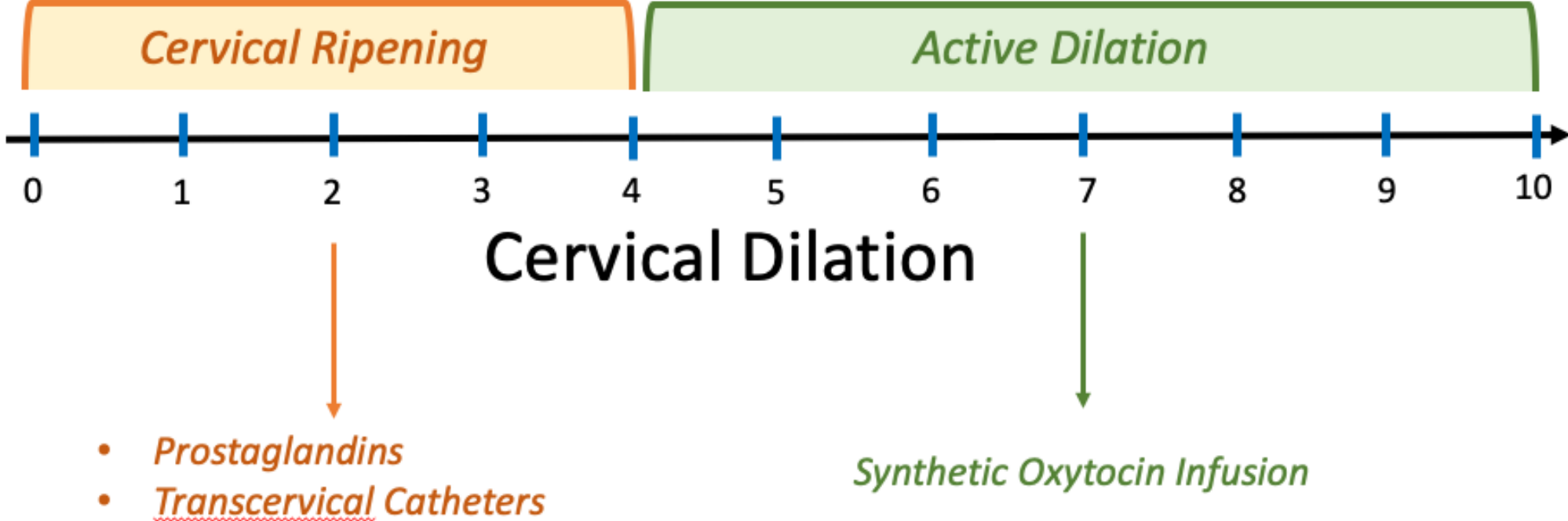
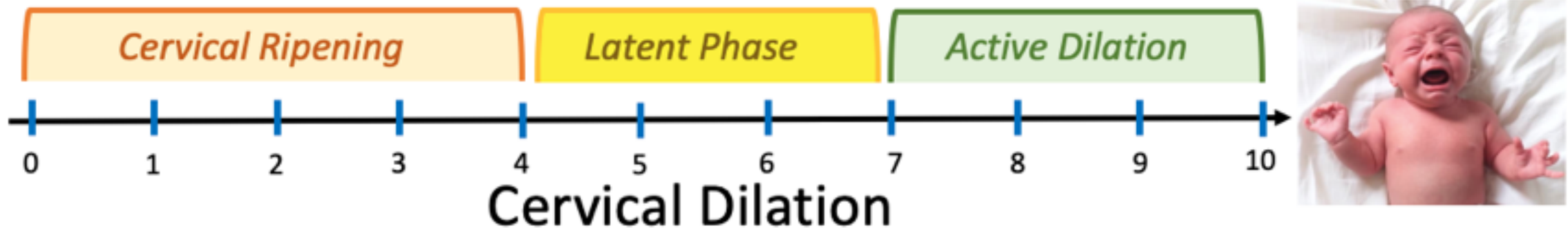(no difference in cases/controls)   (twice as long in cases, requiring nearly 7x more oxytocin)

Induction of Labor: The Process

Cervical Ripening | **Latent Phase** | **Active Dilation**

0   1   2   3   4   5   6   7   8   9   10

Cervical Dilation

No difference in cases/controls

Low Omega-3 fatty acid levels = latent phase twice as long

Very little difference in cases/controls

Modelling maternal obesity: the effects of a chronic high-fat, high-cholesterol diet on uterine expression of contractile-associated proteins and *ex vivo* contractile activity during labour in the rat

Ronan Muir*, Jean Ballan*, Bethan Clifford*, Sarah McMullen*, Raheela Khan†, Anatoly Shmygol†, Siobhan Quenby‡§ and Matthew Elmes*

*Division of Nutritional Science, School of Bioscience, University of Nottingham, Sutton Bonington Campus, Loughborough LE12 5RD, England, U.K.
†Graduate School of Medicine, University of Nottingham, Royal Derby Hospital, Uttoxeter Road, Derby DE22 3DT, England, U.K.
‡Reproductive Health, University of Warwick, Coventry, Warwickshire CV2 2DX, England, U.K.
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Labor

Physiologic Changes

Modelling maternal obesity: the effects of a chronic high-fat, high-cholesterol diet on uterine expression of contractile-associated proteins and *ex vivo* contractile activity during labour in the rat

Ronan Muir*, Jean Ballan*, Bethan Clifford*, Sarah McMullen*, Raheela Khan†, Anatoly Shmygol‡, Siobhan Quenby†§ and Matthew Elmes*

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†Graduate School of Medicine, University of Nottingham, Royal Derby Hospital, Uttoxeter Road, Derby DE22 3DT, England, U.K.
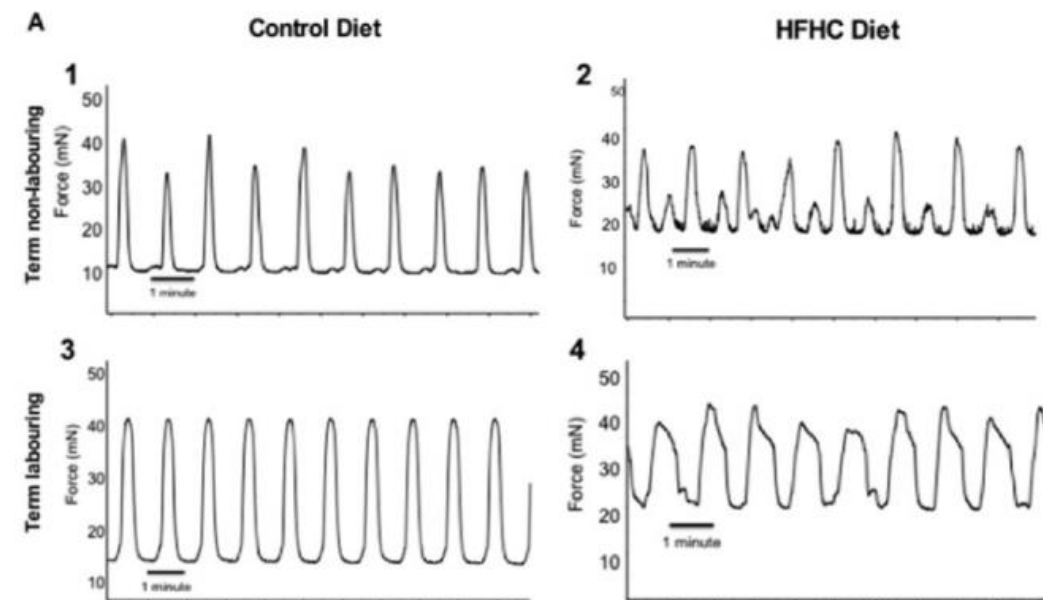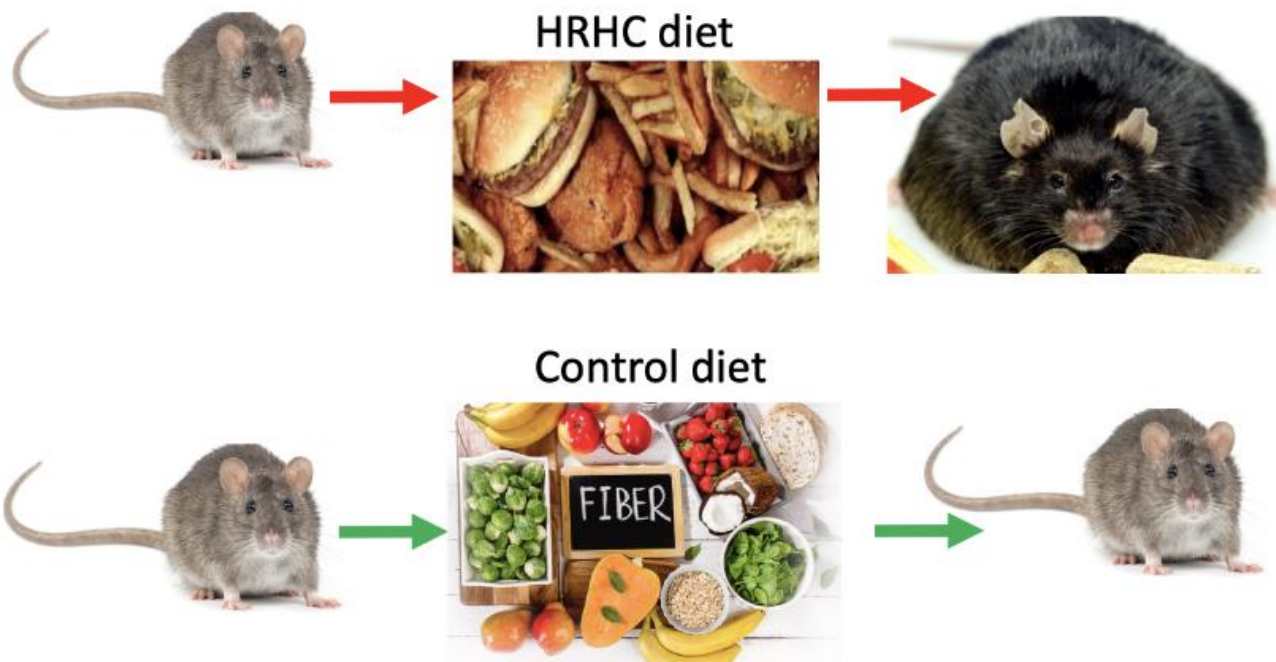‡Reproductive Health, University of Warwick, Coventry, Warwickshire CV2 2DX, England, U.K.
§Biomedical Research Unit in Reproductive Health, University Hospital Coventry and Warwickshire, Coventry, Warwickshire CV2 2DX, U.K.

- ↑ visceral fat
- ↑ cholesterol
- ↑ triglyceride
- ↓ gap junctions
- ↓ COX-2 contractile protein
- No change in oxytocin receptors, but blunted contractile activity in response to oxytocin
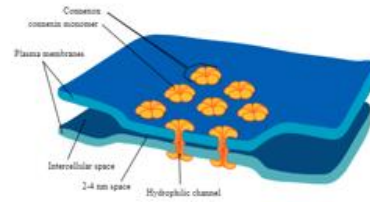
- ↓ visceral fat
- ↓ cholesterol
- ↓ triglyceride
- ↑ gap junctions
- ↑ COX-2 contractile protein
- Contractile activity increased with oxytocin

Control Diet

HFHC Diet
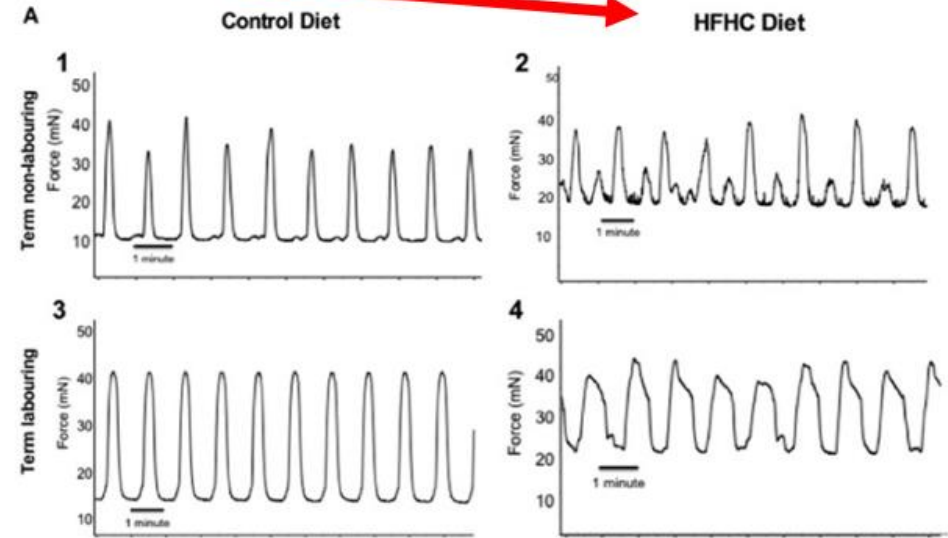
Normal contractions

Unstable, asynchronous contractions

The Caregiving Interaction & Maternal Adiposity: The Role of Intersectional Identities

MATERNAL ADIPOSITY + PROVIDER CHOICES = OUTCOMES

Provider & Biology Interaction: Excess Maternal Adiposity in Labor
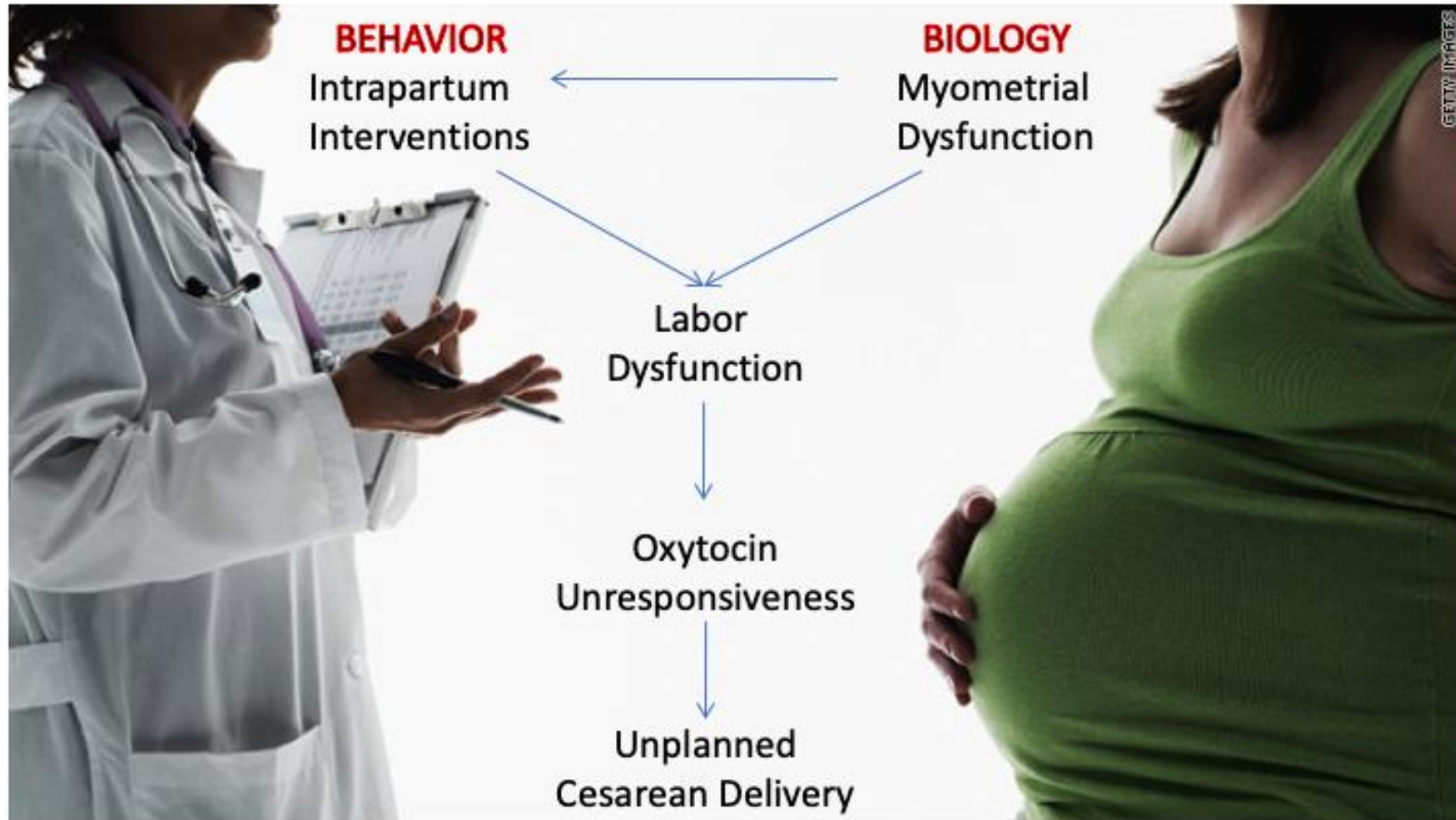
- Used participant-identified Presenting Race: "how do other people in the United States identify and treat you?"

  This allows for examination of racism on outcomes of interest

- Primary Outcome: unplanned cesarean birth

- Dataset: nuMoM2b, from NICHD. Multisite U.S. study of nulliparas (n=5095 healthy participants for secondary analysis)

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10176719/

Table 2 Maternal presenting race/ethnicity and cesarean birth in healthy, laboring nulliparas (*N* = 5095)

	Unadjusted Odds Ratio (95% CI)[a]	*P*-value difference in Model	Adjusted Odds Ratio (95% CI)[b]	*P*-value difference in Model
Presenting Race/Ethnicity				
Black-presenting	Ref	–	Ref	–
White-presenting	0.66 (0.55- 0.79)	<0.001	0.57 (0.45–0.73)	<0.001
Hispanic-presenting	1.04 (0.83- 1.29)	0.761	1.17 (0.88, 1.55)	0.278

Distribution of Presenting Race/Ethnicity + BMI in NuMo Participants with Cesarean for NRFHT (N=322)
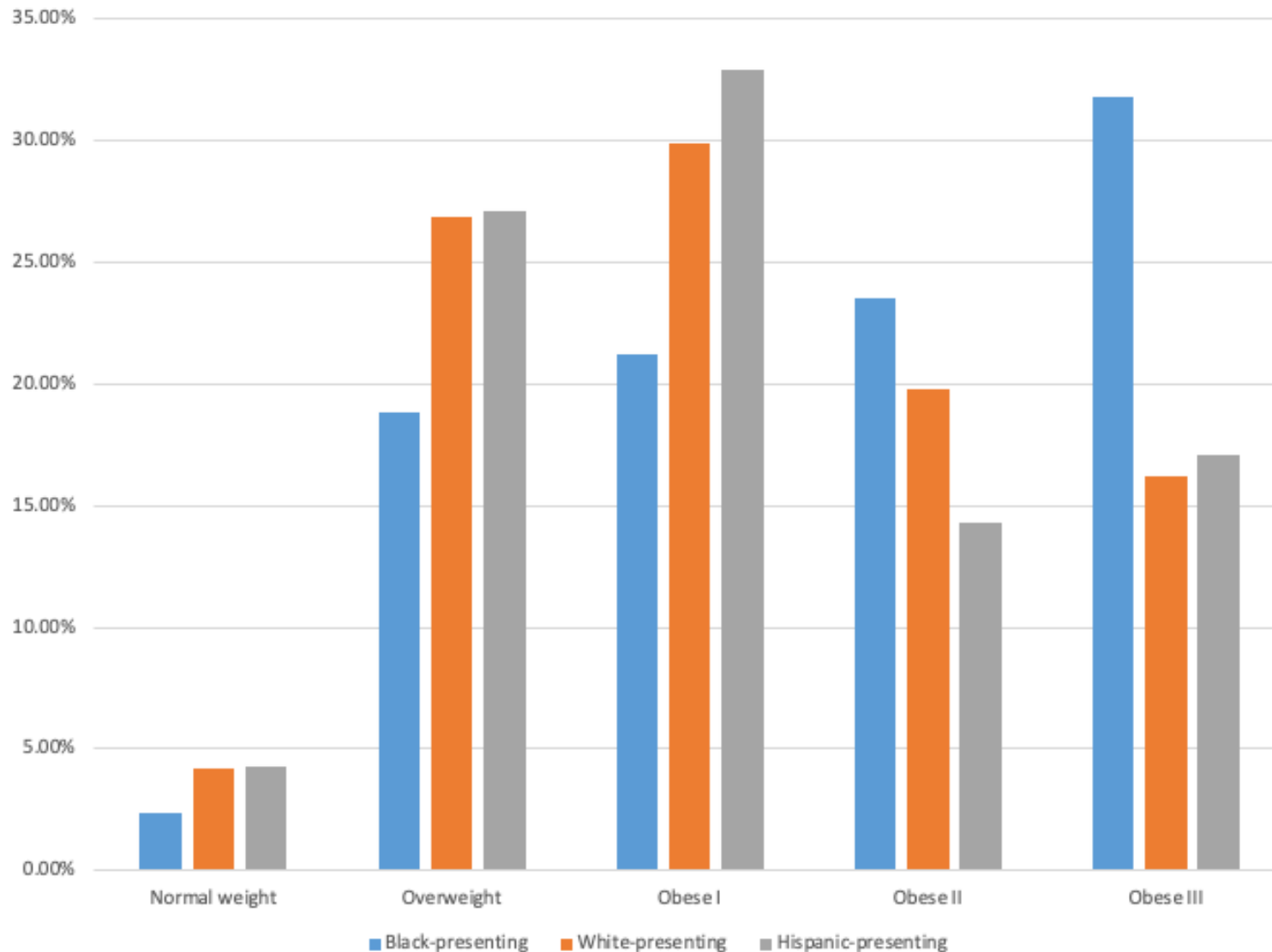
- Maternal BMI at the time of labor accounted for about a quarter of the influence of maternal presenting race/ethnicity on unplanned cesarean
- The relationship between BMI and higher odds for unplanned cesarean birth was unique to the Black-presenting race group.
- Black-presenting people in larger bodies had the highest risks for unplanned cesarean—higher than white- or Hispanic-presenting people in similar sized bodies.

Excess Maternal Adiposity & Labor Induction

STRATEGIES FOR SUCCESS

Continuing Education

Review of Evidence-Based Methods for Successful Labor Induction

Nicole Carlson[1], CNM, PhD, Jessica Ellis[2], CNM, PhD, Katie Page[3], CNM, Alexis Dunn Amore[1], CNM, PhD, Julia Phillippi[4], CNM, PhD

Induction of labor is increasingly a common component of the intrapartum care. Knowledge of the current evidence on methods of labor induction is an essential component of shared decision-making to determine which induction method meets an individual's health needs and personal preferences. This article provides a review of the current research evidence on labor induction methods, including cervical ripening techniques, and contraction stimulation techniques. Current evidence about expected duration of labor following induction, use of the Bishop score to guide induction, and guidance on the use of combination methods for labor induction are reviewed.
J Midwifery Womens Health 2021;00:1–11 © 2021 by the American College of Nurse-Midwives.

American College of Nurse-Midwives Clinical Bulletin Number 18: Induction of Labor

American College of Nurse-Midwives[1], Nicole Smith Carlson[2], CNM, PhD, Alexis Dunn Amore[2], CNM, PhD, Jessica Ann Ellis[3], CNM, PhD, Katie Page[4], CNM, MSN, Robyn Schafer[5], CNM, MSN, EdM

Induction of labor is an increasingly common component of intrapartum care in the United States. This rise is fueled by a nationwide escalation in both medically indicated and elective inductions at or beyond term, supported by recent research showing some benefits of induction over expectant management. However, induction of labor medicalizes the birth experience and may lead to a complex cascade of interventions. The purpose of this Clinical Bulletin is twofold: (1) to guide clinicians on the use of person-centered decision-making when discussing induction of labor and (2) to review evidence-based practice recommendations for intrapartum midwifery care during labor induction.
J Midwifery Womens Health 2022;67:140–149 © 2022 by the American College of Nurse-Midwives.

Duration of Labor Induction with Excess Maternal Adiposity

LONGER DURATION OF LABOR INDUCTION...ESPECIALLY DURING LATENT PHASE

Progress of induced labor is slower for both nulliparous and multiparous people

Fig. 1. Average labor curves stratified by parity and type of labor onset.

Harper. Normal Labor in Induction. Obstet Gynecol 2012.
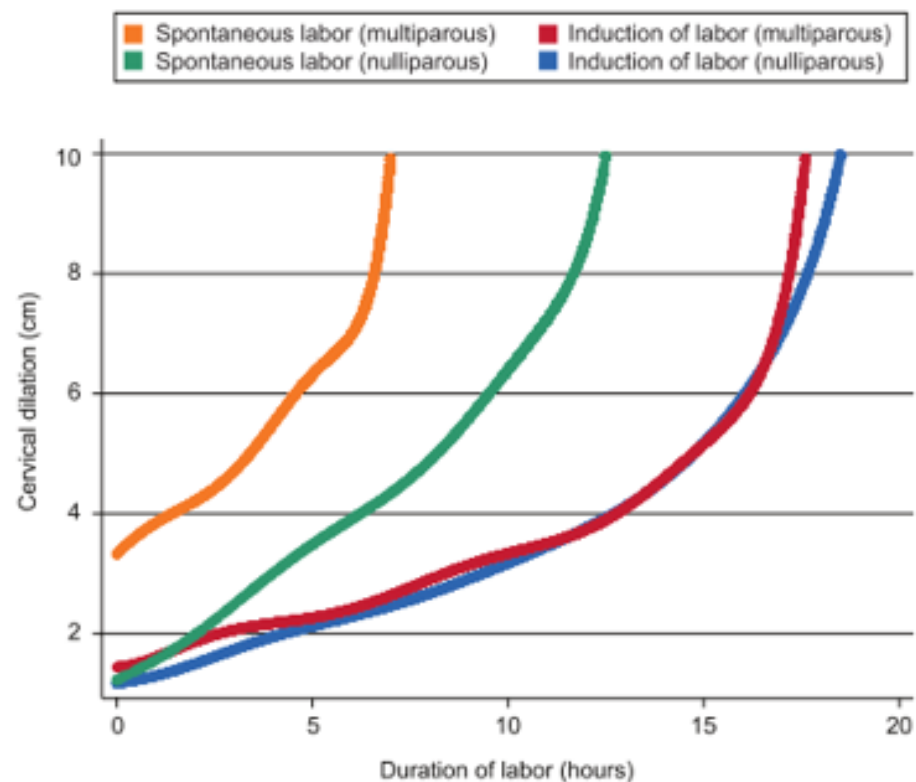
Induced vs. Spontaneous Labor Duration

Nulliparous People: 5.5 (16.8) hr vs. 3.8(11.h) hr

Multiparous People: 4.4 (16.2) hr vs. 2.4 (16.2) hr

Longer Duration of Induced Labor with Higher BMI

TABLE 3 Duration of labor, in hours, in primiparae term women with induction of labor

Maternal body mass index (kg/m^2)	Time from admission to start of active phase in hours (N = 15 073)					Duration of the active phase of labor in hours (N = 15 259)				
		Quartiles			Range		Quartiles			Range
	N	25%	Median	75%	[Min-Max]	N	25%	Median	75%	[Min-Max]
<18.5	322	7.7	12.9	25.0	[1.5-91.7]	325	4.0	6.1	8.9	[0.5-30.5]
18.5-24.9	8434	8.4	14.5	25.1	[0.5-95.9]	8509	4.7	7.4	11.0	[0.5-44.5]
25-29.9	3993	9.2	16.3	28.2	[0.5-95.6]	4044	4.8	7.6	11.2	[0.5-40.3]
30-34.9	1568	9.6	18.2	30.4	[0.7-94.6]	1605	4.6	7.6	11.1	[0.6-46.5]
35-39.9	549	10.2	21.0	31.7	[0.5-80.0]	562	4.5	7.0	11.3	[0.8-30.9]
≥40	207	11.1	22.6	35.1	[1.0-91.0]	214	4.7	7.4	11.8	[1.3-35.7]

75% longest IOL = 36.1 hours

75% longest IOL = 46.9 hours

Carlhall et al (2019). Acta Obstet Gynecol Scand. N=15,259 nulliparous people
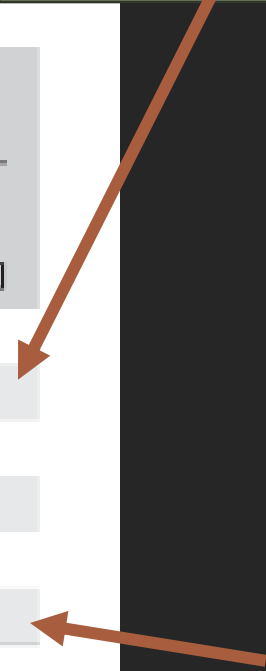
Latent Phase Labor During IOL

- Latent phase labor is not often discussed in the context of IOL

- Grobman et al (ARRIVE PI) defined latent phase during IOL as occurring after cervical ripening, ROM, and oxytocin initiation but prior to 5cm cervical dilation

- N=10,677 term nulliparous people induced in 25 U.S. hospitals

- >40% with an 18 HOUR latent phase achieved safe vaginal birth

- They recommend waiting at least 15 hours for latent phase to complete before thinking about cesarean for failed IOL.

- THIS STUDY DID NOT TAKE BMI INTO ACCOUNT (likely we should wait even longer for latent phase to end in people with excess adiposity)

Grobman et al (2018) Defining failed IOL. Am J Obstet Gynecol
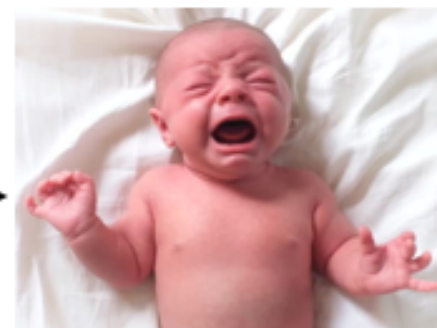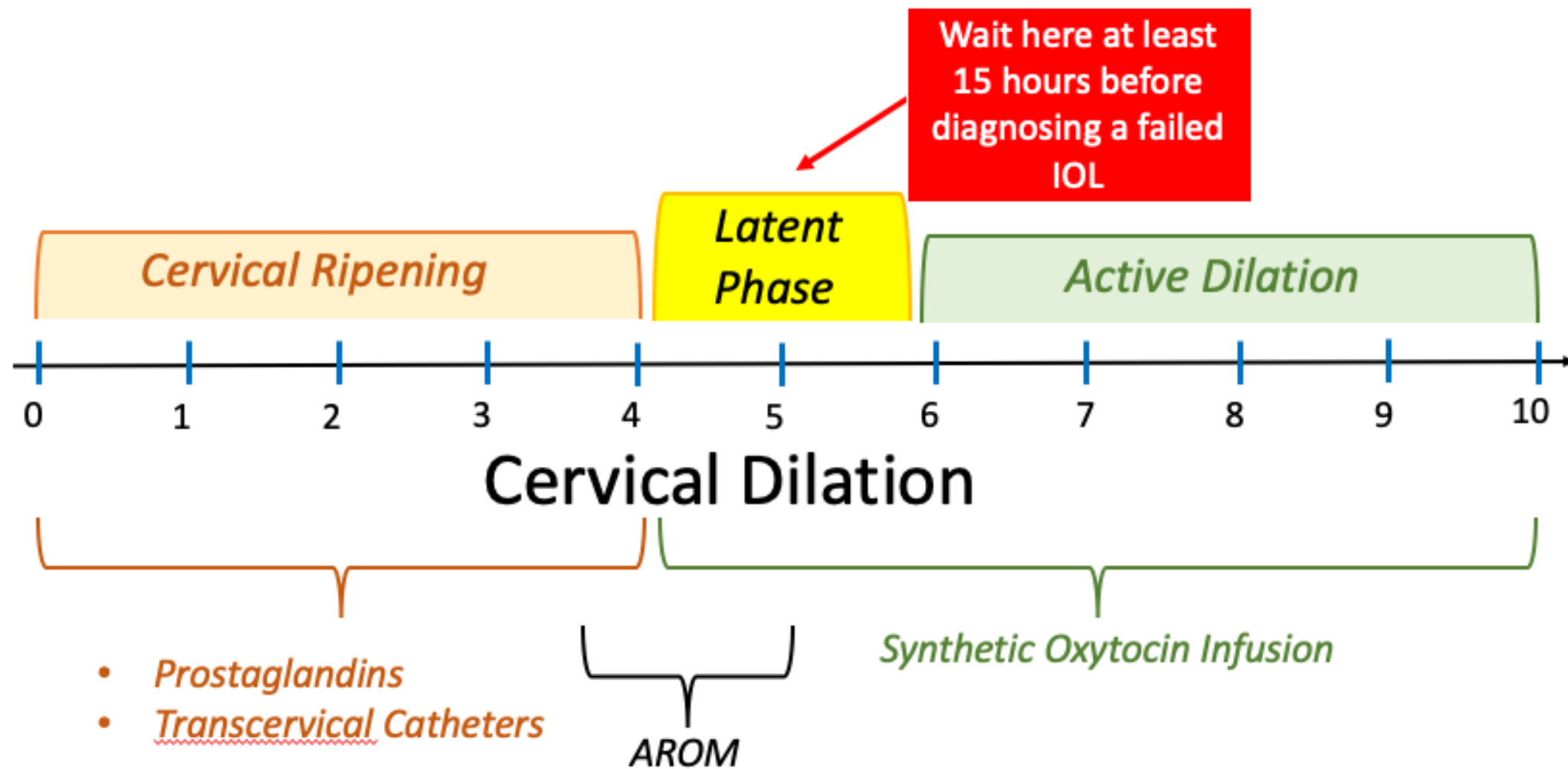
Cervical Ripening

THE MOST ESSENTIAL STEP OF LABOR INDUCTION

Prostaglandins & Excess Maternal Adiposity

- Birthing people with excess adiposity are less likely to respond to prostaglandins for cervical ripening:

  Less likely to reach active labor

  Need longer to birth (much longer; 13 h)

The problem with PGE2 (dinoprostone)

- Exogenous PGE2 shown to not be as effective as misoprostol (PGE1 analog) for labor induction in laboring people with excess adiposity

- *Misoprostol group successful cervical ripening: 78.1%*

- *Cervidil successful cervical ripening: 66.7%*

- Physiologically, dinoprostone is naturally higher in pregnant people with excess adiposity; causing PGE2 receptor activity to be decreased.

Suidan et al, 2015 Labor outcomes of obese patients undergoing IOL with misoprostol compared to dinoprostone.

Mechanical Methods

- Transcervical catheters take longer in laboring persons with higher BMIs

- Combining prostaglandins with mechanical methods does not speed the process nor decrease rates of unplanned cesarean birth:

  Viteri et al (2021) Am J Perinatology PMID 32299108

  RCT of N=236, PGE1 alone vs. PGE1 + Foley

- Tips when using transcervical catheters:

  Higher filling volumes cause quicker labors

  Transition from latent to active phase labor takes place later with transcervical vs.
  Prostaglandin cervical ripening (6cm, vs. 4cm)

The Good News...Outpatient Cervical Ripening Optimizes Outcomes

Table 1 Outcomes for patients with BMI ≥ 30 compared with patients with BMI <30 for inpatient versus outpatient cervical ripening with a CF

	Interaction (p-Value)[a]	BMI ≥ 30 (n = 69)			BMI < 30 (n = 57)		
		Inpatient (n = 38)	Outpatient (n = 31)	p-Value	Inpatient (n = 25)	Outpatient (n = 32)	p-Value
Admission to delivery (hours)	0.08	20.4 (16.6–31.3)	18.0 (13.5–20.9)	0.01	18.9 (12.3–22.8)	16.0 (12.2–18.9)	0.39
Total hospital duration (days)	0.004	3.4 (3.1–4.3)	3.2 (2.5–3.3)	0.02	3.2 (3.1–3.3)	3.2 (2.8–3.9)	0.40
Cesarean birth	0.01	17 (44.7)	6 (19.4)	0.03	3 (12.0)	9 (28.1)	0.14
Simplified Bishop score admission	0.63	1.0 (0.0–1.0)	3.0 (2.0–3.0)	<0.001	1.0 (0.0–1.0)	3.0 (2.0–5.0)	<0.001
Dilation admission (cm)	0.63	1.0 (0.0–1.0)	3.0 (3.0–3.0)	<0.001	1.0 (0.0–1.0)	3.0 (2.0–4.0)	<0.001
Effacement admission	0.15	25.0 (0.0–25.0)	50.0 (25.0–50.0)	<0.001	25.0 (0.0–37.5)	50.0 (25.0–75.0)	<0.001
Station admission	0.15	−5.0 (−5.0 to 5.0)	−5.0 (−5.0 to −3.0)	0.04	−5.0 (−5.0 to −5.0)	−3.0 (−5.0 to −3.0)	0.01
Chorioamnionitis	0.49	5 (13.2)	9 (29.0)	0.10	3 (12.0)	5 (15.6)	>0.99[a]
Endometritis	0.94	2 (5.3)	0 (0)	0.50[a]	0 (0)	1 (3.1)	>0.99[a]

Abbreviations: BMI, body mass index; CF, Foley catheter.
Notes: Interactions evaluated at 0.10 level of significance in logistic regression models for binary outcomes and least squares regression models for continuous outcomes without adjustment.
Stratified data presented as mean ± standard deviation or median (Q1–Q3) for continuous outcomes. Frequencies (%) are presented for binary outcomes.
Bold p-values are statistically significant.
[a]Fisher's exact test.
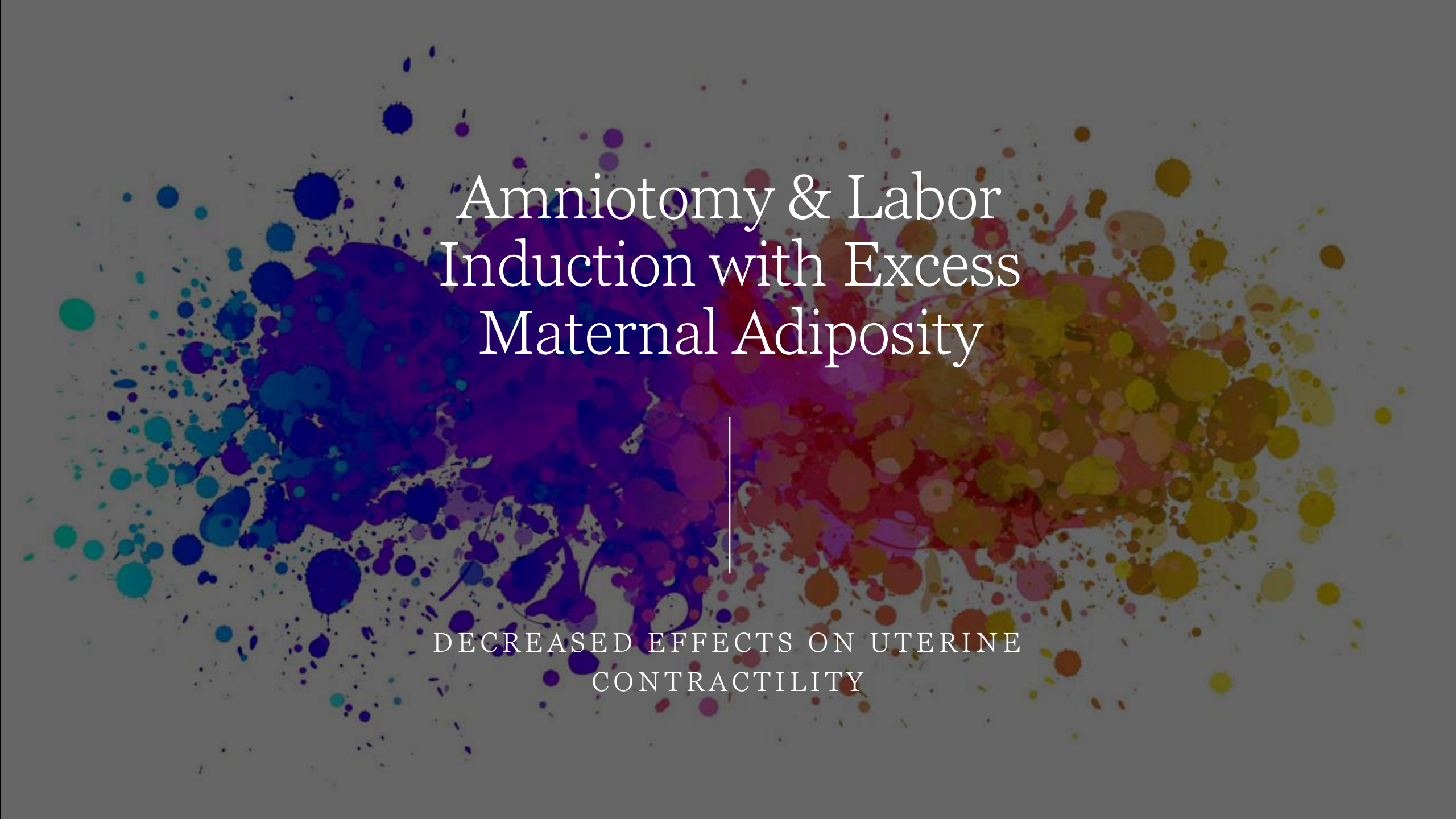
Seasely et al, 2023 Am J Perinatol. PMID 36477716. Secondary analysis of the OFFSITE II RCT.

When to stop cervical ripening?

Nulliparous Person

Bishop = 8 or more

Multiparous Person

Bishop = 6 or more
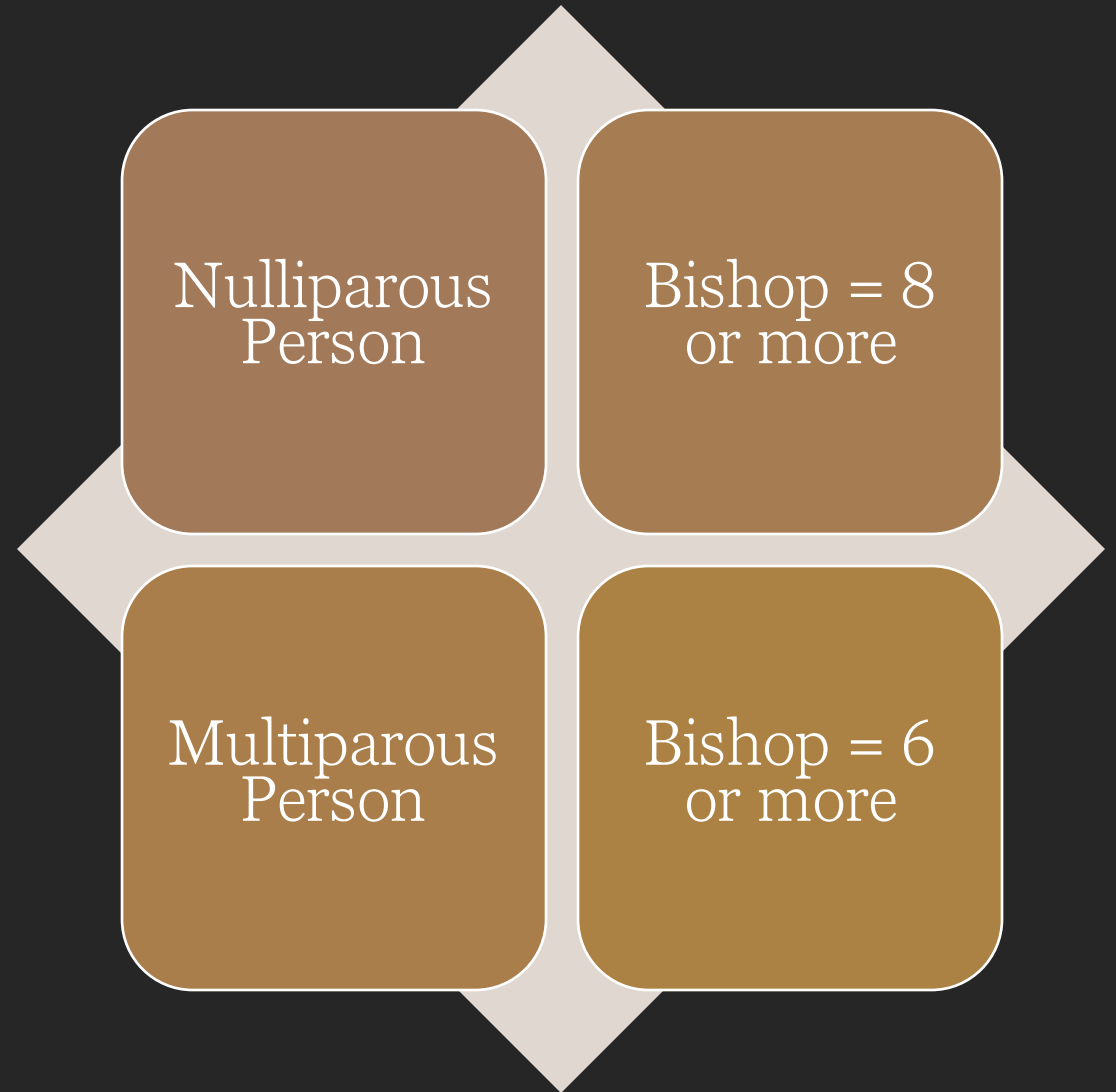
Amniotomy & Labor Induction with Excess Maternal Adiposity

DECREASED EFFECTS ON UTERINE CONTRACTILITY

Artificial Rupture of Membranes

- Electrical uterine myography (EUM) used to measure uterine electrical activity following AROM in women of different cervical dilations (Foroutan et al, 2015)
  - Women with cervix > 4 cm showed significant increase in uterine contraction strength/activation
  - Women with cervix < 4cm at time of AROM showed **no difference in uterine activity**

- Similar study found that as BMI increases, uterine response to AROM decreases (Hiersch et al, 2013)

When to Use AROM During IOL?

- AROM is performed during IOL to increase uterine activity

- Wait until 4cm in people with excess adiposity

- Early amniotomy (< 4cm) associated with cesarean birth in people with BMI >=40kg/m2 (aOR 2.05, 95% CI 1.21-3.47) in a 2019 retrospective cohort study (N=285)

- Subanalysis: this association between early amniotomy & cesarean birth during IOL was only true for nulliparous people.

Pansko et al (2019). Am J Perinatol 35(5); 449-454.

Oxytocin Use During IOL

LONGER DURATION IS THE KEY TO SUCCESS
WITH HIGHER MATERNAL ADIPOSITY

Study	BMI category	Total time (h)	Total dose
Lassiter, 2016	< 30	7.17	
	30-40	8.54	
	>40	10.39	
Maeder, 2017	<25	13.98	6.3 U
	25-29	16.00	5.92 U
	>30	18.30	7.5 U
Pevzner, 2009	<30	14.9	2.6 U
	30-39	16.0	3.5 U
	>40	19.0	5.0 U

Oxytocin & IOL with Higher Maternal Adiposity

- Multiple studies have shown that the total dose of oxytocin during IOL increases with each increase in BMI

- This may have less to do with pathophysiology in oxytocin processing & more to do with the slow pace of labor in the setting of excess adiposity, regardless of oxytocin use

MVUs: Minimal usefulness

- Secondary analysis of MVU and birth outcome data for N=87 nulliparas with BMI >= 30 whose labor was augmented

- Only 13% had MVU >= 200 prior to the final 2 hours of labor

- MVUs minimally responsive to oxytocin infusion

- MVUs not associated with labor progression

- MVUs not associated with birth route

- 200 MVU should not be used as the threshold of 'adequate' uterine activity in people with higher BMI ranges

Kissler, K.J., & Hernandez, T.L, Carlson, N. (2023). https://doi.org/10.1177/10998004221150798 PMID: 36609174.

Clinical Pearls

Successful IOL in People with Excess Adiposity

- Outpatient cervical ripening is safe, faster, & increases chances of vaginal birth

- Avoid AROM until at least 4cm

  AROM does not have the same effect on uterine activation in people with obesity as it does in others

  Especially true for nulliparous people

- MVUs are not helpful measures of uterine strength

- Be patient

  On average, it takes 13 hours longer for a person with excess adiposity to birth after IOL, compared to similar person with 'normal weight' BMI

  Latent phase during IOL is something we should all observe (at least 15 hours after cervical ripening, ROM, and oxytocin infusion onset and prior to 5cm)

COULDN'T DO IT WITHOUT A TEAM

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Questions?

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