SESSION 2
ADULT SESSION

WOMEN'S HEALTH THROUGHOUT THE LIFESPAN

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EPIC DIABETES CONFERENCE

MAY 3, 2025 CU ANSCHUTZ MEDICAL CAMPUS

EMPOWERING PATIENTS FOR INDIVIDUALIZED CARE

Barbara Davis Center for Diabetes • Children's Diabetes Foundation •

DISCLOSURES

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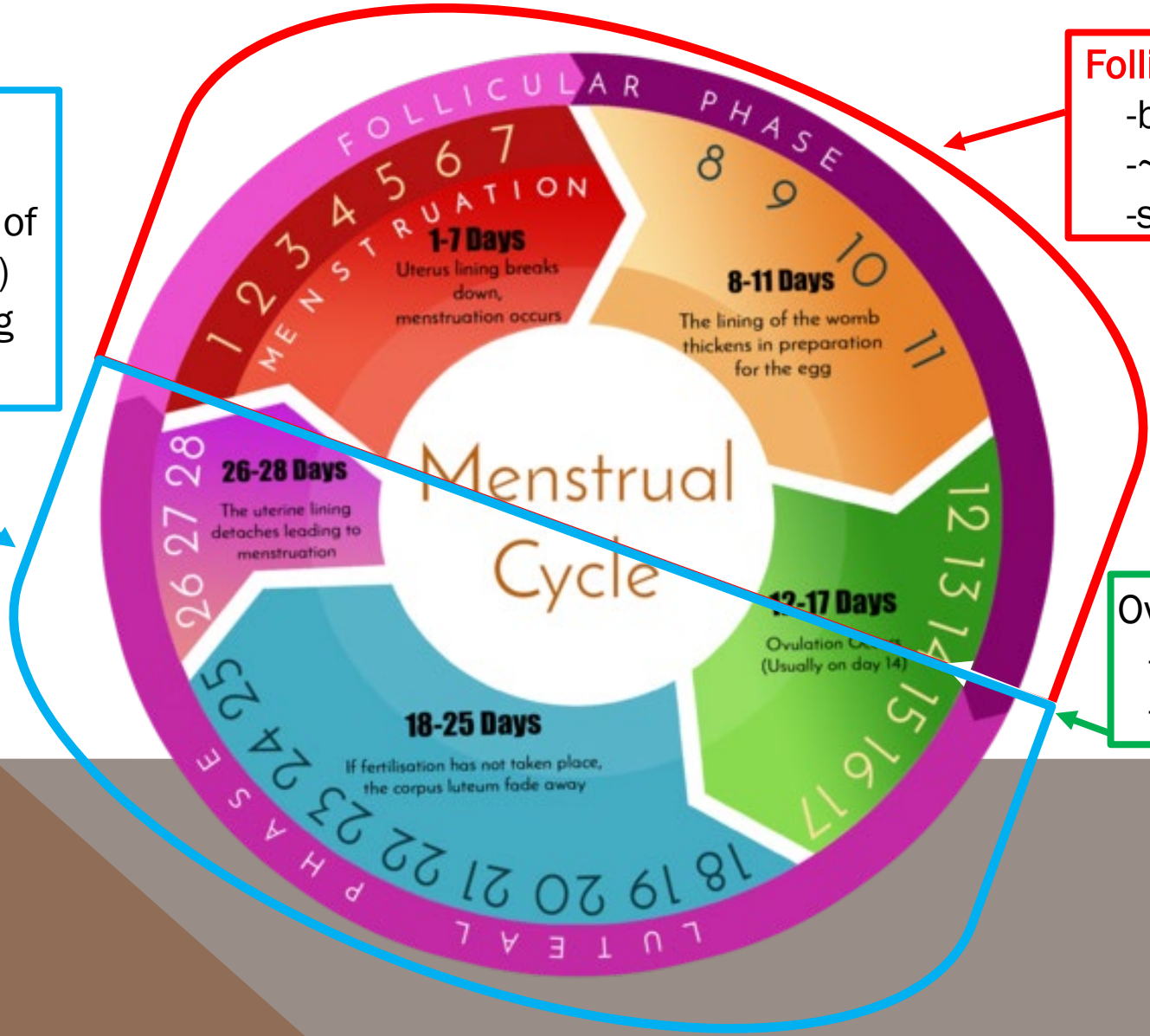
MENSTRUAL CYCLES

MENSTRUAL CYCLES: GENERAL PRINCIPLES

Luteal phase:
-last 14 days of the cycle
-corpus luteum (remains of released follicle in ovary) decays and uterine lining thickens

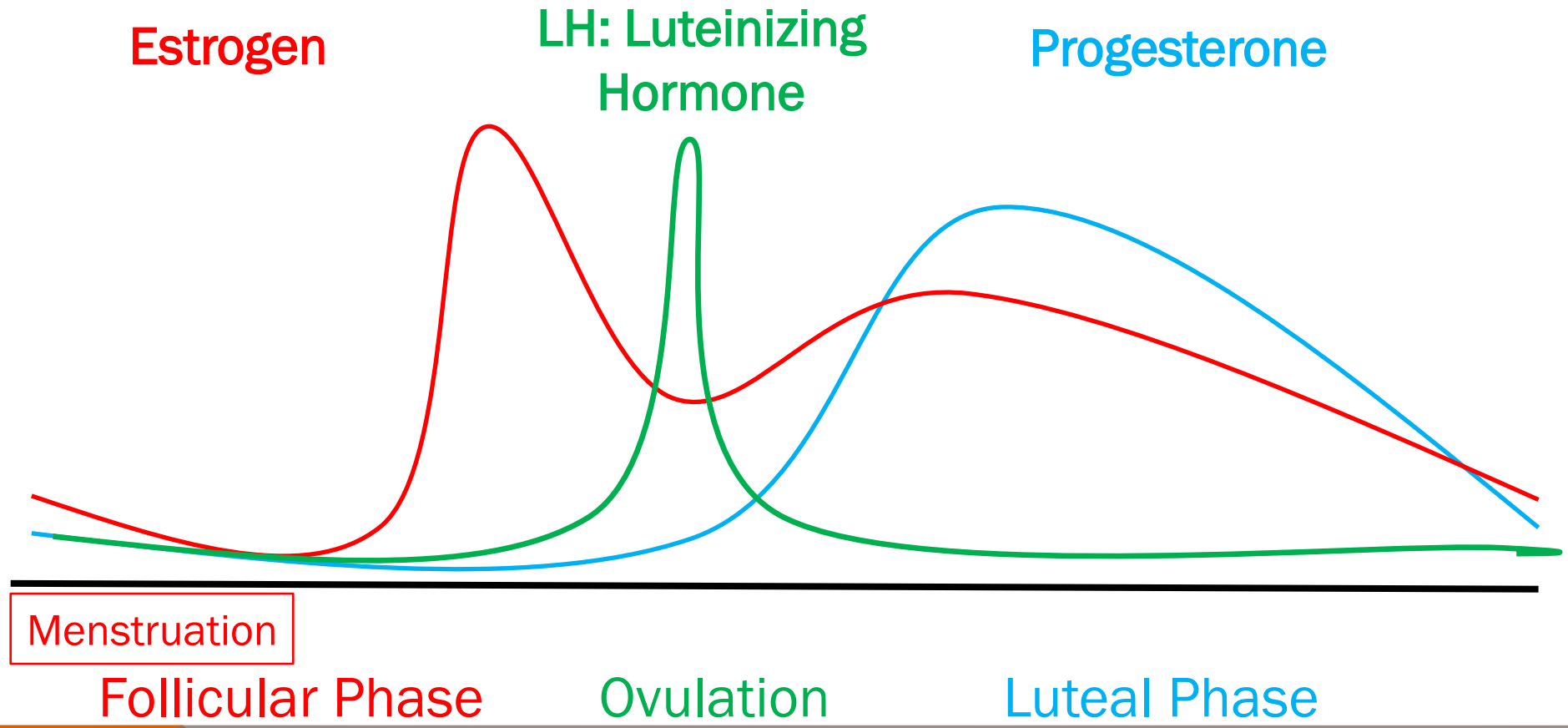
Follicular phase:
-bleeding → ovulation
-~half the cycle, 14-21 days
-some follicles grow within ovary



Ovulation:
-~mid-point of the cycle
-one follicle or "egg" is released

Anigan. All about Menstruation: How Does the Menstrual Cycle Work? www.anigan.com

MENSTRUAL CYCLES: GENERAL PRINCIPLES



MENSTRUAL CYCLES: CHALLENGES IN T1D

- Women with T1D experience more menstrual irregularity than those without it.
- During menstruation, glucose can range (↑,~,↓), depending on the woman.

- There is glucose variability over the cycle.
- Not every woman has a consistent pattern in glucose variability.
- The most common glucose pattern is luteal phase hyperglycemia and is due to shifts in insulin resistance over the course of the cycle.

Walsh CH, Malins JM, *Br Med J*, 1977. Schroeder B et al, *J of Repro Med*, 2000.
Goldner WS et al, *DTT*, 2004. Gaete X et al, *Fertility and Sterility*, 2010. Barata DS et al, *Diab Care*, 2013.

MENSTRUAL CYCLES: CHALLENGES IN T1D

- **High glucose levels can lead to:**
  - a later start date for menses to begin,
  - lack of menses, and
  - skipped menses.

- Menstrual disturbances have been found to be increased when the A1C is over 9%.

Schroeder B et al, *J of Repro Med*, 2000. Arrais RF, Dib SA, *Human Repro*, 2006. Gaete X et al, *Fertility and Sterility*, 2010.

MENSTRUAL CYCLES: OVERCOMING CHALLENGES IN T1D

- Hormone-based contraception can regulate and improve cycle variability and symptoms. Please consult with a medical professional.

- Closely monitor at least 3 menstrual cycles with frequent finger-sticks and/or CGM to identify if a consistent glucose pattern exists.

- Control glucose levels as much as possible.
  - Automated insulin delivery therapy helps reduce high and low glucose values across menstrual cycles.

- Adjust insulin doses to limit the glucose extremes.

Schroeder B et al, *J of Repro Med*, 2000. Arrais RF, Dib SA, *Human Repro*, 2006. Gaete X et al, *Fertility and Sterility*, 2010. Bahamondes L et al, Human Repro Update, 2015. Mesa A et al, *DTT,* 2024. Elhenawy YI et al, *Diab Obes Metab,* 2024.

PREGNANCY

PRECONCEPTION COUNSELING/PLANNING

- **Worldwide, ~48% of pregnancies are unintended.**

- **Discussions with non-pregnant individuals with childbearing potential should occur:**
  - multiple times over the reproductive years.
  - regardless of use of contraception or plan to become pregnant.

UNFPA. Seeing the Unseen. 2022; 9-18. ACOG. *Obstet Gynecol*. 2019; 133(1): e78-e89.

PREGNANCY: GLUCOSE TARGETS FOR WOMEN WITH DIABETES

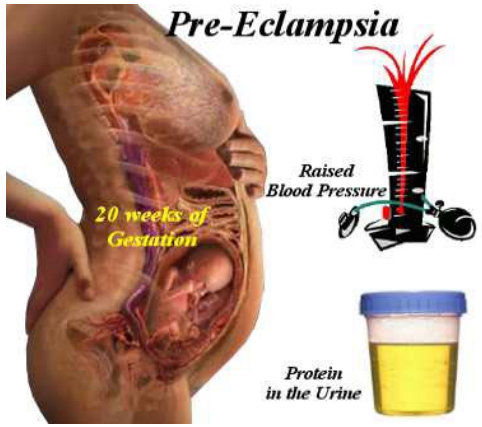
Measurement	Target with Preexisting Diabetes	Target with Significant Hypoglycemia
Hemoglobin A1C (A1C)	<6%	<7%
Fasting glucose	<95 mg/dL	<105 mg/dL
Postprandial glucose	1-hour: <140 mg/dL 2-hour: <120 mg/dL	1-hour: <155 mg/dL 2-hour: <130 mg/dL

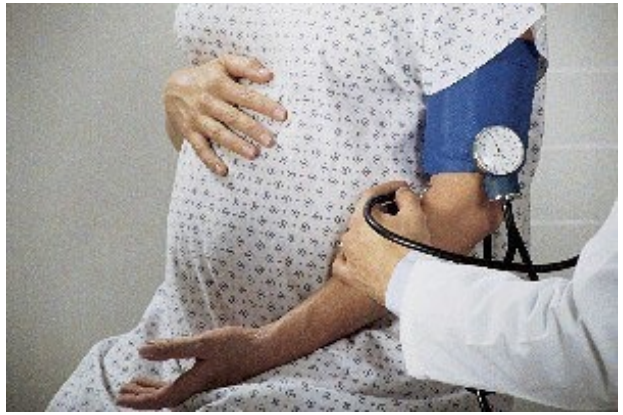
Aim to achieve these targets if they can be met without significant hypoglycemia.

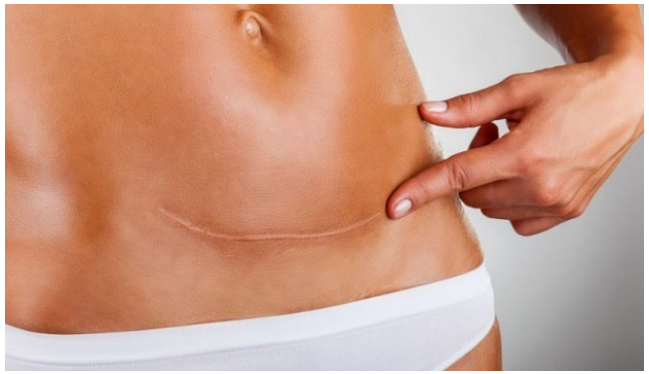
ADA. Management of diabetes in pregnancy. *Diabetes Care* 2025: 48 Suppl 1: S306-S320.
ADA. Management of diabetes in pregnancy. *Diabetes Care* 2016: 39 Suppl 1: S94-S98.

WHY ARE THE GLYCEMIC TARGETS SO STRICT?

- Hyperglycemia is associated with numerous adverse maternal and fetal outcomes.

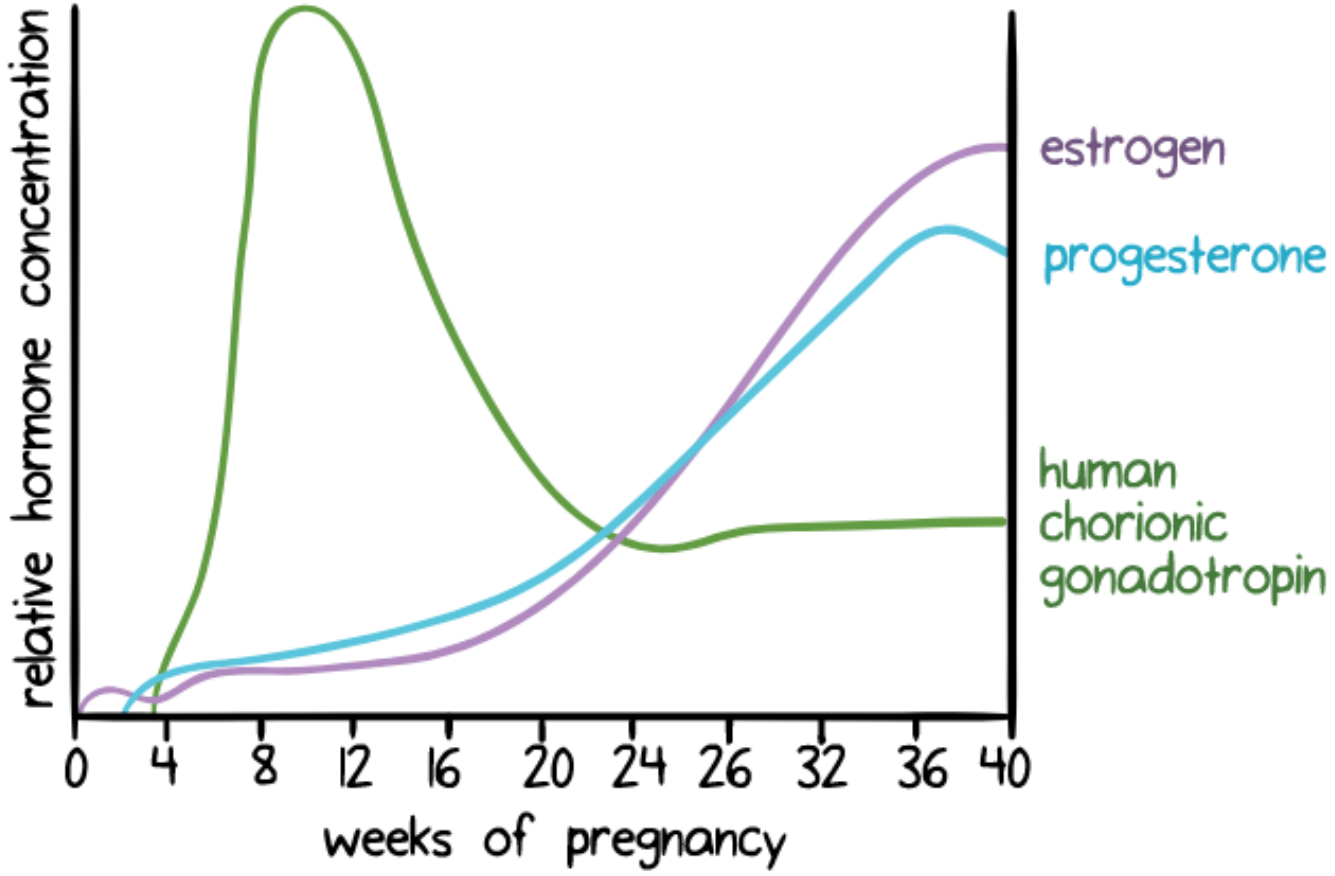






Keely and Barbour, EndoText, 2014; Kitzmiller JL et al, Diabetes Care, 2008; Evers IM et al, Diabetes Care, 2002.

PREGNANCIES: HORMONAL CHANGES



Khan Academy, Physiology of Pregnancy, 2018.

PREGNANCY: INSULIN REQUIREMENTS

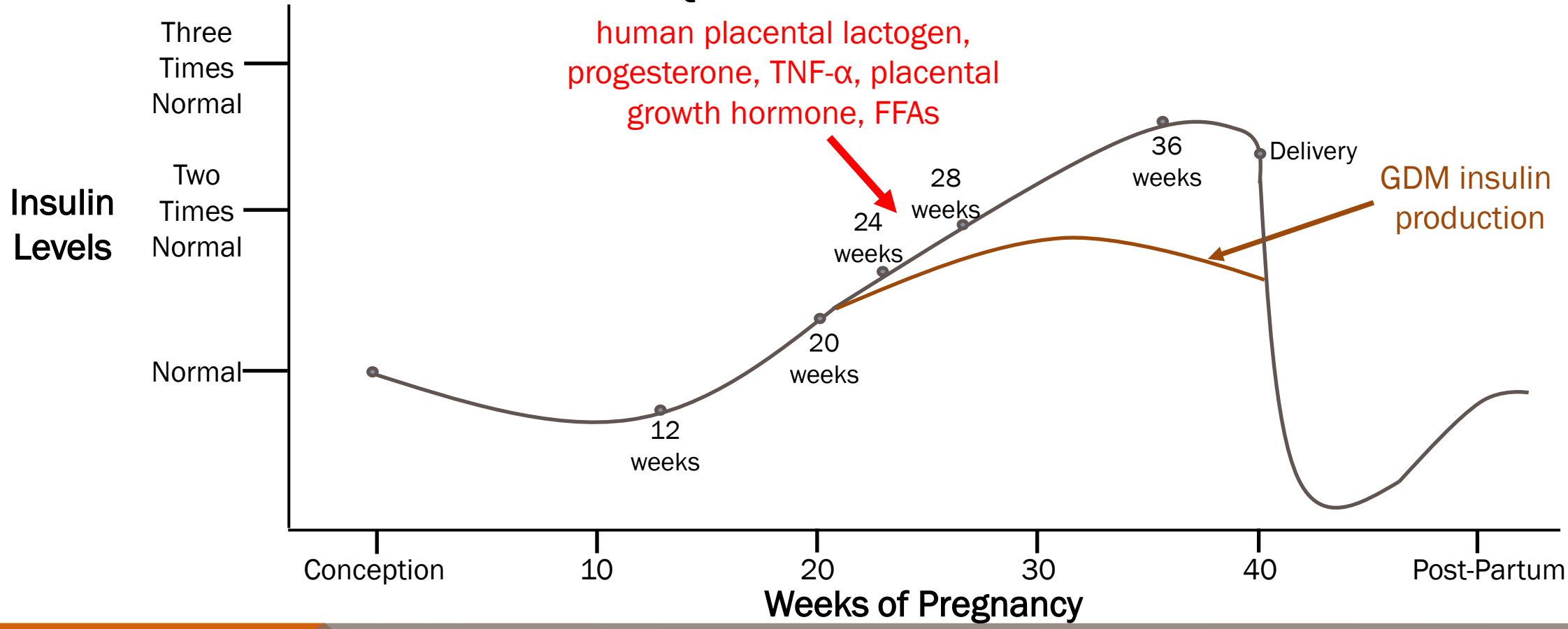


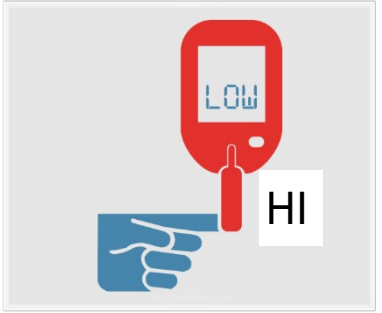
Figure Recreated and Adapted from: Marcinkevage JA and Venkat Narayan KM. *Primary Care Diabetes* 2011; 5(2): 81-88. Keely E, Barbour LA. Management of diabetes in pregnancy. *Endotext*. 2000-. 2014 Feb 14. Ringholm L, et al. Nat Rev Endocrinol. 2012;8(11):659–667. Feldman AZ, et al. *Curr Diab Rep*. 2016.

PHYSIOLOGY OF PREGNANCIES ASSOCIATED WITH DIABETES

- ↑ Insulin sensitivity in the first trimester.

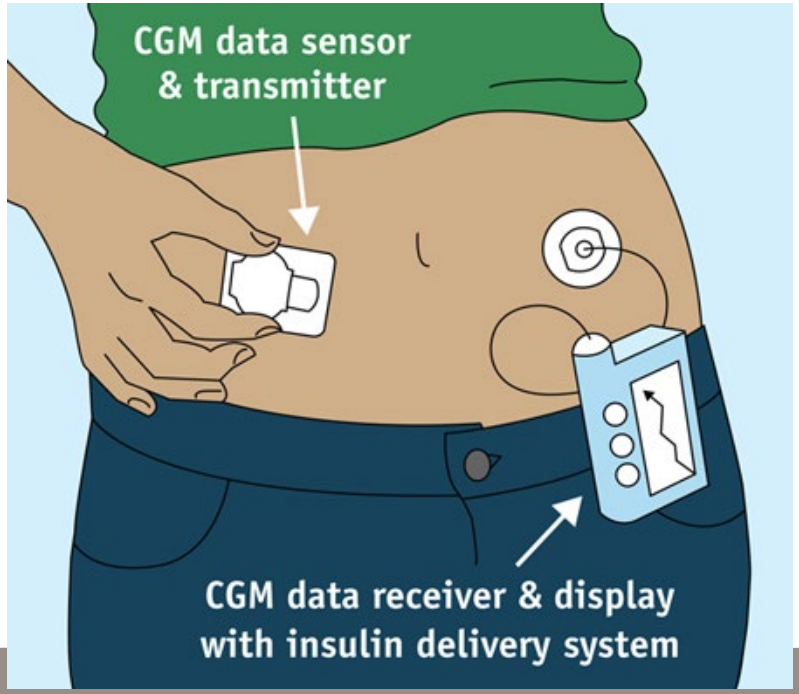
  -Predisposes to nocturnal (fasting) hypoglycemia.

- ↑ Risk for euglycemic DKA.



Keely E, Barbour LA. Management of diabetes in pregnancy. Endotext. 2000-. 2014 Feb 14. Ringholm L, et al. Nat Rev Endocrinol. 2012;8(11):659–667.

CONTINUOUS GLUCOSE MONITORING (CGM)



REAL-TIME CGM IN PREGNANCY: CONCEPTT

Table 3: Maternal Outcomes

Outcome	CGM	Control	P-value
Maternal outcomes	No significant changes between groups		

Table 4: Neonatal Outcomes

Outcome	CGM	Control	P-value
Number assessed	100	100	--
Median customized centile birth weight*	92 (68–99)	96 (84–100)	0.0489
LGA (>90th centile)	53 (53%)	69 (69%)	0.0210
Neonatal hypoglycemia requiring IV dextrose	15 (15%)	28 (28%)	0.0250
NICU >24 hours	27 (27%)	43 (43%)	0.0157
Infant length of hospital stay	3.1 (2.1–5.7)	4.0 (2.4–7.0)	0.0091

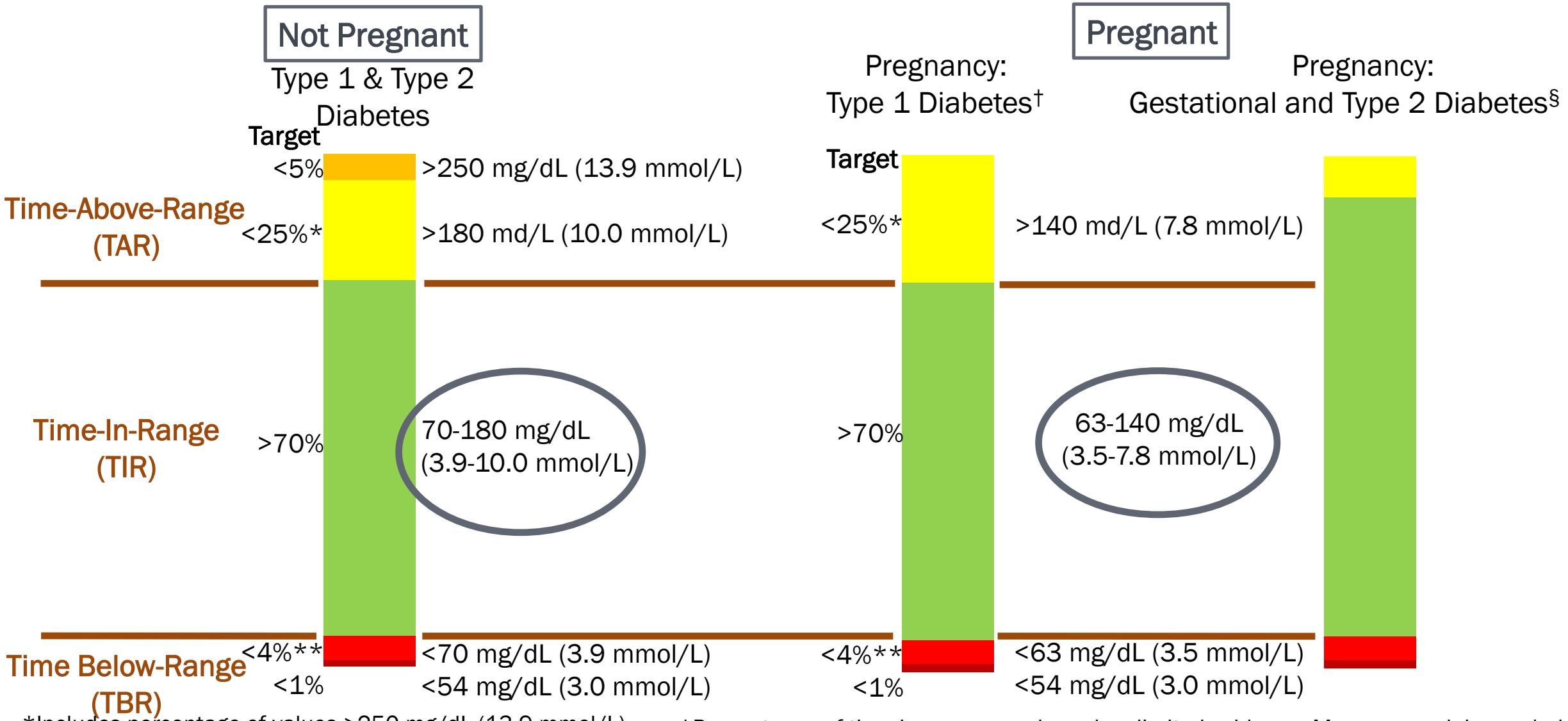
Mean (SD) and median (IQR) as appropriate. *Based on gestation-related optimal weight customised growth charts

Points to consider:

- First RCT intended for constant CGM use in pregnancy.
- Maternal and fetal outcomes may reflect changes in TIR and post-prandial hyperglycemia in a well-controlled cohort.
- Between-group difference in A1C of 0.5% was not achieved.
- CGM use was 70% in pregnancy group and 77% in planning pregnancy group.
- A1C measurements were infrequent.

Feig DS, et al. *Lancet*. 2017; 390(10110): 2347-2359.
Garg SK, Polsky S. *Lancet*. 2017; 390(10110): 2329-31.

CGM TARGETS FOR PEOPLE WITH DIABETES



*Includes percentage of values >250 mg/dL (13.9 mmol/L).
**Includes percentage of values <54 mg/dL (3.0 mmol/L).

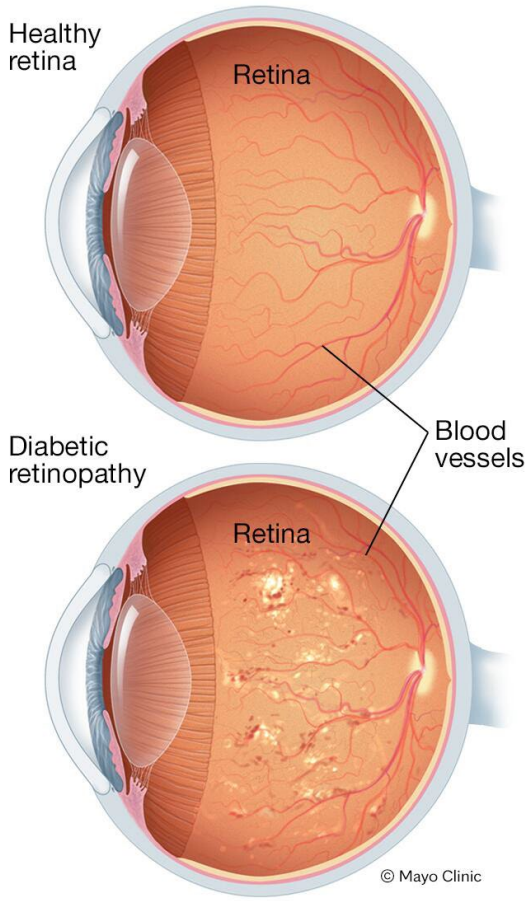
†Percentages of time in ranges are based on limited evidence. More research is needed.
§Percentages of time in ranges have not been included because there is very limited evidence in this are. More research is needed.

Figure Adapted from: Batellino T et al. *Diabetes Care* 2019: 42(8): 1593-1603.

RETINOPATHY AND PREGNANCY

- **High risk of developing or having progression of diabetic retinopathy for individuals with preexisting type 1 and type 2 diabetes.**

- **Dilated eye examinations recommended prior to pregnancy, every trimester, and post-partum.**
  - Degree of retinopathy and recommendation of eye health care professional influence frequency of eye examinations.
  - Post-partum period out to 1 year.



ADA. Management of diabetes in pregnancy. *Diabetes Care* 2024: 47 Suppl 1: S282-S294.
Image from: https://www.mayoclinic.org/diseases-conditions/diabetic-retinopathy/symptoms-causes/syc-20371611

PREECLAMPSIA

High Risk Level

Aspirin for Preeclampsia Prevention in Women with ≥1 High-Risk Factor*	
T1D	History of Preeclampsia
T2D	Multifetal Gestation
Chronic Hypertension	Renal Disease
Autoimmune disease (SLE, antiphospholipid syndrome)	

*Low-dose aspirin (100-150 mg/day), starting 12-16 weeks gestation.

Moderate Risk Level

Aspirin for Preeclampsia Prevention in Women with ≥2 Moderate-Risk Factor*	
Nulliparous	BMI >30 kg/m^2
Age ≥35 Years	*In vitro* Conception
Black Race	Low SES
Family History of Preeclampsia (Mother, Sister)	Personal Pregnancy History (e.g., low birthweight, APO)

APO, adverse pregnancy outcome; BMI, body mass index; SES, socioeconomic status.

ACOG. *Obs & Gyn.* July 2018; 132(1): e44-e51. USPTF. 2021 Sep. Report No.: 21-05274-EF-1.
ADA. Management of diabetes in pregnancy. *Diabetes Care* 2024: 47 Suppl 1: S282-S294.

PREGNANCY: A TEAM APPROACH

- Obstetrician or maternal-fetal specialist (preferably high-risk providers)
- Diabetes provider (diabetologist or endocrinologist)
- Diabetes care and education specialist
- Registered dietician nutritionist
- Nurse
- Social worker
- Ophthalmologist or optometrist
- Nephrologist (if needed)
- Cardiology (if needed)
- Pediatrician or neonatologist

Medical Management of Type 1 Diabetes, 6th Ed. 2012.

MENOPAUSE

IMPACT OF DIABETES ON MENOPAUSE ONSET

Study Title: European Prospective Investigation into Cancer and Nutrition (EPIC)

Study Design:

- Prospective cohort study in 23 centers across 10 European countries
- Questionnaires administered from 1992 through 2000.
- Data from 258,898 out of 367,331 women (70.5%) included.
- Diabetes diagnosis and age of menopause onset based on self-report.

Brand JS et al. *Human Reproduction*. 2014; 30(6): 1491-98.

IMPACT OF DIABETES ON MENOPAUSE ONSET

Results:

- Total cohort median age of natural menopause: 52 years

- Hazard ratio (HR) for risk of earlier menopause:
  - ➢DM diagnosis <10 years: HR = 1.59 (95% CI, 1.03-2.43) ↑
  - ➢DM diagnosis 10-20 years: HR = 1.43 (95% CI, 1.02-2.01) ↑
  - ➢DM diagnosis ≥50 years: HR = 0.81 (95% CI, 0.70-0.95) ↓

Relationships held after adjustments for age, smoking, reproductive factors, or DM risk factors

Brand JS et al. *Human Reproduction*. 2014; 30(6): 1491-98.

IMPACT OF T1D ON MENOPAUSE ONSET

Study Title: The Familial Autoimmune and Diabetes (FAD) Study

Study Participants:

- FAD Study consent obtained from:
  - **T1D** participants
  - Parents/**siblings** of T1D probands
  - Healthy **control** probands, group-matched by age, sex, race, and duration of Pittsburgh residence

Characteristic	T1D (n=143)	Sisters (n=186)	Controls (n=160)	P-value
Mean age at menopause* (years)	41.6	49.9	48.0	**0.05**

Dorman JS et al. *Diabetes*. 2001; 50: 1857-62.

SYMPTOMS OF DIABETES AND OF MENOPAUSE

Diabetes Symptoms		Menopausal Symptoms	
Polyuria, Polydipsia	**Sweating (hypo)**	**Hot flashes**	**Night sweats**
Polyphagia/Hunger	Tremor (hypo)	Nervousness	Sleep disturbances
Weight loss	**Anxiety (hypo)**	**Anxiety**	**Vaginal dryness**
Nausea (hyper, DKA)	Dizziness (hypo)	**Irritability**	Dyspareunia
Headaches	Changes in vision	**Depression**	Breast pain
Vaginal dryness (DM complications)	**Blunted mental activity (hypo)**	**Difficulty concentrating**	**Menstrual migraines**
Abnormal behavior	Confusion (hypo)	Impaired balance	Joint aches/pain
LOC (hypo, DKA)	Convulsions (hypo)	Skin changes	Body composition Δ

Abbreviations: DKA, diabetic ketoacidosis; hyper, hyperglycemia; hypo, hypoglycemia; LOC, loss of consciousness

UpToDate: Clinical Manifestations and Diagnosis of Menopause. Accessed May 7, 2020.
Szmuilowicz ED et al. Nature Review Endocrinology. 2009; 5(10): 553-8. Harrison's Principles of Internal Medicine, 14th Ed. Vol 2. 1998.

T1D EFFECTS ON BONE QUALITY AFTER MENOPAUSE

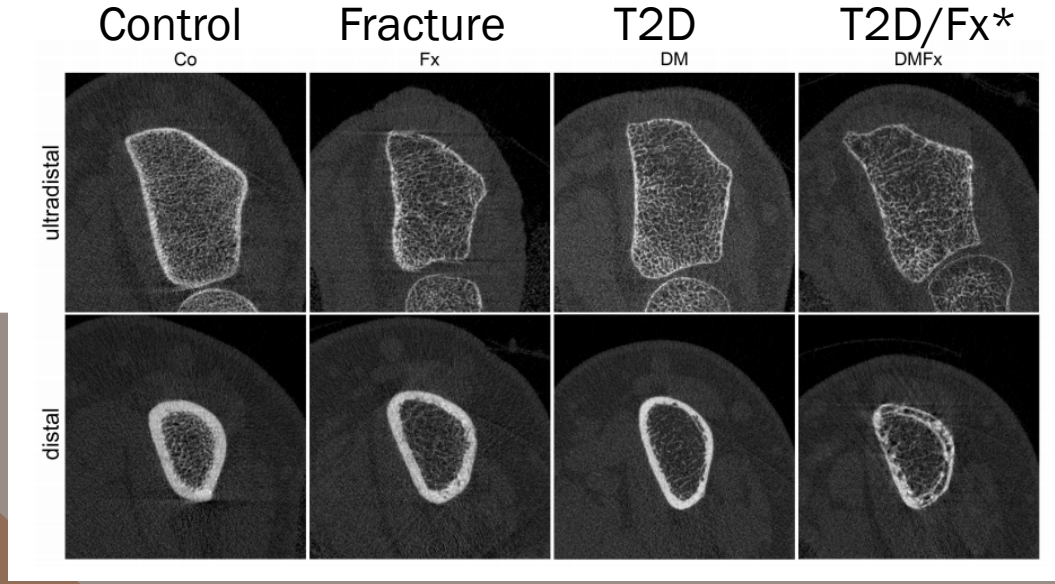
Study Design:

- Cross-sectional study in women with T1D ≥45 years old

- Post-menopausal groups:
  - Young-onset T1D: T1D onset <20 years
  - Adult-onset T1D: T1D onset >20 years

  } n=24

  - Women without DM frequency matched by age, sex, BMI (n=22)



Shah VN et al. *Bone*. 2019; 123: 260-64.

*Image from: Patsch JM et al. *J Bone Miner Res*. 2013; 28(2): 313-24.

T1D EFFECTS ON BONE QUALITY AFTER MENOPAUSE

Results:

- History of fracture ↑ in T1D (79.2% T1D vs 45.5% controls, p=0.03).
- Adjusted results for DEXA scan: no differences between groups.
- Adjusted results for peripheral quantitative CT scan (pQCT) in T1D:
  - ↓ bone quality
  - ↓ bone strength

Shah VN et al. *Bone*. 2019; 123: 260-64.

Take Home Points:

BMD (DEXA) may under-estimate fracture risk in women with DM.

Differences in bone quality contribute to ↑ fracture risk in women with DM.

Thank You

Questions?

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