IS THERE A ROLE FOR CGM IN PREGNANT PATIENTS WITH DIABETES?

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I HAVE NOTHING TO DISCLOSE.

OBJECTIVE

Describe emerging use of continuous glucose monitoring (CGM) in diabetes and pregnancy.

EPIDEMIOLOGY

CURRENT STATISTICS

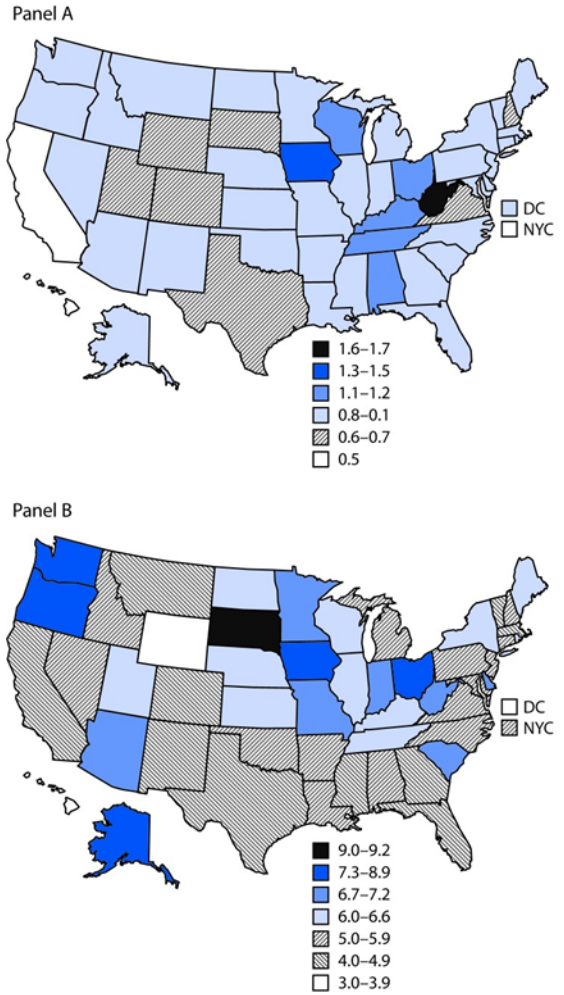
Among births occurring at Kaiser Permanente hospitals in Southern California from 1999-2005:

- Preexisting diabetes complicated approximately 0.8% of pregnancies in 1999;
- Increased to 1.82% in 2005 ($p<0.001$);
- Among deliveries to women with diabetes, 10% are due to preexisting diabetes in 1999;
- Increased to 21% of deliveries to women with diabetes in 2005.

Lawrence, et al. Trends in the Prevalence of Preexisting Diabetes and Gestational Diabetes Mellitus among a Racially/Ethnically Diverse Population of Pregnant Women, 1999-2005. Diabetes Care. 2008.

CURRENT STATISTICS

- Preexisting diabetes complicates 1.5% of pregnancies
- Half of these are secondary to Type 1 DM and half to Type 2 DM
- Prevalence of Type 1 DM among young people is increasing rapidly



Standardized prevalence of preexisting (panel A) and gestational (panel B) diabetes among women who had a live birth — United States, 2016
Abbreviations: DC = District of Columbia; NYC = New York City.
* Standardized to age and race/ethnicity distribution of U.S. resident mothers delivering in 2012.

Feig et al. Trends in incidence of diabetes in pregnancy and serious perinatal outcomes. Diabetes Care. 2014.
Patterson et al., Incidence trends for childhood type 1 diabetes. Lancet. 2009.

CURRENT STATISTICS

- Improvements in stillbirth in pregnancies complicated by Type 1 DM;
- Improvements in congenital abnormalities in pregnancies complicated by Type 1 DM;
- No improvement in other complications associated with maternal hyperglycemia such as LGA, NICU admission, or preterm delivery.

Murphy, H. Intensive Glycemic Treatment During Type 1 Diabetes Pregnancy: A Story of (Mostly) Sweet Success! Diabetes Care. 2018.

CURRENT STATISTICS

Glucose excursions *not adequately evaluated* by FSBG can affect both maternal and fetal wellbeing

- Postprandial hyperglycemia is associated with macrosomia
- Nocturnal and pre-prandial hypoglycemia can increase hypoglycemia unawareness and put pregnant women at risk of trauma, seizures, and death

LONG-TERM VERSUS SHORT-TERM GOALS

LONG-TERM GOALS

- Avoid long-term complications of diabetes;
- Avoid hypoglycemia and associated complications;
- Avoid development of hypoglycemia unawareness.

SHORT-TERM GOALS

- Achieve tight blood glucose control to create a healthy hormonal and nutritional milieu for the developing fetus;
- Avoid hyperglycemia and hypoglycemia and the associated complications for the fetus, child, and adult.

MATERNAL COMPLICATIONS – DIABETES

Miscarriage

Hypertensive disorders of pregnancy

Preterm delivery

Macrosomia

Polyhydramnios

Trauma to pelvic floor

Operative delivery

Hemorrhage

Infectious morbidity

FETAL COMPLICATIONS – DIABETES

Miscarriage
Congenital abnormalities
Macrosomia
NICU admission
Hypoglycemia
Hyperbilirubinemia
RDS

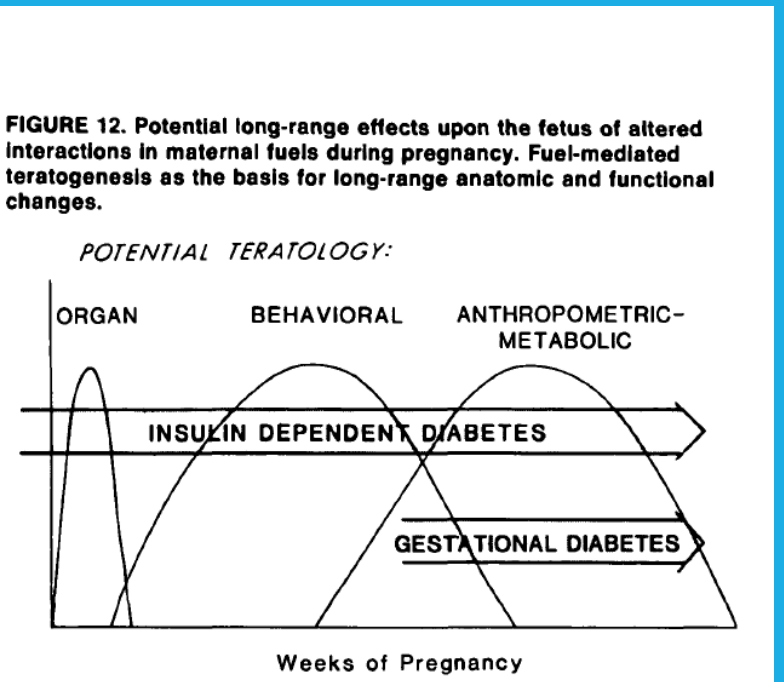
Operative delivery
Shoulder dystocia
Birth trauma
Stillbirth
Childhood/adult obesity
Childhood/adult Type II diabetes

FETAL PROGRAMMING

FREINKEL, BANTING LECTURE 1980

"…might not one effect possibly permanent changes in habitus (that is, anthropometric modifications) or in endocrine or neuroendocrine metabolism by abnormal fuel presentations during the period of intrauterine development for the terminally differentiated cells that determine these functions?"

DIABETES, VOL. 29, DECEMBER 1980



BARKER HYPOTHESIS OF FETAL PROGRAMMING

"…nutritional (and other environmental) exposures during critical developmental windows may induce changes in tissue development and function that contribute to long-term chronic disease risk.

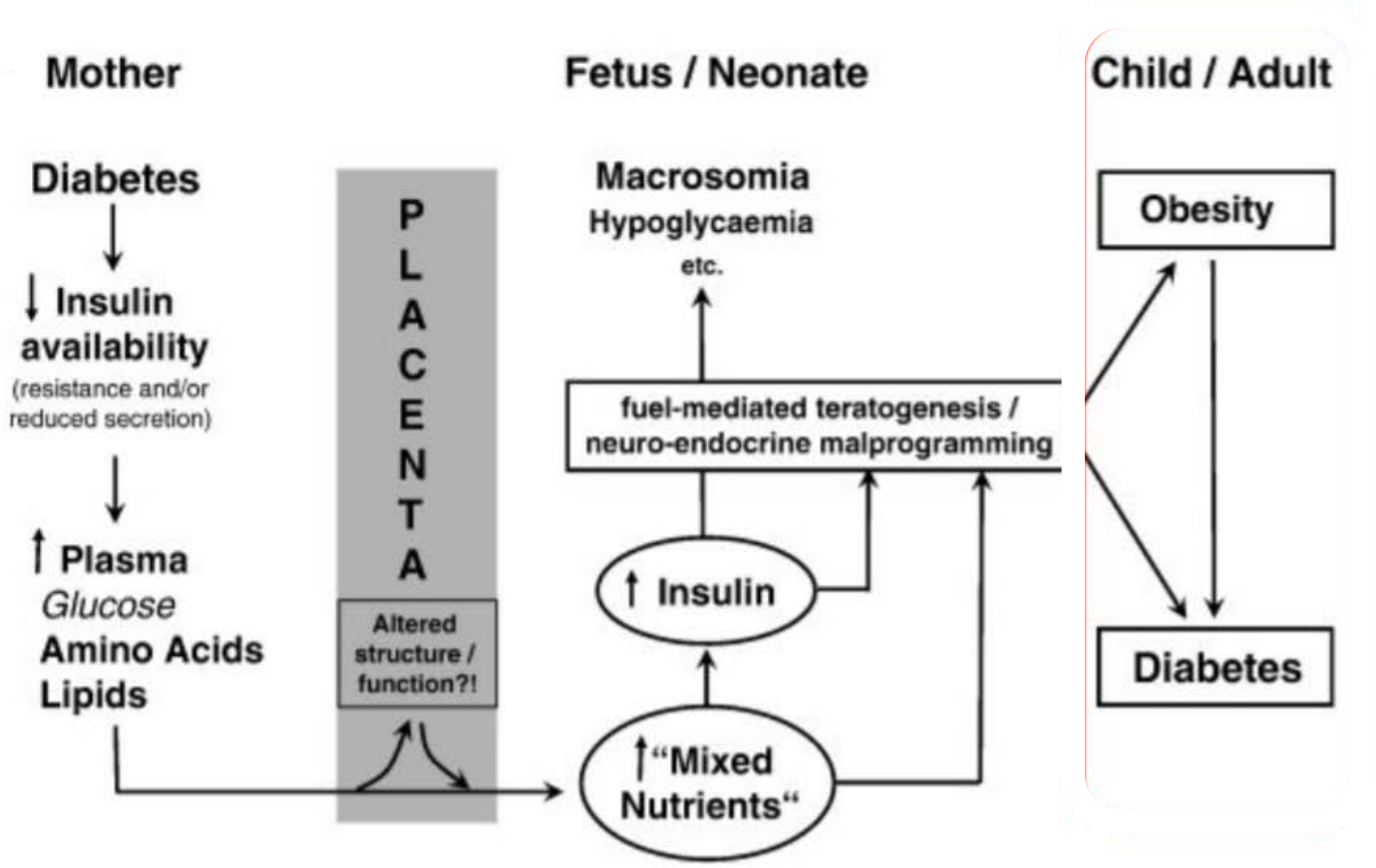
"effects may be mediated through epigenetic changes in the β-cells, liver, and insulin target tissues, along with the hypothalamic appetite signaling, the gut microbiome, plasma metabolites, and other factors."

Barker, Osmond. Infant mortality, childhood nutrition, and ischaemic heart disease in England and Wales. Lancet 1986.
Gingras. Early-life exposures and risk of diabetes mellitus and obesity. Curr Diab Rep 2018.
Chen. Differnetial methylation of genes in individuals exposed to maternal diabetes in utero. Diabetologia 2017.
Brown. Much to HAPO FUS About. Diabetes Care 2019.

BARKER HYPOTHESIS/DOHAD

Fetal environment either nutritionally deprived or over-rich increases risk for child and adult obesity and its sequelae (Catalano, 2003; Oken & Gillman, 2003; Ehrenberg et al., 2004)

Developmental Origins of Adult Health and Disease (DOHaD) (Gluckman et al 2005; Taylor & Poston, 2007)

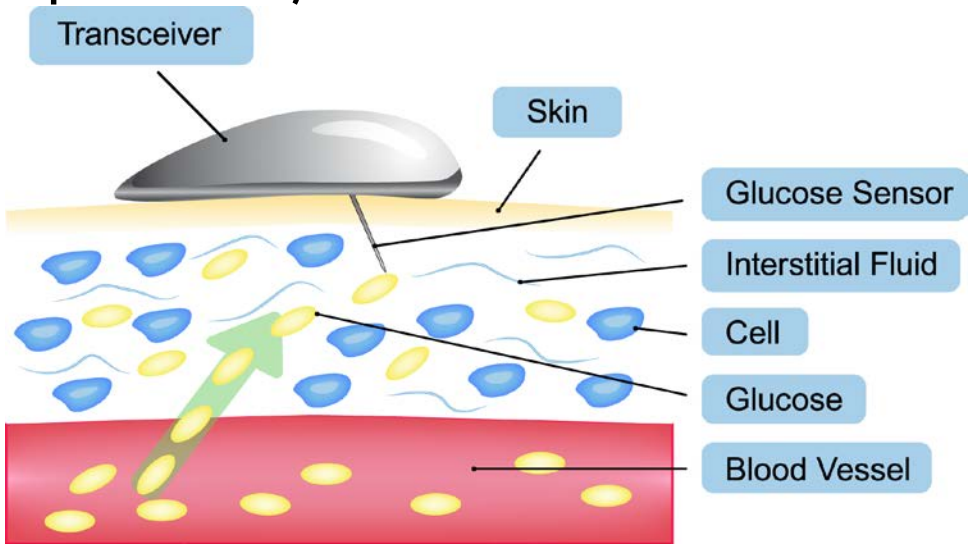


Pedersen et al. "Blood Sugar in Newborn Infants of Diabetic Mothers" Acta Endocrinol 1954
Freinkel N. "Of pregnancy and progeny. Banting lecture 1980. Diabetes 1980
Dorner G. et al. "Perinatal hyperinsulinism as possible predisposing factor for diabetes mellitus, obesity and enhanced cardiovascular risk in later life." Horm Metab Res 1994

CGM VS. SMBG VS. HBA1C

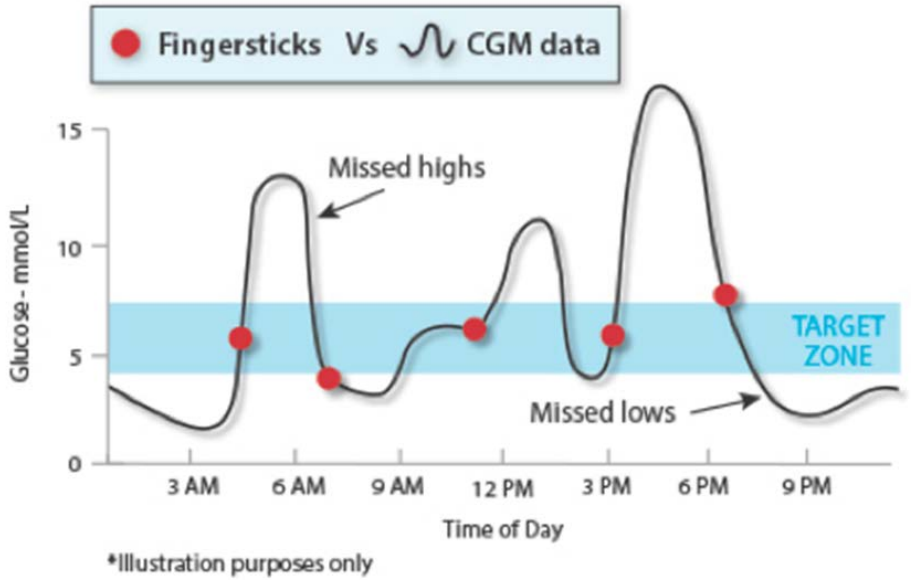
CONTINUOUS GLUCOSE MONITOR (CGM)

"a system that measures interstitial glucose levels on a continuous basis throughout the day and night." (L. Hieronymus. Diabetes Self Management. March/April 2019)



SELF-MONITORED BLOOD GLUCOSE

- Fingerstick BG data misses significant highs and lows that have consequences for both mom and fetus



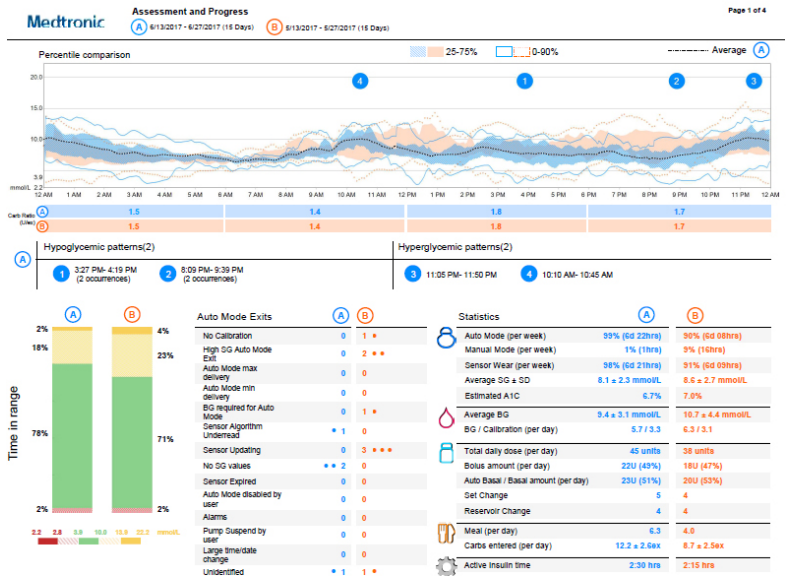
HBA1C

HbA1c is not a helpful measure of blood glucose control in pregnancy:

- HbA1c normally decreases in pregnancy due to physiologic changes of pregnancy;
- HbA1c is an average and does not adequately reflect the blood glucose variability.

CGM DATA

CGM “allows for unprecedented characterization of the day-to-day, within-day, and between-day glycemic variability.”



Murphy, H. Intensive Glycemic Treatment During Type 1 Diabetes Pregnancy: A Story of (Mostly) Sweet Success!. Diabetes Care. August 2018.

STUDIES OF CGM IN PREGNANCY

MURPHY ET AL., 2008

Effectiveness of Continuous glucose monitoring in pregnant women with diabetes: randomized clinical trial

- 71 women with Type 1 DM (n=46) or Type 2 DM (n=25) allocated to antenatal care plus CGM monitoring or to standard antenatal care
- CGM was worn for up to 7 days at intervals of 4-6 weeks between 8- and 32-weeks gestation

Murphy et al., Effectiveness of continuous glucose monitoring in pregnant women with diabetes: randomised clinical trial. BMJ 2008.

MURPHY ET AL., 2008

Women randomized to CGM had:

- Lower mean HbA1c levels from 32 to 36 weeks gestation
  - 5.8% (SD 0.6) v 6.4% (SD 0.7)
- Decreased median birthweight centiles
  - 69% v 93%
- Reduced risk of macrosomia
  - Odds ratio 0.36 (CI 0.13 to 0.98)

Murphy et al., Effectiveness of continuous glucose monitoring in pregnant women with diabetes: randomised clinical trial. BMJ 2008.

SECHER ET AL., 2013.

The effect of real-time continuous glucose monitoring in pregnant women with diabetes: a randomized controlled trial

- 123 women with Type 1 and 31 women with Type 2 diabetes;
- Randomized to intermittent real-time CGM for 6 days on 5 occasions (at 8, 12, 21, 27, and 33 weeks gestation) versus usual care;
- HbA1c and SMBG compared at each time period, prevalence of LGA and other neonatal outcomes were compared at delivery.

Secher et al., The Effect of Real-Time Continuous Glucose Monitoring in Pregnant Women with Diabetes. Diabetes Care. 2013.

SECHER ET AL., 2013.

Women using intermittent real-time CGM had:

- Equivalent HbA1c to usual care patients
  - 6.1% vs 6.1%, p= 0.39
- Equivalent frequency of sever hypoglycemia
  - 16% vs 16%, p=0.91
- Statistically equivalent incidence of LGA
  - 45% vs 34%, p=0.19

Secher et al., The Effect of Real-Time Continuous Glucose Monitoring in Pregnant Women with Diabetes. Diabetes Care. 2013.

FEIG ET AL, 2017

Continuous glucose monitoring in pregnant women with type 1 diabetes (CONCEPTT): a multicenter international randomized controlled trial

- 215 pregnant women, 108 assigned to CGM intervention and 107 assigned to control
- CGM's were worn approximately 6 days per week
- HbA1c was measured at randomization, 24 weeks, and 34 weeks gestation

Feig et al., Continuous glucose monitoring in pregnant women with type 1 diabetes (CONCEPTT): a multicenter international randomized controlled trial. Lancet 2017.

FEIG ET AL, 2017

Women randomized to the CGM group had:

- Greater change in HbA1c from baseline to 34 weeks;
- Spent increased time in recommended glucose control target range;
  - 68% vs 61%, (p=0.0034)
- Reduced time above the target range;
  - Without increased maternal hypoglycaemia
- Decreased proportion of large for gestational age infants
  - Odds ratio 0.51, CI 0.28 to 0.90, (p=0.0210)

Feig et al., Continuous glucose monitoring in pregnant women with type 1 diabetes (CONCEPTT): a multicenter international randomized controlled trial. Lancet 2017.

FEIG ET AL, 2017

Infants of mothers randomized to CGM:

- Fewer NICU admissions > 24hrs;
- Fewer incidences of neonatal hypoglycaemia;
- Reduced total length of hospital stay.

Number of pregnant women needed to treat with CGM to prevent one NICU admission or LGA infant is six.

Feig et al., Continuous glucose monitoring in pregnant women with type 1 diabetes (CONCEPTT): a multicenter international randomized controlled trial. Lancet 2017.

SUMMARY

SUMMARY

- No clear-cut advantage to intermittent and retrospective use of CGM;
- Some evidence to support real time use of CGM for neonatal outcomes;
- More research needed on continuous real time use of CGM;
- More research needed on optimal glucose goals for pregnancy and diabetes.

SUMMARY (MY THOUGHTS)

- Use of CGM during pregnancy is preferred because it allows for increased capture of episodes of hyper- and hypo-glycemia, allowing us to address them with medication changes, and achieve tighter blood glucose control benefitting the fetus and neonate while decreasing the risk of hypoglycemia to the mother.

SUMMARY

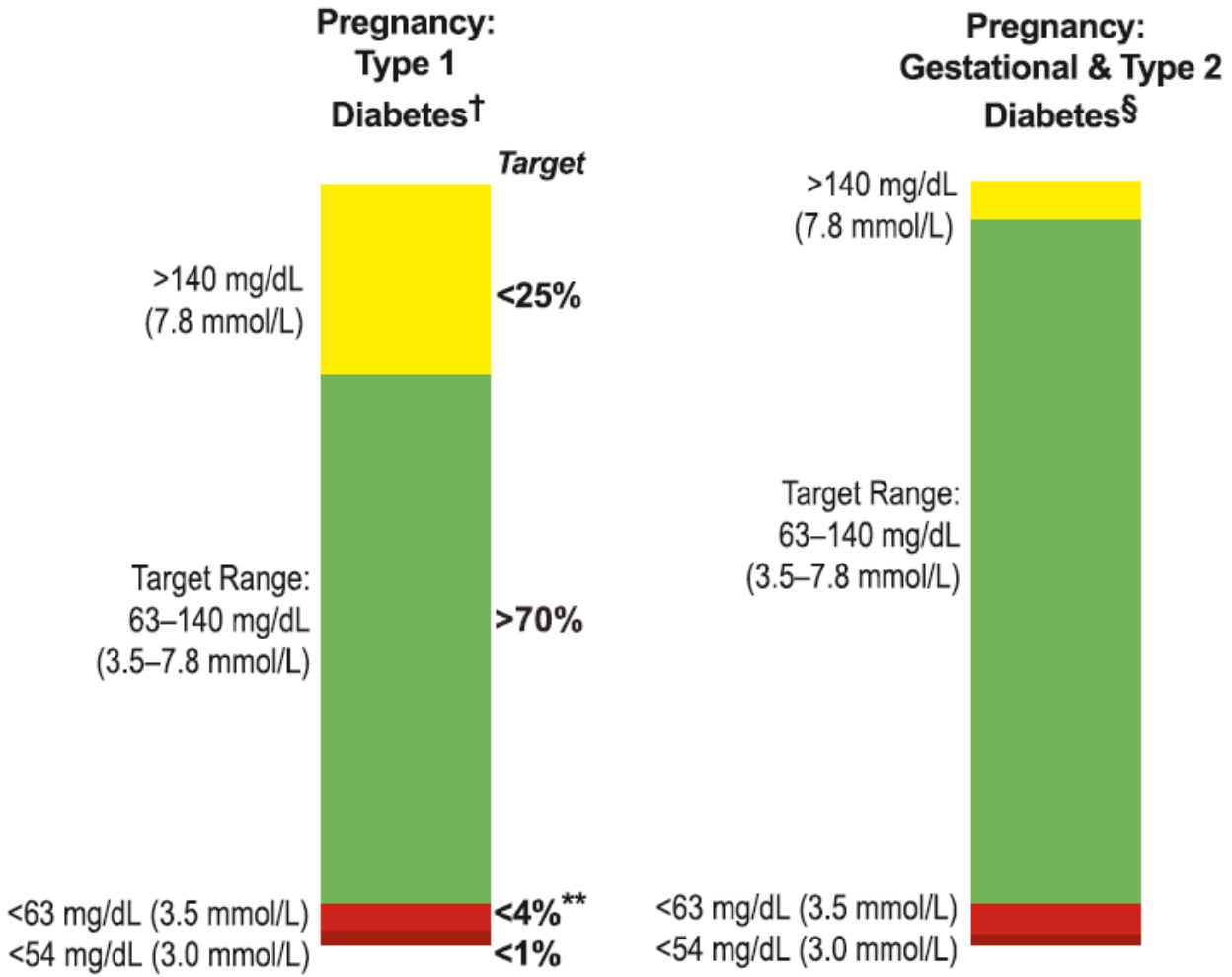
Table 4—Guidance on targets for assessment of glycemic control during pregnancy

	TIR		TBR		TAR	
Diabetes group	% of readings; time per day	Target range	% of readings; time per day	Below target level	% of readings; time per day	Above target level
Pregnancy, type 1§	>70%; >16 h, 48 min	63–140 mg/dL† (3.5–7.8 mmol/L†)	<4%; <1 h <1%; <15 min	<63 mg/dL† (<3.5 mmol/L†) <54 mg/dL (<3.0 mmol/L)	<25%; <6 h	>140 mg/dL (>7.8 mmol/L)
Pregnancy, type 2/GDM§	See PREGNANCY section	63–140 mg/dL† (3.5–7.8 mmol/L†)	See PREGNANCY section	<63 mg/dL† (<3.5 mmol/L†) <54 mg/dL (<3.0 mmol/L)	See PREGNANCY section	>140 mg/dL (>7.8 mmol/L)

Each incremental 5% increase in TIR is associated with clinically significant benefits for pregnancy in women with type 1 diabetes (59,60). †Glucose levels are physiologically lower during pregnancy. §Percentages of TIR are based on limited evidence. More research is needed.

Battelino, et al., Clinical Targets for Continuous Glucose Monitoring Data Interpretation: Recommendations From the International Consensus on Time in Range. Diabetes Care. 2019.

SUMMARY



Battelino, et al., Clinical Targets for Continuous Glucose Monitoring Data Interpretation: Recommendations From the International Consensus on Time in Range. Diabetes Care. 2019.

THE END