

Glucose levels measured with continuous glucose monitoring in uncomplicated pregnancies

Anders L Carlson,¹ Roy W Beck,² Zoey Li ,² Elizabeth Norton,³ Richard M Bergenstal,¹ Mary Johnson,¹ Sean Dunnigan,¹ Matthew Banfield,¹ Katie J Krumwiede,¹ Judy R Sibayan,² Peter Calhoun,² Celeste Durnwald³

To cite: Carlson AL, Beck RW, Li Z, *et al*. Glucose levels measured with continuous glucose monitoring in uncomplicated pregnancies. *BMJ Open Diab Res Care* 2024;**12**:e003989. doi:10.1136/bmjdr-2023-003989

► Additional supplemental material is published online only. To view, please visit the journal online (<https://doi.org/10.1136/bmjdr-2023-003989>).

Received 20 December 2023
Accepted 17 April 2024



© Author(s) (or their employer(s)) 2024. Re-use permitted under CC BY-NC. No commercial re-use. See rights and permissions. Published by BMJ.

¹International Diabetes Center Park Nicollet, St. Louis Park, Minnesota, USA

²Jaeb Center for Health Research, Tampa, Florida, USA

³Maternal Fetal Medicine Research Program, Department of Obstetrics and Gynecology, Perelman School of Medicine, University of Pennsylvania, Philadelphia, Pennsylvania, USA

Correspondence to

Dr Celeste Durnwald; celeste.durnwald@pennmedicine.upenn.edu

ABSTRACT

Introduction To characterize glucose levels during uncomplicated pregnancies, defined as pregnancy with a hemoglobin A1c <5.7% (<39 mmol/mol) in early pregnancy, and without a large-for-gestational-age birth, hypertensive disorders of pregnancy, or gestational diabetes mellitus (ie, abnormal oral glucose tolerance test).

Research design and methods Two sites enrolled 937 pregnant individuals aged 18 years and older prior to reaching 17 gestational weeks; 413 had an uncomplicated pregnancy (mean±SD body mass index (BMI) of 25.3±5.0 kg/m²) and wore Dexcom G6 continuous glucose monitoring (CGM) devices throughout the observed gestational period. Mealtimes were voluntarily recorded. Glycemic levels during gestation were characterized using CGM-measured glycemic metrics.

Results Participants wore CGM for a median of 123 days each. Glucose levels were nearly stable throughout all three trimesters in uncomplicated pregnancies. Overall mean±SD glucose during gestation was 98±7 mg/dL (5.4±0.4 mmol/L), median per cent time 63–120 mg/dL (3.5–6.7 mmol/L) was 86% (IQR: 82–89%), median per cent time <63 mg/dL (3.5 mmol/L) was 1.8%, median per cent time >120 mg/dL (6.7 mmol/L) was 11%, and median per cent time >140 mg/dL (7.8 mmol/L) was 2.5%. Mean post-prandial peak glucose was 126±22 mg/dL (7.0±1.2 mmol/L), and mean post-prandial glycemic excursion was 36±22 mg/dL (2.0±1.2 mmol/L). Higher mean glucose levels were low to moderately associated with pregnant individuals with higher BMIs (103±6 mg/dL (5.7±0.3 mmol/L) for BMI ≥30.0 kg/m² vs 96±7 mg/dL (5.3±0.4 mmol/L) for BMI 18.5–<25 kg/m², r=0.35).

Conclusions Mean glucose levels and time 63–120 mg/dL (3.5–6.7 mmol/L) remained nearly stable throughout pregnancy and values above 140 mg/dL (7.8 mmol/L) were rare. Mean glucose levels in pregnancy trend higher as BMI increases into the overweight/obesity range. The glycemic metrics reported during uncomplicated pregnancies represent treatment targets for pregnant individuals.

Gestational diabetes mellitus (GDM) is among the most common complications of pregnancy and is globally increasing in prevalence.¹ Over the past century, methods to measure and diagnose maternal dysglycemia have evolved, with the most current

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Continuous glucose monitoring technologies can provide glycemic profiles of uncomplicated pregnancies throughout gestation, an area where there are little data for clinicians.

WHAT THIS STUDY ADDS

⇒ Overall mean±SD glucose levels in uncomplicated pregnancies were 98±7 mg/dL, and median per cent time 63–120 mg/dL was 86% (IQR: 82–89%).

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Glycemic metrics reported during uncomplicated pregnancies could inform treatment targets for pregnant individuals and provide data for future research initiatives.

evidence supporting routine use of oral glucose tolerance testing (OGTT), with or without antecedent glucose challenge testing, between 24 and 28 weeks' gestation for GDM screening.² More recently, early screening for GDM has been proposed by some organizations, using hemoglobin A1c (HbA1c), fasting glucose levels and/or OGTT.¹ While there is some association between HbA1c and pregnancy outcomes, this association is not well established.^{3–5} To date, there is no consensus on the glycemic thresholds that would distinguish altered glucose metabolism in early pregnancy from normal glycemic changes of pregnancy, nor on the method to assess such thresholds.

Continuous glucose monitoring (CGM) is a rapidly evolving technology used primarily for people living with diabetes to help manage their insulin or other diabetes treatments to maintain glucose levels within target ranges as much as possible. CGM-derived metrics are also used in clinical research to assess for efficacy and safety of new diabetes therapies and devices.⁶ As the accuracy and patient

tolerability of CGM devices increase, their potential use in clinical research is expanding across broad categories of glucose-related conditions.⁷ To date, few studies have described normative CGM data from a broad non-pregnant population, and there is even less known about CGM data during uncomplicated pregnancies.^{3 8 9}

The Glucose Levels Across Maternity (GLAM) Study was conducted to describe CGM-based glucose metrics throughout the pregnancies of pregnant participants aiming to correlate CGM metrics with OGTT results and obstetrical outcomes. The purpose of this paper is to describe the CGM-derived patterns of glycemia observed throughout pregnancy in a large cohort of individuals with uncomplicated pregnancies.

METHODS

Study design

This observational, non-intervention study was conducted at two academic-based clinical sites: the University of Pennsylvania, Philadelphia, Pennsylvania, USA and the International Diabetes Center at Park Nicollet, St Louis Park, Minnesota, USA.

Major eligibility criteria included age 18 years and older, singleton pregnancy under routine prenatal care at or before gestational time of 16 weeks, 6 days (determined by ultrasound), HbA1c less than 6.5% (48 mmol/mol) and no pre-gravid diabetes diagnosis, no signs of abnormalities in fetal or placental development, no use of oral systemic steroids or medication intended to lower blood glucose, and willing/able to wear a Dexcom CGM device (see online supplemental table 1 for complete listing of inclusion and exclusion criteria). Electronic informed consent was obtained from each participant.

A blinded Dexcom G6 Pro was placed during the clinical visit, and the participant instructed on its care and mailing of the transmitter to the coordinating center after 10 days. A new sensor was placed at each standard care office visit and/or at home approximately every 10 days if a sensor was worn continuously. Training of sensor insertion was performed through virtual methods (ie, video conferencing) remotely or in person. Participants were encouraged to insert new sensors at home between visits, but this was optional. Participants voluntarily entered meal start times onto a mobile application during weeks 18–22 and 32–34 of gestation. As per usual care, an OGTT was performed between 24 and 28 weeks. At conclusion of pregnancy, data were recorded for adverse pregnancy outcomes (APOs).

For this paper, the cohort was limited to participants with an uncomplicated pregnancy, which was defined as a pregnancy without large for gestational age, hypertensive disorders, or GDM based on OGTT. Participants included in the analysis were required to have an HbA1c <5.7% (<39 mmol/mol) at screening, a completed OGTT, an APO assessment at delivery, and at least 14 days of CGM data during their gestational period with at least 10 days of CGM data in the second trimester.

Statistical methods

CGM-measured glycemic metrics were calculated using all available CGM data during gestation. To be included in the main analysis cohort, the participant must have at least 14 days of CGM data with 10 days in the second trimester. A minimum of 252 and 84 hours of CGM data was required for daytime and night-time (defined as midnight–06:00) CGM metric tabulations, respectively. For CGM metrics summarized within each trimester and 4-week period, a minimum of 10 days of CGM data was required within each period. The difference in mean glucose by trimester was tested using a repeated measures linear regression model, and the association between body mass index (BMI) and mean glucose was tested using a linear regression model.

Post-prandial metrics were calculated from CGM data during the 4 hours after a self-reported meal start time. Participants were required to have at least five meals with a CGM-measured glucose level 15 min prior to, 30 min after, 1 hour after, 2 hours after, and 3 hours after the reported mealtime to be included in the analysis. Post-prandial peak was defined as the maximum CGM-measured glucose value within the 4 hours after a reported meal time; time to post-prandial peak was defined as the time between the reported mealtime and post-prandial peak. Meals with another reported meal within the 2 hours prior to 3 hours after were excluded. Post-prandial metrics were also explored by trimester, for which at least five meals meeting the minimum data requirements were also required within each trimester.

Outcomes were summarized as means and SDs or summary statistics appropriate to the distribution. Multiple comparisons were adjusted using the Benjamini-Hochberg adaptive false discovery rate.¹⁰ Significance was assessed at the $\alpha=0.05$ level. Analyses were performed with SAS software, V.9.4 (SAS Institute).

Data and resource availability

Data will be made available on a publicly available website (<https://www.jaeb.org/>) at a later date.

RESULTS

Study participants

Between June 2020 and December 2021, 937 adults enrolled into the study, with the last participant completing the study by August 2022. Of the participants enrolled into the study, 413 met criteria for an uncomplicated pregnancy and had sufficient CGM data to be included in the analyses.

Mean \pm SD age of the 413 participants with uncomplicated pregnancies at enrollment was 32 \pm 4 years (range: 19–42) years. Based on self-report, the cohort consisted of <1% American Indian/Alaskan Native, 5% Asian, 9% African American, 78% white, and 4% multiracial participants. Seven per cent of the participants also identified themselves as being of Hispanic ethnicity. Mean HbA1c was 5.1 \pm 0.2% (32 \pm 2.2 mmol/mol), mean BMI

was $25.3 \pm 5.0 \text{ kg/m}^2$, 16% of participants were classified as obese, 33% were nulligravid, and 2% had a history of GDM in a prior pregnancy. Additional baseline characteristics are listed in [table 1](#).

Glycemic outcomes

A median of 123 days (IQR: 86–147 days) of CGM data was collected from each participant. [Figure 1](#) displays the distribution of CGM values during gestation. Average mean glucose during the gestational period was $98 \pm 7 \text{ mg/dL}$ ($5.4 \pm 0.4 \text{ mmol/L}$). Median per cent time $63\text{--}120 \text{ mg/dL}$ ($3.5\text{--}6.7 \text{ mmol/L}$) was 86% (IQR: 82–89%) and median per cent time $63\text{--}140 \text{ mg/dL}$ ($3.5\text{--}7.8 \text{ mmol/L}$) was 95% (93–96%).

Average mean glucose was 103 ± 7 , 98 ± 7 , and $98 \pm 8 \text{ mg/dL}$ (5.7 ± 0.4 , 5.4 ± 0.4 , and $5.4 \pm 0.4 \text{ mmol/L}$) for the first, second, and third trimesters, respectively ($p < 0.001$ testing difference in mean glucose by trimester, [table 2](#)). Further analyzing CGM metrics by 4-week periods showed the average mean glucose was $104 \pm 7 \text{ mg/dL}$ ($5.8 \pm 0.4 \text{ mmol/L}$) during weeks 9–12 and steadily decreased to 97 ± 8 ($5.4 \pm 0.4 \text{ mmol/L}$) during weeks 21–24 with little change after 24 weeks (online supplemental table 2 and online supplemental figure 1).

Median per cent time >120 and $>140 \text{ mg/dL}$ (>6.7 and $>7.8 \text{ mmol/L}$) was 11% (IQR: 7–16%) and 2.5% (IQR: 1.3–4.1%), respectively. Median per cent time $>120 \text{ mg/dL}$ ($>6.7 \text{ mmol/L}$) was 15% during the first trimester and 11% in the second and third trimesters, while median per cent time $>140 \text{ mg/dL}$ ($>7.8 \text{ mmol/L}$) was 3.5%, 2.2%, and 2.3% during the first, second, and third trimesters, respectively. Additional glycemic metrics during the observed gestational period such as per cent time $<63 \text{ mg/dL}$ ($<3.5 \text{ mmol/L}$) and $<54 \text{ mg/dL}$ ($<3.0 \text{ mmol/L}$) are detailed in [table 2](#).

The average night-time mean glucose was $96 \pm 8 \text{ mg/dL}$ ($5.3 \pm 0.4 \text{ mmol/L}$), decreasing from a mean glucose of $103 \pm 9 \text{ mg/dL}$ ($5.7 \pm 0.5 \text{ mmol/L}$) at midnight to $93 \pm 8 \text{ mg/dL}$ ($5.2 \pm 0.4 \text{ mmol/L}$) by 06:00. During the daytime, average mean glucose was $99 \pm 7 \text{ mg/dL}$ ($5.5 \pm 0.4 \text{ mmol/L}$) and generally increased throughout the day (online supplemental table 3 and [figure 1](#)). The mean glucose appeared to increase more rapidly during times when there may have been meals. There was more glucose variability during the daytime in comparison with the night-time. Mean coefficient of variation was $20\% \pm 3\%$ vs $17\% \pm 3\%$ during daytime and night-time periods, respectively. Hypoglycemia was lower during the day, with a median daytime per cent time $<63 \text{ mg/dL}$ ($<3.5 \text{ mmol/L}$) of 1.6% vs 2.2% during the night. The CGM metrics generally changed by trimester, especially from the first to second trimester, but the differences between daytime and night-time CGM metrics were largely consistent by trimester.

There were 157 participants who voluntarily recorded a total of 3747 meals with sufficient CGM data. Mean fasting glucose (ie, average glucose in the 45 to 15 min prior to the first reported morning meal of the day) was

Table 1 Participant characteristics

	Overall (N=413)
Age (years), mean \pm SD	32 \pm 4
18–24, n (%)	17 (4)
25–34, n (%)	282 (68)
35–45, n (%)	114 (28)
Range	19–42
Race*, n (%)	
American Indian/Alaskan Native	2 (<1)
Asian	19 (5)
Black/African American	36 (9)
White	323 (78)
Multiple	17 (4)
Unknown or not reported	16 (4)
Ethnicity†, n (%)	
Hispanic	29 (7)
Not Hispanic	379 (92)
Unknown or not reported	5 (1)
Body mass index (kg/m ²), mean \pm SD	25.3 \pm 5.0
Underweight (<18.5), n (%)	10 (2)
Normal (18.5–<25.0), n (%)	241 (58)
Overweight (25.0–<30), n (%)	94 (23)
Obese (\geq 30), n (%)	68 (16)
HbA1c (%) (mmol/mol) prior to 20 weeks' gestation, mean \pm SD	5.1 \pm 0.2 (32 \pm 2.2)
4.2–4.9 (22–30), n (%)	99 (24)
5.0–5.4 (31–36), n (%)	272 (66)
5.5–5.6 (37–38), n (%)	42 (10)
Range	4.2–5.6 (22–38)
Gravida, median (IQR)	2 (1–3)
1, n (%)	137 (33)
2, n (%)	128 (31)
3, n (%)	76 (18)
4, n (%)	38 (9)
\geq 5, n (%)	34 (8)
Parity, median (IQR)	1 (0–1)
0, n (%)	192 (46)
1, n (%)	160 (39)
2, n (%)	51 (12)
\geq 3, n (%)	10 (2)
Gestational age at study enrollment (weeks), mean \pm SD	14 \pm 2
1st trimester, n (%)	252 (61)
2nd trimester, n (%)	161 (39)

*Race information was solicited from the participant in response to the following question: 'Which of the following racial designations best describes you?'. The race categories (number of participants) of the 17 participants who self-reported as multiracial are as follows: black and white (4), Asian and white (3), American Indian/Alaskan Native and white (2), Native Hawaiian or Other Pacific Islander and white (2), American Indian/Alaskan Native and Asian and black and white (1), white and unspecified (1), unspecified (4).

†Hispanic ethnicity information was solicited in response to the following question: 'Do you consider yourself to be Hispanic/Latino or not Hispanic/Latino?'. The 'not Hispanic' category includes one participant who self-reported as Jewish in the free response section after participant indicated they identified with more than one race.
HbA1c, hemoglobin A1c.

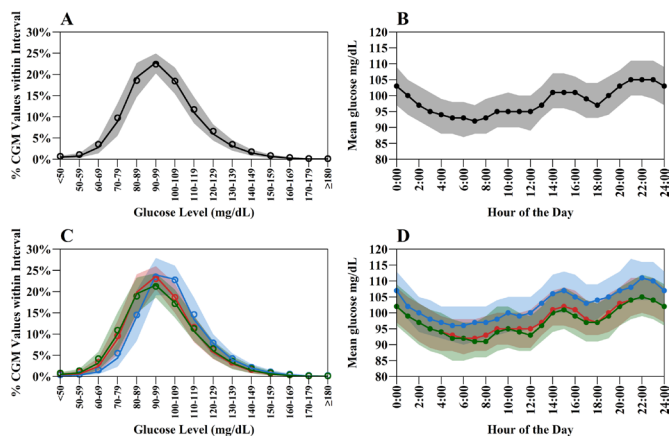


Figure 1 Distribution of CGM-measured glucose levels throughout uncomplicated pregnancies. Envelope plots of the per cent of CGM values within each glucose level interval for each participant during (A) the entire observed gestational period (N=413) and (C) each trimester (N=118, 413, and 355 in the first, second, and third trimester, respectively). Tracings of participant-level mean glucose levels by the hour of the day during (B) the entire observed gestational period and (D) each trimester. Solid dots and lines represent medians, and open circles represent means. Shaded bands represent the IQR (ie, 25th–75th percentiles). The first, second, and third trimesters are represented by the colors blue, red, and green, respectively. CGM, continuous glucose monitoring.

88±14 mg/dL (4.9±0.8 mmol/L). Mean post-prandial peak was 126±22 mg/dL (7.0±1.2 mmol/L), and mean glucose excursion within 4 hours after the meal was 36±22 mg/dL (2.0±1.2 mmol/L) (table 3). The median time to peak glucose was 62 (IQR: 40–124) min. Post-prandial glycemic metrics were similar between the second and third trimesters. Glucose levels averaged 87, 89, and 94 mg/dL (4.8, 4.9, and 5.2 mmol/L) at the start of breakfast, lunch, and dinner, respectively, but the excursion was similar across meal type (mean excursion of 34, 37, and 35 mg/dL (1.9, 2.1, 1.9 mmol/L), respectively; online supplemental table 4). Median time to peak glucose was 50 min at breakfast and 70–71 min for lunch and dinner.

The correlation between BMI and mean glucose during gestation was low to moderate ($r=0.35$). Participants with a higher BMI had higher glucose levels than those with a lower BMI (online supplemental table 5). Participants with a BMI of ≥ 30.0 kg/m² had a mean glucose of 103±6 mg/dL (5.7±0.3 mmol/L) compared with a mean glucose of 96±7 mg/dL (5.3±0.4 mmol/L) for participants with a BMI between 18.5 and <25.0 kg/m² ($p<0.001$). The median per cent time 63–120 mg/dL (3.5–6.7 mmol/L) was 83% vs 87%, respectively. The median per cent time >120 and >140 mg/dL (>6.7 and >7.8 mmol/L) was 15% vs 10% and 3.5% vs 2.1%, respectively.

Post-prandial glucose levels were also elevated for those with higher BMIs, but glucose excursion after the meal was still similar among all the BMI categories. Mean glucose at the start of a meal was 97±17 mg/dL (5.4±0.9 mmol/L) and increased to a peak of 133±23 mg/dL

(7.4±1.3 mmol/L) for those with a BMI ≥ 30.0 kg/m², while mean glucose at the start of a meal was 89±18 mg/dL (4.9±1.0 mmol/L) and increased to a peak of 124±22 mg/dL (6.9±1.2 mmol/L) for those with a BMI of 18.5–<25.0 kg/m². Mean glucose excursion for both BMI groups was 35–36 mg/dL (1.9–2.0 mmol/L) (online supplemental table 6).

DISCUSSION

Overall, CGM-derived mean glucose was slightly higher and per cent time 63–120 mg/dL (3.5–6.7 mmol/L) was slightly lower in the first trimester, but both mean glucose and per cent time 63–120 mg/dL (3.5–6.7 mmol/L) remained steady in the second and third trimesters for participants with uncomplicated pregnancies (table 2). The median per cent time 63–120 mg/dL (3.5–6.7 mmol/L) was 86% (IQR 82–89%) suggesting this range is seen in a large percentage of uncomplicated pregnancies and may be an important metric to use when comparing CGM-derived metrics with obstetrical outcomes in pregnancies complicated by GDM. The median per cent time >140 mg/dL (>7.8 mmol/L) was 2.5% (IQR: 1.3–4.1%), indicating most uncomplicated pregnancies had approximately 30 min per day with glucose above 140 mg/dL (7.8 mmol/L), often occurring after lunch or dinner.

There is no standard CGM-based glucose range for normoglycemic pregnancies; recommendations for glucose levels using CGM are mainly based on studies of participants with type 1 diabetes.¹¹ In one study of 58 normoglycemic participants between gestational age 8 and 20 weeks, CGM data for up to 72 hours showed a per cent time 63–140 mg/dL (3.5–7.8 mmol/L) of 98.2%.¹² Another study used a matched control group based on age, parity and BMI (no GDM), and found a per cent time 63–140 mg/dL (3.5–7.8 mmol/L) of 96.1%, 95.9% and 93.5% in trimesters one, two and three, respectively, among those without GDM.⁹ The CGM-based glucose ranges observed in this study may be representative of glucose levels in all trimesters of uncomplicated pregnancies.

Additionally, in uncomplicated pregnancies, there is a noticeable diurnal pattern to glucose (figure 1), similar to normoglycemic non-pregnant participants.⁸ The stability of mean glucose throughout the 24-hour period going from the second to third trimester suggests that in normoglycemic pregnancies, there is relatively preserved β -cell function and mass when faced with the physiologic changes in insulin and glucose metabolism during pregnancy.

The post-prandial CGM data show the peak glucose remains relatively stable throughout pregnancy. While there is no CGM-based consensus on a post-prandial glucose target in non-pregnant individuals, the post-prandial levels measured by CGM in this pregnant population are in the range of 100–120 mg/dL, which is similar to previously published post-prandial capillary

Table 2 Glycemic profiles of uncomplicated pregnancies, overall and by trimester

	Entire gestational period	1st trimester	2nd trimester	3rd trimester
Number of participants	413	118	413	355
Days of CGM readings, median (IQR)	123 (86–147)	18 (14–25)	69 (50–80)	53 (36–64)
Mean glucose—mg/dL (mmol/L), mean±SD	98±7 (5.4±0.4)	103±7 (5.7±0.4)	98±7 (5.4±0.4)	98±8 (5.4±0.4)
<90 mg/dL (<5.0 mmol/L), n (%)	42 (10)	2 (2)	53 (13)	57 (16)
90–<95 mg/dL (5.0–<5.3 mmol/L), n (%)	89 (22)	10 (8)	83 (20)	74 (21)
95–<100 mg/dL (5.3–<5.6 mmol/L), n (%)	121 (29)	31 (26)	114 (28)	85 (24)
100–<105 mg/dL (5.6–<5.8 mmol/L), n (%)	93 (23)	33 (28)	92 (22)	82 (23)
105–<110 mg/dL (5.8–<6.1 mmol/L), n (%)	44 (11)	26 (22)	45 (11)	31 (9)
110–<120 mg/dL (6.1–<6.7 mmol/L), n (%)	24 (6)	16 (14)	26 (6)	22 (6)
≥120 mg/dL (≥6.7 mmol/L), n (%)	0 (0)	0 (0)	0 (0)	4 (1)
Glucose SD—mg/dL (mmol/L), mean±SD	19±3 (1.1±0.2)	18±3 (1.0±0.2)	18±3 (1.0±0.2)	19±3 (1.1±0.2)
Glucose coefficient of variation (%), mean±SD	19%±3%	18%±2%	19%±3%	20%±3%
% time 63–120 mg/dL (3.5–6.7 mmol/L), mean±SD	85%±7%	83%±8%	85%±7%	84%±8%
Median (quartiles)	86% (82–89%)	84% (79–89%)	87% (83–90%)	85% (80–90%)
95–<99%, n (%)	2 (<1)	2 (2)	5 (1)	6 (2)
90–<95%, n (%)	78 (19)	25 (21)	101 (24)	73 (21)
85–<90%, n (%)	159 (38)	23 (19)	148 (36)	109 (31)
80–<85%, n (%)	94 (23)	35 (30)	92 (22)	76 (21)
70–<80%, n (%)	62 (15)	24 (20)	53 (13)	71 (20)
50–<70%, n (%)	18 (4)	9 (8)	14 (3)	19 (5)
<50%, n (%)	0 (0)	0 (0)	0 (0)	1 (<1)
% time 63–140 mg/dL (3.5–7.8 mmol/L), mean±SD	94%±3%	95%±3%	95%±3%	94%±4%
Median (quartiles)	95% (93–96%)	95% (93–97%)	95% (94–97%)	95% (92–96%)
% time <70 mg/dL (<3.9 mmol/L), median (quartiles)	4.2% (2.1–6.9%)	1.8% (1.0–3.6%)	3.5% (1.8–6.6%)	4.7% (2.1–8.7%)
Area over the curve 70 mg/dL (3.9 mmol/L), median (quartiles)	0.4 (0.2–0.7)	0.2 (0.1–0.3)	0.3 (0.2–0.6)	0.4 (0.2–0.8)
% time <63 mg/dL (<3.5 mmol/L), median (quartiles)	1.8% (0.9–3.2%)	0.8% (0.4–1.6%)	1.5% (0.8–3.0%)	2.0% (0.8–3.9%)
0%, n (%)	0 (0)	2 (2)	2 (<1)	3 (<1)
>0–<0.5%, n (%)	45 (11)	33 (28)	62 (15)	50 (14)

Continued

Table 2 Continued

	Entire gestational period	1st trimester	2nd trimester	3rd trimester
0.5–<1%, n (%)	70 (17)	34 (29)	79 (19)	44 (12)
1–<2%, n (%)	106 (26)	26 (22)	102 (25)	80 (23)
2–<4%, n (%)	117 (28)	18 (15)	102 (25)	91 (26)
≥4%, n (%)	75 (18)	5 (4)	66 (16)	87 (25)
Area over the curve 63 mg/dL (3.5 mmol/L), median (quartiles)	0.2 (0.1–0.3)	0.1 (0.0–0.2)	0.2 (0.1–0.3)	0.2 (0.1–0.4)
% time <54 mg/dL (<3.0 mmol/L), median (quartiles)	0.7% (0.4–1.3%)	0.3% (0.1–0.8%)	0.6% (0.3–1.3%)	0.8% (0.3–1.5%)
Area over the curve 54 mg/dL (3.0 mmol/L), median (quartiles)	0.1 (0.0–0.1)	0.0 (0.0–0.1)	0.1 (0.0–0.1)	0.1 (0.0–0.1)
% time >120 mg/dL (6.7 mmol/L), median (quartiles)	11% (7–16%)	15% (9–19%)	11% (7–16%)	11% (7–17%)
>0–<5%, n (%)	43 (10)	6 (5)	54 (13)	57 (16)
5–<10%, n (%)	135 (33)	26 (22)	134 (32)	101 (28)
10–<15%, n (%)	110 (27)	28 (24)	109 (26)	77 (22)
15–<20%, n (%)	64 (15)	29 (25)	60 (15)	59 (17)
20–<30%, n (%)	46 (11)	23 (19)	43 (10)	46 (13)
30–<50%, n (%)	15 (4)	6 (5)	13 (3)	14 (4)
≥50%, n (%)	0 (0)	0 (0)	0 (0)	1 (<1)
Area under the curve 120 mg/dL (6.7 mmol/L), median (quartiles)	1.5 (0.9–2.4)	2.1 (1.2–3.1)	1.4 (0.8–2.3)	1.5 (0.8–2.7)
% time >140 mg/dL (>7.8 mmol/L), median (quartiles)	2.5% (1.3–4.1%)	3.5% (1.7–5.4%)	2.2% (1.1–3.9%)	2.3% (1.0–4.6%)
Area under the curve 140 mg/dL (7.8 mmol/L), median (quartiles)	0.30 (0.13–0.57)	0.41 (0.19–0.76)	0.25 (0.11–0.53)	0.26 (0.10–0.57)
Morning glucose				
Mean glucose at 05:00*—mg/dL (mmol/L), mean±SD	93±9 (5.2±0.5)	98±9 (5.4±0.5)	93±9 (5.2±0.5)	93±10 (5.2±0.5)
Glucose SD at 05:00* —mg/dL (mmol/L), mean±SD	14±3 (0.8±0.2)	12±5 (0.7±0.3)	13±3 (0.7±0.2)	14±3 (0.8±0.2)
Mean glucose at 06:00†—mg/dL (mmol/L), mean±SD	93±8 (5.2±0.4)	97±9 (5.4±0.5)	93±9 (5.2±0.5)	92±10 (5.1±0.6)
Glucose SD at 06:00†—mg/dL (mmol/L), mean±SD	13±3 (0.7±0.2)	11±6 (0.6±0.3)	13±3 (0.7±0.2)	14±4 (0.8±0.2)
*Includes CGM data from 04:45 to 05:15.				
†Includes CGM data from 05:45 to 06:15.				
CGM, continuous glucose monitoring.				

Table 3 Post-prandial profiles of uncomplicated pregnancies, overall and by trimester

	Entire gestational period	2nd trimester	3rd trimester
Number of participants	157	150	76
Number of meals	3747	2543	1183
Fasting glucose*—mg/dL (mmol/L), mean±SD	88±14 (4.9±0.8)	88±14 (4.9±0.8)	87±14 (4.8±0.8)
Baseline glucose prior to meal†—mg/dL (mmol/L), mean±SD	91±18 (5.1±1.0)	91±18 (5.1±1.0)	90±18 (5.0±1.0)
Post-prandial glucose level—mg/dL (mmol/L), mean±SD			
30 min after meal time	103±22 (5.7±1.2)	104±21 (5.8±1.2)	101±22 (5.6±1.2)
1 hour after meal time	108±23 (6.0±1.3)	107±23 (5.9±1.3)	109±23 (6.1±1.3)
2 hours after meal time	102±21 (5.7±1.2)	102±21 (5.7±1.2)	102±21 (5.7±1.2)
3 hours after meal time	97±20 (5.4±1.1)	97±19 (5.4±1.1)	97±20 (5.4±1.1)
Post-prandial peak glucose—mg/dL (mmol/L), mean±SD	126±22 (7.0±1.2)	126±22 (7.0±1.2)	125±22 (6.9±1.2)
Glucose meal excursion‡—mg/dL (mmol/L), mean±SD	36±22 (2.0±1.2)	36±21 (2.0±1.2)	35±22 (1.9±1.2)
Time to peak glucose—min, median (IQR)	62 (40–124)	60 (39–123)	67 (42–125)
Rate of glucose rise§—mg/dL/min (mmol/L/min), median (IQR)	0.5 (0.2–0.9) (0.03 (0.01–0.05))	0.5 (0.2–1.0) (0.03 (0.01–0.06))	0.5 (0.2,–0.9) (0.03 (0.01–0.05))

Summary statistics are on a meal level, with the exception of fasting glucose, which is on a day level. Post-prandial time period is 4 hours after meal start time. Each period requires participants to have at least five meals (a) with sufficient CGM data (non-missing glucose –15 min, +30 min, +1 hour, +2 hours, and +3 hours after meal start) and (b) without additional meals 2 hours before or 3 hours after the recorded meal time.

*Average glucose in 45 to 15 min prior to first recorded meal of the day. First recorded meal of the day must be before noon.

†Average glucose in the 15 min prior to recorded meal time.

‡Post-prandial peak glucose minus baseline glucose prior to meal.

§Glucose meal excursion divided by time to peak glucose.
CGM, continuous glucose monitoring.

glucose levels in participants with normoglycemic pregnancies.^{13 14} Additional analyses to confirm whether or not the observed time to peak glucose of approximately 60 min is similar in the GDM population of this cohort will help assess the optimal timing for basing post-prandial glycemic targets in pregnancy, particularly when it comes to treatment with insulin.

Further, another important observation is that as BMI increases above normal BMI (normal BMI defined as 18.5–<25.0 kg/m²), the mean fasting and overall glucose increases and per cent time 63–140 mg/dL decreases, although slightly. This is consistent with other studies noting that obesity independent of GDM can increase APOs.^{15 16} The CGM findings in this study further highlight that hyperglycemia in pregnancy is a continuum upon which the binary diagnosis of no GDM versus GDM may not completely describe obstetrical risks.

The strengths of this study include the large number of participants, including 413 participants with a median of 123 days of CGM data throughout the second and third trimesters of pregnancy. It is also notable to have

almost 3800 meals logged and correlated with CGM data to describe post-prandial glucose excursions in normal pregnancies. The limitations of the study are that there were relatively fewer participants with data during the first trimester, and potential limited generalizability of the results to a heterogeneous population due to a predominantly white and non-Hispanic cohort and small percentage of individuals with BMI over 30 kg/m².

In conclusion, we present a large data set of normative glucose data based on CGM throughout pregnancy in predominantly white, non-Hispanic participants without diabetes who had uncomplicated pregnancies. These data will be useful in comparison with the CGM results from the participants in the cohort who did develop GDM or other adverse obstetrical outcomes. Further understanding of glycemic patterns during pregnancy as well as further evaluation of more racially and ethnically diverse individuals will guide future research into the optimal method and timing of screening for GDM and the subsequent timing for intervention in GDM, as well as the optimal glycemic targets throughout pregnancy.

Acknowledgements Study center staff and other individuals who participated in the conduct of the trial are listed in the online supplemental material.

Contributors ALC and ZL wrote and edited the manuscript. RWB, EN, RMB, MJ, SD, MB, KJK, JRS, PC, and CD reviewed and edited the manuscript. ALC is the guarantor of this work and, as such, accepts full responsibility for the finished work and/or the conduct of the study, had access to the data, and controlled the decision to publish.

Funding Study funding was provided by the Leona M and Harry B Helmsley Charitable Trust and UnitedHealth Group. Dexcom provided the devices used in the study.

Competing interests ALC reports no personal financial disclosures but reports that his institution has received funding on his behalf as follows: research support from Medtronic, Tandem, Insulet, Abbott, Dexcom, Eli Lilly, NovoNordisk, Sanofi and UnitedHealth Group and consultancy fees from Mannkind and NovoNordisk. RWB reports no personal financial disclosures but reports that his institution has received funding on his behalf as follows: grant funding and study supplies from Dexcom. RMB has received research support, has acted as a consultant, or has been on the scientific advisory board for Abbott Diabetes Care, Ascensia, Bigfoot Biomedical, CeQur, Dexcom, Eli Lilly, Embecta, Hygieia, Insulet, Medtronic, Novo Nordisk, Onduo, Roche Diabetes Care, Tandem Diabetes Care, Sanofi, UnitedHealthcare, Vertex Pharmaceuticals and Zealand Pharma. RMB's employer, non-profit HealthPartners Institute, contracts for his services and he receives no personal income for any of these activities. CD reports advisory work for Dexcom for GDM patient-facing materials and system implementation.

Patient consent for publication Not applicable.

Ethics approval This study involves human participants. The protocol and informed consent forms were approved by Jaeb Center for Health Research Institutional Review Board (reference ID: GLAM). Participants gave informed consent to participate in the study before taking part.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available upon reasonable request. Data will be made available on a publicly available website (www.jaeb.org) at a later date.

Supplemental material This content has been supplied by the author(s). It has not been vetted by BMJ Publishing Group Limited (BMJ) and may not have been peer-reviewed. Any opinions or recommendations discussed are solely those of the author(s) and are not endorsed by BMJ. BMJ disclaims all liability and responsibility arising from any reliance placed on the content. Where the content includes any translated material, BMJ does not warrant the accuracy and reliability of the translations (including but not limited to local regulations, clinical guidelines, terminology, drug names and drug dosages), and is not responsible for any error and/or omissions arising from translation and adaptation or otherwise.

Open access This is an open access article distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited, appropriate credit is given, any changes made indicated, and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>.

ORCID iD

Zoey Li <http://orcid.org/0000-0002-5950-9317>

REFERENCES

- 1 Sweeting A, Wong J, Murphy HR, *et al*. A clinical update on gestational diabetes mellitus. *Endocr Rev* 2022;43:763–93.
- 2 Gestational diabetes mellitus [article online]. 2018. Available: <https://www.acog.org/clinical/clinical-guidance/practice-bulletin/articles/2018/02/gestational-diabetes-mellitus> [Accessed 21 Jul 2023].
- 3 Hughes RCE, Moore MP, Gullam JE, *et al*. An early pregnancy HbA1c $\geq 5.9\%$ (41 mmol/Mol) is optimal for detecting diabetes and identifies women at increased risk of adverse pregnancy outcomes. *Diabetes Care* 2014;37:2953–9.
- 4 Immanuel J, Simmons D, Desoye G, *et al*. Performance of early pregnancy HbA(1c) for predicting gestational diabetes mellitus and adverse pregnancy outcomes in obese European women. *Diabetes Res Clin Pract* 2020;168:108378.
- 5 Sweeting AN, Ross GP, Hyett J, *et al*. Baseline HbA1c to identify high-risk gestational diabetes: utility in early vs standard gestational diabetes. *J Clin Endocrinol Metab* 2017;102:150–6.
- 6 Battelino T, Alexander CM, Amiel SA, *et al*. Continuous glucose monitoring and metrics for clinical trials: an international consensus statement. *Lancet Diabetes Endocrinol* 2023;11:42–57.
- 7 Ehrhardt N, Al Zaghaf E. Behavior modification in prediabetes and diabetes: potential use of real-time continuous glucose monitoring. *J Diabetes Sci Technol* 2019;13:271–5.
- 8 Shah VN, DuBose SN, Li Z, *et al*. Continuous glucose monitoring profiles in healthy nondiabetic participants: a multicenter prospective study. *J Clin Endocrinol Metab* 2019;104:4356–64.
- 9 Stentebjerg LL, Madsen LR, Staving RK, *et al*. Roux-en-Y gastric bypass increases glycemic excursions during pregnancy and postpartum: a prospective cohort study. *Diabetes Care* 2023;46:502–10.
- 10 Benjamini Y, Hochberg Y. On the adaptive control of the false discovery rate in multiple testing with independent statistics. *Journal of Educational and Behavioral Statistics* 2000;25:60.
- 11 Feig DS, Donovan LE, Corcoy R, *et al*. Continuous glucose monitoring in pregnant women with type 1 diabetes (CONCEPTT): a multicentre international randomised controlled trial. *Lancet* 2017;390:2347–59.
- 12 Gupta Y, Singh C, Goyal A, *et al*. Continuous glucose monitoring system profile of women diagnosed as gestational diabetes mellitus by International Association of diabetes and pregnancy study groups criteria and labeled as normoglycemic by alternate criteria in early pregnancy. *J Diabetes Investig* 2022;13:1753–60.
- 13 Harmon KA, Gerard L, Jensen DR, *et al*. Continuous glucose profiles in obese and normal-weight pregnant women on a controlled diet: metabolic determinants of fetal growth. *Diabetes Care* 2011;34:2198–204.
- 14 Hernandez TL, Friedman JE, Van Pelt RE, *et al*. Patterns of glycemia in normal pregnancy: should the current therapeutic targets be challenged? *Diabetes Care* 2011;34:1660–8.
- 15 Ballesta-Castillejos A, Gómez-Salgado J, Rodríguez-Almagro J, *et al*. Relationship between maternal body mass index and obstetric and perinatal complications. *J Clin Med* 2020;9:707.
- 16 Santos S, Voerman E, Amiano P, *et al*. Impact of maternal body mass index and gestational weight gain on pregnancy complications: an individual participant data meta-analysis of European, North American and Australian cohorts. *BJOG* 2019;126:984–95.