



# Glycaemic control and pregnancy outcomes with real-time continuous glucose monitoring in gestational diabetes (GRACE): an open-label, multicentre, multinational, randomised controlled trial

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## Summary

**Background** Data regarding the impact of real-time continuous glucose monitoring (rt-CGM) on reducing adverse pregnancy outcomes in women with gestational diabetes are contradictory. We aimed to assess differences in the proportion of large-for-gestational-age (LGA) newborns between women using rt-CGM versus self-monitoring of blood glucose (SMBG).

**Methods** For this open-label, parallel-group, multicentre, randomised controlled trial, women aged 18–55 years with singleton pregnancy and gestational diabetes (diagnosed according to the International Association of the Diabetes and Pregnancy Study Groups criteria), were randomly assigned (1:1) to rt-CGM or SMBG. The first allocation was by chance; for subsequent allocations, minimisation was used to balance three prespecified factors: gestational age at study entry, previous gestational diabetes, and preconceptional BMI. SMBG participants used blinded CGM for 10 days after randomisation and at 36–38 weeks; rt-CGM participants used open rt-CGM until delivery. All were managed according to standard care protocols in four university hospitals in Austria, Germany, and Switzerland. The primary endpoint was the proportion of LGA newborns (using the Perinatal Institute's GROW customised birthweight percentiles), assessed in the intention-to-treat population. Secondary endpoints included the requirement for glucose-lowering medication, CGM metrics, and non-glycaemic maternal and neonatal outcomes. Recruitment and follow-up are complete. This study is registered with ClinicalTrials.gov (NCT03981328).

**Findings** Between Aug 24, 2020, and May 30, 2024, 610 women were screened for eligibility, of whom 375 (diagnosed with gestational diabetes at a mean of 25·2 weeks [SD 2·3] of gestation), were randomly assigned to rt-CGM (n=190) or SMBG (n=185) at a mean of 28·6 weeks (SD 1·9) of gestation. 170 intervention and 175 control participants with available data were assessed for the primary endpoint. LGA neonates were born to six (4%) of 170 rt-CGM and 18 (10%) of 175 SMBG participants (OR 0·32, 95% CI 0·10–0·87, p=0·014). Small-for-gestational-age (SGA) neonates were born to 33 (19%) and 23 (13%) participants, respectively (OR 1·59, 0·86–2·99, p=0·11). Serious adverse events occurred in 23 (12%) of 190 versus 28 (15%) of 185 participants (OR 0·77, 0·42–1·40, p=0·39).

**Interpretation** rt-CGM use in women with gestational diabetes reduced LGA births, without differences in serious adverse events. The higher-than-expected overall prevalence of SGA infants, possibly related to the tight glycaemic control in our cohort, requires further research.

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## Introduction

Pregnant women with any form of diabetes are at increased risk of adverse pregnancy outcomes.<sup>1,2</sup> Although gestational diabetes is associated with milder hyperglycaemia as compared with type 1 and type 2 diabetes,<sup>3</sup> its growing prevalence poses an increasing challenge to clinical practice.<sup>4</sup> Another concern lies in the interindividual heterogeneity of gestational diabetes presentation and the progression of its severity during pregnancy. Beyond pregnancy-specific influences,

pre-existing conditions also appear to affect maternal glycaemia.<sup>5</sup> There is a trend for precursors of the disease to be present before conception,<sup>3</sup> revealing a shifting metabolic risk profile of women of reproductive age. One burden of gestational diabetes is the impact of maternal hyperglycaemia on perinatal complications. The HAPO study demonstrated a linear relationship between maternal glycaemia and the risk of large-for-gestational-age (LGA) neonates (birthweight >90th percentile), caesarean delivery, and neonatal hypoglycaemia.<sup>6</sup>

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For the German translation of the abstract see [Online](#) for appendix 1

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## Research in context

### Evidence before this study

We searched PubMed for articles published before Aug 30, 2018, with no restrictions on language or start date. The search terms included (“gestational diabetes mellitus” OR “gestational diabetes”) AND (“pregnancy” OR “diabetes in pregnancy”) AND “continuous glucose monitoring” AND “randomised controlled trial”. We identified four trials, all of which used continuous glucose monitoring (CGM) only intermittently. Two trials reported improvements in either HbA1c concentrations or maternal weight gain, and one trial showed improved identification of women requiring antihyperglycaemic medication. None was large enough to assess meaningful differences in key maternal or neonatal outcomes. Evidence on the clinical benefit of CGM in gestational diabetes therefore remained limited, and larger, adequately powered trials were needed.

### Added value of this study

In this multicentre, randomised controlled trial, 375 pregnant women with gestational diabetes were randomly assigned to monitor their blood glucose using either real-time continuous glucose monitoring (rt-CGM) or standard self-monitoring of blood glucose (SMBG) until delivery. This large trial provides the first adequately powered evidence that rt-CGM improves key neonatal outcomes in gestational diabetes. rt-CGM significantly

reduced the risk of large-for-gestational-age (LGA) neonates without increasing adverse events. The findings show that rt-CGM enables more precise detection and management of hyperglycaemia (reflected by greater use and higher doses of rapid-acting insulin) which likely contributes to improved outcomes. The unexpectedly high prevalence of small-for-gestational-age (SGA) infants also highlights a new area for investigation, suggesting that tighter glycaemic control could influence fetal growth and raising questions about the optimal time in range for women with gestational diabetes. Overall, this study provides the strongest evidence to date that rt-CGM offers clinical benefit beyond standard self-monitoring and could improve management of gestational diabetes.

### Implications of all the available evidence

The use of rt-CGM in women with gestational diabetes was associated with a reduced proportion of LGA neonates compared with SMBG. Additionally, rt-CGM use was linked to a higher frequency of rapid-acting insulin administration and a modest improvement in time in target range. Together, these findings suggest that rt-CGM could be a potentially useful monitoring approach in gestational diabetes by enabling the identification of additional patients who could possibly benefit from pharmacotherapy.

Moreover, the altered intrauterine conditions promoting fetal overgrowth are thought to contribute to long-term metabolic consequences, perpetuating a cycle of transgenerational risk transmission.<sup>7</sup> Evidence from large interventional trials indicates that treating even mild maternal hyperglycaemia can reduce adverse perinatal outcomes, particularly the LGA incidence,<sup>8,9</sup> although previous studies reported an inverse relationship between blood glucose concentrations and the risk of small-for-gestational-age (SGA) neonates,<sup>10,11</sup> indicating that reductions in LGA incidence could be associated with shifts in the overall birthweight distribution.

Continuous glucose monitoring (CGM), a valuable tool for improving glycaemic control, is recommended for use in patients on any type of insulin therapy by the American Diabetes Association.<sup>12</sup> However, evidence for its use in gestational diabetes is contradictory.<sup>13</sup> Observational studies suggest that CGM might improve glycaemic control and reduce neonatal complications compared with self-monitoring of blood glucose (SMBG).<sup>14</sup>

Studies focusing on CGM in pregnancy have often used CGM systems that do not provide real-time glucose data. In contrast, real-time CGM (rt-CGM) offers immediate feedback, allowing users to respond quickly to glucose fluctuations through behavioural adjustments or pharmacological interventions.<sup>15,16</sup> Studies in non-pregnant individuals with type 1 diabetes have shown that rt-CGM enhances diabetes self-management and improves glycaemic control, whereby glycaemic improvement was

found to be greater with modern rt-CGM technology.<sup>17</sup> Focusing on type 1 diabetes and pregnancy, the CONCEPTT trial demonstrated improved perinatal outcomes, likely attributable to reduced hyperglycaemia in mothers randomly assigned to rt-CGM.<sup>18</sup> In contrast, a recent randomised study with focus on gestational diabetes did not show an improvement in pregnancy outcomes and glycaemic control with rt-CGM.<sup>19</sup> Consequently, evidence regarding benefits of rt-CGM in gestational diabetes remains contradictory.

We hypothesise that rt-CGM, by providing real-time feedback to guide lifestyle modifications and pharmacotherapy, can contribute to a reduction in gestational diabetes-specific complications. Therefore, this study aims to assess differences in the proportion of LGA newborns between women with gestational diabetes using rt-CGM and those using SMBG. Secondary objectives include maternal and neonatal outcomes, requirement for glucose-lowering medication, and CGM-derived glucose metrics. Additionally, adverse events and serious adverse events were systematically recorded throughout the trial.

## Methods

### Study design and participants

The study design was previously described in detail.<sup>20</sup> Briefly, pregnant women aged 18–55 years with a recent diagnosis of gestational diabetes were consecutively enrolled in an open-label, multicentre, randomised

controlled trial with two parallel groups. The gestational diabetes diagnosis was made according to international guidelines after 24 weeks and 0 days (24<sup>0</sup> weeks) of gestation using a 2-h 75 g oral glucose tolerance test based on International Association of the Diabetes and Pregnancy Study Groups and WHO criteria.<sup>21,22</sup> When gestational diabetes was diagnosed before 24<sup>0</sup> weeks according to local guidelines,<sup>23</sup> women were eligible for inclusion if they met glycaemic targets without requiring glucose-lowering medication before 24<sup>0</sup> weeks. All women were managed according to standard care, and treatment was not postponed for study purposes. The maximum gestational age for inclusion was 31<sup>6</sup> weeks. Exclusion criteria were: preconceptional type 1 diabetes or type 2 diabetes; history of metabolic surgery; >2 weeks of systemic steroids prior to enrolment; multiple pregnancy; use of glucose-lowering medications (metformin or insulin) before study entry; fetal growth restriction at study entry (assessed by ultrasound); inpatient psychiatric treatment within 1 year before enrolment; and participation in this study during a previous pregnancy.

The study was conducted at four tertiary referral centres: the Department of Obstetrics and Gynecology at the Medical University of Vienna (Austria), the Department of Obstetrics and Prenatal Medicine and Department of Endocrinology at the University Hospital Basel (Switzerland), the Clinic of Obstetrics at Charité – Universitätsmedizin Berlin (Germany), and the Department of Obstetrics at Jena University Hospital (Germany). The study was registered at ClinicalTrials.gov (NCT03981328) on Feb 15, 2019, and approved by the Institutional Review Boards (Vienna: 1863/2018, Basel: BASEC 2022-D000I, Berlin: EA2/133/20, Jena: 2021-2334-BO). The study was performed in accordance with the Declaration of Helsinki and written informed consent was obtained from all participants. Details on funding and responsibilities are provided in appendix 2 (p 19). There was no patient or public involvement in the design, conduct, or reporting of this trial. The original and final protocols and summary of changes are provided in appendix 3.

### Randomisation and masking

Randomisation was performed at visit 2 by using MUW Randomizer, version 2.0 software. Participants were automatically assigned to either rt-CGM or SMBG in a 1:1 ratio by the system, which was exclusively accessed by investigators at each study site with secure login. The first patient was randomly assigned by chance. Subsequent patients were allocated using the minimisation method<sup>24</sup> with a 0.85 assignment probability to minimise the imbalance between groups according to three stratification variables: week of gestation at study entry (four strata: 24<sup>0</sup> to 25<sup>6</sup>, 26<sup>0</sup> to 27<sup>6</sup>, 28<sup>0</sup> to 29<sup>6</sup>, 30<sup>0</sup> to 31<sup>6</sup>); previous pregnancy with gestational diabetes (two strata: yes or no); preconceptional BMI (three strata:

<25.0, 25.0 to <30.0, and ≥30.0 kg/m<sup>2</sup>). All participants were randomly assigned using the minimisation algorithm from the outset.

The control group used a blinded CGM system (Dexcom G6 Pro, Dexcom, San Diego, CA, USA) for 10 days immediately after randomisation and for another 10 days between gestational weeks 36<sup>0</sup> and 38<sup>6</sup>, with the receiver masked in advance and no access to CGM readings for either participants or physicians during the study.

### Procedures

Details on procedures, visits, and treatment goals are specified in appendix 2 (p 19). Briefly, a broad risk evaluation was performed at the initial contact (visit 1) after gestational diabetes diagnosis. All participants received nutrition and lifestyle recommendations and were trained on capillary glucose measurement. Participants were randomly assigned after a run-in period of 6–8 days (visit 2). Visit 3 was scheduled 8–10 days after visit 2, with further follow-up visits every 2 weeks. Both groups were managed with the goal of maintaining blood or CGM glucose concentrations within the pregnancy target range of 65–140 mg/dL (3.6–7.8 mmol/L), including fasting glucose concentrations of 95 mg/dL (5.3 mmol/L) or below, and 1-h postprandial glucose concentrations of 140 mg/dL (7.8 mmol/L) or below, in accordance with the American Diabetes Association guidelines.<sup>25</sup> Patients in the SMBG group were instructed to measure blood glucose concentrations four times daily (fasting and 1 h after breakfast, lunch, and dinner) using a study-provided blood glucose meter (Contour Next One system, Ascensia Diabetes Care Holdings, Basel, Switzerland), whereas patients in the intervention group used rt-CGM (Dexcom G6 Pro), with SMBG performed as needed based on patient discretion. Glycaemic control was evaluated every 2 weeks. CGM data were pseudonymised and uploaded in Dexcom's Clarity platform. Patients were trained to adjust their diet based on rt-CGM and SMBG measurements. Insulin therapy was initiated and titrated by experienced obstetricians or diabetologists when recommended thresholds were exceeded for both groups. Long-acting insulin was initiated in the evening if two or more fasting glucose measurements were 95 mg/dL (5.3 mmol/L) or higher over 1 week. Rapid-acting insulin was initiated if two or more postprandial glucose measurements were 140 mg/dL (7.8 mmol/L) or higher over 1 week. Metformin was used as an alternative or additional treatment in some patients. CGM data were analysed only for participants with at least 96 h of readings during the respective period in accordance with CONCEPTT.<sup>18</sup> CGM data were analysed up to 2359 h on the day before delivery.

At visit 2, women assigned to the intervention group were provided with an rt-CGM device (Dexcom G6 Pro) that records interstitial glucose concentrations every 5 min. The device was used factory calibrated, but manual calibrations were possible. The rt-CGM sensor was

See Online for appendix 2

See Online for appendix 3

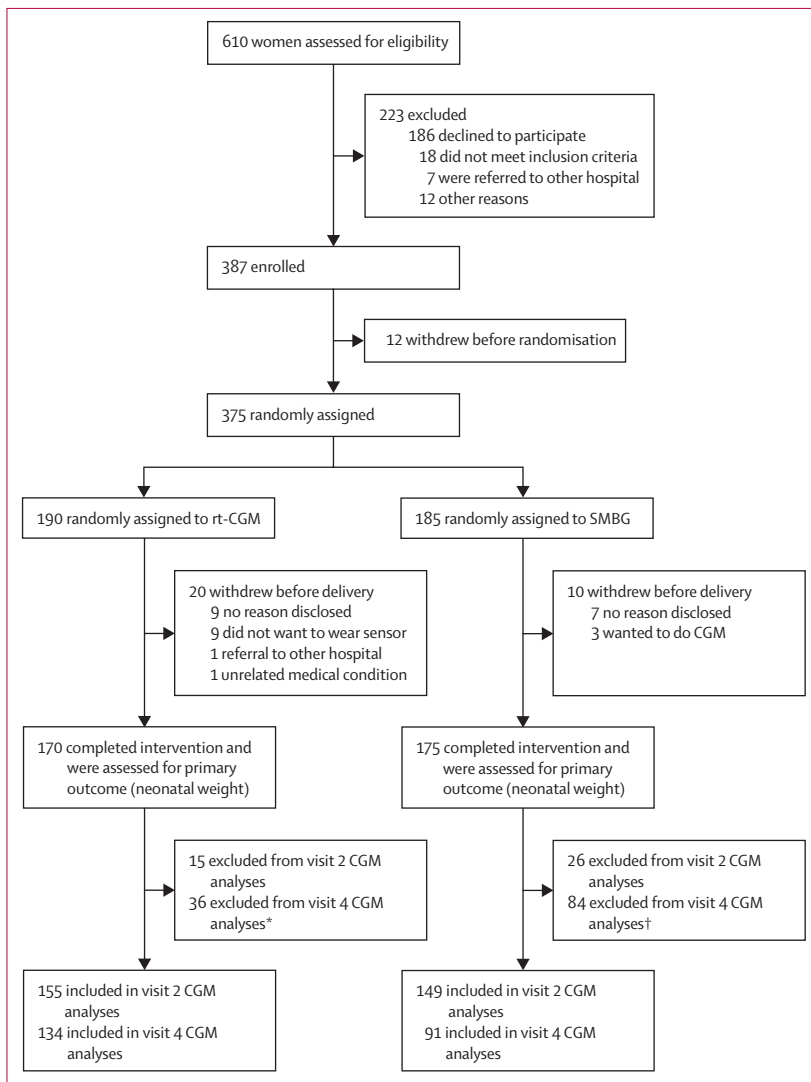
For MUW Randomizer see [www.meduniwien.ac.at/randomizer/login](http://www.meduniwien.ac.at/randomizer/login)

inserted into the subcutaneous tissue of the posterior upper arm. Women were equipped with a receiver, which provided real-time glucose concentrations. Alerts other than the alarm triggered by glucose values of 54 mg/dL (3.0 mmol/L) or below were discretionary. All participants in the intervention group received training on using the system. This included instructions on how to replace the sensor every 10 days and on measuring capillary blood glucose if the glucose readings or alerts did not align with their symptoms.

### Outcomes

The difference in the proportion of LGA newborns (birthweight >90th percentile) in women with

gestational diabetes using rt-CGM as compared with women using routine care SMBG was the primary endpoint of this study. In accordance with the CONCEPTT study, birthweight percentiles were calculated using customised percentiles from the Perinatal Institute's GROW Centile Calculator, which adjusts for maternal pregestational BMI, ethnicity, parity, gestational age at delivery, and fetal sex.<sup>26</sup> National birthweight percentiles, adjusted for fetal sex and gestational age at delivery and derived from a German reference population,<sup>27</sup> were evaluated as a secondary outcome measure. Other secondary endpoints included differences in further obstetric or neonatal complications, such as SGA infants (birthweight <10th percentile), neonatal hypoglycaemia ( $\leq 31$  mg/dL [1.7 mmol/L] in the first 24 h after delivery or  $\leq 45$  mg/dL [2.5 mmol/L] after the first 24 h after delivery and/or treatment with glucose infusion)<sup>6</sup> whereby, if several measurements were available, the lowest value was used, labour induction, stillbirth, preterm birth, caesarean section, shoulder dystocia, neonatal jaundice, admission to a neonatal intensive care unit (NICU), and maternal birth injuries, as well as length of hospital stay, umbilical cord blood pH, glucose, and C-peptide, and Apgar score. Neonatal birthweight and birth length were also recorded as secondary outcomes. Maternal secondary outcomes were differences in CGM metrics such as mean interstitial glucose, glycaemic variability (standard deviation of glucose readings, coefficient of glycaemic variation, and mean amplitude of glycaemic excursions), pregnancy-specific time in range (65–140 mg/dL [3.6–7.8 mmol/L]) as well as time spent above ( $>140$  mg/dL [7.8 mmol/L]) and below ( $<65$  mg/dL [3.6 mmol/L]) target range. Since the Dexcom system only allows for 5.0 mg/dL increments within its settings, the target range for this study and consequently all CGM analyses was set at 65–140 mg/dL [3.6–7.8 mmol/L] instead of 63–140 mg/dL [3.5–7.8 mmol/L] as recommended by some guidelines.<sup>28,29</sup> However, a post-hoc analysis of basic CGM metrics with a target range of 63–140 mg/dL [3.5–7.8 mmol/L] was also done. Daytime and night-time differences were assessed, with daytime defined as 0701 h to 2259 h and night-time as 2300 h to 0700 h. We also assessed HbA<sub>1c</sub>, change in maternal bodyweight, and the frequency and dosage of glucose-lowering therapy. According to the study protocol, only adverse events and serious adverse events, as defined by the Data Safety Monitoring Board, were recorded, without applying a formal grading system. Events were systematically assessed at each visit and documented in the electronic case report form, including onset, resolution, relatedness to the intervention, and seriousness. Any serious adverse event was reported immediately to the principal investigator and relevant local authorities. Other secondary outcomes specified in the study protocol will be analysed and reported



**Figure 1: Trial profile**

rt-CGM=real-time continuous glucose monitoring. SMBG=self-monitoring of blood glucose. \*CGM data unavailable (22 lost or not collected, 8 delivered prematurely, 2 delivered before visit 4, 4 had less than 96 h of recording). †CGM data unavailable (49 lost or not collected, 5 deliveries in other hospital, 11 premature deliveries, 1 lost receiver, 6 refused to wear sensor, 1 medical condition unrelated to study, 2 lost to follow up, 1 delivered before visit 4, 8 had less than 96 h of recording).

separately; a comprehensive list of all outcomes, including those designated for later analysis, is provided in appendix 2 (pp 21–22).

### Statistical analysis

A sample size of  $n=338$  (169 women per group) was estimated to detect a difference between two independent proportions of LGA of 13.7% (intervention group) versus 25.8% (control group) with a power of 80% (according to the results of a previous study<sup>14</sup>) and a two-sided type I error of  $\alpha=0.05$  for Pearson's  $\chi^2$  test. As we expected a dropout rate of 10%, a total sample size of  $n=372$  (186 women per group) was estimated to be necessary for this study. The sample-size calculation was performed by using the software G\*Power (version 3.1.9.2).<sup>30</sup> The conclusion from a predefined sample size review is provided in appendix 2 (p 20).

Analyses were conducted according to the intention-to-treat principle as predefined in the study protocol.<sup>20</sup> The intention-to-treat population is defined as all randomly assigned patients, analysed according to their assigned treatment group, regardless of whether they completed or adhered to the assigned intervention. This corresponds to the treatment policy strategy where intercurrent events, like glucose-lowering medications, are part of routine practice. The safety population is defined as all randomly assigned patients who received the assigned intervention. In this study, all patients who were randomly assigned also initiated treatment with CGM, resulting in identical safety and intention-to-treat population. Categorical variables were summarised by counts and proportions; continuous variables were summarised by mean and SD or by median and IQR in the case of strong deviations from normal distribution. Pearson's  $\chi^2$  test was used to compare differences in the primary outcome (difference in proportion of LGA newborns) and for binary secondary outcomes. For the primary outcome, post-hoc sensitivity analyses were conducted using binary logistic regression to adjust for stratification variables (as defined above), gestational diabetes diagnosis before 24 weeks of gestation, and centre effects, and were repeated after excluding one participant in the intervention group who was not diagnosed with gestational diabetes. In addition, post-hoc subgroup comparisons of the primary outcome were performed by centre, country, stratification variables, and timing of gestational diabetes diagnosis (before or after 24<sup>th</sup> weeks) to explore potential differences between subgroups. Additionally, post-hoc subgroup comparisons of CGM metrics were conducted for participants with and without glucose-lowering pharmacotherapy and according to CGM recording duration ( $\geq 96$  h vs all participants irrespective of wear time). Odds ratios (ORs) and 95% CIs were computed as appropriate. Continuous secondary outcome parameters (such as differences in CGM metrics) were compared by Student's *t*-test or rank based inference (Brunner–Munzel test). Effect estimates

	n	rt-CGM	n	SMBG
Age, years	170	34.8 (5.6)	175	33.9 (5.7)
Parity $\geq 1$	170	94 (55%)	175	88 (50%)
Ethnicity (non-Caucasian)	165	41 (25%)	169	36 (21%)
African	..	5 (3%)	..	3 (2%)
Arabic	..	12 (7%)	..	11 (7%)
South Asian	..	13 (8%)	..	11 (7%)
Central Asian	..	0	..	1 (1%)
East Asian	..	2 (1%)	..	3 (2%)
Southeast Asian	..	2 (1%)	..	2 (1%)
Latin American	..	1 (1%)	..	0
Other	..	4 (2%)	..	2 (1%)
Mixed	..	2 (1%)	..	3 (2%)
Gestational age at diagnosis, weeks	166	25.1 (2.5)	171	25.2 (2.2)
Gestational age at randomisation, weeks	170	28.6 (2.0)	175	28.5 (1.8)
$\geq 24$ to $< 26$ weeks	..	17 (10%)	..	14 (8%)
$\geq 26$ to $< 28$ weeks	..	49 (29%)	..	52 (30%)
$\geq 28$ to $< 30$ weeks	..	58 (34%)	..	66 (38%)
$\geq 30$ weeks	..	46 (27%)	..	43 (25%)
Maternal weight before pregnancy, kg	170	73.9 (17.6)	175	75.0 (17.2)
BMI before pregnancy, kg/m <sup>2</sup>	170	27.2 (6.2)	175	27.7 (6.2)
$< 25$ kg/m <sup>2</sup>	..	72 (42%)	..	65 (37%)
$\geq 25$ to $< 30$ kg/m <sup>2</sup>	..	59 (35%)	..	57 (33%)
$\geq 30$ kg/m <sup>2</sup>	..	39 (23%)	..	53 (30%)
HbA <sub>1c</sub> at randomisation, %	134	5.1 (0.4)	134	5.1 (0.3)
HbA <sub>1c</sub> at randomisation, mmol/mol	134	32.6 (4.2)	134	32.2 (3.7)
Gestational diabetes in previous pregnancy	170	29 (17%)	175	24 (14%)
First degree relative with diabetes	158	53 (34%)	161	60 (37%)
Current smoker	159	14 (9%)	165	10 (6%)
Post-secondary education	95	62 (65%)	95	58 (61%)
OGTT glucose concentration, mg/dL				
0 min	169	91 (10)	172	94 (11)
60 min	158	179 (35)	160	174 (33)
120 min	159	139 (31)	159	135 (36)
Study centre				
Vienna	170	115 (68%)	175	118 (67%)
Berlin	170	30 (18%)	175	31 (18%)
Jena	170	16 (9%)	175	14 (8%)
Basel	170	9 (5%)	175	12 (7%)
Country of randomisation				
Austria	170	115 (68%)	175	118 (67%)
Germany	170	46 (27%)	175	45 (26%)
Switzerland	170	9 (5%)	175	12 (7%)

Data are mean (SD) or n (%). OGTT=oral glucose tolerance test. rt-CGM=real-time continuous glucose monitoring. SMBG=self-monitoring of blood glucose.

**Table 1: Main characteristics of the intention-to-treat population at baseline**

were expressed as mean difference or relative effects (ie, stochastic equivalence) and associated 95% CI. Adjustment for stratification variables were done by linear as well as binary or ordinal logistic regression, resulting in adjusted mean difference or OR. Differences in adverse and serious adverse events are given as absolute risk difference or rate ratios and 95% CI. Except

for patients who withdrew their consent, there were no missing data for the primary outcome or most neonatal outcomes. Therefore, no data imputation was used in line with the study protocol.<sup>20</sup> The two-sided significance level was set to  $p < 0.05$ . There was no adjustment for multiplicity for secondary outcomes, these should consequently be interpreted in an exploratory context.

	n	rt-CGM	n	SMBG	p value	Effect size (95% CI)
<b>Primary outcome</b>						
Large for gestational age (>90th percentile)	170	6 (4%)	175	18 (10%)	0.014	0.32 (0.10 to 0.87)
<b>Secondary obstetric outcomes</b>						
Gestational age at delivery, weeks	170	38.9 (1.3)	175	38.8 (1.5)	0.56	0.09 (-0.21 to 0.39)
Preterm birth (<37 weeks)	170	8 (5%)	175	11 (6%)	0.52	0.74 (0.25 to 2.07)
Induction of labour	163	57 (35%)	165	45 (27%)	0.13	1.43 (0.87 to 2.36)
Caesarean section	170	77 (45%)	172	92 (53%)	0.13	0.72 (0.46 to 1.13)
Shoulder dystocia	169	0	170	0	..	..
Maternal birth injuries (all)	89	61 (69%)	75	52 (69%)	0.91	0.96 (0.47 to 1.97)
Perineal laceration >grade 2	89	1 (1%)	75	2 (3%)	0.46	0.42 (0.01 to 8.16)
Hypertensive disorder	167	8 (5%)	166	9 (5%)	0.79	0.88 (0.29 to 2.64)
Length of hospital stay, days	167	4.0 (3.0-5.0)	167	4.0 (3.1-5.0)	0.33	0.47 (0.41 to 0.53)
<b>Secondary neonatal outcomes</b>						
Birthweight, g	170	3242 (447)	175	3287 (483)	0.37	-45.13 (-143.72 to 53.46)
Birth length, cm	170	51.0 (2.6)	173	50.8 (3.0)	0.49	0.21 (-0.39 to 0.80)
Birthweight, customised percentile	170	38.6 (28.0)	175	45.6 (29.0)	0.024	-6.96 (-13.00 to -0.92)
Birthweight, national percentile	169	40.1 (25.9)	172	46.5 (26.8)	0.028	-6.30 (-11.92 to -0.68)
Birthweight >4000 g	170	9 (5%)	175	8 (5%)	0.76	1.17 (0.39 to 3.57)
Small for gestational age (<10th percentile)	170	33 (19%)	175	23 (13%)	0.11	1.59 (0.86 to 2.99)
Extreme small for gestational age (<5th percentile)	170	20 (12%)	175	14 (8%)	0.24	1.53 (0.71 to 3.41)
Umbilical cord pH	166	7.25 (0.07)	168	7.25 (0.08)	0.73	0.00 (-0.01 to 0.02)
Umbilical cord pH <7.2	166	34 (20%)	168	34 (20%)	0.96	1.01 (0.58 to 1.79)
Cord blood glucose, mg/dL	48	75.4 (19.3)	43	81.8 (24.2)	0.17	-6.40 (-15.61 to 2.80)
Cord blood C-peptide, pmol/L	40	1.6 (1.2)	45	1.7 (1.2)	0.64	-0.12 (-0.64 to 0.39)
Apgar score						
1 min	167	9 (9-9)	168	9 (9-9)	0.39	0.52 (0.47 to 0.57)
5 min	168	10 (10-10)	171	10 (9-10)	0.13	0.54 (0.49 to 0.58)
10 min	168	10 (10-10)	171	10 (10-10)	0.19	0.52 (0.49 to 0.56)
Newborn glucose, mg/dL	154	58 (15)	152	59 (15)	0.42	-1.39 (-4.77 to 2.00)
Newborn hypoglycaemia	153	5 (3%)	152	2 (1%)	0.26	2.51 (0.40 to 26.75)
NICU admission	170	6 (4%)	172	14 (8%)	0.07	0.41 (0.13 to 1.18)
NICU length of stay, days	6	4.0 (2.3-8.0)	14	4.5 (1.3-8.3)	0.85	0.53 (0.19 to 0.87)
Newborn jaundice	166	4 (2%)	170	2 (1%)	0.39	2.07 (0.29 to 23.17)
Stillbirth	170	0	175	0	..	..
<b>Further secondary outcomes</b>						
Large for gestational age (according to national percentile)	169	5 (3%)	172	9 (5%)	0.29	0.55 (0.14 to 1.88)
Small for gestational age (according to national percentile)	169	19 (11%)	172	18 (10%)	0.82	1.08 (0.52 to 2.28)
Maternal weight gain, kg*	155	10.8 (5.8)	150	10.3 (5.4)	0.42	0.51 (-0.74 to 1.77)
HbA <sub>1c</sub> at 36 <sup>th</sup> to 38 <sup>th</sup> weeks, %	132	5.3 (0.4)	130	5.3 (0.3)	0.70	0.02 (-0.07 to 0.11)
HbA <sub>1c</sub> at 36 <sup>th</sup> to 38 <sup>th</sup> weeks, mmol/mol	132	34.4 (4.4)	130	34.2 (3.8)	0.70	0.19 (-0.81 to 1.19)

Data are n (%) for dichotomous outcomes, mean (SD) for normally distributed outcomes, or median (IQR) for non-normally distributed outcomes. Effect sizes are either odds ratios for dichotomous outcomes (expected value under the null hypothesis: 1), mean difference for normally distributed outcomes (expected value under the null hypothesis: 0), or ranked-based relative effects for non-normally distributed continuous outcomes (expected value under the null hypothesis: 0.5). Effect size describes the magnitude of change in outcomes from the control group to the intervention group. NICU=neonatal intensive care unit. rt-CGM=real-time continuous glucose monitoring. SMBG=self-monitoring of blood glucose. \*Difference between visit 4 and pregestational weight.

**Table 2: Primary, secondary, and further secondary obstetric and neonatal outcomes for the intention-to-treat population**

Statistical analysis was performed by using R (version 4.3.2). Information on data handling and processing is provided in appendix 2 (p 20).

### Role of the funding source

The funder of the study (Dexcom) provided all rt-CGM devices, but had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

### Results

Between Aug 24, 2020, and May 30, 2024, 610 women were screened for eligibility, of whom 375 were randomly assigned (rt-CGM,  $n=190$ ; SMBG,  $n=185$ ) at a mean of 28·6 weeks (SD 1·9) of gestation. 345 women completed the study: 170 in the intervention group and 175 in the control group (figure 1). These participants were distributed among the study sites as follows: Vienna, 233; Berlin, 61; Jena, 30; Basel, 21. Among participants for whom gestational age at diagnosis was known, 36 (22%) of 166 participants in the intervention group and 23 (13%) of 171 participants in the control group were diagnosed with gestational diabetes before 24 weeks of gestation. Mean gestational age at diagnosis was 25·2 weeks (SD 2·3).

A comparison of baseline characteristics is provided in table 1. No major differences in baseline parameters were observed after randomisation.

Maternal and neonatal outcomes are provided in table 2, indicating a statistically significant reduction of LGA infants born to women using rt-CGM as compared with SMBG (six [4%] of 170 vs 18 [10%] of 175; OR 0·32, 95% CI 0·10–0·87,  $p=0·014$ ). The statistically significant difference in the primary outcome remained after adjustment for the predefined stratification variables (appendix 2 p 5). Additional sensitivity analyses for the primary outcome, addressing centre effects and the inclusion of a patient who did not meet the eligibility criteria, as well as an adjustment for early gestational diabetes with diagnosis before 24 weeks, are provided in appendix 2 (p 8). These analyses yielded results consistent with the primary findings. Moreover, the average newborn weight percentiles were lower in participants using rt-CGM (figure 2), and remained statistically significant after adjustment for stratification variables, centre effects, and gestational diabetes diagnosis before 24<sup>th</sup> weeks of gestation (appendix 2 pp 5–7). For more detailed insights we conducted further post-hoc descriptive analysis of the primary outcome across centres, countries, stratification variables, and timing of gestational diabetes diagnosis (appendix 2 p 9). When national percentiles were applied, the LGA rate did not differ significantly; however, mean birthweight percentiles were significantly lower in the intervention group (40·1 vs 46·5, mean difference 6·30, 95% CI –11·92 to –0·68,  $p=0·028$ ). Conversely, group-based comparisons of the proportion of SGA newborns (33 [19%] of 170 for rt-CGM vs 23 [13%] of 175 for SMBG

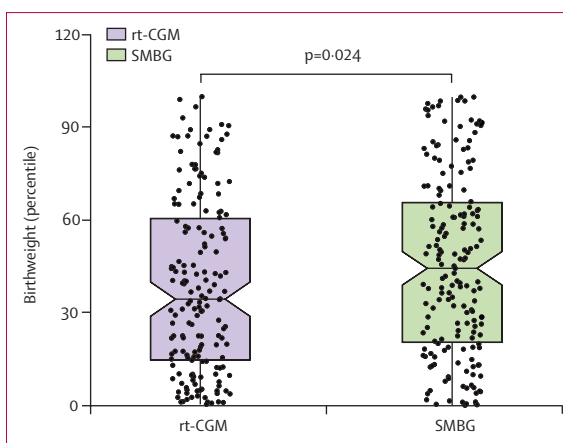


Figure 2: Birthweight percentiles (GROW customised centiles) in participants assigned to either rt-CGM or SMBG

Notch represents the 95% CI of the median. rt-CGM=real-time continuous glucose monitoring. SMBG=self-monitoring of blood glucose

users; OR 1·59, 95% CI 0·86–2·99,  $p=0·11$ ) or the frequency of neonatal hypoglycaemia were not statistically significant. We observed two cases of infants requiring intravenous glucose infusion in the control group, none in the rt-CGM group. NICU admission was reported for the newborns of six (4%) of 170 mothers in the intervention group versus 14 (8%) of 172 in the control group. No cases of shoulder dystocia or intrauterine fetal death were reported in the study. The median time of maternal hospitalisation was similar between groups.

The percentage of participants who received glucose-lowering medications did not differ between groups. However, rapid-acting insulin was more often prescribed in the rt-CGM group, also requiring higher daily doses of insulin (table 3).

A comparison of glucose measurements derived from blinded CGM (control group) and open CGM (intervention group) in the first 10 days after randomisation (appendix 2 p 11) showed no major differences in time in range and time above range. However, participants assigned to rt-CGM showed longer time below range (<65 mg/dL [3·6 mmol/L]). A comparison of CGM measurements from blinded CGM (control group) and open CGM (intervention group) between 36 weeks and 38 weeks of gestation (visit 4) showed a modest, but statistically significant, improvement in time in range (65–140 mg/dL [3·6–7·8 mmol/L]) in the rt-CGM group (table 3), a finding that persisted when the target range was set to 63–140 mg/dL (3·5–7·8 mmol/L, appendix 2 p 17). However, the favourable effect on glycaemic control was larger in participants with need of glucose-lowering medication (appendix 2 pp 14–15). The results remained unchanged when participants with glucose readings of less than 96 h were included (appendix 2 p 16). Differences in occurrence, duration and severity of hyperglycaemic episodes at visit 4 are provided in

	n	rt-CGM	n	SMBG	p-value	Effect size (95% CI)
<b>Glucose-lowering medication</b>						
Pharmacotherapy (metformin and/or insulin)	170	104 (61%)	175	97 (55%)	0.28	1.27 (0.81 to 1.99)
Metformin	169	8 (5%)	175	5 (3%)	0.36	1.69 (0.48 to 6.70)
Basal-acting or rapid-acting insulin	170	102 (60%)	175	95 (54%)	0.28	1.26 (0.81 to 1.98)
Basal-acting or rapid-acting insulin, IU/day*	104	23 (14–39)	97	18 (12–28)	0.029	0.59 (0.51 to 0.67)
Basal-acting or rapid-acting insulin, IU/day†	102	24 (14–40)	95	18 (12–29)	0.026	0.59 (0.51 to 0.67)
Basal-acting insulin	170	101 (59%)	175	92 (53%)	0.20	1.32 (0.84 to 2.07)
Basal-acting insulin, IU/day*	104	14 (10–22)	97	14 (10–20)	0.24	0.55 (0.47 to 0.63)
Basal-acting insulin, IU/day‡	101	14 (10–22)	92	14 (10–20)	0.34	0.54 (0.46 to 0.62)
Rapid-acting insulin	170	70 (41%)	175	53 (30%)	0.035	1.61 (1.01 to 2.58)
Rapid-acting insulin, IU/day*	104	6 (0–18)	97	2 (0–10)	0.007	0.60 (0.53 to 0.68)
Rapid-acting insulin, IU/day§	70	13 (6–26)	53	10 (4–18)	0.056	0.60 (0.50 to 0.70)
Gestational age at start of insulin therapy, weeks	102	30.5 (3.0)	95	29.9 (2.8)	0.21	0.53 (–0.29 to 1.35)
Gestational age at start of maximum insulin dose, weeks	102	36.1 (2.4)	95	34.9 (2.7)	0.0010	1.22 (0.50 to 1.95)
<b>Glucose metrics derived from CGM between 36 and 38 weeks of gestation</b>						
Sensor wear time, h	134	218 (181–237)	91	192 (167–216)	<0.0001	0.68 (0.63 to 0.75)
Mean interstitial glucose, mg/dL	134	103 (9)	91	105 (12)	0.16	–2.04 (–4.87 to 0.79)
Standard deviation of glucose readings, mg/dL	134	19 (4)	91	20 (5)	0.083	–1.20 (–2.56 to 0.16)
Coefficient of glycaemic variation, %	134	18 (4)	91	19 (4)	0.20	–0.73 (–1.84 to 0.38)
MAGE, mg/dL	134	44.4 (11.0)	91	47.0 (13.6)	0.13	–2.63 (–6.01 to 0.75)
Time in, above, and below range, %¶						
Total						
Time in range (65–140 mg/dL)	134	95 (91–97)	91	93 (87–96)	0.026	0.59 (0.51 to 0.66)
Time above range (>140 mg/dL)	134	3.95 (1.3–7.3)	91	5.6 (1.5–10.7)	0.10	0.43 (0.35 to 0.51)
Time below range (<65 mg/dL)	134	0.6 (0.1–1.8)	91	0.5 (0.1–2.3)	0.87	0.49 (0.42 to 0.57)
Time below range (<54 mg/dL)	134	0.0 (0.0–0.4)	91	0.0 (0.0–0.4)	0.92	0.50 (0.42 to 0.57)
Daytime						
Time in range (65–140 mg/dL)	134	94 (89–98)	91	93 (87–96)	0.065	0.57 (0.50 to 0.65)
Time above range (>140 mg/dL)	134	4.6 (1.3–8.8)	91	5.6 (1.8–11.8)	0.13	0.44 (0.36 to 0.52)
Time below range (<65 mg/dL)	134	0.3 (0.0–1.2)	91	0.4 (0.0–1.5)	0.73	0.49 (0.41 to 0.56)
Time below range (<54 mg/dL)	134	0.0 (0.0–0.1)	91	0.0 (0.0–0.2)	0.98	0.50 (0.43 to 0.57)
Night-time						
Time in range (65–140 mg/dL)	134	96 (92–98)	91	94 (91–98)	0.07	0.57 (0.49 to 0.65)
Time above range (>140 mg/dL)	134	1.7 (0.1–4.7)	91	1.9 (0.0–7.0)	0.46	0.47 (0.39 to 0.55)
Time below range (<65 mg/dL)	134	0.6 (0.0–2.4)	91	0.5 (0.0–2.9)	0.82	0.49 (0.41 to 0.57)
Time below range (<54 mg/dL)	134	0.0 (0.0–0.6)	91	0.0 (0.0–1.0)	0.44	0.47 (0.40 to 0.54)

Data are n (%) for dichotomous outcomes, mean (SD) for normally distributed outcomes, or median (IQR) for non-normally distributed outcomes. Effect sizes are either odds ratios for dichotomous outcomes (expected value under the null hypothesis: 1), mean differences for normally distributed outcomes (expected value under the null hypothesis: 0), or ranked-based relative effects for non-normally distributed continuous outcomes (expected value under the null hypothesis: 0.5). Effect size describes the magnitude of change in outcomes from the control group to the intervention group. MAGE=mean amplitude of glycaemic excursions. rt-CGM=real-time continuous glucose monitoring. SMBG=self-monitoring of blood glucose. \*Calculated for participants who received glucose-lowering medications (metformin and/or insulin). †Calculated for participants who received insulin treatment (basal-acting or rapid-acting). ‡Calculated for participants who received basal-acting insulin. §Calculated for participants who received rapid-acting insulin. ¶Percentages refer to percentage of time; daytime is 0701–2259 h and night-time is 2300–0700 h.

**Table 3: Comparison of glucose-lowering medications and glucose metrics derived from CGM assessed between 36 and 38 weeks of gestation for the intention-to-treat population**

appendix 2 (p 17). In the rt-CGM group, sensor use covered 62% of expected wear time from visit 2 to delivery. We found no group-specific differences in HbA<sub>1c</sub> (assessed at visit 4) or maternal weight gain (difference between visit 4 and pregestational weight, table 2). Moreover, the number of visits at the hospital (a post-hoc endpoint) was similar between rt-CGM and SMBG users: median 9 (8–12) versus 10 (7–12) visits.

The study reported 52 serious adverse events among 23 (12%) of 190 women in the rt-CGM group and 28 (15%) of 185 women in the SMBG group, with one woman in the rt-CGM group experiencing two events (table 4). The proportion of participants with serious adverse events showed no difference between groups. Likewise, a total of 59 adverse events were reported among 33 (17%) women in the rt-CGM group and 20 (11%) women in the SMBG

group, with four women in the rt-CGM group and two women in the SMBG group reporting two adverse events. The proportion of participants with adverse events showed no statistically significant difference between groups, although skin reactions were more often observed in the rt-CGM group.

## Discussion

In this randomised controlled trial, we aimed to assess the effectiveness of rt-CGM versus SMBG for the management of gestational diabetes and found that participants assigned to rt-CGM had lower birthweight percentiles and a lower prevalence of LGA neonates.

A lower risk of LGA neonates was also reported in another study involving pregnant women with type 1 diabetes.<sup>18</sup> With regard to gestational diabetes, a small randomised trial using intermittently scanned CGM during the first 4 weeks after diagnosis showed a reduced incidence of fetal macrosomia.<sup>31</sup> Similarly, a larger non-randomised study by Yu and colleagues found that periodic CGM use was associated with lower risks of LGA infants and neonatal hypoglycaemia.<sup>14</sup> A systematic review recently identified a lower risk of LGA infants and improved glycaemic control in pregnancies with type 1 diabetes and gestational diabetes.<sup>32</sup>

The recently published DipGluMo study showed no improvement in perinatal outcomes among gestational diabetes patients using rt-CGM.<sup>19</sup> Although participants reported a higher preference for rt-CGM use, time in range was significantly lower in the rt-CGM group as compared with the SMBG group. These findings are in contrast with the results of our study. While key elements of the study designs were similar, differences in treatment strategies might explain this discrepancy: In DipGluMo, SMBG participants performed six daily glucose measurements compared with four in our trial, which might have enabled tighter control. Rapid-acting insulin use was uncommon in DipGluMo, whereas pharmacotherapy was more frequent in our study and might have contributed to greater TIR among rt-CGM users, particularly in those receiving glucose-lowering medication. Consistent with our findings, a previous, albeit smaller, randomised controlled trial in women with gestational diabetes, also reported that glucose-lowering medications were more often prescribed to CGM users.<sup>33</sup> Moreover, a significantly higher percentage of time in range in CGM users was observed in another recent randomised controlled trial.<sup>34</sup>

A large Chinese prospective cohort study demonstrated a positive association between CGM-derived hyperglycaemia metrics (including time in range and time above range) and an increased risk for LGA and perinatal complications.<sup>35</sup> Notably, while pregnancy-specific CGM glucose targets and time in range goals have been recommended for individuals with pregestational diabetes, international consensus guidelines do not specify treatment targets for time spent within these

	rt-CGM (n=190)	SMBG (n=185)	p value	Effect size (95% CI)
<b>Serious adverse events</b>				
Participants with serious adverse events	23 (12%)	28 (15%)	0.39	0.77 (0.42 to 1.40)*
Number of serious adverse events (total)	24 (13%)	28 (15%)	0.52	0.83 (0.48 to 1.44)†
Obstetric	20 (11%)	17 (9%)	..	1.34 (-5.24 to 7.88)‡
Respiratory or ENT	2 (1%)	2 (1%)	..	-0.03 (-3.33 to 3.20)‡
Gastrointestinal, including nausea and vomiting	0	2 (1%)	..	-1.08 (-4.26 to 1.55)‡
Urinary or genital	0	2 (1%)	..	-1.08 (-4.26 to 1.55)‡
Cardiological or vasovagal	0	3 (2%)	..	-1.62 (-5.05 to 1.13)‡
Headaches or migraines	0	0	..	0 (0 to 0)‡
Skin	1 (<1%)	0	..	0.53 (-2.06 to 3.35)‡
Musculoskeletal	0	1 (<1%)	..	-0.54 (-3.44 to 1.98)‡
Haematological	1 (<1%)	1 (<1%)	..	-0.01 (-2.95 to 2.85)‡
Neurological	0	0	..	0 (0 to 0)‡
Psychological or psychiatric	0	0	..	0 (0 to 0)‡
Other	0	0	..	0 (0 to 0)‡
Maternal deaths	0	0	..	0 (0 to 0)‡
<b>Adverse events</b>				
Participants with adverse events	33 (17%)	20 (11%)	0.067	1.73 (0.96 to 3.19)*
Number of adverse events (total)	37 (19%)	22 (12%)	0.067	1.64 (0.97 to 2.82)†
Obstetric	6 (3%)	8 (4%)	..	-1.17 (-5.87 to 3.37)‡
Respiratory or ENT	4 (2%)	3 (2%)	..	0.48 (-3.23 to 4.23)‡
Gastrointestinal, including nausea and vomiting	4 (2%)	5 (3%)	..	-0.6 (-4.69 to 3.34)‡
Urinary or genital	2 (1%)	1 (<1%)	..	0.51 (-2.51 to 3.65)‡
Cardiological or vasovagal	2 (1%)	4 (2%)	..	-1.11 (-4.85 to 2.32)‡
Headaches or migraines	0	0	..	0 (0 to 0)‡
Skin	14 (7%)	1 (<1%)	..	6.83 (2.57 to 11.79)‡
Musculoskeletal	0	0	..	0 (0 to 0)‡
Haematological	1 (<1%)	0	..	0.53 (-2.06 to 3.35)‡
Neurological	0	0	..	0 (0 to 0)‡
Psychological or psychiatric	3 (2%)	0	..	1.58 (-1.21 to 4.92)‡
Other	1 (<1%)	0	..	0.53 (-2.06 to 3.35)‡

All randomly assigned patients were included (safety population). Data are n (%), odds ratio (95% CI), rate ratio (95% CI), or absolute risk difference (95% CI). Risk difference describes the magnitude of change in outcomes from the control group to the intervention group. Obstetric serious adverse events included: cervix insufficiency (rt-CGM, 5; SMBG, 3; total, 8), pre-eclampsia (rt-CGM, 3; SMBG, 4; total, 7), premature rupture of membranes (rt-CGM, 3; SMBG, 2; total, 5), prepartum or postpartum haemorrhage (rt-CGM, 2; SMBG, 3; total, 5), premature contractions (rt-CGM, 3; SMBG, 1; total, 4), abnormal fetal doppler or cardiotocography patterns (rt-CGM, 2; SMBG, 1; total, 3), intrahepatic cholestasis of pregnancy (rt-CGM, 0; SMBG, 1; total, 1), vasa previa (rt-CGM, 0; SMBG, 1; total, 1), abruption of placenta (rt-CGM, 1; SMBG, 0; total, 1), placenta residuals (rt-CGM, 0; SMBG, 1; total, 1), inpatient admission for abnormal glucose values (rt-CGM, 1; SMBG, 0; total, 1). Adverse event grading was not performed, as no events met the criteria for severe intensity, and the protocol specified recording events only as non-serious or serious. ENT=ear nose throat. rt-CGM=real-time continuous glucose monitoring. SMBG=self-monitoring of blood glucose. \*Effect size is expressed as odds ratio. †Effect size is expressed as rate ratio. ‡Effect size is expressed as risk difference.

**Table 4: Adverse and serious adverse events for the safety population**

ranges in gestational diabetes.<sup>12,28</sup> Some experts recommend a time in range exceeding 90% and a time above range below 5% in women with gestational diabetes.<sup>29,36,37</sup> However, optimal duration targets remain under discussion.

The higher rate of SGA in the rt-CGM group (19% vs 13%) represents a potentially important concern,

and overtreatment needs to be considered as a possible explanation of this finding. In a systematic review, Martis and colleagues pointed out that certain treatment approaches for gestational diabetes may increase the likelihood of labour induction, thereby suggesting potential harm through overtreatment.<sup>38</sup> In our study, the proportion of patients undergoing induction of labour was indeed higher in rt-CGM participants than in SMBG participants (35% vs 27%). In contrast, the rate of caesarean sections was lower (45% vs 53%). Despite neither difference reaching statistical significance, it is important to note that gestational age at delivery (38·9 weeks vs 38·8 weeks) and the frequency of preterm birth (5% vs 6%) were almost the same. Thus, we have no indication that the differences observed in neonatal outcomes were due to an increased incidence of preterm deliveries through induction of labour or caesarean section. Nevertheless, the increased proportion of SGA neonates in the rt-CGM group remains a cause for concern. However, this finding might not necessarily reflect a direct consequence of rt-CGM use, but could be a result of adherence to the tight glycaemic targets recommended for pregnancy with gestational diabetes.<sup>29,36,37</sup> Therefore, our findings could contribute to the ongoing debate regarding the appropriateness of current glycaemic targets in the management of gestational diabetes. Indeed, previous studies reported an inverse relationship between blood glucose concentrations and the risk of SGA.<sup>10,11</sup> It is, however, important to note that the observed difference in the frequency of SGA did not reach statistical significance in our study. In line with our observation for customised percentiles, national birthweight percentiles showed a statistically significant difference on a continuous basis as well (appendix 2 p 10); however, the frequencies of both SGA (11% vs 10%) and LGA (3% vs 5%) derived from national percentiles remained markedly lower and were similar between groups. Although national birthweight percentiles might be inadequate for our multinational study, this finding underscores the need to carefully consider the chosen method, as customised percentiles have been shown to yield higher SGA rates and have been linked to poorer perinatal outcomes.<sup>39–41</sup> In our study, the decision to use customised percentiles was aligned with the CONCEPTT trial, in which they were more strongly associated with adverse pregnancy outcomes in a prespecified analysis.<sup>18,42</sup> However, further research is needed to determine the best approach for LGA definition in the context of gestational diabetes.

Regarding hypoglycaemic events, we observed that immediately after randomisation, rt-CGM users spent more time below the target of 65 mg/dL (3·6 mmol/L), particularly during daytime. Although hypoglycaemia is a concern, the median time below range was modest in both groups (less than 1%) and the difference was no longer statistically significant later in pregnancy. Importantly, time spent below 54 mg/dL (3·0

mmol/L)—the threshold for severe hypoglycaemia according to international guidelines<sup>28,43</sup>—did not differ between the groups. While we do not consider hypoglycaemia a major safety concern for rt-CGM based on these data, the finding warrants further investigation.

With regard to safety outcomes, no statistically significant differences in adverse or serious adverse events were observed, although skin reactions were reported more frequently in the rt-CGM group, as expected. These findings suggest that rt-CGM does not substantially increase the rate of adverse events in women with gestational diabetes.

The advantages and limitations of our trial need to be discussed. Although disproportionate recruitment at one centre and restriction to tertiary care settings are notable limitations, the multinational, randomised controlled study design is a clear strength. Another limitation is that the trial was powered for LGA, and rarer outcomes such as shoulder dystocia or stillbirth could not be meaningfully compared. While the sample size is also small for assessing safety outcomes, this is, to our knowledge, the largest randomised controlled trial of rt-CGM in women with gestational diabetes. Additionally, rt-CGM was used continuously and unblinded for clinical gestational diabetes management from the time of diagnosis until delivery. Notably, the number of assessments of glycaemic control during late gestation (36–38 weeks) was reduced due to preterm birth (before visit 4) and missed follow-up visits. This might be in part explained by the COVID-19 pandemic, which had various implications for both clinical research and routine care in pregnancies affected by diabetes.<sup>44</sup> Other reasons for loss to follow-up include transfer to other hospitals for delivery and low adherence to the use of the blinded CGM device in the control group. COVID-19-related disruptions and transfers to other hospitals are likely unrelated to unobserved outcomes (missing at random). In the control group, some participants might have discontinued CGM use in late pregnancy due to the perceived burden of wearing an additional device without clear benefit, contributing to a higher rate of missing data. As this type of missingness is not directly related to glucose concentrations, it could also be regarded as missing at random. Furthermore, in line with the CONCEPTT study, no adjustment for type I error inflation was made for secondary outcomes, and findings should therefore be interpreted with appropriate caution. Another limitation is that the incidence of LGA neonates in the entire cohort was lower than initially anticipated. This outcome might be attributed to the fact that participants were managed at tertiary care centres with substantial expertise in treating women with gestational diabetes. Generalisability might therefore be limited, and results might differ in other health-care settings. However, also ethnic factors and use of different calculations of birthweight percentiles could explain the generally low event rate. The already low incidence of

LGA, along with acceptable time in range even in the control group, could potentially mitigate the impact of CGM. The open-label character of this study could also be considered a limitation, but is consistent with other similar studies.<sup>18,19</sup> Moreover, multiple pregnancies were excluded from this study. Finally, patients diagnosed with gestational diabetes before 24 weeks of gestation were included in the study if pharmacotherapy had not been initiated, which might be considered another limitation. However, the results remained unchanged when this factor was accounted for in the multivariable analysis.

In summary, use of rt-CGM in women with gestational diabetes was associated with a lower incidence of LGA infants and reduced birthweight percentiles compared with SMBG. However, the overall high prevalence of SGA warrants further research, as reductions in the proportion of LGA neonates might potentially be accompanied by an increased risk of SGA. Rt-CGM use also led to increased administration of rapid-acting insulin and modest enhancement in time in range. Consequently, until glycaemic targets for CGM use in gestational diabetes are better defined, rt-CGM could be considered for selected patients under the supervision of an experienced care team.

#### Contributors

CG, as Principal Investigator, was responsible for the conceptualisation of the study, secured funding, developed the methodology, led the investigation, and was responsible for visualisation, validation, and writing of the original draft. TL contributed to data curation, investigation, project administration, and visualisation, and took the lead in writing the original draft as well as reviewing and editing the manuscript. ID-S contributed to the conceptualisation of the study, data curation, investigation, and project administration. SW was involved in the study's conceptualisation, data curation, investigation, and project administration. KS contributed to conceptualisation, data curation, investigation, and project administration. SS was responsible for conceptualisation, data curation, investigation, and project administration. DE contributed to data curation, investigation, and project administration. CM was involved in conceptualisation, investigation, and project administration. FH contributed to conceptualisation, data curation, formal analysis, and validation. KR contributed to conceptualisation, data curation, investigation, and project administration. BW was involved in conceptualisation, data curation, investigation, and project administration. FW and TG contributed to conceptualisation, data curation, investigation, and project administration. BM contributed to data curation, investigation, and project administration. MMi was responsible for data curation, formal analysis, methodology, and validation. JJ contributed to conceptualisation, funding acquisition, validation, and manuscript review and editing. WH was involved in conceptualisation and funding acquisition. MMo contributed to data curation, formal analysis, and validation. LB contributed to conceptualisation and writing of the original draft as well as reviewing and editing the manuscript. AT was responsible for conceptualisation, data curation, formal analysis, methodology, and review and editing of the manuscript. CG, TL, FH, MMi, and AT accessed and verified the underlying data. All authors had full access to all the data in the study and had final responsibility for the decision to submit for publication. All authors reviewed and approved the final manuscript.

#### Declaration of interests

We declare no competing interests.

#### Data sharing

De-identified individual participant data underlying the results reported in this Article (including text, tables, figures, and appendices), together with the study protocol, will be made available after publication. Data

will be shared with investigators who submit a methodologically sound proposal to the corresponding author, have their proposed use approved by an independent review committee ("learned intermediary") identified for this purpose, sign a data access agreement, and agree to use the data only for the purposes outlined in the approved proposal.

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