Continuous Glucose Monitoring in Women With Type 1 Diabetes in Pregnancy Trial

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Introduction

- Despite advances in care, pregnant women with Type 1 Diabetes continue to have increased rates of adverse maternal and neonatal outcomes

- There is good evidence that adverse outcomes are associated with poor glycaemic control

- Continuous Glucose Monitoring (CGM) may assist women in achieving optimal glycaemic control

Continuous Glucose Monitor (CGM)

CONCEPTT

- **Aim**: to evaluate the impact of CGM on glycaemic control in women with Type 1 diabetes who were pregnant or planning pregnancy
- International multi-centre, randomised controlled trial of 2 parallel cohorts

Inclusion Criteria

- Women aged 18-40 years with Type 1 diabetes > 1 year
- Suboptimal glucose control
  - HbA1c 7-10% in cohort planning pregnancy
  - HbA1c 6.5-10% in pregnant cohort
- Intensive insulin therapy using either insulin pump or multiple daily injections

Study Design: Pregnant Cohort

Enrolment: first trimester (singleton <14 w gestation on US)

Run-in phase with blinded CGM: sensor wear for 6 of 7 days, ≥4 capillary glucose tests/day

Randomisation

Stratified by:

Pump v. MDI

Baseline HbA1c (<7.5% v. ≥7.5%)

Intervention: RT-CGM

Device education

Algorithms for insulin titration

Treatment decisions based on capillary glucose tests

BGL Target

3.5-7.8 mmol/L

Control: SMBG

≥7 capillary glucose tests/day

Algorithms for insulin titration

Blinded CGM at 24 and 34 w

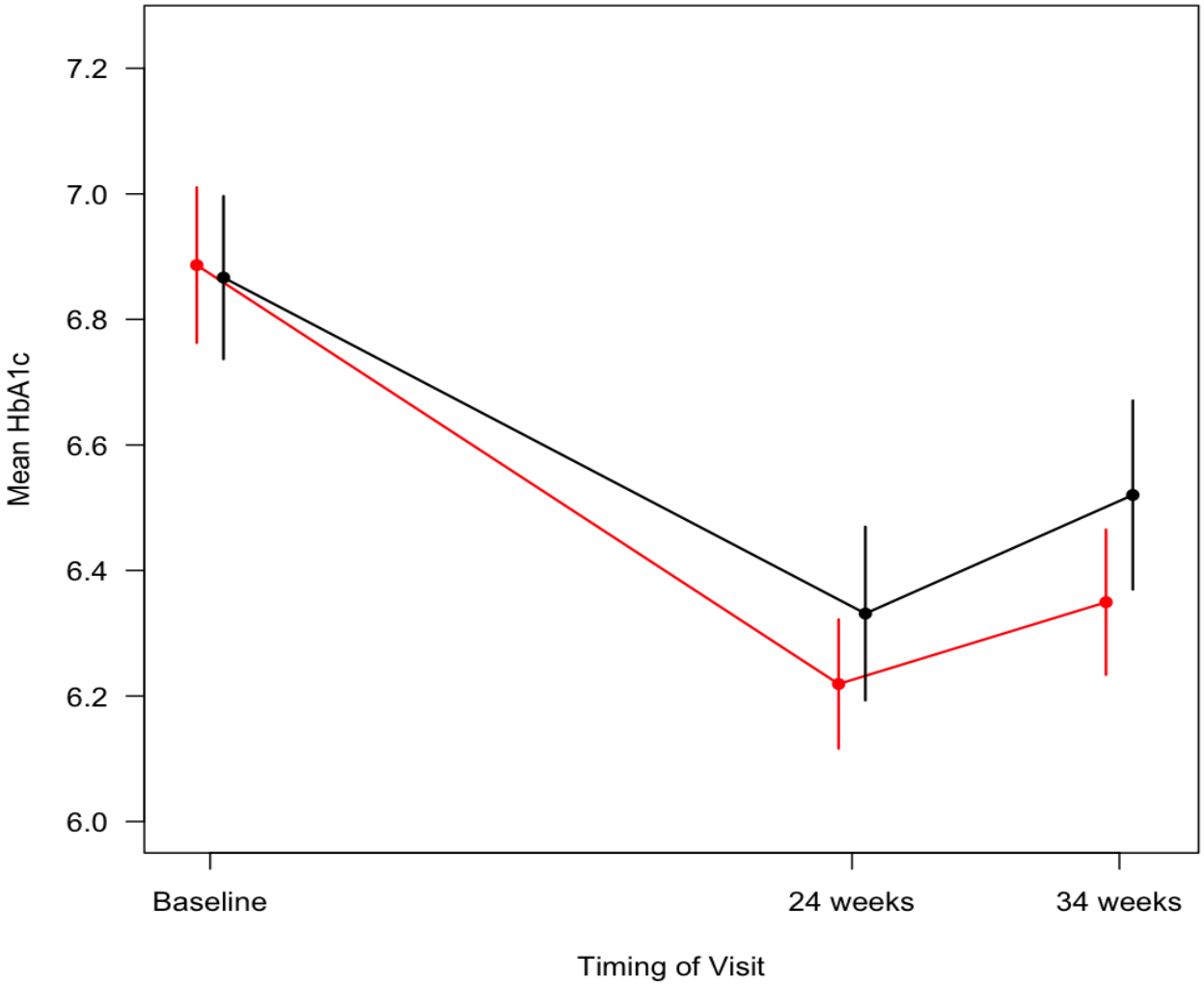
Q4w visits and usual obstetric care until delivery

Baseline Participant Characteristics

	CGM (n=108)	CONTROL (n=107)
Age (years)	31.4 ± 4.5	31.5 ± .4.9
BMI (kg/m^2)	26.1 ± 5.1	25.3 ± 3.8
European origin (n, %)	94 (87%)	90 (84%)
Gestational Age (weeks)	10.5 ± 2.2	11.0 ± 2.0
Post-secondary education (n, %)	88 (81%)	77 (72%)
Duration of diabetes (years)*	17 (6-28)	16 (7-26)
HbA1c at randomisation (%)	6.83 (0.67)	6.95 (0.66)
Insulin pump (n, %)	50 (46%)	48 (45%)
Total Insulin Dose (u/kg/day)	0.69 ± 0.25	0.76 ± 0.31
Smoking (n, %)	13 (12%)	23 (21%)
Preconception Folic Acid (n, %)	54 (50%)	55 (51%)
Presence of DM Complications	27 (25%)	30 (28%)

*Data are mean ± SD or n(%). *median (10th to 90th percentile)*

Primary Outcome: Change in HbA1c from randomisation to 34 weeks' gestation



CGM

Control

mean difference

-0.19%

95% CI -0.34, -0.03

p = 0.0207

CGM measures, % time

	Baseline	
	CGM N=107	**Control N=107**
WITHIN TARGET 3.5-7.8 mmol/L	52% ± 13% 12.5 h/day	52% ± 14% 12.5 hrs/day
Hyperglycaemia >7.8 mmol/L	39% (28-49) 9.4 h/day	40% (32-51) 9.6 h/day
Hypoglycaemia <3.5 mmol/L	8% (4-14) 2 h/day	6% (3-11) 1.4 h/day

Values are mean (SD) and median (IQR)

CGM measures, % time

	Baseline		34 weeks' gestation		
	CGM N=107	**Control N=107**	**CGM N=77**	**Control N=77**	**P-value**
WITHIN TARGET 3.5-7.8 mmol/L	52% ± 13% 12.5 h/day	52% ± 14% 12.5 hrs/day	68% ± 13% 16.3 hrs/day	61% ± 15% 14.6 hrs/day	**0.003**
Hyperglycaemia >7.8 mmol/L	39% (28-49) 9.4 h/day	40% (32-51) 9.6 h/day	27% (19-37) 6.5 h/day	32% (25-39) 7.7 h/day	**0.028**
Hypoglycaemia <3.5 mmol/L	8% (4-14) 2 h/day	6% (3-11) 1.4 h/day	3% (1-6) 0.7 h/day	4% (2-8) 1 h/day	**0.10**

Values are mean (SD) and median (IQR)

Women using CGM spent an extra 100 minutes per day within glucose target

72 minutes less time per day above the glucose target range

Other Outcomes

- No significant between-group differences in
  - Number of episodes of severe hypoglycaemia (18 CGM and 21 control)
  - Diabetic Ketoacidosis
  - Total Insulin Dose (unit/kg/day)
    - 0.99 (0.41) CGM v. 1.07 (0.42) Control, p=0.14
  - Maternal weight gain (Median, IQR) from entry to 34w
    - 13.1 kg (9.9-16.6) CGM v. 13.7 kg (10.9-17.6) Control, p=0.22
  - Gestational age at delivery (Median, IQR)
    - 37.4 (36.7-38.1) CGM v. 37.3 (36.0-38.0) Control, p=0.50

Neonatal Outcomes

- **LGA**: 53% CGM v. 69% control
  OR 0.51; 95% CI 0.28-0.90
  p=0.0210
  NNT 6

- **Hypoglycaemia** requiring dextrose infusion:
  15% CGM v. 28% control
  OR 0.45; 95%CI 0.22-0.89
  p=0.0250
  NNT 8

- **NICU admission** >24h: 27% CGM v 43% control
  OR 0.48; 95% CI 0.26-0.86;
  p=0.0157
  NNT 6

Adverse Outcomes

- Skin reactions in 48% CGM v. 8% Control
- 15 SAEs with no between-group differences
- Adverse Pregnancy outcomes: 1 stillbirth and 1 termination (control), 5 congenital anomalies (2 in CGM group, 3 in control)
- CGM “frustrations” reported in 80% women including problems with connectivity from transmitter to receiver, insertion, discomfort at sensor site
- CGM users had more scheduled (7.2 CGM v. 6.8 control visits, p=0.017) and unscheduled contacts (1530 v. 1026) attributable to sensor issues

CONCEPTT Summary

Use of CGM during pregnancy in women with Type 1 diabetes:

- Improved glycaemia: mean HbA1c change -0.2% and 100 min/day more time in target
- Improved neonatal outcomes: lower proportions of LGA, neonatatal hypoglycaemia and NICU admission
- NNT is low at 6-8 with potential for cost-savings

CGM should be offered to all pregnant women with Type 1 diabetes using intensive insulin therapy

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

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Extra Slides

Statistical Analysis

- Sample size of 214 pregnant women calculated to detect a between group difference in HbA1c of 0.5% (SD 0.8) with 90% power at a 2-sided significance level of 5%, assuming 20% loss to follow-up
- Primary Outcome: ANCOVA used to compare treatment arms, adjusting for baseline HbA1c and mode of insulin delivery. Included all randomised women with a baseline HbA1c with multiple imputation if missing ≥5% HbA1c values

Severe Hypoglycaemia

	Pregnant	
	CGM (n=108)*	Control (n=107)
Severe hypoglycaemia in past year**	13/107 (12%)	7 (7%)
Severe hypoglycaemia during early pregnancy (pre-randomisation)	7/107 (7%)	4 (4%)
Hypoglycaemia awareness symptoms		
Always aware	74/107 (69%)	76 (71%)
Sometimes	30/107 (28%)	28 (26%)
Never aware	3/107 (3%)	3 (3%)

	Baseline		34 weeks' gestation		p value*
	CGM	Control	CGM	Control	
Severe hypoglycaemia¶					
Number of women	7 (7%)	4 (4%)	11 (11%)	12 (12%)	1·0
Number of episodes‡	11	5	18	21	..

Neonatal Outcomes

	CGM N=100	Control N=100	P-value
Birthweight (g)	3545.4±649	3582.5±777	0.37
Median customised centile◊	**92 (68-99)**	**96 (84-100)**	**0.0489**
LGA >90th centile	**53.0%**	**69.0%**	**0.0210**
Extreme LGA >97.7th centile	36.0%	44.0%	0.31
Macrosomia ≥4000g	23.0%	27.0%	0.62
SGA <10th centile	2.0%	2.0%	1.0

LGA Odds ratio 0.51; 95%CI 0.28—0.90, p=0.0210

◊ Birthweight for maternal ethnicity, height, weight and neonatal sex and gestational age at delivery

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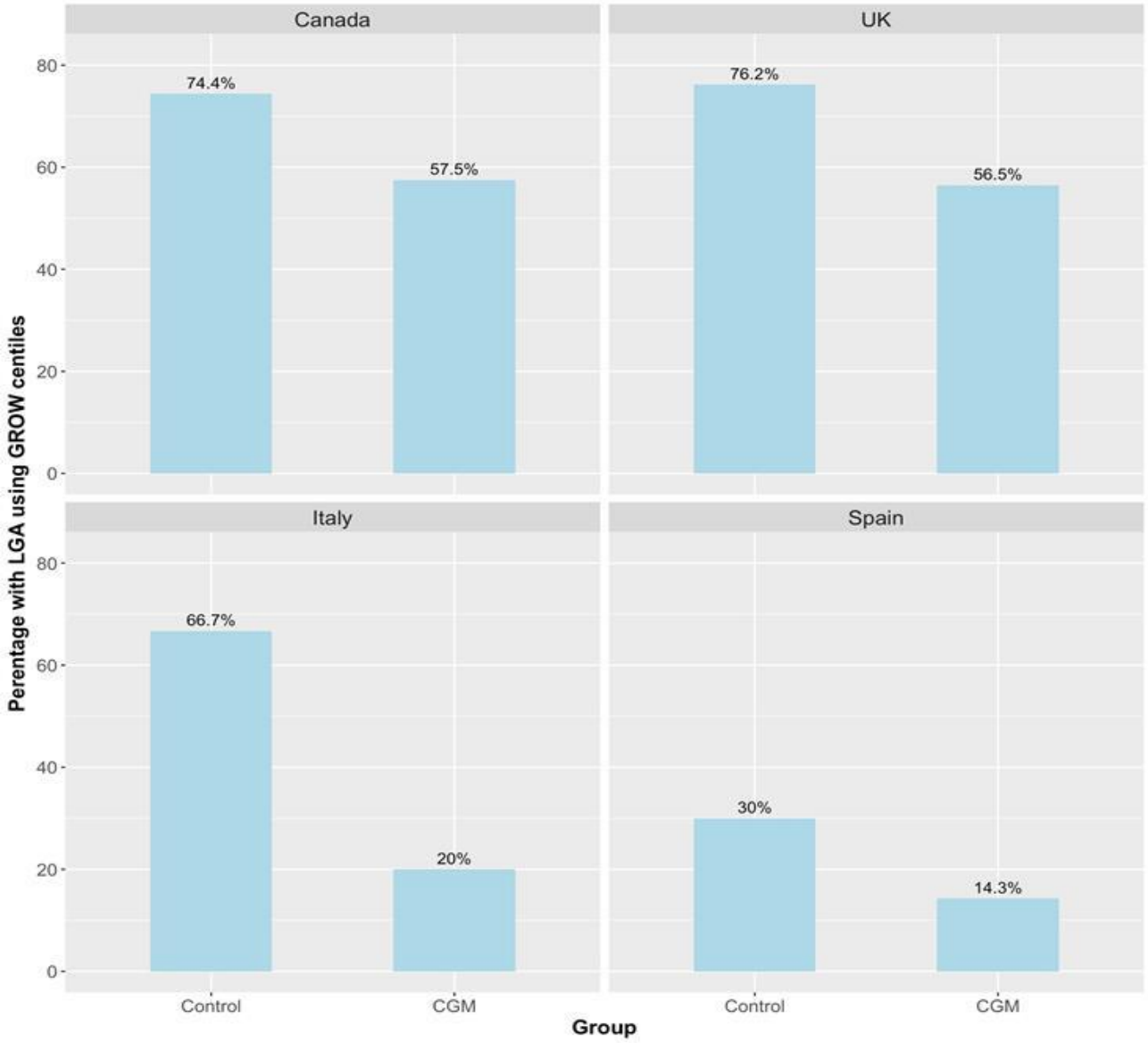
LGA by country



Neonatal outcomes

	CGM	Control	P-value
	N=100	**N=100**	
Birth injury	1	0	1.0
Shoulder dystocia	1	0	1.0
Neonatal hypoglycaemia	**15.0%**	**28.0%**	**0.0250**
Hyperbilirubinaemia	25.0%	31.0%	0.43
Respiratory Distress	9.0%	9.0%	1.0
High level neonatal care (NICU) >24 hours	**27.0%**	**43.0%**	**0.0157**
Composite neonatal outcome[1]	42.9%	52.8%	0.17

[1] Composite outcome comprises of pregnancy loss (miscarriage, stillbirth, neonatal death); birth injury; neonatal hypoglycaemia; hyperbilirubinemia; respiratory distress; and high-level neonatal care for more than 24 h.

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