THE LANCET
Child & Adolescent Health

Supplementary appendix

This appendix formed part of the original submission and has been peer reviewed. We post it as supplied by the authors.

Supplement to: Beardsall K, Thomson L, Guy C, et al. Real-time continuous glucose monitoring in preterm infants (REACT): an international, open-label, randomised controlled trial. *Lancet Child Adolesc Health* 2021; published online Feb 9. http://dx.doi.org/10.1016/S2352-4642(20)30367-9.

Supplementary Data

Sensor Glucose mmol/l	Falling	Stable	Rising
<2.6	**Check Blood Glucose** Stop any Insulin & Check all lines Give additional Dextrose Consider starting 20% Dextrose at 1ml/kg/hr	**Check Blood Glucose** Stop any Insulin & Check all lines Give additional Dextrose Consider starting 20% Dextrose at 1ml/kg/hr	**Check Blood Glucose** Review infusions & check lines Ensure Insulin is not running Consider starting/increasing 20% Dextrose at 1ml/kg/hr
2.6-4.0	**Check Blood Glucose** Stop any Insulin & Check all lines Give additional Dextrose Consider starting 20% Dextrose at 1ml/kg/hr	**Check Blood Glucose** Stop any Insulin & Check all lines Give additional Dextrose Consider starting 20% Dextrose at 1ml/kg/hr	**Observe the rate of rise** Review infusions & check lines Ensure Insulin is not running Consider need for additional Dextrose
Target Range 4.0 - 8.0	**IN TARGET** If the rate of fall means you will be <4.0mmol/l within 1 hour consider reducing Insulin	**IN TARGET**	**IN TARGET** Consider weaning any additional 20% Dextrose
8.0-10.0	**Observe the rate of fall** Consider ***reducing*** Insulin infusion rate by 25%	Stop any additional 20% Dextrose or Start Insulin at 0.05 units/kg/hr or if Insulin is already running ***increase*** Insulin infusion rate by 50%	Stop any additional 20% Dextrose or Start Insulin at 0.05 units/kg/hr or if Insulin is already running ***increase*** Insulin infusion rate by 50%
10-15.0	**Observe the rate of fall** Consider ***increasing*** Insulin infusion rate by 25%	Stop any additional 20% Dextrose or Start Insulin at 0.05 units/kg/hr or if Insulin is already running ***increase*** Insulin infusion rate by 50%	Stop any additional 20% Dextrose or Start Insulin at 0.05 units/kg/hr or if Insulin is already running ***increase*** Insulin infusion rate by 50%
> 15	**Observe the rate of fall** Consider ***increasing*** Insulin infusion rate by 50%	Start Insulin at 0.05 units/kg/hr **or** consider ***increasing*** Insulin infusion rate by 100% (that is: Double) **Always check infusion lines if there is little or no response to an intervention**	Start Insulin at 0.05 units/kg/hr **or** consider ***increasing*** Insulin infusion rate by 100% (that is: Double) **Always check infusion lines if there is little or no response to an intervention**
CRITICAL	Please remember continuous glucose sensor readings are provided to support clinical management. They provide additional information on trends in glucose levels which should be used to guide the need for blood glucose measurement. Capillary/venous blood glucose levels are more accurate. ***Always check infusion lines if there is little or no response to an intervention***		
CONCERN			
IN TARGET			

Figure 1 Paper Guideline

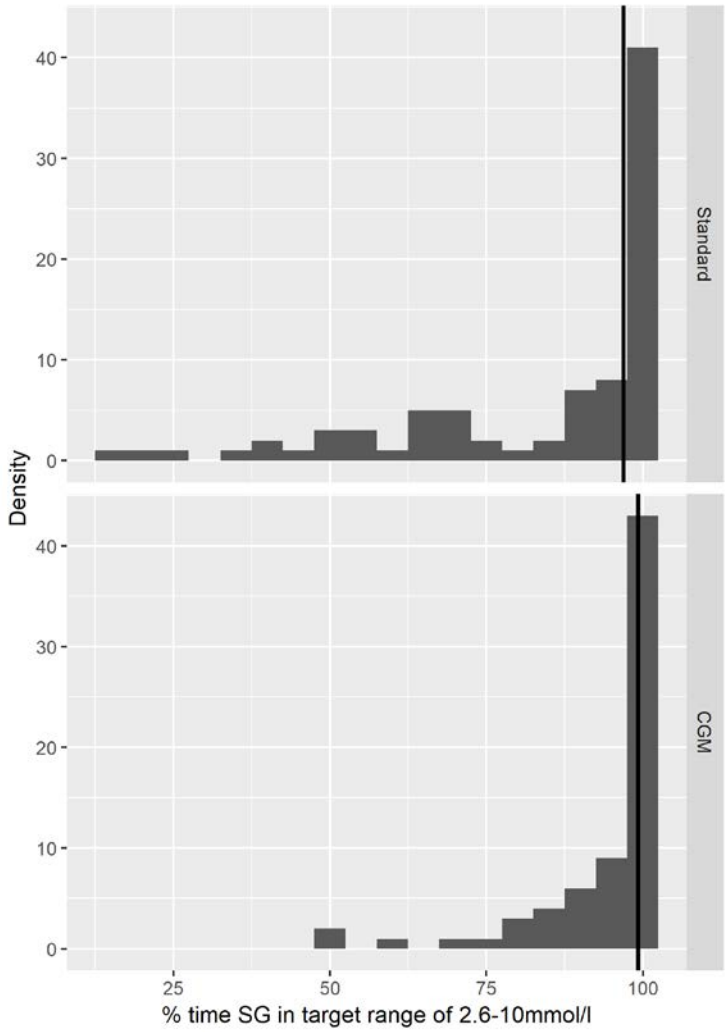

Figure 2 Histogram of the primary outcome by treatment group (n=179)

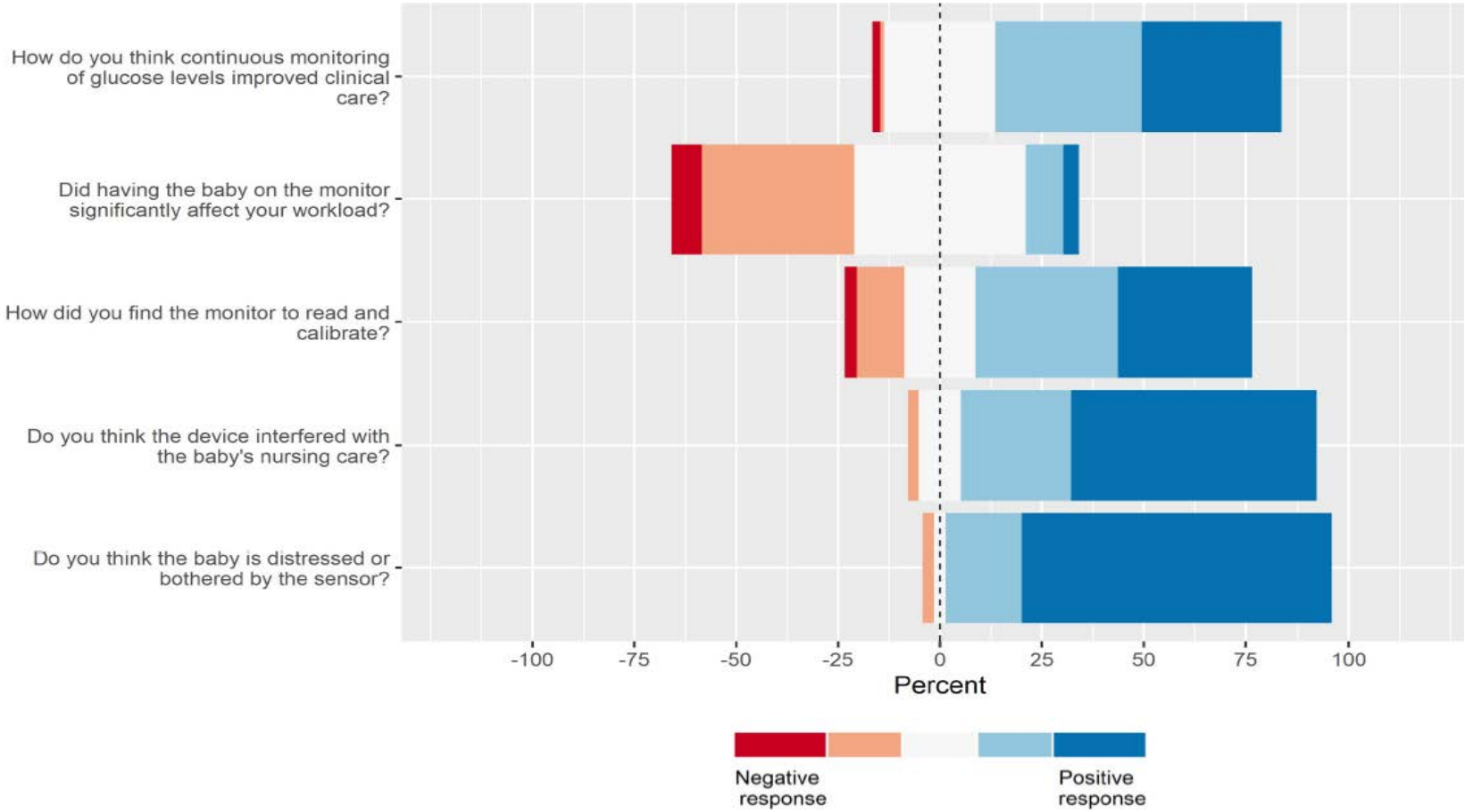

Figure 3 Staff Questionnaire of acceptability.

Stacked bar chart showing proportion of response for each Likert question Pooled data from day 3 and day 7 (n=54).

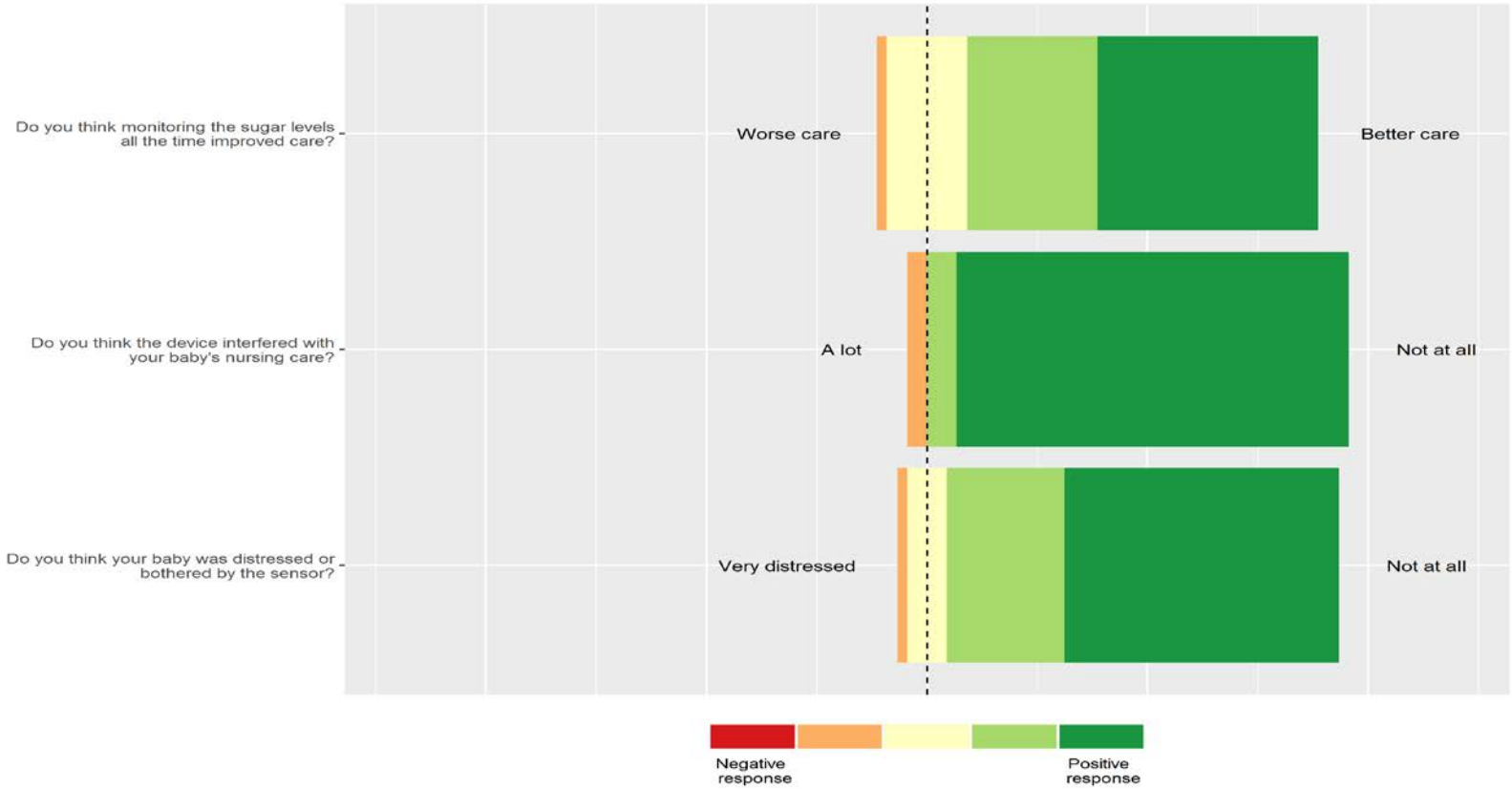

Figure 4 Parent Questionnaire of acceptability.

Stacked bar chart showing proportion of response for each Likert question (n=45)

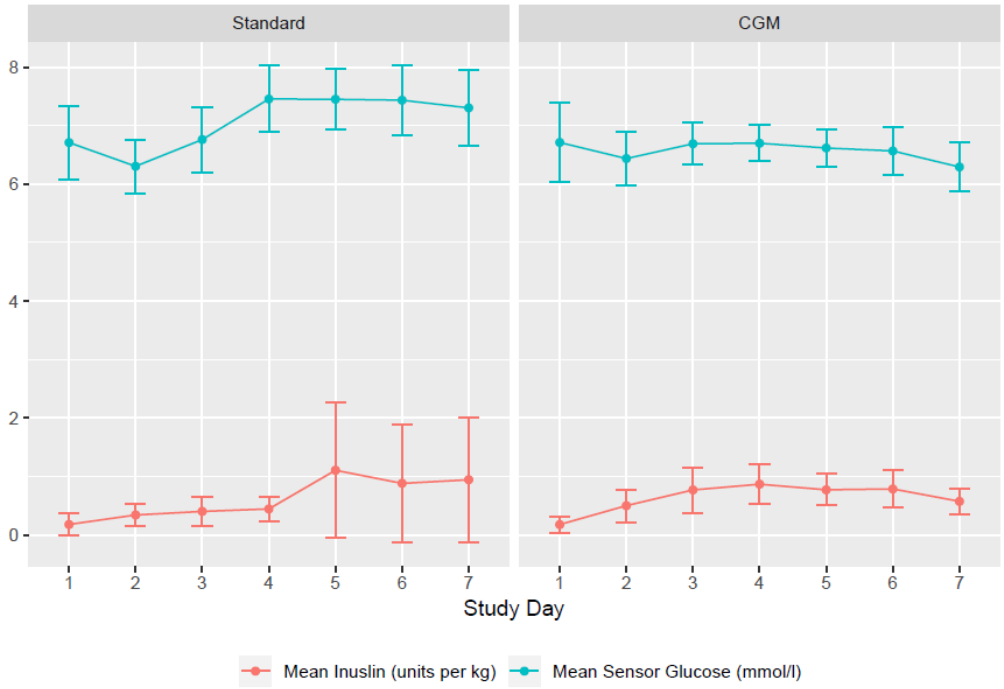

Figure 5 Mean glycaemia and mean insulin infused by treatment arm

CGM: Continuous glucose monitoring intervention

	mean	sd	median	Min	maz
Standard Care	**7.31**	**5**	**7.19**	**2**	**28**
Real Time CGM	**6.46**	**3**	**7.62**	**1**	**28**

Sites were adjusted for using a fixed effects model in the primary analysis. This was borderline case as to whether fixed- or random-effects for site were more appropriate. We report based on the pre-specified choice. Sensitivity analysis show the treatment effect is consistent with either modelling assumtpion: 9.26 (2.79) [estimate (SE)] in the random effects model

eTable 1. Summary Data of Number of Subjects per Centre

Outcome	Standard	CGM	Adjusted Estimate[a] (95% CI)	P-value
Mortality	6% (6/95)	2% (2/84)	0·263 [0·0353, 1·3]	0·13
Infection	62% (53/85)	58% (50/74)	1 [0·46, 2·2]	0·99
NEC	28% (24/85)	13% (10/75)	0·328 [0·129, 0·78]	0·014
PDA	31% (26/85)	26% (19/74)	0·52 [0·199, 1·3]	0·16
Intracerebral pathology	32% (27/84)	33% (25/75)	1·02 [0·51, 2·1]	0·95
BPD	66% (56/85)	60% (45/75)	1·2 [0·52, 2·8]	0·66
Maximum ROP	1·5 (3·6)	1·1 (3·8)	-0·26 (-1·37, 0·85)	0·64
Weight SDS – day 7	-1·3 (0·75)	-1·26 (0·79)	0·05 (-0·19, 0·28)	0·69
Weight SDS – 36 weeks gestation	-1·54 (0·94)	-1·56 (0·93)	-0·04 (-0·34, 0·25)	0·78
Body length SDS – day 7	-1·81 (1·07)	-1·78 (0·87)	-0·02 (-0·36, 0·31)	0·89
Body length SDS – 36 weeks gestation	-2·6 (1·6)	-2·9 (1·8)	-0·38 (-1·19, 0·42)	0·34
Head circumference – day 7	-1·84 (0·77)	-1·76 (0·83)	0·07 (-0·2, 0·35)	0·60
Head circumference – 36 weeks gestation	-1·3 (1·6)	-1·1 (1·7)	0·13 (-0·44, 0·7)	0·65
Total insulin – week 2 (units per kg)	1·1 (2·6)	1·1 (3·0)	0·1 (-0·76, 0·96)	0·82

Data presented as mean (SD) or percentage (frequency). [a]Adjusted for gestation and centre: data presented as mean difference (95% CI) and odds ratio [95% CI]. NEC: necrotizing enterocolitis; PDA: patent ductus arteriosus; BPD: bronchopulmonary dysplasia; ROP: retinopathy of prematurity; SDS: standard deviation score

eTable 2 Clinical Outcomes Exploratory Analyses

Variable	Statistics	Standard	CGM	Logistic regression	
				Adjusted Odds Ratio[a] (95% CI)	P-value
2.2mmol/l< BG <2.6mmol/l	Yes	11.8% (11/93)	14.7% (11/75)	1.2 (0.48, 3.2)	0.7
BG ≤2.2mmol/l	Yes	6.5% (6/93)	13.3% (10/75)	2.2 (0.7, 7.1)	0.2
Continuous episode of SG <2.6mmol/l for >1 hr	Yes	15.3% (13/85)	5.7% (4/70)	0.361 (0.0919, 1.2)	0.1
Length of time SG <2.6mmol/l (hours)	n	85	70		
	Mean (SD)	1.0 (3.2)	0.5 (1.7)		
	Median	0	0		
	Min, Max	0, 22	0, 11.2		
% time SG <2.6mmol/l	n	85	70		
	Mean (SD)	1.1 (3.2)	1 (5.3)		
	Median	0	0		
	Min, Max	0, 16.7	0, 41		

[a]Adjusted for centre and gestation (<26 weeks, ≥26 weeks)

eTable 3 Safety analyses of real time continuous glucose monitoring versus standard care

Title: Primary outcome
Population: Full Analysis (N = 179)
Subtitle: Model fitting results - sensitivity analyses

Model	Outcome	Covariate	Estimate (Std. Error)	95% CI	P-value
LM weighted by number of SG observations	% time SG in target of 2.6-10mmol/l	(Intercept)	80 (3.39)	(73.3, 86.7)	<0.001
		CGM versus standard	8.5 (2.58)	(3.4, 13.6)	0.001
		N36 (ref: N01)	-4.57 (15.1)	(-34.4, 25.3)	0.763
		N42	7.04 (5.5)	(-3.85, 17.9)	0.203
		N43	-0.0351 (3.82)	(-7.59, 7.52)	0.993
		N68	1.73 (3.95)	(-6.09, 9.54)	0.663
		N73	3.55 (5.39)	(-7.1, 14.2)	0.511
		N74	10 (12.4)	(-14.6, 34.6)	0.422
		N85	8.28 (6.43)	(-4.42, 21)	0.2
		N86	-21 (8.66)	(-38.1, -3.89)	0.017
		N87	-16.5 (12)	(-40.3, 7.31)	0.173
		N88	-26.5 (7.21)	(-40.8, -12.2)	<0.001
		ND3	6.33 (6.22)	(-5.96, 18.6)	0.311
		SP3	9.19 (7.64)	(-5.91, 24.3)	0.231
		Gestation >= 26 weeks	6.07 (3.29)	(-0.431, 12.6)	0.067
RSD = 15.8					
LM adjusted for start time of first SG and first SG	% time SG in target of 2.6-10mmol/l	(Intercept)	82.8 (4.66)	(73.6, 92)	<0.001
		CGM versus standard	9.09 (2.64)	(3.86, 14.3)	<0.001
		Time from birth (hours) to first SG	0.0353 (0.132)	(-0.226, 0.297)	0.79
		First SG measurement (mmol/l)	-2.3 (0.553)	(-3.4, -1.21)	<0.001
		N36 (ref: N01)	-12.8 (12.3)	(-37.1, 11.6)	0.302
		N42	2.77 (6.01)	(-9.11, 14.6)	0.645
		N43	0.00483 (4.03)	(-7.97, 7.98)	0.999
		N68	-2.76 (4.17)	(-11, 5.49)	0.51
		N73	-0.444 (5.29)	(-10.9, 10)	0.933

Model	Outcome	Covariate	Estimate (Std. Error)	95% CI	P-value
		N74	3.84 (12.2)	(-20.2, 27.9)	0.753
		N85	4.94 (6.61)	(-8.13, 18)	0.456
		N86	-14.6 (8.54)	(-31.4, 2.31)	0.09
		N87	-16.4 (11.9)	(-39.9, 7.16)	0.171
		N88	-26.9 (7.74)	(-42.2, -11.6)	<0.001
		ND3	2.7 (6.72)	(-10.6, 16)	0.688
		SP3	7.13 (8.46)	(-9.59, 23.9)	0.401
		Gestation >= 26 weeks	1.25 (3.51)	(-5.68, 8.18)	0.721
RSD = 16.14					
LM with interaction between time to first SG and treatment	% time SG in target of 2.6-10mmol/l	(Intercept)	82.6 (5.71)	(71.3, 93.9)	<0.001
		CGM versus standard	9.47 (6.83)	(-4.04, 23)	0.168
		Time from birth (hours) to first SG	0.043 (0.183)	(-0.319, 0.405)	0.815
		First SG measurement (mmol/l)	-2.3 (0.555)	(-3.4, -1.2)	<0.001
		N36 (ref: N01)	-12.8 (12.4)	(-37.4, 11.7)	0.303
		N42	2.71 (6.1)	(-9.35, 14.8)	0.657
		N43	-0.00716 (4.05)	(-8.02, 8.01)	0.999
		N68	-2.76 (4.19)	(-11, 5.52)	0.51
		N73	-0.467 (5.32)	(-11, 10.1)	0.93
		N74	3.96 (12.4)	(-20.5, 28.5)	0.749
		N85	4.93 (6.63)	(-8.18, 18)	0.458
		N86	-14.6 (8.62)	(-31.7, 2.42)	0.092
		N87	-16.5 (12)	(-40.3, 7.33)	0.173
		N88	-27 (7.97)	(-42.7, -11.2)	<0.001
		ND3	2.7 (6.75)	(-10.6, 16)	0.689
		SP3	7.11 (8.49)	(-9.68, 23.9)	0.404
		Gestation >= 26 weeks	1.26 (3.52)	(-5.7, 8.23)	0.72
		[CGM - treatment:Time from birth (hours) to first SG]	-0.0147 (0.242)	(-0.494, 0.465)	0.952
RSD = 16.2					

Model	Outcome	Covariate	Estimate (Std. Error)	95% CI	P-value
LM with interaction between first SG and treatment	% time SG in target of 2.6-10mmol/l	(Intercept)	80 (4.63)	(70.8, 89.1)	<0.001
		CGM versus standard	10.3 (2.61)	(5.17, 15.5)	<0.001
		First SG measurement (mmol/l)	-3.49 (0.673)	(-4.82, -2.16)	<0.001
		Time from birth (hours) to first SG	0.0591 (0.129)	(-0.196, 0.314)	0.648
		N36 (ref: N01)	-11.6 (12)	(-35.3, 12.2)	0.337
		N42	1.84 (5.86)	(-9.75, 13.4)	0.754
		N43	0.839 (3.94)	(-6.95, 8.63)	0.831
		N68	-2.56 (4.06)	(-10.6, 5.47)	0.53
		N73	-0.185 (5.15)	(-10.4, 10)	0.971
		N74	2.68 (11.9)	(-20.8, 26.1)	0.822
		N85	4.75 (6.43)	(-7.97, 17.5)	0.461
		N86	-19.1 (8.46)	(-35.9, -2.42)	0.025
		N87	-16.8 (11.6)	(-39.7, 6.12)	0.149
		N88	-27.1 (7.54)	(-42, -12.2)	<0.001
		ND3	3.11 (6.54)	(-9.83, 16.1)	0.635
		SP3	5.63 (8.25)	(-10.7, 21.9)	0.496
		Gestation >= 26 weeks	3.38 (3.49)	(-3.52, 10.3)	0.334
		[CGM - treatment:First SG measurement (mmol/l)]	3.07 (1.04)	(1, 5.13)	0.004
RSD = 15.71					
GLS allowing for heteroscedastic variances between treatment groups	% time SG in target of 2.6-10mmol/l	(Intercept)	81.9 (3.44)	(75.2, 88.7)	<0.001
		CGM versus standard	8.92 (2.7)	(3.63, 14.2)	0.001
		N36 (ref: N01)	2.88 (9.38)	(-15.5, 21.3)	0.759
		N42	8.28 (5.15)	(-1.82, 18.4)	0.11
		N43	3.87 (3.3)	(-2.59, 10.3)	0.242
		N68	-0.0845 (3.22)	(-6.4, 6.23)	0.979
		N73	4.67 (4.24)	(-3.63, 13)	0.272

Model	Outcome	Covariate	Estimate (Std. Error)	95% CI	P-value
		N74	9.2 (9.38)	(-9.18, 27.6)	0.328
		N85	8.46 (5.5)	(-2.33, 19.2)	0.126
		N86	-23.2 (8.15)	(-39.2, -7.26)	0.005
		N87	-11.8 (15.7)	(-42.5, 18.9)	0.453
		N88	-12.2 (6.5)	(-25, 0.523)	0.062
		ND3	7.3 (5.5)	(-3.48, 18.1)	0.187
		SP3	9.02 (6.79)	(-4.28, 22.3)	0.186
		Gestation >= 26 weeks	1.53 (2.93)	(-4.21, 7.27)	0.603
RSD = 9.59					
Random intercept for site	% time SG in target of 2.6-10mmol/l	(Intercept)	79.5 (4.14)	(71.3, 87.7)	<0.001
		CGM versus standard	9.26 (2.79)	(3.75, 14.8)	0.001
		Gestation >= 26 weeks	5.19 (3.56)	(-1.84, 12.2)	0.146
RSD = 17.15					
LM adjusting for gestation only	% time SG in target of 2.6-10mmol/l	(Intercept)	80.1 (3.45)	(73.3, 86.9)	<0.001
		CGM versus standard	9.38 (2.88)	(3.7, 15.1)	0.001
		Gestation >= 26 weeks	5.28 (3.62)	(-1.87, 12.4)	0.147
RSD = 17.8					

RSD = residual error standard deviation; LM = linear regression model; GLS = generalised least squares

eTable 4: Sensitivity Analyses for Primary outcome