Changes in the glycaemic profiles of women with type 1 and type 2 diabetes during pregnancy

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Running title: glycaemic profiles during pregnancy

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Abstract

Aims – To examine the changes in glycaemic excursions which occur during pregnancy using continuous glucose monitoring and to compare patterns of glycaemia in pregnant women with type 1 and type 2 diabetes.

Research design and methods – Observational data analysis from a prospective randomised study of continuous glucose monitoring in 57 women with pregestational type 1 (n=40) or type 2 diabetes (n=17) with 7-day CGMS profiles during each trimester. Serial glucose measurements were divided into periods of euglycaemia (70-140mg/dl), hyperglycaemia (>140mg/dl) and hypoglycaemia (< 70mg/dl). Generalised linear mixed effects models were fitted to the repeated measures data to determine how these glycaemic characteristics varied during gestation and by diabetes type.

Results – 180 continuous glucose profiles were examined (140 type 1 diabetes, 40 type 2 diabetes) providing 20,433 hours of data for analysis (16,117 hours type 1 diabetes, 4,316 type 2 diabetes). Women with type 2 diabetes spend ~33% less time hyperglycaemic throughout pregnancy compared to women with type 1 diabetes (p=0.005), with a significantly more rapid reduction in time spent hyperglycaemic in early pregnancy (p=0.02). Although women with type 2 diabetes spend less overall time hypoglycaemic (p=0.04), their risk of nocturnal hypoglycaemia is equivalent to women with type 1 diabetes (BGL<70mg/dl, p = 0.9; BGL<50mg/dl, p = 0.2).

Conclusions – Continuous glucose monitoring reveals clear differences in the level of glycaemic control that exist in women with type 1 and type 2 diabetes. These data will guide therapeutic interventions aimed at optimising glycaemic control and improving the pregnancy outcomes of both type 1 and type 2 diabetes.
Recent nationwide studies from both the United Kingdom and the Netherlands confirm that the outcomes of pregnancy for women with diabetes remain poor, with increased rates of congenital malformation, perinatal mortality, premature delivery and macrosomia. It has also been shown that the outcomes of pregnancy in women with type 2 diabetes are at least as poor as for women with type 1 diabetes. Some studies, including our own regional audit, suggest that women with type 2 diabetes, who are older, more obese and more likely to belong to an ethnic minority group, may have even poorer pregnancy outcomes than women with type 1 diabetes. With the increasing prevalence of obesity in developed countries, type 2 diabetes has become the most common form of diabetes in women of reproductive age, accounting for 1/3 to 1/2 of all diabetic pregnancies. Yet compared to pregnancies complicated by type 1 diabetes, very little is known about blood glucose control during pregnancy for women with type 2 diabetes. The published series suggest minimal differences in overall measures of glycaemia, with a possible small decrease in HbA1c for women with type 2 diabetes during the second trimester.

Continuous glucose monitoring systems (CGMS) provide greater insight into glucose levels throughout the day, yielding information on the magnitude, frequency and duration of glucose excursions not available with conventional glucose self-monitoring. The importance of CGMS data is well recognised, described as a “stepping stone in the journey towards a cure” and “a roadmap for effective diabetes management”. The slow kinetics of glycosylated haemoglobin accumulation and physiological changes in erythrocyte formation during pregnancy mean that HbA1c is only a limited predictor of acute blood glucose changes, providing an explanation for the poor pregnancy outcomes, even in women with apparently “good” glycaemic control. Recent attention has therefore focused on evaluating the role of CGMS in pregnancy with studies providing normative data in non-diabetic pregnancies and highlighting the prevalence of glycaemic excursions during early pregnancy, in women with type 1 diabetes.

Because CGMS is still a relatively new tool and remains expensive for routine clinical use, there is a paucity of longitudinal data throughout pregnancy, even for women with type 1 diabetes. Furthermore, despite their poor pregnancy outcomes, there are no continuously monitored data detailing the glycaemic characteristics of women with type 2 diabetes. This study using 7-day CGMS profiles provides serial data regarding the glycaemic profiles of women with both type 1 and type 2 diabetes. The objectives were firstly, to examine changes in the daily patterns of glucose excursions with increasing gestation and secondly, to compare differences between women with type 1 and type 2 diabetes.

**Research design and methods**

A prospective randomised study comparing CGMS to conventional blood glucose monitoring in pregnancies complicated by pregestational diabetes was undertaken at 2 specialist diabetic antenatal clinics in the United Kingdom from September 2003-2006. Here, we have analysed the profiles collected during the study to evaluate the changes in glycaemic profiles over gestation and the differences between type 1 and type 2 diabetes in pregnancy. Appropriate research governance and ethics committee approval was obtained at both sites. Women with documented pregestational type 1 and type 2 diabetes were enrolled if they had a confirmed positive pregnancy test and ultrasound dating scan, were between 16-45 years old, provided written informed consent and were willing to wear the continuous glucose monitoring device for up to 7-days during each trimester. Women randomised
to the CGMS intervention were encouraged to wear the device at 4-6 weekly intervals from the booking visit through to 34 weeks gestation as our clinical experience suggests greater discomfort associated with wearing the device in later pregnancy. The prepregnancy and antenatal care at these centres has been recently documented.

From the 79 consecutive women with pregestational diabetes approached, 57 women agreed to participate (72%), were trained in the use of the continuous glucose monitor, and had sensors implanted into the upper outer buttock alternating between sides, by research nurses at antenatal diabetes clinics. Subjects continued their usual finger-stick blood glucose monitoring with at least 7 measurements per day, aiming for fasting blood glucose of <95mg/dl, 130-140mg/dl 1-hour after meals and <120 2-hours after meals. The data were downloaded to a personal computer using the software (Medtronic Com-station, version 1.7B) provided by the manufacturer after 1 week and shared with women and their health care team. Therapeutic adjustments were made by the usual combined obstetric/diabetes team, based on both finger-stick and continuous data. Women were managed with short-acting insulin analogues before meals, with once or twice daily intermediate acting insulin, long acting insulin analogues or insulin pump therapy if started prior to pregnancy. All women with type 2 diabetes were commenced on insulin before pregnancy or as soon as pregnancy was confirmed if they had not attended for prepregnancy care.

**Study population**

40/57 (70%) women had type 1 diabetes and 17/57 (30%) had type 2 diabetes. The mean age of the entire study group was 31.5 ± 7.1 years (31.1 ± 6.1 type 1 vs 32.7 ± 9.1 years type 2; p=0.4), with 70% of women having planned their pregnancies (73% type 1, 65% type 2; p=0.6). Women with type 1 diabetes had a longer duration since diagnosis (18.5 ± 9.3 vs 5.8 ± 7.1 years; p <0.0001) and were less obese at the booking visit (mean BMI 25.5 ± 4.5 vs 38.0 ± 10.7; p=0.0001) than women with type 2 diabetes. There was no significant difference between the HbA1c at booking between women with type 1 and type 2 diabetes (7.2 ± 1.7% and 7.0 ± 1.1%; p=0.6).

There were no statistically significant differences between the 57 subjects who participated in the study and those who declined to participate (n=22) in mean age, duration of diabetes, ethnicity, type of diabetes, uptake of pre-pregnancy counselling or parity. This suggests the patients studied were representative of women with diabetes attending our antenatal clinics.

**Study device**

The CGMS device (CGMS Gold Medtronic-MiniMed, Northridge, USA) consists of a disposable subcutaneous glucose-sensing device and a glucose oxidase-impregnated electrode connected by a cable to a lightweight monitor. Interstitial glucose values in subcutaneous tissues, within a range of 40-400mg/dl, are measured electrochemically every 10 seconds and an average value is stored in the monitor every 5 minutes, providing up to 288 blood glucose measurements per day. The subjects are unaware of the results of the sensor measurements during monitoring. The system is recalibrated each time a blood glucose measurement is entered into the device and subjects are asked to do this at least 4 times per day. The accuracy, reliability and measurement of glycaemic control by CGMS has been confirmed with sensor modification allowing the device to be worn for up to 7 days.

**Statistical methods**

Serial glucose measurements for all subjects were analysed using summary measures to characterise each subject’s glucose profile. Each profile was divided into periods of euglycaemia (70-140mg/dl),
hypoglycaemia (<70mg/dl) and hyperglycaemia (>140mg/dl). Extreme hypoglycaemic excursions were defined as <50mg/dl and extreme hyperglycaemic excursions as >200mg/dl. An excursion into either the hypoglycaemic or hyperglycaemic range required a duration of at least 30 minutes per definitive episode.

For each subject, the proportions of time spent euglycaemic, hyperglycaemic and hypoglycaemic were determined from the continuously monitored data. The total area under the curve (AUC) for each glucose threshold was determined, representing both the duration and magnitude of the glucose excursions. Mean blood glucose values from the CGMS data and HbA1c measurements taken at 4-weekly intervals, assayed using the DCCT aligned Biomen 8140 method (normal reference range 3.6-5.8%) were calculated for each trimester with the first trimester defined as up to 13 weeks gestation, 2nd trimester 13-28 weeks gestation and 3rd trimester from 28 weeks gestation onwards.

To provide statistical comparisons for and estimates of the summary measures for type 1 and 2 diabetes at different stages of gestation, generalised linear mixed effects models were fitted to the repeated measures data. The main hypotheses to be tested was whether each summary measure showed differences between type 1 and type 2 diabetes, whether it changed over gestation, and whether the rate of change differed between type 1 and 2 diabetes (time x diabetes interaction). Normally distributed random effects were fitted to the inter-individual differences in change over gestation (slope) and starting point (intercept). Within-patient correlation over time was fitted using a continuous autoregressive function. A Poisson family model with the canonical log link function was used for the amount of time spent in euglycaemia, hyperglycaemia, or hypoglycaemia, and the number of such episodes, with the total length of recorded time taken as the offset. Since AUC is always ≥0 (and often =0), a log link function was used for this response variable as well, without an offset. For HbA1c and mean blood glucose models, simple linear mixed effects models were used. These comprehensive models were fitted using a restricted penalized quasi-likelihood algorithm in S-plus v7.0 (Insightful Corp, Seattle, WA).

Results
During the study, 40 women with type 1 diabetes (70%) and 17 women with type 2 diabetes (30%) had a total of 180 CGMS profiles (140 type 1 diabetes, 40 type 2 diabetes). There were 40 CGMS profiles obtained during the first trimester (30 type 1 diabetes, 10 type 2 diabetes; 14 ≤8 weeks, 26 ≤12 weeks), 90 in the second trimester (69 type 1 diabetes, 21 type 2 diabetes; 28 ≤16 weeks, 24 ≤20 weeks, 26 ≤24 weeks, 12 <28 weeks) and 50 in the third trimester (41 type 1 diabetes, 9 type 2 diabetes; 24 ≤32 weeks, 19 ≤36 weeks, 7 >36 weeks). Overall 20,433 hours of continuously monitored data (16,117 type 1 diabetes, 4,316 type 2 diabetes) were obtained.

To analyse the data, we extracted summary measures from each CGMS trace, and fitted generalized linear mixed effects models to analyse the differences between type 1 and type 2 diabetes in these measures over the three trimesters of pregnancy. This is the most accurate approach to model multiple profiles from individual women, taken at varying gestational ages throughout pregnancy, and is a well-established technique for analysing longitudinal data. In particular, we explicitly modelled and compensated for the differing number of traces downloaded for each subject and the varying gestational ages at which traces were obtained; the correlation between serial measurements in time within a given subject; and the inter-individual differences in both the starting point for glycaemic
glycaemic profiles during pregnancy

control and its change during pregnancy. Table 1 provides values estimated from the models for the total proportion of time spent euglycaemic, hyperglycaemic and hypoglycaemic, as well as the AUCs, per trimester for both types of diabetes.

**Euglycaemia**

The duration of time spent within the euglycaemic range for pregnancy increased with each week of advancing gestation for women with both types of diabetes (Figure 1A). The proportion of time in the euglycaemic range rose from an average of 43% at the end of the first trimester to 56% at the end of the third trimester for type 1 diabetes and from 58% to 75% for women with type 2 diabetes (p<0.0001 for the change over pregnancy). Women with type 2 diabetes spent approximately a third more time in the euglycaemic range than women with type 1 diabetes (Ratio of proportion of time in euglycaemic range, 1.33; 95% CI, 1.17 – 1.52; p=0.0001). There was extensive variability among subjects with respect to the overall duration of time spent euglycaemic, and the rate of change over gestation for both types of diabetes (Figure 1A). The differences between type 1 and 2 diabetes, and the changes over gestation, were very similar in magnitude when just daytime (06.00-22.00) measurements (p=0.0002 for change over time; p=0.0005 for diabetes type) and just nighttime (22.00-06.00) measurements were analysed (p=0.0005 for change over time; p<0.0001 for diabetes type). In summary, euglycaemia increased over gestation as expected, but was significantly greater throughout pregnancy for type 2 diabetes.

**Hyperglycaemia**

The increase in time spent euglycaemic over gestation could be due to a decrease either in time spent hyperglycaemic or time spent hypoglycaemic or both. We therefore explored the changes in patterns of hyperglycaemia and hypoglycaemia over gestation (Figures 1B and 1C). The time spent hyperglycaemic decreased with advancing gestation for women with both types of diabetes (p= 0.007). Women with type 2 diabetes spent only two thirds of the amount of time hyperglycaemic compared to women with type 1 diabetes (ratio of proportion of time with BGL>140mg/dl, 0.69; 95% CI, 0.53 – 0.89; p=0.005). Furthermore, the rate of decrease was significantly greater in women with type 2 diabetes than type 1 (p=0.02, interaction term), meaning that hyperglycaemia decreased both more quickly and earlier in gestation for type 2 diabetes (Figure 1B). Thus, women with type 1 diabetes showed a reduction from 41% of time spent hyperglycaemic at the end of the first trimester, to 33% at the end of the third trimester, whereas the decrease between the corresponding time-points for women with type 2 diabetes was from 33% to 12%. However, it should be noted that at 8 weeks gestation, women with both types of diabetes spend >40% time (i.e. approximately 10 hours/day) with BGL >140mg/dl.

The same patterns were seen at extreme levels of hyperglycaemia (glucose excursions >200mg/dl). Extreme hyperglycaemia decreased over gestation (p=0.0006). Type 2 diabetes was associated with shorter duration of extreme hyperglycaemia than type 1 diabetes (p=0.0004), and showed a more rapid reduction in levels through gestation (p=0.04, interaction term), mirroring the above findings for milder hyperglycaemia.

**Hypoglycaemia**

Notably, the proportion of time spent hypoglycaemic did not show significant change over gestation either for milder (BGL<70mg/dl) (p=0.6; Figure 1C) or more extreme hypoglycaemic excursions (BGL<50mg/dl) (p=0.1). However, women with type 1 diabetes spent more time hypoglycaemic than type 2 diabetes (BGL<70mg/dl, p=0.04; BGL<50mg/dl, p=0.02), having 2.3 episodes and spending 3.3 hr/day with BGL<70mg/dl compared to 1.8 episodes and 2.3 hr/day for women
with type 2 diabetes. Interestingly, there were no significant differences in nocturnal hypoglycaemia between women with type 1 and type 2 diabetes (p=0.9 and p=0.2 for BGL<70mg/dl (Figure 1D) and BGL<50mg/dl respectively), with the increased risk of hypoglycaemia in women with type 1 diabetes occurring during daytime hours (p=0.003 and p=0.009 below each threshold). Very similar results were obtained when the number of hypoglycaemic episodes and the AUC<70mg/dl was analysed (Table 1). Thus, in contrast to the results for hyperglycaemia, we found that the risk of hypoglycaemia did not significantly change over gestation, and although women with type 2 diabetes spend less time during the day hypoglycaemic, their risk of nocturnal hypoglycaemia is equivalent to women with type 1 diabetes.

**Changes in HbA1c and mean blood glucose**

These CGMS data therefore reveal significant differences between type 1 and type 2 diabetes in both hyperglycaemia and hypoglycaemia, and the changes in these variables over pregnancy. Thus we explored whether the complexity of these differences were captured by the commonly used measures of glycaemic control: mean BGL and HbA1c. Mean BGL showed a significant decrease over gestation (p=0.009), but showed only a trend towards lower levels in type 2 diabetes (p=0.08), and did not show differences between type 1 and type 2 diabetes in the rate of change over pregnancy (p=0.3, interaction term). HbA1c levels similarly showed significant decreases over gestation (p=0.004), but showed no significant differences between type 1 and type 2 diabetes in either the overall levels (p=0.2) or the rate of change over pregnancy (p=0.2). It therefore appears that these overall measures of glycaemia do not fully capture the striking differences in blood glucose profiles between women with type 1 and type 2 diabetes seen with CGMS.

**Conclusions**

This study provides the first opportunity to document the changes in glycaemic patterns throughout pregnancy using the continuous glucose monitoring systems in women with both type 1 and type 2 diabetes. Unlike earlier studies, these data are longitudinal, with repeated measures, providing on average 358 hours (~15 days) of continuous glucose data from each woman throughout her pregnancy. With the use of appropriate statistical methodology, this has allowed detailed analysis of the changes in several clinically relevant glycaemic measures during pregnancy. These provide detailed observations regarding the duration, magnitude and frequency of glucose fluctuations throughout pregnancy, extending previous preliminary, cross-sectional data in type 1 diabetes and describing the first continuous glucose data in pregnancies complicated by type 2 diabetes.

It is particularly alarming that during the critical stages of early pregnancy women with diabetes on average spend only 50% or 12 hours/day with blood glucose levels in the euglycaemic range. Furthermore, despite intensive multidisciplinary team advice and support, including the use of CGMS as an educational and therapeutic tool, the proportion of time spent euglycaemic has risen to only 66% or approximately 16 hours/day by the end of pregnancy. This is remarkably similar to a recent report in non-pregnant subjects, for whom 65% of the time was spent euglycaemic, although outside pregnancy the definition of euglycaemia (70-180mg/dl) is less stringent. That even a population of motivated pregnant women, with “good” HbA1c levels, willing to wear the CGMS device, are so far from achieving euglycaemia suggests that we are still a long way off achieving the aims set out by the 1989 St Vincent declaration, both for women with type 1 and type 2 diabetes.
Comparisons in glycaemic control between women with type 1 and type 2 diabetes

Continuous glucose monitoring demonstrated clear differences between the level of glycaemic control achieved by women with type 1 and type 2 diabetes, which were not apparent from mean blood glucose or HbA1c measurements. Women with type 2 diabetes achieved a significantly greater reduction in hyperglycaemia, beginning earlier and lasting throughout pregnancy. Indeed, the level of hyperglycaemia achieved by women with type 2 diabetes, by the end of the first trimester (33% of time >140mg/dl), was not achieved by women with type 1 diabetes until the very end of pregnancy. It is intriguing that although women with type 2 diabetes in this study spend 33% less time hyperglycaemic, even during early pregnancy, large series confirm that their risks of congenital malformation and perinatal mortality are equivalent to type 1 diabetes. Some authors, based on HbA1c measurements, have concluded that congenital malformations in type 2 diabetes are unrelated to glycaemic control. While other well documented factors such as poor pregnancy preparation, older age and obesity clearly contribute to the poor outcomes in type 2 pregnancies, our data nonetheless suggest that during the critical stages of organogenesis, up to 8 weeks gestation, women with type 2 diabetes are spending as much time hyperglycaemic as those with type 1 diabetes (see Figure 1B). The reduction in hyperglycaemia achieved by the end of the first trimester may therefore be too late to reduce rates of malformation.

Glycaemic control in women with type 1 diabetes

By the end of the first trimester, women with type 1 diabetes are still spending more than 9 hours per day hyperglycaemic (>140mg/dl), with approximately 3 hours extremely hyperglycaemic (>200mg/dl), offering an explanation for why “near optimal glycaemic control (HbA1c <7%) is not good enough” to prevent congenital malformation. Clearly prepregnancy care plays an important role, improving early glycaemic control and reducing major malformation and perinatal mortality. However, our recent data suggest that even the significant improvements in glycaemic control achieved by women attending prepregnancy care are still “not good enough”, in that they fail to reduce rates of pre-eclampsia and macrosomia. These complications are believed to be related to hyperglycaemic excursions during the second and third trimesters, which are clearly demonstrated in this study. The majority of our subjects had near-optimal glycaemic control, attended prepregnancy care and believed that wearing CGM was beneficial (data not shown). The modest improvements in hyperglycaemia (40% to 33%) achieved by the end of pregnancy lead us to speculate that newer technologies such as real-time continuous glucose monitoring perhaps combined with insulin pump therapy, and ultimately closed loop systems, may be required to avoid hyperglycaemia and reduce the risk of pre-eclampsia and macrosomia.

Hypoglycaemia

Our study is the first to document the duration of hypoglycaemia throughout pregnancy, examining the differences between daytime and night-time hypoglycaemia for women with both type 1 and type 2 diabetes. Contrary to our expectations that the amount of time spent hypoglycaemic would diminish with the increasing insulin resistance of advancing gestation, we in fact found that the duration of time spent hypoglycaemic remained constant throughout pregnancy, both for women with type 1 and type 2 diabetes. Of course, it is also noteworthy that the reductions in hyperglycaemia were achieved without increased hypoglycaemia. To preclude the vicious cycle of impaired glucose counter-regulation and consequent loss of hypoglycaemic warning symptoms by antecedent hypoglycaemia, prevention
of BGL$<70$mg is a recommended treatment goal$^{32}$. In our study, this was not achieved, either for women with type 1 or type 2 diabetes, despite the use of regular CGMS.

It is important to distinguish biochemical episodes of hypoglycaemia from severe hypoglycaemia (SH), defined as requiring third party assistance. The large studies required to document frequency of SH consistently demonstrate increased SH during the late first and/or early second trimester$^{32,33}$. Our findings show no change in the overall time spent hypoglycaemic during gestation, suggesting that duration of biochemical hypoglycaemia alone is not sufficient to explain this peak of SH at the end of the first trimester. Although our study found a high incidence of nocturnal hypoglycaemia (as suggested in earlier studies$^{36}$), there were no differences between type 1 and type 2 diabetes in the amount of time spent hypoglycaemic overnight. Surprisingly, therefore, the increased hypoglycaemia for women with type 1 diabetes was limited to daytime. In non-pregnant subjects with type 1 diabetes, impaired hypoglycaemic awareness predisposed to a six-fold increase in SH, much of which also occurred during the waking hours$^{34}$. Further research should try, within the ethical limitations, to examine the changes in hypoglycaemia awareness and glucose counter-regulation during both type 1 and type 2 diabetic pregnancies.

We recognise that like all monitoring systems, CGMS is not without limitations, in particular with regard to the quality of readings during rapid blood glucose changes and in the lower hypoglycaemic ranges$^{35}$. However, from this vast quantity of continuously monitored data, we have gained unprecedented insights into the magnitude, frequency and duration of blood glucose fluctuations in women with type 1 and type 2 diabetes during pregnancy. We have demonstrated clear differences in the patterns of glycaemia, with better glycaemic control earlier in pregnancy for women with type 2 diabetes. Strikingly, the data highlight just how difficult it is to reach current targets for euglycaemia, particularly for women with type 1 diabetes. These data are important for all clinicians seeking to limit hypoglycaemia and optimise maternal glycaemic control in daily practice, as well as researchers seeking to improve therapeutic interventions aimed at achieving normoglycaemia during pregnancy.

**Acknowledgements**

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References


Table 1. Estimates of glycaemic characteristics at the end of each trimester for type 1 and type 2 diabetes, obtained from generalized linear mixed effects models.

<table>
<thead>
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<th>Glycaemic measure</th>
<th>Trimester 1</th>
<th>Trimester 2</th>
<th>Trimester 3</th>
<th>P value</th>
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<td><strong>Euglycaemia</strong></td>
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<td>Percentage of time 70-140mg/dl (hrs per 24 hours)</td>
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<tr>
<td>Type 1</td>
<td>43.2% (10.4hrs)</td>
<td>49.3% (11.8hrs)</td>
<td>56.3% (13.5hrs)</td>
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<td>57.6% (13.8hrs)</td>
<td>65.8 % (15.8hrs)</td>
<td>75.1% (18.0hrs)</td>
<td>Gestational period: 0.0001</td>
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<td><strong>Hyperglycaemia</strong></td>
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<td>Type 1</td>
<td>40.5% (9.7hrs)</td>
<td>36.4% (8.7hrs)</td>
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<td>Type 2</td>
<td>32.8% (7.9hrs)</td>
<td>19.5% (4.7hrs)</td>
<td>11.6% (2.8hrs)</td>
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<td>AUC &gt;140mg/dl</td>
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<td>Type 1</td>
<td>16% (3.8hrs)</td>
<td>11.8% (2.8hrs)</td>
<td>8.7% (2.0hrs)</td>
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<td>7.9% (1.9hrs)</td>
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<td>1.0% (0.2hrs)</td>
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<td>Percentage of time &lt;70mg/dl (hrs per time period)</td>
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<tr>
<td>Overall (24 hours)</td>
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<tr>
<td>Type 1</td>
<td>14.6% (3.5hrs)</td>
<td>13.7% (3.3hrs)</td>
<td>12.9% (3.0hrs)</td>
<td>DM type: 0.04</td>
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<td>10.2% (2.4hrs)</td>
<td>9.6% (2.3hrs)</td>
<td>9.1% (2.2hrs)</td>
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<td>Nocturnal (2200 – 0600)</td>
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<td>14.6% (1.1hrs)</td>
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<td>Overall (24 hours)</td>
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<tr>
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<td>5.7% (1.4hrs)</td>
<td>4.6% (1.1hrs)</td>
<td>3.7% (0.9hrs)</td>
<td>DM type: 0.02</td>
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<td>Type 2</td>
<td>3.0% (0.7hrs)</td>
<td>2.5% (0.6hrs)</td>
<td>2.0% (0.5hrs)</td>
<td>Gestational period: NS</td>
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<td>Nocturnal (2200 – 0600)</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Type 1</td>
<td>7.3% (0.6hrs)</td>
<td>6.3% (0.5hrs)</td>
<td>5.4% (0.4hrs)</td>
<td>DM type: NS</td>
</tr>
<tr>
<td>Type 2</td>
<td>5.1% (0.4hrs)</td>
<td>4.4% (0.3hrs)</td>
<td>3.8% (0.3hrs)</td>
<td>Gestational period: NS</td>
</tr>
<tr>
<td><strong>Mean BG (mg/dl)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Type 1</td>
<td>137</td>
<td>128</td>
<td>119</td>
<td>DM type: 0.08</td>
</tr>
<tr>
<td>Type 2</td>
<td>126</td>
<td>117</td>
<td>106</td>
<td>Gestational period: 0.009</td>
</tr>
<tr>
<td><strong>HbA1c (%)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Type 1</td>
<td>6.84</td>
<td>6.37</td>
<td>5.90</td>
<td>DM type: NS</td>
</tr>
<tr>
<td>Type 2</td>
<td>6.56</td>
<td>6.09</td>
<td>5.62</td>
<td>Gestational period: 0.004</td>
</tr>
</tbody>
</table>
Figure 1 – Estimates of glycaemic characteristics for women with type 1 and type 2 diabetes obtained from applying generalized linear mixed effects models to the intermittent 7-day continuous glucose profiles. Changes in the overall proportion of time spent euglycaemic (70-140mg/dl) (A), hyperglycaemic (>140mg/dl) (B), hypoglycaemic (<70mg/dl) (C) and hypoglycaemia overnight (D) during pregnancy are shown for women with type 1 (green) and type 2 diabetes (red). The thick lines represent the mean changes in duration of time spent at each threshold, while the thin lines reflect changes across gestation for individual subjects.