

## Research: Pregnancy

# Effect of pregnancy planning on maternal and neonatal outcomes in women with Type 1 diabetes

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### Abstract

**Aims** To assess the effect of pregnancy planning on maternal and neonatal outcomes in women with Type 1 diabetes.

**Methods** Pregnancy planning was assessed retrospectively in a cohort of women who participated in the Diabetes and Pre-eclampsia Intervention Trial (DAPIT). Pregnancy planning was determined based on self-report as to whether pregnancy was planned or unplanned. The effect of pregnancy planning on maternal and neonatal outcomes was examined, controlling for confounding variables.

**Results** A total of 747 women were included in the study, of whom 39% considered their pregnancy unplanned. Characteristics associated with unplanned pregnancy included being younger ( $P<0.001$ ), being a current smoker ( $P<0.001$ ), being from a lower social class ( $P<0.001$ ) and having higher HbA<sub>1c</sub> values prior to and throughout pregnancy ( $P\leq 0.005$ ). Significantly fewer women with unplanned vs planned pregnancies received pre-pregnancy counselling (24% vs 64%;  $P<0.001$ ). Infants of women with unplanned pregnancies were more likely to be small for gestational age (<5<sup>th</sup> centile;  $P=0.004$ ), to be admitted to the neonatal care unit ( $P=0.001$ ) and to have a longer stay in hospital ( $P=0.01$ ). Outcomes did not differ between the groups in relation to pre-eclampsia, congenital malformations or a composite adverse outcome.

**Conclusions** Risks associated with diabetes in pregnancy need to be highlighted to all women, their partners and families, and healthcare professionals. Further research is required to determine if these groups are fully aware of the risks associated with diabetes in pregnancy.

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### Introduction

Approximately half of women in the UK describe their pregnancy as unplanned or are ambivalent towards it [1]. There are a range of behaviours that are known to be detrimental during pregnancy, including smoking and alcohol use [2,3], many of which are associated with pregnancies that are unplanned. Such behaviours may contribute to the increased risks associated with unplanned pregnancy [2,4]. Planning a pregnancy is considered particularly important for women with diabetes, as they are at increased risk of a number of adverse pregnancy outcomes, including fetal malformation, stillbirth and pre-eclampsia [5,6]. Poor

glucose control in the preconception period and early pregnancy has been linked to an increased risk of adverse outcomes [7].

From adolescence, it is recommended that all women with diabetes, regardless of pregnancy intention, receive preconception counselling [8]. This is a discussion between women and their healthcare professionals about the importance of planning for pregnancy and should inform women of the need for pre-pregnancy care prior to conception. Pre-pregnancy care is specialist care delivered by the multidisciplinary diabetes care team to help ensure a woman is prepared for pregnancy, and includes optimization of glycaemic control [8], the prescription of high-dose folic acid supplements (5 mg) and review of their current medications.

Despite these recommendations, ~60% of women with diabetes still do not plan their pregnancy [9,10], and enter pregnancy unprepared, increasing their risk of adverse outcomes. The Confidential Enquiry into Maternal and

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**What's new?**

- Being young, a smoker and from a lower social class were associated with unplanned pregnancy.
- Outcomes that were associated with unplanned pregnancy were very low birth weight and greater neonatal and maternal care requirements post-delivery
- Poor preconception counselling rates among women who did not plan pregnancy suggests an urgent need for strategies to ensure all women receive preconception counselling, regardless of pregnancy intention.

Child Health (CEMACH) reported an increased risk of poor pregnancy outcomes in women with unplanned pregnancies [9]. The effect of pre-pregnancy care on adverse outcomes in women with diabetes has been studied in some detail. Evidence shows that attending pre-pregnancy care is associated with decreased HbA<sub>1c</sub> levels in early pregnancy and with a reduced incidence of adverse outcomes, including congenital malformations, preterm birth and perinatal mortality [11,12].

The aim of the present study was to assess the effect of pregnancy planning on maternal and neonatal outcomes in women with Type 1 diabetes.

## Participants and methods

A total of 747 women from the Diabetes and Pre-eclampsia Intervention Trial (DAPIT) were included. DAPIT was a multi-centre randomized double-blind placebo-controlled trial to investigate the use of antioxidants (vitamins C and E) for the prevention of pre-eclampsia in women with Type 1 diabetes [13]. Pregnancy planning was determined as part of a patient questionnaire completed by each woman at study randomization. Women were asked if their pregnancy was planned, with the response categorized as 'yes', 'no' or 'not known'. Women were also asked if they had received pre-pregnancy counselling (yes or no option), described to women as structured advice about the need to maintain good blood glucose control and healthy lifestyle (with respect to diet, exercise, BMI, smoking status and alcohol consumption) before trying to become pregnant, including the need to take folate supplements. This information was not independently confirmed or cross-checked against clinical records.

Other maternal characteristics collected at baseline included BMI, smoking status, alcohol consumption and social class. Social class was classified according to occupation of the main earner in the household, based on the 1990 classifications [14]. Each class was defined by occupation as: I, professional; II, managerial and technical; IIIN, skilled non-manual; IIIM, skilled manual; IV, partly skilled; and V, unskilled.

Maternal and neonatal outcomes were collected as part of DAPIT and included pre-eclampsia, gestational hypertension,

eclampsia, fetal death, fetal malformation, caesarean section delivery, birth weight, admission to neonatal care unit, maternal stay in hospital and failure to attend a 6-week postnatal visit. Pre-eclampsia was defined as gestational hypertension with proteinuria, in accordance with international guidelines [15,16]. Gestational hypertension was defined as two diastolic blood pressure readings of  $\geq 90$  mmHg at least 4 h apart, or one reading of at least 110 mmHg after 20 weeks' gestation. Proteinuria was defined as a result of at least 1+ for dipstick analysis of a midstream specimen on at least two occasions or 300 mg urinary protein per 24-h period [13]. Late fetal loss was defined as a baby born dead at a gestational age of 20–23 weeks. Neonatal death was categorized into early (death within the first 6 complete days of life) and late (death at age 7–27 completed days of life). Stillbirth was categorized into antepartum (fetal death occurring before labour at  $\geq 24$  weeks' gestation) and intrapartum (fetal death occurring during labour at  $\geq 24$  weeks' gestation). Birth weight centile was calculated from customized birth weight charts [17]. Small for gestational age (SGA) was defined as birth weight below the 5<sup>th</sup> centile and below the 10<sup>th</sup> centile, while large for gestational age (LGA) was defined as birth weight above the 90<sup>th</sup> centile. Informed written consent was obtained and the West Midlands Multicentre Ethics Research Committee provided ethical approval for DAPIT (MREC 02/7/016). DAPIT was carried out in accordance with the Declaration of Helsinki.

## Statistical analysis

Group comparisons were performed using chi-squared and independent-samples *t*-tests. Logistic regression analysis was used to identify outcomes that were associated with unplanned pregnancies. A number of infrequent outcomes were combined *a priori* to create a composite adverse outcome: miscarriage; late fetal loss; stillbirth; neonatal death; termination; and major fetal malformation. All outcomes were adjusted for smoking, social class, maternal age, BMI, parity and centre. All statistical analyses were performed using spss version 20 (IBM Corp, Armonk, NY, USA).

## Results

### Characteristics

The maternal characteristics of women with planned and unplanned pregnancy are summarized in Table 1. Of the 747 women included in the study, 455 (60.9%) described their pregnancy as planned and 292 (39.1%) as unplanned. Women who reported having an unplanned pregnancy were significantly younger and more likely to smoke compared with women who had a planned pregnancy ( $P < 0.001$ ). Women with unplanned pregnancies tended to be in a lower social class ( $P < 0.001$ ) and to book later at their first antenatal visit than those who planned their pregnancy

**Table 1** Maternal characteristics of women with planned and unplanned pregnancies

| Characteristic  | Planned pregnancy<br><i>n</i> <sub>max</sub> =455 | Unplanned pregnancy<br><i>n</i> <sub>max</sub> =292 | <i>P</i> |
|---|---|---|----------|
| Age, years  | 30.9 (4.8)  | 27.6 (6.3)  | <0.001   |
| Gestational age at first antenatal visit, weeks                         | 8.6 (2.7)   | 9.1 (2.9)   | 0.01     |
| BMI, kg/m <sup>2</sup>  | 27.5 (4.6)  | 27.4 (4.7)  | 0.80     |
| Woman's ethnic origin non-white, <i>n</i> (%)                           | 13 (3)  | 10 (3)  | 0.66     |
| Marital status, <i>n</i> (%)  |   |   |          |
| Married   | 366 (74)  | 104 (36)  |          |
| Cohabiting  | 96 (21)   | 90 (31)   | <0.001   |
| Never married   | 15 (3)  | 85 (29)   |          |
| Social class, <i>n</i> (%)  |   |   |          |
| Professional/managerial and technical occupations (I,II)                | 222 (49)  | 79 (27)   |          |
| Skilled, partly-skilled and unskilled occupations (III,IV,V)            | 202 (46)  | 160 (55)  | <0.001   |
| Not known/not classified  | 31 (7)  | 53 (18)   |          |
| ≤12 years in education, <i>n</i> (%)                                    | 155 (34)  | 135 (47)  | <0.001   |
| Duration of diabetes, years   | 14.8 (8.2)  | 14.1 (8.2)  | 0.25     |
| Current smoker, <i>n</i> (%)  | 67 (15)   | 78 (27)   | <0.001   |
| Alcohol use, <i>n</i> (%)   |   |   |          |
| Never/stopped before pregnancy  | 255 (56)  | 154 (53)  |          |
| Stopped during pregnancy  | 150 (33)  | 150 (36)  | 0.66     |
| Current   | 50 (11)   | 32 (11)   |          |
| Primiparous, <i>n</i> (%)   | 215 (47)  | 154 (53)  | 0.14     |
| Abnormal renal status before this pregnancy*, <i>n</i> (%)              | 22 (5)  | 19 (7)  | 0.31     |
| Retinal status before this pregnancy, <i>n</i> (%)                      |   |   |          |
| Normal  | 322 (72)  | 210 (74)  |          |
| Background retinopathy  | 84 (19)   | 55 (19)   | 0.60     |
| Abnormal**  | 39 (9)  | 19 (7)  |          |
| Recall receiving pre-pregnancy counselling, <i>n</i> (%)                | 292 (64)  | 70 (24)   | <0.001   |
| HbA <sub>1c</sub> , mmol/mol  |   |   |          |
| Pre-pregnancy (≤6 months prior)   | 61 (16)   | 74 (21)   | <0.001   |
| Randomisation (8–22 weeks' gestation)                                   | 52 (12)   | 59 (12)   | <0.001   |
| 34 weeks' gestation   | 48 (7)  | 50 (8)  | 0.005    |
| HbA <sub>1c</sub> , %   |   |   |          |
| Pre-pregnancy (≤6 months prior)   | 7.7 (1.5)   | 8.9 (1.9)   |          |
| Randomisation (8–22 weeks' gestation)                                   | 7.0 (0.8)   | 7.5 (1.1)   |          |
| 34 weeks' gestation   | 6.5 (0.6)   | 6.7 (0.8)   |          |
| Proportion with HbA <sub>1c</sub> ≤50 mmol/mol, <i>n</i> (%)            |   |   |          |
| Pre-pregnancy (≤6 months prior)   | 88 (25)   | 18 (9)  | <0.001   |
| Randomization (8–22 weeks' gestation)                                   | 165 (41)  | 67 (27)   | <0.001   |
| 34 weeks' gestation   | 225 (69)  | 105 (58)  | 0.01     |
| Systolic blood pressure at randomisation (8–22 weeks' gestation), mmHg  | 119.2 (11.9)                                      | 118.4 (12.0)  | 0.35     |
| Diastolic blood pressure at randomization (8–22 weeks' gestation), mmHg | 75.1 (8.4)  | 73.9 (8.7)  | 0.05     |
| Taking folic acid prior to conception, <i>n</i> (%)                     | 325 (72)  | 29 (10)   | <0.001   |

Data are mean (SD) unless otherwise stated.

\*Includes microalbuminuria, macroalbuminuria and 24h urinary protein >3 g/24 h.

\*\*Includes proliferative retinopathy, maculopathy, previous vitrectomy and blindness.

(*P*=0.01). Women with planned pregnancies were significantly more likely to have received pre-pregnancy counselling than women with unplanned pregnancies (*P*<0.001). Those with unplanned pregnancies had significantly higher HbA<sub>1c</sub> values 6 months prior to and throughout pregnancy, compared with those with planned pregnancies (*P*≤0.005). A significantly higher proportion of women who planned their pregnancy were taking folic acid prior to conception than those who did not plan pregnancy (*P*<0.001).

### Maternal and neonatal outcomes

Maternal and neonatal outcomes are reported in Table 2. Gestational age at delivery was significantly lower in women with unplanned vs planned pregnancies (*P*=0.02).

Rates of pre-eclampsia and gestational hypertension did not differ significantly between the two groups. There were no significant differences between planned and unplanned pregnancies with regard to type of delivery, with similar proportions having vaginal and caesarean section deliveries.

There was a significant difference in birth weight between planned and unplanned pregnancies (*P*=0.008). This difference persisted after correction for gestational age; infants of women with unplanned pregnancies were more likely to be SGA, whether defined by the 5<sup>th</sup> centile (*P*=0.001) or the 10<sup>th</sup> centile (*P*=0.01). After adjusting for other covariates, SGA defined by the 10<sup>th</sup> centile was no longer significant (*P*=0.10), but remained significant for SGA defined by the 5<sup>th</sup> centile (*P*=0.004).

**Table 2** Maternal and fetal outcomes of women with planned and unplanned pregnancies

| Outcome                                   | Planned pregnancy<br>( <i>n</i> =455)<br><i>n</i> / <i>N</i> (%) | Unplanned pregnancy<br>( <i>n</i> =292)<br><i>n</i> / <i>N</i> (%) | Odds ratio (95%CI) for unplanned vs planned |                       |
|---|--|--|---|-----------------------|
|   |  |  | Unadjusted                                  | Adjusted <sup>†</sup> |
| Pre-eclampsia                             | 74/448 (17)  | 49/286 (17)  | 1.05 (0.70, 1.55)                           | 1.23 (0.77, 1.95)     |
| Gestational hypertension                  | 53/448 (12)  | 30/286 (11)  | 0.87 (0.54, 1.40)                           | 0.76 (0.45, 1.30)     |
| Eclampsia                                 | 0/447 (0)  | 3/286 (1)  | –   | –                     |
| Caesarean delivery                        | 307/454 (68)   | 200/286 (69)   | 1.04 (0.76, 1.43)                           | 1.38 (0.96, 1.98)     |
| Foetal death                              | 12/449 (3)   | 6/284 (2)  | 0.79 (0.29, 2.12)                           | 0.70 (0.24, 2.05)     |
| SGA <5 <sup>th</sup> centile              | 13/446 (3)   | 24/284 (9)   | 3.08 (1.54, 6.14)**                         | 3.10 (1.42, 6.75)**   |
| SGA <10 <sup>th</sup> centile             | 26/446 (6)   | 31/284 (11)  | 1.98 (1.15, 3.41)*                          | 1.68 (0.91, 3.11)     |
| LGA >90 <sup>th</sup> centile             | 230/446 (52)   | 149/284 (53)   | 1.04 (0.77, 1.40)                           | 1.19 (0.84, 1.68)     |
| Major fetal malformation                  | 15/454 (3)   | 13/291 (5)   | 1.37 (0.64, 2.92)                           | 0.96 (0.41, 2.24)     |
| Adverse outcome <sup>‡</sup>              | 30/455 (7)   | 26/292 (9)   | 1.39 (0.80, 2.39)                           | 1.06 (0.57, 1.95)     |
| Admission to neonatal intensive care unit | 218/436 (50)   | 178/277 (64)   | 1.80 (1.32, 2.45)**                         | 1.84 (1.28, 2.66)**   |
| Infant stayed >10 days in hospital        | 65/434 (15)  | 64/277 (23)  | 1.71 (1.16, 2.51)**                         | 1.75 (1.13, 2.70)*    |
| Did not attend 6-week postnatal visit     | 34/436 (12)  | 27/275 (15)  | 1.35 (0.88, 2.07)                           | 1.15 (0.69, 1.93)     |

SGA, small for gestational age; LGA, large for gestational age.

<sup>†</sup>Odds ratio (95% CI) from logistic regression adjusted for smoking, social class, maternal age, BMI, parity and centre.

\**P*<0.05, \*\**P*<0.01.

<sup>‡</sup>Includes miscarriage, late fetal loss, stillbirth, neonatal deaths, termination and major malformation.

Rates of major congenital malformations and adverse outcomes did not differ significantly between the groups. Infants of women with unplanned pregnancies were significantly more likely to be admitted to a neonatal intensive care unit (*P*<0.001), a finding which remained significant after adjustment for covariates. A significantly higher proportion of infants from unplanned compared with planned pregnancies remained in hospital for > 10 days; *P*=0.006). This difference also remained significant after adjustment for covariates.

## Discussion

The majority of research to date has focused on the association of pre-pregnancy care with pregnancy outcomes in women with diabetes, with only a small number of studies investigating pregnancy planning [18,19]. The present study showed that almost 40% of women with Type 1 diabetes did not plan their pregnancy, with only a quarter of women reporting having received preconception counselling. Younger women and those of lower social class were significantly less likely to plan their pregnancies. Unplanned pregnancy was associated with higher HbA<sub>1c</sub> levels prior to and throughout pregnancy, lower folic acid uptake, more smoking in pregnancy and higher rates of SGA infants, infant neonatal intensive care unit admission and neonatal hospital stay exceeding 10 days. Previous studies in the general population have similarly found that women with an unplanned pregnancy were more likely to be younger, classed as socially deprived, and to engage in detrimental behaviours, including smoking [1,2,20], and were also more likely to have adverse outcomes [18].

With regard to HbA<sub>1c</sub> levels in pregnancy, evidence has shown that higher levels are associated with a number of

adverse outcomes, including congenital malformations, macrosomia and pre-eclampsia [21,22]. In the present study, although women with unplanned pregnancies had significantly higher HbA<sub>1c</sub> levels before and throughout their pregnancies, rates of outcomes such as those mentioned, were not significantly higher when compared to women with planned pregnancies. Smoking has previously been shown to reduce the risk of pre-eclampsia [23] and also to increase the risk of SGA infants [24], and so may explain similar rates of pre-eclampsia and LGA infants in the present study. The adjustment for smoking status in our logistic regressions, however, did not suggest that it had much of a confounding effect.

The proportion of women who reported receiving pre-pregnancy counselling was significantly lower among those with unplanned pregnancies. It is important that all women with diabetes receive advice about pregnancy planning, with previous evidence showing a reduction in adverse outcomes associated with pre-pregnancy care [11]; however, it is interesting to note the similar rates of alcohol consumption between the two groups, and that a small proportion of women with unplanned pregnancies were taking folic acid prior to pregnancy, which may demonstrate that some messages are getting through. Those who attend pre-pregnancy counselling/care are a self-selecting group, so other more pragmatic solutions may be needed. These may include education about relationships and safe sex, and access to safe, effective contraception, particularly for women of lower social class.

It is unclear why women in the present study did not plan their pregnancies, but previous research suggests that both women and healthcare professionals are not aware of the full range of risks and complications associated with diabetes in

pregnancy [10,25,26]. It is important that pregnancy planning is seen as a shared responsibility among women, their partners, their families and their healthcare providers. Further research is needed to determine the extent to which these groups are aware of the risks and complications associated with diabetes in pregnancy.

The present study has a number of strengths. Firstly, DAPIT includes one of the largest contemporary datasets of women with Type 1 diabetes, with 762 women from across the UK. The study comprises a well characterized cohort of women with Type 1 diabetes, with extensive information being collected about pregnancy and pregnancy outcomes. Secondly, the study protocol included details of an extensive number of maternal and neonatal outcomes in these women.

The study also has a number of limitations. Participants in the study were those who consented to take part and, as a result, they may not be truly representative of the total population of women with diabetes. Pregnancy planning was a self-reported response and not all participants may have answered honestly, which could have led to a bias towards under-reporting of unplanned pregnancies. Additionally, it is possible that women biased their answers in relation to other questions, such as questions surrounding the use of alcohol in pregnancy. The study was also unable to determine if women specifically received specialized pre-pregnancy care or pre-pregnancy counselling as it was not possible to relate the data back to pre-pregnancy care clinics. It is therefore likely that those who reported having received preconception counselling represent a mixture of women who received counselling and specialized pre-pregnancy care.

In conclusion, although pregnancy planning did not affect the rates of all maternal and neonatal outcomes, unplanned pregnancy was associated with higher rates of SGA infants, admission to a neonatal intensive care unit and a longer neonatal stay in hospital. This study showed an association between lower social class and unplanned pregnancy in women with Type 1 diabetes. It is important that the risks associated with diabetes in pregnancy are highlighted to all women, their partners and families, and also to healthcare professionals. In addition to this, women, particularly those from lower social classes, should have access to good sex education and safe effective contraception, which may go some way to reducing unplanned pregnancies. Further research is required to determine the awareness among both women with diabetes and their healthcare professionals of the risks associated with diabetes in pregnancy.

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#### Competing interests

None declared.

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