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DIABETIC Medicine

SYSTEMATIC REVIEW

Interventions to enhance pre-pregnancy care for women with type 2 diabetes: A systematic review of the literature

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Abstract

Aims: The aim of the study was to examine the content and impact of interventions that have been used to increase the uptake of pre-pregnancy care for women with type 2 diabetes, and their impact on maternal and fetal outcomes.

Methods: A systematic search of multiple databases was conducted in November 2021, and updated July 2022, to identify studies assessing interventions to enhance pre-pregnancy care for women with type 2 diabetes. Over 10% of articles were screened by two reviewers at title and abstract phase, after which all selected full-text articles were screened by two reviewers. Quality assessment was conducted using the Critical Appraisal Skills Programme checklist for cohort studies. Meta-analysis was not possible due to study heterogeneity; therefore, narrative synthesis was conducted.

Results: Four eligible cohort studies were identified. The conclusions able to be drawn by this review were limited as women with type 2 diabetes ($n = 800$) were in the minority in all four studies (35%–40%) and none of the interventions were exclusively tailored for them. The uptake of pre-pregnancy care was lower in women with type 2 diabetes (8%–10%) compared with other participant groups in the studies. Pregnancy preparation indicators generally improved among

all groups exposed to pre-pregnancy care, with varying impact on pregnancy outcomes.

Conclusions: This review demonstrates that previous interventions have had a limited impact on pre-pregnancy care uptake in women with type 2 diabetes. Future studies should focus on tailored interventions for improving pre-pregnancy care for women with type 2 diabetes, particularly those from ethnic minorities and living in poorer communities.

KEYWORDS

pregnancy, pre-pregnancy care, systematic review, type 2 diabetes

1 | INTRODUCTION

The number of women living with early-onset type 2 diabetes (diagnosed between 18 and 39 years) is rising.[1] In England and Wales, pregnancies in women with early-onset type 2 diabetes now account for over half of pre-existing diabetes pregnancies (54% type 2 compared to 44% type 1).[1,2] Relative to the general population women with type 2 diabetes; are older, have higher BMI and are more ethnically diverse.[2] Without adequate preparation, these pregnancies can be hazardous for both the fetus and mother, with increased risk of obstetric complications (caesarean section, preterm births, large or small birthweight, neonatal care unit admission) and serious adverse pregnancy outcomes (congenital anomaly, perinatal death).[1–3] These unfavourable outcomes are not only physically and emotionally hazardous for women and their offspring, they also increase health service costs considerably.

Multiple factors are associated with adverse pregnancy outcomes among women with type 2 diabetes. This group generally have less adequate pregnancy preparation compared to women with type 1 diabetes, showing lower rates of 5 mg folic acid supplementation (22.6% vs. 42.9%); inadequate glycaemic management with 25% untreated, 50% taking metformin alone, and 15% taking insulin before pregnancy; later antenatal booking (9 (5–14) weeks vs. 7 (4–12) weeks) and more exposure to potentially harmful medications (11.5% vs. 3.1%).[2] Furthermore, many women with type 2 diabetes have multimorbidity features including hypertension and obesity which may contribute to their obstetric risks.[4,5] Therefore, it is important to ensure that these issues are addressed with effective pre-pregnancy care if pregnancy outcomes are to be improved in this population.

In the United Kingdom (UK), pre-pregnancy care focuses on supporting women to meet the National Institute for Health and Care Excellence (NICE) guidelines for pre-pregnancy care: to cease potentially harmful medicines, to optimize glucose levels to achieve a HbA_{1c} ≤48 mmol/mol (6.5%) and to start high dose 5 mg folic acid.[6] However, the uptake of pre-pregnancy care among women with type 2 diabetes is low, with less than 12% of women with type 2 diabetes currently meeting the NICE pre-pregnancy targets.[2]

What's new?

- Women who access pre-pregnancy care are better prepared for pregnancy and are more likely to have improved pregnancy outcomes.
- Existing interventions have not adequately increased the uptake of pre-pregnancy care among women with type 2 diabetes.
- Interventions designed for women with type 2 diabetes are needed to increase the use of effective contraception and enhance pre-pregnancy care uptake.

Studies investigating the factors underlying sub-optimal pre-pregnancy care uptake have identified: a lack of understanding about the need for such care both among women with type 2 diabetes and healthcare professionals; insufficient communication between women and health professionals; poor awareness among women and professionals of the severe metabolic consequences of early-onset type 2 diabetes, a lack of systemic processes to ensure access to safe effective contraceptive methods; and considerable negative perceptions or stigma associated with obesity and type 2 diabetes.[7,8] Therefore, if the uptake of pre-pregnancy care is to improve in this population, new approaches are required to increase access to this care, improve pregnancy outcomes and reduce healthcare costs.

This review aimed to identify the key components of interventions to enhance pregnancy planning for women

with type 2 diabetes and assess their impact on the uptake of pre-pregnancy care. The objectives of the review were to:

- Identify and critically appraise studies evaluating interventions to increase pre-pregnancy care uptake;
- Identify the components and active mechanisms of the interventions;
- Estimate the impact of the interventions in promoting pre-pregnancy care uptake and on pregnancy outcomes.

2 | METHODS

The current review has been prepared in accordance with Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. The review was not registered, and a protocol was not prepared, however, the researchers used: explicit search terms and screening criteria; and a common data extraction framework.

A systematic review was conducted to identify studies of interventions aiming to enhance pre-pregnancy care for women with type 2 diabetes. The study inclusion criteria were:

- Studies reporting evaluations of interventions to promote pregnancy planning that included women with type 2 diabetes
- Studies assessing the effect of interventions on pre-pregnancy care uptake and pregnancy outcomes in women with type 2 diabetes

The criteria for excluding studies were:

- Non-intervention studies
- Studies not reporting pre-pregnancy care indicators as outcomes
- Studies that did not differentially report outcomes for women with type 2 diabetes
- Studies without full-text accessible papers (e.g. conference abstracts or posters)
- Protocol papers

2.1 | Search strategy

Searches of MEDLINE, Embase, Web of Science, PUBMED and Cochrane databases were conducted in November 2021 to identify intervention studies of pre-pregnancy care for women with Type 2 diabetes. A citation search and a review of the reference lists of the full-text papers were also conducted. The search was conducted without date or language limitation using a combination of keywords and Medical Subject Heading (MeSH) terms (see File S1 for the full search strategy). The search was updated in July 2022, with no new eligible citations identified. All retrieved citations were exported to Endnote citation manager and then to Covidence systematic review software to support the screening process. Two reviewers (LH and RF) screened ≥10% of studies at title and abstract stage and all articles at full-text stage. Conflicts were resolved through discussion.

2.2 | Data extraction

A data extraction tool was developed to identify the principal information from the selected articles. Data were extracted independently by two researchers (LH and RF) and consolidated through discussion. Data extraction included:

- Author (year)
- Type of study
- Study population
- Intervention components
- Pre-pregnancy care uptake findings
- Pregnancy outcome data

2.3 | Critical appraisal

Each study was appraised using the Critical Appraisal Skills Programme (CASP) tool for cohort studies,[9] to reflect the type of studies included (no clinical trials were identified). There is no numerical scoring for this tool, rather the studies are categorized into low, medium or high quality. The tool was used to assess data quality, rather than to eliminate articles from this review.[10,11] Critical appraisal was undertaken separately by two researchers and then discussed until a consensus was reached to award the final score.

2.4 | Synthesis

Due to the heterogeneity of the studies, conducting a meta-analysis was not appropriate, therefore the main findings of the included studies were tabulated to detail the intervention components and the observed outcomes.[12,13] A narrative synthesis, in line with the methods outlined by Snilstveit et al. (2012), was also undertaken, to explicate the active elements of the interventions.[13] The synthesis involved tabulating the data; producing a text-based description of the studies; and providing an exploration of relationships in the data of the included studies.[13]

3 | RESULTS

Searches identified 3187 citations, including 1693 duplicates which were excluded, leaving 1494 citations for screening. Following title and abstract screening, 1427 citations were excluded based on the eligibility criteria, resulting in 67 citations for full-text screening. Following full-text screening, all but four studies were excluded. The results of this search are summarized in the PRISMA diagram in Figure 1.

3.1 | Study quality

All included studies were prospective cohort studies, limiting the quality of the evidence they can provide. This is considered when making inferences from the data. The included studies were categorized as medium[16] and high[14,17,18] quality using the CASP appraisal tool.[9] There was a lack of measurement or consideration for the role of ethnicity as a confounding factor in the Willhoite[16] and Yamamoto[18] papers, now recognized as an important factor when considering type 2 diabetes.[1] Willhoite et al.[16] also used a surrogate classification of type 2 diabetes, assuming those diagnosed over the age of 20 had type 2 diabetes, which may not be a valid measure as many women are diagnosed with type 1 in adulthood. However, all studies had appropriate follow-up of participants, addressed a clearly focused research question and had clear and appropriate methods for recruitment.

3.2 | Study characteristics

Two of the four identified studies were conducted in the UK (Murphy et al.[17]; Yamamoto et al.[18]), with one each in the USA (Willhoite et al.[16]) and Ireland (Egan et al.[14]). All studies reported on interventions addressing pregnancy planning for women with diabetes, although women with type 2 diabetes formed the minority of the participants (ranging from 35% to 40%). Two studies reported on the rates of pre-pregnancy care attendance, pre-pregnancy care indicators and pregnancy outcomes within their population (Murphy et al.[17]; Egan et al.[14]). Yamamoto et al.[18] reported on pre-pregnancy care indicators and pregnancy outcomes during/after implementation of a primary care-based intervention, compared to pre-implementation. While Willholte[16] reported on rates of pre-pregnancy care

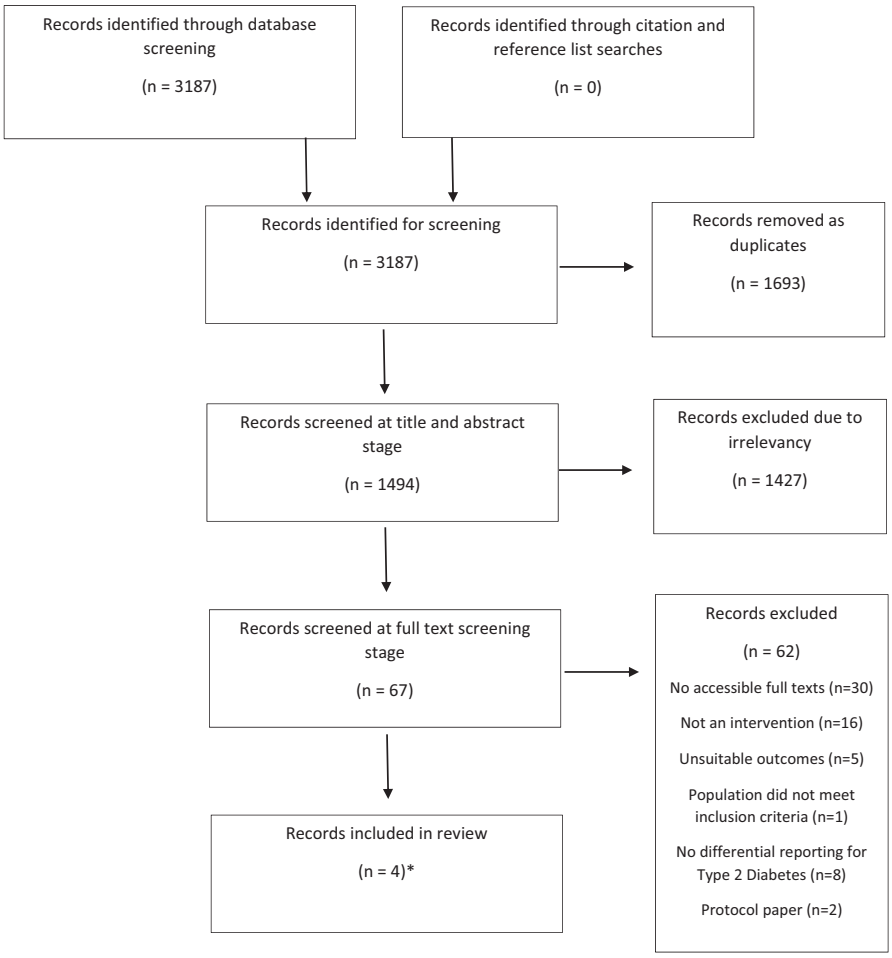

FIGURE 1 PRISMA chart of data flow throughout the review*Two papers relating to the Atlantic DIP intervention were identified as eligible for inclusion in the review; Egan et al[14] and Dunne et al.[15] The Egan et al[14] paper was used as the index paper for completeness as its scope covered a wider time frame, including that outlined in the Dunne et al[15] paper.

attendance, they did not report on pregnancy preparation indicators (HbA_{1c}, folic acid, potentially harmful medications). The characteristics of the study design, the sample, the intervention contents, pre-pregnancy care uptake and pregnancy outcomes are presented in Tables 1 and 2. Where available the specific data for the women with type 2 diabetes were extracted (see Table 3).

Summarized below is a narrative synthesis which considers the impact of the interventions on indicators of effective pre-pregnancy care for women with pregestational diabetes.[19] The narrative considers the following aspects of the included studies:

- Maternal characteristics
- Intervention components and theoretical framework
- Uptake of pre-pregnancy care
- Measures of pregnancy preparation
- Obstetric and neonatal outcomes

The data on participant characteristics of pre-pregnancy care outcomes for women with type 2 diabetes were only presented in three of the studies (Murphy et al.[17]; Egan et al.[14]; and Yamamoto et al.[18]). Limited data on participant characteristics in the study by Willhoite et al.[16] have been included where available.

3.3 | Maternal characteristics

In total, the studies reported data on 800 women with type 2 diabetes. The proportion of women with type 2 diabetes was low in all studies ranging from 35% to 40%, with the remainder being women with type 1 diabetes, which may be reflective of when these studies were conducted, as the proportion of women with type 2 diabetes prior to pregnancy has increased in recent years.[2] In the studies reporting pre-pregnancy care attendance, women with type 2 diabetes were less likely to attend than women with type 1 diabetes (Willhoite et al.[16]; Murphy et al.[17]; Egan et al.[14]). Women with type 2 diabetes who attended pre-pregnancy care had a longer diabetes duration, were more likely to be Caucasian, live in less deprived areas and be non-smokers (Murphy et al.[17]; Egan et al.[14];). Attenders had lower BMIs compared to non-attenders, although this only reached statistical significance in one study (Murphy et al.[17]; Tables 1 and 2).

3.4 | Intervention components and theoretical framework

In all studies, the interventions used multimodal approaches, comprising combinations of: patient and health professional education; clinical practice guidelines and proformas; and patient information leaflets (Table 1). It was not possible to assess the benefit of each approach, as the impacts on the uptake of the individual elements were not evaluated in any of the studies. All the studies had multiple targets with intervention components aimed at patient and healthcare professional behaviours along with healthcare system changes. The interventions were all evaluated in multi-centred settings within defined geographical regions.

There was variation in the delivery approach between the interventions: one study was opportunistic (Willhoite et al.[16]), with participants being identified on presentation to their healthcare provider; two studies (Murphy et al.[17]; Egan et al.[14]) used census models, which involved proactively posting information to all women with diabetes aged 15–50 years; and the fourth (Yamamoto et al.[18]) used a combination of these approaches.

None of the included studies explicitly outlined any theoretical frameworks or models to underpin their interventions. Murphy et al.[17] and Yamamoto et al.[18] both indicated that the information leaflet used in their studies was 'theoretically guided' although this was not explicitly detailed.

3.5 | Uptake of pre-pregnancy care

Pre-pregnancy care attendance was reported in three studies (Willhoite et al.[16]; Murphy et al.[17]; Egan et al.[14]). Uptake was modest, with attendance rates ranging from 26% to 36% for women with both types of diabetes. However, uptake was considerably lower among women with type 2 diabetes, with only 8% to 10% engaging with pre-pregnancy care (Table 2). Pre-pregnancy care attendance rates were not reported by Yamamoto et al.[18] which focused exclusively on markers of pregnancy preparation. They reported individual components (maternal $HbA_{1c} < 48$/mmol/mol, no harmful medications, 5 mg preconception folic acid supplementation, first antenatal contact <8 weeks gestation) and a composite 'optimal pregnancy preparedness' outcome which included all of these. They reported that the number of women with type 2 diabetes with 'optimal pregnancy preparedness' increased from 5.8% prior to the intervention to 15.1% post-intervention.

3.6 | Impact on pregnancy preparation criteria

3.6.1 | Glycaemic control

Two studies reported HbA_{1c} levels prior to and during the first trimester of pregnancy (Murphy et al.[17]; Egan et al.[14]).

TABLE 1 Studies included in the review.

Study	Method	Population	Intervention	Measures of pregnancy preparedness
Maine Diabetes in Pregnancy Programme (MDPP) Willhoite et al. (1993) USA	Prospective cohort study. Study period 1985 to 1990	All pregnancies complicated by diabetes in the study region during the intervention period Type 2 diabetes ($n=65$)	Components: 1. Pre-pregnancy care Guideline 2. Professional education 3. Group education for patients and families 4. Individual education for patients 5. Mass media campaign Setting: Specialist clinics in education centres Delivery: Diabetes nurse educators and dietitian	Receipt of pre-pregnancy counselling
East Anglia Study Group Murphy et al. (2010) UK	Prospective cohort study. Study period January 2006 to December 2009	All pregnancies complicated by diabetes in the study region during the intervention period Type 2 diabetes ($n=271$)	Components: 1. Pre-pregnancy care Guideline 2. Standardized clinic proforma 3. Pre-pregnancy care information leaflet (EPSIPOD) 4. Regional Pre-pregnancy care team Setting: Specialist clinics in secondary care Delivery: Diabetes physician, diabetes specialist nurses, midwives and obstetricians	Attendance at pre-pregnancy care in specialist clinics HbA_{1c}, Folic acid, teratogenic medications
Atlantic DIP Egan et al. (2016) Ireland	Prospective cohort and cost-analysis study. Study period January 2006 to December 2014	All pregnancies for women living with diabetes attending antenatal centres in the study region during the study period (after the implementation of the intervention) Type 2 diabetes ($n=146$)	Components: 1. Pre-pregnancy care Guideline 2. Professional education 3. Individual education for patients 4. Regional Pre-pregnancy care team 5. Invitation letter to women with DM Setting: Specialist clinics in secondary care Delivery: Diabetes physician, nurse and dietician	Attendance at pre-pregnancy care HbA_{1c}, Folic acid, Teratogenic medications
Yamamoto et al. (2018) UK	Prospective cohort study Study period June 2013 to February 2017	All pregnancies for women living with diabetes attending antenatal care in the region before, during and after the implementation of the intervention Type 2 diabetes ($n=318$)	Components: 1. Pre-pregnancy care Guideline 2. Standardized clinic proforma 3. Pre-pregnancy care information leaflet (EASIPOD) 4. Primary Care electronic records alerts to identify women Setting: Specialist clinics in secondary care and primary care Delivery: Diabetes physician, diabetes specialist nurses, midwives and obstetricians, primary care HCPs	Meeting criteria for optimal pregnancy preparation[a] HbA_{1c}, Folic acid, Teratogenic medications

Abbreviations: BMI body mass index, PPC pre-pregnancy care.

[a]Women in the study population meeting criteria for optimal diabetes management for pregnancy (on 5 mg folic acid prior to last period, booking at ≤8 weeks gestation, no harmful medications prior to last period, first HbA_{1c} ≤48 mmol/mol).

Murphy et al.[17] reported an improvement in HbA_{1c} levels in women with type 1 and type 2 diabetes attending pre-pregnancy care at both time points. Similarly, Egan et al.[14] found significantly lower HbA_{1c} levels during the first trimester in those who had received pre-pregnancy care in both the type 1 and type 2 diabetes groups. Yamamoto

TABLE 2 Participant characteristics and outcomes by whether or not they attended pre-pregnancy care.

Study	Characteristics	No pre-pregnancy care	Pre-pregnancy care	*p* value	Preparedness/ outcomes	No pre-pregnancy care	Pre-pregnancy care	*p* values
Maine Diabetes in Pregnancy Programme (MDPP) Willhoite et al. (1993)	Age[a]	26.3 ± 5.6	28.3 ± 5.7	0.02	Optimal Preparedness[l]	Not reported	Not reported	
	Duration of DM[a]	9.0 ± 7.4	11.2 ± 7.3	0.02	HbA_{1c} pre-pregnancy	Not reported	Not reported	
	BMI	Not reported	Not reported		HbA_{1c}	Not reported	Not reported	
	Ethnicity	Not reported	Not reported		Folic Acid	Not reported	Not reported	
	Smoker	31% (*n* = 38)	13% (*n* = 8)	0.01	Medications	Not reported	Not reported	
	Type 1 diabetes	64.7% (*n* = 77)	35.3% (*n* = 42)		**Maternal outcomes:**			
	Type 2 diabetes[h]	71% (*n* = 46)	29% (*n* = 19)		Caesarean section	66% (*n* = 47)	81% (*n* = 30)	
					Fetal outcomes:			
					Congenital abnormalities	6.5% (*n* = 8)	1.6% (*n* = 1)	
					Fetal death[c]	17% (*n* = 21)	5% (*n* = 3)	
					Neonatal death	4% (*n* = 5)	1.6% (*n* = 1)	
East Anglia Study Group Murphy et al. (2010)	Age[b]	31 (22–39)	33 (26–39)	0.002	Optimal Preparedness[l]	Not reported	Not reported	
	Duration of DM[b]	7 (1–22)	10 (2–27)	0.01	HbA_{1c} pre-pregnancy[b]	8.1% (6.1–11.7)	7.2% (6.0–8.8)	<0.001
	BMI[b]	27.9 (22.2–38.1)	26.1 (21.3–36.2)	0.005	HbA_{1c}[b,e]	7.4% (6.0–9.7)	6.9% (5.8–8.4)	<0.001
	Ethnicity[f]	77.6% (*n* = 387)	91.7% (*n* = 166)		Folic Acid[g]	26.7% (*n* = 112)	88.2% (*n* = 157)	<0.001
	Smoker	21.6% (*n* = 105)	7.7% (*n* = 14)		*ACE Inhibitors*[m]	4.6% (*n* = 23)	1.1% (*n* = 2)	0.05
	Type 1 diabetes	68.6% (*n* = 278)	31.4% (*n* = 127)		*Statins*[m]	7.6% (*n* = 38)	(*n* = 0)	<0.001
	Type 2 diabetes	80.4% (*n* = 218)	19.6% (*n* = 53)		**Maternal outcomes:**			
					Caesarean section	55.6% (*n* = 222)	65.1% (*n* = 99)	
					Fetal outcomes:			
					Congenital abnormalities	5.6% (*n* = 23)	0.7% (*n* = 1)	0.02
					Stillbirth	1.5% (*n* = 6)	0.7% (*n* = 1)	0.7
					Neonatal death	0.7 (*n* = 3)	(*n* = 0)	0.7
Atlantic DIP Egan et al. (2016)	Age[a]	31.9 ± 5.7	33.8 ± 4.6	<0.001	Optimal Preparedness[l]	Not reported	Not reported	
	Duration of DM[a]	9.5 ± 8.7	11.7 ± 9.7	0.02	HbA_{1c} pre-pregnancy[a]	8.1% ± 2.5	7.4% ± 1.3	0.002
	BMI[a]	29.4 ± 6.9	28.3 ± 5.6	0.09	HbA_{1c}[a,e]	7.7% ± 1.8	6.8% ± 1.2	
	Ethnicity[f]	86.4% (*n* = 229)	96% (*n* = 143)	0.003	Folic Acid[g]	57.7% (*n* = 153)	97.3% (*n* = 145)	<0.001
	Smoker	16.6% (*n* = 44)	8.7% (*n* = 13)	0.03	Harmful medications[d]	6% (*n* = 16)	0.7% (*n* = 1)	0.008
	Type 1 diabetes	58.7% (*n* = 158)	41.3% (*n* = 111)		**Maternal outcomes:**			
	Type 2 diabetes	73.4% (*n* = 107)	26% (*n* = 38)		Caesarean section	62% (*n* = 142)	68.6% (*n* = 85)	0.22
					Fetal outcomes:			
					Congenital abnormalities	5.2% (*n* = 12)	0.8% (*n* = 1)	0.04
					Stillbirth	3% (*n* = 8)	1.3% (*n* = 2)	
					Neonatal death	(*n* = 0)	(*n* = 0)	

(Continues)

TABLE 2 (Continued)

Study	Characteristics	No pre-pregnancy care	Pre-pregnancy care	*p* value	Preparedness/ outcomes	No pre-pregnancy care	Pre-pregnancy care	*p* values
Yamamoto et al. (2018)	Age[a]	32.5 ± 5.9[k]	31.4 ± 5.9[i]	0.0074	Optimal Preparedness[l]	9.5% (*n* = 36)[k]	16% (*n* = 50)[i]	0.011
	Duration of DM	Not reported	Not reported		HbA_{1c} pre-pregnancy	Not reported	Not reported	
	BMI[a]	29.3 ± 7.2[k]	29.8 ± 6.9[i]	0.29	HbA_{1c}[a,n]	7.5% ± 3.8[k]	7.4% ± 3.7[i]	0.34
	Ethnicity	Not reported	Not reported		Folic Acid[g]	47.6% (*n* = 217)[k]	51.9% (*n* = 166)[i]	0.24
	Smoker	Not reported	Not reported		Harmful medications[d]	8.2% (*n* = 37)[k]	5.6% (*n* = 19)[i]	0.21
	Type 1 diabetes	61.4% (*n* = 308)[k]	60.3% (*n* = 205)[i]		**Maternal outcomes:**			
	Type 2 diabetes	37.1% (*n* = 186)[k]	38.8% (*n* = 132)[i]		Caesarean section	Not reported	Not reported	
					Fetal outcomes:			
					Congenital abnormalities	3.4% (*n* = 15)[k]	6% (*n* = 18)[i]	0.10
					Stillbirth	0.9% (*n* = 4)[k]	1% (*n* = 3)[i]	1.00
					Neonatal death	0.7% (*n* = 3)[k]	(*n* = 0)[i]	0.28

Abbreviations: BMI, body mass index; and PPC pre-pregnancy care.

[a]Reported as mean ± standard deviation.

[b]Reported as median average (10th–90th centile).

[c]Fetal deaths including stillbirths.

[d]Taking at least one teratogenic medication (ACE inhibitors and statins) at first antenatal visit.

[e]First trimester HbA_{1c}.

[f]White ethnicity.

[g]Taking folic acid 5 mg.

[h]Surrogate classification; assumed women >20 years of age at diagnosis were type 2 diabetes.

[i]Relates to pregnancies occurring during or after the implementation of the intervention.

[k]Relates to pregnancies occurring before the intervention was implemented.

[l]Reports % (*n*) of women in the study population meeting criteria for optimal diabetes management for pregnancy (on 5 mg folic acid prior to last period, booking at ≤8 weeks gestation, no harmful medications prior to last period, first HbA_{1c} ≤48 mmol/mol).

[m]Taking medication at first antenatal visit.

[n]HbA_{1c} at first antenatal visit.

et al.[18] recorded HbA_{1c} levels at first antenatal contact, finding no significant differences in mean HbA_{1c} levels before and after the intervention. However, there was a 14-percentage point increase in the percentage of women with type 2 diabetes achieving $HbA_{1c} < 48$ mmol/mol after the intervention.

3.6.2 | Use of potentially harmful medications and folic acid

There was inconsistent reporting between the studies about the use of potentially harmful medications and folic acid. Willhoite et al.[16] did not address folic acid supplementation or the use of medications, although this may be reflective of the time period of the study (early 1990s). Murphy et al.[17] and Egan et al.[14] reported that supplementation with folic acid 5 mg was more likely among those who attended pre-pregnancy care in both the women with type 1 and type 2 diabetes. Yamamoto et al.[18] reported a significant increase in the percentage of women with type 2 diabetes taking folic acid 5 mg after (41.8%) as compared to before (23.5%) the intervention.

Additionally, both Murphy et al.[17] and Egan et al.[14] reported that the use of potentially harmful medications was less likely among women who attended pre-pregnancy care. Egan et al.[14] found this difference was only significant among women with type 1 diabetes. Murphy et al.[17] reported the use of potentially harmful medications was less likely among those with type 2 diabetes who attended pre-pregnancy care, with none taking statins at conception compared with over 14% ($n = 31$) of non-attenders ($p < 0.01$). The use of ACE Inhibitors was also more frequently reported among those with type 2 diabetes who had not attended pre-pregnancy care (8.3%, $n = 18$). Yamamoto et al.[18] found no significant differences in the percentage of women with type 2 diabetes using at least one potentially harmful medication during/after the introduction of their intervention (12.2%) compared to pre-intervention exposure (16%).

3.7 | Pregnancy outcomes

The reporting of fetal and maternal outcomes differed between the included studies, with only limited data available in three of the studies (Willhoite et al.[16]; Murphy et al.[17]; Egan et al.[14]). Three studies reported that the infants of women who attended pre-pregnancy care were less likely to have congenital abnormalities compared with the infants of the non-attenders; although this was only observed in women with type 1 diabetes in Egan et al.'s,[14] and Murphy et al.'s[17] studies. Stillbirths were lower for those who had attended pre-pregnancy care across all three studies (Willhoite et al.[16]; Murphy et al.[17]; Egan et al.[14]). These results were not statistically significant but interpretations from this analysis are problematic due to the low incidence of this event. The rates of caesarean section delivery were inconsistent across the studies.

4 | DISCUSSION

In summary, only four studies met the inclusion criteria for this review. This low yield of studies reflects the relatively low level of attention to diabetes care processes, glycaemic targets and pre-pregnancy care for women with type 2 diabetes, despite the fact that this is a growing population with a high prevalence of preventable adverse pregnancy outcomes, which have implications for future health and outcomes of future pregnancies. While the sample sizes are small, reflecting low prevalence of type 2 diabetes when these studies were performed, the data suggest that women who attend pre-pregnancy care are more likely to achieve their pregnancy glucose targets, take high dose folic acid and less likely to be exposed to potentially harmful medicines in early pregnancy. However, all these studies showed that increasing the uptake of pre-pregnancy care in women with type 2 diabetes is challenging, with much lower uptake rates in women with type 2 diabetes compared to those with type 1 diabetes.

It is well established that serious adverse pregnancy outcomes such as congenital anomalies and perinatal deaths are higher among women with diabetes compared to those without diabetes.[1–3] We found that women who attended pre-pregnancy care had fewer serious adverse outcomes compared with the non-attenders, however it is important to note that there are also differences in the maternal characteristics of women who do and do not attend, introducing the possibility of a bias in the observed effects of pre-pregnancy care. It is possible that the women who attended were more motivated to engage with healthcare support than those who did not. This is further supported by recent national pregnancy data demonstrating striking structural healthcare inequalities in access to pre-pregnancy care with significant impact of maternal deprivation and ethnicity.[1] Therefore, developing interventions that will improve the uptake of pre-pregnancy care among all women with type 2 diabetes is a priority. Furthermore, the American Diabetes Association Standard Guidelines highlight the need for early pre-pregnancy care interventions and awareness raising for women and adolescents with type 2 diabetes, from puberty.[20] It is important to ensure that such interventions are acceptable to all women of reproductive age with type 2 diabetes and that they are appropriately targeted to women from diverse backgrounds

TABLE 3 Participant characteristics and pregnancy preparedness by pre-pregnancy care attendance and diabetes type.

Study	Type 1 Characteristic/pregnancy preparedness	No pre-pregnancy care	Pre-pregnancy care
Willhoite et al. (1993)	Differentiated results by diabetes type not reported		
Murphy et al. (2010)		$n=278$	$n=127$
	Age[b]	29 (20–38)	31 (25–38)
	White Ethnicity[g]	95.7% ($n=266$)	96.1 ($n=122$)
	BMI[b]	25.7 (22–32)	24.7 (21–31)
	Folic acid[c]	28.6% ($n=69$)	89.5% ($n=111$)
	ACE inhibitors	1.8% ($n=5$)	0.8% ($n=1$)
	Statins	2.5% ($n=7$)	($n=0$)
	Booking gestation[b,e]	7.6 (5–14)	6.6 (4.4–9.9)
	HbA_{1c} pre-pregnancy[b]	8.6 (6.5–12.1)	7.4 (6.5–9)
	HbA_{1c} [b,f]	7.8 (6.1–9.8)	6.9 (6.2–8.4)
	Optimal preparedness	Not reported	Not reported
	Caesarean section	Not reported	Not reported
	Congenital anomaly	5.7% ($n=13$)	0.9% ($n=1$)
	Stillbirth	1.8% ($n=4$)	0.9% ($n=1$)
	Neonatal death	1.3% ($n=3$)	($n=0$)
Egan et al. (2016)	Age[a]	$n=158$	$n=111$
	White Ethnicity[g]	30.7 ± 5.7	34.0 ± 4.9
	BMI[a]	99.4% ($n=157$)	100% ($n=111$)
	Folic acid[c]	26.3 ± 4.9	26.5 ± 4.2
	Harmful meds[d]	59.5% ($n=94$)	98.1% ($n=109$)
	Booking gestation[e]	9.5% ($n=15$)	0.9% ($n=1$)
	HbA_{1c} pre-pregnancy	Not reported	Not reported
	HbA_{1c} [a,f]	Not reported	Not reported
	Optimal preparedness[j]	8.1 ± 1.7	6.9 ± 1.0
	Caesarean section	Not reported	Not reported
	Congenital anomaly	58.2% ($n=92$)	55% ($n=61$)
	Stillbirth	6.3% ($n=10$)	($n=0$)
	Neonatal death	3.8% ($n=6$)	1.8% ($n=2$)
		($n=0$)	($n=0$)
Yamamoto et al. (2018)	Age[a]	$n=308$	$n=205$
	White Ethnicity[g]	31.2 ± 5.9[i]	30.2 ± 5.8[h]
	BMI[a]	Not reported	Not reported
	Folic acid[c]	26.5 ± 4.6[i]	27.3 ± 5.3[h]
	Harmful meds[d]	60.6% ($n=174$)[i]	58% ($n=113$)[h]
	Booking gestation[a,e]	3.7% ($n=10$)[i]	1.5% ($n=3$)[h]
	HbA_{1c} pre-pregnancy	8.4 ± 3.5[i]	7.6 ± 3.7[h]
	HbA_{1c} [a,k]	Not reported	Not reported
	Optimal preparedness[j]	7.8 ± 3.8[i]	7.8 ± 3.7[h]
	Caesarean section	10.6% ($n=25$)[i]	16.3% ($n=31$)[h]
	Congenital anomaly	Not reported	Not reported
	Stillbirth	3.8% ($n=10$)[i]	7.9% ($n=14$)[h]
	Neonatal death	1.1% ($n=3$)[i]	($n=0$)[h] ($n=0$)[h]
		0.74% ($n=2$)[i]	

[a]Reported as mean ± standard deviation.

[b]Reported as median average (10th–90th centile).

[c]Taking folic acid 5 mg.

[d]Teratogenic medications (ACE inhibitors and statins).

[e]Gestational age in weeks at booking.

[f]First trimester HbA_{1c} %.

[g]White ethnicity.

[h]Relates to pregnancies occurring during or after the implementation of the intervention.

[i]Relates to pregnancies occurring before the intervention was implemented.

[j]Reports % (n) of women in the study population meeting criteria for optimal diabetes management for pregnancy (on 5 mg folic acid prior to last period, booking at ≤8 weeks gestation, no harmful medications prior to last period, first HbA_{1c} ≤48 mmol/mol).

[k]HbA_{1c} at first antenatal visit.

p value	Type 2 Characteristic/pregnancy preparedness	No pre-pregnancy care	Pre-pregnancy care	*p* value
	Differentiated results by diabetes type not reported			
<0.001	Age[b]	*n* = 218	*n* = 53	0.3
0.6	White ethnicity[g]	34 (25–40)	35 (27–39)	.001
0.04	BMI[b]	54.6% (*n* = 119)	83% (*n* = 44)	0.8
<.0001	Folic acid[c]	32.2 (24–43)	33.9 (26–40)	<0.001
0.7	*ACE inhibitors*	23.3% (*n* = 41)	84.9% (*n* = 45)	0.2
0.2	*Statins*	8.3% (*n* = 18)	1.9% (*n* = 1)	0.007
<.0001	Booking gestation[b,e]	14.2% (*n* = 31)	(*n* = 0)	0.04
<.0001	HbA_{1c} pre-pregnancy[b]	7.9 (5–15)	7.3 (5–12)	<0.001
<.0001	HbA_{1c} [b,f]	7.1 (5.7–10.8)	6.6 (5.6–8.1)	0.007
0.08	Optimal preparedness[j]	6.8 (5.7–8.8)	6.4 (5.5–7.7)	0.2
0.9	Caesarean section	Not reported	Not reported	0.9
0.6	Congenital anomaly	Not reported	Not reported	
	Stillbirth	5.6% (*n* = 10)	(*n* = 0)	
	Neonatal death	1% (*n* = 2)	(*n* = 0)	
		(*n* = 0)	(*n* = 0)	
<.001	Age[a]	*n* = 107	*n* = 38	0.59
0.86	White ethnicity[g]	33.7 ± 5.3	33.3 ± 3.5	0.93
<.001	BMI[a]	67.3% (*n* = 72)	84.2% (*n* = 32)	<.001
0.003	Folic acid[c]	33.7 ± 7.1	33.6 ± 5.8	1.00
<.001	Harmful meds[d]	55.1% (*n* = 59)	94.7% (*n* = 36)	0.05
0.89	Booking gestation[e]	0.9% (*n* = 1)	(*n* = 0)	0.07
0.007	HbA_{1c} pre-pregnancy	Not reported	Not reported	1
	HbA_{1c} [a,f]	Not reported	Not reported	
	Optimal preparedness[j]	7.0 ± 1.7	6.3 ± 1.5	
	Caesarean section	Not reported	Not reported	
	Congenital anomaly	52.6% (*n* = 50)	70.6% (*n* = 24)	
	Stillbirth	2.1% (*n* = 2)	2.9% (*n* = 1)	
	Neonatal death	1.9% (*n* = 2)	(*n* = 0)	
		(*n* = 0)	(*n* = 0)	
0.058	Age[a]	*n* = 186	*n* = 132	0.026
0.068	White ethnicity[g]	34.7 ± 5.2[i]	33.4 ± 5.4[h]	0.71
1.00	BMI[a]	Not reported	Not reported	0.001
0.17	Folic acid[c]	34.3 ± 8.0[i]	33.9 ± 7.2[h]	0.41
0.020	Harmful meds[d]	23.5 (*n* = 38)[i]	41.8% (*n* = 51)[h]	0.25
0.65	Booking gestation[a,e]	16% (*n* = 27)[i]	12.2% (*n* = 16)[h]	0.30
0.086	HbA_{1c} pre-pregnancy	10.5 ± 4.5[i]	9.8 ± 4.9[h]	0.021
0.084	HbA_{1c} [a,k]	Not reported	Not reported	0.72
0.28	Optimal preparedness[j]	6.9 ± 3.5[i]	6.8 ± 3.5[h]	0.31
0.52	Caesarean section	5.8% (*n* = 8)[i]	15.1% (*n* = 18)[h]	1
	Congenital anomaly	Not reported	Not reported	
	Stillbirth	2.4% (*n* = 4)[i]	3.3% (*n* = 4)[h]	
	Neonatal death	0.6% (*n* = 1)[i]	2.4% (*n* = 3)[h]	
		0.6% (*n* = 1)[i]	(*n* = 0)[h]	

and those living in the most deprived regions, where most type 2 diabetes pregnancies occur (40.3 vs 5.8% for type 2 diabetes pregnancies in women living in the most compared to least deprived quintiles).[2]

An important consideration in developing interventions to improve women's engagement with pre-pregnancy care, is to understand some of the factors that might influence their reproductive health choices and behaviours. Pre-pregnancy care requires several adjustments, such as changes in their personal behaviour, lifestyle modification, enhancing their understanding or changes to their therapeutic modalities.[8,21] In addition, there are multiple barriers to women with type 2 diabetes' engagement in pregnancy planning; previous studies have shown that women's reproductive behaviours can be regulated by stigma, interpersonal relations, cultural expectations and their visibility as having reproductive potential to healthcare providers.[7] Therefore, interventions need to incorporate behavioural models that address these, underpinning psychosocial factors. Unfortunately, none of the interventions reported in these studies were underpinned by any theoretical models to explicate how the different intervention components might target the barriers to women's access to pre-pregnancy care. Hence, future studies need to be theoretically modelled to demonstrate how they will facilitate behaviour change in both the women and the health professionals who provide their diabetes care.[22] An example of one such theoretically modelled intervention is the 'READY-Girls Preconception Counselling Programme', which focuses on early intervention and awareness raising for adolescents with Type 1 and Type 2 diabetes.[23] However, this intervention is currently not specifically tailored towards adult women and the associated study includes adolescents with type 1 and type 2 diabetes, but does not differentially report outcomes for the type 2 diabetes group. As the number of adolescent and younger adult females with type 2 diabetes continues to increase, developing pre-pregnancy interventions targeting this younger population is important as current interventions are limited.[24]

Additionally, as women with type 2 diabetes experience most of their diabetes care in primary care settings, focused interventions delivering better one-stop reproductive support to women with type 2 diabetes are needed. It is well recognized that complex problems require multifaceted interventions that target patient and healthcare professional behaviour change along with changes in organizational processes to support improved care.

4.1 | Review limitations

As with all reviews, the conclusions are limited by the characteristics and quality of the included studies. A particular challenge was that studies were conducted at a time when the population of women with type 2 diabetes was much lower, and they included only a minority of the women with type 2 diabetes. These limitations emphasize that future studies need to be better focused on women with type 2 diabetes as their needs and context of care are divergent from women with type 1 diabetes. Addressing inequalities in the provision and access to diabetes and contraceptive services are priorities for women with both types of diabetes.

Eight studies which included women with type 2 diabetes were excluded from the review as they did not differentially report outcomes for women with type 2 from those with type 1 diabetes, such that independent inferences could not be made. While the exclusion of these studies may have introduced some publication bias, it is unlikely they would have altered our findings given the small proportion of women with type 2 diabetes in these studies. However, we would recommend that future studies report sub-group outcome data for women with type 2 diabetes.

Encouragingly, some emerging studies have been identified which may provide such interventions. The Preconception and Diabetes Information (PADI) app is a developing intervention involving a pregnancy planning information application for women with pregestational diabetes.[25] While not exclusively tailored towards women with type 2 diabetes, the centring of this intervention in mobile health, rather than specialist secondary care centres as in the reviewed studies, may contribute to making the intervention more accessible to this population. Two studies have been published relating to this protocol, exploring the feasibility and acceptability of the PADI app among women with pregestational diabetes and their clinicians, with both studies supporting its use.[26,27] However, to the authors knowledge, no studies assessing the effectiveness of the PADI app have yet been published. There are two ongoing studies of relevance, with one based in the UK (the PREPARED study),[28] while the other is based in the US.[29] These studies both aim to integrate pre-pregnancy care for women with type 2 diabetes into primary care. The proposed interventions components for these studies include: modified electronic health record technology to promote pre-pregnancy care discussions[28,29]; health professional education[28]; education resources for women with type 2 diabetes[28,29]; and text message prompts to promote health behaviours.[29] Both of these studies address many of the limitations identified in the previous studies as they are theoretically grounded and focused on primary care settings. Both the UK PREPARED study and the US study explicitly target organizational processes to support pre-pregnancy care, recognizing that care outcomes emerge from interactions between healthcare professionals and women in an organizational context.[7]

5 | CONCLUSION

In conclusion, this review has highlighted that women with type 2 diabetes who access pre-pregnancy care are better prepared for pregnancy and likely to have better pregnancy outcomes. However, current models have not adequately increased the uptake of pre-pregnancy care among women with type 2 diabetes. Future interventions should be tailored to the needs of women with type 2 diabetes, considering: their diverse sociodemographic profiles; and integrating pre-pregnancy care within the context of primary care settings as well as in specialist services. Future studies should also report disaggregated data for women with type 2 diabetes from other included populations. Encouragingly there are a few studies in progress that are developing and testing such interventions.

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CONFLICT OF INTEREST STATEMENT

A co-author (HRM) was the principal investigator on two of the studies included in this review.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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