Preconception care and the risk of congenital anomalies in the offspring of women with diabetes mellitus: a meta-analysis

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Authors' objectives
To assess the effect of preconception care (PCC) interventions in reducing congenital malformation in the offspring of women with diabetes mellitus (DM).

Searching
MEDLINE (from 1970 to June 2000) and EMBASE (from 1980 to June 2000) were searched, merging the following textwords and MeSH terms: ('diabetes' or 'diabetes mellitus') and ('anomalies', 'congenital anomalies', 'malformations', 'congenital malformations' or 'birth defects') and ('prevention', 'preconception', 'preconception care' or 'counseling'). In addition, the references of review articles and retrieved studies were checked for further studies. Only studies published in English were eligible for inclusion.

Study selection
Study designs of evaluations included in the review
Studies with a concurrent control group who did not receive PCC were eligible for inclusion. Both prospective and retrospective cohort studies were included in the review.

Specific interventions included in the review
Studies that had a PCC intervention were included. Three studies included an early in-patient phase for PCC followed by out-patient care, while the remaining 13 studies focused on out-patient care alone. There were several different approaches to the type and duration of PCC. Interventions included the use of the following: screening for retinal and renal disease; specific contraceptive advice; advice to delay conception until glucose levels were optimised; special dietary advice; advice regarding the quantity and route of daily insulin injections; advice to target blood glucose levels; and supplemental folic acid use.

Participants included in the review
Women with pregestational DM, with at least 50% with type 1 DM, were included. Most of the participants had type 1 DM, but 3 studies also included women with type 2 DM. The mean age of women who received PCC was 27 years, an average of 1.8 years older than those who did not receive PCC.

Outcomes assessed in the review
Studies that reported the frequency of major congenital anomalies were included. A major congenital anomaly was typically defined as one which causes death, or a serious handicap necessitating surgical correction or medical therapy.

How were decisions on the relevance of primary studies made?
The authors did not state explicitly how the papers were selected for the review, but did report that two authors independently conducted the searches.

Assessment of study quality
The authors did not state that they assessed validity, but the blinding of study investigators (infant examiners) was recorded.

Data extraction
Two reviewers extracted the data; the authors did not state whether this was undertaken independently. Data on the frequency of major and minor congenital anomalies, and the earliest available first-trimester glycosylated haemoglobin
values in the PCC and non-PCC groups, were also included where available. In situations where the standard deviation (SD) of the mean was not provided, the SD was approximated from the average SD of all other studies.

**Methods of synthesis**

How were the studies combined?
The unadjusted relative risk (RR) and its 95% confidence interval (CI) were calculated, and then pooled using the random-effects model of DerSimonian and Laird. The crude event rates in the PCC and non-PCC groups were also pooled using a random-effects model. Continuous data were pooled using an inverse variance-weighted method.

How were differences between studies investigated?
Heterogeneity across the studies was assessed using the Breslow and Day test, with statistical significance set at a P-value of less than 0.20. Three sensitivity analyses were also undertaken: the first excluded all retrospective studies; the second excluded study programmes that had an in-patient phase; the third only included studies where investigators were blind to maternal PCC status during the assessment of congenital malformations.

**Results of the review**

Eight prospective and 8 retrospective cohort studies (total number of offspring in the analysis = 2,651) were included.

Among 2,104 offspring, the crude pooled rate of major and minor anomalies was 2.4% (95% CI: 1.2, 4.6) in the PCC group, compared with 7.7% (95% CI: 6.3, 9.4) in the non-PCC group; the RR was 0.32 (95% CI: 0.17, 0.59). Among 2,651 offspring, the crude pooled rate of major malformations was lower in the PCC group (2.1%, 95% CI: 1.4, 3.2) than the non-PCC group (6.5%, 95% CI: 1.4, 9.2); the pooled RR was 0.36 (95% CI: 0.22, 0.59).

When the results of the 8 prospective studies were considered alone, the risk for major malformations remained significantly lower among PCC recipients than non-recipients (RR 0.42, 95% CI: 0.24, 0.74). When the 3 in-patient studies were excluded, there was a significantly lower risk for both major (RR 0.36, 95% CI: 0.22, 0.60) as well as major and minor (RR 0.29, 95% CI: 0.12, 0.72) congenital anomalies among PC recipients. When the studies in which infant examiners were blind to the mothers' PCC status, there was a significantly lower risk for major malformation in the PCC group (RR 0.38, 95% CI: 0.17, 0.87).

Seven studies also reported on the early first trimester glycosylated haemoglobin (HbA1 and HbA1c) values in the PCC and non-PCC groups. In each study, the mean glycosylated haemoglobin level was lower in the PCC group, as was the pooled absolute mean difference (2.3%, 95% CI: 2.1, 2.4). However, heterogeneity was present in this pooled estimate.

**Cost information**
The authors quoted cost data from other studies. One compared the combination of PCC plus prenatal care with prenatal care alone, and found a net cost-saving of $1,720 (1989 US$) per hypothetical enrollee, with a desirable benefit-cost ratio of 1.86. More recent estimates using real-time, direct cost measures suggested a saving of approximately $34,000 (1992 US$) per PCC (see Other Publications of Related Interest nos.1-2).

**Authors' conclusions**

Out-patient PCC probably reduces the risk of major congenital anomalies among the offspring of women with pregestational DM.

**CRD commentary**
The authors addressed a well-defined review question in terms of the interventions, participants and outcome measures. The literature search was restricted to studies published in English only. This means that publication and language bias could have been introduced and that other relevant studies might have been missed. The observational (cohort) studies included in the review were appropriate to the question addressed. However, the authors' conclusions were based primarily on a meta-analysis of these observational data, without adequate attention to potential sources of confounding.
and bias in the individual studies. Such an approach is frequently associated with an over-estimation of the treatment effects (see Other Publications of Related Interest no.3).

**Implications of the review for practice and research**

**Practice:** The authors stated that because many women with diabetes neither plan their pregnancy nor achieve adequate glycaemic control before conception, strategies are needed to improve access to PCC programmes and to maximise those interventions associated with improved pregnancy outcome (e.g. smoking cessation and folic acid use).

**Research:** The authors stated that in order to optimally address some of the issues raised in the review, a large multicentre cohort study should be conducted to collect important information about the influence of PCC on adverse pregnancy outcomes.

**Bibliographic details**


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**Other publications of related interest**


**Indexing Status**

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**MeSH**

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