A systematic review of the effectiveness of antenatal care programmes to reduce infant mortality and its major causes in socially disadvantaged and vulnerable women

Final Report

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Executive summary

The systematic review described in this report is part of a programme of work, commissioned by the Department of Health, to strengthen the evidence base on interventions to reduce infant mortality, with a particular focus on reducing inequalities in infant mortality.

Aim

To identify the best available evidence on the effectiveness of interventions focused on the delivery and organisation of antenatal care to reduce infant mortality, or one of its three major causes (preterm birth (PTB), congenital anomalies, sudden infant death syndrome/ sudden unexpected death in infancy (SIDS/SUDI)) in:

- socially disadvantaged and vulnerable groups of women; and
- other groups defined in terms of pre-specified risk factors for adverse birth outcomes where the risk factor is strongly associated with social disadvantage.

Methods

Searches

We searched the major bibliographic databases, specialist databases and online resources to identify primary reports and relevant secondary sources (guidelines, HTA reports, Cochrane reviews). We additionally checked reference lists and citations of included studies and of relevant guidelines and systematic reviews.

Inclusion criteria

Studies which met the following criteria were eligible for inclusion.

Population

- Study evaluated the intervention in a relevant disadvantaged or vulnerable population.
- Population recruited in a member country of the Organisation for Economic Co-operation and development (OECD), but excluding Turkey and Mexico.

Intervention

- Study evaluated an antenatal care programme involving the provision of health or social care to pregnant women, but not:
  - clinical interventions, unless evaluated in the context of a broader antenatal care programme
  - interventions with a focus on labour/birth or on the periconceptional period
  - interventions aiming to improve the outcome of a subsequent pregnancy
  - interventions which only involved opiate substitution including methadone

Comparator

- Study included a control/comparator group(s) receiving 'standard' comprehensive antenatal care or a specified alternative model of comprehensive antenatal care.

Outcome

- Study evaluated the effect of the intervention on one of the following outcomes:
  - PTB/preterm labour
  - neonatal/infant mortality
  - presence of any congenital anomalies in liveborn infants
  - SIDS/SUDI.

Quality assessment

Internal validity was assessed as 'good', 'mixed' or 'poor' using the GATE checklist. Randomised controlled trials (RCTs) were rated by a single reviewer; observational studies were rated by two reviewers.

Results

Forty articles relating to 36 distinct interventions/evaluations met the inclusion criteria:

- Twenty-six (72%) of the studies were conducted in the USA, four in Australia, four in the UK, one in Canada and one in Greece.
- The vast majority (89%) of studies reported PTB/preterm labour as an outcome (81% PTB, 8% preterm labour); eleven (31%) reported infant mortality or neonatal mortality. Six studies (17%) reported the occurrence of congenital anomalies. None of the studies reported deaths from SIDS/SUDI.
- Nine (25%) of the studies were randomised controlled trials (RCTs) (seven individually randomised, two cluster randomised), six were prospective cohort studies, twelve were retrospective cohort studies, two were cohort studies (unspecified), one had a mixed prospective/retrospective design and six were before and after studies, two of which included some form of contemporaneous geographical comparator group, and one of which included a geographical comparator group during the 'after' period only.
- Eight of the nine RCTs were assessed as having 'good' or 'mixed' internal validity, and one was rated 'poor'. Of the 27 observational studies, six were assessed as having 'mixed' internal validity and 21 as 'poor'.
- Twenty studies related to interventions targeting and/or evaluated in socioeconomically disadvantaged populations: 12 of these were aimed at disadvantaged pregnant women in general, and eight were aimed at disadvantaged women with additional clinical risk factors for PTB. Seventeen of these 20 studies were conducted in the USA, with most targeting medically indigent and/or Medicaid eligible women.
- Sixteen primary reports related to interventions targeting or evaluated in specific, predominantly disadvantaged groups at risk of adverse pregnancy outcomes: nine targeted pregnant teenagers, four targeted pregnant substance users, two targeted pregnant indigenous Australians, and one targeted pregnant women who were HIV positive. One secondary report provided data on the effectiveness of an intervention in a subgroup of substance using, HIV positive women.

The interventions studied fell under the broad headings summarised below.

Socioeconomically disadvantaged pregnant women	
• without risk factors for PTB	**Comprehensive antenatal care:** • Group antenatal care • Comprehensive multidisciplinary service with outreach • Nurse/midwife clinic for low risk women • Other US public antenatal care programme **Programmes provided as an adjunct to comprehensive antenatal care:** • Case management/care co-ordination • Nurse home visits • 'Healthy Start' programme

Socioeconomically disadvantaged pregnant women	
• with risk factors for PTB	**Clinic-based PTB programmes providing enhanced care to higher risk women:** • Broad, multifaceted enhanced care programme • PTB prevention programme primarily focusing on patient education regarding signs of preterm labour plus additional visits/pelvic examinations • Hospital clinic vs. 'managed care' **Programmes provided as an adjunct to comprehensive antenatal care:** • Home visits/telephone support
Specific populations of interest	
• Teenagers	• 'Teen' clinic • Adolescent group antenatal care *(CenteringPregnancy)* • Stand alone nutritional intervention
• Substance users	• Substance abuse programme provided as an adjunct to standard antenatal care • Comprehensive care in accredited general antenatal clinic providing an enhanced range of services
• Indigenous women	• Culturally sensitive comprehensive antenatal care including community/outreach services
• Low-income, HIV positive women	• Comprehensive care in accredited general antenatal clinic providing an enhanced range of services

Effectiveness

Socioeconomically disadvantaged women – comprehensive antenatal care

Of the four studies that were assessed as having adequate interval validity, two assessed group antenatal care, one assessed an antenatal care model involving outreach, and one evaluated a managed care model of providing antenatal care.

Group antenatal care: Two linked studies evaluated the group care model: the first an observational study conducted in clinics serving low-income, predominantly minority women in Atlanta, Georgia and New Haven, and the second a larger RCT conducted at university-affiliated hospitals in Connecticut and Georgia. The initial evaluation was inconclusive, largely because of the potential risk of selection bias and the lack of study power. The subsequent trial reported a significant reduction in PTB in the group care arm (adjusted odds ratio 0.67, 95% confidence interval (CI) 0.44-0.98).

Comprehensive antenatal care with outreach: An observational evaluation of the Temple Infant and Parent Support Services (TIPPS) programme, a 'customised' comprehensive multidisciplinary service designed to meet the specific needs of the local population in North Philadelphia, Pennsylvania, reported a statistically significant effect on PTB (4.3% preterm vs. 12% in those not enrolled in TIPPS). Because of the risk of selection bias the reviewers considered the findings inconclusive but consistent with a possible beneficial effect.

Managed care: One study (a before and after study with a contemporaneous comparison group) evaluated a 'managed care' model of delivering antenatal care in one US state (Tennessee) against a standard antenatal care model in an adjacent

state (North Carolina). The study did not provide evidence of a beneficial effect of managed care on either PTB or neonatal mortality although some implementation problems occurred during the evaluation which may have affected the outcome.

Socioeconomically disadvantaged women – 'add on' interventions

Of the three studies considered to have good or adequate internal validity, one evaluated the effect of case management/care coordination on infant mortality, and two (one individually randomised RCT and one cluster randomised RCT) evaluated the effect of nurse home visiting programmes on PTB. One of the evaluations of nurse home visiting also reported neonatal mortality but was not adequately powered to detect an effect on this outcome.

Case management/care coordination: A retrospective observational evaluation of a care coordination programme provided to Medicaid recipients in North Carolina reported a statistically significant effect on infant mortality (9.9 deaths per 1000 live births vs. 12.2 per 1000 (unadjusted)). The reviewers considered the findings inconclusive but consistent with a possible beneficial effect of the intervention on infant mortality.

Nurse home visits: Two studies evaluated the effect of nurse home visits: the first a well-designed RCT to evaluate the antenatal home visiting component of the *Prenatal and Early Childhood Nurse Home Visitation Program* in Tennessee; and the second a cluster RCT of the antenatal component of a home visiting programme with a focus on nutritional education, delivered to an isolated rural population in Northern Greece. The first trial provided no evidence of a beneficial effect on PTB (11% PTB in the intervention group vs. 13% in the comparator group; adjusted odds ratio 0.8 (95% CI 0.6-1.2)) and the second trial reported a significant effect on PTB (3.7% PTB in the intervention group vs. 8.3% in the comparator group, $p<0.04$, but no adjustment for clustering). Findings relating to the effectiveness of the home visiting programme evaluated in this latter study were assessed as inconclusive but consistent with a possible beneficial effect of the intervention on PTB.

Clinic-based PTB programmes providing enhanced care to higher risk women

Of the five evaluations of clinic based programmes two were considered to have adequate internal validity. Both of these evaluated 'multifaceted PTB prevention programmes'.

Broad, multifaceted enhanced care programmes: Two studies evaluated broad, multifacteted PTB prevention programmes targeting a range of risk factors: the first a cluster randomised RCT and the second an individually randomised RCT. An evaluation of the *West Los Angeles Preterm Prevention Project* reported a statistically significant reduction in PTB, based on a *one-sided test* for an intervention effect (7.4% PTB in the intervention clinics vs. 9.1% in the control clinics, p=.063; adjusted odds ratio 0.78, *two-sided* 95% CI 0.58-1.04); while the evaluation of an augmented antenatal programme in Alabama reported a non-significant reduction in PTB (10.6% PTB vs. 14%). Findings of the former evaluation were considered inconclusive but consistent with a possible beneficial effect of the intervention on PTB. The latter study was inconclusive.

Other PTB prevention programmes aimed at socioeconomically disadvantaged women with additional clinical risk factors for PTB

All three of the studies that evaluated non clinic-based PTB prevention programmes were considered to have adequate internal validity.

Home visits: An RCT of home visits/social support in Western Australia did not demonstrate a significant beneficial effect on PTB overall (odds ratio 0.84; 95% CI 0.65-1.09), and the stratified analysis by social class suggested that the beneficial effect, if any, was confined to the most advantaged women in the study. Odds ratios for women classified as 'clerical' and 'manual' were close to one. A second trial of a similar intervention in the UK similarly found no effect on PTB (18% PTB in the intervention group vs. 19% in the usual care arm; odds ratio not reported).

Telephone support: An RCT of telephone assessment/advice in North Carolina also found no significant beneficial effect on PTB overall but a subgroup analysis (assumed to have been pre-specified) showed a beneficial effect in a subgroup of black women aged ≥19 years (relative risk 0.56, 95% CI 0.38-0.84).

Antenatal care interventions targeting specific vulnerable/at risk populations

Of the 16 studies that evaluated interventions in specific populations, only three were considered to have adequate internal validity.

Teenagers: An observational evaluation of the *Higgins Nutrition Intervention Program* in adolescents reported a substantial, statistically significant effect on PTB (<37 weeks) (adjusted odds ratio 0.59, 95% CI 0.45-0.78) and on early PTB (<34 weeks) (adjusted odds ratio 0.53, 95% CI 0.35-0.81). Although the study was inconclusive due to the risk of selection bias, the reviewers considered the findings consistent with a possible beneficial effect on PTB.

HIV positive substance users: The observational evaluation of the *Prenatal Care Assistance Program* (PCAP) reported a significant effect on PTB (<37 weeks) in substance-abusing, HIV positive women attending a PCAP-accredited clinic compared with those who received care in a non-PCAP participating clinic (adjusted odds ratio 0.57, 95% CI 0.34-0.97). The reviewers considered that the evidence was inconclusive due to the risk of selection bias but consistent with a possible beneficial effect of the intervention on PTB.

HIV positive women: A second observational evaluation of the *Prenatal Care Assistance Program* (PCAP) reported a significant effect on PTB (<37 weeks) in HIV positive women attending a PCAP-accredited clinic compared with those who received care in a non PCAP-participating clinic (adjusted odds ratio 0.53, 95% CI 0.40-0.70). The reviewers considered that the evidence was inconclusive due to the risk of selection bias but consistent with a possible beneficial effect of the intervention on PTB in both the populations studied.

Conclusions

We found no evidence relating to the effect of antenatal care interventions on mortality from SIDS/SUDI and limited evidence relating to effects on congenital anomalies.

We found insufficient evidence of adequate quality to conclude that interventions involving alternative models of organising or delivering antenatal care reduce infant mortality or PTB in socially disadvantaged or vulnerable populations compared with standard models of antenatal care. A small number of the interventions reviewed were considered 'promising' in terms of their effect on PTB in socially disadvantaged or vulnerable populations, but the effects, if any, are likely to be modest and further robust evaluation would be required before routine adoption of these interventions could be recommended in the NHS.

A systematic review of the effectiveness of antenatal care programmes to reduce infant mortality and its major causes in socially disadvantaged and vulnerable women

1 Introduction

The systematic review described in this report is part of a programme of work, commissioned by the Department of Health, to strengthen the evidence base on interventions to reduce infant mortality, with a particular focus on reducing inequalities in infant mortality. The review focuses on interventions involving the delivery or organisation of antenatal care as a means of reducing infant mortality or its three major causes (preterm birth (PTB), congenital anomalies, sudden infant death syndrome/sudden unexpected death in infancy (SIDS/SUDI)) in disadvantaged and vulnerable women.

2 Background to the review

In recent years, infant mortality in England and Wales has shown a steady decline from around 12 deaths per 1000 live births in 1980 to 4.7 deaths per 1000 live births in 2007. But throughout this period infant mortality has shown a marked and persistent socioeconomic gradient with the highest rates occurring in the most socioeconomically disadvantaged groups. In 2007, for example, the infant mortality rate amongst those in 'routine and manual' social groups was 5.2 deaths per 1000 live births, compared with 3.0 deaths per 1000 births amongst those in 'managerial and professional' occupations and 3.7 deaths per 1000 births amongst those in intermediate occupations. A number of other disadvantaged and vulnerable groups also suffer disproportionately high rates of infant mortality and other adverse perinatal outcomes or are known to have a high prevalence of risk factors for poor pregnancy outcome/infant health: these include teenagers,[1,2] certain black and minority ethnic populations,[2,3] homeless women,[4,5] prisoners,[4,6] victims of domestic violence,[7] asylum seekers and refugees,[4] women with mental illness[8] and women with substance abuse problems.[4,9,10]

A review of UK interventions to improve perinatal outcomes in disadvantaged groups found limited UK evidence of effective and promising interventions for disadvantaged childbearing women.[4] A further scoping review of the international effectiveness literature conducted by the NPEU in 2008 confirmed the paucity of relevant systematic review level evidence relating to disadvantaged populations.

Immaturity related conditions and congenital anomalies together account for 75% of infant deaths in England and Wales. Both groups of conditions are associated with socioeconomic disadvantage: the risk of PTB[11] and infant mortality rates from immaturity related conditions show a clear socioeconomic gradient[i] (although the proportions of infant deaths attributable to immaturity does not vary markedly by socioeconomic status[1]); and non-chromosomal anomalies in general, including neural tube defects, are significantly more common in less affluent areas of the UK.[12]

Antenatal care is generally thought to be an effective method of improving outcomes in pregnant women and their babies, although many specific antenatal care practices have not been subject to rigorous evaluation.[13] One review from the early 1990s evaluated 'prenatal care packages' [14] but found only five studies of adequate quality which evaluated

i Unpublished analysis of ONS data (table 12, Series DH3, no 40)

the effect of the programme on gestational age at birth and/or infant mortality, two of which (Nurse Home Visitation [15]; and case management[16]) were found to have a positive effect on the relevant outcome measure.

Other systematic reviews have evaluated the effect of specific antenatal care packages on PTB and infant mortality, including:

- Changes in the delivery of antenatal care to Australian indigenous women.[17]
- Telephone support for pregnant and postpartum women, covering effects nn smoking, preterm birth, low birthweight, breastfeeding, and postpartum depression.[18]
- Social support for pregnant women who are believed to be at risk of giving birth to preterm or low birthweight babies.[91]
- Home visits offering social support to high-risk women or providing medical care to women with complications.[19]
- Continuity of caregiver during pregnancy and childbirth (two reviews[20,21]).
- Timing and frequency of antenatal care visits (3 reviews, all with an emphasis on the safety of reducing the number of routine antenatal visits in low risk women[22-24]).

These reviews found that telephone support,[18] home visits/social support[19,91] and continuity of care[20,21] had beneficial effects on a range of measures of maternal and infant health and wellbeing, but none of these interventions was found to have a statistically significant effect on infant mortality or PTB. The review by Rumbold et al.[17] found some studies that reported beneficial effects of some interventions targeting Australian indigenous women, but the authors concluded that the evidence was flawed.

2.1 Aims of the review

In the light of the paucity of up to date evidence relating to the effectiveness of antenatal care programmes as a means of reducing infant mortality in disadvantaged and vulnerable groups of women, the aim of this review was:

> *To identify the best available evidence on the effectiveness of interventions focused on the delivery and organisation of antenatal care to reduce infant mortality, or one of its three major causes (PTB, congenital anomalies, SIDS/SUDI) in:*
>
> - *socially disadvantaged and vulnerable groups of women; and*
> - *other specified groups defined in terms of pre-specified risk factors for adverse birth outcomes where the risk factor is strongly associated with social disadvantage*

3 Definitions and scope of the review

3.1 Antenatal care

Antenatal care may be broadly defined as encompassing pregnancy-related services provided between conception and the onset of labour with the aim of improving pregnancy outcome and/or the heath of the mother or child. This care involves a series of assessments and appropriate treatments[25] covering three components:

- monitoring of the health status of the woman and the fetus;
- provision of medical and psychosocial interventions and support;
- health promotion.

Given the context of the Infant Mortality Project, we were primarily interested in interventions which might be implemented in the context of the NHS. We therefore restricted the review to antenatal care interventions involving the delivery or organisation of health or social care to pregnant women.

Additionally, because we were primarily interested in interventions which might strengthen or enhance antenatal health care, we considered 'stand alone' antenatal care interventions, such as social support programmes, only where they were delivered and/or evaluated in conjunction with some form of normal antenatal health care.

Clinical interventions, such as drug therapies (for example, to treat genito-urinary infections, to prevent or delay labour or for fetal maturation, vitamins and nutritional supplements have been extensively reviewed[26] so were excluded unless they formed part of a broader package of antenatal care.

Methadone/opiate substitution programmes were also explicitly excluded since an initial scoping review of the literature indicated that many of the evaluations concerned the safety of such programmes rather than their effectiveness in terms of improving infant outcomes.

Finally, because some interventions may be initiated pre-conceptionally but continue through into pregnancy, and others may commence prior to the onset of labour but be primarily concerned with labour and delivery, we explicitly excluded peri-conceptional interventions and interventions with a focus on labour and birth.

3.2 Standard antenatal care

Our aim was to evaluate interventions against 'standard antenatal care' (typically involving periodic attendance at a hospital or office based ambulatory clinic). However, because of the range of different healthcare systems covered and the nature of some of the target populations (e.g. substance users) we did not attempt to further define what constituted 'standard care': we required only that the control/comparator group received some form of comprehensive antenatal care or a specified alternative model of comprehensive antenatal care.

3.3 Disadvantaged and vulnerable groups

Our aim was to cover interventions targeting and/or evaluated in disadvantaged populations at high risk of adverse perinatal outcomes, including both socioeconomically deprived and vulnerable groups of women and specific groups such as teenagers, women with mental illness and women with substance use problems who also suffer disproportionately high rates of infant mortality and other adverse perinatal outcomes.[4] These groups included:

a) Disadvantaged and vulnerable women:
   - Disadvantaged minority ethnic/racial groups
   - Women in prison
   - Travellers
   - Homeless women
   - Asylum seekers and refugees
   - Recently arrived migrants
   - Other immigrant groups
   - Victims of abuse
   - Women living in deprived areas
   - Women with mental illness/mental health problems
   - Women with learning disabilities
   - Sex workers

b) Specific groups with risk factors for adverse birth outcomes that are strongly associated with social disadvantage:
   - Teenagers
   - Obese pregnant women
   - Women who are HIV positive
   - Substance users

- Alcohol misusers

We did not include pregnant smokers as a group of interest. However, a recent Cochrane review is available covering smoking cessation interventions during pregnancy.[27]

4 Methods

4.1 Criteria for considering studies for this review

4.1.1 Types of studies

We included both experimental and observational studies and did not place any restriction on study design other than that the study had to include a control or comparator group and the study must be an effectiveness evaluation broadly addressing the review question.

4.1.2 Types of participants

We required that the study evaluated the intervention in a relevant disadvantaged or vulnerable population of pregnant women (see section 3.3).

Studies recruiting a broader population of pregnant women but which explicitly evaluated the effect of an intervention in a relevant subgroup were also included.

4.1.3 Types of intervention

We included evaluations relating to the organisation and/or delivery of:

- comprehensive antenatal care;
- components of antenatal care provided in the context of normal antenatal care;
- stand-alone interventions involving the provision of health or social care to pregnant women delivered as an adjunct to standard antenatal care.

We excluded:

- stand-alone intervention targeting pregnant women and not delivered and/or evaluated in conjunction with standard antenatal care
- clinical interventions, unless evaluated in the context of a broader package of antenatal care
- interventions with a focus on labour/birth or in the peri-conceptional period e.g. folic acid supplementation
- interventions aiming to improve the outcome of a subsequent pregnancy
- interventions which only involved opiate substitution, including methadone

4.1.4 Comparator

We required that the study included a control/comparator group receiving comprehensive antenatal care which might be either standard antenatal care or a specified alternative model of comprehensive antenatal care (e.g. 'managed care' [i]).

In the case of studies evaluating an intervention at a community level, we required that the study compared a population with **access** to the intervention with a comparator population with access only to standard antenatal care or some other specified alternative model of comprehensive antenatal care.

i Managed care plans are health insurance plans that contract with health care providers and medical facilities to provide care for members at reduced costs. For a fuller description of managed care see, for example: *http://www.americanheart.org/presenter.jhtml?identifier=4663*

4.1.5 Types of outcome measure

We included studies reporting one or more of the following outcomes:

- preterm birth or "preterm labour"
- neonatal/infant mortality
- presence of any congenital anomalies in liveborn infants
- SIDS/SUDI

We required PTB to be reported as the number/proportion of women delivering before 37 weeks or before some other cut-off point less than 37 weeks. We did not include studies that reported only a change in the mean/median gestational age at birth.

4.1.6 Language

Non-English language studies were considered for inclusion provided that an abstract was available in English.

4.1.7 Time period

Models of antenatal care have shifted in recent decades from predominantly obstetrician-led/hospital-based models of care to more diverse models with greater involvement of midwives, primary care physicians and others in the provision of antenatal care for non-high risk pregnancies. In order to focus on models of antenatal care that are relevant in the current context, we included only studies published from 1990 onwards.

4.1.8 Geographical areas

In order to focus the review on interventions relevant to the NHS, we included only interventions from high income counties with relatively low infant mortality rates and well- developed healthcare systems. We therefore included only studies conducted in Organisation for Economic Co-Operation and Development (OECD) member countries, but excluding Mexico and Turkey both of which have markedly higher infant mortality than the rest of the OECD.

4.1.9 Types of publication

We included journal articles reporting primary research in English (with or without an abstract) and also non-English journal articles with an English language abstract.

4.2 Methods for identification of studies

4.2.1 Bibliographic databases

We searched the following databases for reports of primary studies published between January 1990 and July 2008:

- Medline
- Embase
- Cinahl
- PsycINFO
- HMIC
- CENTRAL
- Database of Abstracts of Reviews of Effects (DARE)
- MIDIRS

Medline, Embase, PsycINFO and HMIC were searched using the Ovid SP interface; Cinahl, was searched using the EBSCO interface; Central and DARE were searched via the Cochrane Library; MIDIRS was searched by the MIDIRS librarian using a keyword search adapted from the MEDLINE search strategy. All searches were run in mid-August 2008

We applied limits and filters to restrict the searches to articles:

- published from 1990 onwards
- relating to human subjects
- in English (with or without an abstract) or non-English with an English language abstract

The Medline search strategy is given in Annex A. Details of searches run in other databases are available from the authors.

4.2.2 Other online searchable resources

We additionally searched the following specialist databases and online resources to identify potentially eligible primary reports and/or guidelines, reviews and reports which might contain relevant citations:

- Cochrane Database of Systematic Reviews
- Health Technology Assessment Database
- NHS Economic Evaluations Database
- System for information on Grey Literature in Europe (OpenSigle)
- National Guideline Clearing House
- National Institute for Health and Clinical Excellence (NICE)
- National Library for Health
- Health Development Agency National Institute for Health Research Service Delivery and Organisation Programme (SDO)
- Social Care Online
- Research Register for Social Care

The Cochrane Database of Systematic Reviews, the Health Technology Assessment Database and the NHS Economic Evaluations Database were all searched via the Cochrane Library advanced search facility using the Medline search strategy; all other online databases were searched using relevant keywords such as: antenatal care, prenatal care, maternity care, pregnancy, socioeconomic, vulnerable, socially disadvantaged, ethnicity, teenagers, adolescents

4.2.3 Reference lists and citations

We inspected the bibliographies of relevant guidelines, reviews and reports to identify further relevant primary reports.

Following the initial two stages of screening (see Table 1 below) the reference list of all included studies were reviewed and the full-text of any possibly relevant new studies retrieved and screened. Articles citing included studies were also identified using the ISI Web of Science database and relevant articles retrieved and screened.

4.3 Review methods

4.3.1 Screening

Table 1: Exclusion criteria applied during abstract/full-text screening

	Stage 1: Abstract/title screening	Stage 2: Full-text screening
		Stage 1 criteria PLUS:
General	• Not primary research • Not a journal article	
Population	• Not conducted in an eligible OECD country • Not pregnant women	• Intervention not evaluated in a relevant disadvantaged/vulnerable population
Intervention	• No intervention • Not an antenatal care intervention • Intervention focus on labour/birth	• Not a relevant antenatal care intervention, for example: - standard antenatal care only - ineligible clinical intervention - peri-conceptional intervention - methadone/opiate substitution
Comparator	• No comparator/control group	• Comparator population did not receive antenatal care
Outcome	• No potentially relevant quantitative outcome	• Relevant outcome (PTB, infant mortality, etc.) not reported or not reported in all relevant study groups/ populations
Other	• Not an effectiveness evaluation	• Relationship between antenatal care and outcome assessed but not an effectiveness evaluation, e.g. epidemiological association/risk factor study

Abstracts were screened independently by two reviewers using the exclusion criteria shown in Table 1. Discrepancies were discussed and the opinion of a third reviewer sought where necessary. Where there was lack of agreement following discussion, the article was included for full-text review.

Full-text of all remaining articles was retrieved and reviewed independently by two reviewers using the *exclusion* criteria shown in Table 1; the opinion of a third reviewer was sought if there were disagreements or queries.

Finally, the following two *inclusion* criteria were independently applied to the remaining articles by two reviewers with the opinion of a third reviewer sought in the case of disagreements:

- Does the study evaluate an intervention involving the organisation and/or delivery of:
  - comprehensive antenatal care;
  - a component of antenatal care provided in the context of normal antenatal care; or
  - a stand-alone intervention providing health or social care to pregnant women provided as an adjunct to (i.e. evaluated in conjunction with) standard antenatal care or some other specific model of antenatal care?

- Is this study designed to assess whether the study intervention affects the risk of an outcome of interest in a population of interest compared with standard antenatal care or some other specific model of antenatal care?

4.3.2 Quality assessment

Internal validity was assessed using the 'Graphical appraisal tool for epidemiological studies' (GATE) developed by Jackson and colleagues.[28] GATE is a generic quality appraisal tool which can be applied to a wide range of experimental and observational study designs[29] and thus avoided the need to use different tools according to the study design.

Randomised studies were assessed by a single reviewer; observational studies were assessed independently by two reviewers. Each reviewer completed the checklist and assigned an overall assessment of internal validity according to the GATE criteria:

++	Good: well reported and reliable
+	Mixed: some weaknesses but insufficient to have an important effect on usefulness of the study
-	Poor: study not reliable, not useful

Where the two assessments (observational studies only) differed, a third reviewer with particular expertise in observational research re-assessed the studies and a final rating was assigned following review and discussion of the three independently completed checklists.

Prior to undertaking the study GATE assessments, reviewers completed and discussed a minimum of five 'training assessments' to ensure that the tool was being correctly and consistently applied.

4.3.3 Data extraction

A data extraction and coding form was developed and loaded into the Eppi-Reviewer software.[30] Descriptive data were extracted and entered into Eppi-Reviewer by one reviewer; data were checked by a second reviewer. Outcome data were extracted and coded independently by two reviewers and checked for agreement.

4.3.4 Assessment of evidence of effectiveness

4.3.4.1 Authors' conclusions

Two reviewers independently assessed the authors' conclusions regarding the effect of the intervention on the main outcomes of interest (PTB and infant/neonatal mortality):

+	Statistically significant beneficial effect on PTB/infant mortality
(+)	Effect consistent with beneficial effect but effect not statistically significant and/or cautious interpretation of finding suggested
X	No evidence of beneficial effect
0	No conclusion stated
N/A	Not applicable – outcome not assessed

Reported conclusions regarding the effects on the incidence of congenital anomalies and SIDS/SUDI were not assessed because in the few instances where one of these outcomes was reported, the sample size was too small for the author to draw a conclusion.

4.3.4.2 Reviewers' assessment of effectiveness

The same two reviewers assessed and coded the evidence of effectiveness, taking into account the strength and limitations noted in the GATE checklist.

+	Study demonstrates a beneficial effect on PTB/Infant Mortality

(+?) Study inconclusive but may demonstrate a beneficial effect

X Study does not provide convincing evidence of a beneficial effect

N/A Not applicable – outcome not assessed

Discrepancies in coding were resolved by discussion with the opinion of a third reviewer sought where necessary.

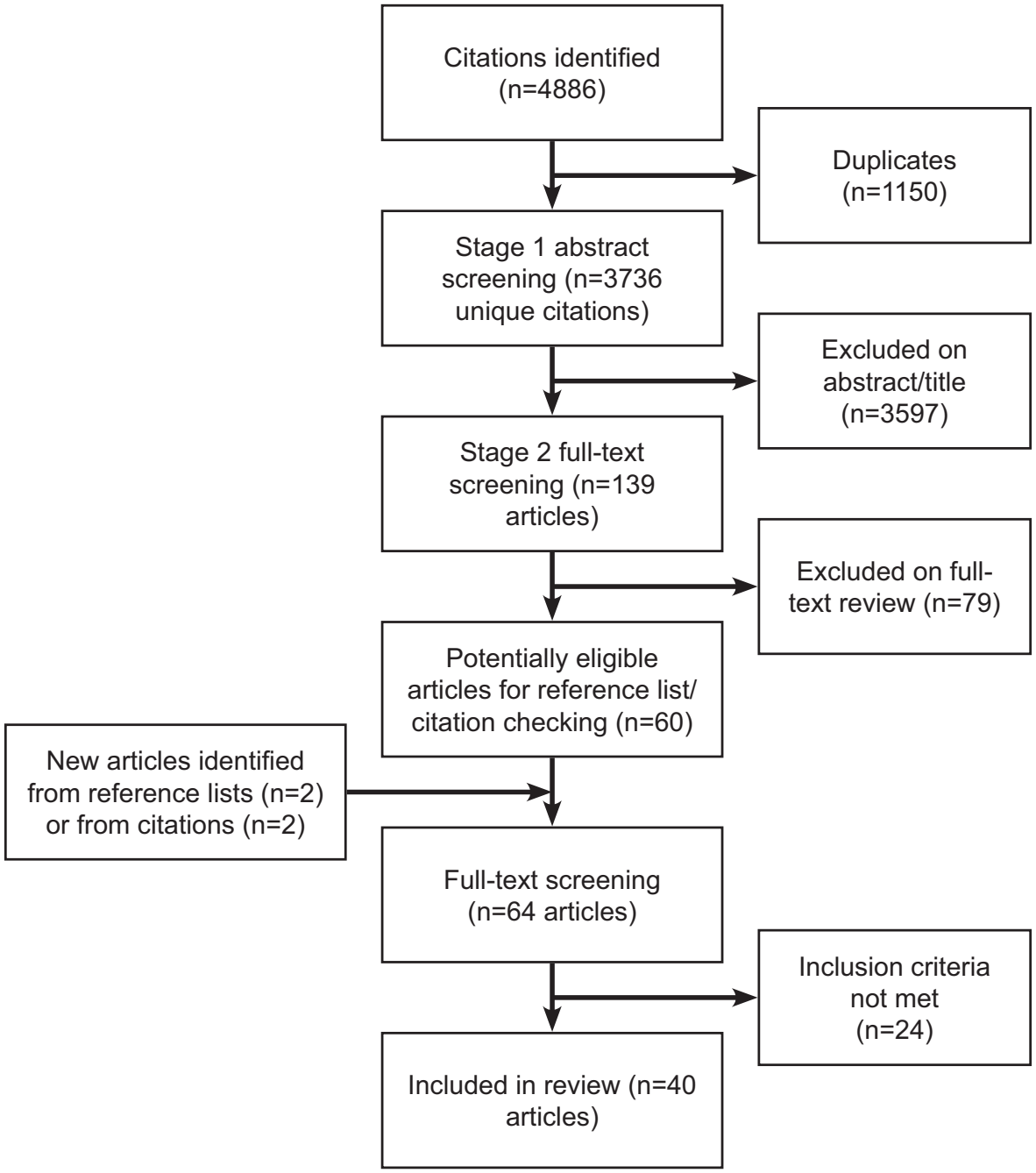
The evidence of effectiveness was assessed only for studies having 'adequate' internal validity ('good' or 'mixed' GATE quality assessment). Studies rated as having poor internal validity (i.e. GATE quality assessment 'Poor: study not reliable, not useful') were not considered further.

5 Results

Our initial searches identified 4886 citations of which 1150 were duplicates, yielding 3736 unique citations. Of these, 3597 were excluded on title/abstract alone and a further 79 were excluded following initial full-text review. Four new articles were identified from the reference lists and citations of the 60 articles which remained after the first round of full-text review (see Figure 1).

Of these, 18 were excluded because they involved stand alone interventions which were not evaluated in conjunction with antenatal care (or the reviewers considered that it was unclear whether or not the intervention was provided in conjunction with antenatal care); and six were excluded because the design failed to meet the review criteria for an eligible effectiveness evaluation. Forty reports satisfied all eligibility criteria.

Figure 1: Screening flow chart



Reasons for exclusion are summarised in Table 2.

Table 2: Reasons for exclusion during screening

	Number excluded	
	Screened on:	
	Title/abstract	Full-text
General		
Not primary research	997	5
Not a journal article	3	
Population		
Not OECD	758	1
Not relevant population (pregnant women)	153	
Intervention		
No intervention	1345	
Not antenatal care intervention	2	4
Management of labour/birth	13	2
Standard antenatal care only		2
Ineligible clinical intervention		15
Peri-conceptional intervention		6
Methadone or opiate substitution		3
Comparator		
No comparator/control group	106	6
Care in comparator group not standard antenatal care		1
Outcome		
No relevant outcome	126	15
Outcome not reported in relevant population		16
Other		
Not effectiveness evaluation	94	3
Did not meet inclusion criteria:		
Stand alone intervention - not delivered/ evaluated in conjunction with antenatal care or unclear if delivered/evaluated in conjunction with antenatal care.		18
Study not designed to address review questions		6
TOTAL EXCLUDED	**3597**	**103**

5.1 Overview of included studies

We identified 40 eligible publications relating to 36 distinct interventions and/or studies (designated 'primary studies'). Of the four 'duplicate' reports, one reported less comprehensive findings from an earlier 'interim' analysis,[31] one was a report of a cost-benefit analysis and provided no new effectiveness data,[32] one provided effectiveness data for a subgroup of substance using women who were also included in a separate evaluation of the same intervention in a broader population,[33] and one provided data from a single site in a multi-centre trial.[34] For these four interventions/studies we designated the most comprehensive and/or relevant report as the primary report (Panaretto et al.[69] took precedence over Panaretto et al.[31]; Moore et al.[39] took precedence over Muender et al.[32]; Turner et al.[59] took precedence over Newschaffer et al.[33]; and the Collaborative Group on Preterm Birth Prevention report[35] took precedence over Goldenberg et al.[34].

Two of these secondary reports included additional data supplementing that provided in the 'primary' reports: Newschaffer et al.[33] reported outcome data on HIV positive substance users and Goldenberg et al.[34] reported neonatal mortality data which were not included in the later Collaborative group report.[35] We include these data where appropriate.

The following descriptive sections relate to the 36 included primary studies, unless otherwise stated.

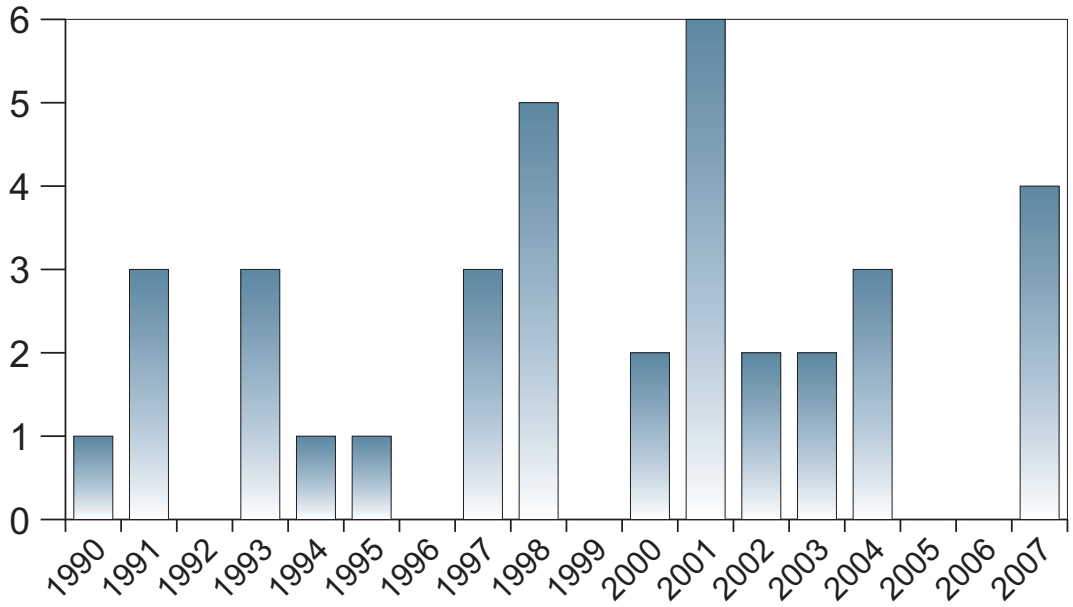
5.1.1 Countries

Just under three quarters of the included studies (26 of 36) were conducted in the USA, 4 in Australia, 4 in the UK, 1 in Canada and 1 in Greece.

5.1.2 Year of publication/study

Included studies were published between 1990 (the start year for the searches) and 2007. There was no marked temporal trend in year of publication (Figure 2).

Figure 2: Year of publication



Only 31 studies explicitly reported the study recruitment/eligibility period: of these 8 (26%) were completed before 1990, a further 17 (55%) were completed before 2000, and the remaining six (19%) were completed between 2000 and 2005. Just over half of the studies (17/31) were completed in 1995 or earlier.

5.1.3 Study design

Nine (25%) of the studies were randomised controlled trials (7 individually randomised,[35-41] 2 cluster randomised[42,43]), 6 were prospective cohort studies,[44-49] 12 were retrospective cohort studies,[16,50-60] two were cohort studies (unspecified),[61,62] one had a mixed prospective/retrospective design,[63] and six were before and after studies,[64-69] two of which included some form of contemporaneous geographical comparator group,[64,66] and one of which included a geographical comparator group during the 'after' period only.[69]

Most of the evaluations (28 of 36) compared outcomes in women who had received the intervention (or had been randomised to receive the intervention) with women who had not received the intervention (or had been randomised to receive 'standard care'); five of the evaluations compared outcomes in populations of women with and without **access** to the intervention [56,61,64,66,67] (i.e. women with access to the intervention were compared with women without access to the intervention); and in two[53,68] it was not possible to determine with certainty which of these two categories applied.

5.1.4 Control/comparator

In all instances, by definition, the comparator/control group received (or had access to in the case of studies comparing women with and without access to the intervention) some form of standard antenatal care. The care received was not always fully described but most commonly involved antenatal care provided in some form of antenatal clinic. Two studies compared one model of antenatal care against another specified model ('fee for service' model vs. 'managed care' [52,64]) and in one of the studies in substance users, all study subjects (intervention and comparator groups) received enhanced antenatal care provided by an antenatal substance abuse programme.[44] The latter study evaluated the addition of drug rehabilitation services to women in the programme.

5.1.5 Outcome measures

The numbers of primary studies reporting each of the four outcome measures of interest are summarised in Table 3. The vast majority (89%) of studies reported PTB/preterm labour as an outcome. In 27 of these 32 studies, PTB was defined as birth before 37 weeks; in two, PTB was not defined;[38,44] and in three, the study reported preterm labour,[49,51,60] with only one of these three explicitly defining this as premature onset of labour before 37 weeks gestation.[49]

Four of the studies additionally reported on early PTB (PTB <28 weeks, 28-33 weeks, 34-36 weeks;[65] PTB <34 weeks;[54] PTB <33 weeks, 33-36 weeks;[45] PTB <28 weeks, 28-32 weeks, 33-36 weeks[41]).

Table 3: Reported outcome measures

	Number of studies reporting outcome
PTB/preterm labour	32
Infant mortality	5
Neonatal mortality	6
Congenital anomalies	6

Five of the studies reported infant mortality as an outcome, and one reported postneonatal deaths before hospital discharge in addition to neonatal deaths.[36] Four of the five studies reporting infant mortality[16,53,56,64] were evaluations of Statewide Medicaid/welfare-based programmes in the USA which were considered to have limited or uncertain relevance to the NHS. Only one study[64] reported neonatal mortality as a primary outcome.

Six studies reported congenital anomalies as an outcome.[38,43,44,49,54,68] This outcome is not considered further in this review because the low event rate, small combined sample size across studies and diversity of interventions meant that no conclusions could be drawn regarding intervention effects on this outcome.

5.1.6 Quality

Eight of the nine randomised controlled trials (RCTs) were assessed as having 'good' (two trials[37,41]) or 'mixed' (6 trials[36,38-40,42,43]) internal validity, and one was rated 'poor'.[35]

Inter-rater reliability of the GATE tool was found to be poor for the observational studies, with 7 of 27 initial ratings found to be discordant. All discrepancies between the two initial reviewers were in the same direction, indicating that the two reviewers systematically applied different thresholds for 'adequate' internal validity. The discordant ratings were resolved following the procedures described in section 4.3.2.

Of the 27 observational studies, 6 were assessed as having 'mixed' internal validity[16,45,48,54,59,64] and 21 as 'poor'.[44,46,47,49-53,55-58,60-63,65-69] Of the 21 studies rated as 'poor', thirteen (see Table 4) were noted to have at least one major design weakness or flaw.

Table 4: Observational studies - major design weaknesses/flaws

Design weakness/flaw	Number of studies
Before and after (BA) study - no protection against effects of secular changes[65,67-69]	4
Comparator and intervention populations differ[51,53,56]	3
Comparator population consists of individuals who refused the intervention[44,49,62]	3
Comparator population not drawn from target population[58]	1
Non-comparable sampling frames for intervention and control groups[63]	1
Other/Multiple[50]	1

5.1.7 Replicability of intervention content

Eight of the interventions studied were defined primarily in terms of staffing, organisational aspects of delivery of care or reimbursement rather than in terms of the content of care: these included four studies of 'teen' clinics,[51,57,58,60] two studies of nurse/midwife led clinics for low-risk women,[46,61] and two US interventions that were defined primarily in terms of mode of reimbursement ('Managed care'[64]; 'fee-for-service' hospital clinic[52]).

Only eight of the remaining 28 primary reports were considered to describe the content of the intervention in sufficient detail for the intervention to be replicable: six of the 8 PTB prevention programmes[35,36,38,39,41,55] were adequately described, as were two group

antenatal care programmes.[40,45] The remaining 20 primary reports were not considered to provide sufficient detail of the intervention evaluated for the intervention to be replicated although in some cases the intervention evaluated was known to be more fully described elsewhere. For example, the CenteringPregnancy model evaluated by Grady et al.[63] in a teenage population is well described elsewhere.[70]

5.2 Interventions studied

5.2.1 Intervention recipients/target populations

Twenty studies related to interventions targeting and/or evaluated in socioeconomically disadvantaged/deprived populations[i]: 8 of the interventions were aimed specifically at socioeconomically disadvantaged women with additional risk factors for PTB; and 12 were aimed at socioeconomically disadvantaged pregnant women in general (see Table 5) one of which included screening for risk of PTB and enhanced services for those identified as being at high risk.[53] Seventeen of these 20 studies were conducted in the USA, with most targeting medically indigent[ii] and/or Medicaid eligible women.

The remaining sixteen primary reports related to interventions targeting or evaluated in specific populations of interest: nine targeted pregnant teenagers,[47,49,51,54,57,58,60,63,65] 4 targeted pregnant substance users,[44,50,62,68] 2 targeted pregnant indigenous Australians,[67,69] and one targeted pregnant women who were HIV positive.[59] One secondary report additionally provided data on the effectiveness of an intervention in a subgroup of substance using, HIV positive women.[33]

One intervention (Group antenatal care) was the subject of three studies in two separate target populations (socioeconomically disadvantaged women[40,45] and teenagers[63]); and one intervention (comprehensive care in accredited general antenatal clinics) targeted socioeconomically disadvantaged women in general but was evaluated in two specific populations (HIV positive women,[59] and HIV positive substance users[33]).

Five of the studies evaluated programmes involving home visiting and/or telephone support.[36,37,39,41,43] All could be characterized as providing social support but one[43] had a nutritional focus, and one targeting women at increased risk of PTB[36] appeared to have a lesser emphasis on social support and instead focused more on monitoring the woman's health status and encouraging healthy behaviours.

i Excluding one study relating to low-income predominantly black teenagers[63] which is included under interventions targeting teenagers.

ii Women who lack health insurance but are ineligible for healthcare coverage under Medicaid (A Federal-State health insurance program provided in the USA for certain low-income individuals and their families). The medically indigent generally earn too much to be eligible for Medicaid but earn too little to be able to purchase health insurance.

Table 5: Overview of interventions by target population/recipients

Socioeconomically disadvantaged pregnant women	
• without risk factors for PTB	**Comprehensive antenatal care:** • Group antenatal care[40,45] • Comprehensive multidisciplinary service with outreach[48] • Nurse/midwife clinic for low risk women[46,61] • Other US public antenatal care programmes[53,64] **PTB programmes provided as an adjunct to comprehensive antenatal care:** • Case management/care coordination[16,56] • Nurse home visits[37,43] • 'Healthy Start' programme[66]
• with risk factors for PTB	**Clinic-based PTB programmes providing enhanced care to higher risk women:** • Broad, multifaceted enhanced care programme[38,42,55] • PTB prevention programme primarily focusing on patient education regarding signs of preterm labour plus additional visits/pelvic examinations[35] • Hospital clinic vs. 'managed care'[52] **PTB programmes provided as an adjunct to comprehensive antenatal care:** • Home visits/telephone support[36,39,41]
Specific populations of interest	
• Teenagers	• 'Teen' clinics[47,49,51,57,58,60,65] • Adolescent group antenatal care (*CenteringPregnancy*)[i] [63] • Stand alone nutritional programme[54]
• Substance users	• Substance abuse programme provided as an adjunct to standard antenatal care[44,50,62,68] • Comprehensive care in accredited general antenatal clinic providing an enhanced range of services[33]
• Indigenous women	• Culturally sensitive comprehensive antenatal care including community/outreach services[67,69]
• Low-income, HIV positive women	• Comprehensive care in accredited general antenatal clinic providing an enhanced range of services[59]

i See also Ickoviks (2003) and Ickoviks (2007) for an evaluation of the group model in adolescents and young women.

5.2.2 Antenatal care interventions targeting socioeconomically disadvantaged pregnant women without specific clinical risk factors for PTB

The interventions targeting or evaluated in socioeconomically disadvantaged women fell into two broad groups: comprehensive antenatal care and interventions provided as an adjunct to comprehensive antenatal care:

Comprehensive antenatal care:

- Group antenatal care[40,45]
- Comprehensive multidisciplinary service with outreach[48]
- Nurse/midwife clinic for low risk women[46,61]
- Other US public antenatal care programme[53,64]
- Comprehensive care in accredited general antenatal clinic, providing an enhanced range of services[i]

Services provided as an adjunct to comprehensive antenatal care:

- Case management/care coordination[16,56]
- Nurse home visits[37,43]
- 'Healthy Start' programme[66]

Beyond this broad grouping, the characteristics and content of the interventions generally differed markedly from study to study and did not readily fall into homogeneous groups.

All but one of the interventions described in this section were evaluated in the USA; the evaluation of nurse home visits by Kafatos et al.[43] was conducted in Greece.

5.2.2.1 Comprehensive antenatal care

Group antenatal care

Two related studies evaluated group antenatal care, firstly in an observational cohort study[45] and subsequently in an RCT.[40] One further study evaluated group antenatal care (the *CenteringPregnancy* model) specifically in a teenage population (Grady et al.,[63] see section 5.2.4.1). Under the group care model, pregnant women – typically younger women – were placed in groups of perhaps 8–10 women, all with similar estimated due dates, and received the vast majority of their antenatal care (including clinical assessments) in a communal/group setting:

> *"When participants arrive, they first engage in self-care activities of weight and blood pressure assessment; they record and chart their own progress in their medical records. Then, individual prenatal assessments are completed by the practitioner during the first 30 minutes of each session (e.g. fetal heart rate, fundal height). Each session focuses on formal discussion, education, and skills-building on issues related to pregnancy, childbirth and parenting. The curriculum is designed to include relevant content that is developmentally appropriate, but facilitators are trained to be sufficiently flexible to meet the needs of individual patients or to address specific topics as they arise in the group. Session themes include: 1. prenatal nutrition and fetal development, 2. common discomforts of pregnancy, 3. relaxation and labor, 4. family and parenting, 5. the birth experience, 6. decisions of pregnancy and developing a birth plan, 7. infant feeding, 8. postpartum adjustment, 9. new baby care, 10. baby and mother care (including post partum contraception). Providers are trained in a facilitative process, such that group sessions are not didactic lectures but rather an integrated discussion with input from health care providers as well as patients."* [45]

i This intervention is described in this section since it is aimed at socioeconomically disadvantaged women in general. The two included evaluations, however, evaluate the intervention in specific populations (HIV positive women,[59] and HIV positive substance users.[33]

Groups met periodically – typically fortnightly – for 1.5 to 2 hour sessions, with each group led by a trained practitioner. The group care model emphasised education, skills building, peer support and personal empowerment.

Further information about the CenteringPregnancy model can be found elsewhere.[70]

Comprehensive multidisciplinary antenatal care with outreach services

Reece and colleagues[48] evaluated an intensive, comprehensive, multidisciplinary service developed to target the high infant mortality rates in an area of North Philadelphia (the *Temple Infant and Parent Support Services (TIPPS)* program). This was a multi-component community-based intervention which included complete antenatal and delivery care, well-baby care, health education, nutritionist care and counselling and psychosocial care. The programme included a range of components to increase uptake and remove barriers to care. For example, outreach teams consisting of nurses and social workers interfaced with community-based organisations to enhance case finding and identify pregnant women who were not receiving antenatal care. Once identified, women received a home visit, during which the programme was explained and a commitment to participate and comply with the therapeutic regimen sought. Assistance with transportation and childcare during appointments was provided to eliminate access barriers, and missed appointments were actively followed up. Antenatal, labour, delivery and postpartum care were provided by certified nurse/midwives with complex and high-risk pregnancies supervised by a medical director and senior obstetric residents. Although some elements of the intervention were specific to the US context – for example, elements designed to target the uptake of services by uninsured American women – some elements of this multifaceted intervention could be relevant in the UK.

Nurse/midwife antenatal clinics

Two studies evaluated care of medically low-risk women in nurse/midwife clinics.[46,61] One study[46] evaluated antenatal care provided in a community-based neighbourhood clinic (*Neighborhood Pregnancy Care*), providing both antenatal care and family planning services in a low-income area adjacent to two housing projects in New Orleans. Care at the clinic was largely provided by advanced practice nurses (clinical nurse specialists, nurse practitioners and certified nurse/midwives) with each woman being seen at least twice by an obstetrician: once shortly after the initial visit and again in the third trimester. The intervention included patient reminders to ensure attendance at scheduled appointments and aimed to provide continuity of care, patient education, case management and coordination of referrals.

A second study[61] evaluated a nurse/midwife antenatal care model provided to low-income women in public clinics in a mixed suburban/rural area of Colorado. To receive this service woman were first referred to the health department for financial and medical risk screening. Antenatal, delivery, and postpartum care was provided at these clinics to qualifying low-risk, low-income women by certified nurse/midwives, nurse practitioners and public health nurses, guided by protocols provided by the supervising obstetrician. The content of the intervention was not further described.

Although both interventions shared some common elements, neither was described in sufficient detail to enable similarities and differences and to be assessed. Both interventions were defined largely in terms of staffing and mode of delivery; and in neither case were the key components of the intervention described in sufficient detail to be replicable.

Other US public antenatal care programmes

Two studies[53,64] evaluated statewide public antenatal care programmes, both of which were considered to have limited relevance/applicability outside the USA.

Clarke and colleagues[53] evaluated Florida's *Improved Pregnancy Outcome (IPO)* programme, which provided comprehensive antenatal care to medically indigent women.

> *"IPO services included regularly scheduled medical examinations and lab work, health and nutritional counseling, pregnancy and parenting education, assistance with delivery arrangements, postpartum and well baby care, and family planning services. Program participants were also routinely referred from enrollment into WIC[i] and the Medicaid program."* [53]

The programme also included a specific PTB prevention component in which all participants were screened for risk of PTB on entry to the programme and at 28 weeks of gestation, using the Creasy risk assessment instrument; those found to be at increased risk were provided with more frequent visits, intensive education concerning the signs of pre-term labour, stress management and nutritional education. The antenatal care component of the programme can be characterised as encompassing basic, standard antenatal care with the addition of PTB screening and enhanced care for women at high risk of PTB.

Conover and colleagues[64] evaluated a Medicaid Managed Care programme in the state of Tennessee (*TennCare*) which aimed to increase access to care by expanding Medicaid coverage to previously uninsured women, and to improve the quality and cost-effectiveness of care by channelling Medicaid eligible women into 'managed care'[ii]. Pregnant women were also guaranteed Medicaid eligibility through the first six weeks post-partum. The intervention is defined primarily in terms of a model of delivery/ reimbursement of care and has limited relevance to the NHS.

Comprehensive care in accredited general antenatal clinics providing an enhanced range of services

New York's *Prenatal Care Assistance Program (PCAP)*, evaluated in specific populations by Turner et al. and Newschaffer et al.,[33,59] provided enhanced antenatal care to low-income Medicaid-eligible women through a network of accredited hospital clinics. The programme aimed to improve birth outcomes by providing Medicaid service providers with financial incentives to improve basic elements of management and coordination of antenatal care. To be accredited (and receive enhanced payments) each clinic had to provide evidence that they provided the required range of services which included:

> *"(1) patient outreach to facilitate timely prenatal care, (2) meeting frequency and content of care standards set by the American College of Obstetricians and Gynaecologists, (3) comprehensive risk assessment for adverse outcomes, (4) development of prenatal care plan and coordination of care, (5) nutritional services, (6) health education, (7) psychological assessment and (8) HIV related services involving testing, counselling and management referrals."* [59]

5.2.2.2 Services provided as an adjunct to comprehensive care

Case management/care coordination

Two studies evaluated interventions involving the provision of case managers/care coordinators alongside standard antenatal care[iii]. There were significant differences between the two programmes evaluated, but both aimed to eliminate barriers to the use of services and in particular to encourage and facilitate the uptake of antenatal care.

Maternity care coordination, evaluated by Buescher and colleagues,[16] was a programme provided to pregnant and postpartum Medicaid recipients in North Carolina. The maternity care coordinators aimed to help Medicaid-eligible women receive services and also

i The Special Supplemental Food Program for Women, Infants and Children (WIC) Program is a federally funded nutritional programme in the USA designed to meet the special nutritional needs of low-income individuals, who are at risk of inadequate nutrition during the critical periods of pregnancy, infancy, and early childhood. WIC supplies supplemental food, health care referrals, and nutrition education to low-income women, who are pregnant or postpartum, and also serves infants and children at 'nutritional risk'. See *http://www.fns.usda.gov/wic/aboutwic/wicataglance.htm*

ii Further details of the programme can be found at *http://www.state.tn.us/tenncare/.*

iii Further details of the two programmes can be found elsewhere.[71 72]

to provide social and emotional support. The programme had a number of elements, including outreach, to help women apply for Medicaid, assessment (psychosocial, nutritional, medical, educational and financial), service planning (development of an individualized plan and provision of assistance to access services), coordination and referral, follow up and monitoring and education and counselling.

The *Illinois Family Case Management Program*, evaluated by Keeton and colleagues[56] delivered case management services (individualised assessment of needs, planning of services, referral, monitoring, and advocacy to assist a client in gaining access to appropriate services) to Medicaid eligible and medically indigent pregnant women, infants and high-risk children. The antenatal component focused on education to promote healthy behaviour and on facilitating access to antenatal care and other services.

Nurse home visits

Two eligible studies evaluated services involving nurse home visits to pregnant women: one[43] had a nutritional focus and one[37] provided social and other support.

Kafatos and colleagues[43] evaluated an outreach health education/counselling service, provided by nurses attached to primary health clinics in Florina, a remote, mountainous rural area in Northern Greece, in which uptake of antenatal care tends to be poor. The intervention was part of a wider intervention programme designed to reduce perinatal and infant mortality and morbidity and to promote infant health in Greece. The Florina intervention involved regular (fortnightly) nurse home visits initiated during pregnancy to all pregnant women in the villages served by the participating primary health clinics. The emphasis of the visits was on nutritional counselling. Instruction in the basics of nutrition during pregnancy included: food sources and the methods for selecting a balanced diet as well as instruction in practical techniques to improve the quality of women's diets, including selection of foods with a high nutrient value and preparation/preservation techniques to reduce the loss of nutrients. Other themes covered during pregnancy included general hygiene, preparation for delivery, breastfeeding and care of the newborn[i]. Home visits continued after delivery until the infant was 12 months old; these visits focused on infant health topics.

A home visiting programme based on the 'Elmira model' developed by Olds and colleagues (and similar to the Family Nurse Partnership model currently being tested and evaluated at 20 pilot sites in England[ii])was evaluated in one eligible study[iii] by Kitzman and colleagues.[37] The full intervention (which included both antenatal and postnatal home visits) was designed to improve the health, well-being and self-sufficiency of young first-time parents and their children.

> *"The program protocols were based on theories of human ecology, human attachment and self-efficacy. The nurses helped families make use of needed health and human services and attempted to involve other family members and friends in the pregnancy, birth and early care of the child. They established trusting relationships with parents and helped mothers set small, achievable behavioural objectives between visits that, when met, would increase mothers' confidence in their ability to master greater challenges."* [37]

i See also earlier report for further details of intervention.[73]

ii Further information about the Family Nurse Partnership project in England is available elsewhere[74,75]

> *'[The program] involves weekly or fortnightly structured home visits by a specially trained nurse from early pregnancy until children are 24 months old. The curriculum is well specified and detailed with a plan for the number, timing and content of visits. Supervision is ongoing and careful records of visits are maintained. The programme has strong theoretical underpinnings, with the formation of a strong therapeutic relationship between nurse and mother at its heart. The programme is designed for low-income mothers who have had no previous live births and starts in the second trimester of pregnancy'*

iii Note: Family Case Management Programmes have been extensively evaluated but only one eligible study was found which (a) reported on a relevant outcome (PTB in the included evaluation by Kitzman et al.[37]) (b) evaluated the effect of the intervention when provided as an adjunct to standard antenatal care vs. standard antenatal care alone.

The antenatal aspect of the intervention involved an average of 7 home visits focusing on improving health-related behaviour (nutrition, smoking, alcohol and illegal drug use). Women were also taught to recognise the signs and symptoms of pregnancy complications and to act appropriately if these occurred; attention was also paid to compliance with treatment and to urinary tract infections (UTIs) and sexually transmitted diseases (STDs).

'Healthy Start' programme

The *Syracuse Health Start (SHS)* programme evaluated by Lane and colleagues[66] was a multi-component Healthy Start programme targeting pregnant women, infants and their families. The programme aimed to reduce infant mortality and teenage pregnancies and was based around a central registry, which was used to facilitate access to a range of services. Components of the programme included: enrolment of women in a central Healthy Start registry to ensure they received antenatal care, follow up to ensure that appointments were kept, screening for social risk, home visiting/case management, education (risk reduction, infant care, family planning), referral to WIC, and access to adolescent programmes, including a teen clinic (see Lane et al.[66] for a fuller programme description). Clients could self-refer by calling a widely advertised 'hotline' number that appeared in advertisements on television, radio, buses, and print media.

5.2.3 PTB prevention programmes aimed at socioeconomically disadvantaged women with additional clinical risk factors for PTB

The interventions are described below under two main headings: clinic-based programmes providing enhanced care to higher risk women; and home visits/support interventions.

All of these interventions/programmes targeted women at higher risk of PTB. The included studies (six of which were randomised trials) used a variety of methods to identify women at higher risk of PTB: two studies[35,42] used the Creasy score to determine PTB risk, one[38] used Goldenberg's abbreviated scale,[76,77] one[39] used a combination of race, age and the Wake Forest University School of Medicine risk assessment tool,[78,79] and four (including the two non-randomised studies) included only women with obstetric risk factors (women with a prior LBW baby,[41] women with a prior PTB,[52] women with twin gestations,[55] women with poor obstetric histories[36]).

5.2.3.1 Clinic-based PTB programmes providing enhanced care to higher risk women

Five studies evaluated clinic-based programmes for women with additional risk factors for PTB. Three of the studies evaluated broad, multifaceted enhanced care programmes targeting a broad range of risk factors; and one study evaluated a more focused programme that involved additional patient education regarding the signs and symptoms of pre-term labour and weekly visits/observation including cervical examination. The fifth study evaluated different models of providing antenatal care to higher risk women, but did not describe the content of care.

Broad, multifaceted enhanced care programmes

Three studies evaluated broad, multifaceted enhanced care programmes targeting a broad range of risk factors in socioeconomically disadvantaged women at higher risk of PTB.

Hobel and colleagues[42] evaluated a programme targeting predominantly Hispanic, medically indigent women in West Los Angeles. Women in the programme received more frequent visits (every two weeks), pre-term prevention education (three classes covering "identification of pre-term labour, steps to take if signs or symptoms occurred, prevention strategies and what to expect at the hospital") as well as psychosocial and nutritional screening and crisis intervention. Women attending the intervention clinics in this cluster randomised RCT (i.e. those randomised to receive enhanced antenatal care) were additionally randomised to receive one of five treatments (control, bed rest, psychological support, oral progestin or placebo).

Klerman and colleagues[38] evaluated a programme of augmented care targeting high-risk black American women in Jefferson County, Alabama. Women in the intervention arm received augmented care at a specially created *Mother and Family Specialty Center*. In the light of research indicating that women in the target population were "significantly less likely than white women to have been informed about the harmful effects of maternal smoking and alcohol consumption and the value of weight gain during pregnancy", the programme focused on informing women about their risk conditions and about what behaviour might improve their pregnancy. The programme included three specific elements relating to major risk factors: smoking cessation, weight gain and vitamin-mineral supplementation and amelioration of psychosocial stress/isolation. The programme also included a range of other features, such as group sessions, regular standing appointments, evening hours where needed, appointment reminders, transportation, and on-site childcare.[i]

Edwards and colleagues[55] evaluated a comprehensive preterm prevention programme provided at a specialist PTB prevention clinic located in an inner-city hospital in the Bronx, New York, serving a predominantly minority, low-income population. The *Program to Reduce Obstetrical Problems and Prematurity (PROPP)* was a programme designed for women with a range of risk factors for PTB. In the study included here, the intervention was evaluated only in women with twin gestations. The focus of PROPP was on:

> *"…early, comprehensive, continuous prenatal care; interconceptional health promotion; ongoing risk assessment; modification of life-style-related behaviour risk/ actions; and a specialized clinic for high risk women. The program includes preterm prevention education, including a video-tape describing the signs and symptoms of preterm labour, information on life-style modification, and other printed educational material."* [55]

Care also included "biweekly visits with frequent cervical assessment and hospital admission when premature cervical dilation is documented"; and "frequent ultrasound studies to assess fetal growth."[55]

Programme with focus on patient education regarding signs of preterm labour plus additional visits/pelvic examinations

One multi-centre trial[35] evaluated a more focused pre-term prevention programme that involved patient education regarding the signs and symptoms of pre-term labour weekly in combination with weekly visits/observation including cervical examination. Results from a single site participating in the trial are reported separately.[34]

The intervention was evaluated in women at increased risk of PTB (Creasy score ≥10) drawn from centres in five US regions chosen to reflect different geographical racial and ethnic groups within the United States. The intervention was designed to commence in women who were ≤ 20 weeks of gestation, but women initially deemed to be low-risk could enter the trial up to 32 or 34 weeks of gestation (depending on centre) if their risk status changed (provided that pre-term labour did not occur within 72 hours of the change of status).

> *"The intervention group patients had visits scheduled weekly after 20 to 24 weeks' gestation and at these visits received routine obstetric care and patient education regarding the subtle symptoms of preterm labor and the importance of early detection of preterm labor and self-detection of uterine contractions, pelvic examination to determine the status of the cervix, reinforcement for patient cooperation and awareness with educational handouts, a weekly questioning concerning the presence or absence of preterm labor symptoms or uterine activity, and ultrasonographic examination of any patients for whom the length of gestation was in question."* [35]

i For fuller details see table 1 of Klerman's article.[38]

Hospital clinic vs. 'managed care'

Bienstock and colleagues[52] compared the rate of recurrent PTB and costs in an inner-city 'house staff' hospital clinic vs. 'managed care' for low-income women with a prior PTB in Baltimore. This study was a retrospective comparison of two models of delivery of care; the content of the 'intervention' was not described.

5.2.3.2 Home visits/telephone support to women at higher risk of PTB

Bryce and colleagues[36] evaluated a programme of additional antenatal social support delivered via home visits and telephone calls to women at higher risk of PTB. The intervention targeted women with poor obstetric histories (prior PTB, prior low birthweight (LBW) birth, prior perinatal death, previous antepartum haemorrhage, prior second trimester (12–19 weeks) miscarriage or three or more first trimester miscarriages) and did not specifically target socioeconomically disadvantaged women, but a stratified (post hoc) sub-group analysis of the effects of the intervention on PTB by social class was reported. The intervention consisted of home visits by midwives at roughly 4–6 weekly intervals (more frequently if requested by the woman) with intervening telephone calls:

> *"Each midwife aimed at increasing expressive support by providing sympathy, empathy, understanding, acceptance and affection, and attempted to act as a confidante… The midwives were instructed to provide instrumental support*[i] *only on request and first to encourage the women to find their own answers. Physical antenatal care could be provided only in an emergency."* [36]

Moore and colleagues[39] evaluated a telephone support programme in a disadvantaged population in North Carolina. The trial targeted women at risk of a premature LBW birth and included black women and women aged 18 years of age or younger, irrespective of PTB risk score, and white or 'other' women with an increased risk of pre-term labour assessed using the Wake Forest University of Medicine Assessment tool. The intervention was delivered by registered nurses. Women received a booklet and additional instruction about the signs and symptoms of preterm labour followed by scheduled nurse phone calls. Women additionally received instructions about contacting the nurse on her pager. The timing of calls was designed to suit the woman's convenience with a goal of three telephone contacts a week:

> *"...each telephone call addressed three major areas: assessment of health status (perception of uterine contractions and other pregnancy changes, color of urine as an assessment of hydration, number of meals eaten, number of cigarettes smoked, alcohol and drug use, and ingestion of a prenatal vitamin capsule on the previous day); recommendations based on assessment; and discussion of any additional issues important to the mother."* [39]

A limitation of this intervention in this low-income population was that a substantial minority of women lacked a phone and/or permanent address and hence could not participate.

Oakley and colleagues[41] evaluated a social support intervention consisting of a 'minimum package' of three home visits carried out at 14, 20 and 28 weeks gestation, plus two telephone contacts or brief home visits in between these times. The midwives carried pagers and were 'on call' to the mothers 24 hours a day. The trial enrolled women with a prior LBW baby.

> *"[The midwives used] a semi-structured interview schedule to provide a basis for flexible and open-ended communication between the midwives and the mothers, so that the mothers would feel able to discuss any topic concerning their pregnancy needs or circumstances that was important to them. The research midwives were asked to give advice or information about specific topics only if requested to do so by the mother. They did not provide clinical care, but referred women to the hospital,*

i Defined as "information, advice and material aid".

general practitioner, or community midwives where appropriate: other referrals, for example to social workers, were also carried out as judged necessary by the mother and midwife." [41]

5.2.4 Antenatal care interventions targeting specific vulnerable/at risk populations

The included interventions targeted four specific groups: teenagers (9 studies), substance users (5 studies), Australian indigenous women (2 studies) and women who were HIV positive (one study):

5.2.4.1 Interventions targeting teenagers

Nine studies evaluated the following interventions targeting (or evaluated in) teenagers:

- 'Teen' clinics [47,49,51,57,58,60,65]
- Adolescent group antenatal care[i]/CenteringPregnancy[63]
- Stand alone nutritional programme[54]

'Teen' clinics

Seven studies evaluated dedicated teen antenatal clinics in a variety of settings and populations.

Bensusson-Wall and colleagues[51] evaluated two interdisciplinary teen clinics in Washington State: the *Young Women's Clinic (YWC)* at the University of Washington Medical Center; and the *Teen Pregnancy and Parenting Clinic (TPPC)* at the Group Health Cooperative, Puget Sound (a staff-model Health Maintenance Organization (HMO)[ii]). Both clinics were established to improve care for pregnant and parent teens, with one of the two programmes (*YWC*) particularly focusing on the needs of high-risk and out-of-home pregnant and parenting teens. The evaluation focused on the antenatal component of the intervention.

The services provided by the clinics were described largely in terms of staffing. The *YWC* team consisted of a public health nurse and a social worker, who provided services in the clinic or community, a registered dietician, certified nurse midwives and an adolescent physician who provides non-obstetric medical care in the clinic. The *TPPC* clinic team consisted of a nurse clinician, social worker, registered dietician, WIC certifier, health educator and a family physician as medical director. The TPPC team provided care in the clinic and hospital; home visits were conducted by the HMO's Home Care Services.

Das and colleagues[65] evaluated the *Young and Pregnant (YAP)* clinic, a dedicated teen clinic provided in a District General Hospital in the North of England. The YAP clinic philosophy was to provide continuity of care and to build up a relationship of trust with the teenagers.

> *"The clinic provides psychosocial support and maternity care appropriate to need by a named midwife and a single named consultant… Appointments are arranged as soon as possible in the pregnancy to commence early health promotion advice, including postnatal contraception, breast-feeding and smoking cessation. Parent education sessions are provided in both group and one-to-one sessions. These sessions provide information regarding parenting skills, health in the pregnancy continuum, labour and care of the neonate."* [65]

Morris and colleagues[57] evaluated a teen clinic provided to an ethnically mixed, predominantly low-income (uninsured) population of teenagers in Galveston, Texas. The philosophy and content of care are not fully described:

i See also section 5.2.2.1 for evaluations of the group model in other age ranges.

ii A form of 'managed care' in which patients are generally reimbursed only for care within the HMO's network of providers.

> *"The teen clinic provides general monitoring of pregnancy in addition to special emphasis on educational, social and nutritional support. The care is provided by a team of nurses, physicians assistants, obstetrician-gynaecologist residents, a social worker and a nutritionist."* [57]

Quinlivan and colleagues[47] evaluated multi-disciplinary teenage antenatal clinics in three metropolitan hospitals in Australia. These clinics, staffed by a multidisciplinary team of obstetric doctors, clinical midwives, midwife nurse educators, social workers and a psychiatrist, aimed to provide comprehensive, teenage-specific care including rigorous infection screening and social support.

> *"Staff had guidelines for the management of teenage pregnancy and these included, in addition to the routine investigations, evaluation of anaemia with multiple vitamin screens (B12, folate, iron studies) and dietician referral, intensive social work appraisal with psychosocial assessments for domestic violence, housing environment and support levels, screening for STDs and genital tract pathogens, Pap smear irregularities and drug use and an open hospital admission policy."* [47]

Staff from the government financial support agency (*Centrelink*), indigenous health and dietician services, also attended the clinic regularly to see patients.

Ukil and Esen[60] evaluated outcomes in younger teenagers (aged 16 years or less) attending a dedicated teenage clinic provided in a District General Hospital in the North East of England.

> *"...optional, dedicated, teenage antenatal clinic in a friendly and informal setting, with appropriate back-up by the relevant agencies. This unit is run by midwives with medical back-up as required, and there is also a high midwife to patient ratio. The clinic is also highly flexible accepting patients on a 'drop-in' basis if necessary."* [60]

Van-Winter and colleagues[49] evaluated the *Young Moms' Clinic* at the Mayo Medical Center in Rochester, Minnesota, which served a non-urban, primarily white population of both teens and young single women (aged 23 years or younger). The clinic aimed to address the physical, psychosocial, educational and financial needs of young mothers in a developmentally appropriate manner throughout pregnancy and the neonatal period. The goals of the programme were to:

> *"(1) teach participants about pregnancy, child birth, early parenting, healthy lifestyles, and contraception, (2) facilitate open communication, trust and cooperative interaction between young mothers and their healthcare providers, (3) provide information about and access to appropriate supportive services in the community, (4) increase compliance in adolescent patients by coordinating their prenatal classes with obstetric clinic appointments, (5) provide a confidential and supportive atmosphere for peer interaction and (6) assess medical, educational and affective outcomes."* [49]

Perez and colleagues[58] evaluated a teen focused obstetric clinic for unmarried pregnant teens provided at a military facility in Tacoma, Washington. Little further information is provided other than that the facility in which the clinic was located served a socioeconomically and ethnically diverse population with unlimited access to free health care in the Department of Defence; and that the clinic was staffed by a single, rotating senior resident who followed the patients for 3-month rotations as the primary provider of obstetrical care.

Adolescent group antenatal care

Grady and colleagues[63] evaluated a *CenteringPregnancy* model group teen clinic provided at the Teen Pregnancy Center, an urban hospital-based clinic which provides specialized antenatal care to teenagers aged 17 years and younger in St Louis, Missouri. The *CenteringPregnancy* model is a comprehensive antenatal care programme which emphasizes assessment, education and support.

> *"Adolescents are grouped with 8 to 12 other young women with an estimated due date within a 6-week period of time. Centering group sessions begin between 12 and 18 weeks' gestation and continue every 2 weeks throughout pregnancy for a total of 12 sessions. Each Centering Group has two cofacilitators that include one CNM [certified nurse midwife] and either the nurse facilitator or the education coordinator at the Teen Pregnacy Center. Teens follow-up with the social worker once a month. The CenteringPregnancy curriculum has been modified adding content on sexually transmitted diseases, abuse issues and parenting issues to meet the specific needs and requests of the adolescents at the clinic. Games including Breastfeeding Bingo and Contraception Jeopardy have been added for enjoyment and reinforce knowledge about breastfeeding and contraception."* [63]

The intervention also included a peer assistance programme in which an adolescent who had 'graduated' was paired with each CenteringPregnancy Group.

Nutritional programme

Dubois and colleagues[54] evaluated the *Higgins Nutrition Intervention Program* in a population of pregnant teenagers drawn from 15 Canadian hospitals in the Montreal area. The programme, delivered as an adjunct to routine antenatal care, consisted of an assessment of each pregnant adolescent's risk profile for adverse birth outcomes and an individualized nutritional rehabilitation programme based on that profile. The programme, which is delivered by trained dieticians, has four elements (described in greater detail elsewhere[80,81]):

> *"(a) Assessment of the risks for the pregnancy; (b) determination of individual dietary prescriptions based on the normal requirements for pregnancy and rehabilitation allowances for diagnosed risk; (c) teaching of food consumption patterns that meet individual dietary prescriptions while respecting pre-existing food habits; and follow-up and supervision by the same dietician at 2-week intervals."* [54]

5.2.4.2 Interventions targeting substance users

Four studies evaluated interventions targeting substance users[44,50,62,68] and one evaluated a general (i.e., untargeted) enhanced antenatal care programme in substance-abusing, HIV positive women.[33]

Substance abuse programmes provided as an adjunct to antenatal care

Armstrong and colleagues[50] evaluated an *Early Start Program* in ten outpatient obstetric clinics run by a group model managed care organisation in Northern California. The programme provided pregnant women with screening and early identification of substance abuse problems, early intervention, ongoing counselling, and case management by an Early Start Specialist, a licensed clinical therapist with expertise in substance abuse. Potential clients were identified by a variety of means: a self-administered antenatal substance-abuse screening questionnaire completed at the first antenatal appointment, clinician referral, self-referral, or by positive urine toxicology screen. Women identified as having some risk for alcohol, tobacco or other drug use during pregnancy were referred to the Early Start Specialist for an in-depth psychosocial assessment; and those assessed as chemically dependent, substance-abusing, problem drinkers or problem drug-users at risk for substance abuse problems during pregnancy were seen for counseling at appointments schedules to coincide with subsequent antenatal visits. Counseling techniques included: motivational therapy, cognitive/behavioural therapy, and psychodynamic therapy. Early Start clients were referred to other intervention programmes as needed. Further details of the programme, including the screening questionnaire, are available elsewhere.[82]

Miles and colleagues[68] evaluated a shared care approach to the management of pregnant drug users and their infants in an inner-city hospital in Manchester, UK. The programme was evaluated in women on methadone treatment. The intervention involved the appointment of a Drug Liaison Midwife (DLM), based in the Manchester Drug Service

(MDS), who provided liaison with the hospital-based services, including the neonatologists who were informed monthly of forthcoming deliveries and involved pre-delivery where appropriate.

The DLM received notification of all known pregnant drug users and received referrals from a wide variety of sources (MDS, GPs, staff in antenatal clinics at local hospitals, local charities providing advice and support to drug users and sex workers, social services, the probation service, and self-referral).

> *"At the first visit to an antenatal clinic, a consultant obstetrician or a senior registrar saw the woman and where possible the DLM would be there. The subsequent antenatal appointments were offered monthly. If the woman missed a clinic appointment, the DLM would carry out a home visit. … The DLM provided specialist advice regarding methadone treatment, care of the newborn and the advantages of breastfeeding. Careful records were kept of declared illicit drug use, smoking and alcohol use, and reduction was encouraged. Each woman was given written information about pregnancy and substance misuse and caring for her baby."* [68]

The intervention also aimed to change the clinical management of the women's infants:

> *"The DLM, community midwives and nurses working on the NMU [Neonatal Medical Unit] shared information. … Liaison between the midwifery services and social services had often occurred by the time of the monthly review meeting [with the neonatologist]. This ensured that any potential child protection issues were identified and follow-up arrangements were in place by the time the infant was born."* [68]

Neonatal management was modified and in-service training in looking after these infants was offered to medical, midwifery and nursing staff by the DLM. Following introduction of the service, neonates, who had previously been routinely admitted to the Neonatal Medical Unit, were admitted only if required on clinical grounds. The DLM continued to supervise the infant's care after discharge from hospital.

Sweeney and colleagues[62] evaluated *Project Link* an intensive hospital-based substance abuse programme for pregnant and postpartum women in Providence, Rhode Island, USA. The programme, provided as an adjunct to standard antenatal care from offices close to the hospital where the antenatal clinic was situated, provided a comprehensive package of substance abuse treatment services. All women attending for standard antenatal care in the local hospital were routinely asked about past and/or present substance abuse and were referred to Project Link if "illicit substance abuse" was admitted or suspected. Women could also be referred postnatally.

> *"Project staff consisted of a Project Director, a clinical Coordinator, three Clinical Social Workers, three case managers, an Office Coordinator and a Project assistant. The staff [Project Director, clinical Coordinator, Clinical Social Workers, Case Managers] combined expertise in maternal-child health and substance abuse treatment with cultural competence, knowledge of community resources, and commitment to women and their children. Services were individualized to the needs of the enrollees and included crisis intervention, comprehensive psychosocial and substance use assessment, individualized treatment plan development, individual and group therapy, child and family therapy, home visiting, parenting education and support, and infant developmental assessment. … Transportation, on-site child-care and other services were provided in an effort to address barriers to women accessing treatment."* [62]

Burkett and colleagues[44] evaluated a drug rehabilitation programme provided to cocaine-dependent women attending a dedicated *Prenatal Substance Abuse Clinic* in Miami, Florida. The *Substance Abuse Clinic* provided a comprehensive package of antenatal care targeting the needs of substance users, including drug rehabilitation (the focus of the evaluation).

"The clinic drug counsellors assess drug dependency and recommend appropriate treatment - inpatient, residential or outpatient intensive care. Interventions include psychiatric or psychological evaluation, counselling and treatment, drug use avoidance strategies, crisis intervention, individual and group counselling, detoxification, family counselling, and long-term aftercare. The first month is usually intensive with all-day sessions, which are gradually reduced as the patient responds." [44]

Comprehensive care in accredited general antenatal clinic providing an enhanced range of services

Newschaffer and colleagues evaluated the *Prenatal Care Assistance Program (PCAP)* in substance-abusing, HIV positive women. See section 5.2.2.1 for a description of the programme which provides enhanced antenatal care to low-income women in New York State. The programme was also evaluated in a broader population of HIV positive women.[59]

5.2.4.3 Interventions targeting indigenous women

Two evaluations related to maternal and child health programmes targeting the needs of pregnant and non-pregnant aboriginal and indigenous women in Australia.

Mackerras and colleagues[67] evaluated a programme known as the *Strong Women Strong Babies Strong Culture Program*, a community based pilot programme developed in conjunction with Aboriginal people to try to improve the birthweight of infants in the Top End region in the Northern Territory, Australia. The particular health aims of the programme were:

"… to increase attendance for antenatal care in the first trimester to allow identification and modification of factors which might affect the health of the mother or child; to introduce nutritional assessment and monitoring into prenatal care with evaluation of their use and to evaluate strategies to improve maternal nutrition by increased weight gain during pregnancy…" [67]

A well-respected Aboriginal woman was employed to develop the programme. She trained Strong Women Workers (SWWs), selected by the communities, who implemented a programme that "included traditional cultural practices related to childbirth as well as informing pregnant women about Western health and medical practices related to pregnancy and encouraging greater use of antenatal health care." The SWWs were community based and worked with both pregnant and non-pregnant women, including pregnant women who had not yet presented for antenatal care.

Panaretto and colleagues[69] evaluated a community-based, collaborative shared antenatal care programme (the *Mums and Babies program*) delivered to Australian indigenous women at maternal and child health clinics run by the Townsville Aboriginal and Islander Heath Service in Queensland. Standard antenatal shared-care protocols were used with some additional infection screening. Patients were seen by a multidisciplinary team which included Aboriginal Health workers, midwives/child health nurses, female doctors, members of the obstetric team and indigenous outreach health workers. Other elements of the programme included: a pregnancy register (with monthly recalls); daily walk-in clinics; family orientation (clinics were open to all pregnant women and families with children up to the age of eight and facilities and activities were provided for children); care plans emphasising essential elements of care (investigations, education, nutritional supplementation); testing for STIs and vaginal strep B infections; transport services; and brief intervention for risk factors (smoking cessation, nutrition, antenatal education, breastfeeding, SIDS).[31,69]

Comprehensive care in accredited general antenatal clinics providing an enhanced range of services

Newschaffer and colleagues evaluated the *Prenatal Care Assistance Program (PCAP)* in substance-abusing, HIV positive women. See section 5.2.2.1 for a description of the programme which provides enhanced antenatal care to low-income women in New York State. The programme was also evaluated in a broader population of HIV positive women.[59]

5.2.4.4 Interventions targeting women who are HIV positive

Turner and colleagues[59] evaluated the *Prenatal Care Assistance Program (PCAP)* in HIV positive women. The programme, which is aimed at low-income Medicaid eligible women in general, is described in section 5.2.2.1.

5.3 Effectiveness

5.3.1 Antenatal care interventions targeting socioeconomically disadvantaged pregnant women

5.3.1.1 Comprehensive antenatal care

Of the seven studies evaluating comprehensive antenatal care interventions in socioeconomically disadvantaged populations (see Table 6) six reported the effect on PTB (two of which reported PTB only as a secondary outcome[45,46]); and three of the studies additionally reported the effect on measures of infant or neonatal mortality.

The quality of evidence was generally poor: only one of the seven evaluations was a randomised controlled trial and only four were considered to have adequate internal validity.

Of the four studies that were assessed as having adequate interval validity ('good' or 'mixed' GATE quality assessment), two assessed group antenatal care,[40,45] one assessed an antenatal care model involving outreach,[48] and one evaluated a managed care model of providing antenatal care.[64]

Group antenatal care

Ickovics and colleagues[40,45] conducted two studies to evaluate the group care model: an initial observational study followed by a larger RCT. The initial evaluation was inconclusive, largely because the potential risk of selection bias and the lack of study power. The subsequent trial reported a significant reduction in PTB in the group care arm (adjusted odds ratio 0.67, 95% CI 0.44-0.98) (see Annex B, Ickovics 2007, page 62).

Comprehensive antenatal care with outreach (TIPPS programme)

Reece and colleagues[48] evaluated the effectiveness of the TIPPS programme, a 'customised' comprehensive multidisciplinary service designed to meet the specific needs of the local target population. They reported a statistically significant effect on PTB (4.3% preterm vs. 12% in a "matched" comparator group receiving antenatal care at the same hospital but not enrolled in TIPPS). Because of the risk of selection bias the reviewers considered the findings inconclusive but consistent with a possible beneficial effect.

Other US public antenatal care programmes

Conover and colleagues[64] evaluated a 'managed care' model of delivering antenatal care in Tennessee against a standard antenatal care model in North Carolina. The study did not provide evidence of a beneficial effect of managed care on either PTB or neonatal mortality although some implementation problems occurred during the evaluation which may have affected the outcome.

Results are summarised in Table 6.

5.3.1.2 Interventions provided as an adjunct to comprehensive antenatal care

Of the five studies that evaluated interventions provided as an adjunct to antenatal care in socioeconomically disadvantaged populations (see Table 7), two evaluated effects on PTB and four reported effects on infant mortality.

Of the three studies considered to have adequate internal validity, one evaluated the effect of case management/care coordination on infant mortality,[16] and two (one RCT and one cluster RCT[43]) evaluated the effect of nurse home visiting programmes on PTB.[37,43] One of the evaluations of nurse home visits also reported neonatal mortality as an outcome[43] but did not have an adequate sample size to detect an effect on this outcome.

Case management/care co-ordination

Buescher et al.[16] reported a statistically non-significant effect of the *North Carolina care coordination program* on infant mortality (9.9 deaths per 1000 live births vs. 12.2 per 1000 (unadjusted); adjusted odds ratio[i] 1.20, 95% CI 0.98–1.47) (See Annex B, Buescher 1991, page 64). The reviewers considered the findings inconclusive but consistent with a possible beneficial effect of the intervention on infant mortality.

Nurse home visits

Two studies evaluating the effect of nurse home visits provided contrasting results. Kitzman et al.[37] conducted a well-designed RCT to evaluate the antenatal home visiting component of the *Prenatal and Early Childhood Nurse Home Visitation Program*. The study (assessed as having 'good' internal validity) provided no evidence of a beneficial effect on PTB (11% PTB in the intervention group vs. 13% in the comparator group; adjusted odds ratio 0.8 (95% CI 0.6-1.2)). In contrast, a cluster RCT of the antenatal component of the Florina intervention programme (a home visiting programme with a focus on nutritional education[43]) reported a significant effect on PTB (3.7% PTB in the intervention group vs. 8.3% PTB in the comparator group). Findings relating to the effectiveness of the home visiting programme evaluated by Kafatos et al. were assessed as inconclusive but consistent with a possible beneficial effect of the intervention on PTB.

Results are summarised in Table 7. For detailed results see Annex B, Kitzman 1997, page 65; Kafatos 1991, page 65.

5.3.2 PTB prevention programmes aimed at socioeconomically disadvantaged women with additional clinical risk factors for PTB

The quality of evidence relating to interventions targeting 'high risk' disadvantaged women was higher than that relating to interventions in 'general-risk' disadvantaged pregnant women: seven of the nine evaluations were randomised controlled trials and six (all RCTs) were considered to have adequate internal validity.

5.3.2.1 Clinic-based PTB programmes providing enhanced care to higher risk women

Of the five evaluations of clinic based programmes (see Table 8), two (both RCTs) were considered to have adequate internal validity. Both of these evaluated broad multifaceted PTB prevention programmes (see section 5.2.3.1 for a fuller description of the programmes).

The evaluation of the *West Los Angeles Preterm Prevention Project*[42] reported a "significant"[ii] beneficial effect on PTB (19% reduction in unadjusted % PTB; adjusted odds ratio 0.78, 95% confidence interval 0.58-1.04); while the evaluation of an augmented

i Expessed as the effect of not receiving the intervention.

ii Significance based on a one-sided test; 95% confidence interval for odds ratio includes 1.0 indicating two-sided test not significant at the 5% level.

antenatal programme in Alabama[38] reported a non-significant reduction in PTB between the intervention and control arms (unadjusted % PTB: 10.6% vs. 14%). Findings of the former evaluation[42] were considered inconclusive but consistent with a possible beneficial effect of the intervention on PTB. The latter study[38] was inconclusive.

Individually these studies are inconclusive but, taken together, may indicate a modest beneficial effect of such programmes on PTB.

Results are summarised in Table 8. For detailed results see Annex B, Hobel 1994, page 66; Klerman 2001, page 67

5.3.2.2 PTB prevention programmes provided as an adjunct to comprehensive antenatal care

All three of the studies that evaluated non clinic-based PTB prevention programmes were randomised controlled trials considered to have adequate internal validity (see Table 9).

Two interventions involved the delivery of antenatal social support through home visits and telephone calls by midwives[36,41]; the third was a more 'health-focussed' telephone intervention involving frequent assessment of health status and provision of advice/ recommendations by a nurse practitioner[39]. In one of these studies[36], the study population was not restricted to socially disadvantaged women but a stratified analysis by social class was reported.

The first trial of home visits/social support[36] did not demonstrate a significant beneficial effect on PTB overall (odds ratio 0.84; 95% CI 0.65-1.09), and the stratified analysis by social class suggested that the beneficial effect, if any, was confined to the most advantaged women in the study (see Annex B, Bryce 1991, page 68). Odds ratios for women classified as 'clerical' and 'manual' were close to one. Oakley and colleagues[41] conducted an RCT of a nurse home visiting programme, and similarly found no effect on PTB (18% PTB in the intervention group vs. 19% PTB in the usual care arm).

The trial of telephone assessment/advice[39] also found no significant beneficial effect on PTB overall but reported a beneficial effect in a subgroup of black women aged ≥19 years (relative risk 0.56, 95% CI 0.38-0.84, p=0.004) (see Annex B, Moore 1998, page 69). It is unclear if the analysis by age and ethnicity was a pre-specified sub-group, however the authors reduced the level of significance required for a positive effect to p<0.006 to allow for multiple comparisons.

5.3.3 Antenatal care interventions targeting specific vulnerable/at risk populations

5.3.3.1 Interventions targeting teenagers

Of the eight studies that evaluated interventions targeting teenagers (Table 10), only one[54] was considered to have adequate internal validity.

Stand alone nutritional programme

The evaluation of the *Higgins Nutrition Intervention Program*[54] reported a substantial statistically significant effect on PTB (<37weeks) (adjusted odds ratio 0.59, 95% CI 0.45-0.78) and on early PTB (<34 weeks) (adjusted odds ratio 0.53, 95% CI 0.35-0.81) (See Annex B, Dubois 1997, page 72), Although the study was inconclusive due to the risk of selection bias, the reviewers considered the findings consistent with a possible beneficial effect on PTB.

5.3.3.2 Interventions targeting substance users

Four of the five studies evaluating interventions targeting substance users (see Table 11) were considered to have poor internal validity, reflecting the considerable methodological challenges of evaluating interventions in this population. One study, an evaluation of the

Prenatal Care Assistance Program (PCAP) in substance-abusing, HIV positive women was considered to have adequate internal validity.[33] The effectiveness of PCAP is also discussed in section 5.3.3.4 below.

Care of substance users in accredited general antenatal clinics providing an enhanced range of services

The evaluation of the *Prenatal Care Assistance Program (PCAP)*[33] reported a significant effect on PTB (<37 weeks) in substance-abusing, HIV positive women attending a PCAP-accredited clinic compared with those who received care in a non-PCAP participating clinic (adjusted odds ratio 0.57, 95% CI 0.34-0.97) (see Annex B, Newschaffer 1998, page 74). The reviewers considered that the evidence was inconclusive due to the risk of selection bias but consistent with a possible beneficial effect of the intervention on PTB.

5.3.3.3 Interventions targeting indigenous women

Two studies evaluated interventions in indigenous women (Table 12) but both were considered to have poor internal validity.

5.3.3.4 Interventions targeting low-income HIV positive women

One study with adequate internal validity (Table 12) evaluated an antenatal care programme in HIV positive women.[59] A second study[33] evaluated the effectiveness of the same programme in the subgroup of substance-abusing, HIV positive women (see section 5.3.3.2 above).

Care of HIV positive women in accredited general antenatal clinics providing an enhanced range of services

The evaluation of the *Prenatal Care Assistance Program (PCAP)*[59] reported a significant effect on PTB (<37 weeks) in HIV positive women attending a PCAP- accredited clinic compared with those who received care in a non-PCAP participating clinic (adjusted odds ratio 0.53, 95% CI 0.40-0.70). A second, partially overlapping, study of the same intervention in the subgroup of substance-abusing, HIV positive women also reported a significant effect (adjusted odds ratio 0.57, 95% CI 0.34-0.97) (See Annex B, Turner 2000, page 75). The reviewers considered that the evidence was inconclusive due to the risk of selection bias but consistent with a possible beneficial effect of the intervention on PTB in both the populations studied.

Table 6: Effectiveness of interventions targeting socioeconomically disadvantaged pregnant women without specific risk factors for PTB - comprehensive antenatal care interventions

	Design	Quality assessment[1]	PTB outcome		Neonatal/infant mortality outcome		Reviewer comments
			Authors' conclusion [2]	Reviewer Assessment [3]	Authors' Conclusion [2]	Reviewer Assessment [3]	
Group antenatal care*							
Ickovics (2003)[45]	Prospective cohort	Mixed	(+)	X	(+)	X	Self-selection bias (volunteers). Sample size based on birth weight outcome, not neonatal mortality or PTB.
Ickovics (2007)[40]	RCT	Mixed	+	+	N/A	N/A	Generally well designed/reported RCT.
Comprehensive antenatal care with outreach							
Reece (2002)[48]	Prospective cohort	Mixed	+	(+?)	N/A	N/A	High risk of selection bias but the intervention group was recruited by outreach workers from high risk populations and thus might be expected to have a higher risk profile than those entering antenatal care voluntarily.
Nurse/midwife antenatal clinics							
Lenaway (1998)[61]	Cohort	Poor	(+)	X	N/A	N/A	High risk of selection bias; impossible to assess comparability of comparator counties; substantial 'baseline differences', no adjustment for confounding.
Mvula (1998)[46]	Prospective cohort	Poor	(+)	X	N/A	N/A	Risk of selection bias; potential for channelling of higher risk women to hospital clinic not adequately addressed.
Other US public antenatal care programmes							
Clark (1993)[53]	Retrospective cohort	Poor	N/A	N/A	(+)	X	Selection bias. No controlling for confounders. Intervention and comparator groups arguably not drawn from the same target population (differed with respect to income).
Conover (2001)[64]	Other observational	Mixed	0	X	X	X	Implementation problems occurred during the evaluation period leading to possible failure to fully deliver the intervention.

[1] **Quality assessment (GATE criteria)**		[2] **Authors' conclusion**		[3] **Reviewers' assessment**	
Good	Well reported and reliable;	+	Statistically significant beneficial effect on PTB/Infant Mortality	+	Study demonstrates a beneficial effect
Mixed	Some weaknesses but insufficient to have an important effect on usefulness of study;	(+)	Effect consistent with beneficial effect but effect not statistically significant and/or cautious interpretation of finding suggested	(+?)	Study inconclusive but may demonstrate a beneficial effect
Poor	Study not reliable, not useful	X	No evidence of beneficial effect	X	Study does not provide convincing evidence of a beneficial effect
		0	No conclusion stated		
		N/A	Not applicable – outcome not assessed	N/A	Not applicable – outcome not assessed

* Group care also evaluated in teenagers by Grady (2004)[63] – see Table 10

Table 7: Effectiveness of interventions targeting socioeconomically disadvantaged pregnant women without specific risk factors for PTB – interventions provided as an adjunct to comprehensive antenatal care

	Design	Quality assessment[1]	PTB outcome		Neonatal/infant mortality outcome		Reviewer comments
			Authors' conclusion [2]	Reviewer Assessment [3]	Authors' Conclusion [2]	Reviewer Assessment [3]	
Case management/care coordination							
Buescher (1991)[16]	Retrospective cohort	Mixed	N/A	N/A	(+)	(+?)	Design subject to risk of selection bias but adequate adjustment for a range of confounders and various additional analyses conducted to investigate potential biases. Adjustment for inadequate quality of antenatal care may have over-adjusted for an effect of the intervention. Results considered consistent with a modest effect of the intervention on infant mortality.
Keeton (2004)[56]	Retrospective cohort	Poor	N/A	N/A	(+)	X	Strong selection bias with high risk of residual confounding despite statistical adjustment for a range of confounders.
Nurse home visits							
Kafatos (1991)[43]	Cluster RCT	Mixed	+	(+?)	X	X	Details of randomization process (i.e. concealment) unclear but groups appeared to be generally well balanced with a marginally higher prevalence of obstetric risk factors present in the intervention group. Analytic methods did not take account of cluster randomization.
Kitzman (1997)[37]	RCT	Good	X	X	N/A	N/A	Well designed/reported RCT. No evidence of treatment effect.
'Healthy Start' programme							
Lane (2001)[66]	Before and after with geographic comparator	Poor	N/A	N/A	(+)	X	Before and after study: changes in infant mortality cannot be reliably attributed to the study intervention. The comparison with temporal trends in the surrounding area is inconclusive since the socioeconomic and racial mix of the two areas differs.

[1] **Quality assessment (GATE criteria)**		[2] **Authors' conclusion**		[3] **Reviewers' assessment**	
Good	Well reported and reliable;	+	Statistically significant beneficial effect on PTB/Infant Mortality	+	Study demonstrates a beneficial effect
Mixed	Some weaknesses but insufficient to have an important effect on usefulness of study;	(+)	Effect consistent with beneficial effect but effect not statistically significant and/or cautious interpretation of finding suggested	(+?)	Study inconclusive but may demonstrate a beneficial effect
Poor	Study not reliable, not useful	X	No evidence of beneficial effect	X	Study does not provide convincing evidence of a beneficial effect
		0	No conclusion stated		
		N/A	Not applicable – outcome not assessed	N/A	Not applicable – outcome not assessed

Table 8: Effectiveness of PTB prevention programmes targeting socioeconomically disadvantaged pregnant women with additional clinical risk factors for PTB – clinic-based programmes

	Design	Quality assessment[1]	PTB outcome		Neonatal/infant mortality outcome		Reviewer comments
			Authors' conclusion [2]	Reviewer Assessment [3]	Authors' Conclusion [2]	Reviewer Assessment [3]	
Broad, multifaceted PTB prevention programmes							
Hobel (1994)[42]	Cluster RCT	Mixed	+ * see note under reviewer comments	(+?)	N/A	N/A	Cluster randomization of small number of sites did not adequately balance groups with respect to PTB risks; not possible to assess likelihood of residual confounding. Analysis did not take account of cluster randomization so significance level of the reported effect on PTB overestimated. * Note: Significance based on one-sided test.
Klerman (2001)[38]	RCT	Mixed	X	X	N/A	N/A	Generally well designed/reported RCT but underpowered for PTB outcome.
Edwards (1995)[55]	Retrospective cohort	Poor	X	X	N/A	N/A	Risk of selection bias and no adjustment for confounding.
Programmes with focus on patient education (signs of preterm labour) plus additional visits/examinations							
Collaborative Group on PTB Prevention (1993)[35]	RCT	Poor	X	X	N/A	N/A	Author notes that results did not show a consistent effect with significant, unexplained heterogeneity between the five study sites. Possible contamination of control group (i.e. exposure to intervention)
Goldenberg* (1990)[34]	RCT		N/A*	N/A*	X	X	More neonatal deaths in the intervention group (difference not statistically significant)
Hospital clinic vs. 'managed care'							
Bienstock (2001)[52]	Retrospective cohort	Poor	+	X	N/A	N/A	Potential selection bias; managed care compared with a single hospital site

[1] **Quality assessment (GATE criteria)**		[2] **Authors' conclusion**		[3] **Reviewers' assessment**	
Good	Well reported and reliable;	+	Statistically significant beneficial effect on PTB/Infant Mortality	+	Study demonstrates a beneficial effect
Mixed	Some weaknesses but insufficient to have an important effect on usefulness of study;	(+)	Effect consistent with beneficial effect but effect not statistically significant and/or cautious interpretation of finding suggested	(+?)	Study inconclusive but may demonstrate a beneficial effect
Poor	Study not reliable, not useful	X	No evidence of beneficial effect	X	Study does not provide convincing evidence of a beneficial effect
		0	No conclusion stated		
		N/A	Not applicable – outcome not assessed	N/A	Not applicable – outcome not assessed

* Results relating to PTB included in preceding row. Goldenberg et al. report additional results relating to neonatal mortality based on a single site participating in the Collaborative Group study

Table 9: Effectiveness of PTB prevention programmes targeting socioeconomically disadvantaged pregnant women with additional clinical risk factors for PTB – programmes provided as an adjunct to comprehensive antenatal care

	Design	Quality assessment[1]	PTB outcome		Neonatal/infant mortality outcome		Reviewer comments
			Authors' conclusion [2]	Reviewer Assessment [3]	Authors' Conclusion [2]	Reviewer Assessment [3]	
Home visits/telephone support							
Bryce (1991)[36]	RCT	Mixed	X	X	0	X	RCT with randomisation before consent. Trial not restricted to socioeconomically disadvantaged women but stratified analysis by social class reported.
Moore (1998)[39]	RCT	Mixed	X/+ * See reviewer comments for explaination	X*	N/A	N/A	Well designed/reported RCT which did not demonstrate a significant intervention effect on PTB overall. The reported intervention effect on PTB in black women aged ≥19 was based on a subgroup analysis and hence must be interpreted with caution. It is unclear if the sub-group analysis was pre-specified, however, the level of significance was set at 0.6% level to allow for multiple comparisons.
Oakley (1990)[41]	RCT	Good	0	X	0	X	Well designed/reported RCT. No evidence of treatment effect.

[1] **Quality assessment (GATE criteria)**		[2] **Authors' conclusion**		[3] **Reviewers' assessment**	
Good	Well reported and reliable;	+	Statistically significant beneficial effect on PTB/Infant Mortality	+	Study demonstrates a beneficial effect
Mixed	Some weaknesses but insufficient to have an important effect on usefulness of study;	(+)	Effect consistent with beneficial effect but effect not statistically significant and/or cautious interpretation of finding suggested	(+?)	Study inconclusive but may demonstrate a beneficial effect
Poor	Study not reliable, not useful	X	No evidence of beneficial effect	X	Study does not provide convincing evidence of a beneficial effect
		0	No conclusion stated		
		N/A	Not applicable – outcome not assessed	N/A	Not applicable – outcome not assessed

Table 10: Effectiveness of interventions targeting teenagers

	Design	Quality assessment[1]	PTB outcome		Neonatal/infant mortality outcome		Reviewer comments
			Authors' conclusion [2]	Reviewer Assessment [3]	Authors' Conclusion [2]	Reviewer Assessment [3]	
'Teen' clinics							
Benussen-Wall (2001)[51]	Retrospective cohort	Poor	0	X	N/A	N/A	Small study; groups differed due to imperfect matching on nine matching criteria; high risk of confounding.
Das (2007)[65]	Before and after	Poor	(+)	X	N/A	N/A	Before and after study: high risk of bias due to secular changes in outcome; possible difference in prognostic factors (particularly age) in the intervention and control groups. Small sample size.
Morris (1993)[57]	Retrospective cohort	Poor	X	X	N/A	N/A	High risk of selection bias and inadequate adjustment for confounding.
Perez (1998)[58]	Retrospective cohort	Poor	(+) * see reviewer comments	X	N/A	N/A	* Authors' conclusion based on achieving outcomes comparable to general population.
Quinlivan (2004)[47]	Prospective cohort	Poor	+	X * see reviewer comments	N/A	N/A	Multi-site study. * Results inconclusive due to high risk of selection bias but groups were broadly comparable at 'baseline' with respect to a range of risk factors .
Ukil (2002)[60]	Retrospective cohort	Poor	+	X	N/A	N/A	Small study; characteristics of study groups not reported; no adjustment for confounding; multiple outcomes compared (high risk of type I error).
Van Winter (1997)[49]	Prospective cohort	Poor	(+)	X	N/A	N/A	High risk of selection bias: intervention recipients compared with those who refused the intervention.
Adolescent group antenatal care							
Grady (2004)[63]	Mixed prospective/ retrospective cohort	Poor	(+)	X	N/A	N/A	High risk of selection bias and no control of confounding.
Stand alone nutritional programme							
Dubois (1997)[54]	Retrospective observational	Mixed	+	(+?)	N/A	N/A	High risk of selection bias but the risk profiles of the intervention and comparator groups suggest that the intervention group had a higher baseline risk of adverse pregnancy outcome.

[1] **Quality assessment (GATE criteria)**	
Good	Well reported and reliable;
Mixed	Some weaknesses but insufficient to have an important effect on usefulness of study;
Poor	Study not reliable, not useful

[2] **Authors' conclusion**	
+	Statistically significant beneficial effect on PTB/Infant Mortality
(+)	Effect consistent with beneficial effect but effect not statistically significant and/or cautious interpretation of finding suggested
X	No evidence of beneficial effect
0	No conclusion stated
N/A	Not applicable – outcome not assessed

[3] **Reviewers' assessment**	
+	Study demonstrates a beneficial effect
(+?)	Study inconclusive but may demonstrate a beneficial effect
X	Study does not provide convincing evidence of a beneficial effect
N/A	Not applicable – outcome not assessed

Table 11: Effectiveness of interventions targeting or evaluated in substance users

	Design	Quality assessment[1]	PTB outcome		Neonatal/infant mortality outcome		Reviewer comments
			Authors' conclusion [2]	Reviewer Assessment [3]	Authors' Conclusion [2]	Reviewer Assessment [3]	
Substance abuse programme provided as an adjunct to standard antenatal care							
Armstrong (2003)[50]	Retrospective cohort	Poor	(+)	X	X	X	Authors' conclusion based on comparison with non-substance abusing comparator
Burkett (1998)[44]	Prospective cohort	Poor	(+)	X	N/A	N/A	High risk of selection bias (intervention group compared with those who refused the intervention); no adjustment for potential confounders.
Miles (2007)[68]	Before and after	Poor	X	X	N/A	N/A	Small before and after study.
Sweeney (2000)[62]	Cohort	Poor	+	X	X	X	Small study with strong selection bias (intervention group compared with women who enrolled in substance abuse treatment postnatally but refused the intervention while pregnant).
Comprehensive care in general antenatal clinics providing an enhanced range of services							
Newschaffer* (1998)[33]	Retrospective cohort	Mixed	+	(+?)	N/A	N/A	Large, generally well designed/reported multi-site retrospective observational study. Risk of selection bias but adequate statistical adjustment for range of potential confounders. Analysis did not take account of clustering so confidence intervals over-estimated.

[1] **Quality assessment (GATE criteria)**		[2] **Authors' conclusion**		[3] **Reviewers' assessment**	
Good	Well reported and reliable;	+	Statistically significant beneficial effect on PTB/Infant Mortality	+	Study demonstrates a beneficial effect
Mixed	Some weaknesses but insufficient to have an important effect on usefulness of study;	(+)	Effect consistent with beneficial effect but effect not statistically significant and/or cautious interpretation of finding suggested	(+?)	Study inconclusive but may demonstrate a beneficial effect
Poor	Study not reliable, not useful	X	No evidence of beneficial effect	X	Study does not provide convincing evidence of a beneficial effect
		0	No conclusion stated		
		N/A	Not applicable – outcome not assessed	N/A	Not applicable – outcome not assessed

* Secondary report (subgroup analysis) – see Turner (2000) for primary report

Table 12: Effectiveness of interventions targeting or evaluated in (a) indigenous women and (b) low-income HIV positive women

	Design	Quality assessment[1]	PTB outcome		Neonatal/infant mortality outcome		Reviewer comments
			Authors' conclusion [2]	Reviewer Assessment [3]	Authors' Conclusion [2]	Reviewer Assessment [3]	
(a) Indigenous women							
Culturally sensitive antenatal care including community/outreach services							
Mackerras (2001)[67]	Before and after	Poor	(+)	X	N/A	N/A	Before and after study; the authors note that it is not possible to separate the effects of concurrent changes in the health services in the communities studied from the effects of the intervention.
Panaretto (2007)[69]	Before and after with additional contemporary comparator group	Poor	(+)	X	N/A	N/A	Before and after study; high risk of selection bias; increased use of ultrasound during the study period could have led to more accurate dating of gestational age.
(b) Low-income, HIV positive women							
Comprehensive care in general antenatal clinics providing an enhanced range of services							
Turner (2000)[59]	Retrospective cohort	Mixed	+	(+?)	N/A	N/A	Large, generally well designed/reported multi-site retrospective observational study. Risk of selection bias but adequate statistical adjustment for range of potential confounders. Analysis did not take account of clustering so confidence intervals over-estimated.

[1] **Quality assessment (GATE criteria)**		[2] **Authors' conclusion**		[3] **Reviewers' assessment**	
Good	Well reported and reliable;	+	Statistically significant beneficial effect on PTB/Infant Mortality	+	Study demonstrates a beneficial effect
Mixed	Some weaknesses but insufficient to have an important effect on usefulness of study;	(+)	Effect consistent with beneficial effect but effect not statistically significant and/or cautious interpretation of finding suggested	(+?)	Study inconclusive but may demonstrate a beneficial effect
Poor	Study not reliable, not useful	X	No evidence of beneficial effect	X	Study does not provide convincing evidence of a beneficial effect
		0	No conclusion stated		
		N/A	Not applicable – outcome not assessed	N/A	Not applicable – outcome not assessed

* Secondary report (subgroup analysis) – see Turner (2000) for primary report

6 Discussion and conclusions

6.1 Summary of main findings

The purpose of this review was to evaluate the effectiveness of interventions involving the delivery or organisation of antenatal care as a means of reducing infant mortality or its three major causes (PTB, congenital anomalies, SIDS/SUDI) in disadvantaged and vulnerable women. In total, we included 40 eligible published reports of which 36 were primary reports relating to distinct interventions and/or evaluations.

The included studies evaluated interventions in a range of disadvantaged and vulnerable populations including socioeconomically disadvantaged/low-income women in general, socioeconomically disadvantaged/low-income women with additional clinical risk factors for adverse pregnancy outcome, and four other specific groups at risk of adverse pregnancy outcome: teenagers, substance users, indigenous women and HIV positive women.

Overall, the quality of evidence was poor and, for most of the interventions considered, there was insufficient evidence to evaluate consistency of findings across multiple studies. Less than half (14 of 36) of the included evaluations were considered to have good or adequate internal validity, of which eight were RCTs, two were prospective cohort studies, three were retrospective cohort studies, and one was a before and after study with a contemporaneous comparator group. Even in these higher quality studies, we found that none of the antenatal care interventions were demonstrably effective in reducing PTB or neonatal mortality in the disadvantaged and vulnerable populations considered.

We concluded that the evidence relating to seven interventions, although inconclusive, indicated a possible beneficial effect on PTB or on infant mortality.

The following four models of comprehensive antenatal care were considered promising:

- Findings of one well-conducted RCT[40] suggested that group antenatal care might reduce PTB in socioeconomically disadvantaged women. An earlier cohort study evaluating the same model of group antenatal care[45] did not show a consistent beneficial effect on PTB, but the study was underpowered to detect an effect on this outcome. The group antenatal care model is well defined and described and would appear to be transferable to the NHS.
- Trials of two broad, multifaceted, clinic-based PTB prevention programmes targeting disadvantaged women with additional clinical risk factors for PTB suggested that such interventions might be effective in reducing PTB. The two interventions evaluated[38,42] were not identical but appeared to share the common approach of targeting a broad range of risk factors. Such programmes would potentially be transferable to the NHS although only one of the two reports provided sufficient detail to enable replication of the main elements of the programme.[38]
- The intensive, multi-component *TIPPS* programme evaluated by Reece[48] was considered promising with regard to possible effects on PTB despite methodological limitations of the evaluation. The *TIPPS* intervention itself was designed specifically to address the problems and needs of a disadvantaged local population in North Philadelphia and it is unclear whether the intervention is transferable or the findings generaliseable to other setting. However, some elements of the intervention and the need-based approach to developing 'locally customised' services may merit further examination and evaluation.
- The two overlapping evaluations of the *New York Prenatal Care Assistance Program (PCAP)*[33,59] suggested that the PCAP programme might be effective in reducing PTB in HIV positive women. The programme aims to improve outcomes by improving the quality of care through a process of clinic accreditation with financial incentives to 'accredited' antenatal clinics. The effect of PCAP on other outcomes has also been evaluated in a wider population of socioeconomically disadvantaged women.[83] The

use of enhanced payments to providers providing enhanced services is potentially transferable to the NHS but it is unclear whether the specific services covered by PCAP accreditation would be relevant to the UK setting.

Three interventions provided as an adjunct to standard antenatal care were also considered promising:

- Two nutritional programmes were tentatively considered promising. An evaluation of the *Higgins Nutrition Intervention Program* in pregnant teenagers indicated a possible beneficial effect on PTB in this population, despite the methodological limitations of the study[54]; and the evaluation of a home visiting programme focussing on nutritional education (the *Florina Intervention Program*) also suggested a possible beneficial effect on PTB in a low-income rural population in Greece.[43,73] The *Higgins Nutrition Intervention Program* is potentially transferable and replicable. The intervention is not described in full in the included report[54] but details are available elsewhere.[80,81] The *Florina Intervention Program* was evaluated in isolated agricultural population in Greece with a low-calorie, seasonal diet based on home produce and domestic livestock[73]: the relevance and generalisability of the nutritional elements of the intervention to the UK population is therefore questionable.

A single US-based study indicated that maternity care coordination might have a beneficial effect on infant mortality in socially disadvantaged women in the USA.[16] However, it is unclear to what extent these findings can be generalised to the NHS since some elements of the intervention may be specific to the healthcare and welfare systems in the USA.

No conclusions could be drawn regarding the effectiveness of 'teen' clinics because of problems of study design and selection bias in the included studies. The effectiveness of 'teen' clinics has not therefore, in our view, been established and would merit further, more rigorous, evaluation.

We considered that the studies reviewed did not provide sufficient evidence to draw any conclusions regarding the effectiveness of the other interventions evaluated.

We recognised at the outset that studies were unlikely to be of sufficient size to detect an effect on congenital anomalies or SIDS/SUDI. Nevertheless, we explicitly searched for evaluations reporting these outcome measures. We found six studies that reported on the occurrence of congenital anomalies, but none, as anticipated, was sufficiently large to detect an intervention effect. We did not find any eligible studies that reported on SIDS.

6.2 Strengths and limitations of this systematic review

In line with our aim to identify the best available evidence on antenatal care interventions targeting socially disadvantaged and vulnerable women we did not restrict ourselves to particular study designs and we designed our searches to reflect this breadth of interest. This lack of specificity may be seen as both a strength and a weakness of this review.

The inclusion of less methodologically rigorous evaluations increased the volume of material identified and reviewed and also presented methodological challenges with regard to quality assessment. However, it did not greatly add to the evidence regarding effectiveness. Nevertheless, the inclusion and systematic quality appraisal of such evaluations may have served the useful function of highlighting the lack of robust evidence supporting the effectiveness of some widely studied interventions, e.g. 'teen' clinics.

The decision to review a broad category of interventions - antenatal care interventions involving the delivery or organisation of health and social care to pregnant women - rather than identifying specific interventions a *priori*, has enabled us to provide an overview of a wide range of interventions. A more focussed approach examining a smaller range of specific interventions would have been more consistent with standard systematic reviewing methods, although developing and applying precise interventions definitions - required to ensure reproducible selection of studies - would potentially have been challenging.[84] Furthermore, such an approach would have lacked the flexibility to review

a broad, rather diffuse and poorly defined evidence base which was possible with our more comprehensive approach. However, a disadvantage is that a more comprehensive approach necessitates a degree of *post hoc* decision making.[85] For example, following our initial searches we had to decide how best to classify and group the interventions. It is possible that different ways of classifying and grouping the interventions might have changed the 'weight of evidence' in favour of an interventions within scope of the review, but, given the limitations of the evidence, we think it unlikely that this would have resulted in major changes to our conclusions.

We were primarily interested in evidence on interventions relating to present day practice. Given the advances in antenatal care made over the past few decades, for pragmatic reasons, we applied a uniform year-of-publication cut off point of 1990. This enabled us to focus on models of antenatal care most likely to be relevant in the current context but may have led to the exclusion of potentially relevant older studies.

An unanticipated consequence of our 'generic' inclusion/exclusion criteria was the exclusion of some seemingly relevant interventions provided as an 'add on' to normal antenatal care. For example, studies relating to some welfare-based US programmes (WIC, care co-ordination) were excluded not because the intervention was ineligible but because studies evaluating the intervention typically compared 'intervention recipients' with 'non-recipients', with the latter group including women who received no antenatal care, i.e. the comparator groups did not receive standard antenatal care, as required by our inclusion criteria. However, although we did not fully quality appraise the studies excluded on the basis of lack of standard antenatal care in the comparator group, we did note two common methodological flaws in the excluded material: firstly, many did not adequately address the risk of gestational age bias[i], and secondly such strong selection biases were often present that adequate adjustment for differences between the intervention and comparator groups was impossible.

It is possible that we may have missed some relevant 'add on' interventions as a result of using non-specific antenatal care search terms (e.g. 'prenatal care') instead of more intervention specific terms. For example, studies relating to the WIC intervention are not consistently indexed under the broad 'catch all' terms that we used (e.g. maternal health services and prenatal care as indexed terms) nor are the majority picked-up by the freetext terms that we used (see Annex A). Similarly, socioeconomically disadvantaged study populations are not consistently indexed or mentioned in searchable elements of the bibliographic record. We took some additional steps to increase ascertainment of relevant material, including using an adapted version of an 'equity filter' developed by the Eppi-Centre in our searches, and 'snowballing',[87] i.e. checking citations of all included studies and checking reference lists of other reviews and guidelines.

6.3 Findings in relation to other published evidence

One previous review conducted in the early 1990s sought to evaluate the "best" evidence relating to the effect of antenatal healthcare programmes on pregnancy outcomes, including infant mortality and gestational age at birth.[14] The review identified 22 relevant reports published between 1981 and 1991, only seven of which the authors considered to have adequate methodological rigour according to a checklist that they had developed. Only two of their seven included studies evaluated PTB or infant/neonatal mortality as an outcome (the evaluation of maternity care coordination by Buescher et al. included in the present review,[16] and a pre-1990 evaluation of a social support programme[88]). They concluded that maternal care coordination, home visits by nurses and specially targeted smoking and nutritional programmes were associated with "optimized pregnancy outcomes for certain groups of women, including the poor and very young." However, as in the present review, and for similar reasons, they urged caution in applying these findings.

i Women giving birth prematurely have less time to enrol in a programme and may therefore be more likely to fall in the 'non-recipient' group in an observational study. See Joyce et al.[86] for a detailed discussion of this in relation to evaluation of the WIC programme.

Other published reviews, discussed below, have addressed the effectiveness of a range of specific antenatal care interventions in socioeconomically mixed populations of pregnant women. We are aware of only two reviews that have evaluated the effect of antenatal care interventions on PTB and infant survival/mortality in specific vulnerable populations (indigenous women[17] and women with alcohol or drug problems[89]). The latter Cochrane review of home visits during pregnancy and after birth from women with alcohol or drug problems did not identify any studies where the intervention contained a significant antenatal element and none of the included studies reported effects on PTB.

The reviews discussed below predominantly considered only RCT evidence[18,19,21,23,90-92]; one was a review of reviews.[93] The three systematic reviews that included evidence from non-randomised studies did not appear to have conducted any form of formal quality assessment.[17,94,95]

Overall, the findings of other published reviews appear consistent with our assessments of the effectiveness of the interventions in disadvantaged or vulnerable populations.

- **PTB prevention educational programmes for high risk women.** Hueston and colleagues reviewed RCT evidence to evaluate whether PTB prevention educational programmes were effective at reducing neonatal mortality, LBW and preterm delivery.[94] The authors concluded that such programmes appeared to have little benefit in reducing PTB and might result in an increased rate of diagnosis of preterm labour. Our conclusion that the Collaborative Group on Preterm Birth Prevention evaluation of a PTB patient education programme[35] did not provide evidence of a beneficial effect of the programme in a low-income population is consistent with Hueston's meta-analysis which was based on four studies, including the Collaborative Group trial.
- **Home visiting programmes.** Blondel and colleagues conducted a systematic review of RCTs to assess the effect of home visits on a range of pregnancy outcomes including PTB (<37 weeks).[19] The review separately examined home visiting programmes providing social support and those providing medical care to women with complications. The authors concluded that home visits, both overall, and in each of the two sub-categories considered (i.e., social support and medical care) did not improve the preterm delivery rate or other pregnancy outcomes. A second review of interventions involving support during pregnancy for women at increased risk of LBW babies,[91] which included a meta-analysis of 11 trials reporting PTB as an outcome, found no effect on PTB (Risk ratio 0.96, 95% CI 0.86 – 1.07). A further 'review of reviews' conducted more recently by the UK Health Development Agency[93] similarly concluded that there was insufficient evidence to suggest that home-visiting programmes had a beneficial impact on low birth weight or other pregnancy outcomes.

  In the present review, we considered evaluations of four home visiting interventions falling within Blondel and/or Hodnett's 'social support' category.[36,37,39,41] Our conclusions regarding lack of evidence of effectiveness were consistent with the reviews discussed above.
- **Telephone support.** A recent systematic review by Dennis and Kingston[18] (which partially overlaps with Hodnett's review of social support discussed above[91]) evaluated the effectiveness of telephone support interventions on a range of outcomes. Based on a meta-analysis of the results of five RCTs reporting PTB (including the studies by Bryce[36] and Moore,[39] included in the present review), they concluded that telephone interventions were ineffective at reducing PTB.
- **Nutritional interventions.** A review by Nielson and colleagues of the effectiveness of interventions to optimize gestational weight gain and diet in pregnant adolescents[95] concluded that such interventions had achieved "promising results" with regard to a range of pregnancy outcomes (predominantly measures of birthweight and/or gestational weight gain), but found little evidence relating to effects on PTB. Nielson and colleagues did not systematically assess the quality of the included material but noted that much of the evidence was methodologically flawed. A second review by Kramer and Kakuma assessed the effects of a range of nutritional interventions

during pregnancy, including advice to increase or reduce energy or protein intake.[92] The authors concluded that although dietary advice appeared to be effective in increasing pregnant women's energy and protein intakes it was unlikely to confer major benefits on infant or maternal health. The latter review was not restricted to teenagers and included the evaluation of the Florina[43] home visiting programme. These findings do not support our tentative conclusions regarding the potentially 'promising' effect of the two programmes with a nutritional focus included in the present review (the Higgins nutritional intervention in teenagers,[54] and the Florina home visiting programme which has a nutritional counselling focus[43]) and, on balance, may suggest that a more cautious interpretation of the evidence in favour of these two interventions would be warranted.

- **Midwife-led antenatal care.** A recent Cochrane systematic review by Hatem and colleagues evaluated midwife-led care versus other models of care for childbearing women.[90] A meta-analysis of data from five antenatal care trials did not find a significant beneficial effect of midwife-led antenatal care on PTB (risk ratio 0.87, 95% CI 0.73-1.04). The trials included in the review varied with regard to the risk status of participants and did not all focus on low-risk women as in the two evaluations of midwife-led clinics included in the present review.[46,61] The lack of a significant effect on PTB in Hatem's well conducted analysis is consistent with our cautious interpretation of the findings of the two evaluations of midwife-led clinics.[46,61] A second review by Waldenstrom and Turnbull of continuity of midwifery care vs. standard care[21] analysed outcome data from many of the same trials as the Hatem review, but additionally conducted a meta-analysis of studies reporting neonatal mortality. This latter analysis found no significant effect on neonatal mortality (odds ratio 1.27, 95% CI 0.49 – 3.34). A third review by Khan-Neelofur and colleagues examined the evidence relating to various aspects of antental care for low-risk women including the effectiveness of midwife/general practitioner-managed care vs. obstetrician/gynaecologist-led shared care.[23] Based on two trials, (including one of the trials[96] included in the Hatem review) the results showed no significant effect on PTB (relative risk 0.80, 95% CI 0.59 – 1.10).
- **Antenatal care targeting specific vulnerable groups.** Rumbold and Cunningham reviewed the impact of antenatal care interventions on Australian indigenous women.[17] They found that two of the four included studies that considered PTB as an outcome (which included the Townsville study considered in the present review[69]) reported a reduction in PTB, but their review did not assess the quality of the included studies so the interpretation of these findings is uncertain.

We are unaware of other relevant systematic reviews considering the effectiveness of the other interventions considered here. A recent Cochrane review of specialised antenatal clinics for women with multiple pregnancy found no relevant randomised controlled trials[97]; and a protocol for a Cochrane review of specialised antenatal clinics for women with a pregnancy at high risk of PTB (excluding multiple pregnancy) was published in 2007[98] indicating that a review is in progress but yet to be published.

6.4 Implications and recommendations

Our findings, together with related evidence from the literature, indicate that there is insufficient robust evidence to recommend that any of the interventions covered in this review be routinely adopted by the NHS as a means of reducing infant mortality in socially disadvantaged and vulnerable groups of women. However, in line with the aims of the infant mortality project, our review focussed specifically on effects of interventions on infant mortality and PTB rates and on other related outcomes. We did not consider other potentially important beneficial effects of the interventions.

Furthermore, many of the included studies were small and would only be able to detect a substantial reduction in infant mortality and/or PTB. As we note above, a number of the included studies with adequate internal validity observed a non-significant effect on PTB or

infant mortality in the desired direction. Thus, although not providing conclusive evidence of a beneficial effect, our findings are suggestive of a modest beneficial effect of some of the interventions on the outcomes of interest.

Policy makers, health care commissioners, service providers and others increasingly look for high quality evidence to support their policies and decisions, and the lack of adequate, high quality research relating to complex health care interventions, such as antenatal care, has serious implications for the development and implementation of evidence based policy and practice. We would echo an observation of the House of Commons Health Committee on Health inequalities:

> *"Policy cannot be evidence-based if there is no evidence and evidence cannot be obtained without proper evaluation"* [99]

While small, exploratory studies may have value during the design stages of an intervention or the planning of a larger evaluation[100] more robust methods are required to adequately evaluate intervention effectiveness. As the material reviewed here powerfully illustrates, small, underpowered evaluations of effectiveness using weak, observational designs tend to provide little evidence of value; and while non-experimental methods may sometimes be justified on the basis of feasibility, acceptability, or cost, the conditions under which observational methods can yield reliable estimates are limited.[101,102] A number of robust experimental and quasi-experimental methods to evaluate complex evaluations are available[101] and would merit more widespread use. Such methods however require earlier and closer collaboration between researcher, policy makers, and those involved in developing and implementing new services.

6.5 Conclusion

In summary, we found insufficient evidence of adequate quality to conclude that interventions involving alternative models of organising or delivering antenatal care reduce infant mortality or PTB in socially disadvantaged or vulnerable populations compared with standard models of antenatal care. A small number of the interventions reviewed here were considered 'promising' in terms of their effect on PTB in socially disadvantaged or vulnerable populations, but the effects, if any, are likely to be modest and further robust evaluation would be required before routine adoption of these interventions could be recommended in the NHS.

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Annex A: Medline search strategy

Outcome terms

3. exp Infant Mortality/
4. exp Perinatal Mortality/
5. ((infant$ or perinat$ or neonat$ or postneonat$) adj2 (death$ or mortalit$ or surviv$)).ti,ab.
6. ((newborn$ or infant$ or perinat$ or neonat$ or postneonat$) adj2 (death$ or dead or died or mortalit$ or surviv$)).ti,ab.
7. or/1-4
8. exp Infant, Premature/
9. exp obstetric labor, premature/ or exp premature birth/
10. ((preterm or prematur$) adj2 (labour$ or labor$ or birth$ or deliver$ or infant$)).ti,ab.
11. (prematurity or preterm).ti,ab.
12. or/6-9
13. exp Sudden Infant Death/
14. "sudden unexpected death in infancy".ti,ab.
15. "sudden unexplained death in infancy".ti,ab.
16. cot death$.ti,ab.
17. crib death$.ti,ab.
18. (SIDS or SUDI).ti,ab.
19. "sudden infant death syndrome".ti,ab.
20. or/11-17
21. exp Congenital Abnormalities/
22. ((birth or congenital) adj2 (defect$ or deform$ or abnorm$ or anomal$ or malform$)).ti,ab.
23. or/19-20
24. 5 or 10 or 18 or 21

Intervention terms

25. exp Prenatal Care/ or maternal health services/
26. exp Midwifery/
27. ((antenatal or prenatal) adj2 (care or clinic or program* or service*)).ti,ab.
28. or/23-25

Disadvantaged and vulnerable group terms

29. exp Socioeconomic Factors/ or exp Social Class/
30. (equity or inequalit$ or equalit$ or unequal$ or inequit$ or disparit$ or gap or gaps or gradient$ or disadvantag$ or socioeconomic$).ti,ab.
31. health inequalit$.mp. or Health Status Indicators/ or *Health Status Disparities/ or *Healthcare Disparities/
32. exp Poverty/ or exp Medical Indigency/ or vulnerable populations/
33. exp Minority Health/ or exp Minority Groups/ or population groups/ or exp ethnic groups/ or health services, indigenous/
34. (ethnic or (black adj2 asian)).ti,ab.
35. (multiethnic$ or multi ethnic$ or multiracial$ or multi racial$).ti,ab.
36. exp Prisoners/ or prison*.ti,ab.
37. exp refugees/ or "Emigrants and Immigrants"/ or "Transients and Migrants"/
38. (immigrant* or refugee* or migrant* or asylum seeker*).ti,ab.
39. exp gypsies/ or travel?er*.ti,ab.

40. exp Homeless Youth/ or exp Homeless Persons/ or homeless$.ti,ab.
41. exp Spouse Abuse/ or Domestic Violence/ or exp battered women/
42. ((abuse$ or violen$) adj4 (partner$ or wife or wives or spouse$ or domestic)).ti,ab.
43. ((neighbo?rhood or economic or rural or urban) adj2 (depriv$ or poverty)).ti,ab.
44. (disadvantag* or deprived area* or innercit* or inner cit*).ti,ab.
45. Mental Disorders/ or exp eating disorders/ or exp mood disorders/ or exp "schizophrenia and disorders with psychotic features"/
46. ((mental$ or psych$) adj2 (ill$ or disorder$ or impair$ or disturb$ or disabil$)).ti,ab.
47. Learning Disorders/ or Mental Deficiency/
48. ((mental$ or learning or cognitiv$) adj2 (retard$ or handicap$ or disab$ or difficult$ or impair$)).ti,ab.
49. exp Prostitution/ or sex worker*.ti,ab.
50. Adolescent Health Services/ or exp Adolescent/ or exp Pregnancy in Adolescence/
51. (teen$ or youth$ or adolescen$).ti,ab.
52. (late adj2 (book$ or initiat$ or attend$)).ti,ab.
53. exp Obesity/ or exp Obesity, Morbid/
54. (obese or obesity).ti,ab.
55. exp HIV Infections/ or HIV/
56. (HIV or HIV-pos$ or HIV-inf$).ti,ab.
57. exp Street Drugs/ or exp Narcotics/ or exp Cocaine/ or exp Crack Cocaine/ or exp Heroin/ or exp amphetamines/ or exp methadone/
58. exp substance-related disorders/ or exp Substance Abuse, Intravenous/ or exp amphetamine-related disorders/ or exp cocaine-related disorders/ or exp marijuana abuse/ or exp opioid-related disorders/ or exp heroin dependence/ or exp phencyclidine abuse/ or exp psychoses, substance-induced/ or exp substance abuse, intravenous/ or substance withdrawal syndrome/
59. exp alcohol-related disorders/ or exp alcoholism/ or exp alcohol-induced disorders/
60. or/27-57
61. 22 and 26 and 58

Limits

62. limit 59 to (humans and yr="1990 - 2008")
63. limit 60 to abstracts
64. limit 60 to english language
65. 61 or 62
66. Case Reports/
67. 63 not 64

Annex B: Description of included studies and summary of results

Notes – how to read this table

- Intervention groups are described in column 6. In most studies there is only one intervention group, labelled 'I'; where there is more than one intervention group, groups are labelled 'I1', 'I2,' etc.
- Comparator/control group(s) are described in column 7. Where there is only one comparator/control group this is labelled 'C'; where there are multiple comparator groups these are labelled 'C1', 'C2', etc.
- Results are generally presented as a comparison of the outcomes in the intervention group compared with the control group(s), i.e. I vs. C for studies with one intervention group and one control/comparator group. Where there are multiple control/comparator groups, multiple comparisons are shown.
- Subgroup analyses are presented where the author comments on differential effectiveness across subgroups
- Both unadjusted and adjusted results are presented where available; where the authors have fitted multiple adjustment models we present the results considered most relevant – usually involving adjustment for maternal characteristics/risk factors present at booking.
- 95% confidence interval, "p-values" and/or a statement that a difference is "not significant" are included where reported by the authors.

To find a particular study, see index below.

Abbreviations

RCT = Randomised controlled trial;
OR = Odds ratio;
RR = Relative Risk;
95% CI = 95% confidence interval;
NS = Not statistically significant at the 5% level;
% PTB = percentage of births that were preterm.

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Table B2: Description of included studies and summary of results

Author, year	Country/Setting	Study design	Study population	Method of allocation to study group(s)	Intervention group(s)	Control/ comparator group(s)	Results - PTB (I vs. C)	Results - neonatal/ infant mortality (I vs. C)
1 Interventions targeting socioeconomically disadvantaged women without specific risk factors for PTB								
1.1 Comprehensive antenatal care interventions								
1.1.1 Group antenatal care								
Ickovics, 2003	USA. Three public antenatal clinics in Atlanta, Georgia and New Haven, serving predominantly low-income, uninsured (Medicaid or self-pay) minority women.	Prospective observational cohort study Matched.	Women without severe medical or psychiatric problems who entered antenatal care at one the three study clinics at 24 or less weeks' gestation between August 1999 and March 2002.	Non-random selection from antenatal care population Women who opted to receive antenatal care in a group setting vs. matched controls attending antenatal care at the same institution.	229 antenatal care attendees who volunteered to receive group antenatal care.	229 antenatal care attendees selected from the women who did not volunteer to receive group antenatal care, matched on age, race/ ethnicity, parity and date of delivery.	Unadjusted % PTB (<37 weeks): 9.2% vs. 9.6%, p = 0.83. Unadjusted % early PTB (<33 weeks): 0.9% vs. 3.1% Unadjusted % late PTB (33-36.9 weeks): 8.3% vs. 6.5%	Neonatal deaths, n (%): I1 vs. C1: 0 (0%) vs. 3 (1.3%)
Ickovics, 2007	USA. Publicly funded obstetric clinics in two university-affiliated hospitals in Connecticut and Georgia.	RCT	Women aged less than 25 entering antenatal care at the two study sites between September 2001 and December 2004; less than 24 weeks gestation; no "high-risk" medical problems (e.g. HIV); consenting to randomization. Multiple gestations excluded in PTB analysis.	Randomised - individual	625 women randomised to group antenatal care.	370 women randomised to individual antenatal care.	Adjusted % PTB (<37 weeks): 9.8% vs. 13.8%, p=.045 Adjusted odds ratio (95% CI) for PTB: 0.67 (0.44-0.98)	
1.1.2 Comprehensive multidisciplinary service with outreach								
Reece, 2002	USA. Community and hospital based maternity services in North Philadelphia, Pennsylvania.	Prospective observational cohort study	Medically indigent women who enrolled in the intensive maternity care programme (TIPPS) or who enrolled in usual antenatal care at the study hospital	Non-random selection from antenatal care population. Matched controls were selected from the population of women who received antenatal care but did not participate in the comprehensive care programme.	380 women enrolled in the Temple Infant and Parent Support Services (TIPPS).	437 women not enrolled in the TIPPS programme.	% PTB* (<37 weeks): 4.3% vs. 12.0%, p< 0.005 * "Matched" comparison group	
1.1.3 Nurse/midwife led clinics for low risk women								
Lenaway, 1998	USA. Public maternity services in mixed suburban/rural areas of Colorado.	Observational cohort study Population based comparison of outcomes in an area where women had access to the study intervention vs. outcomes in two comparator non-intervention areas.	Medically indigent women residing in three contiguous counties in Colorado (Boulder county and two adjacent comparator counties) who delivered a live-born singleton infant between Sept 1989 and Dec 1990.	Non-randomised - selection by area of treatment/birth	692 Women resident in Boulder County (intervention area) who delivered a live-born singleton infant (n=692) during the study period.	Women resident in two non-intervention counties (A and B) who delivered a live-born singleton infant during the study period. Area A(C1): n=726; Area B(C2): n=1373	Prematurity (<37 weeks): Intervention area (I): 5.9% vs. C1: 8.4% C2: 7.8% C1+C2: 8.0% OR (95% CI), I vs.(C1+C2):	

Author, year	Country/Setting	Study design	Study population	Method of allocation to study group(s)	Intervention group(s)	Control/ comparator group(s)	Results - PTB (I vs. C)	Results - neonatal/ infant mortality (I vs. C)
Mvula, 1998	USA. Publicly funded antenatal care in low-income areas of new Orleans, Louisiana.	Prospective observational cohort study	Low-risk women registered for antenatal care at the two study clinics in 1994. Women with multiple gestations and specific medical problems (hypertension, diabetes, etc) excluded	Non-randomised - selection by site of treatment/birth	179 low-risk women registered for antenatal care at the Neighbourhood Pregnancy Care clinic.	181 low-risk women randomly sampled from a traditional antenatal care clinic	Unadjusted % PTB (<37 weeks): 7.3% vs. 17.7%, p < 0.003 Odds Ratios (95% CI): Unadjusted OR: 0.37 (0.19 - 0.72)* Adjusted OR: 0.36 (0.16-0.78)** Adjusted OR: 1.01 (0.39 - 2.63)*** * OR C vs. I reported; I vs. C calculated from data. **Adjusted for baseline characteristics only. ***Additionally adjusted for number of antenatal visits, Medicaid and delivery hospital	
1.1.4 Other US public antenatal care programmes								
Clarke, 1993	USA. State-wide public antenatal care for low-income women, provided at local county public health departments and community health centres across Florida	Retrospective observational cohort study	Florida residents who delivered a live born infant in the period 1985-1988. Different criteria for intervention and comparator groups: Intervention group: women with income <150% of state poverty level Comparator group: "near poor" women with incomes above the 150% of the poverty level. Women who did not obtain antenatal care excluded.	Other - retrospective assignment based on treatment received with matched control group	Women who enrolled in the *Improved Pregnancy Outcome Program* (IPO). Number of subjects not stated (~139940 IPO enrolees).	Women who did not enrol in (and were not eligible for) the IPO programme. Number of subjects not reported.		Unadjusted mortality rates** (rate difference) per 1000 births: Black, by year: 1985: 9.51 vs.9.14 (+0.37) 1986: 9.98 vs.11.18 (-1.2)* 1987: 5.86 vs.8.77 (-2.91)* 1988: 8.09 vs.9.76 (-1.67)* White, by year: 1985: 7.06 vs.8.05 (-0.99)* 1986: 6.72 vs.8.13 (-1.41)* 1987: 3.88 vs.5.57 (-1.69)* 1988: 4.66 vs.6.42 (-1.76)* * p<.001 for rate difference I vs. C ** Reported results described as "neonatal mortality" but believed to be infant mortality

Author, year	Country/Setting	Study design	Study population	Method of allocation to study group(s)	Intervention group(s)	Control/ comparator group(s)	Results - PTB (I vs. C)	Results - neonatal/ infant mortality (I vs. C)
Conover, 2001	USA. Antenatal services for Medicaid eligible women in Tennessee and North Carolina.	Other A pre- and post-design (Before and After) coupled with a difference-in-difference approach using another state as a control.	Women resident in the two study areas delivering a singleton live births in 1993 and 1995. Study populations NOT restricted to Medicaid eligible women	Non-randomised - selection by area of treatment/birth	Intervention area, 'after'(I): ~70045 births, 1995, Tennessee residents	Intervention area, 'before'(C1): ~69329 births, 1993, Tennessee residents Comparator area, 'before' (C2): ~94012 births, 1993, North Carolina residents Comparator area, 'after'(C3): ~94910 births, 1995, North Carolina residents	Adjusted Odds Ratio (95% CI) for PTB (<37 weeks): C1 vs. C2 (TN vs. NC, 'before'): 0.764 (0.74-0.79) I vs. C3 (TN vs. NC, 'after'): 0.796 (0.77-0.82) Ratio I vs. C3/(C1 vs. C2): 1.042 (1.00-1.09)	Adjusted Odds Ratios (95% CI) for neonatal death (<28 days): C1 vs. C2 (TN vs. NC, 'before'): 0.862 (0.74-1.00) I vs. C3 (TN vs. NC, 'after'): 1.012 (0.87-1.18) Ratio (I vs. C3) /(C1 vs. C2): 1.174 (0.95-1.46) Adjusted Odds Ratios (95% CI) for death in the first 60 days: C1 vs. C2 (TN vs. NC, 'before'): 0.915 (0.80-1.05) I vs. C3 (TN vs. NC, 'after'): 1.071 (0.93-1.24) Ratio (I vs. C3) /(C1 vs. C2): = 1.170 (0.96-1.43) Adjusted Odds Ratios (95% CI) for infant death (<1 year): C1 vs. C2 (TN vs. NC, 'before'): 0.990 (0.88-1.11) I vs. C3 (TN vs. NC, 'after'): 1.146 (1.02-1.29) Ratio(I vs. C3) (/C1 vs. C2): 1.158 (0.98-1.37)
1.2 Programmes provided as an adjunct to comprehensive antenatal care								
1.2.1 Case management/care co-ordination								
Buescher, 1991	USA. Services for Medicaid eligible women, North Carolina.	Retrospective observational cohort study	North Carolina residents on Medicaid delivering a live, singleton infant in 1988-89. Women without antenatal care excluded.	Other - retrospective assignment based solely on treatment received	15,526 women who received maternity care coordination.	34,463 women who did not receive maternity care coordination.		Unadjusted infant deaths per 1000 live births: 9.9 vs. 12.2, p=0.02 Adjusted Odds Ratio (95% CI) for infant death: C vs. I: 1.20 (0.98-1.47)

Author, year	Country/Setting	Study design	Study population	Method of allocation to study group(s)	Intervention group(s)	Control/ comparator group(s)	Results - PTB (I vs. C)	Results - neonatal/ infant mortality (I vs. C)
Keeton, 2004	USA. Case management services provided via federally qualified health centers and community based organisations in Illinois	Retrospective observational cohort study	Medicaid participating pregnant women who entered antenatal care before the third trimester and delivered a live singleton infant in 1996 in the State of Illinois.	Other - retrospective assignment based solely on treatment received Intervention subjects recruited from WIC, Medicaid and community outreach; comparator group drawn from non-recipients of case management.	42,683 recipients of Family Case Management services.	31982 women who did not receive Family Case Management services.		Adjusted Odds Ratio (95% CI) for infant mortality: 0.98 (0.82-1.17)
1.2.2 Nurse home visits								
Kafatos, 1991	Greece. Rural primary health care clinics in Florina, a socioeconomically disadvantaged rural region in Northern Greece.	RCT	Pregnant women in the Florina region proactively identified by clinic staff and enrolled in a broader child health programme targeting infant mortality/ morbidity and infant development.	Randomised - cluster	296 women attending one of the clinics randomised to provide the interventions.	263 women attending one of the clinics randomised to provide normal care.	Unadjusted % PTB (<37 weeks): 3.7% vs. 8.3%, p<0.04	Neonatal deaths, n (%) (<27 days): 6 (2.1%) vs. 5 (2.0%)
Kitzman, 1997	USA. Public system of obstetric care, Memphis, Tennessee.	RCT	Women less than 29 weeks pregnant; without previous live birth or chronic illness thought to contribute to PTB or fetal growth retardation; and with at least 2 of the following sociodemographic risk conditions: unmarried, <12 yrs education, unemployed.	Randomised - individual	518 women randomised to receive intensive nurse home-visitation services during pregnancy. Treatment arms 3 and 4 combined (these differed only in the postpartum period).	681 women randomised to receive normal care during pregnancy. Treatment arms 1 and 2 combined (these differed only in the postpartum period).	Unadjusted % PTB (<37 weeks): 11% vs. 13% Unadjusted % spontaneous PTB (<37 weeks): 8% vs. 9% Adjusted Odds Ratio (95% CI) for PTB (<37 weeks): 0.8 (0.6-1.2) Adjusted Odds Ratio (95% CI) for spontaneous PTB (<37 weeks): 0.8 (0.5-1.3)	

Author, year	Country/Setting	Study design	Study population	Method of allocation to study group(s)	Intervention group(s)	Control/ comparator group(s)	Results - PTB (I vs. C)	Results - neonatal/ infant mortality (I vs. C)
1.2.3 'Healthy Start' programme								
Lane, 2001	USA. Public Health system, Syracuse/ Onondaga county, New York State.	Other "Non experimental" population-based before and after comparison used to compare changes in infant mortality rates in the project area with infant mortality rates in the wider county area.	Infants born to women resident in Onondaga county during the "before" and "after" study periods (1994-94 and 1997-99)	Non-randomised - selection by area of treatment/birth Geographic concurrent comparator group. Non-randomised - selection by year of treatment/birth Before and after component.	Intervention area, 'after': Infants born to women resident in the Syracuse Healthy Start (SHS) project area (30 census tracts in central Syracuse) after the inception of SHS (1997-99).	Intervention area, 'before'(C1): Infants born to women resident in the Syracuse Healthy Start (SHS) project area (30 census tracts in central Syracuse) prior to the inception of SHS (1994-96). 'before' and 'after' geographic comparator area (C2): Infants born to women in the surrounding county (Onondaga county) minus the SHS project area, 1994-96 and 1997-99.		Unadjusted infant Mortality per 1,000 live births All races: 'before'(C1) vs. 'after'(I): 12.9% vs.10.8%, Geographic comparator (C2) 'before' vs. 'after'(I): 7.0% vs.7.2% African-American: 'before'(C1) vs. 'after'(I): 18.8% vs.16.6% White: 'before'(C1) vs. 'after'(I): 8.8% vs.5.3%
2 Interventions targeting socioeconomically disadvantaged women with additional clinical risk factors for PTB								
2.1 Clinic based PTB prevention programmes								
2.1.1 Broad, multifaceted enhanced care programmes								
Edwards, 1995	USA. Two inner-city hospitals in the Bronx, New York.	Retrospective observational cohort study	Consecutive women delivering twins at ≥20 weeks gestation at one of the two study hospitals from 1985 to 1992.	Non-randomised - selection by site of treatment/birth	134 eligible women who received care at the PROPP (intervention) clinic.	161 eligible women who received care at the conventional antenatal care site.	Unadjusted % PTB (<37weeks): 54% vs. 49%	
Hobel, 1994	USA. Public antenatal clinics in West Los Angeles, California.	RCT Main intervention evaluated by means of a cluster RCT; the design additionally included an RCT conducted within the experimental sites to evaluate further clinical interventions.	Women with a first antenatal clinic visit at one of the study sites between 1983 and 1986 and with a completed risk assessment indicating high-risk of PTB. Multiple pregnancies, those that aborted at <20 weeks gestation and those that resulted in stillbirth or major congenital anomaly excluded.	Randomised - cluster	1774 high-risk women attending a clinic randomised to provide the PTB prevention programme.	880 high-risk women attending a clinic randomised to usual care (clinics unaware of women's risk scores).	Unadjusted % PTB (<37 weeks): 7.4% vs. 9.1%, p=0.063. Adjusted* Odds Ratio (95% CI) for PTB (<37 weeks): 0.78 (0.58-1.04). One-sided test for treatment effect: p=.045. * Adjusted for number of high risk problems.	

Author, year	Country/Setting	Study design	Study population	Method of allocation to study group(s)	Intervention group(s)	Control/ comparator group(s)	Results - PTB (I vs. C)	Results - neonatal/ infant mortality (I vs. C)
Klerman, 2001	USA. Public health care system, Jefferson County, Alabama.	RCT	African-American, Medicaid-eligible pregnant women seeking antenatal care from the Jefferson County Department of Health between March 1994 and June 1996; women at least 16 yrs old, less than 26 weeks' gestation, with a score of 10 or higher on a risk assessment scale (medical and social factors, including prior PTB, low pre-pregnancy weight, no car for transportation) and without alcoholism, substance abuse, asthma, cancer, diabetes, epilepsy, high blood pressure, sickle cell disease or HIV/ AIDS.	Randomised - individual	318 women randomised to receive augmented care.	301 women randomised to usual care.	Unadjusted % PTB (undefined): 10.6% vs. 14.0%, p = 0.22	
2.1.2 Programmes with focus on patient education regarding signs of preterm labour plus additional visits/pelvic examinations								
Collaborative Group on Preterm Birth Prevention, 1993	USA. Medical Centres/ hospitals serving predominantly low-income populations in five states (Illinois, Ohio, Alabama, California, Tennessee).	RCT	Women at high risk for preterm labour, receiving antenatal care at one of the study sites between 1983 and 1986 and seen before 32 or 34 weeks of gestation. Some additional exclusion criteria were applied at individual sites.	Randomised - individual	1200 consenting, eligible women randomised to the intervention.	1195 consenting, eligible women randomised to receive normal care.	Unadjusted % spontaneous PTB (<37 weeks): 16.1% vs. 15.4% Unadjusted % spontaneous PTB (<36 weeks): 11.9% vs. 10.9%* Unadjusted overall % PTB (<37 weeks): 20.4% vs. 20.2%* * Significant heterogeneity, i.e. intervention effects differed significantly between sites (site specific intervention effects ranged from +13% to -6%)	
Goldenberg, 1990	USA. Health department clinics, Jefferson County, Alabama.	RCT	Women who registered for antenatal care in the Jefferson County Health Department System at <30 weeks gestation with an estimated delivery date between November 1982 and April 1986; and who screened as high-risk for preterm delivery.	Randomised - individual	491 high-risk women randomised to receive the PTB prevention programme.	478 high-risk women randomised to receive usual antenatal care.	Unadjusted % PTB (<37 weeks): 15.9% vs. 14.2% Unadjusted % PTB (<36 weeks): 11.8% vs. 10.5% Unadjusted % PTB (<28 weeks): 2.7% vs. 1.3%	Unadjusted neonatal death rate (deaths per 1000 births): 20 per 1000 (10 deaths) vs. 10 per 1000 (5 deaths)* *Not significant at 5% level.

Author, year	Country/Setting	Study design	Study population	Method of allocation to study group(s)	Intervention group(s)	Control/ comparator group(s)	Results - PTB (I vs. C)	Results - neonatal/ infant mortality (I vs. C)
2.1.3 Hospital clinic vs. 'managed care'								
Bienstock, 2001	USA. Antenatal care (hospital obstetric clinic and care by neighbourhood Managed Care Organisation), Johns Hopkins Hospital, Baltimore, Maryland.	Retrospective observational cohort study	Medically indigent inner-city patients with a history of previous preterm delivery; delivery at Johns Hopkins hospital, Baltimore in period 1994-1996; women with private attending physician or no antenatal care excluded.	Non-randomised - selection by site of treatment/birth Treatment received (managed care vs. hospital clinic) retrospectively assessed from medical records.	164 women who received antenatal care from the study hospital's Medicaid accepting Managed Care Organisation (MCO) (I1). 96 women who received antenatal care from the study hospital's House Staff Obstetric Clinic (fee-for-service) (I2). Note: Comparison of outcomes in two models of antenatal care. Neither group designated as 'Intervention' or 'control'.	See intervention groups for definitions.	Unadjusted % PTB (<37 weeks): MCO vs. fee for service (I1 vs. I2): 36% vs. 24%, p=0.04	
2.2 Programmes provided as an adjunct to comprehensive antenatal care								
2.2.1 Home visits/telephone support								
Bryce, 1991	Australia. Three public hospital antenatal clinics in Perth and the offices of 87 obstetricians and general practitioners in western Australia.	RCT Relevant results derived from a subgroup analysis.	Pregnant women presenting for antenatal care at any of the study clinics/offices with a prior PTB or other specified risk factors for adverse pregnancy outcome.	Randomised - individual Randomised before consent.	981 women randomised to receive additional antenatal social support.	986 women randomised to receive standard antenatal care.	Stratified Odds Ratio (95% CI) for PTB (stratified by social class) 0.84 (0.65-1.09) OR by social class: Professional: 0.59 (0.36-0.96) Clerical: 1.00 (0.64-1.56) Manual: 0.96 (0.59-1.56)	Neonatal deaths before hospital discharge: 1.4% vs. 0.6% Postneonatal deaths before hospital discharge: 0% vs. 0.2%

Author, year	Country/Setting	Study design	Study population	Method of allocation to study group(s)	Intervention group(s)	Control/ comparator group(s)	Results - PTB (I vs. C)	Results - neonatal/ infant mortality (I vs. C)
Moore, 1998	USA. Public health clinic, Winston-Salem, North Carolina	RCT	Black women (all ages), white/ "other" women with a high risk for preterm labour, and white/"other women aged 18 yrs or less; English speaking and with access to a telephone; 22 to 32 weeks gestation, receiving antenatal care at a community public clinic.	Randomised - individual	775 women randomised to receive the nurse telephone intervention.	779 women randomised to receive usual care.	% PTB (<37 weeks) and Relative Risk (95% CI): 9.7% vs. 11.0%; RR: 0.87 (0.62-1.22), p = 0.415 Stratified analysis: Black women, aged <=18 years: 11.0% vs. 7.9% RR: 1.39 (0.72 - 2.67), p = 0.039 Black women, aged >=19 years: 8.7% vs. 15.4% RR: 0.56 (0.38- 0.84), p = 0.004 White or other women, aged <=18 years: 7.8% vs. 4.1% RR: 1.92 (0.61-6.02), p = 0.255 White or other women, aged >=19 years: 19.6% vs. 6.6% RR: 2.99; (0.98-9.09), p = 0.041	
Oakley 1990	UK. Four hospital antenatal clinics	RCT	Women booking for delivery at a study site between January 1986 and May 1987 with at least one previously normal baby weighing less than 2500g following spontaneous onset of labour; less that 24 weeks gestation at booking; singleton pregnancy; fluent in English.	Randomised - individual	255 women randomised to receive social support plus usual care.	254 women randomised to receive usual care.	% PTB (<37 weeks): 18% vs. 19% % by gestational age: <28 weeks: 2% vs. 1% 28-32 weeks: 3% vs. 4% 33-36 weeks: 13% vs. 14% 37+ weeks: 82% vs. 81%	Neonatal deaths (%): 1% vs. 1%

Author, year	Country/Setting	Study design	Study population	Method of allocation to study group(s)	Intervention group(s)	Control/ comparator group(s)	Results - PTB (I vs. C)	Results - neonatal/ infant mortality (I vs. C)
3 Interventions targeting specific populations								
3.1 Interventions targeting teenagers								
3.1.1 'Teen' clinics								
Bensussen-Walls, 2001	USA. Teen and adult-focused obstetric clinics, Washington State.	Retrospective observational cohort study	Pregnant teens aged 13-18 who delivered December 1996 to November 1997 at (i) the Out of Home and Teen Pregnancy Project and the Young Women's' Clinic (YWC) at the University of Washington, (ii) the Group Health Cooperative Teen Pregnancy and Parenting Clinic (TPPC), (iii) the Maternal and Infant Center at the University of Washington Medical Center (UWMC, and (iv) the Group Health Cooperative Women's Center (GHC).	Non-randomised - selection by site of treatment/birth Matched. Patients chosen from TPPC, UWMC, and GHC to act as comparison groups for 27 index group clients from YWC group - subjects matched on age, parity, out-of-home status, past juvenile justice involvement, history of depression or suicidality, illegal drug use, history of sexual and/or physical abuse, ethnicity, and trimester of entry into antenatal care.	27 pregnant teens receiving care from the YWC teen clinic (I1). 27 pregnant teens receiving care from the TPPC teen clinic (I2).	C1: 27 pregnant teens receiving care from the UWMC adult-focused obstetric clinic (C1). C2: 27 pregnant teams receiving care from the GHC adult-focused obstetric clinic (C2).	Raw data presented but no statistical comparison of PTB in intervention and comparator groups.	
Das, 2007	UK. Antenatal clinics in a district general hospital, Manchester.	Before and after (BA) study	Selection criteria not fully described. Adolescents aged 11-17 at booking who delivered at the study site in 2001 and 2004 (before and after the introduction of the intervention clinic). Unclear if all women in the 2004 group attended the intervention clinic.	Non-randomised - selection by year of treatment/birth	128 teenagers receiving antenatal care/delivering at the study hospital in 2004 (after the introduction of the teenage clinic)	132 teenagers receiving antenatal care/ delivering at the study hospital in 2001 (before the introduction of the teenage clinic).	Unadjusted % PTB (<37 weeks): 'After' (I) vs. 'before' (C): 4% vs. 8%, NS Unadjusted % PTB, 'after' vs. 'before': <28 weeks: 0% vs. 2%, NS 29-32 weeks: 2% vs. 2%, NS 33-36 weeks: 2% vs. 5%, NS	
Morris, 1993	USA. Public health clinic, Galveston, Texas	Retrospective observational cohort study	Medically indigent adolescents aged <18 who received antenatal care at one of the study clinics (teen or traditional) provided by the University of Texas Medical Branch at Galveston and who delivered from 1985 to 1986.	Non-randomised - selection by site of treatment/birth Teenagers self-selected teen clinic vs. traditional care	660 medically indigent teenagers (<18yrs) attending the teen clinic	227 medically indigent teenagers (<18yrs) attending a traditional antenatal clinic.	Adjusted* % PTB (<37 weeks): 10.5% vs. 8.7%, NS (p value not reported) * Adjusted only for gynaecologic age	

Author, year	Country/Setting	Study design	Study population	Method of allocation to study group(s)	Intervention group(s)	Control/ comparator group(s)	Results - PTB (I vs. C)	Results - neonatal/ infant mortality (I vs. C)
Perez, 1998	USA. Obstetric clinics provided by a tertiary level Army Medical Center providing free health care to eligible Military/ Department of Defence personnel, Washington State.	Retrospective observational cohort study	Women enrolled in antenatal care at the study site (an Army Medical Centre) between January 1993 and December 1995.	Non-randomised - selection by site of treatment/birth Selection process unclear: unmarried teens were eligible to attend the teen clinic (intervention); others attended the traditional clinic.	611 unmarried teenage patients of the Madigan Army Medical Center teen-focussed obstetrical clinic.	No comparator group of unmarried teens. Other groups: 424 unmarried 20-24 year old patients of routine antenatal clinic (C1). 847 married teenage patients of routine antenatal clinic (C2). 4,433 married 20-24 year old patients of routine antenatal clinic (C3).	Unadjusted % PTB (<37 weeks): unmarried teens (I): 4.1% vs. unmarried, aged 20-24 (C1): 6.6% married teens(C2): 5.8% married, aged 20-24 (C3): 6.5% No significant differences between the 4 groups.	Neonatal deaths, % (no. of deaths): unmarried teens (I): 0.4% (3 deaths) vs. unmarried, aged 20-24 (C1): 0.7% (3 deaths) married teens(C2): 0% (0 deaths) married, aged 20-24 (C3): 0.2% (10 deaths)
Quinlivan, 2004	Australia. Antenatal clinics provided at three metropolitan hospitals.	Prospective observational cohort study	Adolescents aged <18 with a dating ultrasound before 20 gestational weeks attending a clinic at one of the three study hospitals.	Non-randomised - selection by site of treatment/birth Teenagers could self-select teenage or traditional clinics - traditional clinics were more widely available.	448 pregnant teenagers attending a teenage antenatal clinic.	203 pregnant teenagers attending a general antenatal clinic.	Unadjusted % PTB (<37 weeks): 12.0% vs. 26.0% p = <0.0001 Unadjusted Odds Ratio (95% CI) for PTB: 0.40 (0.25-0.62)	
Ukil, 2002	UK Teenage and adult clinics at a district general hospital, South Tyneside.	Retrospective observational cohort study	Teenagers aged 16 years or less who delivered at the study hospital between January 1996 and December 1999.	Non-randomised - selection by site of treatment/birth Teenagers could self-select teenage or traditional clinics	78 teenagers (≤16) who attended the study hospital teenage antenatal clinic.	34 teenagers attending the adult antenatal clinic at the study hospital.	Unadjusted % "premature labour": 2.5% vs. 15% Unadjusted Odds Ratio for "preterm deliveries" (95%* CI): 0.15 (0.028 - 0.83), p=.026 * Stated to be "98%" CI in article	
Van Winter, 1997	USA. Antenatal clinics at the Mayo Medical Center, Rochester, Minnesota serving a predominantly white non-urban population.	Prospective observational cohort study	Adolescents (13-21) and single young women (21-23) invited to attend the Young Moms' Clinic at their initial antenatal visit over a two year period (undefined).	Non-random selection from antenatal care population. Eligible women were invited to attend the Young Moms' clinic - those that consented (52%) formed the intervention group, those that declined formed the control group.	101 eligible women who accepted the invitation to attend the Young Moms' Clinic.	95 eligible women attending the standard antenatal clinic who declined the invitation to attend the Young Moms' Clinic.	Premature onset of labour % (<37 weeks): 7.9% vs. 19.0%, p = 0.023 Prematurity % (undefined): 2.0% vs. 10.5%, p = 0.013	

Author, year	Country/Setting	Study design	Study population	Method of allocation to study group(s)	Intervention group(s)	Control/ comparator group(s)	Results - PTB (I vs. C)	Results - neonatal/ infant mortality (I vs. C)
3.1.2 Adolescent group antenatal care								
Grady, 2004	USA. Urban, hospital-based clinics in St Louis, Missouri.	Other Intervention group studied prospectively; comparator group identified retrospectively.	Adolescents aged 17 or younger who received antenatal care and/or delivered at the study hospital in the relevant time period (see intervention/comparator group descriptions for specification of study periods).	Non-random selection from antenatal care population. Intervention group self-selected with those who opted out of group care entering the comparator group. Comparator group consisted of adolescent births at the study hospital, excluding those who had received group care, but report does not clearly describe what proportion were intervention "refusers"	124 adolescents who have given birth after completing the *CenteringPregnancy* programme between March 2001 and April 2003.	144 adolescents who gave birth at the study hospital in 2001 excluding adolescents who received no antenatal care and those who participated in the CenteringPregnancy Groups.	Unadjusted % PTB (<37 weeks): 10.5% vs. 25.7%, p<.02	
3.1.3 Stand alone nutritional programme								
Dubois,1997	Canada. Subjects recruited from 15 Montreal area hospitals but location/setting of the Montreal Diet Dispensary unclear.	Retrospective observational cohort study	Adolescent mothers at 15 Montreal area hospitals who delivered between 1981 and 1991.	Non-random selection from antenatal care population Not described.	1203 adolescents who participated in the Higgins Nutritional Intervention during pregnancy.	1203 adolescents (matched on site, year and age) who did not participate in the Higgins Nutritional Intervention during pregnancy.	Unadjusted % PTB (<37 weeks): 8.2% vs. 12.8% Unadjusted % very preterm (<34 weeks): 2.3% vs. 5.1% Adjusted Odds Ratio (95% CI) for PTB (<37 weeks): 0.59 (0.45 - 0.78), p≤0.001 Adjusted Odds Ratio (95% CI) for very preterm birth (<34 weeks) 0.53 (0.35 -0.81), p≤0.001 Odds ratios also reported for subsamples - pregravid weight <50kg; pregravid weight 50kg or more; 13-17yrs; 18-19yrs.	

Author, year	Country/Setting	Study design	Study population	Method of allocation to study group(s)	Intervention group(s)	Control/ comparator group(s)	Results - PTB (I vs. C)	Results - neonatal/ infant mortality (I vs. C)
3.2 Interventions targeting substance users								
3.2.1 Substance abuse programmes provided as an adjunct to standard antenatal care								
Armstrong, 2003	USA. 10 group model managed care outpatient obstetric clinics in Northern California.	Retrospective observational cohort study	Substance users (including problem drinkers) receiving outpatient antenatal care from a study clinic who delivered a singleton baby between July 1995 and June 1998. The subgroups considered relevant in this review are those who screened positive for substance abuse and who were subsequently diagnosed as chemically dependent or substance-abusing by an early Start Specialist.	Non-random selection from antenatal care population	783 pregnant women receiving antenatal care at a study site who screened positive for substance abuse and received at least one follow-up Early Start appointment.	348 pregnant substance abusing or chemically dependent women who received antenatal care and were seen by an Early Start Specialist but did not receive a follow-up Early Start appointments (C1). Other groups: 262 pregnant women receiving antenatal care at a study site who screened positive for substance abuse but who were not assessed or followed-up by an Early Start specialist (C2). 5382 women receiving antenatal care at a study site who screened negative for substance abuse (non substance abusing controls) (C3).	Adjusted Odds Ratio (95% CI) for PTB (<37 weeks). I vs. C3*: 1.3 (0.9-1.8), p=0.11 C1 vs. C3*: 1.6 (1.1-2.4), p=0.02 C2 vs.C3*: 1.7 (1.2-2.8), p=.006 * Indirect comparison with non-substance abusing comparator group (C3)	Neonatal deaths (%): I: 0% (0 deaths) C1: 0.57% (2 deaths) C2: 0.76% (2 deaths) C3 (non-users): 0.37% (20 deaths)
Burkett, 1998	USA. Outpatient antenatal care clinic, Miami, Florida.	Prospective observational cohort study	HIV negative, cocaine or crack using pregnant women diagnosed and recruited prospectively at the study hospital between January and December 1989.	Non-random selection from antenatal care population Self-selected (women who accepted drug rehabilitation (I1) vs. refusers(C1)).	278 HIV negative, cocaine/crack using women receiving antenatal care plus drug rehabilitation	206 HIV negative, cocaine/crack using pregnant women receiving antenatal care but no drug rehabilitation	Unadjusted % PTB (undefined): 8.3% vs. 13.1%	
Miles, 2007	UK. Outpatient antenatal clinic at St Mary's hospital, Manchester.	Before and after (BA) study	Pregnant women on methadone treatment with a live born infant 1991-94 (pre-intervention) and 1997-2001 (post implementation of intervention)	Non-randomised - selection by year of treatment/birth	98 methadone using women delivering 1997-2001 after the implementation of the enhanced service(shared care/ Drug Liaison Midwife)	78 methadone using women delivering 1991-94 prior to the implementation of the enhanced service.	Unadjusted % PTB (<37 weeks): 'Before' (C) vs. 'after' (I): 21% vs. 36%, p = 0.03	
Sweeney, 2000	USA. Hospital based outpatient programme, Women and Infants Hospital, Providence, Rhode Island.	Observational cohort study	Women identified as substance misusers antenatally who enrolled in Project Link either antenatally (intervention group) or postnatally (comparator group) and who delivered a singleton at the study hospital between May 1992 and December 1995.	Non-random selection from antenatal care population Pregnant substance misusers who refused enrolment in Project Link during pregnancy but subsequently enrolled postpartum.	87 substance misusers who enrolled in Project Link antenatally.	87 substance misusers (identified antenatally) who did not receive Project Link services while pregnant but enrolled in Project Link postnatally.	Adjusted % PTB (<37 weeks): 14.9% vs. 40.2%, p < 0.001 Adjusted Odds Ratio for PTB: I1 vs. C1: 0.20, p < 0.001	

Author, year	Country/Setting	Study design	Study population	Method of allocation to study group(s)	Intervention group(s)	Control/ comparator group(s)	Results - PTB (I vs. C)	Results - neonatal/ infant mortality (I vs. C)
3.2.2 Comprehensive care in accredited general antenatal clinic providing an enhanced range of services								
Newschaffer, 1998	USA. New York State Medicaid antenatal clinics.	Retrospective observational cohort study	HIV infected, drug abusing, Medicaid claimants who delivered a singleton between January 1993 and September 1994.	Unclear Retrospective assignment to intervention and control groups based on treatment received. Allocation by site assumed but not stated.	240 HIV infected, drug abusing, Medicaid claimants who received antenatal care at a *Prenatal Care Assistance Program (PCAP)* participating clinic.	113 HIV infected, drug abusing, Medicaid claimants who received antenatal care at a non PCAP- participating clinic.	Unadjusted % PTB (<37 weeks): 13% vs. 22.6%, p=.001 Adjusted* Odds Ratio (95% CI) for PTB (<37 weeks): 0.57 (0.34-0.97) * Adjusted for maternal characteristics only. Additional adjustment for antenatal care adequacy, care continuity and receipt of other treatments/ services attenuates the estimated effect.	
3.3 Interventions targeting indigenous women								
3.3.1 Culturally sensitive comprehensive antenatal care including community/outreach services								
Mackerras, 2001	Australia. Community based programme in three aboriginal communities in the rural Top End region of the Northern Territories.	Before and after (BA) study	Not fully described. Study cohorts were assembled using antenatal charts for births in 1990/91 ('before') and 1994-96 ('after') from three pilot aboriginal communities.	Other This is a before and after study evaluated at a community level. 'Before' group had access to available services; 'after' group had access to available services including the study intervention.	'After' (I): Aboriginal women delivering 1994-1996 in three pilot communities after implementation of the *Strong Women Strong Babies Strong Culture Program* (SWSBSCP).	'Before' (C): Aboriginal women delivering 1990-91 in three pilot communities before implementation of the SWSBSCP programme.	Unadjusted % PTB (<37 weeks): 'Before' (C) vs. 'after' (I): 22% vs. 13%	
Panaretto, 2007	Australia. Community based clinics in Townsville, Queensland.	Other Before and after study with an additional contemporary control group.	Aboriginal and Torres Strait Islanders who delivered a singleton infant at Townsville hospital between January 1998 and June 1999 ("before") or between January 2000 and December 2005 ("after").	Non-randomised - selection by year of treatment/birth	'After' (I): 781 indigenous women who made at least one visit to the *Mums and Babies program* and gave birth in the study period after implementation of the programme.	'Before' (C): 84 indigenous women who received antenatal care from the Townsville Aboriginal and Islander Health Service and gave birth in the pre-intervention study period.	Unadjusted % PTB (<37 weeks): 'Before' (C) vs. 'after' (I): 16.7% vs. 9.5%, p=.055	

Author, year	Country/Setting	Study design	Study population	Method of allocation to study group(s)	Intervention group(s)	Control/ comparator group(s)	Results - PTB (I vs. C)	Results - neonatal/ infant mortality (I vs. C)
3.4 Interventions targeting HIV positive women								
3.4.1 Comprehensive care in general antenatal clinics providing an enhanced range of services								
Turner, 2000	USA. Public antenatal care services, New York, New York State	Retrospective observational cohort study	HIV-infected, New York State Medicaid enrolled women delivering a live-born singleton infant between January 1993 and October 1995	Non-randomised - selection by site of treatment/birth	298 HIV-infected women who received antenatal care from a *Newschaffer* participating clinic.	425 HIV-infected women who received antenatal care from a non PCAP-participating clinic.	Adjusted Odds Ratio (95% CI) for PTB (<37 weeks): 0.53 (0.40-0.70)* *Adjusted for maternal characteristics Additional adjustment for health care and social service use during pregnancy, illicit drug use, and for adequacy of antenatal care attenuates the effect, but effects remain statistically significant.	

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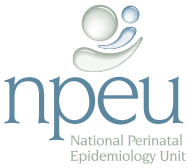
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