Australian Perinatal Mental Health Guideline Evidence Review

Technical Report Part C

Effectiveness of treatment and prevention interventions

Prepared by

hereco
clinical evidence for the real world

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ABBREVIATIONS

ASQ:SE	Ages and Stages Questionnaire: Social-Emotional
AQS	Attachment Q Set
BAI	Beck Anxiety Inventory
BDI	Beck Depression Inventory
BSI	Brief Symptom Inventory
CES-D	Center for Epidemiologic Studies Depression Scale
CBCL	Child Behaviour Checklist
CGI-I	Clinical Global Impression – Improvement scale
CGI	Clinical Global Impression scale
CORE-OM	Clinical Outcomes in Routine Evaluation-Outcome Measure
CBT	cognitive behaviour therapy
CIS-R	Computerised version of the Clinical Interview Schedule – Revised
CI	confidence interval
CAGE	cut-annoyed-guilty-eye
DASS	Depression Anxiety Stress Scale
DSM-IV	Diagnostic and Statistical Manual of Mental Disorders, 4th Edition
EPDS	Edinburgh Postnatal Depression Scale
EAS	Emotional Availability Scales
GHQ	General Health Questionnaire
GAD-7	Generalised Anxiety Disorder Assessment
HRSD	Hamilton Rating Scale for Depression
HSCL	Hopkins Symptom Checklist
HADS	Hospital Anxiety and Depression Scale
IES	Impact of Events Scale
IES-R	Impact of Events Scale – Revised
ES-R	Impact of Events Scale – Revised
ICEP	Infant and Caregiver Engagement Phases
ITT	intention-to-treat
IPT	interpersonal psychotherapy
IPT	interpersonal therapy
LOCF	last observation carried forward
LIFE	Longitudinal Interval Follow-up Examination
MDD	major depressive disorder
MMS	Maternal Mood Screener
MD	mean difference
MINI	Mini International Neuropsychiatric Interview
MADRS	Montgomery–Åsberg Depression Rating Scale
NICU	neonatal intensive care unit
NE	not estimable (from data in SR)
NR	not reported
NCAST	Nursing Child Assessment Satellite Training Scale
OCD	obsessive-compulsive disorder
OR	odds ratio
PIRGAS	Parent-Infant Relationship Global Assessment Scale
PSCS	Parenting Sense of Competence Scale
PSS	Perceived Stress Scale
PPQ	Perinatal PTSD Questionnaire
PICS	Pictoral Infant Communication Scales
PND	postnatal depression
PTSD	post-traumatic stress disorder
QIDS	Quick Inventory of Depressive Symptoms
RCT	randomised controlled trial
RR	relative risk
RDC	Research Diagnostic Criteria
SADS	Schedule for Affective Disorders and Schizophrenia
SCAN	Schedules for Clinical Assessment in Neuropsychiatry
SSRI	selective serotonin reuptake inhibitor
SF	Short Form Health Survey
STSI	Short Temperament Scale for Infants

SD	standard deviation
SMD	standardised mean difference
STAI	State-Trait Anxiety Inventory
STAI-S	State-Trait Anxiety Inventory-State
STAI-T	State-Trait Anxiety Inventory-Trait
KID-SCID	Structured Clinical Interview for Childhood Diagnoses
SCID	Structured Clinical Interview for DSM Disorders
SR	systematic review
TAU	treatment as usual
VAS	visual analogue scale
WHO	World Health Organization
WCS	worst case scenario
YBOCS	Yale–Brown Obsessive Compulsive Scale

C1 INTRODUCTION

The aim of this Evidence Review is to assess the evidence relating to the identification and treatment or prevention of mental health problems in women during pregnancy or the postnatal period. The following Technical Reports and associated Appendices are related to this assessment:

- Part B Technical Report and Part B Appendix – Psychosocial Assessment and Screening
- Part C Technical Report and Part C Appendix – Effectiveness of Treatment and Prevention
- Part D Technical Report and Part D Appendix – Harm

This Technical Report and associated Appendix (Part C) present the findings of the assessment of evidence of the effectiveness of *interventions* used for the treatment and prevention of mental health problems in women during the antenatal or postnatal period.

C2 METHODOLOGY

C2.1 CLINICAL QUESTIONS

The two main questions relating to the effectiveness of interventions for the treatment of mental health problems in pregnant or postpartum women, or prevention of mental health problems in pregnant or postpartum women identified as being at risk of developing mental health problems, were each broken down into five sub-questions based on different intervention types. Each sub-question is also broken down further into individual interventions and outcomes; the detailed definitions associated with these interventions and outcomes can be found in **Section C2.2.** All questions were addressed via systematic review.

It should be noted that while the side effects of treatment experienced by the mother were captured in this part of the Technical Report (Part C), the harms to the fetus, infant, child or mother are assessed in **Part D** of the **Technical Report**.

C2.1.1.1 Treatment interventions

Main question:

4. What is the effectiveness of interventions for the treatment of mental health problems in women in the antenatal or postnatal period?

Sub-questions:

4a. What is the effectiveness of psychosocial interventions for the treatment of mental health problems in women in the antenatal or postnatal period?

4b. What is the effectiveness of psychological interventions for the treatment of mental health problems in women in the antenatal or postnatal period?

4c. What is the effectiveness of pharmacological interventions for the treatment of mental health problems in women in the antenatal or postnatal period?

4d. What is the effectiveness of complementary interventions for the treatment of mental health problems in women in the antenatal or postnatal period?

4e. What is the effectiveness of physical interventions for the treatment of mental health problems in women in the antenatal or postnatal period?

C2.1.1.2 Prevention interventions

Main question:

5. What is the effectiveness of interventions for the prevention of mental health problems in women identified as being at risk of developing a mental health problem in the antenatal or postnatal period?

Sub-questions:

5a. What is the effectiveness of psychosocial interventions for the prevention of mental health problems in women identified as being at risk of developing a mental health problem in the antenatal or postnatal period?

5b. What is the effectiveness of psychological interventions for the prevention of mental health problems in women identified as being at risk of developing a mental health problem in the antenatal or postnatal period?

5c. What is the effectiveness of pharmacological interventions for the prevention of mental health problems in women identified as being at risk of developing a mental health problem in the antenatal or postnatal period?

5d. What is the effectiveness of complementary interventions for the prevention of mental health problems in women identified as being at risk of developing a mental health problem in the antenatal or postnatal period?

5e. What is the effectiveness of physical interventions for the prevention of mental health problems in women identified as being at risk of developing a mental health problem in the antenatal or postnatal period?

C2.2 CRITERIA FOR DETERMINING STUDY ELIGIBILITY

To determine the effectiveness of an intervention, a systematic review (SR) of randomised controlled trials (RCTs) provides the highest level of evidence, as shown in the evidence hierarchy for examination of intervention questions (**Table C2-1**).

For each of the intervention-based questions to be assessed by the Evidence Review (effectiveness of treatment and prevention, and harm), the Expert Working Group (EWG) agreed to the appropriate level of evidence for inclusion. For the review of effectiveness of treatment and prevention using psychosocial, psychological and most physical interventions, the EWG agreed that Level I evidence (SR of RCTs) should be used as the basis of the review, with preference given to those SRs that used a GRADE approach for assessment of the evidence. For online, pharmacological, complementary and selected physical interventions (electroconvulsive therapy [ECT] and transcranial magnetic stimulation [TMS]), Level II evidence was to be included if Level I evidence was unavailable or out of date (i.e. pre-2014).

Table C2-1 NHMRC Evidence Hierarchy: designation of levels of evidence according to type of research question[1]

Level	Intervention
I	A systematic review of level II studies
II	A randomised controlled trial
III-1	A pseudorandomised controlled trial (i.e. alternate allocation or some other method)
III-2	A comparative study with concurrent controls: • Non-randomised, experimental trial[2] • Cohort study • Case-control study • Interrupted time series with a control group
III-3	A comparative study without concurrent controls: • Historical control study • Two or more single arm studies[3] • Interrupted time series without a parallel control group
IV	Case series with either post-test or pre-test/post-test outcomes

Table C2-2 summarises the criteria used to determine study eligibility. The populations of interest for interventions that treat and/or prevent mental health problems are pregnant and postpartum women. A comprehensive range of interventions were reviewed under the categories of psychosocial, psychological, online, pharmacological, complementary and physical. Eligible comparators included treatment as usual,

[1] NHRMC (2009) NHMRC additional levels of evidence and grades for recommendations for developers of guidelines. Accessed on 12 May 2017 from https://www.nhmrc.gov.au/_files_nhmrc/file/guidelines/developers/nhmrc_levels_grades_evidence_120423.pdf.

[2] This also includes controlled before-and-after (pre-test/post-test) studies, as well as adjusted indirect comparisons (ie. utilise A vs B and B vs C, to determine A vs C with statistical adjustment for B).

[3] Comparing single arm studies ie. case series from two studies. This would also include unadjusted indirect comparisons (ie. utilise A vs B and B vs C, to determine A vs C but where there is no statistical adjustment for B).

enhanced treatment as usual, no treatment/placebo, waitlist control, or other active interventions. The included outcomes were:

- Maternal mental health outcomes – antenatal or postnatal development of, or change in, a mental health diagnosis or symptomatology using validated instruments.
- Mother-infant interactions – postnatal assessment of attachment problems, positive interactions, and maternal sensitivity, using validated instruments.
- Safety – in terms of side effects to the mother.

Harms due to pharmacological, complementary or physical interventions are assessed in **Part D** of the **Technical Report**.

Table C2-2 PICO criteria used to inform the literature search

Populations	Interventions	Comparators	Outcomes
Pregnant women Post-partum women	Psychosocial interventions Psychoeducation Psychoeducational booklet Social/peer support Home visits Non-mental-health-focused education/support Pre-delivery discussion Post-delivery discussion Post-miscarriage self-help Seeing and/or holding stillborn infant Mother-infant relationship interventions Co-parenting interventions Mindfulness Psychological interventions Structured psychological interventions (CBT and IPT) Directive counselling Non-directive counselling Case management/individualised treatment Self-help or facilitated self-help Post-traumatic birth counselling Post-miscarriage counselling Online interventions Pharmacological interventions Antidepressants Antipsychotics Mood stabilisers (including anticonvulsants,[4] benzodiazepines and z-drugs) Lithium Complementary interventions Omega-3 fatty acids St John's wort Gingko biloba Physical interventions Exercise Yoga Acupuncture Electroconvulsive therapy Transcranial magnetic stimulation	Treatment as usual, enhanced treatment as usual, no treatment/placebo, or waitlist control Other active interventions	Maternal mental health symptomatology or diagnosis Depression/anxiety/PTSD diagnosis Depression/anxiety/PTSD symptomatology Negative thoughts/mood Mother-infant interactions Mother-infant attachment problems Positive mother-infant interaction Maternal sensitivity Safety Side effects

Abbreviations: CBT, cognitive behaviour therapy; IPT, interpersonal psychotherapy; PTSD, post-traumatic stress disorder.

[4] Sodium valproate, carbamazepine and lamotrigine only.

C2.3 LITERATURE SEARCH

C2.3.1 Search strategy

A two-tiered search strategy was undertaken. An initial search was undertaken to identify SRs that assessed various treatments for the main mental health problems seen during the perinatal period; these included depression, anxiety, schizophrenia and bipolar disorder. Full details of the SR search can be found in **Appendix C1.1.1**. It should be noted that this search was conducted to identify studies not only for the assessment of efficacy for treatment and prevention, but also for screening interventions, and the harms associated with pharmacological, complementary and selected physical interventions.

From this search, a list was compiled of SRs that assessed the effectiveness of various interventions for the treatment and prevention of mental health problems during the perinatal period; evidence regarding harms was also identified by this search. The individual studies included in each SR were tabulated and, where possible, a 'foundation review' was selected. The process for identifying the foundation reviews is outlined in **Appendix C2** (treatment) and **Appendix C3** (prevention). The foundation review was defined as the SR that included the most recent and comprehensive set of data for a particular intervention and outcome; SRs that assessed the body of evidence and produced a Summary of Findings table using GRADE methodology were preferentially included where available.

Based on the findings of the SR search, a second series of literature searches were carried out for the online, pharmacological, complementary and selected physical interventions. These 'updated' searches were also aimed at identifying individual studies for the consideration of harms. Full details of the updated searches can be found in **Appendix C1.1.2**.

Searches were conducted in the MEDLINE, Embase and PsychINFO databases (via the OVID and/or Embase.com interfaces), the Cochrane Library, and included examination of the reference lists of included SRs.

C2.3.2 Study eligibility

The aim of the literature search was to identify the highest possible quality evidence for each intervention/outcome. As noted previously, SRs of RCTs provide the highest level of evidence for assessment of the effects of interventions, and for the assessment of treatment and prevention effectiveness, eligibility was limited to this study type for the assessment of psychosocial and psychological interventions, most physical interventions, anticonvulsants and omega-3 fatty acids; individual RCTs were eligible for inclusion for pharmacological, other complementary, and electroconvulsive therapy and transcranial magnetic stimulation.

Citations identified in the literature searches were reviewed and evidence selection criteria were applied hierarchically.

As shown in **Table C2 3**, there was a set of standard inclusion/exclusion criteria that applied to both the SR search for all interventions, and the updated searches for online, pharmacological, complementary and the physical (ECT and TMS) interventions.

Details of the assessment of study eligibility can be found in **Part C Appendix Section C1.2**.

Table C2-3 Evidence selection criteria

Criterion	Description
SR search	
Not a SR	Excludes individual clinical studies, narrative reviews, editorials, animal studies and in vitro studies
Wrong population	Excludes studies that are not conducted in pregnant or postnatal women, or children exposed to intervention antenatally or postnatally
Wrong intervention/exposure	Excludes studies that do not examine one of the exposures included in Table C2-2
Wrong outcome	Excludes studies that do not examine one of the outcomes included in Table C2-2
Not in English	Excludes SRs not available in English.
Updated searches – all	
Not a clinical study	Excludes narrative reviews, editorials, animal studies and in vitro studies
Not a SR	Excludes reviews described as systematic that are not, or that limit identification of evidence to MEDLINE/PubMed only.
Wrong population	Excludes studies that are not conducted in pregnant or postnatal women (or children exposed to intervention antenatally or postnatally for the assessment of infant harms)
Wrong intervention/exposure	Excludes studies that do not examine one of the interventions included in Table C2-2
Wrong/no comparator	Excludes studies that do not compare the intervention with no intervention or a relevant active intervention
Wrong outcome	Excludes studies that do not examine one of the outcomes included in Table C2-2
Wrong study type	Excludes RCTs where SR evidence is available and all observational studies (assessment of effectiveness using individual studies limited to RCT evidence only)
Protocol only	Excludes publications describing a study protocol only
Duplicate data	Excludes studies that include data that has already been included from another publication
Not in English	Excludes studies not available in English
Abstract only	Excludes studies available as a conference abstract only. Where identified, an additional search is conducted to see if the study was subsequently published.

Abbreviations: SR, systematic review.

C2.4 Assessment of the evidence

Grading of Recommendations, Assessment, Development and Evaluations (GRADE) methodology has been used (either within the identified foundation SR or performed specifically for this Evidence Review) to grade the quality of the evidence for each intervention and outcome and translate this into recommendations and practice points. For further details about GRADE see http://www.gradeworkinggroup.org/.

According to the GRADE process, the body of evidence is summarised in either an Evidence Profile (EP) table or Summary of Findings (SoF) table. For the purpose of the assessment of effectiveness of treatment and prevention, the evidence is presented in SoF tables.

C2.5 Evidence to recommendations process

C2.5.1 Grading of the certainty of the body of evidence

Assessing the certainty of a body of evidence using GRADE involves consideration of the following five domains: risk of bias, inconsistency, indirectness, imprecision and publication bias. For an evidence base drawn from RCTs, the grading of the certainty of the body of evidence starts at 'high' (⊕⊕⊕⊕) and can be downgraded for each of the five domains depending on whether the limitation is considered serious (downgrade one level) or very serious (downgrade two levels).

For this Evidence Review, the aim of the assessment of effectiveness was to identify existing SRs that had assessed and presented the body of evidence using GRADE methodology. Where this was available, the assessment performed by the SR was accepted, and the SoF table was taken directly from the SR and presented in this Technical Report. Where this was not available, relevant SRs or original studies were identified and the body of evidence was assessed using GRADE methodology and presented in SoF or EP tables.

C2.5.2 Determining the absolute increase in risk

The absolute increase in risk can be calculated for dichotomous outcomes that are reported as risk ratios (RRs). The baseline risk generally comes from the control group of the SR of RCTs, and is multiplied by the RR and 95% confidence interval (CI) to determine the increase or decrease in risk associated with an intervention.

Where an existing SoF table was available, the absolute increase in risk reported in the table was used. Where an SoF table was developed de novo, the absolute increase in risk was calculated.

C2.5.3 Drafting of Evidence Statements

Evidence Statements have been derived from the data presented in the SoF tables. Although Evidence Statements are not a requirement for GRADE, it was agreed that describing the data in words is a useful bridge from the SoF tables to the Recommendations and Practice Points. All of the summary findings presented below are based on data from RCTs. Consequently, the following general 'phrasing rules' have been applied to the Evidence Statements:

- Where there is a statistically significant effect, and the quality of the evidence has been rated 'high' or 'moderate', the phrasing "improves [outcome]" has been used.
- Where there is a statistically significant effect, and the quality of the evidence has been rated 'low' or 'very low', the phrasing "may improve [outcome]" has been used.
- Where no statistically significant effect is observed, and the quality of the evidence has been rated 'high' or 'moderate', the phrasing "has no effect on [outcome]" has been used.
- Where no statistically significant effect is observed, and the quality of the evidence has been rated 'low' or 'very low', the phrasing "appears to have no effect on [outcome]" has been used.

In some circumstances, where there is a large but not statistically significant effect, and the quality of the evidence has been rated 'high' or 'moderate', the phrasing "may have an effect on [outcome]" is used. Likewise, in some circumstances, where there is a large effect that is close to being statistically significant (P=0.05-1.0), irrespective of the quality of the evidence, the phrasing "may have an effect on [outcome]" is used.

C3 RESULTS – TREATMENT

For the majority of psychosocial, psychological, physical and pharmacological interventions, the National Institute for Health and Care Excellence Clinical Guideline Number 192 (NICE 2015) was chosen as the foundation review, primarily due to its currency, comprehensiveness, and high quality. The EWG agreed that the current Review would reproduce the Summary of Findings (SoF) tables from NICE 2015, and that replication of data extraction tables, risk-of-rias assessment, or Evidence Profile (EP) tables was not required. Readers are referred to the NICE guideline CG192 and appendices for this information.

NICE 2015 did not specifically assess evidence relating to online (web-based or computer-based) interventions. As such, the current Evidence Review relied on other published SRs, together with a literature search update to identify recent RCTs not included in the published reviews. For all relevant RCTs relating to online interventions, a full assessment of the evidence was required, including data extraction, risk-of-bias assessment, and EP tables; these are available in the **Part C Appendix**. Evidence from additional SRs was used for yoga (treatment) and antidepressants (treatment); the quality of the SR was assessed, the SR evidence was transcribed directly into an SoF table, and the certainty of the body of evidence was informed by the SR assessment of risk of bias of the individual studies.

C3.1 TREATMENT WITH PSYCHOSOCIAL INTERVENTIONS

C3.1.1 Psychoeducation

Only one SR (NICE 2015) was identified for psychoeducation in the literature search. NICE 2015 included a total of 17 individual RCTs, two of which were from Australia. Sixteen RCTs (N=2,955) compared psychologically informed psychoeducation with treatment as usual or enhanced treatment as usual[5]. Psychoeducation was cognitive behaviour therapy (CBT)-informed in 10 RCTs, IPT-informed in five RCTs, and CBT- and IPT-informed in one RCT. In one of these RCTs the intervention was aimed at women with subthreshold symptoms of OCD, and in the remaining 15 RCTs the intervention was intended for women with symptoms (or subthreshold symptoms) of depression. The timing of the intervention was antenatal in four RCTs, postnatal in four RCTs, and both antenatal and postnatal in eight RCTs. In all RCTs the intervention was delivered face-to-face but one study also involved one postnatal telephone follow-up.

NICE 2015 also included one RCT from the United States (N=38) that compared face-to-face IPT-informed high-intensity group psychoeducation with an active intervention (non-mental health-focused education and support group) in pregnant women with a diagnosis of MDD.

C3.1.1.1 Psychologically (CBT/IPT) informed psychoeducation versus treatment as usual or enhanced treatment as usual

NICE 2015 did not consider the timing of the intervention, format or mode of delivery in their analyses.

[5] Enhanced treatment as usual was a psychoeducational booklet (two RCTs), non-mental-health-focused education and support group (two RCTs), and a psychoeducation group without the CBT component (one RCT). In some cases, these comparators could be considered to be active interventions.

Evidence from up to eight studies showed moderate effects of psychoeducation on depression diagnosis at endpoint using an ITT approach; however, the confidence in these effect estimates is very low due to imprecision (**Table C3-1**). There was also high-certainty evidence from five studies for small-to-moderate, statistically significant benefits associated with psychoeducation on depression symptomatology. However, treatment effects on mean depression scores at endpoint, while statistically significant in many cases, failed to reach the threshold for clinically significant benefits, either at endpoint or at short- or long-term follow up. There was also no evidence for any statistically or clinically significant treatment effects for any outcome measures at intermediate follow up or for depression diagnosis at long-term follow up (using an ITT approach).

There was no evidence for statistically or clinically significant benefits of psychologically informed psychoeducation for anxiety diagnosis at endpoint or at long-term follow-up in women with symptoms (or subthreshold symptoms) of depression. Furthermore, there was no evidence for statistically significant benefits associated with psychoeducation for any of the PTSD outcome measures; the very low certainty of evidence due to risk-of-bias concerns, very serious imprecision and selective outcome reporting prohibits any clear conclusions being drawn from the evidence.

There was very low quality single-study evidence for delayed but statistically significant moderate-to-large effects of psychoeducation on mean OCD symptoms at intermediate and long-term followup, with statistically and clinically non-significant effects at endpoint.

Thirteen studies (N=2,375) found no evidence for clinically or statistically significant effects of psychologically (CBT/IPT) informed psychoeducational interventions relative to treatment as usual or enhanced treatment as usual on attrition (as a proxy measure for retention in services and treatment acceptability).

Table C3-1 Summary of findings (treatment) – psychologically (CBT/IPT) informed psychoeducation versus treatment as usual or enhanced treatment as usual

Outcomes (follow-up)	Illustrative comparative risks*		Relative effect (95% CI)	No. of participants (studies)	Quality of the evidence (GRADE)
	Assumed risk Control	Corresponding risk Intervention			
Depression diagnosis					
Post-treatment – ITT analysis MINI, Schedule for Affective Disorders and Schizophrenia (SADS), Maternal Mood Screener (MMS), SCID or Longitudinal Interval Follow-up Examination (LIFE) (4-52 weeks)	*Study population*		RR 0.67 (0.41, 1.08)	985 (8 studies)	●○○○ Very low (a,b,c)
	163 per 1000	109 per 1000 (67, 176)			
	Moderate				
	239 per 1000	160 per 1000 (98, 258)			
Post-treatment – available case analysis SADS, MMS or SCID or LIFE (4-52 weeks)	*Study population*		RR 0.50 (0.22, 1.14)	464 (6 studies)	●○○○ Very low (a,b,c,d)
	170 per 1000	71 per 1000 (-31, 180)			
	Moderate				
	219 per 1000	92 per 1000 (-39, 232)			
Intermediate follow-up (17-24 weeks post-intervention) – ITT analysis MINI, SADS or MMS (6-36 weeks)	*Study population*		RR 1.1 (0.75, 1.6)	734 (4 studies)	●○○○ Very low (a,b,c,f)
	113 per 1000	125 per 1000 (85, 181)			
	Moderate				
	86 per 1000	95 per 1000 (65, 138)			
Intermediate follow-up (17-24 weeks post-intervention) – available case analysis SADS or MMS (26-36 weeks)	*Study population*		RR 1.1 (0.58, 2.09)	233 (2 studies)	●○○○ Very low (a,b,c)
	128 per 1000	141 per 1000 (74, 268)			
	Moderate				
	77 per 1000	85 per 1000 (45, 161)			
Long Follow-up (25-103 weeks post-intervention) – ITT analysis MINI, SADS, MMS or SCID (32-75 weeks)	*Study population*		RR 0.8 (0.56, 1.13)	812 (5 studies)	●○○○ Very low (a,b,c)
	217 per 1000	173 per 1000 (121, 245)			
	Moderate				
	250 per 1000	200 per 1000 (140, 282)			
Long Follow-up (25-103 weeks post-intervention) – available case analysis SADS, MMS or SCID (32-75 weeks)	*Study population*		RR 0.6 (0.36, 1.03)	266 (3 studies)	●○○○ Very low (a,b,c)
	227 per 1000	136 per 1000 (82, 233)			
	Moderate				
	250 per 1000	150 per 1000 (90, 257)			
Depression symptomatology					
Post-treatment – ITT analysis HSCL: Sum/20 >0.75 depression, EPDS≥13, Leverton Questionnaire (Elliott et al., 2000) ≥12, QIDS ≥11 or BDI: Treatment non-response (4-26 weeks)	*Study population*		**RR 0.74 (0.62, 0.88)**	1,518 (5 studies)	●●●● High
	351 per 1000	260 per 1000 (218, 309)			
	Moderate				
	480 per 1000	355 per 1000 (298, 422)			
Post-treatment – available case analysis HSCL: Sum/20 >0.75 depression, QIDS≥11 or BDI: Treatment non-response (4-26 weeks)	*Study population*		**RR 0.82 (0.68, 0.98)**	997 (3 studies)	●●●○ Moderate (a)
	320 per 1000	262 per 1000 (218, 314)			
	Moderate				
	458 per 1000	376 per 1000 (311, 449)			
Depression mean scores					
Post-treatment – ITT analysis EPDS or CES-D (4-31 weeks)	SMD -0.25 (-0.58, 0.08)		-	436 (4 studies)	●●●○ Moderate (d)
Post-treatment – available case analysis BDI-II, BDI, EPDS or CES-D (4-31 weeks)	**SMD -0.26 (-0.48, -0.05)**		-	351 (7 studies)	●●●○ Moderate (e)

Outcomes (follow-up)	Illustrative comparative risks*		Relative effect (95% CI)	No. of participants (studies)	Quality of the evidence (GRADE)
	Assumed risk Control	Corresponding risk Intervention			
Short Follow-up (9-16 weeks post-intervention) – ITT analysis EPDS (13-27 weeks)	**SMD -0.37 (-0.63, -0.11)**		-	235 (2 studies)	●●●○ Moderate (e)
Short Follow-up (9-16 weeks post-intervention) – available case analysis EPDS or BDI-II (19-27 weeks)	**SMD -0.42 (-0.82, -0.02)**		-	100 (2 studies)	●○○○ Very low (c,e)
Intermediate follow-up (17-24 weeks post-intervention) – ITT analysis EPDS (26-36 weeks)	SMD -0.07 (-0.35, 0.21)		-	197 (2 studies)	●●○○ Low (e)
Intermediate follow-up (17-24 weeks post-intervention) – available case analysis EPDS (mean 36 weeks)	SMD -0.28 (-0.89, 0.34)		-	41 (1 study)	●○○○ Very low (b,c,e,f)
Long Follow-up (25-103 weeks post-intervention) – ITT analysis EPDS (57-75 weeks)	SMD -0.43 (-0.86, 0)		-	86 (2 studies)	●●○○ Low (e)
Long Follow-up (25-103 weeks post-intervention) – available case analysis EPDS or BDI-II (32-75 weeks)	**SMD -0.44 (-0.75, -0.12)**		-	161 (3 studies)	●○○○ Very low (c,e)
Anxiety diagnosis					
Post-treatment – ITT analysis MINI or SADS (9-52 weeks)	*Study population*		RR 0.97 (0.61, 1.54)	476 (2 studies)	●○○○ Very low (a,b,c,f)
	136 per 1000	132 per 1000 (83, 209)			
	Moderate				
	138 per 1000	134 per 1000 (84, 213)			
Post-treatment – available case analysis SADS (mean 9 weeks)	*Study population*		RR 0.78 (0.32, 1.88)	199 (1 study)	●○○○ Very low (a,b,c)
	102 per 1000	80 per 1000 (33, 192)			
	Moderate				
	102 per 1000	80 per 1000 (33, 192)			
Long Follow-up (25-103 weeks post-intervention) – ITT analysis MINI	*Study population*		RR 1 (0.56, 1.78)	277 (1 study)	●○○○ Very low (a,b,c,f)
	163 per 1000	163 per 1000 (91, 290)			
	Moderate				
	163 per 1000	163 per 1000 (91, 290)			
PTSD diagnosis					
Post-treatment – ITT analysis LIFE (mean 13 weeks)	*Study population*		RR 0.74 (0.22, 2.47)	54 (1 study)	●○○○ Very low (a,b,c,g)
	192 per 1000	142 per 1000 (42, 475)			
	Moderate				
	192 per 1000	142 per 1000 (42, 474)			
Post-treatment – available case analysis LIFE (mean 13 weeks)	*Study population*		RR 2.54 (0.11, 59.23)	46 (1 study)	●○○○ Very low (a,b,c,g)
	0 per 1000	0 per 1000 (0, 0)			
	Moderate				

Outcomes (follow-up)	Illustrative comparative risks*		Relative effect (95% CI)	No. of participants (studies)	Quality of the evidence (GRADE)
	Assumed risk Control	Corresponding risk Intervention			
	0 per 1000	0 per 1000 (0, 0)			
PTSD mean scores					
Post-treatment – available case analysis Davidson Trauma Scale or LIFE: Psychiatric Status Ratings mean PTSD score (6-13 weeks)	SMD -0.4 (-0.81, 0)		-	96 (2 studies)	●○○○ Very low (c,e)
OCD mean scores					
Post-treatment – available case analysis Yale–Brown Obsessive Compulsive Scale (YBOCS) (mean 4 weeks)	SMD -0.41 (-0.94, 0.11)		-	58 (1 study)	●○○○ Very low (b,c,e)
Intermediate follow-up (17-24 weeks post-intervention) – available case analysis YBOCS (mean 19 weeks)	**SMD -0.71 (-1.29, -0.12)**		-	50 (1 study)	●○○○ Very low (c,e)
Long follow-up (25-103 weeks post-intervention) – available case analysis YBOCS (mean 32 weeks)	**SMD -0.76 (-1.35, -0.17)**		-	49 (1 study)	●○○○ Very low (c,e)

Evidence Statements:

Psychologically (CBT/IPT) informed psychoeducation has inconsistent effects on depression diagnosis at endpoint or first measurement (very low certainty evidence), at intermediate follow-up (17-24 weeks post-intervention) (very low certainty evidence), and at long follow-up (25-103 weeks post-intervention) (very low certainty evidence) compared with treatment as usual or enhanced treatment as usual in women who have symptoms (or subthreshold symptoms) of depression in the perinatal period.

Psychologically (CBT/IPT) informed psychoeducation improves depression symptomatology (high certainty evidence) at endpoint or first measurement compared with treatment as usual or enhanced treatment as usual in women who have symptoms (or subthreshold symptoms) of depression in the perinatal period.

Psychologically (CBT/IPT) informed psychoeducation has inconsistent effects on depression mean scores at endpoint or first measurement (moderate certainty evidence), at short follow-up (9-16 weeks post-intervention) (moderate certainty evidence), at intermediate follow-up (17-24 weeks post-intervention) (low certainty evidence), and at long follow-up (25-103 weeks post-intervention) (low certainty evidence) compared with treatment as usual or enhanced treatment as usual in women who have symptoms (or subthreshold symptoms) of depression in the perinatal period; however, the magnitude of any benefit may not be clinically significant.

Psychologically (CBT/IPT) informed psychoeducation appears to have no effect on anxiety diagnosis at endpoint or first measurement (very low certainty evidence) or at long follow-up (25-103 weeks post-intervention) (very low certainty evidence) compared with treatment as usual or enhanced treatment as usual in women who have symptoms (or subthreshold symptoms) of depression in the perinatal period.

Psychologically (CBT/IPT) informed psychoeducation appears to have no effect on PTSD diagnosis at endpoint or first measurement (very low certainty evidence) compared with enhanced treatment as usual in women who have experienced intimate partner violence and have subthreshold symptoms of depression in the perinatal period.

Psychologically (CBT/IPT) informed psychoeducation appears to have no effect on PTSD mean scores at endpoint or first measurement (very low certainty evidence) compared with treatment as usual or enhanced treatment as usual in women who have experienced intimate partner violence or have infants in the neonatal intensive care unit, and have subthreshold symptoms of depression in the perinatal period.

Psychologically (CBT/IPT) informed psychoeducation may improve OCD mean scores at endpoint or first measurement at post-treatment (very low certainty evidence), at intermediate follow-up (17-24 weeks post-intervention) (very low certainty evidence) and at long follow-up (25-103 weeks post-intervention) (very low certainty evidence) compared with enhanced treatment as usual in pregnant women who have subthreshold symptoms of OCD; however, the magnitude of the benefits may not be clinically significant.

Outcomes (follow-up)	Illustrative comparative risks*		Relative effect (95% CI)	No. of participants (studies)	Quality of the evidence (GRADE)
	Assumed risk Control	Corresponding risk Intervention			
Footnotes: * The 'assumed risk' for the *study population* is calculated using the mean baseline risk from the studies in the meta-analysis (i.e. total number of events in the control/comparison group divided by the total number of patients in the control/comparison group). The *moderate* risk scenario is calculated using the median control/comparison group risk from the studies in the meta-analysis. The 'corresponding risk' (and its 95% CI) is based on the assumed risk in the control/comparison group and the relative effect of the intervention (and its 95% CI). a. Total number of events is less than 300 (a threshold rule-of-thumb) b. 95% CI crosses both line of no effect and measure of appreciable benefit or harm (SMD -0.5/0.5 or RR 0.75/1.25) c. Papers omit data d. There was evidence of substantial heterogeneity between effect sizes e. Total population size is less than 400 (a threshold rule-of-thumb) f. Risk of bias due to statistically significant group differences at baseline g. Risk of bias due to unclear blinding of outcome assessment					

Source: NICE 2015, Table 141, Table 164, Table 172, Table 174, Table 183

Abbreviations: BDI, Beck Depression Inventory; CBT, cognitive behaviour therapy; CES-D, Center for Epidemiologic Studies Depression Scale; CI, confidence interval; EPDS, Edinburgh Postnatal Depression Scale; HSCL, Hopkins Symptom Checklist; IPT, interpersonal psychotherapy; ITT, intention-to-treat; LIFE, Longitudinal Interval Follow-up Examination; MINI, Mini International Neuropsychiatric Interview; MMS, Maternal Mood Screener; OCD, obsessive-compulsive disorder; PSCS, Parenting Sense of Competence Scale; PTSD, post-traumatic stress disorder; QIDS, Quick Inventory of Depressive Symptoms; RR, relative risk; SADS, Schedule for Affective Disorders and Schizophrenia; SCID, Structured Clinical Interview for DSM Disorders; SMD, standardised mean difference; VAS, Visual Analogue Scale; YBOCS, Yale–Brown Obsessive Compulsive Scale.

Note: Statistically significant differences are shown in bold.

C3.1.1.2 IPT-informed psychoeducation versus non-mental-health-focused education and support

There was no evidence that IPT-informed psychoeducation was more effective than non-mental-health-focused education and support for treating depression symptomatology (**Table C3-2**).

Table C3-2 Summary of findings (treatment) – IPT-informed psychoeducation versus non-mental health-focused education and support

Outcomes (follow-up)	Illustrative comparative risks*		Relative effect (95% CI)	No. of participants (studies)	Certainty of the evidence (GRADE)
	Assumed risk Control	Corresponding risk Intervention			
Depression symptomatology					
Post-treatment – ITT Analysis	*Study population*		RR 0.76 (0.53, 1.07)	38 (1 study)	●●○○ Low (a,b)
EPDS	882 per 1000	671 per 1000 (468, 944)			
(mean 16 weeks)	*Moderate*				
	882 per 1000	670 per 1000 (467, 944)			
Evidence Statement: *IPT-informed group psychoeducation appears to have no effect on depressive symptomatology at endpoint or first measurement (low certainty evidence) compared with non-mental-health-focused education and support in pregnant women with a diagnosis of MDD.*					

Footnotes:

* The 'assumed risk' for the *study population* is calculated using the mean baseline risk from the studies in the meta-analysis (i.e. total number of events in the control/comparison group divided by the total number of patients in the control/comparison group). The *moderate* risk scenario is calculated using the median control/comparison group risk from the studies in the meta-analysis. The 'corresponding risk' (and its 95% CI) is based on the assumed risk in the control/comparison group and the relative effect of the intervention (and its 95% CI).

a. Total number of events is less than 300 (a threshold rule-of-thumb).

b. 95% CI crosses both line of no effect and measure of appreciable benefit or harm (SMD -0.5/0.5 or RR 0.75/1.25).

Source: NICE 2015, Table 142

Abbreviations: CI, confidence interval; EPDS, Edinburgh Postnatal Depression Scale; ITT, intention-to-treat; MDD, major depressive disorder; RR, relative risk; SMD, standardised mean difference.

C3.1.2 Psychoeducational booklet

The literature search identified no SRs that relate to this intervention.

Table C3-3 Summary of findings (treatment) – psychoeducational booklet

Evidence Statement: *There is no RCT evidence for psychoeducational booklet in women who have mental health problems in the perinatal period.*

C3.1.3 Social/peer support

Of the three SRs identified in the literature search, NICE 2015 was chosen as the foundation review due to its high quality and comprehensiveness. NICE 2015 included four RCTs that compared social support (peer-mediated support or support group) with treatment as usual (or waitlist) in postnatal women with symptoms of depression. One RCT was from Taiwan and the other three were from Canada. The Taiwanese RCT assessed face-to-face group support, whereas the Canadian RCTs assessed individual telephone support. In one RCT, peer-mediated support was provided at home and/or via the telephone and the intervention included mother-infant relationship content.

NICE 2015 also included one Australian RCT that compared a combined psychosocial (informal support group) and physical exercise (pram walking) intervention with enhanced treatment as usual (telephone support), and another Australian RCT that compared social support group with physical exercise (a pram walking exercise program). In both RCTs, the interventions were aimed at postnatal women with symptoms of depression.

C3.1.3.1 Social support versus treatment as usual

NICE 2015 did not consider the format or mode of delivery of the intervention in their analyses.

There were mixed results for treatment effects on depression outcomes associated with peer-mediated support or support groups (mutual support). There was low-to-moderate-certainty evidence from three studies (N=807) for moderate benefits of social support on depression symptomatology at endpoint using an ITT approach (**Table C3-4**). However, these effects appeared to be transient as no clinically or statistically significant benefits were observed on depression symptomatology at short-term follow-up. Moreover, there was no evidence for clinically or statistically significant benefits of social support on depression diagnosis at endpoint using ITT analysis or for mean depression symptoms at endpoint or short-term follow-up.

There was no evidence for clinically or statistically significant benefits of social support on anxiety symptomatology or anxiety mean symptoms, and no clinically or statistically significant benefits of social support for positive mother-infant feeding or teaching interactions.

Three studies (N=807) found evidence for a moderate effect of social support relative to treatment as usual on attrition with higher drop-out associated with peer-mediated support or a support group. However, this effect was not statistically significant due to very serious imprecision.

Table C3-4 Summary of findings (treatment) – social support versus treatment as usual

Outcomes (follow-up)	Illustrative comparative risks*		Relative effect (95% CI)	No. of participants (studies)	Certainty of the evidence (GRADE)
	Assumed risk Control	Corresponding risk Intervention			
Depression diagnosis					
Post-treatment – ITT analysis SCID (mean 12 weeks)	*Study population*		RR 1.11 (0.81, 1.52)	701 (1 study)	●○○○ Very low (a,b,c)
	170 per 1000	189 per 1000 (138, 259)			
	Moderate				
	171 per 1000	190 per 1000 (139, 260)			
Post-treatment – available case analysis SCID (mean 12 weeks)	*Study population*		RR 0.65 (0.34, 1.23)	612 (1 study)	●○○○ Very low (a,b,c)
	73 per 1000	47 per 1000 (13, 83)			
	Moderate				
	73 per 1000	47 per 1000 (13, 83)			
Depression symptomatology					
Post-treatment – ITT analysis BDI≥10 or EPDS≥12 (8-14 weeks)	*Study population*		RR 0.69 (0.47, 1.01)	807 (3 studies)	●●○○ Low (a,b)
	359 per 1000	248 per 1000 (169, 363)			
	Moderate				
	546 per 1000	377 per 1000 (257, 551)			
Post-treatment – available case analysis BDI≥10 or EPDS≥12 (8-14 weeks)	*Study population*		**RR 0.52 (0.39, 0.7)**	713 (3 studies)	●●●○ Moderate (a)
	292 per 1000	152 per 1000 (114, 205)			
	Moderate				
	524 per 1000	272 per 1000 (204, 367)			
Short Follow-up (9-16 weeks post-intervention) – ITT analysis EPDS≥12 (mean 24 weeks)	*Study population*		RR 1.12 (0.87, 1.44)	701 (1 study)	●●○○ Low (a,b)
	239 per 1000	267 per 1000 (208, 344)			
	Moderate				
	239 per 1000	268 per 1000 (208, 344)			
Short Follow-up (9-16 weeks post-intervention) – available case analysis EPDS≥12 (mean 24 weeks)	*Study population*		RR 0.83 (0.54, 1.26)	600 (1 study)	●●○○ Low (a,b)
	138 per 1000	115 per 1000 (75, 174)			
	Moderate				
	138 per 1000	115 per 1000 (75, 174)			
Depression mean scores					
Post-treatment – available case analysis BDI or EPDS (12-14 weeks)	SMD -0.12 (-0.68, 0.45)		-	723 (3 studies)	●○○○ Very low (b,d)
Short Follow-up (9-16 weeks post-intervention) – available case analysis EPDS (mean 24 weeks)	SMD -0.13 (-0.29, 0.03)		-	600 (1 study)	●●●● High
Anxiety symptomatology					
Post-treatment – ITT analysis STAI-S >44 (mean 12 weeks)	*Study population*		RR 0.93 (0.75, 1.14)	701 (1 study)	●●○○ Low (a,c)
	349 per 1000	325 per 1000 (262, 398)			
	Moderate				
	349 per 1000	325 per 1000 (262, 398)			
Post-treatment – available case analysis STAI-S>44 (mean 12 weeks)	*Study population*		RR 0.75 (0.56, 1)	612 (1 study)	●○○○ Very low (a,c)
	273 per 1000	205 per 1000 (153, 273)			
	Moderate				
	273 per 1000	205 per 1000 (153, 273)			

Outcomes (follow-up)	Illustrative comparative risks*		Relative effect (95% CI)	No. of participants (studies)	Certainty of the evidence (GRADE)
	Assumed risk Control	Corresponding risk Intervention			
Depression diagnosis					
Anxiety mean scores					
Post-treatment – available case analysis STAI-S (mean 12 weeks)	SMD -0.14 (-0.3, 0.02)		-	612 (1 study)	●●●○ Moderate (c)
Short follow-up (9-16 weeks post-intervention) – available case analysis STAI-S (mean 24 weeks)	SMD -0.07 (-0.23, 0.09)		-	600 (1 study)	●●●○ Moderate (c)
Mother-infant interaction					
Post-treatment – available case analysis NCAST: Feeding (mean 12 weeks)	SMD -0.18 (-0.79, 0.42)		-	43 (1 study)	●●○○ Low (b,e)
Post-treatment – available case analysis NCAST: Teaching (mean 12 weeks)	SMD -0.45 (-1.04, 0.13)		-	46 (1 study)	●●○○ Low (b,e)

Evidence Statement:

Social support (peer-mediated support or support group) may have an effect[6] on depression symptomatology at endpoint or first measurement (low certainty evidence) compared with treatment as usual in women who have symptoms of depression in the postnatal period; however, the effect is not maintained at short-term follow-up (9-16 weeks post-intervention) (low certainty evidence).

Social support (peer-mediated support or support group) appears to have no effect on depression mean scores at endpoint or first measurement (very low certainty evidence) compared with treatment as usual in women who have symptoms of depression in the postnatal period.

Telephone peer-mediated support appears to have no effect on depression diagnosis at endpoint or first measurement (very low certainty evidence) compared with treatment as usual in women who have symptoms of depression in the postnatal period.

Telephone peer-mediated support has no effect on anxiety mean scores (moderate certainty evidence) and appears to have no effect or on anxiety symptomatology (low certainty evidence) at endpoint or first measurement compared with treatment as usual in women who have symptoms of depression in the postnatal period.

Peer-mediated support (with mother-infant relationship intervention content) appears to have no effect on mother-infant feeding interactions at endpoint or first measurement (low certainty evidence) compared with treatment as usual in women who have symptoms of depression in the postnatal period.

Footnotes:

* The 'assumed risk' for the *study population* is calculated using the mean baseline risk from the studies in the meta-analysis (i.e. total number of events in the control/comparison group divided by the total number of patients in the control/comparison group). The *moderate* risk scenario is calculated using the median control/comparison group risk from the studies in the meta-analysis. The 'corresponding risk' (and its 95% CI) is based on the assumed risk in the control/comparison group and the relative effect of the intervention (and its 95% CI).

a. Total number of events is less than 300 (a threshold rule-of-thumb).

b. 95% CI crosses both line of no effect and measure of appreciable benefit or harm (SMD -0.5/0.5 or RR 0.75/1.25).

c. Papers omit data.

d. There was evidence of considerable heterogeneity between effect sizes.

e. Total population size is less than 400 (a threshold rule-of-thumb).

Source: NICE 2015, Table 140, Table 163, Table 190

Abbreviations: BDI, Beck Depression Inventory; CI, confidence interval; EPDS, Edinburgh Postnatal Depression Scale; ITT, intention-to-treat; NCAST, Nursing Child Assessment Satellite Training Scale; RR, relative risk; SCID, Structured Clinical Interview for DSM Disorders; SMD, standardised mean difference; STAI-S, State-Trait Anxiety Inventory-State.

Note: Statistically significant differences are shown in bold.

[6] RR 0.69 (95% CI 0.47, 1.01); P=0.05

C3.1.3.2 Combined social support and physical exercise versus enhanced treatment as usual

There was single-study evidence (N=20) for large benefits of a combined informal social support group and pram walking exercise program on depression symptomatology and mean depression symptoms; however, confidence in these effect estimates is low due to the extremely low event rate and very small sample size (**Table C3-5**).

Table C3-5 Summary of findings (treatment) – combined social support and physical exercise versus enhanced treatment as usual

Outcomes (follow-up)	Illustrative comparative risks*		Relative effect (95% CI)	No. of participants (studies)	Certainty of the evidence (GRADE)
	Assumed risk Control	Corresponding risk Intervention			
Depression symptomatology					
Post-treatment – ITT analysis EPDS ≥12 (mean 12 weeks)	*Study population*		RR 0.07 (0, 1.03)	20 (1 study)	●●○○ Low (a,b)
	700 per 1000	49 per 1000 (0, 721)			
	Moderate				
	700 per 1000	49 per 1000 (0, 721)			
Post-treatment – available case analysis EPDS ≥12 (mean 12 weeks)	*Study population*		RR 0.07 (0, 1.03)	20 (1 study)	●●○○ Low (a,b)
	700 per 1000	49 per 1000 (0, 721)			
	Moderate				
	700 per 1000	49 per 1000 (0, 721)			
Depression mean symptoms					
Post-treatment – ITT analysis EPDS (mean 12 weeks)	**SMD -1.64 (-2.68, -0.59)**		-	20 (1 study)	●●○○ Low (c)
Post-treatment – available case analysis EPDS (mean 12 weeks)	**SMD -1.64 (-2.68, -0.59)**		-	20 (1 study)	●●○○ Low (c)
Evidence Statement: *Social support group combined with physical exercise (a pram walking exercise program) may improve depression mean symptoms (low certainty evidence) and may have an effect[7] on depression symptomatology (low certainty evidence) at endpoint or first measurement compared with enhanced treatment as usual (telephone support) in women who have symptoms of depression in the postnatal period.*					
Footnotes: * The 'assumed risk' for the *study population* is calculated using the mean baseline risk from the studies in the meta-analysis (i.e. total number of events in the control/comparison group divided by the total number of patients in the control/comparison group). The *moderate* risk scenario is calculated using the median control/comparison group risk from the studies in the meta-analysis. The 'corresponding risk' (and its 95% CI) is based on the assumed risk in the control/comparison group and the relative effect of the intervention (and its 95% CI). a. Total number of events is less than 300 (a threshold rule-of-thumb). b. 95% CI crosses both line of no effect and measure of appreciable benefit or harm (SMD -0.5/0.5 or RR 0.75/1.25). c. Total population size is less than 400 (a threshold rule-of-thumb).					

Source: NICE 2015, Table 152

Abbreviations: CI, confidence interval; EPDS, Edinburgh Postnatal Depression Scale; ITT, intention-to-treat; RR, relative risk; SMD, standardised mean difference.

Note: Statistically significant differences are shown in bold.

[7] RR 0.07 (95% CI 0, 1.03)

C3.1.3.3 Social support versus physical exercise

In order to tease apart the combined intervention discussed above and assess the individual contribution of psychosocial and physical interventions, the same researchers compared social support and physical exercise in a head-to-head trial and provided single-study evidence (N=20) for a large effect of social support (social support group) relative to physical exercise (pram walking exercise program) on depression mean symptoms. However, confidence in this effect estimate was low due to imprecision as a result of the very small sample size.

Table C3-6 Summary of findings (treatment) – social support versus physical exercise

Outcomes (follow-up)	Illustrative comparative risks*		Relative effect (95% CI)	No. of participants (studies)	Certainty of the evidence (GRADE)
	Assumed risk Control	Corresponding risk Intervention			
Depression mean symptoms					
Post-Treatment – available case analysis EPDS (mean 12 weeks)	**SMD -1.09 (-2.07, -0.11)**		-	19 (1 study)	●●○○ Low (a)
Evidence Statement: *Social support group may improve depression mean symptoms at endpoint or first measurement (low certainty evidence) compared with physical exercise (a pram walking exercise program) in women who have symptoms of depression in the postnatal period.*					
Footnotes: * The 'assumed risk' for the *study population* is calculated using the mean baseline risk from the studies in the meta-analysis (i.e. total number of events in the control/comparison group divided by the total number of patients in the control/comparison group). The *moderate* risk scenario is calculated using the median control/comparison group risk from the studies in the meta-analysis. The 'corresponding risk' (and its 95% CI) is based on the assumed risk in the control/comparison group and the relative effect of the intervention (and its 95% CI). a. Total population size is less than 400 (a threshold rule-of-thumb)					

Source: NICE 2015, Table 153

Abbreviations: CI, confidence interval; EPDS, Edinburgh Postnatal Depression Scale; SMD, standardised mean difference.

Note: Statistically significant differences are shown in bold.

C3.1.4 Home visits

Only one SR (NICE 2015) was identified for home visits in the literature search. NICE 2015 included five RCTs, one of which was from Australia. The five RCTs compared face-to-face, home-based listening visits (non-directive counselling) with treatment as usual or enhanced treatment as usual[8] in women with a diagnosis of depression or symptoms (or subthreshold symptoms) of depression. The intervention was postnatal in two RCTs and antenatal and postnatal in the remaining three RCTs.

The intervention in the Australian study (Armstrong 1999; N=181) was a structured program of weekly child health nurse visits for vulnerable, or 'high risk', families. 'High risk' was defined at two levels: a) at least one of the following four: sole parenthood; ambivalence to the pregnancy (sought termination, no antenatal care); physical forms of domestic violence; childhood abuse of either parent; and b) three or more of the following: maternal age<18 years old; unstable housing; financial stress; maternal education <10 years; low family income; social isolation; history of mental health disorder (either parent); alcohol or drug

[8] Enhanced treatment as usual involved Medicaid enhanced prenatal/postnatal services.

abuse; domestic violence other than physical abuse. At baseline, 23% of study participants had an Edinburgh Postnatal Depression Scale (EPDS) score of >12 (mean baseline EPDS 8.7 [SD 3.5]). The intervention aimed to enhance parenting self-esteem and confidence, provide anticipatory guidance for normal child development problems, promote preventive child health care, and facilitate access to appropriate community services.

A French RCT (N=364) assessed a manualised multifocal perinatal home-visiting program that was specifically tailored to empower mothers in terms of developing parenting skills, using the health and social care system, and making the most of their personal networks and local community services. Study participants were first-time mothers aged less than 26 years old, who had at least one of the following: less than 12 years' education; were planning to bring up their child without the child's father; or had low income. At baseline, 45% of study participants had EPDS >11. The home visitations were undertaken by a team of psychologists specifically trained to promote mental health and attachment quality, provide social and emotional support within a solid working alliance, and address depression should it occur.

An RCT from the United States (N=440) assessed a voluntary intensive, long-term home visiting program (the Healthy Families Alaska Program). Families were eligible if they scored ≥25 on the Kempe's Family Stress Checklist. Trained home visitors provided information, made referrals to community resources, helped parents prepare for developmental milestones, screened and referred for developmental delay, and promoted child environmental safety. They also supported positive parent–child interaction via role modelling and reinforcement of positive interactions and parental empathy. Visits were offered weekly for the first 6–9 months and less frequently as the family functioning improved. At baseline, 57% of women had a CES-D >15.

Another RCT from the United States (N=613) assessed a Nurse-Community Health Worker (Nurse-CHW) home visiting team intervention in the context of Medicaid enhanced pre/postnatal services. Nurses guided the CHW care, led a multidisciplinary team assessment, provided crisis intervention and case management, assessed and managed health problems (including screening for depression), and had periodic office visits with prenatal providers. CHWs provided relationship-based support through phone and face-to-face contacts. Although a study exclusion criterion was diagnosis or treatment for a pre-existing mental health condition within the last two years, 56% of study participants had CES-D ≥16.

A Japanese RCT (N=18) assessed home visits provided by mental health nurses to women with a diagnosis of minor or major depression using the Structural Clinical Interview for DSM Disorders, modified for postnatal depression (SCID-PND) and EPDS >9. The intervention involved active listening, providing support and acceptance, psychoeducation on depressive symptoms, and advice on coping strategies for problematic life issues, including parenting and increasing access to social or family support. The intervention was provided flexibly according to the individual's needs and the nurse's assessment of each woman's self-care level and mental state.

C3.1.4.1 Home visits versus treatment as usual or enhanced treatment as usual

There was single-study evidence (N=18) for moderate benefits of postnatal home visits on depression diagnosis in Japanese women with a diagnosis of minor or major depression, using an ITT approach (**Table C3-7**). However, confidence in these effect estimates is very low due to the 95% CI including estimates of both no effect and clinically meaningful treatment benefits. The intervention was provided by mental health nurses and involved active listening, providing support and acceptance of the woman, psychoeducation on depressive symptoms, and advice on coping strategies for problematic life issues, including parenting and increasing access to social or family support.

There was no evidence from three studies of clinically or statistically significant treatment effects on depression symptomology, or clinically significant treatment effects on mean depression symptoms.

There was no evidence of clinically or statistically significant benefits of home visits on mother-infant attachment problems.

Table C3-7 Summary of findings (treatment) – home visits versus treatment as usual or enhanced treatment as usual

Outcomes (follow-up)	Illustrative comparative risks*		Relative effect (95% CI)	No. of participants (studies)	Certainty of the evidence (GRADE)
	Assumed risk Control	Corresponding risk Intervention			
Depression diagnosis					
Post-treatment – ITT analysis SCID (mean 6 weeks)	*Study population*		RR 0.67 (0.28, 1.58)	18 (1 study)	●○○○ Very low (a,b,c)
	667 per 1000	447 per 1000 (187, 1000)			
	Moderate				
	667 per 1000	447 per 1000 (187, 1000)			
Post-treatment – available case analysis SCID (mean 6 weeks)	*Study population*		RR 0.43 (0.12, 1.51)	16 (1 study)	●○○○ Very low (a,b,c)
	667 per 1000	287 per 1000 (-173, 740)			
	Moderate				
	667 per 1000	287 per 1000 (-173, 740)			
Depression symptomatology					
Post-treatment – ITT analysis EPDS ≥10/12 or CES-D ≥24 (22-104 weeks)	*Study population*		RR 0.92 (0.8, 1.06)	985 (3 studies)	●●●○ Moderate (d)
	451 per 1000	415 per 1000 (361, 479)			
	Moderate				
	477 per 1000	439 per 1000 (382, 506)			
Post-treatment – available case analysis EPDS ≥10/12 or CES-D ≥24 (22-104 weeks)	*Study population*		RR 0.87 (0.69, 1.1)	754 (3 studies)	●○○○ Very low (b,c,d)
	279 per 1000	243 per 1000 (193, 307)			
	Moderate				
	220 per 1000	191 per 1000 (152, 242)			
Depression mean scores					
Post-treatment – available case analysis EPDS or CES-D (22-52 weeks)	**SMD -0.17 (-0.3, -0.05)**		-	960 (3 studies)	●●●● High
Mother-infant attachment problems					
Post-treatment – ITT analysis NCAST ≤35 (mean 104 weeks)	*Study population*		RR 0.87 (0.69, 1.09)	364 (1 study)	●○○○ Very low (b,c,e)
	476 per 1000	414 per 1000 (328, 518)			
	Moderate				
	476 per 1000	414 per 1000 (328, 519)			
Post-treatment – available case analysis NCAST ≤35 (mean 104 weeks)	*Study population*		RR 0.79 (0.47, 1.32)	249 (1 study)	●○○○ Very low (b,c,e)
	211 per 1000	167 per 1000 (99, 279)			
	Moderate				
	211 per 1000	167 per 1000 (99, 279)			

Outcomes (follow-up)	Illustrative comparative risks*		Relative effect (95% CI)	No. of participants (studies)	Certainty of the evidence (GRADE)
	Assumed risk Control	Corresponding risk Intervention			
Depression diagnosis					
Evidence Statements: *Home visits improve depression mean scores at endpoint or first measurement (high certainty evidence) compared with treatment as usual in women who have symptoms of depression in the perinatal period; however, the magnitude of the benefit may not be clinically significant.* *Home visits have no effect on depression symptomatology (moderate certainty evidence) and appear to have no effect on depression diagnosis (very low certainty evidence) at endpoint or first measurement compared with treatment as usual in women who have a diagnosis of depression in the postnatal period.* *A long-term home visiting program to prevent child abuse appears to have no effect on mother-infant attachment problems (very low certainty evidence) at endpoint or first measurement compared with treatment as usual in families that screen positive for family stress in the perinatal period.*					
Footnotes: * The 'assumed risk' for the *study population* is calculated using the mean baseline risk from the studies in the meta-analysis (i.e. total number of events in the control/comparison group divided by the total number of patients in the control/comparison group). The *moderate* risk scenario is calculated using the median control/comparison group risk from the studies in the meta-analysis. The 'corresponding risk' (and its 95% CI) is based on the assumed risk in the control/comparison group and the relative effect of the intervention (and its 95% CI). a. Risk of bias due to unclear blinding of outcome assessment. b. Total number of events is less than 300 (a threshold rule-of-thumb). c. 95% CI crosses both line of no effect and measure of appreciable benefit or harm (SMD -0.5/0.5 or RR 0.75/1.25). d. Papers omit data. e. Risk of bias due to statistically significant group differences at baseline.					

Source: NICE 2015, Table 144, Table 184, Table 192

Abbreviations: CAGE, cut-annoyed-guilty-eye; CBCL, Child Behaviour Checklist; CES-D, Center for Epidemiologic Studies Depression Scale; CI, confidence interval; EPDS, Edinburgh Postnatal Depression Scale; ITT, intention-to-treat; NCAST, Nursing Child Assessment Satellite Training Scale; RR, relative risk; SCID, Structured Clinical Interview for DSM Disorders; SMD, standardised mean difference.

Note: Statistically significant differences are shown in bold.

C3.1.5 Non-mental-health-focused education/support

Only one SR (NICE 2015) was identified for non-mental-health-focused education/support in the literature search. NICE 2015 included one RCT from Tanzania (N=331) that compared a face-to-face group counselling intervention for HIV-positive women (antenatal and postnatal) with treatment as usual. Approximately 73% of the study sample had symptoms of depression (Hopkins Symptom Checklist [HSCL]-25>1.06).

C3.1.5.1 Non-mental-health-focused education and support versus treatment as usual

Based on one RCT, there was no evidence for clinically or statistically significant benefits associated with non-mental health-focused education and support for depression symptomatology in HIV-positive women (**Table C3-8**).

Table C3-8 Summary of findings (treatment) – non-mental health-focused education and support versus treatment as usual

Outcomes (follow-up)	Illustrative comparative risks*		Relative effect (95% CI)	No. of participants (studies)	Certainty of the evidence (GRADE)
	Assumed risk Control	Corresponding risk Intervention			
Depression symptomatology					
Post-treatment – ITT analysis HSCL-25 >1.06 (mean 12 weeks)	*Study population*		RR 0.91 (0.82, 1.01)	331 (1 study)	●●●○ Moderate (a)
	847 per 1000	770 per 1000 (694, 855)			
	Moderate				
	847 per 1000	771 per 1000 (695, 855)			
Post-treatment – available case analysis HSCL-25 >1.06 (mean 12 weeks)	*Study population*		RR 0.82 (0.67, 1.01)	188 (1 study)	●●○○ Low (a,b)
	725 per 1000	595 per 1000 (486, 733)			
	Moderate				
	725 per 1000	595 per 1000 (486, 732)			
Evidence Statement: *Non-mental-health-focused education and support during the perinatal period has no effect on depression symptomatology at endpoint or first measurement compared with treatment (moderate certainty evidence) as usual in HIV-positive women.*					
Footnotes: * The 'assumed risk' for the study population is calculated using the mean baseline risk from the studies in the meta-analysis (i.e. total number of events in the control/comparison group divided by the total number of patients in the control/comparison group). The moderate risk scenario is calculated using the median control/comparison group risk from the studies in the meta-analysis. The 'corresponding risk' (and its 95% CI) is based on the assumed risk in the control/comparison group and the relative effect of the intervention (and its 95% CI). a. Total number of events is less than 300 (a threshold rule-of-thumb). b. 95% CI crosses both line of no effect and measure of appreciable benefit or harm (SMD -0.5/0.5 or RR 0.75/1.25).					

Source: NICE 2015, Table 143

Abbreviations: CI, confidence interval; HSCL, Hopkins Symptom Checklist; ITT, intention-to-treat; RR, relative risk; SMD, standardised mean difference.

C3.1.6 Pre-delivery discussion

The literature search identified one SR (NICE 2015) relating to the assessment of pre-delivery discussion/psychoeducation for fear of childbirth (symptoms of tokophobia). However, the outcomes reported in the included RCTs are not relevant to the current Review.

Table C3-9 Summary of findings (treatment) – pre-delivery discussion

Evidence Statement: *There is no RCT evidence for pre-delivery discussion in pregnant women who have mental health problems.*

C3.1.7 Post-delivery discussion

The literature search identified no SRs that relate to this intervention.

Table C3-10 Summary of findings (treatment) – summary of findings: post-delivery discussion

Evidence Statement: *There is no RCT evidence for post-delivery discussion in women who have mental health problems in the perinatal period.*

C3.1.8 Post-miscarriage self-help

Only one SR (NICE 2015) was identified for post-miscarriage self-help in the literature search. NICE 2015 included one RCT from Germany that compared online post-miscarriage self-help (internet-based cognitive behaviour therapy (CBT) involving 10 written assignments with therapist feedback on each) with treatment as usual in self-referring women with complicated grief (mean baseline IES was 33.7 [SD 10.1]), and one multi-armed RCT from the United States that compared post-miscarriage self-help (three 18-minute video accompanied by his and her workbooks) with post-miscarriage facilitated self-help (video and workbook delivery and face-to-face nurse-led counselling) with treatment as usual in women with symptoms of depression (mean baseline CES-D was 21).

C3.1.8.1 Post-miscarriage self-help versus treatment as usual

There was low quality, single-study evidence for moderate benefits of post-miscarriage self-help on depression symptomatology compared with treatment as usual in women with complicated grief (**Table C3-11**); however, the measure for depression symptomatology was treatment non-response (based on reverse scale rating of reliable change index) on the BSI Depression subscale rather than a depression-specific validated checklist. No clinically or statistically significant benefits on mean depression symptoms were observed.

Based on one, low quality study, there was no evidence for statistically or clinically significant benefits of post-miscarriage self-help on anxiety symptomatology or mean symptoms in women with complicated grief.

There was low quality, single-study evidence for moderate effects of post-miscarriage self-help on PTSD symptomatology (analysed using an ITT approach) and large effects on mean PTSD symptoms.

Table C3-11 Summary of findings (treatment) – post-miscarriage self-help versus treatment as usual

Outcomes (follow-up)	Illustrative comparative risks*		Relative effect (95% CI)	No. of participants (studies)	Certainty of the evidence (GRADE)
	Assumed risk Control	Corresponding risk Intervention			
Depression symptomatology					
Post-treatment – ITT analysis BSI: Depression (Treatment nonresponse: reliable change index) (mean 5 weeks)	*Study population*		**RR 0.65 (0.45, 0.92)**	78 (1 study)	⨁⨁◯◯ Low (a)
	758 per 1000	492 per 1000 (341, 697)			
	Moderate				
	758 per 1000	493 per 1000 (341, 697)			
Post-treatment – available case analysis BSI: Depression (Treatment nonresponse: reliable change index) (mean 5 weeks)	*Study population*		**RR 0.44 (0.25, 0.78)**	59 (1 study)	⨁⨁◯◯ Low (a)
	692 per 1000	305 per 1000 (173, 540)			
	Moderate				
	692 per 1000	304 per 1000 (173, 540)			
Depression mean scores					
Post-treatment – ITT analysis BSI: Depression or CES-D (5-12 weeks)	SMD -0.3 (-1.19, 0.6)		-	250 (2 studies)	⨁◯◯◯ Very low (b,c)
Long Follow-up (25-103 weeks post-intervention) – ITT analysis CES-D (mean 46 weeks)	SMD -0.15 (-0.45, 0.15)		-	172 (1 study)	⨁⨁◯◯ Low (c)
Anxiety symptomatology					
Post-treatment – ITT analysis BSI: Anxiety (Treatment nonresponse: reliable change index) (mean 5 weeks)	*Study population*		RR 0.95 (0.71, 1.26)	78 (1 study)	⨁⨁◯◯ Low (a,d)
	727 per 1000	691 per 1000 (516, 916)			
	Moderate				
	727 per 1000	691 per 1000 (516, 916)			
Post-treatment – available case analysis BSI: Anxiety (Treatment nonresponse: reliable change index) (mean 5 weeks)	*Study population*		RR 0.83 (0.56, 1.23)	59 (1 study)	⨁⨁◯◯ Low (a,d)
	692 per 1000	575 per 1000 (388, 852)			
	Moderate				
	692 per 1000	574 per 1000 (388, 851)			
Anxiety mean scores					
Post-treatment – ITT analysis BSI: Anxiety (mean 5 weeks)	SMD -0.23 (-0.68, 0.23)		-	78 (1 study)	⨁⨁◯◯ Low (c,d)
PTSD symptomatology					
Post-treatment – ITT analysis IES: Treatment nonresponse (reliable change index) (mean 5 weeks)	*Study population*		**RR 0.59 (0.38, 0.94)**	78 (1 study)	⨁⨁◯◯ Low (a)
	636 per 1000	375 per 1000 (242, 598)			
	Moderate				
	636 per 1000	375 per 1000 (242, 598)			
Post-treatment – available case analysis IES: Treatment nonresponse (reliable change index) (mean 5 weeks)	*Study population*		**RR 0.32 (0.14, 0.7)**	59 (1 study)	⨁⨁◯◯ Low (a)
	577 per 1000	185 per 1000 (81, 404)			
	Moderate				
	577 per 1000	185 per 1000 (81, 404)			
PTSD mean scores					
Post-treatment – ITT analysis IES: Traumatic stress (mean 5 weeks)	**SMD -0.84 (-1.31, -0.37)**		-	78 (1 study)	⨁⨁◯◯ Low (c)

Outcomes (follow-up)	Illustrative comparative risks*		Relative effect (95% CI)	No. of participants (studies)	Certainty of the evidence (GRADE)
	Assumed risk Control	Corresponding risk Intervention			
Evidence Statements: ***Women with symptoms of depression*** *Post-miscarriage self-help appears to have no effect on depression mean scores at long follow-up (25-103 weeks post-intervention) (low certainty evidence) compared with treatment as usual in women with symptoms of depression.* ***Women with subthreshold symptoms of PTSD*** *Post-miscarriage self-help may improve depression symptomatology (low certainty evidence) but appears to have no effect on depression mean scores (very low certainty evidence) at endpoint or first measurement compared with treatment as usual in women with subthreshold symptoms of PTSD.* *Post-miscarriage self-help appears to have no effect on anxiety symptomatology (low certainty evidence) or on anxiety mean scores (low certainty evidence) at endpoint or first measurement compared with treatment as usual in women with subthreshold symptoms of PTSD.* *Post-miscarriage self-help may improve PTSD symptomatology (low certainty evidence) and PTSD mean scores (low certainty evidence) at endpoint or first measurement compared with treatment as usual in women with subthreshold symptoms of PTSD.*					

Footnotes:

* The 'assumed risk' for the *study population* is calculated using the mean baseline risk from the studies in the meta-analysis (i.e. total number of events in the control/comparison group divided by the total number of patients in the control/comparison group). The *moderate* risk scenario is calculated using the median control/comparison group risk from the studies in the meta-analysis. The 'corresponding risk' (and its 95% CI) is based on the assumed risk in the control/comparison group and the relative effect of the intervention (and its 95% CI).

a. Total number of events is less than 300 (a threshold rule-of-thumb)
b. There was evidence of considerable heterogeneity between effect sizes
c. Total population size is less than 400 (a threshold rule-of-thumb)
d. 95% CI crosses both line of no effect and measure of appreciable benefit or harm (SMD -0.5/0.5 or RR 0.75/1.25)

Source: NICE 2015, Table 134, Table 158, Table 170, Table 179

Abbreviations: BSI, Brief Symptom Inventory; CES-D, Center for Epidemiologic Studies Depression Scale; CI, confidence interval; IES, Impact of Events Scale; ITT, intention-to-treat; PTSD, post-traumatic stress disorder; RR, relative risk; SMD, standardised mean difference.

Note: Statistically significant differences are shown in bold.

C3.1.8.2 Post-miscarriage facilitated self-help versus treatment as usual

There was no evidence for clinically or statistically significant benefits of post-miscarriage facilitated self-help on mean depression symptoms (**Table C3-12**).

Table C3-12 Summary of findings (treatment) – post-miscarriage facilitated self-help versus treatment as usual

Outcomes (follow-up)	Illustrative comparative risks*		Relative effect (95% CI)	No. of participants (studies)	Certainty of the evidence (GRADE)
	Assumed risk Control	Corresponding risk Intervention			
Depression mean scores					
Post-treatment – ITT analysis CES-D (mean 12 weeks)	SMD 0.13 (-0.17, 0.43)		-	171 (1 study)	●●○○ Low (a)
Long Follow-up (25-103 weeks post-intervention) – ITT analysis CES-D (mean 46 weeks)	SMD -0.1 (-0.4, 0.2)		-	171 (1 study)	●●○○ Low (a)
Evidence Statement: *Post-miscarriage facilitated self-help (video and workbook delivery and face-to-face support) appears to have no effect on depression mean scores at endpoint or first measurement (low certainty evidence), or at long follow-up (25-103 weeks post-intervention) (low certainty evidence), compared with treatment as usual in women with symptoms of depression.*					
Footnotes: * The 'assumed risk' for the *study population* is calculated using the mean baseline risk from the studies in the meta-analysis (i.e. total number of events in the control/comparison group divided by the total number of patients in the control/comparison group). The *moderate* risk scenario is calculated using the median control/comparison group risk from the studies in the meta-analysis. The 'corresponding risk' (and its 95% CI) is based on the assumed risk in the control/comparison group and the relative effect of the intervention (and its 95% CI). a. Total population size is less than 400 (a threshold rule-of-thumb).					

Source: NICE 2015, Table 135

Abbreviations: CES-D, Center for Epidemiologic Studies Depression Scale; CI, confidence interval; ITT, intention-to-treat; SMD, standardised mean difference.

C3.1.9 Seeing and/or holding stillborn infant

The literature search identified no SRs that relate to this intervention.

Table C3-13 Summary of findings (treatment) – seeing and/or holding stillborn infant

Evidence Statement: *There is no RCT evidence for seeing and/or holding a stillborn infant in women who have mental health problems in the perinatal period.*

C3.1.10 Mother-infant relationship interventions

Of the three SRs identified for mother-infant relationship interventions in the literature search, NICE 2015 was chosen as the foundation review due to its high quality and comprehensiveness. NICE 2015 included six RCTs that compared mother-infant relationship interventions with treatment as usual. The intervention was individual in five RCTs and involved a group intervention in the sixth. Participants had a diagnosis of MDD in two RCTs, symptoms of depression in three RCTs, and subthreshold symptoms of depression in one RCT. However, none of the interventions were specifically designed to treat maternal depression; treatment was primarily directed at improving the quality of the mother-infant interaction. Across the studies, several of the outcome measures for maternal-infant interactions were observed rather than based solely on maternal report.

Of the two RCTs that recruited women with a diagnosis of MDD, one assessed a relationship/attachment-based (CBT-informed) therapy that was directed at problems identified by the mother in the management of her infant (concerning, for example, feeding or sleeping), as well as at observed problems in the quality of the mother-infant interaction. The mother was provided with advice about managing particular infant problems, was helped to solve such problems in a systematic way, was encouraged to examine her patterns of thinking about her infant and herself as a mother, and was helped through modelling and reinforcement to alter aspects of her interactional style. In the second RCT, 95% of study participants met DSM-IV criteria for a major depressive episode or dysthymia (mean baseline BDI was 23.6 [SD 8.6]). The intervention involved a home visitor (qualified prevention specialist) who monitored and videotaped the mother and child during everyday activities, and subsequently discussed the interactions with the mother.

NICE 2015 also included two RCTs with active comparators. One Australian RCT (N=51) assessed an in-hospital mother-infant relationship intervention with video feedback compared with a mother-infant relationship intervention with verbal feedback in women with a diagnosis of MDD. NICE 2015 also included an RCT from the United Kingdom (N=80) that assessed a home-based mother-infant relationship intervention compared with listening visits in women with a diagnosed eating disorder (participants in both study arms also received facilitated self-help aimed at their eating disorder).

One additional RCT from the United States that was published after the NICE 2015 literature search compared home-based, nurse-delivered perinatal dyadic psychotherapy with usual care plus depression monitoring by phone in depressed first-time mothers. The pilot RCT (N=42) found no effect of the intervention on depression remission (RR 0.95; 95% CI 0.84, 1.09) or depression symptoms (mean difference in change from baseline -53 (95% CI: -3.74, 0.68). The SR that identified the RCT did not include any mother-infant relationship data from this RCT.

C3.1.10.1 Mother-infant relationship interventions versus treatment as usual or enhanced treatment as usual

NICE 2015 did not consider the format of the intervention in their analyses.

There was mixed evidence for the effects of mother-infant relationship interventions on mother-infant attachment outcomes (**Table C3-14**). Very low certainty evidence from two studies (one using mother-infant psychotherapy and the other using CBT-informed relationship/attachment-based therapy) showed a statistically significant, moderate benefit of mother-infant relationship interventions on reducing attachment problems at endpoint in women with a diagnosis of MDD or symptoms of depression (EPDS = 12), but the positive effect was not maintained in the one study with long follow-up, which showed mild risk of harm (not statistically significant) of the CBT-informed therapy. The same RCT (in women with a diagnosis of MDD) showed a statistically significant, moderate benefit of mother-infant relationship interventions on mother-infant behavior management problems at endpoint.

Evidence from up to four studies found no evidence for statistically or clinically significant effects on continuous measures of mother-infant attachment or positive interactions at endpoint or at intermediate or long-term follow-up. There was single study evidence, in women with a diagnosis of a major depressive episode or dysthymia, for a large harm of a mother–baby intervention on mother-infant positive interaction mean scores at very long follow-up with effects favouring enhanced treatment as usual (telephone support). The 15-week intervention from the Netherlands involved a home visitor videotaping mother and child everyday activities and subsequently discussing the observed interactions with the mother.

There was single-study evidence for moderate benefits of mother-infant relationship interventions on maternal sensitivity treatment response; however, confidence in the effect estimate was very low due to risk-of-bias concerns (statistically significant differences in infant age at baseline and selective reporting bias) and very serious imprecision. Evidence from four studies found no evidence for statistically or clinically significant effects on continuous measures of maternal sensitivity at endpoint or intermediate follow-up; however, there was low quality single-study evidence for moderate benefits of mother-infant relationship interventions on maternal sensitivity at long follow-up.

Evidence for treatment effects of mother-infant relationship interventions on depression outcome measures was very inconsistent (**Table C3-14**). There was single-study evidence (N=95) in women that met DSM-III-R criteria for MDD for moderate benefits of a relationship/attachment-based (CBT-informed) therapy on depression diagnosis at endpoint, but evidence suggestive of harms at long and very long follow-up. However, the certainty of the evidence was low and there was serious imprecision. Low certainty evidence from meta-analyses of up to six studies provided no evidence of clinically or statistically significant benefits of mother-infant relationship interventions on depression symptomatology at endpoint, or depression mean symptoms at endpoint or long-term follow-up. Evidence from one study showed moderate harms of mother-infant relationship interventions on depression symptomatology at intermediate follow-up; however, there was very serious imprecision associated with this effect.

Based on one RCT, there was no evidence for clinically or statistically significant benefits of a mother-infant relationship intervention on anxiety symptomatology (using an ITT approach) or anxiety mean scores; however, there was very serious imprecision.

One RCT showed no evidence for clinically or statistically significant benefits or harms associated with mother-infant relationship interventions for PTSD symptomatology at endpoint or at intermediate follow-up using an ITT analysis approach, and no clinically or statistically significant effects on PTSD mean symptoms.

Five studies (N=576) found no evidence for clinically or statistically significant effects of mother-infant relationship interventions relative to treatment as usual or enhanced treatment as usual on attrition (as a proxy measure for retention in services and treatment acceptability).

Table C3-14 Summary of findings (treatment) – mother-infant relationship interventions versus treatment as usual or enhanced treatment as usual

Outcomes (follow-up)	Illustrative comparative risks*		Relative effect (95% CI)	No. of participants (studies)	Certainty of the evidence (GRADE)
	Assumed risk Control	Corresponding risk Intervention			
Depression diagnosis					
Post-treatment – ITT analysis SCID (mean 20 weeks)	*Study population*		RR 0.72 (0.48, 1.07)	95 (1 study)	⨁⨁◯◯ Low (a,b)
	615 per 1000	443 per 1000 (295, 658)			
	Moderate				
	615 per 1000	443 per 1000 (295, 658)			
Post-treatment – available case analysis SCID (mean 20 weeks)	*Study population*		RR 0.71 (0.47, 1.08)	92 (1 study)	⨁⨁◯◯ Low (a,b)
	600 per 1000	426 per 1000 (228, 630)			
	Moderate				
	600 per 1000	426 per 1000 (228, 630)			
Intermediate follow-up (17-24 weeks post-intervention) – ITT analysis SCID (mean 39 weeks)	*Study population*		RR 0.83 (0.46, 1.48)	95 (1 study)	⨁⨁◯◯ Low (a,b)
	365 per 1000	303 per 1000 (168, 541)			
	Moderate				
	365 per 1000	303 per 1000 (168, 540)			
Intermediate follow-up (17-24 weeks post-intervention) – available case analysis SCID (mean 39 weeks)	*Study population*		RR 0.8 (0.4, 1.58)	88 (1 study)	⨁⨁◯◯ Low (a,b)
	312 per 1000	250 per 1000 (125, 494)			
	Moderate				
	313 per 1000	250 per 1000 (125, 495)			
Long Follow-up (25-103 weeks post-intervention) – ITT analysis SCID (mean 78 weeks)	*Study population*		RR 1.21 (0.63, 2.33)	95 (1 study)	⨁⨁◯◯ Low (a,b)
	250 per 1000	302 per 1000 (157, 582)			
	Moderate				
	250 per 1000	302 per 1000 (157, 582)			
Long Follow-up (25-103 weeks post-intervention) – available case analysis SCID (mean 78 weeks)	*Study population*		RR 1.52 (0.71, 3.25)	90 (1 study)	⨁⨁◯◯ Low (a,b)
	188 per 1000	285 per 1000 (133, 609)			
	Moderate				
	188 per 1000	286 per 1000 (133, 611)			
Very long Follow-up (≥104 weeks post-intervention) – ITT analysis SCID (mean 260 weeks)	*Study population*		RR 1.21 (0.63, 2.33)	95 (1 study)	⨁⨁◯◯ Low (a,b)
	250 per 1000	302 per 1000 (157, 582)			
	Moderate				
	250 per 1000	302 per 1000 (157, 582)			
Very long Follow-up (≥104 weeks post-intervention) – available case analysis SCID (mean 260 weeks)	*Study population*		RR 0.69 (0.27, 1.73)	73 (1 study)	⨁⨁◯◯ Low (a,b)
	243 per 1000	168 per 1000 (66, 421)			
	Moderate				
	243 per 1000	168 per 1000 (66, 420)			
Depression symptomatology					
Post-treatment - ITT analysis EPDS: Treatment nonresponse (reliable change index-no improvement)/EPDS ≥12 or CES-D ≥16 (5-26 weeks)	*Study population*		RR 0.87 (0.69, 1.1)	396 (3 studies)	⨁⨁◯◯ Low (a,b)
	565 per 1000	492 per 1000 (390, 622)			
	Moderate				
	717 per 1000	624 per 1000 (495, 789)			
Post-treatment – available case analysis EPDS: Treatment nonresponse (reliable change index-no improvement)/EPDS ≥12 or CES-D ≥16 (5-26 weeks)	*Study population*		RR 0.85 (0.58, 1.25)	288 (3 studies)	⨁⨁◯◯ Low (a,b)
	379 per 1000	322 per 1000 (220, 473)			
	Moderate				
	472 per 1000	401 per 1000 (274, 590)			

Outcomes (follow-up)	Illustrative comparative risks*		Relative effect (95% CI)	No. of participants (studies)	Certainty of the evidence (GRADE)
	Assumed risk Control	Corresponding risk Intervention			
Intermediate follow-up (17-24 weeks post-intervention) – ITT analysis EPDS≥12 (mean 25 weeks)	*Study population*		RR 1.27 (0.73, 2.21)	121 (1 study)	●●○○ Low (a,b)
	262 per 1000	333 per 1000 (191, 580)			
	Moderate				
	262 per 1000	333 per 1000 (191, 579)			
Intermediate follow-up (17-24 weeks post-intervention) – available case analysis EPDS ≥12 (mean 25 weeks)	*Study population*		RR 1.63 (0.49, 5.41)	96 (1 study)	●●○○ Low (a,b)
	80 per 1000	130 per 1000 (39, 433)			
	Moderate				
	80 per 1000	130 per 1000 (39, 433)			
Depression mean scores					
Post-treatment – available case EPDS, BDI, BDI-II or CES-D (5-28 weeks)	SMD 0.02 (-0.38, 0.41)		-	566 (6 studies)	●●○○ Low (c)
Intermediate follow-up (17-24 weeks post-intervention) – available case analysis EPDS (mean 39 weeks)	SMD -0.11 (-0.53, 0.31)		-	88 (1 study)	●●○○ Low (b,d)
Long Follow-up (25-103 weeks post-intervention) – available case analysis EPDS or BDI (57-78 weeks)	SMD 0.08 (-0.23, 0.39)		-	161 (2 studies)	●●○○ Low (d)
Very long Follow-up (≥104 weeks post-intervention) – available case analysis EPDS (mean 260 weeks)	SMD -0.17 (-0.66, 0.32)		-	65 (1 study)	●●○○ Low (b,d)
Anxiety symptomatology					
Post-treatment – ITT analysis STAI-S >40 (mean 7 weeks)	*Study population*		RR 0.94 (0.47, 1.89)	121 (1 study)	●●○○ Low (a,b)
	213 per 1000	200 per 1000 (100, 403)			
	Moderate				
	213 per 1000	200 per 1000 (100, 403)			
Post-treatment – available case analysis STAI-S >40 (mean 7 weeks)	*Study population*		RR 0.21 (0.01, 4.23)	98 (1 study)	●●○○ Low (a,b)
	40 per 1000	8 per 1000 (0, 169)			
	Moderate				
	40 per 1000	8 per 1000 (0, 169)			
Anxiety mean scores					
Post-treatment – available case analysis STAI-S (mean 7 weeks)	SMD -0.16 (-0.55, 0.24)		-	98 (1 study)	●●○○ Low (b,d)
Intermediate follow-up (17-24 weeks post-intervention) – available case analysis STAI-S (mean 25 weeks)	SMD -0.3 (-0.7, 0.11)		-	96 (1 study)	●●○○ Low (b,d)
PTSD symptomatology					
Post-treatment – ITT analysis PPQ: Scores in clinical range (no further detail) (mean 7 weeks)	*Study population*		RR 1.18 (0.71, 1.94)	121 (1 study)	●●○○ Low (a,b)
	311 per 1000	368 per 1000 (221, 604)			
	Moderate				
	312 per 1000	368 per 1000 (222, 605)			
Post-treatment – available case analysis PPQ: Scores in clinical range (no further detail) (mean 7 weeks)	*Study population*		RR 1.3 (0.56, 3.02)	98 (1 study)	●●○○ Low (a,b)
	160 per 1000	208 per 1000 (90, 483)			
	Moderate				
	160 per 1000	208 per 1000 (90, 483)			

Outcomes (follow-up)	Illustrative comparative risks*		Relative effect (95% CI)	No. of participants (studies)	Certainty of the evidence (GRADE)
	Assumed risk Control	Corresponding risk Intervention			
Intermediate follow-up (17-24 weeks post-intervention) – ITT analysis PPQ: Scores in clinical range (no further detail) (mean 25 weeks)	*Study population*		RR 1.02 (0.63, 1.63)	121 (1 study)	●●○○ Low (a,b)
	361 per 1000	368 per 1000 (227, 588)			
	Moderate				
	361 per 1000	368 per 1000 (227, 588)			
Intermediate follow-up (17-24 weeks post-intervention) – available case analysis PPQ: Scores in clinical range (no further detail) (mean 25 weeks)	*Study population*		RR 0.79 (0.35, 1.79)	96 (1 study)	●●○○ Low (a,b)
	220 per 1000	174 per 1000 (77, 394)			
	Moderate				
	220 per 1000	174 per 1000 (77, 394)			
PTSD mean scores					
Post-treatment – available case analysis PPQ (mean 7 weeks)	SMD -0.1 (-0.5, 0.29)		-	98 (1 study)	●●○○ Low (b,d)
Intermediate follow-up (17-24 weeks post-intervention) – available case analysis PPQ (mean 25 weeks)	SMD -0.25 (-0.66, 0.15)		-	96 (1 study)	●●○○ Low (b,d)
Mother-infant attachment problems					
Post-treatment – ITT analysis Maternal report: Mother-infant relationship problems or Parent-Infant Relationship Global Assessment Scale (PIRGAS): Treatment nonresponse (no improvement-reliable change index) (20-26 weeks)	*Study population*		**RR 0.55 (0.42, 0.72)**	175 (2 studies)	●○○○ Very low (a,f)
	793 per 1000	436 per 1000 (333, 571)			
	Moderate				
	789 per 1000	434 per 1000 (331, 568)			
Post-treatment – available case analysis Maternal report: Mother-infant relationship problems or PIR-GAS: Treatment non-response (no improvement-reliable change index) (20-26 weeks)	*Study population*		**RR 0.55 (0.41, 0.74)**	151 (2 studies)	●○○○ Very low (a,f)
	736 per 1000	405 per 1000 (302, 545)			
	Moderate				
	736 per 1000	405 per 1000 (302, 545)			
Long follow-up (25-103 weeks post-intervention) – ITT analysis Maternal report: Mother-infant relationship problems (mean 78 weeks)	*Study population*		RR 1.16 (0.79, 1.71)	95 (1 study)	●●○○ Low (a,b)
	481 per 1000	558 per 1000 (380, 822)			
	Moderate				
	481 per 1000	558 per 1000 (380, 823)			
Long follow-up (25-103 weeks post-intervention) – available case Maternal report: Mother-infant relationship problems (mean 78 weeks)	*Study population*		RR 1.26 (0.81, 1.95)	88 (1 study)	●●○○ Low (a,b)
	426 per 1000	536 per 1000 (345, 830)			
	Moderate				
	426 per 1000	537 per 1000 (345, 831)			
	371 per 1000	316 per 1000 (171, 591)			
	Moderate				
	371 per 1000	315 per 1000 (171, 590)			
Mother-infant positive interaction mean scores					
Post-treatment – available case analysis Dyadic Mutuality Code, PIR-GAS, Behavioural observation: Positive mother-infant interaction or Global Rating Scales of Mother-infant Interaction: Overall mother-infant interaction (5-26 weeks)	SMD 0.15 (-0.26, 0.56)		-	378 (4 studies)	●○○○ Very low (b,d,g)
Intermediate follow-up (17-24 weeks post-intervention) – available case analysis Global Rating Scales of Mother-infant Interaction: Overall mother-infant interaction (mean 25 weeks)	SMD 0 (-0.4, 0.4)		-	96 (1 study)	●●○○ Low (d)
Very long follow-up (>104 weeks post-intervention) – available case analysis Behavioural observation: Positive mother-infant interaction (mean 271 weeks)	**SMD -1.82 (-2.44, -1.2)**		-	58 (1 study)	●●○○ Low (d)

Outcomes (follow-up)	Illustrative comparative risks*		Relative effect (95% CI)	No. of participants (studies)	Certainty of the evidence (GRADE)
	Assumed risk Control	Corresponding risk Intervention			
Maternal sensitivity treatment response					
Post-treatment – ITT analysis Emotional Availability Scales (EAS): Maternal sensitivity: Treatment response (improvement-reliable change index) (mean 26 weeks)	*Study population*		RR 1.67 (0.43, 6.51)	80 (1 study)	●○○○ Very low (a,b,e,h)
	75 per 1000	125 per 1000 (32, 488)			
	Moderate				
	75 per 1000	125 per 1000 (32, 488)			
Post-treatment – available case analysis EAS: Maternal sensitivity: Treatment response (improvement-reliable change index) (mean 26 weeks)	*Study population*		RR 1.62 (0.42, 6.31)	75 (1 study)	●○○○ Very low (a,b,e,h)
	81 per 1000	131 per 1000 (34, 512)			
	Moderate				
	81 per 1000	131 per 1000 (34, 511)			
Maternal sensitivity mean scores					
Post-treatment – available case analysis EAS: Maternal sensitivity or Behavioural observation: Maternal sensitivity or Global Rating Scales of Mother-infant Interaction: Maternal sensitive behaviour (5-28 weeks)	SMD 0.23 (-0.08, 0.53)		-	332 (4 studies)	●○○○ Very low (b,d,i)
Intermediate follow-up (17-24 weeks post-intervention) – available case analysis Global Rating Scales of Mother-infant Interaction: Maternal sensitive behavior (mean 25 weeks)	SMD 0.15 (-0.25, 0.55)		-	96 (1 study)	●●○○ Low (b,d)
Long follow-up (25-103 weeks post-intervention)- Available case analysis EAS: Maternal sensitivity (mean 57 weeks)	**SMD 0.81 (0.33, 1.3)**		-	71 (1 study)	●●○○ Low (d)

Evidence Statements:

Individual mother-infant relationship interventions

Mother-infant relationship interventions (individual) may improve mother-infant attachment problems (very low certainty evidence) at endpoint or first measurement compared with treatment as usual in women with a diagnosis of MDD or symptoms of depression.

Mother-infant relationship interventions (individual) appear to have no effect on (or may be harmful to) mother-infant attachment problems at long follow-up (25-103 weeks post-intervention) (low certainty evidence) compared with treatment as usual in women with a diagnosis of MDD.

Mother-infant relationship interventions (individual) appear to have no effect on mother-infant positive interaction mean scores at intermediate follow-up (17-24 weeks post-intervention) (low certainty evidence) compared with enhanced treatment as usual (a booklet about infant care) in women with symptoms of depression.

Mother-infant relationship interventions (individual) appear to be harmful to mother-infant positive interaction mean scores at very long follow-up (>104 weeks post-intervention) (low certainty evidence) compared with enhanced treatment as usual (telephone support) in women with a diagnosis of a major depressive episode or dysthymia.

Mother-infant relationship interventions (individual mother-infant psychotherapy) appear to have no effect on maternal sensitivity treatment response at endpoint or first measurement (very low certainty evidence) compared with treatment as usual in women with symptoms of depression.

Mother-infant relationship interventions (individual) may have an effect[9] on depression diagnosis at endpoint or first measurement (low certainty evidence), but appear to have no effect on depression diagnosis at intermediate follow-up (17-24 weeks post-intervention) (low certainty evidence), at long follow-up (25-103 weeks post-intervention) (low certainty evidence), or at very long follow up (>103 weeks post-intervention) (low certainty evidence) compared with treatment as usual in women with a diagnosis of MDD.

Mother-infant relationship interventions (individual) appear to have no effect on depression mean scores (low certainty evidence) at intermediate (17-24 weeks post-intervention), long (25-103 weeks post-intervention), or very long (>103 weeks post-treatment) follow-up compared with treatment as usual or enhanced treatment as usual in women with a diagnosis of depression.

Mother-infant relationship interventions (individual) appear to have no effect on depression symptomatology (low certainty evidence) at intermediate follow-up (17-24 weeks post-intervention) than enhanced treatment as usual (a booklet about infant care) in women with symptoms of depression.

[9] RR 0.72 (95% CI 0.48, 1.07); P=0.10

Outcomes (follow-up)	Illustrative comparative risks*		Relative effect (95% CI)	No. of participants (studies)	Certainty of the evidence (GRADE)
	Assumed risk Control	Corresponding risk Intervention			
Mother-infant relationship interventions (individual) appear to have no effect on anxiety symptomatology at endpoint or first measurement (low certainty evidence), and appear to have no effect on anxiety mean scores at endpoint or first measurement (low certainty evidence) or at intermediate follow-up (17-24 weeks post-intervention) (low certainty evidence), compared with enhanced treatment as usual (a booklet about infant care) in women with symptoms of depression. *Mother-infant relationship interventions (individual) appear to have no effect on PTSD symptomatology (low certainty evidence) or on PTSD mean symptoms (low certainty evidence) at endpoint or first measurement, or at intermediate follow-up (17-24 weeks post-intervention), compared with enhanced treatment as usual (a booklet about infant care) in women with symptoms of depression.* ***Individual or group mother-infant relationship interventions*** *Mother-infant relationship interventions (individual or group) appear to have no effect on mother-infant positive interaction mean scores at endpoint or first measurement (very low certainty evidence) compared with treatment as usual or enhanced treatment as usual in women with a diagnosis of MDD or symptoms (or subthreshold symptoms) of depression.* *Mother-infant relationship interventions (individual or group) appear to have no effect on maternal sensitivity mean scores at endpoint or first measurement (very low certainty evidence) compared with treatment as usual or enhanced treatment as usual in women with symptoms (or subthreshold symptoms) of depression or a diagnosis of a major depressive episode or dysthymia, but may improve maternal sensitivity mean scores at long follow-up (low certainty evidence).* *Mother-infant relationship interventions (individual or group) appear to have no effect on depression symptomatology (low certainty evidence) or on depression mean scores (low certainty evidence) at endpoint or first measurement compared with treatment as usual or enhanced treatment as usual in women with a diagnosis of depression or symptoms (or subthreshold symptoms) of depression.*					

Footnotes:

* The 'assumed risk' for the *study population* is calculated using the mean baseline risk from the studies in the meta-analysis (i.e. total number of events in the control/comparison group divided by the total number of patients in the control/comparison group). The *moderate* risk scenario is calculated using the median control/comparison group risk from the studies in the meta-analysis. The 'corresponding risk' (and its 95% CI) is based on the assumed risk in the control/comparison group and the relative effect of the intervention (and its 95% CI).

a. Total number of events is less than 300 (a threshold rule-of-thumb).
b. 95% CI crosses both line of no effect and measure of appreciable benefit or harm (SMD -0.5/0.5 or RR 0.75/1.25).
c. There was evidence of considerable heterogeneity between effect sizes.
d. Total population size is less than 400 (a threshold rule-of-thumb).
e. Risk of bias due to statistically significant group differences at baseline.
f. Risk of bias due to statistically significant group differences at baseline and non-blind outcome assessment.
g. There is evidence of substantial heterogeneity of study effect sizes.
h. Paper omits data.
i. There is evidence of moderate heterogeneity of study effect sizes.

Source: NICE 2015, Table 145, Table 165, Table 173, Table 193

Abbreviations: AQS, Attachment Q Set; ASQ:SE, Ages and Stages Questionnaire: Social-Emotional; BDI, Beck Depression Inventory; CBCL, Child Behaviour Checklist; CES-D, Center for Epidemiologic Studies Depression Scale; CI, confidence interval; EAS, Emotional Availability Scales; EPDS, Edinburgh Postnatal Depression Scale; ITT, intention-to-treat; MDD, major depressive disorder; PIRGAS, Parent-Infant Relationship Global Assessment Scale; PPQ, Perinatal PTSD Questionnaire; PTSD, post-traumatic stress disorder; RR, relative risk; SCID, Structured Clinical Interview for DSM Disorders; SMD, standardised mean difference; STAI-S, State-Trait Anxiety Inventory-State; TAU, treatment as usual.

Note: Statistically significant differences are shown in bold.

C3.1.10.2 Mother-infant relationship intervention with video feedback versus mother-infant relationship intervention with verbal feedback

A single study (N=51) found no advantage of video feedback compared with verbal feedback for effects of mother-infant relationship interventions on mean depression symptoms (**Table C3-15**). There was no clinically or statistically significant difference between study arms on attrition.

The study outcomes relating to mother-infant interactions (maternal confidence/competence mean scores; maternal perceptions of infant behavior mean scores) are not captured in **Table C3-15** as they are not considered to be key outcomes for the current Review.

Table C3-15 Summary of findings (treatment) – mother-infant relationship intervention with video feedback versus mother-infant relationship intervention with verbal feedback

Outcomes (follow-up)	Illustrative comparative risks*		Relative effect (95% CI)	No. of participants (studies)	Certainty of the evidence (GRADE)
	Assumed risk Control	Corresponding risk Intervention			
Depression mean scores					
Post-treatment – available case analysis EPDS (mean 3 weeks)	SMD 0.29 (-0.36, 0.94)		-	37 (1 study)	●●○○ Low (a,b)
Evidence Statement: *Mother-infant relationship intervention (individual) with video feedback appears to have no effect on depression mean scores at endpoint or first measurement (low certainty evidence) compared with a mother-infant relationship intervention (individual) with verbal feedback in women with a diagnosis of MDD.*					
Footnotes: * The 'assumed risk' for the *study population* is calculated using the mean baseline risk from the studies in the meta-analysis (i.e. total number of events in the control/comparison group divided by the total number of patients in the control/comparison group). The *moderate* risk scenario is calculated using the median control/comparison group risk from the studies in the meta-analysis. The 'corresponding risk' (and its 95% CI) is based on the assumed risk in the control/comparison group and the relative effect of the intervention (and its 95% CI). a. Total population size is less than 400 (a threshold rule-of-thumb) b. 95% CI crosses both line of no effect and measure of appreciable benefit or harm (SMD -0.5/0.5 or RR 0.75/1.25)					

Source: NICE 2015, Table 146

Abbreviations: CI, confidence interval; EPDS, Edinburgh Postnatal Depression Scale; MDD, major depressive disorder; RR, relative risk; SMD, standardised mean difference.

C3.1.10.3 Mother-infant relationship intervention (and facilitated self-help for eating disorders) versus listening visits (and facilitated self-help for eating disorders

There was very low quality single-study evidence (N=80) for moderate-to-large benefits of a mother-infant relationship intervention relative to listening visits for women with eating disorders for reducing mealtime conflict, maternal inappropriate verbal responses, and infant autonomy, but not for maternal intrusions. However, none of these outcomes are considered to be key outcomes for the current Review.

There was higher dropout observed in the mother-infant relationship intervention group; however, this effect was not statistically significant due to very serious imprecision.

Table C3-16 Summary of findings (treatment) – mother-infant relationship intervention (and facilitated self-help for eating disorders) versus listening visits (and facilitated self-help for eating disorders)

Evidence Statement: *There is no RCT evidence for any pre-defined important outcomes for mother-infant relationship interventions relative to listening visits for women with eating disorders.*

C3.1.11 Co-parenting interventions

Only one SR (NICE 2015) was identified for co-parenting interventions in the literature search. NICE 2015 identified one RCT from Canada (N=29; Misri 2000), which compared a face-to-face co-parenting intervention with enhanced treatment as usual (monitoring) in postpartum women with a diagnosis of MDD.

C3.1.11.1 Co-parenting intervention versus enhanced treatment as usual

There was single-study evidence for a moderate effect of a co-parenting intervention on depression diagnosis; however, confidence in this effect estimate was very low due to very serious imprecision (**Table C3-17**). In addition, the same study showed no evidence for statistically or clinically significant benefits of a co-parenting intervention on mean depression symptoms. There were no drop-outs in either arm.

Table C3-17 Summary of findings (treatment) – co-parenting intervention versus enhanced treatment as usual

Outcomes (follow-up)	Illustrative comparative risks*		Relative effect (95% CI)	No. of participants (studies)	Certainty of the evidence (GRADE)
	Assumed risk Control	Corresponding risk Intervention			
Depression diagnosis					
Post-treatment – ITT analysis MINI (mean 6 weeks)	*Study population*		RR 0.51 (0.22, 1.18)	29 (1 study)	●○○○ Very low (a,b,c)
	615 per 1000	314 per 1000 (135, 726)			
	Moderate				
	615 per 1000	314 per 1000 (135, 726)			
Post-treatment – available case analysis MINI (mean 6 weeks)	*Study population*		RR 0.51 (0.22, 1.18)	29 (1 study)	●○○○ Very low (a,b,c)
	615 per 1000	314 per 1000 (-37, 665)			
	Moderate				
	615 per 1000	314 per 1000 (-37, 664)			
Depression mean scores					
Post-treatment – available case analysis EPDS (mean 6 weeks)	SMD -0.47 (-1.22, 0.29)		-	28 (1 study)	●○○○ Very low (a,c,d)
Evidence Statement: *Co-parenting interventions appear to have no effect on depression diagnosis (very low certainty evidence) or depression mean scores (very low certainty evidence) at endpoint or first measurement compared with enhanced treatment as usual (monitoring) in postpartum women with a diagnosis of MDD.*					

Footnotes:

* The 'assumed risk' for the *study population* is calculated using the mean baseline risk from the studies in the meta-analysis (i.e. total number of events in the control/comparison group divided by the total number of patients in the control/comparison group). The *moderate* risk scenario is calculated using the median control/comparison group risk from the studies in the meta-analysis. The 'corresponding risk' (and its 95% CI) is based on the assumed risk in the control/comparison group and the relative effect of the intervention (and its 95% CI).

a. Risk of bias as blinding of outcome assessment was unclear.

b. Total number of events is less than 300 (a threshold rule-of-thumb).

c. 95% CI crosses both line of no effect and measure of appreciable benefit or harm (SMD -0.5/0.5 or RR 0.75/1.25).

d. Total population size is less than 400 (a threshold rule-of-thumb).

Source: NICE 2015, Table 147

Abbreviations: CI, confidence interval; EPDS, Edinburgh Postnatal Depression Scale; ITT, intention-to-treat; MDD, major depressive disorder; MINI, Mini International Neuropsychiatric Interview; RR, relative risk; SMD, standardised mean difference.

C3.1.12 Mindfulness

Of the four SRs identified in the literature search, NICE 2015 was chosen as the foundation review due to its high quality and comprehensiveness. NICE 2015 included two RCTs from the United States that compared antenatal, face-to-face, group mindfulness training with enhanced treatment as usual[10] or waitlist. The intervention in one RCT (N=47) was aimed at women with elevated levels of perceived stress or pregnancy-specific anxiety, and the other RCT (N=34) was aimed at women with mood concerns (31% of all participants exceeded a score of 16 on the CES-D, and the mean baseline CES-D score in the intervention group was 20.4, which is above the clinical cut-off of 16).

C3.1.12.1 Mindfulness training versus treatment as usual or enhanced treatment as usual

There was no evidence for statistically or clinically significant benefits associated with mindfulness training on mean depression symptoms or negative affect mean scores, or on mean anxiety symptoms (**Table C3-18**).

There was evidence for a moderate effect of mindfulness training relative to enhanced treatment as usual on attrition, with higher drop-out in the mindfulness training group; however, this effect was not statistically significant due to very serious imprecision.

Table C3-18 Summary of findings (treatment) – mindfulness training versus treatment as usual or enhanced treatment as usual

Outcomes (follow-up)	Illustrative comparative risks*		Relative effect (95% CI)	No. of participants (studies)	Certainty of the evidence (GRADE)
	Assumed risk Control	Corresponding risk Intervention			
Depression mean scores					
Post-treatment – available case analysis CES-D (mean 10 weeks)	SMD -0.13 (-0.85, 0.58)		-	31 (1 study)	●○○○ Very low (a,b,c)
Anxiety mean scores					
Post-treatment – ITT analysis STAI-S (mean 6 weeks)	SMD 0.23 (-0.35, 0.8)		-	47 (1 study)	●●○○ Low (a,b)
Post-treatment – available case analysis STAI-S (mean 10 weeks)	SMD -0.02 (-0.74, 0.69)		-	31 (1 study)	●○○○ Very low (a,b,c)
Evidence Statement: *Group mindfulness training appears to have no effect on depression mean scores at endpoint or first measurement (very low certainty evidence) compared with waitlist in pregnant women with mood concerns.* *Group mindfulness training appears to have no effect on anxiety mean scores at endpoint or first measurement (low certainty evidence) compared with enhanced treatment as usual (non-mental health-focused education and support booklet) in pregnant women with elevated levels of perceived stress or pregnancy-specific anxiety.*					

[10] Enhanced treatment as usual involved non-mental health-focused education and support (book).

Outcomes (follow-up)	Illustrative comparative risks*		Relative effect (95% CI)	No. of participants (studies)	Certainty of the evidence (GRADE)
	Assumed risk Control	Corresponding risk Intervention			
Footnotes: * The 'assumed risk' for the *study population* is calculated using the mean baseline risk from the studies in the meta-analysis (i.e. total number of events in the control/comparison group divided by the total number of patients in the control/comparison group). The *moderate* risk scenario is calculated using the median control/comparison group risk from the studies in the meta-analysis. The 'corresponding risk' (and its 95% CI) is based on the assumed risk in the control/comparison group and the relative effect of the intervention (and its 95% CI). a. Total population size is less than 400 (a threshold rule-of-thumb) b. 95% CI crosses both line of no effect and measure of appreciable benefit or harm (SMD -0.5/0.5 or RR 0.75/1.25) c. Paper omits data					

Source: NICE 2015, Table 151, Table 168

Abbreviations: CES-D, Center for Epidemiologic Studies Depression Scale; CI, confidence interval; ITT, intention-to-treat; RR, relative risk; SMD, standardised mean difference; STAI-S, State-Trait Anxiety Inventory-State.

C3.2 TREATMENT WITH PSYCHOLOGICAL INTERVENTIONS

C3.2.1 Structured psychological interventions (CBT or IPT)

Of the 10 SRs identified for structured psychological interventions in the literature search, NICE 2015 was chosen as the foundation review due to its currency, high quality and comprehensiveness. While the NICE 2015 SR separated structured psychological interventions (CBT or IPT) from psychologically (CBT/IPT) informed psychoeducation (which is covered in **Section C3.1.1**), several of the other identified SRs combined these interventions.

NICE 2015 included 14 RCTs (N=2,099) that compared face-to-face structured psychological interventions (CBT or IPT) with treatment as usual or enhanced treatment as usual in women with a diagnosis of depression (MDD, major depressive episode, minor depression, depressive disorder) or symptoms of depression. The intervention was IPT in four RCTs and CBT in the remaining 10 RCTs. Four of the included RCTs were from Australia (three CBT studies and one IPT study). Across the 14 RCTs, the timing and format of the intervention varied considerably. In nine RCTs (including the four Australian studies) the intervention was postnatal, two RCTs assessed antenatal interventions, and in three RCTs the intervention was both antenatal and postnatal. The format was individual in 12 RCTs, group in one RCT, and both individual and group in one RCT.

The comparator also varied across the 14 included RCTs. One RCT compared CBT plus home visits with home visits only, one RCT compared IPT with waitlist, six RCTs compared CBT or IPT with treatment as usual, and six RCTs compared CBT or IPT with enhanced treatment as usual[11].

NICE 2015 also included four RCTs that compared CBT or IPT with active interventions. One RCT from the United States (N=34[12]) compared face-to-face individual CBT with listening visits in pregnant women with a diagnosis of MDD. One RCT from the United Kingdom (N=3,449) compared face-to-face individual CBT with listening visits in postpartum women with symptoms of depression. One RCT from Brazil (N=60) compared face-to-face individual CBT with relational constructivist

[11] Enhanced treatment as usual varied across the six RCTs: single session psychoeducation; GP training; single session post-delivery discussion; non-specific emotional support and mothercraft advice; and psychoeducation booklet, monitoring and improved access to support.

[12] In Hayden 2012 the number of randomised women is unclear but there were 34 participants in the completer analysis.

therapy in postpartum women with symptoms of depression. One RCT from the United States (N=48) compared face-to-face group IPT with a support group in pregnant women with a diagnosis of MDD or dysthymia.

Although NICE 2015 included only two RCTs of group CBT (one of which also had an individual component), one of the identified SRs (Scope 2013) specifically assessed the effectiveness of group CBT on PND. Scope 2013 used a broad definition of CBT in their review to include studies of group programs that included elements derived from cognitive behaviour principles, including psychoeducational activities. Three RCTs[13], two non-RCTs, and two observational studies met the inclusion criteria. No RCTs directly compared individual CBT with group CBT. Meta-analyses showed that group CBT appeared to be clinically effective when compared to routine primary care, usual care or a waiting list group, although the reduction in depression scores was not consistent across time. The authors note that the results should be interpreted with caution due to the limited number and quality of the studies. In addition, some of the studies included concurrent therapy, the effects of which are difficult to separate from group treatment. There was also uncertainty as to how accurately some of the described group treatments reflect CBT.

C3.2.1.1 Structured psychological interventions versus treatment as usual or enhanced treatment as usual

NICE 2015 did not separately consider CBT and IPT interventions in their analyses. Furthermore, NICE 2015 did not consider the timing of the intervention, format, setting or mode of delivery in their analyses.

Very low-to-high certainty evidence from up to ten studies showed that structured psychological interventions (CBT or IPT) were more effective than treatment as usual or enhanced treatment as usual in reducing depression diagnosis, depression symptomatology, and depression mean scores at post-treatment, with large to moderate effects observed for all outcomes and some low certainty evidence for maintained moderate-to-large effects at short-term follow-up (**Table C3-19**). At intermediate follow-up periods, there was evidence for moderate benefits associated with structured psychological interventions; however, confidence that these were true measures of effect was low to very low due to wide confidence intervals. At longer-term follow-ups (>24 weeks post-intervention), the evidence for structured psychological interventions is very inconsistent with point estimates of effect in favour of CBT or IPT for depression symptomatology, but in favour of treatment as usual or enhanced treatment as usual for depression diagnosis.

There was low quality, single-study evidence for a large effect of a structured psychological intervention on mean state anxiety symptoms (using an ITT analysis approach; however, an available case analysis approach (two studies) revealed no evidence for clinically significant benefits (although differences were statistically significant) associated with mean state anxiety symptoms, and the small benefit for trait anxiety symptoms found in a single-study analysis also failed to reach the threshold for appreciable benefit despite meeting statistical-significance criteria.

There was low-to-very low certainty evidence from up to two studies for moderate-to-large benefits of structured psychological interventions (CBT or IPT) on general mental health outcomes at endpoint, and at short-term and intermediate follow-ups. There was also evidence for a statistically significant, but not clinically significant, effect of CBT on reducing the risk of self-harm.

[13] One of the RCTs was included in NICE 2015, one was specifically excluded, and one was classified by NICE 2015 as a psychoeducational intervention.

There was high to very low certainty evidence from up to two studies for moderate-to-large benefits of structured psychological interventions (CBT or IPT) in reducing mother-infant attachment problems at endpoint and at long-term follow-up, mother-infant attachment mean scores and mother-infant play frequency. There was, however, no evidence for clinically or statistically significant benefits on mother-infant attachment mean scores at short-term follow-up.

Twelve studies (N=1,983) found no evidence for clinically or statistically significant effects of structured psychological interventions (CBT or IPT) relative to treatment as usual or enhanced treatment as usual on attrition (as a proxy measure for retention in services and treatment acceptability).

Table C3-19 Summary of findings (treatment) – structured psychological interventions (CBT or IPT) versus treatment as usual or enhanced treatment as usual

Outcomes (follow-up)	Illustrative comparative risks*		Relative effect (95% CI)	No. of participants (studies)	Certainty of the evidence (GRADE)
	Assumed risk Control	Corresponding risk Intervention			
Depression diagnosis					
Post-treatment – ITT SCID or CIS-R (12-44 weeks)	*Study population*		**RR 0.48 (0.39, 0.6)**	1307 (6 studies)	●●●● High
	652 per 1000	313 per 1000 (254, 391)			
	Moderate				
	687 per 1000	330 per 1000 (268, 412)			
Post-treatment – available case analysis SCID or CIS-R (12-44 weeks)	*Study population*		**RR 0.38 (0.24, 0.58)**	1,066 (5 studies)	●●○○ Low (a)
	602 per 1000	229 per 1000 (145, 349)			
	Moderate				
	615 per 1000	234 per 1000 (148, 357)			
Short Follow-up (9-16 weeks post-intervention) – ITT SCID (mean 28 weeks)	*Study population*		**RR 0.39 (0.19, 0.8)**	93 (1 study)	●●○○ Low (e)
	435 per 1000	170 per 1000 (83, 348)			
	Moderate				
	435 per 1000	170 per 1000 (83, 348)			
Intermediate follow-up (17-24 weeks post-intervention) – ITT CIS-R or SCID (mean 33 weeks)	*Study population*		RR 0.59 (0.24, 1.41)	138 (2 studies)	●○○○ Very low (a,e,f)
	471 per 1000	278 per 1000 (113, 665)			
	Moderate				
	572 per 1000	337 per 1000 (137, 807)			
Intermediate follow-up (17-24 weeks post-intervention) – available case analysis CIS-R or SCID (mean 33 weeks)	*Study population*		RR 0.5 (0.23, 1.08)	118 (2 studies)	●●○○ Low (e,f)
	373 per 1000	186 per 1000 (86, 403)			
	Moderate				
	474 per 1000	237 per 1000 (109, 512)			
Long Follow-up (25-103 weeks post-intervention) – ITT SCID (mean 78 weeks)	*Study population*		RR 1.68 (0.95, 2.98)	102 (1 study)	●●○○ Low (e,f)
	250 per 1000	420 per 1000 (237, 745)			
	Moderate				
	250 per 1000	420 per 1000 (237, 745)			
Long Follow-up (25-103 weeks post-intervention) – available case analysis SCID (mean 78 weeks)	*Study population*		RR 1.56 (0.73, 3.33)	89 (1 study)	●●○○ Low (e,f)
	188 per 1000	292 per 1000 (137, 624)			
	Moderate				
	188 per 1000	293 per 1000 (137, 626)			
Very long Follow-up (>104 weeks post-intervention) – ITT SCID (mean 260 weeks)	*Study population*		**RR 1.92 (1.11, 3.33)**	102 (1 study)	●●○○ Low (e)
	250 per 1000	480 per 1000 (278, 832)			
	Moderate				
	250 per 1000	480 per 1000 (278, 832)			
Very long Follow-up (>104 weeks post-intervention) – available case analysis SCID (mean 260 weeks)	*Study population*		RR 0.87 (0.37, 2.08)	70 (1 study)	●●○○ Low (e,f)
	243 per 1000	212 per 1000 (90, 506)			
	Moderate				
	243 per 1000	211 per 1000 (90, 505)			

Outcomes (follow-up)	Illustrative comparative risks*		Relative effect (95% CI)	No. of participants (studies)	Certainty of the evidence (GRADE)
	Assumed risk Control	Corresponding risk Intervention			
Depression symptomatology					
Post-treatment – ITT EPDS ≥10/EPDS ≥12/Treatment nonresponse (baseline to endpoint decrease <4 points and EPDS >13)/Treatment nonresponse (<50% improvement) or BDI ≥16 or BDI-II ≥14 (6-44 weeks)	*Study population*		**RR 0.69 (0.56, 0.85)**	969 (10 studies)	⨁⨁◯◯ Low (b,c)
	643 per 1000	444 per 1000 (360, 547)			
	Moderate				
	626 per 1000	432 per 1000 (351, 532)			
Post-treatment – available case analysis EPDS ≥10/EPDS ≥12/Treatment nonresponse (baseline to endpoint decrease <4 points and EPDS >13) or BDI ≥ 16 or BDI-II ≥ 14 (6-16 weeks)	*Study population*		**RR 0.62 (0.53, 0.73)**	702 (9 studies)	⨁⨁⨁⨁ High
	559 per 1000	347 per 1000 (296, 408)			
	Moderate				
	588 per 1000	365 per 1000 (312, 429)			
Short Follow-up (9-16 weeks post-intervention) – ITT BDI-II ⩾14 (mean 29 weeks)	*Study population*		RR 0.89 (0.54, 1.47)	55 (1 study)	⨁⨁◯◯ Low (e,f)
	560 per 1000	498 per 1000 (302, 823)			
	Moderate				
	560 per 1000	498 per 1000 (302, 823)			
Short Follow-up (9-16 weeks post-intervention) – available case analysis BDI-II ⩾14 (mean 29 weeks)	*Study population*		RR 0.57 (0.31, 1.07)	42 (1 study)	⨁⨁◯◯ Low (e)
	667 per 1000	380 per 1000 (207, 713)			
	Moderate				
	667 per 1000	380 per 1000 (207, 713)			
Long Follow-up (25-103 weeks post-intervention) – ITT EPDS ≥10 (mean 32 weeks)	*Study population*		RR 0.71 (0.2, 2.53)	37 (1 study)	⨁◯◯◯ Very low (e,f,g)
	250 per 1000	178 per 1000 (50, 632)			
	Moderate				
	250 per 1000	178 per 1000 (50, 632)			
Long Follow-up (25-103 weeks post-intervention) – available case analysis EPDS ⩾10 (mean 32 weeks)	*Study population*		RR 0.4 (0.05, 3.46)	33 (1 study)	⨁◯◯◯ Very low (e,f,g)
	167 per 1000	67 per 1000 (8, 577)			
	Moderate				
	167 per 1000	67 per 1000 (8, 578)			
Depression mean scores					
Post-treatment – ITT EPDS or BDI-II (6-44 weeks)	**SMD -1.31 (-2.36, -0.26)**		-	306 (5 studies)	⨁⨁⨁◯ Moderate (a,d)
Post-treatment – available case analysis EPDS, BDI, BDI-II or HRSD (6-16 weeks)	**SMD -0.6 (-0.8, -0.4)**		-	1,508 (10 studies)	⨁⨁⨁◯ Moderate (b)
Short Follow-up (9-16 weeks post-intervention) – ITT EPDS or BDI-II (28-29 weeks)	SMD -1.84 (-4.31, 0.64)		-	148 (2 studies)	⨁◯◯◯ Very low (a,d,f)
Short Follow-up (9-16 weeks post-intervention) – available case analysis EPDS or BDI-II (21-29 weeks)	**SMD -0.66 (-1.14, -0.18)**		-	89 (2 studies)	⨁⨁◯◯ Low (d)
Intermediate Follow-up (17-24 weeks post-intervention) – available case analysis EPDS (mean 33 weeks)	SMD -0.51 (-1.72, 0.7)		-	118 (2 studies)	⨁◯◯◯ Very low (a,d,f)
Long Follow-up (25-103 weeks post-intervention) – available case analysis EPDS or BDI (32-78 weeks)	SMD -0.28 (-0.8, 0.23)		-	142 (3 studies)	⨁⨁◯◯ Low (d,f)
Very long Follow-up (>104 weeks post-intervention) – available case analysis EPDS (mean 260 weeks)	SMD -0.17 (-0.67, 0.33)		-	62 (1 study)	⨁⨁◯◯ Low (d,f)

Outcomes (follow-up)	Illustrative comparative risks*		Relative effect (95% CI)	No. of participants (studies)	Certainty of the evidence (GRADE)
	Assumed risk Control	Corresponding risk Intervention			
Negative thoughts/mood mean scores					
Available case analysis Automatic Thought Questionnaire (mean 4 weeks)	**SMD -0.94 (-1.83, -0.04)**		-	22 (1 study)	●○○○ Very low (d,g)
Anxiety mean scores					
Post-treatment – ITT analysis Beck Anxiety Inventory (BAI) (mean 44 weeks)	**SMD -1.34 (-1.94, -0.74)**		-	53 (1 study)	●●○○ Low (d)
Post-treatment – available case analysis BAI or STAI-S (12-26 weeks)	**SMD -0.35 (-0.58, -0.13)**		-	315 (2 studies)	●●○○ Low (c,d)
Mother-infant attachment problems					
Post-treatment – ITT analysis Maternal report: Mother-infant relationship problems (mean 20 weeks)	*Study population*		**RR 0.65 (0.49, 0.87)**	102 (1 study)	●●○○ Low (e)
	827 per 1000	537 per 1000 (405, 719)			
	Moderate				
	827 per 1000	538 per 1000 (405, 719)			
Post-treatment – available case analysis Maternal report: Mother-infant relationship problems (mean 20 weeks)	*Study population*		**RR 0.63 (0.43, 0.91)**	78 (1 study)	●●○○ Low (e)
	743 per 1000	468 per 1000 (319, 676)			
	Moderate				
	743 per 1000	468 per 1000 (319, 676)			
Long follow-up (25-103 weeks post-intervention) – ITT analysis Maternal report: Mother-infant relationship problems (mean 78 weeks)	*Study population*		RR 1.29 (0.9, 1.84)	102 (1 study)	●●○○ Low (e,f)
	481 per 1000	620 per 1000 (433, 885)			
	Moderate				
	481 per 1000	620 per 1000 (433, 885)			
Long follow-up (25-103 weeks post-intervention) – available case analysis Maternal report: Mother-infant relationship problems (mean 78 weeks)	*Study population*		RR 1.23 (0.79, 1.92)	87 (1 study)	●●○○ Low (e,f)
	426 per 1000	523 per 1000 (336, 817)			
	Moderate				
	426 per 1000	524 per 1000 (337, 818)			
Mother-infant attachment mean scores					
Post-treatment – available case analysis Prenatal Attachment Inventory or Maternal Attachment Inventory (8-15 weeks)	SMD 2.28 (-1.17, 5.73)		-	76 (2 studies)	●○○○ Very low (d,f,h)
Short follow-up (9-16 weeks post-intervention) – available case analysis Maternal Attachment Inventory (mean 21 weeks)	SMD 0.32 (-0.27, 0.91)		-	45 (1 study)	●●○○ Low (d,f)

Evidence Statements:

CBT or IPT

Structured psychological interventions (individual CBT or IPT) improve depression diagnosis at endpoint or first measurement (high certainty evidence) compared with treatment as usual or enhanced treatment as usual in pregnant or postpartum women with a diagnosis of depression.

Structured psychological interventions (individual CBT or IPT) appear to have no effect on depression diagnosis at intermediate follow-up (17-24 weeks post-intervention) (low certainty evidence) compared with treatment as usual in pregnant or postpartum women with a diagnosis of MDD or depression.

Structured psychological interventions (individual or group CBT or IPT) may improve depression symptomatology at endpoint or first measurement (low certainty evidence) compared with treatment as usual or enhanced treatment as usual in pregnant or postpartum women with a diagnosis of depression or symptoms of depression.

Structured psychological interventions (individual CBT or IPT) improve depression mean scores at endpoint or first measurement (moderate certainty evidence) compared with treatment as usual or enhanced treatment as usual in pregnant and postpartum women with a diagnosis of depression or symptoms of depression.

Outcomes (follow-up)	Illustrative comparative risks*		Relative effect (95% CI)	No. of participants (studies)	Certainty of the evidence (GRADE)
	Assumed risk Control	Corresponding risk Intervention			
Structured psychological interventions (individual CBT or IPT) appear to have no effect on depression mean scores at intermediate follow-up (17-24 weeks post-intervention) (very low certainty evidence) compared with treatment as usual in pregnant or postpartum women with a diagnosis of MDD or depression. *Structured psychological interventions (individual or group CBT or IPT) appear to have no effect on depression mean scores at long follow-up (>24 weeks post-intervention) (low certainty evidence) compared with treatment as usual or enhanced treatment as usual in postpartum women with a diagnosis of MDD or depression.* *Structured psychological interventions (individual or group CBT or IPT) appear to have no effect on mother-infant attachment mean scores at endpoint or first measurement (very low certainty evidence) compared with treatment as usual in pregnant or postpartum women with a diagnosis of depression or MDD.* ***CBT*** *Structured psychological interventions (individual CBT and home visits) may improve depression diagnosis at short follow-up (9-16 weeks post-intervention) (low certainty evidence) compared with home visits alone in postpartum women with a diagnosis of MDD.* *Structured psychological interventions (individual CBT) appear to have no effect on depression symptomatology at short follow-up (9-16 weeks post-intervention) (low certainty evidence) compared with treatment as usual in pregnant or postpartum women with a diagnosis of MDD.* *Structured psychological interventions (individual CBT) appear to have no effect on depression symptomatology at long follow-up (>24 weeks post-intervention) (very low certainty evidence) compared with enhanced treatment as usual non-specific emotional support and mothercraft advice) in postpartum women with a diagnosis of MDD.* *Structured psychological interventions (individual CBT with or without home visits) appear to have no effect on depression mean scores at short follow-up (9-16 weeks post-intervention) (very low certainty evidence) compared with treatment as usual or home visits alone in pregnant or postpartum women with a diagnosis of MDD.* *Structured psychological interventions (individual CBT) may improve negative thoughts/mood mean score at endpoint or first measurement (very low certainty evidence) compared with enhanced treatment as usual (single session psychoeducation) in pregnant women with a diagnosis of depressive disorder.* ***IPT*** *Structured psychological interventions (individual IPT) may improve anxiety mean scores at endpoint or first measurement (low certainty evidence) compared with enhanced treatment as usual (psychoeducation booklet, monitoring and improved access to support) in pregnant or postpartum women with a diagnosis of depression; however, the magnitude of the benefit may not be clinically significant.* *Structured psychological interventions (individual and group IPT) appear to have no effect on mother-infant attachment mean scores at short follow-up (9-16 weeks post-intervention) (low certainty evidence) compared with treatment as usual in postpartum women with a diagnosis of MDD.* ***IPT – psychodynamic therapy*** *Structured psychological interventions (individual IPT [psychodynamic therapy]) appear to be less effective at improving depression diagnosis at long follow-up (>24 weeks post-intervention) (low certainty evidence) and at very long follow-up (>104 weeks post-intervention) (low certainty evidence) than treatment as usual in postpartum women with a diagnosis of MDD.* *Structured psychological interventions (individual IPT [psychodynamic therapy]) appear to have no effect on depression mean scores at very long follow-up (>104 weeks post-intervention) (low certainty evidence) compared with treatment as usual in postpartum women with a diagnosis of MDD.* *Structured psychological interventions (individual IPT [psychodynamic therapy]) may improve mother-infant attachment problems at endpoint or first measurement (low certainty evidence) compared with treatment as usual in postpartum women with a diagnosis of MDD.* *Structured psychological interventions (individual IPT [psychodynamic therapy]) appear to have no effect on (and may be harmful to) mother-infant attachment problems at long follow-up (>24 weeks) (low certainty evidence) compared with treatment as usual in postpartum women with a diagnosis of MDD.*					

Outcomes (follow-up)	Illustrative comparative risks*		Relative effect (95% CI)	No. of participants (studies)	Certainty of the evidence (GRADE)
	Assumed risk Control	Corresponding risk Intervention			
Footnotes: * The 'assumed risk' for the *study population* is calculated using the mean baseline risk from the studies in the meta-analysis (i.e. total number of events in the control/comparison group divided by the total number of patients in the control/comparison group). The *moderate* risk scenario is calculated using the median control/comparison group risk from the studies in the meta-analysis. The 'corresponding risk' (and its 95% CI) is based on the assumed risk in the control/comparison group and the relative effect of the intervention (and its 95% CI). a. There was evidence of substantial heterogeneity between effect sizes. b. There was evidence of moderate-to-substantial heterogeneity between effect sizes. c. Papers omit data. d. Total population size is less than 400 (a threshold rule-of-thumb). e. Total number of events is less than 300 (a threshold rule-of-thumb). f. 95% CI crosses both line of no effect and measure of appreciable benefit or harm (SMD -0.5/0.5 or RR 0.75/1.25). g. Risk of bias due to statistically significant group differences at baseline. h. There is evidence of considerable heterogeneity of study effect sizes. i. Risk of bias due to unclear blinding of outcome assessment.					

Source: NICE 2015, Table 129, Table 154, Table 177, Table 187

Abbreviations: CBT, cognitive behaviour therapy; BAI, Beck Anxiety Inventory; BDI, Beck Depression Inventory; BSI, Brief Symptom Inventory; CI, confidence interval; CIS-R, Computerised version of the Clinical Interview Schedule – Revised; CORE-OM, Clinical Outcomes in Routine Evaluation-Outcome Measure; ES-R, Impact of Events Scale – Revised; IPT, interpersonal psychotherapy; ITT, intention-to-treat; MDD, major depressive disorder; PTSD, post-traumatic stress disorder; RR, relative risk; SCID, Structured Clinical Interview for DSM Disorders; SF, Short Form Health Survey; SMD, standardised mean difference; STAI-S, State-Trait Anxiety Inventory-State; STAI-T, State-Trait Anxiety Inventory-Trait; WHO, World Health Organization.

Note: Statistically significant differences are shown in bold.

C3.2.1.2 CBT versus listening visits

There was no evidence for benefits associated with CBT relative to listening visits on mean depression symptoms at endpoint or first measurement (**Table C3-20**).

Table C3-20 Summary of findings (treatment) – CBT versus listening visits

Outcomes (follow-up)	Illustrative comparative risks*		Relative effect (95% CI)	No. of participants (studies)	Certainty of the evidence (GRADE)
	Assumed risk Control	Corresponding risk Intervention			
Depression mean scores					
Post-treatment – available case analysis BDI or EPDS (mean 26 weeks)	SMD -0.06 (-0.33, 0.22)		-	301 (2 studies)	●●○○ Low (a)
Evidence Statement: *Individual CBT appears to have no effect on depression means scores at endpoint or first measurement (low certainty evidence) compared with listening visits in pregnant or postpartum women with a diagnosis of MDD or symptoms of depression.*					
Footnotes: * The 'assumed risk' for the *study population* is calculated using the mean baseline risk from the studies in the meta-analysis (i.e. total number of events in the control/comparison group divided by the total number of patients in the control/comparison group). The *moderate* risk scenario is calculated using the median control/comparison group risk from the studies in the meta-analysis. The 'corresponding risk' (and its 95% CI) is based on the assumed risk in the control/comparison group and the relative effect of the intervention (and its 95% CI). a. Papers omit data					

Source: NICE 2015, Table 130

Abbreviations: BDI, Beck Depression Inventory; CI, confidence interval; EPDS, Edinburgh Postnatal Depression Scale; MDD, major depressive disorder; SMD, standardised mean difference.

C3.2.1.3 IPT versus support group

There was no evidence for clinically or statistically significant effects of IPT relative to a support group on mean depression or anxiety symptoms (**Table C3-21**).

Table C3-21 Summary of findings (treatment) – IPT versus support group

Outcomes (follow-up)	Illustrative comparative risks*		Relative effect (95% CI)	No. of participants (studies)	Certainty of the evidence (GRADE)
	Assumed risk Control	Corresponding risk Intervention			
Depression mean scores					
Post-treatment – available case analysis CES-D (mean 12 weeks)	SMD -0.49 (-1.09, 0.11)		-	44 (1 study)	●○○○ Very low (a,b,c)
Anxiety mean scores					
Post-treatment – available case STAI-S (mean 12 weeks)	SMD -0.48 (-1.09, 0.12)		-	44 (1 study)	●○○○ Very low (a,b,c)
Evidence Statement: *Group IPT appears to have no effect on depression mean scores (very low certainty evidence) or on anxiety mean scores (very low certainty evidence) at endpoint or first measurement compared with a support group in pregnant women with a diagnosis of MDD or dysthymia.*					

Footnotes:
* The 'assumed risk' for the *study population* is calculated using the mean baseline risk from the studies in the meta-analysis (i.e. total number of events in the control/comparison group divided by the total number of patients in the control/comparison group). The *moderate* risk scenario is calculated using the median control/comparison group risk from the studies in the meta-analysis. The 'corresponding risk' (and its 95% CI) is based on the assumed risk in the control/comparison group and the relative effect of the intervention (and its 95% CI).
a. Risk of bias due to statistically significant group differences at baseline.
b. Total population size is less than 400 (a threshold rule-of-thumb).
c. 95% CI crosses both line of no effect and measure of appreciable benefit or harm (SMD -0.5/0.5 or RR 0.75/1.25).

Source: NICE 2015, Table 132, Table 156

Abbreviations: CES-D, Center for Epidemiologic Studies Depression Scale; CI, confidence interval; MDD, major depressive disorder; SMD, standardised mean difference; STAI-S, State-Trait Anxiety Inventory-State.

C3.2.2 Directive counselling

Only one SR (NICE 2015) was identified for directive counselling in the literature search. NICE 2015 included one Australian RCT that compared face-to-face directive counselling (individual and group) with treatment as usual in postpartum women with a diagnosis of minor depression or MDD.

C3.2.2.1 Directive counselling versus treatment as usual

There was low quality, single-study evidence that directive counselling was more effective than treatment as usual for depression symptomatology with moderate effects observed on dichotomous measures at endpoint and a large effect observed on a continuous measure at long-term follow-up; however, the effects on mean depression symptoms at endpoint were not statistically or clinically significant.

There was low quality single-study evidence for moderate effects of directive counselling on mean anxiety symptoms using an available case analysis approach.

There was no evidence for clinically or statistically significant effects of directive counselling relative to treatment as usual on attrition (as a proxy measure for retention in services and treatment acceptability).

Table C3-22 Summary of findings (treatment) – directive counselling versus treatment as usual

Outcomes (follow-up)	Illustrative comparative risks*		Relative effect (95% CI)	No. of participants (studies)	Certainty of the evidence (GRADE)
	Assumed risk Control	Corresponding risk Intervention			
Depression symptomatology					
Post-treatment – ITT analysis BDI≥16 (mean 12 weeks)	*Study population*		**RR 0.72 (0.59, 0.88)**	146 (1 study)	⨁⨁◯◯ Low (a)
	848 per 1000	611 per 1000 (501, 747)			
	Moderate				
	849 per 1000	611 per 1000 (501, 747)			
Post-treatment – available case analysis BDI≥16 (mean 12 weeks)	*Study population*		**RR 0.54 (0.36, 0.81)**	90 (1 study)	⨁⨁◯◯ Low (a)
	722 per 1000	390 per 1000 (260, 585)			
	Moderate				
	722 per 1000	390 per 1000 (260, 585)			
Depression mean scores					
Post-treatment – available case analysis BDI (mean 12 weeks)	SMD -0.42 (-0.95, 0.1)		-	90 (1 study)	⨁⨁◯◯ Low (b,c)
Long Follow-up (25-103 weeks post-intervention) – available case analysis BDI (mean 52 weeks)	**SMD -1.46 (-2.29, -0.63)**		-	45 (1 study)	⨁⨁◯◯ Low (b)
Anxiety mean scores					
Post-treatment – available case analysis BAI (mean 12 weeks)	**SMD -0.56 (-1.09, -0.04)**		-	90 (1 study)	⨁⨁◯◯ Low (b)

Evidence Statements:

Directive counselling may improve depression symptomatology (low certainty evidence) at endpoint or first measurement compared with treatment as usual in postpartum women with a diagnosis of minor depression or MDD.

Directive counselling appears to have no effect on depression mean scores at endpoint or first measurement (low certainty evidence) but may improve depression mean scores at long follow-up (25-103 weeks post-intervention) (low certainty evidence) compared with treatment as usual in postpartum women with a diagnosis of minor depression or MDD.

Directive counselling may improve anxiety mean scores at endpoint or first measurement (low certainty evidence) compared with treatment as usual in postpartum women with a diagnosis of minor depression or MDD.

Footnotes:

* The 'assumed risk' for the *study population* is calculated using the mean baseline risk from the studies in the meta-analysis (i.e. total number of events in the control/comparison group divided by the total number of patients in the control/comparison group). The *moderate* risk scenario is calculated using the median control/comparison group risk from the studies in the meta-analysis. The 'corresponding risk' (and its 95% CI) is based on the assumed risk in the control/comparison group and the relative effect of the intervention (and its 95% CI).

a. Total number of events is less than 300 (a threshold rule-of-thumb).

b. Total population size is less than 400 (a threshold rule-of-thumb).

c. 95% CI crosses both line of no effect and measure of appreciable benefit or harm (SMD -0.5/0.5 or RR 0.75/1.25).

Source: NICE 2015, Table 137, Table 160

Abbreviations: BAI, Beck Anxiety Inventory; BDI, Beck Depression Inventory; CI, confidence interval; ITT, intention-to-treat; MDD, major depressive disorder; RR, relative risk; SMD, standardised mean difference.

Note: Statistically significant differences are shown in bold.

C3.2.3 Non-directive counselling

Of the three SRs of non-directive counseling identified in the literature search, NICE 2015 was chosen as the foundation review due to its high quality and comprehensiveness. NICE 2015 included five RCTs that compared face-to-face non-directive counselling (listening visits) in the home with treatment as usual in postpartum women with symptoms (or subthreshold symptoms) of depression or a diagnosis of depression or MDD.

One additional RCT from the United States (N=66) published after the NICE 2015 literature search assessed listening visits provided by point-of-care providers (e.g. home visitor or physician's assistant) and delivered to low-income, ethnic minority, depressed pregnant women or mothers of young children. Listening visits provided clinically and statistically significant benefits on depression mean scores compared with waitlist controls (women receiving standard social/health services).

C3.2.3.1 Listening visits/non-directive counselling versus treatment as usual

There was no evidence for statistically significant benefits of listening visits on depression diagnosis at endpoint, using an ITT approach (**Table C3-23**). At follow-up, there was some evidence that listening visits may be less effective than treatment as usual, with point estimates suggestive of clinically significant harms on depression diagnosis at long and very long follow-up. There was no statistically or clinically significant effect of listening visits on depression symptomatology at endpoint or at follow-up and no clinically significant effect of listening visits on depression mean scores at endpoint or at follow-up.

There was low quality single-study evidence for statistically significant effects of listening visits on mean state anxiety symptoms; however, the effect was small and failed to reach a threshold indicative of clinically significant treatment benefits. In addition, the confidence in the effect estimate was low due to small sample size and selective outcome reporting.

There was low quality, single-study evidence for moderate benefits of listening visits on reducing mother-infant attachment problems and behavior management problems. However, the effect on behavior management problems was not statistically significant and effects on mother-infant attachment problems were not maintained at long-term follow-up.

Three studies (N=1,211) found no evidence for clinically or statistically significant effects of listening visits relative to treatment as usual on attrition (as a proxy measure for retention in services and treatment acceptability).

Table C3-23 Summary of findings (treatment) – listening visits/non-directive counselling versus treatment as usual

Outcomes (follow-up)	Illustrative comparative risks*		Relative effect (95% CI)	No. of participants (studies)	Certainty of the evidence (GRADE)
	Assumed risk Control	Corresponding risk Intervention			
Depression diagnosis					
Post-treatment – ITT analysis SCID (mean 20 weeks)	*Study population*		RR 0.74 (0.51, 1.08)	100 (1 study)	●●○○ Low (a,b)
	615 per 1000	455 per 1000 (314, 665)			
	Moderate				
	615 per 1000	455 per 1000 (314, 664)			
Post-treatment – available case analysis SCID or Goldberg's standardised psychiatric interview: Research diagnostic criteria or psychiatric interview using Montgomery–Åsberg Depression Rating Scale (MADRS) (7-20 weeks)	*Study population*		**RR 0.54 (0.31, 0.93)**	179 (3 studies)	●○○○ Very low (a,c,d)
	633 per 1000	317 per 1000 (82, 551)			
	Moderate				
	625 per 1000	312 per 1000 (81, 544)			
Intermediate follow-up (17-24 weeks post-intervention) – ITT analysis SCID (mean 20 weeks)	*Study population*		RR 0.97 (0.57, 1.64)	100 (1 study)	●●○○ Low (a,b)
	365 per 1000	354 per 1000 (208, 599)			
	Moderate				
	365 per 1000	354 per 1000 (208, 599)			
Intermediate follow-up (17-24 weeks post-intervention) – available case analysis SCID (mean 20 weeks)	*Study population*		RR 1.09 (0.61, 1.94)	95 (1 study)	●●○○ Low (a,b)
	312 per 1000	341 per 1000 (191, 606)			
	Moderate				
	313 per 1000	341 per 1000 (191, 607)			
Long Follow-up (25-103 weeks post-intervention) – ITT analysis SCID (mean 20 weeks)	*Study population*		RR 1.42 (0.77, 2.6)	100 (1 study)	●●○○ Low (a,b)
	250 per 1000	355 per 1000 (192, 650)			
	Moderate				
	250 per 1000	355 per 1000 (192, 650)			
Long Follow-up (25-103 weeks post-intervention) – available case analysis SCID (mean 20 weeks)	*Study population*		RR 1.66 (0.8, 3.45)	93 (1 study)	●●○○ Low (a,b)
	188 per 1000	311 per 1000 (150, 647)			
	Moderate				
	188 per 1000	312 per 1000 (150, 649)			
Very long Follow-up (>104 weeks post-intervention) – ITT analysis SCID (mean 260 weeks)	*Study population*		RR 1.83 (1.04, 3.22)	100 (1 study)	●●○○ Low (a)
	250 per 1000	458 per 1000 (260, 805)			
	Moderate				
	250 per 1000	458 per 1000 (260, 805)			
Very long Follow-up (>104 weeks post-intervention) – available case analysis SCID (mean 260 weeks)	*Study population*		RR 0.87 (0.37, 2.08)	70 (1 study)	●●○○ Low (a,b)
	243 per 1000	212 per 1000 (90, 506)			
	Moderate				
	243 per 1000	211 per 1000 (90, 505)			
Depression symptomatology					
Post-treatment – ITT analysis EPDS≥12 (26-52 weeks)	*Study population*		RR 0.96 (0.84, 1.09)	1,111 (2 studies)	●●●○ Moderate (d)
	452 per 1000	434 per 1000 (380, 493)			
	Moderate				
	494 per 1000	474 per 1000 (415, 538)			

Outcomes (follow-up)	**Illustrative comparative risks***		Relative effect (95% CI)	**No. of participants (studies)**	**Certainty of the evidence (GRADE)**
	Assumed risk Control	**Corresponding risk Intervention**			
Post-treatment – available case analysis EPDS≥12 (26-52 weeks)	*Study population*		RR 0.82 (0.66, 1.01)	885 (2 studies)	●●○○ Low (a,b,d)
	331 per 1000	271 per 1000 (218, 334)			
	Moderate				
	373 per 1000	306 per 1000 (246, 377)			
Long Follow-up (25-103 weeks post-intervention) – ITT analysis GHQ≥12 (mean 78 weeks)	*Study population*		RR 0.98 (0.87, 1.11)	731 (1 study)	●●●○ Moderate (d)
	651 per 1000	638 per 1000 (567, 723)			
	Moderate				
	652 per 1000	639 per 1000 (567, 724)			
Long Follow-up (25-103 weeks post-intervention) – available case analysis GHQ≥12 (mean 78 weeks)	*Study population*		RR 0.96 (0.79, 1.15)	549 (1 study)	●●○○ Low (a,d)
	538 per 1000	516 per 1000 (425, 618)			
	Moderate				
	538 per 1000	516 per 1000 (425, 619)			
Depression mean scores					
Post-treatment – available case analysis EPDS (20-26 weeks)	**SMD -0.34 (-0.55, -0.14)**		-	375 (2 studies)	●●●○ Moderate (d)
Intermediate follow-up (17-24 weeks post-intervention) – by intervention EPDS or CES-D (4-12 weeks)	SMD -0.07 (-0.35, 0.21)		-	197 (2 studies)	●●●○ Moderate (e)
Intermediate follow-up (17-24 weeks post-intervention) – available case analysis EPDS (mean 20 weeks)	SMD 0.07 (-0.33, 0.48)		-	94 (1 study)	●●○○ Low (e)
Long Follow-up (25-103 weeks post-intervention) – available case analysis EPDS (mean 78 weeks)	SMD 0.14 (-0.26, 0.55)		-	92 (1 study)	●●○○ Low (b,e)
Very long Follow-up (>104 weeks post-intervention) – available case analysis EPDS (mean 260 weeks)	SMD -0.19 (-0.67, 0.29)		-	67 (1 study)	●●○○ Low (b,e)
Anxiety mean scores					
Post-treatment – available case analysis STAI-S (mean 26 weeks)	**SMD -0.29 (-0.53, -0.04)**			260 (1 study)	●●○○ Low (d,e)
Mother-infant attachment problems					
Post-treatment – ITT analysis Maternal report: Mother-infant relationship problems (mean 20 weeks)	*Study population*		**RR 0.71 (0.54, 0.92)**	100 (1 study)	●●○○ Low (a)
	827 per 1000	587 per 1000 (447, 761)			
	Moderate				
	827 per 1000	587 per 1000 (447, 761)			
Post-treatment – available case analysis Maternal report: Mother-infant relationship problems (mean 20 weeks)	*Study population*		RR 0.72 (0.51, 1.01)	78 (1 study)	●●○○ Low (a,b)
	743 per 1000	535 per 1000 (379, 750)			
	Moderate				
	743 per 1000	535 per 1000 (379, 750)			
Long follow-up (25-103 weeks post-intervention) – ITT analysis Maternal report: Mother-infant relationship problems (mean 78 weeks)	*Study population*		RR 1.08 (0.73, 1.6)	100 (1 study)	●●○○ Low (a,b)
	481 per 1000	519 per 1000 (351, 769)			
	Moderate				
	481 per 1000	519 per 1000 (351, 770)			

Outcomes (follow-up)	**Illustrative comparative risks***		Relative effect (95% CI)	**No. of participants (studies)**	**Certainty of the evidence (GRADE)**
	Assumed risk Control	**Corresponding risk Intervention**			
Long follow-up (25-103 weeks post-intervention) – available case analysis Maternal report: Mother-infant relationship problems (mean 78 weeks)	*Study population*		RR 0.96 (0.58, 1.59)	86 (1 study)	⨁⨁◯◯ Low (a,b)
	426 per 1000	409 per 1000 (247, 677)			
	Moderate				
	426 per 1000	409 per 1000 (247, 677)			

Evidence Statements:

Non-directive counselling in the home appears to have no effect on depression diagnosis at endpoint or first measurement (low certainty evidence) or at intermediate follow-up (17-24 weeks post-intervention) (low certainty evidence) or at long follow-up (25-103 weeks post-intervention) (low certainty evidence), and may be less effective on depression diagnosis at very long follow-up (>104 weeks post-intervention) (low certainty evidence) than treatment as usual in postpartum women with a diagnosis of MDD.

Listening visits in the home have no effect on depression symptomatology at endpoint or first measurement (moderate certainty evidence), or at long follow-up (25-103 weeks post-intervention) (moderate certainty evidence), compared with treatment as usual in postpartum women with symptoms (or subthreshold symptoms) of depression.

Non-directive counselling/listening visits in the home improve depression mean scores at endpoint or first measurement (moderate certainty evidence) compared with treatment as usual in postpartum women with a diagnosis of depression or symptoms of depression; however, the magnitude of the benefit is not clinically significant.

Non-directive counselling in the home appears to have no effect on depression mean scores at intermediate follow-up (17-24 weeks post-intervention) (low certainty evidence), long follow-up (>24 weeks post-intervention) (low certainty evidence) and very long follow-up (>104 weeks post-intervention) (low certainty evidence) compared with treatment as usual in postpartum women with a diagnosis of MDD.

Non-directive counselling in the home may improve state anxiety mean scores (low certainty evidence) at endpoint or first measurement compared with treatment as usual in postpartum women with symptoms of depression; however, the magnitude of the benefits may not be clinically significant.

Non-directive counselling in the home may improve mother-infant attachment problems at endpoint or first measurement (low certainty evidence), but appears to have no effect on mother-infant attachment problems at long follow-up (25-103 weeks post-intervention) (low certainty evidence) compared with treatment as usual in postpartum women with a diagnosis of MDD.

Footnotes:

* The 'assumed risk' for the *study population* is calculated using the mean baseline risk from the studies in the meta-analysis (i.e. total number of events in the control/comparison group divided by the total number of patients in the control/comparison group). The *moderate* risk scenario is calculated using the median control/comparison group risk from the studies in the meta-analysis. The 'corresponding risk' (and its 95% CI) is based on the assumed risk in the control/comparison group and the relative effect of the intervention (and its 95% CI).

a. Total number of events is less than 300 (a threshold rule-of-thumb)

b. 95% CI crosses both line of no effect and measure of appreciable benefit or harm (SMD -0.5/0.5 or RR 0.75/1.25)

c. There was evidence of moderate-to-substantial heterogeneity between effect sizes

d. Papers omit data

e. Total population size is less than 400 (a threshold rule-of-thumb)

Source: NICE 2015, Table 136, Table 159, Table 180, Table 189

Abbreviations: CI, confidence interval; CIS-R, Computerised version of the Clinical Interview Schedule – Revised; EPDS, Edinburgh Postnatal Depression Scale; GHQ, General Health Questionnaire; ITT, intention-to-treat; MADRS, Montgomery–Åsberg Depression Rating Scale; MDD, major depressive disorder; PTSD, post-traumatic stress disorder; RR, relative risk; SCID, Structured Clinical Interview for DSM Disorders; SMD, standardised mean difference; STAI-S, State-Trait Anxiety Inventory-State.

Note: Statistically significant differences are shown in bold.

C3.2.4 Case management/individual treatment

The literature search identified no SRs that relate to this intervention.

Table C3-24 Summary of findings (treatment) – case management/individual treatment

Evidence Statement:
There is no RCT evidence for case management or individualised treatment in women who have mental health problems in the perinatal period.

C3.2.5 Self-help and facilitated self-help

Only one SR on self-help or facilitated self-help was identified in the literature search; NICE 2015 included three RCTs that compared facilitated self-help with treatment as usual. One Australian study assessed facilitated self-help (workbook delivery and telephone support) in pregnant women with subthreshold symptoms of depression. The other two RCTs from the United Kingdom assessed internet-delivered self-help, one of which also offered online (chat room) support for postpartum women with symptoms of depression, while the other offered telephone support to postpartum women with a diagnosis of MDD.

C3.2.5.1 Facilitated self-help versus treatment as usual

There was very low-to-high quality data from up to three studies for moderate benefits of facilitated self-help relative to treatment as usual for depression symptomatology and mean depression symptoms (**Table C3-25**). There was very low quality, single-study evidence for moderate benefits of facilitated self-help relative to treatment as usual for treating anxiety symptomatology and for mean anxiety symptoms.

Table C3-25 Summary of findings (treatment) – facilitated self-help versus treatment as usual

Outcomes (follow-up)	Illustrative comparative risks*		Relative effect (95% CI)	No. of participants (studies)	Certainty of the evidence (GRADE)
	Assumed risk Control	Corresponding risk Intervention			
Depression symptomatology					
Post-treatment – ITT Analysis BDI-II≥14 or EPDS>12 (15-20 weeks)	*Study population*		**RR 0.73 (0.53, 0.99)**	1,136 (3 studies)	●○○○ Very low (a,b)
	817 per 1000	596 per 1000 (433, 809)			
	Moderate				
	762 per 1000	556 per 1000 (404, 754)			
Post-treatment – available case analysis BDI-II≥14 or EPDS>12 (15-20 weeks)	*Study population*		**RR 0.58 (0.44, 0.77)**	503 (3 studies)	●●○○ Low (b,c)
	567 per 1000	329 per 1000 (250, 437)			
	Moderate				
	586 per 1000	340 per 1000 (258, 451)			
Depression mean scores					
Post-treatment – available case analysis EPDS (15-17 weeks)	**SMD -0.56 (-0.76, -0.37)**		-	414 (2 studies)	●●●● High
Anxiety symptomatology					
Post-treatment – ITT analysis Depression Anxiety Stress Scale (DASS): Anxiety ≥8 (mean 20 weeks)	*Study population*		**RR 0.67 (0.47, 0.96)**	143 (1 study)	●○○○ Very low (b,c)
	569 per 1000	382 per 1000 (268, 547)			
	Moderate				
	569 per 1000	381 per 1000 (267, 546)			

Outcomes (follow-up)	**Illustrative comparative risks***		**Relative effect (95% CI)**	**No. of participants (studies)**	**Certainty of the evidence (GRADE)**
	Assumed risk Control	**Corresponding risk Intervention**			
Post-treatment – available case analysis Depression Anxiety Stress Scale (DASS): Anxiety ≥8 (mean 20 weeks)	*Study population*		**RR 0.24 (0.07, 0.81)**	89 (1 study)	●○○○ Very low (b,c)
	262 per 1000	63 per 1000 (18, 212)			
	Moderate				
	262 per 1000	63 per 1000 (18, 212)			
Anxiety mean scores					
Post-treatment – available case analysis Generalised Anxiety Disorder Assessment (GAD-7) (mean 17 weeks)	SMD -0.5 (-1.02, 0.02)		-	59 (1 study)	●○○○ Very low (b,d,e)
Evidence Statements: *Facilitated self-help (internet delivery with online or telephone support) improves depression mean scores at endpoint or first measurement (high certainty evidence) compared with treatment as usual in postpartum women with a diagnosis of MDD or symptoms of depression.* *Facilitated self-help (workbook or internet delivery with online or telephone support) may improve depression symptomatology at endpoint or first measurement (very low certainty evidence) compared with treatment as usual in pregnant or postpartum women with a diagnosis of MDD or symptoms (or subthreshold symptoms) of depression.* *Facilitated self-help (workbook delivery with telephone support) may improve anxiety symptomatology at endpoint or first measurement (very low certainty evidence) compared with treatment as usual in pregnant women with subthreshold symptoms of depression.* *Facilitated self-help (internet delivery with telephone support) appears to have no effect on anxiety mean scores at endpoint or first measurement (very low certainty evidence) compared with treatment as usual in postpartum women with a diagnosis of MDD.*					
Footnotes: * The 'assumed risk' for the *study population* is calculated using the mean baseline risk from the studies in the meta-analysis (i.e. total number of events in the control/comparison group divided by the total number of patients in the control/comparison group). The *moderate* risk scenario is calculated using the median control/comparison group risk from the studies in the meta-analysis. The 'corresponding risk' (and its 95% CI) is based on the assumed risk in the control/comparison group and the relative effect of the intervention (and its 95% CI). a. There was evidence of considerable heterogeneity between effect sizes. b. Papers omit data. c. Total number of events is less than 300 (a threshold rule-of-thumb). d. Total population size is less than 400 (a threshold rule-of-thumb). e. 95% CI crosses both line of no effect and measure of appreciable benefit or harm (SMD -0.5/0.5 or RR 0.75/1.25).					

Source: NICE 2015, Table 133, Table 157

Abbreviations: BDI, Beck Depression Inventory; CI, confidence interval; DASS, Depression Anxiety Stress Scale; EPDS, Edinburgh Postnatal Depression Scale; GAD-7, Generalised Anxiety Disorder Assessment: ITT, intention-to-treat; MDD, major depressive disorder; RR, relative risk; SMD, standardised mean difference.

Note: Statistically significant differences are shown in bold.

C3.2.6 Post-traumatic birth counselling

Only one SR (NICE 2015) was identified for post-traumatic birth counselling in the literature search. NICE 2015 included one Australian RCT (N=103) that compared individual post-traumatic birth counselling (face-to-face and telephone) with treatment as usual in women with a diagnosis of PTSD.

C3.2.6.1 Post-traumatic birth counselling versus treatment as usual

There was low quality, single-study evidence for large effects of post-traumatic birth counselling on depression symptomatology (**Table C3-26**). The same study showed a large effect of post-traumatic birth counselling on anxiety symptomatology; however, confidence that this is a true measure of the effect is low due to the low number of events and imprecision. There was no evidence for statistically or clinically significant benefits of post-traumatic birth counselling on PTSD diagnosis and no evidence for a clinically significant effect (despite meeting statistical significance criteria) on mean PTSD symptoms. The study reported no drop-outs from either study arm.

Table C3-26 Summary of findings (treatment) – post-traumatic birth counseling versus treatment as usual

Outcomes (follow-up)	Illustrative comparative risks*		Relative effect (95% CI)	No. of participants (studies)	Certainty of the evidence (GRADE)
	Assumed risk Control	Corresponding risk Intervention			
Depression symptomatology					
Post-treatment – ITT analysis EPDS≥12 (mean 13 weeks)	*Study population*		**RR 0.25 (0.09, 0.69)**	103 (1 study)	●●○○ Low (a)
	321 per 1000	80 per 1000 (29, 221)			
	Moderate				
	321 per 1000	80 per 1000 (29, 221)			
Post-treatment – available case analysis EPDS≥12 (mean 13 weeks)	*Study population*		**RR 0.25 (0.09, 0.69)**	103 (1 study)	●●○○ Low (a)
	321 per 1000	80 per 1000 (29, 221)			
	Moderate				
	321 per 1000	80 per 1000 (29, 221)			
Anxiety symptomatology					
Post-treatment – ITT analysis Depression Anxiety Stress Scale (DASS): Anxiety >9 (mean 13 weeks)	*Study population*		RR 0.18 (0.02, 1.42)	103 (1 study)	●●○○ Low (a,b)
	113 per 1000	20 per 1000 (2, 161)			
	Moderate				
	113 per 1000	20 per 1000 (2, 160)			
Post-treatment – available case analysis Depression Anxiety Stress Scale (DASS): Anxiety >9 (mean 13 weeks)	*Study population*		RR 0.18 (0.02, 1.42)	103 (1 study)	●●○○ Low (a,b)
	113 per 1000	20 per 1000 (2, 161)			
	Moderate				
	113 per 1000	20 per 1000 (2, 160)			
PTSD diagnosis					
Post-treatment – ITT analysis Mini- PTSD Diagnosis Interview (mean 13 weeks)	*Study population*		RR 0.35 (0.1, 1.23)	103 (1 study)	●●○○ Low (a,b)
	170 per 1000	59 per 1000 (17, 209)			
	Moderate				
	170 per 1000	59 per 1000 (17, 209)			
Post-treatment – available case analysis Mini- PTSD Diagnosis Interview (mean 13 weeks)	*Study population*		RR 0.35 (0.1, 1.23)	103 (1 study)	●●○○ Low (a,b)
	170 per 1000	59 per 1000 (17, 209)			
	Moderate				
	170 per 1000	59 per 1000 (17, 209)			

Outcomes (follow-up)	Illustrative comparative risks*		Relative effect (95% CI)	No. of participants (studies)	Certainty of the evidence (GRADE)
	Assumed risk Control	Corresponding risk Intervention			
PTSD mean scores					
Post-treatment – ITT analysis Mini- PTSD Diagnosis Interview: 'Trauma symptoms', rating scale unclear (mean 13 weeks)	**SMD -0.41 (-0.81, -0.02)**		-	103 (1 study)	⨁⨁◯◯ Low (c)
Post-treatment – available case analysis Mini- PTSD Diagnosis Interview: 'Trauma symptoms', rating scale unclear (mean 13 weeks)	**SMD -0.41 (-0.81, -0.02)**		-	103 (1 study)	⨁⨁◯◯ Low (c)
Evidence Statements: *Individual post-traumatic birth counselling may improve depression symptomatology at endpoint or first measurement (low certainty evidence) compared with treatment as usual in postpartum women with a diagnosis of PTSD.* *Individual post-traumatic birth counselling appears to have no effect on anxiety symptomatology at endpoint or first measurement (low certainty evidence) compared with treatment as usual in postpartum women with a diagnosis of PTSD.* *Individual post-traumatic birth counselling may improve PTSD mean scores (low certainty evidence), but appears to have no effect on PTSD diagnosis (low certainty evidence) at endpoint or first measurement compared with treatment as usual in postpartum women with a diagnosis of PTSD.*					
Footnotes: * The 'assumed risk' for the *study population* is calculated using the mean baseline risk from the studies in the meta-analysis (i.e. total number of events in the control/comparison group divided by the total number of patients in the control/comparison group). The *moderate* risk scenario is calculated using the median control/comparison group risk from the studies in the meta-analysis. The 'corresponding risk' (and its 95% CI) is based on the assumed risk in the control/comparison group and the relative effect of the intervention (and its 95% CI). a. Total number of events is less than 300 (a threshold rule-of-thumb). b. 95% CI crosses both line of no effect and measure of appreciable benefit or harm (SMD -0.5/0.5 or RR 0.75/1.25). c. Total population size is less than 400 (a threshold rule-of-thumb).					

Source: NICE 2015, Table 139, Table 162, Table 171

Abbreviations: CI, confidence interval; DASS, Depression Anxiety Stress Scale; EPDS, Edinburgh Postnatal Depression Scale; ITT, intention-to-treat; PTSD, post-traumatic stress disorder; RR, relative risk; SMD, standardised mean difference.

Note: Statistically significant differences are shown in bold.

C3.2.7 Post-miscarriage counselling

Only one SR (NICE 2015) was identified for post-miscarriage counselling in the literature search. NICE 2015 included three RCTs that compared post-miscarriage counselling with treatment as usual or enhanced treatment as usual[14]. One RCT from the United States assessed face-to-face nurse-led counselling in postpartum women with symptoms of depression. Another RCT from the United States assessed interpersonal counselling via telephone in postpartum women with symptoms of depression. One RCT from the United Kingdom assessed face-to-face psychological counselling (with medical investigations into causes of miscarriage) in postpartum women with symptoms of anxiety.

[14] Enhanced treatment as usual involved medical investigations into causes of miscarriage without counselling.

C3.2.7.1 Post-miscarriage counselling versus treatment as usual

NICE 2015 did not consider the setting or mode of delivery of the intervention in their analyses.

There was no evidence for clinically or statistically significant benefits associated with post-miscarriage counselling on mean depression symptoms or anxiety mean scores at endpoint or at follow-up (**Table C3-27**).

There was no evidence for clinically or statistically significant effects of post-miscarriage counselling relative to treatment as usual or enhanced treatment as usual on attrition (as a proxy measure for retention in services and treatment acceptability).

Table C3-27 Summary of findings (treatment) – post-miscarriage counselling versus treatment as usual

Outcomes (follow-up)	Illustrative comparative risks*		Relative effect (95% CI)	No. of participants (studies)	Certainty of the evidence (GRADE)
	Assumed risk Control	Corresponding risk Intervention			
Depression mean scores					
Post-treatment – ITT analysis CES-D or HRSD (7-12 weeks)	SMD 0.17 (-0.12, 0.46)		-	189 (2 studies)	⨁⨁◯◯ Low (a)
Post-treatment – available case analysis HRSD or HADS – Depression (2-7 weeks)	SMD 0.14 (-0.29, 0.58)		-	81 (2 studies)	⨁⨁◯◯ Low (a,b)
Intermediate follow-up (17-24 weeks post-intervention) – available case analysis HADS – Depression (mean 17 weeks)	SMD -0.23 (-0.71, 0.26)		-	66 (1 study)	⨁⨁◯◯ Low (a,b)
Long Follow-up (25-103 weeks post-intervention) – ITT analysis CES-D (mean 46 weeks)	SMD -0.08 (-0.38, 0.22)		-	170 (1 study)	⨁⨁◯◯ Low (a)
Anxiety mean scores					
Post-treatment – available case analysis HADS – Anxiety (mean 2 weeks)	SMD 0.11 (-0.38, 0.59)		-	66 (1 study)	⨁⨁◯◯ Low (a,b)
Intermediate follow-up (17-24 weeks post-intervention) – available case analysis HADS – Anxiety (mean 17 weeks)	SMD -0.31 (-0.8, 0.17)		-	66 (1 study)	⨁⨁◯◯ Low (a,b)
Evidence Statements: *There is that individual post-miscarriage counselling (telephone or face-to-face at home) appears to have no effect on depression mean scores at endpoint or first measurement (low certainty evidence), or on depression mean scores at long follow-up (25-103 weeks post-intervention) (low certainty evidence) compared with treatment as usual in women with symptoms of depression.* *Individual post-miscarriage counselling (face-to-face clinic-based psychological counselling plus medical investigations into causes of miscarriage) appears to have no effect on depression mean scores at intermediate follow-up (17-24 weeks post-intervention) (low certainty evidence) or on anxiety mean scores at intermediate follow-up (17-24 weeks post-intervention) (low certainty evidence) compared with enhanced treatment as usual (medical investigations into causes of miscarriage without counselling) in women with symptoms of anxiety.*					
Footnotes: * The 'assumed risk' for the *study population* is calculated using the mean baseline risk from the studies in the meta-analysis (i.e. total number of events in the control/comparison group divided by the total number of patients in the control/comparison group). The *moderate* risk scenario is calculated using the median control/comparison group risk from the studies in the meta-analysis. The 'corresponding risk' (and its 95% CI) is based on the assumed risk in the control/comparison group and the relative effect of the intervention (and its 95% CI). a. Total population size is less than 400 (a threshold rule-of-thumb) b. 95% CI crosses both line of no effect and measure of appreciable benefit or harm (SMD -0.5/0.5 or RR 0.75/1.25)					

Source: NICE 2015, Table 138, Table 161

Abbreviations: CES-D, Center for Epidemiologic Studies Depression Scale; CI, confidence interval; HADS, Hospital Anxiety and Depression Scale; HRSD, Hamilton Rating Scale for Depression; ITT, intention-to-treat; RR, relative risk; SMD, standardised mean difference.

C3.3 TREATMENT WITH ONLINE INTERVENTIONS

Two SRs (Ashford 2016; Lee 2016) were identified in the literature search. Ashford 2016 included five RCTs (plus two studies with a quasi-experimental pretest/post-test design) of web- or computer-based interventions for the treatment of mental health problems. With the exception of the RCT of the 'Maternal Depression Online' intervention that was published in a thesis, all other RCTs included in Ashford 2016 were included in NICE 2015 (as self-help or post-miscarriage self-help interventions) and have been included in other sections of the current report (**Section C3.2.5, Section C3.1.8, Section C4.1.8**).[15]

The majority of interventions were developed for the treatment of depression in pregnant women or postpartum women; however, one intervention (with two publications) targeted complicated grief and mental health in women and their partners after pregnancy loss. The therapeutic approach used in the web-based interventions was CBT (three RCTs) or behavioural activation (two RCTs). The majority of interventions also included therapist contact (either on the phone, via email, or in real-time online), which occurred mostly on a weekly basis. In the studies that targeted women and their partners after pregnancy loss, support was provided in the form of written feedback for writing assignments, with assignments personalised by a therapist. The duration of the interventions ranged from 5 weeks to 17 weeks across the studies. Sample attrition between pre- and post-intervention time points was up to 62%.

Across the five RCTs included in Ashford 2016, the comparator was either waitlist control or treatment as usual. *No studies compared an online intervention with an offline version of the same intervention for the treatment of mental health problems.* The authors concluded that computer- or web-based mental health interventions, particularly those targeting depression or complicated grief, may be a promising approach to the treatment and reduction of maternal mental health issues during the perinatal period; however, there are significant gaps in the current evidence base so further research is needed.

A literature search was conducted to identify RCTs of online interventions published after the literature search date of the Ashford 2016 SR. Only those studies that compared an online intervention with an offline version of the same intervention were considered eligible. *No additional studies, published in full, were identified in the literature search update.*

Table C3-28 Summary of findings (treatment) – online interventions

Evidence Statement: *There is no RCT evidence for online interventions compared with offline versions of the same intervention in women who have mental health problems in the perinatal period.*

[15] Of note, Ashford 2016 classified an RCT of a cognitive behaviour web-based intervention (Kersting 2013) as a treatment study (see **Section C3.3**), whereas NICE 2015 classified this study as a preventive intervention (see **Section C4.1.8** on post-miscarriage self-help interventions).

C3.4 TREATMENT WITH PHARMACOLOGICAL INTERVENTIONS

C3.4.1 Antidepressants

Of the eight SRs of antidepressants identified in the scoping and updated searches, NICE 2015 and Molyneaux 2014 were chosen as the foundation reviews due to their currency, high quality and comprehensiveness. It should be noted that both SRs reporting on treatment with antidepressants (NICE 2015; Molyneaux 2014) included the same set of six RCTs, which included one comparing antidepressants as a group with general supportive care and a psychological therapy (listening visits), two comparing SSRIs with placebo, two comparing SSRIs plus psychological therapy with placebo plus psychological therapy,[16] and one comparing SSRIs with TCAs. Rather than choosing a single foundation SR for the assessment of treatment, both reviews are included because they analysed the available data in slightly different ways.

C3.4.1.1 Any antidepressants

Two comparisons were available for the assessment of the efficacy and side effects of treatment with antidepressants as a group – one against general supportive care and one against listening visits – in one identified study (Sharp 2010).

Table C3-29 summarises the evidence and provides Evidence Statements relating to the comparison between antidepressants as a group and general supportive care. The type of antidepressant used was at the discretion of the general practitioner (GP), although use of SSRIs as first-line treatment was encouraged and the majority of women received citalopram, fluoxetine or sertraline. General supportive care was described as women seeing their GP or practice health visitor (PHV) as often as they liked, with no antidepressant prescription from the GP and no listening visit with the PHV, unless the severity of the depression required a protocol deviation. The results of this comparison, based on very low certainty evidence, show that antidepressants may be significantly beneficial compared with general supportive care in terms of increasing remission at 4 weeks post-treatment, reducing depression symptomatology and decreasing depression mean score.

Table C3-30 summarises the evidence and provides Evidence Statements relating to the comparison between antidepressants as a group and listening visits. Listening visits were described as "a psychotherapeutic intervention that uses a form of non-directive counselling, often referred to as 'active listening'." The results of this comparison, based on very low certainty evidence, show that there does not appear to be a difference in remission rate at 4 weeks post-treatment between antidepressants and listening visits.

Table C3-29 Summary of findings (treatment) – antidepressants versus general supportive care

Outcomes (follow-up)	Illustrative comparative risks*		Relative effect (95% CI)	No. of participants (studies)	Certainty of the evidence (GRADE)
	Assumed risk Control	Corresponding risk Intervention			
Remission					
Remission rate at post-treatment	*Study population*		**RR 2.11**	254	●○○○
Post-treatment	176 per 1000	371 per 1000 (239, 577	**(1.36, 3.28)**	(1 RCT)[17]	Very low (a,b)

[16] While listed as included in the Molyneaux 2014 review, one of these (Appleby 1997) did not contribute to any of the presented analyses.
[17] Molyneaux 2014 (Sharp 2010).

Outcomes (follow-up)	Illustrative comparative risks*		Relative effect (95% CI)	No. of participants (studies)	Certainty of the evidence (GRADE)
	Assumed risk Control	Corresponding risk Intervention			
< 13 EPDS	*Moderate*				
(4 weeks)	NR	NR			
Depression symptomatology					
Depression symptomatology	*Study population*		**RR 0.76**	254	●○○○
Post-treatment – ITT analysis	824 per 1000	626 per 1000 (536, 733)	**(0.65, 0.89)**	(1 RCT)[18]	Very low (c,d)
EPDS > 13	*Moderate*				
(4 weeks)	NR	NR			
Depression symptomatology	*Study population*		**RR 0.68**	218	●○○○
Post-treatment – available case analysis	804 per 1000	546 per 1000 (450, 667)	**(0.56, 0.83)**	(1 RCT)[19]	Very low (c,d)
EPDS > 13	*Moderate*				
(mean 4 weeks)	NR	NR			
Depression mean scores					
Depression mean scores	**SMD -0.48**		-	218	●○○○
Post-treatment – available case analysis	**(-0.75, -0.21)**			(1 RCT)	Very low (c,d)
EPDS					
(4 weeks)					

Evidence Statements:

Treatment with antidepressants may improve remission rate at 4 weeks post-treatment compared with general supportive care, in women with postnatal depression, from a rate of 18% to 37% (very low certainty evidence).

Treatment with antidepressants may improve depression symptomatology at 4 weeks post-treatment compared with general supportive care, in women with postnatal depression, from a rate of 82% to 55% (very low certainty evidence).

Treatment with antidepressants may improve depression mean score at 4 weeks post-treatment compared with general supportive care, in women with postnatal depression (very low certainty evidence).

Footnotes:

* The 'assumed risk' for the study population is calculated using the mean baseline risk from the studies in the meta-analysis (i.e. total number of events in the control/comparison group divided by the total number of patients in the control/comparison group). The moderate risk scenario is calculated using the median control/comparison group risk from the studies in the meta-analysis. The 'corresponding risk' (and its 95% CI) is based on the assumed risk in the control/comparison group and the relative effect of the intervention (and its 95% CI).

a. Downgraded twice due to high risk of bias in two domains (lack of blinding of outcome assessors and low adherence).

b. Downgraded due to imprecision (only one study available for this comparison).

c. High risk of performance bias and only 56% reporting taking antidepressants in intervention group.

d. Total population size is less than 400 (a threshold rule-of-thumb).

Source: Molyneaux 2014 – Analysis 2.1; NICE 2015 – Table 297.

Abbreviations: CI, confidence interval; EPDS, Edinburgh Postnatal Depression Scale; ITT, intention-to-treat; NR, not reported; PND, postnatal depression; RCT, randomised controlled trial; RR, relative risk; SMD, standardised mean difference.

[18] NICE 2015 (Sharp 2010).

[19] NICE 2015 (Sharp 2010).

Table C3-30 Summary of findings (treatment) – antidepressants versus listening visits

Outcomes (follow-up)	Illustrative comparative risks*		Relative effect (95% CI)	No. of participants (studies)	Certainty of the evidence (GRADE)
	Assumed risk Control	Corresponding risk Intervention			
Remission					
Remission rate at post-treatment	*Study population*		RR 1.04	254	●○○○
Post-treatment	448 per 1000	466 per 1000 (354, 609)	(0.79, 1.36)	(1 RCT)[20]	Very low (a,b)
As defined in individual studies	*Moderate*				
(4 weeks)	NR	NR			
Evidence Statements:					
Treatment with antidepressants appears to have no effect on remission rate at 4 weeks post-treatment compared with treatment with listening visits, in women with postnatal depression (very low certainty evidence).					

Footnotes:

* The 'assumed risk' for the study population is calculated using the mean baseline risk from the studies in the meta-analysis (i.e. total number of events in the control/comparison group divided by the total number of patients in the control/comparison group). The moderate risk scenario is calculated using the median control/comparison group risk from the studies in the meta-analysis. The 'corresponding risk' (and its 95% CI) is based on the assumed risk in the control/comparison group and the relative effect of the intervention (and its 95% CI).

a. Downgraded twice due to high risk of bias in two domains (lack of blinding of outcome assessors and low adherence).

b. Downgraded due to imprecision (only one study available for this comparison).

Source: Molyneaux 2014 – Analysis 3.1.

Abbreviations: CI, confidence interval; EPDS, Edinburgh Postnatal Depression Scale; ITT, intention-to-treat; NR, not reported; PND, postnatal depression; RCT, randomised controlled trial; RR, relative risk; SMD, standardised mean difference.

C3.4.1.2 SSRIs

Two comparisons were available for the use of SSRIs in postnatal depression – one against placebo and one against TCAs – in two SRs (NICE 2015, Molyneaux 2014), which each included four studies (Hantsoo 2014, Bloch 2012, Yonkers 2008 and Wisner 2006). It should be noted that the study by Bloch 2012 compared SSRIs plus psychological therapy with placebo plus psychological therapy. In the Molyneaux 2014 SR, the findings from the Bloch 2012 study have been included in the 'versus placebo' comparison, while in the NICE 2015 SR they have been included in a separate comparison 'versus placebo plus psychological therapy'. Both comparisons are presented in the SoF tables below

Table C3-31 summarises the evidence and provides Evidence Statements relating to the comparison between SSRIs as a group and placebo. Two of the three RCTs included in the SRs examined sertraline (Hantsoo 2014, Bloch 2012) while the remaining RCT examined paroxetine (Yonkers 2008). The analyses of three RCTs conducted by Molyneaux 2014 provides very low certainty evidence that use of SSRIs may improve response and remission at 6-8 weeks post-treatment compared with placebo. There was also low certainty evidence that SSRIs may significantly reduce mean global severity and improvement scores compared with placebo. There was no difference between SSRIs and placebo in terms of mean depression scores and adverse events; these findings were based on very low certainty evidence and were subject to imprecision. As shown in **Table C3-32**, when the comparison between SSRIs plus psychological therapy and placebo plus psychological therapy was considered separately, based on very low certainty evidence there was no difference in response, remission, global improvement mean

[20] Molyneaux 2014 (Sharp 2010).

score and mean distress score; however, there was low-to-moderate certainty evidence that SSRIs plus psychological therapy may result in greater reduction in mean depression and mean global severity scores.

Table C3-33 summarises the evidence and provides Evidence Statements relating to the comparison between SSRIs and TCAs; however, the single included study compared only one of each class – sertraline and nortriptyline (Wisner 2006). Based on the analyses of data from this study, there was low-to-very low certainty evidence of no difference between SSRIs and TCAs for any of the outcomes assessed, including response score, remission score, global severity and improvement, depression mean score, global assessment of functioning mean score, and social problems.

Table C3-31 Summary of findings (treatment) – SSRIs versus placebo

Outcomes (follow-up)	Illustrative comparative risks*		Relative effect (95% CI)	No. of participants (studies)	Certainty of the evidence (GRADE)
	Assumed risk Control	Corresponding risk Intervention			
Response					
Response rate at post-treatment	*Study population*		**RR 1.43**	146	●○○○
Post-treatment	365 per 1000	522 per 1000 (369, 741)	**(1.01, 2.03)**	(3 RCTs)[21]	Very low (a,b,c)
As defined in individual studies	*Moderate*				
(6-8 weeks)	NR	NR			
Response rate at post-treatment	*Study population*		RR 1.62	106	●○○○
Post-treatment	296 per 1000	480 per 1000 (290, 790)	(0.98, 2.67)	(2 RCTs)[22]	Very low (b,c)
As defined in individual studies	*Moderate*				
(6-8 weeks)	NR	NR			
Non-response to postnatal treatment	*Study population*		RR 0.74	106	●○○○
Post-treatment – ITT[23]	704 per 1000	521 per 1000 (366, 746)	(0.52, 1.06)	(2 RCTs)[24]	Very low (e)
> 10 HRSD, > 50% decrease, improvement on CGI or CGI -I=1 or 2	*Moderate*				
(6 weeks)	711 per 1000	526 per 1000 (370, 754)			
Non-response to postnatal treatment	*Study population*		RR 0.46	33	●●○○
Post-treatment – available case analysis[25]	722 per 1000	332 per 1000 (152, 722)	(0.21, 1.00)	(1 RCT)[26]	Low (d)
> 10 HRSD, > 50% decrease, improvement on CGI	*Moderate*				
(6 weeks)	722 per 1000	332 per 1000 (152, 722)			
Remission					
Remission rate at post-treatment	*Study population*		**RR 1.79**	146	●○○○
Post-treatment	257 per 1000	460 per 1000 (278, 766)	**(1.08, 2.98)**	(3 RCTs)[27]	Very low (a,b,c)
As defined in individual studies	*Moderate*				
(6-8 weeks)	NR	NR			
Remission rate at post-treatment	*Study population*		**RR 2.56**	106	●○○○
Post-treatment	167 per 1000	428 per 1000 (219, 835)	**(1.31, 5.00)**	(2 RCTs)[28]	Very low (b,c)
As defined in individual studies	*Moderate*				
(6-8 weeks)	NR	NR			
Non-remission	*Study population*		**RR 0.70**	106	●○○○
Post-treatment – ITT[23]	883 per 1000	583 per 1000 (450, 758)	**(0.54, 0.91)**	(2 RCTs)[29]	Very low (d,e)
HRSD > 7 or HRSD > 8	*Moderate*				
(6 weeks)	823 per 1000	576 per 1000 (444, 749)			
Non-remission	*Study population*		RR 0.51	33	●●○○
Post-treatment – available case analysis[25]	778 per 1000	397 per 1000 (202, 778)	(0.26, 1.00)		Low (d)

[21] Molyneaux 2014 (Hantsoo 2014, Bloch 2012 and Yonkers 2008). In NICE 2015, the results for Bloch 2012 (SSRIs + psychotherapy versus placebo + psychotherapy) were assessed separately.
[22] Molyneaux 2014 (Hantsoo 2014 and Yonkers 2008). Excludes the Bloch 2012 study (SSRIs + psychotherapy versus placebo + psychotherapy).
[23] Method of ITT unclear.
[24] NICE 2015 (Hantsoo 2014 and Yonkers 2008).
[25] Completers: participants with at least three post-randomisation assessments.
[26] NICE 2015 (Hantsoo 2014).
[27] Molyneaux 2014 (Hantsoo 2014, Bloch 2012 and Yonkers 2008). In NICE 2015, the results for Bloch 2012 (SSRIs + psychotherapy versus placebo + psychotherapy) were assessed separately.
[28] Molyneaux 2014 (Hantsoo 2014 and Yonkers 2008). Excludes the Bloch 2012 study (SSRIs + psychotherapy versus placebo + psychotherapy).
[29] NICE 2015 (Hantsoo 2014 and Yonkers 2008).

Outcomes (follow-up)	Illustrative comparative risks*		Relative effect (95% CI)	No. of participants (studies)	Certainty of the evidence (GRADE)
	Assumed risk Control	Corresponding risk Intervention			
Response					
HRSD > 7 (6 weeks)	*Moderate*			(1 RCT)[30]	
	778 per 1000	397 per 1000 (202, 778)			
Depression mean scores					
Depression mean scores Post-treatment – available case analysis HRSD (6 weeks)	SMD -0.6 (-1.33, 0.12)		-	31 (1 RCT)[31]	●○○○ Very low (e,f)
Global severity and improvement mean scores					
Global severity mean scores Post-treatment – available case analysis CGI (8 weeks)	**SMD -0.9** **(-1.65, -0.16)**		-	31 (1 RCT)[32]	●●○○ Low (d,e)
Adverse events					
Decreased appetite Post-treatment – available case analysis (8 weeks)	*Study population*		RR 1.50 (0.27, 8.43)	70 (1 RCT)[33]	●○○○ Very low (e,f)
	57 per 1000	86 per 1000 (15, 482)			
	Moderate				
	57 per 1000	85 per 1000 (15, 481)			
Diarrhoea Post-treatment – available case analysis (6-8 weeks)	*Study population*		RR 1.02 (0.32, 3.30)	106 (2 RCTs)[34]	●○○○ Very low (e,f)
	93 per 1000	94 per 1000 (30, 306)			
	Moderate				
	84 per 1000	86 per 1000 (27, 277)			
Dizziness Post-treatment – available case analysis (8 weeks)	*Study population*		RR 2.00 (0.54, 7.37)	70 (1 RCT)[35]	●○○○ Very low (e,f))
	86 per 1000	171 per 1000 (46, 632)			
	Moderate				
	86 per 1000	172 per 1000 (46, 632)			
Headache Post-treatment – available case analysis (6-8 weeks)	*Study population*		RR 0.75 (0.37, 1.49)	106 (2 RCTs)[36]	●○○○ Very low (e,f)
	241 per 1000	181 per 1000 (89, 359)			
	Moderate				
	186 per 1000	140 per 1000 (69, 277)			
Nausea Post-treatment – available case analysis (6-8 weeks)	*Study population*		RR 0.97 (0.35, 2.71)	106 (2 RCTs)[37]	●○○○ Very low (e,f)
	111 per 1000	108 per 1000 (39, 301)			
	Moderate				
	86 per 1000	83 per 1000 (30, 233)			

[30] NICE 2015 (Hantsoo 2014).
[31] NICE 2015 (Yonkers 2008).
[32] NICE 2015 (Yonkers 2008).
[33] NICE 2015 (Yonkers 2008).
[34] NICE 2015 (Hantsoo 2014 and Yonkers 2008).
[35] NICE 2015 (Yonkers 2008).
[36] NICE 2015 (Hantsoo 2014 and Yonkers 2008).
[37] NICE 2015 (Hantsoo 2014 and Yonkers 2008).

Outcomes (follow-up)	Illustrative comparative risks*		Relative effect (95% CI)	No. of participants (studies)	Certainty of the evidence (GRADE)
	Assumed risk Control	Corresponding risk Intervention			
Response					
Somnolence Post-treatment – available case analysis (8 weeks)	*Study population*		RR 1.00 (0.32, 3.15)	70 (1 RCT)[38]	⨁◯◯◯ Very low (e,f)
	143 per 1000	143 per 1000 (46, 450)			
	Moderate				
	143 per 1000	143 per 1000 (46, 450)			
Dry mouth Post-treatment – available case analysis (8 weeks)	*Study population*		RR 9.00 (0.5, 161)	70 (1 RCT)[39]	⨁◯◯◯ Very low (e,f)
	0 per 1000	0 per 1000 (0, 0)			
	Moderate				
	0 per 1000	0 per 1000 (0, 0)			

Evidence Statements:

Treatment with an SSRI may improve response rate at 6-8 weeks post-treatment compared with placebo, in women with postnatal depression, from a rate of 37% to 52% (very low certainty evidence).

Treatment with an SSRI may improve remission rate at 6-8 weeks post-treatment compared with placebo, in women with postnatal depression, from a rate of 26% to 46% (very low certainty evidence).

Treatment with an SSRI appears to have no effect on depression mean score at 6 weeks post-treatment compared with placebo, in women with postnatal depression (very low certainty evidence).

Treatment with an SSRI may improve global severity mean score at 6 weeks post-treatment compared with placebo, in women with postnatal depression (very low certainty evidence).

Treatment with an SSRI does not appear to be associated with an increased risk of maternal adverse events at 6-8 weeks post-treatment compared with placebo, in women with postnatal depression (very low certainty evidence).

Footnotes:

* The 'assumed risk' for the study population is calculated using the mean baseline risk from the studies in the meta-analysis (i.e. total number of events in the control/comparison group divided by the total number of patients in the control/comparison group). The moderate risk scenario is calculated using the median control/comparison group risk from the studies in the meta-analysis. The 'corresponding risk' (and its 95% CI) is based on the assumed risk in the control/comparison group and the relative effect of the intervention (and its 95% CI).

a. Downgraded due to indirectness (in one of the studies included in the meta-analysis participants in both arms additionally received brief dynamic psychotherapy).

b. Downgraded due to risk of bias (incomplete outcome data owing to loss to follow-up)

c. Downgraded due to high imprecision (wide confidence intervals owing to the small number and small samples of included studies)

d. Total population size is less than 400 (a threshold rule-of-thumb).

e. Risk of bias due to high attrition.

f. Total population size is less than 400 (a threshold rule-of-thumb) and 95% CI crosses both line of no effect and measure of appreciable benefit or harm (SMD -0.5/0.5 or RR 0.75/1.25).

Source: Molyneaux 2014 – SoF table (p4-5) and Table 1; NICE 2015 – Table 291, table 294, Table 302 and Table 313.

Abbreviations: CGI, Clinical Global Impression scale; CGI-I, Clinical Global Impression – Improvement scale; CI, confidence interval; HRSD, Hamilton Rating Scale for Depression; ITT, intention-to-treat; PND, postnatal depression; RCT, randomized controlled trial; RR, relative risk; SMD, standardised mean difference; SSRI, selective serotonin reuptake inhibitor.

[38] NICE 2015 (Yonkers 2008).

[39] NICE 2015 (Yonkers 2008).

Table C3-32 Summary of findings (treatment) – SSRIs + psychological interventions versus placebo + psychological interventions

Outcomes (follow-up)	Illustrative comparative risks*		Relative effect (95% CI)	No. of participants (studies)	Certainty of the evidence (GRADE)
	Assumed risk Control	Corresponding risk Intervention			
Response					
Non-response to treatment Post-treatment – ITT analysis[40] MADRS or EPDS > 50% (8 weeks)	*Study population*		RR 0.60 (0.27, 1.32)	42 (1 RCT)[41]	●●○○ Low (a)
	500 per 1000	300 per 1000 (135, 660)			
	Moderate				
	500 per 1000	300 per 1000 (135, 660)			
Remission					
Non-remission to treatment Post-treatment – ITT analysis[40] (8 weeks)	*Study population*		RR 0.64 (0.32, 1.30)	42 (1 RCT)[42]	●●○○ Low (a)
	545 per 1000	349 per 1000 (175, 709)			
	Moderate				
	546 per 1000	349 per 1000 (175, 710)			
Depression mean scores					
Depression mean scores Post-treatment – ITT analysis EPDS (8-12 weeks)	**SMD -0.42 (-0.77, -0.07)**		-	127 (2 RCTs)[43]	●●○○ Low (b,c)
Depression mean scores Post-treatment – available case analysis EPDS (12 weeks)	**SMD -0.56 (-1.07, -0.04)**		-	61 (1 RCT)[44]	●●○○ Low (b,c)
Global severity					
Global severity mean scores Post-treatment – ITT analysis CGI (8 weeks)	**SMD -1.37 (-2.06, -0.67)**		-	40 (1 RCT)[45]	●●●○ Moderate (c)
Global improvement mean scores Post-treatment – ITT CGI (8 weeks)	SMD -0.29 (-0.91, 0.33)		-	40 (1 RCT)[46]	●●○○ Low (d)
Distress					
Distress mean scores Post-treatment – ITT analysis Mental Health Inventory (8 weeks)	SMD -0.15 (-0.77, 0.47)		-	40 (1 RCT)[47]	●●○○ Low (d)

[40] Calculated based on LOCF and WCS for those not included in LOCF.
[41] NICE 2015 (Bloch 2012). Bloch 2012 included in 'versus placebo' analysis in Molyneaux 2014 SR.
[42] NICE 2015 (Bloch 2012). Bloch 2012 included in 'versus placebo' analysis in Molyneaux 2014 SR.
[43] NICE 2015 (Bloch 2012 and Appleby 1997).
[44] NICE 2015 (Appleby 1997).
[45] NICE 2015 (Bloch 2012).
[46] NICE 2015 (Bloch 2012).
[47] NICE 2015 (Bloch 2012).

Outcomes (follow-up)	Illustrative comparative risks*		Relative effect (95% CI)	No. of participants (studies)	Certainty of the evidence (GRADE)
	Assumed risk Control	Corresponding risk Intervention			
Evidence Statement: *Treatment with an SSRI plus a psychological intervention appears to have no effect on response rate at 8 weeks post-treatment compared with placebo plus a psychological intervention, in women with postnatal depression (low certainty evidence).* *Treatment with an SSRI plus a psychological intervention appears to have no effect on remission rate at 8 weeks post-treatment compared with placebo plus a psychological intervention, in women with postnatal depression (low certainty evidence).* *Treatment with an SSRI plus a psychological intervention for postnatal depression may improve depression mean score at 8-12 weeks post-treatment compared with placebo plus a psychological intervention, in women with postnatal depression (low certainty evidence).* *Treatment with an SSRI plus a psychological intervention improves global severity mean score at 8 weeks post-treatment compared with placebo plus a psychological intervention, in women with postnatal depression (moderate certainty evidence).* *Treatment with an SSRI plus a psychological intervention appears to have no effect on distress mean score at 8 weeks post-treatment compared with placebo plus a psychological intervention, in women with postnatal depression (low certainty evidence).*					

Footnotes:

* The 'assumed risk' for the study population is calculated using the mean baseline risk from the studies in the meta-analysis (i.e. total number of events in the control/comparison group divided by the total number of patients in the control/comparison group). The moderate risk scenario is calculated using the median control/comparison group risk from the studies in the meta-analysis. The 'corresponding risk' (and its 95% CI) is based on the assumed risk in the control/comparison group and the relative effect of the intervention (and its 95% CI).

a. Number of events is less than 300 (a threshold rule of thumb) and 95% CI crosses both line of no effect and measure of appreciable benefit or harm (SMD -0.5/0.5 or RR 0.75/1.25).

b. Risk of bias due to high and unbalanced attrition rate.

c. Total population size is less than 400 (a threshold rule-of-thumb).

d. Total population size is less than 400 (a threshold rule-of-thumb) and 95% CI crosses both line of no effect and measure of appreciable benefit or harm (SMD -0.5/0.5 or RR 0.75/1.25).

Source: NICE 2015 – Table 292, Table 296 and Table 301.

Abbreviations: CI, confidence interval; EPDS, Edinburgh Postnatal Depression Scale; ITT, intention-to-treat; LOCF, last observation carried forward; MADRS, Montgomery–Åsberg Depression Rating Scale; RCT, randomized controlled trial; RR, relative risk; SSRI, selective serotonin reuptake inhibitor; WCS, worst case scenario.

Table C3-33 Summary of findings (treatment) – SSRIs versus TCAs

Outcomes (follow-up)	Illustrative comparative risks*		Relative effect (95% CI)	No. of participants (studies)	Certainty of the evidence (GRADE)
	Assumed risk Control	Corresponding risk Intervention			
Response					
Response rate at post-treatment	*Study population*		RR 0.82	109	●○○○
Post-treatment	685 per 1000	562 per 1000 (418, 754)	(0.61, 1.10)	(1 RCT)[48]	Very low (a,b)
As defined in individual study	*Moderate*				
(8 weeks)	NR	NR			
Non-response to treatment	*Study population*		RR 1.39	109	●○○○
Post-treatment – ITT analysis	315 per 1000	438 per 1000 (264, 715)	(0.84, 2.27)	(1 RCT)[49]	Very low (c,d)
HRSD < 50% reduction	*Moderate*				
(8 weeks)	315 per 1000	438 per 1000 (265, 715)			
Non-response to treatment	*Study population*		RR 2.81	29	●○○○
Intermediate follow-up – available case analysis	0 per 1000	0 per 1000 (0, 0)	(0.12, 63.8)	(1 RCT)[49]	Very low (c,d)
HRSD < 50% reduction	*Moderate*				
(22 weeks post-intervention)	0 per 1000	0 per 1000 (0, 0)			
Remission					
Remission rate at post-treatment	*Study population*		RR 0.94	109	●○○○
Post-treatment	481 per 1000	452 per 1000 (303, 678)	(0.63, 1.41)	(1 RCT)[50]	Very low (a,b)
As defined in individual study	*Moderate*				
(8 weeks)	NR	NR			
Non-remission to treatment	*Study population*		RR 1.05	109	●○○○
Post-treatment – ITT analysis	519 per 1000	544 per 1000 (384, 778)	(0.74, 1.50)	(1 RCT)[49]	Very low (c,d)
HRSD > 7	*Moderate*				
(8 weeks)	519 per 1000	545 per 1000 (384, 779)			
Non-remission to treatment	*Study population*		RR 1.24	29	●○○○
Post-treat Intermediate follow-up – available case analysis	214 per 1000	266 per 1000 (73, 986)	(0.34, 4.64)	(1 RCT)[49]	Very low (c,d)
HRSD > 7	*Moderate*				
(22 weeks post-intervention)	214 per 1000	265 per 1000 (73, 984)			
Depression symptomatology					
Depression mean scores	SMD 0.03 (-0.40, 0.47)		-	83	●●○○
Post-treatment - available case analysis				(1 RCT)[49]	Low (c,e)
HRSD					
(8 weeks)					
Depression mean scores	SMD 0.20 (-0.53, 0.93)		-	29	●○○○
Intermediate follow-up - available case analysis				(1 RCT)[51]	Very low (c,d)
HRSD					
(22 weeks post-intervention)					

[48] Molyneaux 2014 (Wisner 2006).
[49] NICE 2015 (Wisner 2006).
[50] Molyneaux 2014 (Wisner 2006).
[51] NICE 2015 (Wisner 2006).

Outcomes (follow-up)	Illustrative comparative risks*		Relative effect (95% CI)	No. of participants (studies)	Certainty of the evidence (GRADE)
	Assumed risk Control	Corresponding risk Intervention			
Global assessment of functioning					
Global assessment of functioning mean score Post-treatment – available case analysis Global Assessment Scale (8 weeks)	SMD 0.06 (-0.38, 0.49)		-	83 (1 RCT)[51]	●●○○ Low (b)
Global assessment of functioning mean score Intermediate follow-up – available case analysis Global Assessment Scale (22 weeks)	SMD 0.03 (-0.69, 0.76)		-	29 (1 RCT)[51]	●●○○ Low (b)
Social problems					
Social problems Post-treatment – available case analysis Social problems questionnaire (8 weeks)	*Study population*		RR 0.91 (0.57, 1.45)	83 (1 RCT)[51]	●●○○ Low (b)
	489 per 1000	445 per 1000 (279, 710)			
	Moderate				
	489 per 1000	445 per 1000 (279, 710)			
Social problems Intermediate follow-up – available case analysis Social problems questionnaire (22 weeks)	*Study population*		RR 0.93 (0.29, 3.03)	29 (1 RCT)[51]	●●○○ Low (b)
	286 per 1000	266 per 1000 (83, 866)			
	Moderate				
	286 per 1000	266 per 1000 (83, 867)			
Global severity and improvement symptomatology					
Global severity and improvement symptomology Post-treatment – available case analysis CGI ≥ 4 (8 weeks)	*Study population*		RR 0.65 (0.06, 6.92)	83 (1 RCT)[51]	●●○○ Low (b)
	43 per 1000	28 per 1000 (3, 294)			
	Moderate				
	43 per 1000	28 per 1000 (3, 298)			

Evidence Statements:

Treatment with a SSRI appears to have no effect on response rate at 8 weeks or up to 22 weeks post-treatment compared with treatment with TCAs, in women with postnatal depression (very low certainty evidence).

Treatment with an SSRI appears to have no effect on remission rate at 8 weeks or up to 22 weeks post-treatment compared with treatment with TCAs, in women with postnatal depression (very low certainty evidence).

Treatment with an SSRI appears to have no effect on depression means at 8 weeks or up to 22 weeks post-treatment compared with treatment with TCAs, in women with postnatal depression (low certainty evidence).

Treatment with an SSRI appears to have no effect on global assessment of functioning means score at 8 weeks or up to 22 weeks post-treatment compared with treatment with TCAs, in women with postnatal depression (low certainty evidence).

Treatment with an SSRI appears to have no effect on social problems at 8 weeks or up to 22 weeks post-treatment compared with treatment with TCAs, in women with postnatal depression (low certainty evidence).

Treatment with an SSRI appears to have no effect on global severity and improvement symptomatology at 8 weeks post-treatment compared with treatment with TCAs, in women with postnatal depression (low certainty evidence).

Footnotes:

* The 'assumed risk' for the study population is calculated using the mean baseline risk from the studies in the meta-analysis (i.e. total number of events in the control/comparison group divided by the total number of patients in the control/comparison group). The moderate risk scenario is calculated using the median control/comparison group risk from the studies in the meta-analysis. The 'corresponding risk' (and its 95% CI) is based on the assumed risk in the control/comparison group and the relative effect of the intervention (and its 95% CI).

a. Downgraded due to risk of bias (incomplete outcome data owing to loss to follow-up)

b. Downgraded due to imprecision (only 1 study available for this comparison).

c. Risk of bias due to incomplete outcome data (discontinuation between groups unbalanced).

d. Total population size is less than 400 (a threshold rule-of-thumb) and 95% CI crosses both line of no effect and measure of appreciable benefit or harm (SMD -0.5/0.5 or RR 0.75/1.25).

e. Total population size is less than 400 (a threshold rule-of-thumb).

Source: Molyneaux 2014 – Table 3; NICE 2015 – Table 293, Table 205 and Table 300.

C3.4.2 Antipsychotics

No SRs or individual RCTs were identified that assessed the effect of antipsychotics on the treatment of antenatal or postnatal mental health problems or maternal side effects.

Table C3-34 Summary of findings (treatment) – antipsychotics

Evidence Statement: *There is no RCT evidence for antipsychotics as an intervention for women with mental health problems in the perinatal period.*

C3.4.3 Anticonvulsants

No SRs or individual RCTs were identified that assessed the effect of anticonvulsants on the treatment of antenatal or postnatal mental health problems or maternal side effects.

Table C3-35 Summary of findings (treatment) – anticonvulsants

Evidence Statement: *There is no RCT evidence for anticonvulsants as an intervention for women with mental health problems in the perinatal period.*

C3.4.4 Benzodiazepines and z-drugs

No SRs or individual RCTs were identified that assessed the effect of benzodiazepines and z-drugs on the treatment of antenatal or postnatal mental health problems or maternal side effects.

Table C3-36 Summary of findings (treatment) – benzodiazepines and z-drugs

Evidence Statement: *There is no RCT evidence for benzodiazepines and z-drugs as an intervention for women with mental health problems in the perinatal period.*

C3.4.5 Lithium

No SRs or individual RCTs were identified that assessed the effect of lithium on the treatment of antenatal or postnatal mental health problems or maternal side effects.

Table C3-37 Summary of findings (treatment) – lithium

Evidence Statement: *There is no RCT evidence for lithium as an intervention for women with mental health problems in the perinatal period.*

C3.5 TREATMENT WITH COMPLEMENTARY THERAPIES

C3.5.1 Omega-3 fatty acids

One comparison was available for the use of omega-3 fatty acids in perinatal depression in the foundation review by NICE 2015 – against placebo.

Table C3-38 summarises the evidence and provides Evidence Statements relating to the comparison between omega-3 fatty acids and placebo. Three of the four RCTs included in the NICE 2015 SR examined different ratios of EPA and DHA (Mozurkewich 2013 [0.2:1], Freeman 2008 [1.4:1] and Su 2008 [1.8:1]), while the remaining study by Rees 2008 examined 'fish oil'. The analyses presented in NICE 2015 provide very low certainty evidence that treatment with omega- fatty acids does not appear to increase remission, reduce depression scores, or cause mild/transient side effects compared with placebo in women with perinatal depression. While there is also very-low-certainty evidence that treatment with omega-3 fatty acids does not increase response compared with placebo, the reduction in risk is substantial and the finding is close to being statistically significant (P=0.09).

Table C3-38 Summary of findings (treatment) – omega-3 fatty acids versus placebo

Outcomes (follow-up)	Illustrative comparative risks*		Relative effect (95% CI)	No. of participants (studies)	Certainty of the evidence (GRADE)
	Assumed risk Control	Corresponding risk Intervention			
Response					
Non-response to treatment Post treatment – ITT analysis HRSD < 50% reduction (8 weeks)	*Study population*		RR 0.67 (0.42, 1.06)	36 (1 RCT)[52]	●○○○ Very low (a,b)
	833 per 1000	558 per 1000 (350, 883)			
	Moderate				
	833 per 1000	558 per 1000 (350, 883)			
Non-response to treatment Post-treatment – available case analysis HRSD < 50% reduction (8 weeks)	*Study population*		RR 0.53 (0.24, 1.15)	24 (1 RCT)[52]	●○○○ Very low (a,b)
	727 per 1000	385 per 1000 (175, 836)			
	Moderate				
	727 per 1000	385 per 1000 (174, 836)			
Remission					
Non-remission to treatment Post-treatment – ITT analysis HRSD > 7 (8 weeks)	*Study population*		RR 0.81 (0.58, 1.13)	36 (1 RCT) [52]	●○○○ Very low (a,b)
	889 per 1000	720 per 1000 (516, 1000)			
	Moderate				
	889 per 1000	720 per 1000 (516, 1000)			

[52] NICE 2015 (Su 2008).

Outcomes (follow-up)	Illustrative comparative risks*		Relative effect (95% CI)	No. of participants (studies)	Certainty of the evidence (GRADE)
	Assumed risk Control	Corresponding risk Intervention			
Non-remission to treatment Post-treatment – available case analysis HRSD > 7 (8 weeks)	*Study population*		RR 0.75 (0.45, 1.26)	24 (1 RCT) [52]	⨁◯◯◯ Very low (a,b)
	818 per 1000	614 per 1000 (368, 1000)			
	Moderate				
	818 per 1000	614 per 1000 (368, 1000)			
Depression mean scores					
Depression mean scores Post treatment – ITT analysis EPDS or BDI (6-36 weeks)	SMD -0.08 (-0.61, 0.46)		-	228 (4 RCTs)[53]	⨁◯◯◯ Very low (a,b,c)
Adverse events					
Any mild/transient side effects Post-treatment – available case analysis (6-8 weeks)	*Study population*		RR 1.15 (0.64, 2.06)	118 (3 RCTs) [54]	⨁⨁◯◯ Low (b)
	246 per 1000	282 per 1000 (157, 506)			
	Moderate				
	NR	NR			

Evidence Statements:

Treatment with omega-3 fatty acids appears to have no effect on response rate at 8 weeks post-treatment compared with placebo, in women with antenatal or postnatal depression (very low certainty evidence).

Treatment with omega-3 fatty acids appears to have no effect on remission rate at 8 weeks post-treatment compared with placebo, in women with antenatal or postnatal depression (very low certainty evidence).

Treatment with omega-3 fatty acids appears to have no effect on depression mean score at 6-36 weeks post-treatment compared with placebo, in women with antenatal or postnatal depression (very low certainty evidence).

Treatment with omega-3 fatty acids does not appear to be associated with an increased risk of mild/transient side effects at 6-8 weeks post-treatment compared with placebo, in antenatal or postnatal depression (very low certainty evidence).

Footnotes:

* The 'assumed risk' for the study population is calculated using the mean baseline risk from the studies in the meta-analysis (i.e. total number of events in the control/comparison group divided by the total number of patients in the control/comparison group). The moderate risk scenario is calculated using the median control/comparison group risk from the studies in the meta-analysis. The 'corresponding risk' (and its 95% CI) is based on the assumed risk in the control/comparison group and the relative effect of the intervention (and its 95% CI).

a. Risk of bias due to unclear selection bias, detection bias and attrition bias.

b. Total population size is less than 400 (a threshold rule-of-thumb) and 95% CI crosses both line of no effect and measure of appreciable benefit or harm (SMD -0.5/0.5 or RR 0.75/1.25).

c. There was evidence of substantial heterogeneity between effect sizes

Source: NICE 2015 – Table 290 and Table 312.

Abbreviations: CI, confidence interval; BDI, Beck Depression Inventory; EPDS, Edinburgh Postnatal Depression Scale; HRSD, Hamilton Rating Scale for Depression; PND, postnatal depression; RCT, randomised controlled trial; RR, relative risk; SMD, standardised mean difference.

C3.5.2 St John's wort

No SRs or individual RCTs were identified that assessed the effectiveness of St John's wort on the treatment of antenatal or postnatal mental health problems.

[53] NICE 2015 (meta-analysis of data from Rees 2008, Su 2008, Freeman 2008 and Mozurkewich 2013).

[54] NICE 2015 (meta-analysis of data from Rees 2008, Su 2008 and Freeman 2008).

Table C3-39 Summary of findings (treatment) – St John's wort

Evidence Statement:
There is no RCT evidence for St John's wort as an intervention for women with mental health problems in the perinatal period.

C3.5.3 Gingko biloba

No SRs or individual RCTs were identified that assessed the effectiveness of gingko biloba on the treatment of antenatal or postnatal mental health problems.

Table C3-40 Summary of findings (treatment) – gingko biloba

Evidence Statement:
There is no RCT evidence for gingko biloba as an intervention for women with mental health problems in the perinatal period.

C3.6 TREATMENT WITH PHYSICAL INTERVENTIONS

C3.6.1 Exercise

Of the three SRs identified in the literature search, NICE 2015 was chosen as the foundation review due to its currency and high quality. NICE 2015 included three RCTs that compared physical activity with treatment as usual, and one RCT that compared physical activity with a mutual support group. The NICE 2015 SR did not separate out different forms of physical activity (i.e. yoga was analysed with other types of exercise interventions).

Of the three RCTs that compared physical activity with treatment as usual, there were two RCTs from the United Kingdom that examined the effect of exercise consultations on postpartum women. One RCT (N=38) assessed individual exercise consultations in the home setting (with follow-up support calls) in women with symptoms of depression (>12 on the EPDS), while the other RCT (N=94) assessed individual and group exercise consultations with support follow-up calls in women with a diagnosis of MDD. A third RCT from the United States (N=92) compared group tai-chi/yoga, specifically designed for women in their second and third trimester of pregnancy, with waitlist control in pregnant women who met diagnostic criteria for depression.

NICE 2015 also included an Australian RCT that compared a 12-week group pram walking exercise program with a 12-week mutual support group in postpartum women with symptoms of depression (N=24). The mutual support group was facilitated by a nurse/social worker and involved unstructured discussion for social and emotional but not practical support.

C3.6.1.1 Physical interventions versus treatment as usual

NICE 2015 did not consider the timing or format of the intervention in their analyses.

There was no evidence for a statistically or clinically meaningful effect of physical activity on mean depression scores at the end of the intervention, although the effect favoured physical activity compared with control (**Table C3-41**). There was no statistically or clinically significant effect of physical activity on mean anxiety scores.

Table C3-41 Summary of findings (treatment) – physical activity versus treatment as usual

Outcomes (follow-up)	Illustrative comparative risks*		Relative effect (95% CI)	No. of participants (studies)	Certainty of the evidence (GRADE)
	Assumed risk Control	Corresponding risk Intervention			
Depression mean scores					
Post-intervention, first available endpoint data – available case analysis Follow-up: 12-26 weeks	SMD -0.23 (-0.52, 0.05)		-	191 (3 studies)	⨁⨁◯◯ Low (a,b)
Anxiety mean scores					
Post-treatment (0-9 weeks) – available case analysis	SMD 0.18 (-0.27, 0.63)		-	75 (1 study)	⨁◯◯◯ Very low (a,b)
Evidence Statements: *Physical activity (individual and group exercise consultations or Tai Chi/yoga) appears to have no effect on depression mean scores at endpoint or first measurement (low certainty evidence) compared with treatment as usual in pregnant or postpartum women who have a diagnosis of depression or symptoms of depression.* *Group physical activity (Tai Chi/yoga) appears to have no effect on anxiety mean scores at endpoint or first measurement (very low certainty evidence) compared with waitlist control in pregnant women who met diagnostic criteria for depression.*					
Footnotes: * The 'assumed risk' for the *study population* is calculated using the mean baseline risk from the studies in the meta-analysis (i.e. total number of events in the control/comparison group divided by the total number of patients in the control/comparison group). The *moderate* risk scenario is calculated using the median control/comparison group risk from the studies in the meta-analysis. The 'corresponding risk' (and its 95% CI) is based on the assumed risk in the control/comparison group and the relative effect of the intervention (and its 95% CI). a. Unclear risk of bias in several domains b. 95% CI crosses both line of no effect and measure of appreciable benefit or harm (SMD -0.5/0.5) or RR 0.75/1.25 and optimal information size (400 participants) not met.					

Source: NICE 2015, Table 349

Abbreviations: CI, confidence interval; RR, relative risk; SMD, standardised mean difference.

C3.6.1.2 Physical activity versus mutual support

There was very low quality, single-study evidence for a large beneficial effect of physical activity compared with mutual support on mean depression scores at post-treatment and at short-term follow-up (**Table C3-42**). However, the confidence in this estimate was very low due to serious imprecision (very small population size) and risk of bias in several domains.

Table C3-42 Summary of findings (treatment) – physical activity versus mutual support

Outcomes (follow-up)	Illustrative comparative risks*		Relative effect (95% CI)	No. of participants (studies)	Certainty of the evidence (GRADE)
	Assumed risk Control	Corresponding risk Intervention			
Depression mean scores					
Post-treatment, 0-9 weeks – available case analysis	**SMD -1.05 (-2.02, -0.07)**		-	19 (1 study)	●○○○ Very low (a,b)
Short-term follow-up, 9-16 weeks – available case analysis	**SMD -1.09 (-2.07, -0.11)**		-	19 (1 study)	●○○○ Very low (a,b)
Evidence Statement: *Physical activity (pram walking exercise program) may improve depression mean scores at endpoint or first measurement (very low certainty evidence), and at short follow-up (9-16 weeks post-intervention) (very low certainty evidence) compared with mutual support group in postpartum women with symptoms of depression.*					

Footnotes:
* The 'assumed risk' for the *study population* is calculated using the mean baseline risk from the studies in the meta-analysis (i.e. total number of events in the control/comparison group divided by the total number of patients in the control/comparison group). The *moderate* risk scenario is calculated using the median control/comparison group risk from the studies in the meta-analysis. The 'corresponding risk' (and its 95% CI) is based on the assumed risk in the control/comparison group and the relative effect of the intervention (and its 95% CI).
a. Risk of bias in several domains
b. Optimal information size for dichotomous outcomes (300 events) and for continuous outcomes (400 participants) not met.

Source: NICE 2015, Table 349
Abbreviations: CI, confidence interval; RR, relative risk; SMD, standardised mean difference.

C3.6.2 Yoga

Of the two SRs identified in the literature search, Gong 2015 was chosen as the foundation review due to its currency and comprehensiveness. Gong 2015 included four RCTs that assessed yoga in pregnant women with a diagnosis of depression. Three RCTs (N=200) compared the effect of 12 weeks of exercise-based yoga with a control group that involved massage and standard prenatal care, parenting education sessions, or a social support group. The fourth RCT (N=92) compared 12 weeks of integrated yoga (yoga with Tai Chi) with a social support group.

One RCT that was not included in Gong 2015 was identified in another SR. The RCT (Vieten 2008) assessed an eight-week mindfulness intervention that incorporated experiential exercises and was facilitated by a licensed clinical psychologist trained in mindfulness-based interventions, as well as a certified prenatal yoga instructor. This RCT, which reported no benefits of the intervention on depression or anxiety symptoms, is included in the current report as a mindfulness intervention (see **Section C3.1.12**.)

C3.6.2.1 Yoga versus control group

Overall, there was a statistically significant reduction in depressive symptoms in the yoga group compared with control (**Table C3-43**); however, this reduction may not be clinically significant. Results of the subgroup analyses showed that exercise-based yoga did not significantly reduce depression symptoms relative to control, whereas integrated yoga appeared to have a beneficial effect (based on one RCT).

Table C3-43 Summary of findings (treatment) – yoga versus control group

Outcomes (follow-up)	Illustrative comparative risks*		Relative effect (95% CI)	No. of participants (studies)	Certainty of the evidence (GRADE)**
	Assumed risk Control	Corresponding risk Intervention			
Depression mean scores					
Post-treatment – available case analysis All studies of women with depressive symptoms CES-D	**SMD -0.46 (-0.90, -0.03)**		-	208 (4 studies)	●○○○ Very low
Post-treatment – available case analysis Subgroup analysis – exercise-based yoga CES-D	SMD -0.41 (-1.01, 0.18)		-	159 (3 studies)	●○○○ Very low
Post-treatment – available case analysis Subgroup analysis – integrated yoga CES-D	**SMD -0.64 (-1.11, -0.18)**		-	75 (1 study)	●○○○ Very low
Evidence Statements: *Exercise-based yoga appears to have no effect on depression mean scores at endpoint or first measurement (very low certainty evidence) compared with a control group (massage and standard prenatal care, parenting education sessions, or a social support group) in pregnant women with a diagnosis of depression.* *Integrated yoga (with Tai Chi) may improve depression mean scores at endpoint or first measurement (very low certainty evidence) compared with a social support group in pregnant women with a diagnosis of depression.*					
Footnotes: * The 'assumed risk' for the *study population* is calculated using the mean baseline risk from the studies in the meta-analysis (i.e. total number of events in the control/comparison group divided by the total number of patients in the control/comparison group). The *moderate* risk scenario is calculated using the median control/comparison group risk from the studies in the meta-analysis. The 'corresponding risk' (and its 95% CI) is based on the assumed risk in the control/comparison group and the relative effect of the intervention (and its 95% CI). ** Risk of bias was assessed in Gong 2015 and was translated for the purposes of this report into a GRADE quality of the evidence rating. For each quality criteria rated by Gong 2015 as 'unclear', the evidence was downgraded.					

Source: Gong 2015, Figure 3, Figure 4

Abbreviations: CI, confidence interval; RR, relative risk; SMD, standardised mean difference.

C3.6.3 Acupuncture

Of the three SRs identified in the literature search, NICE 2015 was chosen as the foundation review due to its currency, high quality and comprehensiveness. NICE 2015 included two RCTS from the United States (N=210) that compared depression-specific acupuncture with non-depression specific acupuncture and with massage in pregnant women with a diagnosis of MDD. NICE 2015 also included one RCT from China (Chung 2012; N=20) that compared electro-acupuncture with non-invasive sham acupuncture in postpartum women with a diagnosis of MDD.

C3.6.3.1 Acupuncture versus massage

There was no statistically or clinically significant difference in effect for acupuncture compared with massage on depression outcomes at post-treatment (**Table C3-44**).

There was no statistically or clinically significant difference in effect for acupuncture (depression and non-depression specific acupuncture combined) compared with massage on mean depression scores at post-treatment or short term follow-up. There was very low certainty evidence for a moderate beneficial effect of acupuncture compared with massage on depression diagnosis at short term follow-up; however, this was not statistically significant and the confidence in the estimate of the effect is low due to very serious imprecision.

Table C3-44 Summary of findings (treatment) – acupuncture versus massage

Outcomes (follow-up)	Illustrative comparative risks*		Relative effect (95% CI)	No. of participants (studies)	Certainty of the evidence (GRADE)
	Assumed risk Control	Corresponding risk Intervention			
Non-response to treatment					
HRSD >=14 and >=50% reduction from baseline Post-treatment (0-8 weeks)	*Study population*		RR 0.8 (0.54, 1.19)	188 (2 studies)	⨁◯◯◯ Very low (a,b)
	442 per 1000 (298, 657)	355 per 1000 (224, 562)			
	Moderate				
	466 per 1000 (315, 694)	379 per 1000 (239, 600)			
Depression diagnosis					
Above depression threshold (DSM-IV) Short term follow-up (9-16 weeks) – available case analysis	*Study population*		RR 0.44 (0.09, 2.13)	46 (1 study)	⨁◯◯◯ Very low (a,b)
	286 per 1000	71 per 1000 (9, 660)			
	Moderate				
	286 per 1000	72 per 1000 (9, 661)			
Depression mean scores					
Post-treatment (0-8 weeks) – available case analysis	SMD 0.19 (-0.47, 0.85)		-	54 (1 study)	⨁◯◯◯ Very low (a,b)
Short term follow-up (9-16 weeks) – available case analysis	SMD -0.16 (-0.77, 0.45)		-	49 (1 study)	⨁◯◯◯ Very low (a,b)

Evidence Statements:

Acupuncture appears to have no effect on response to treatment (measured using the HRSD) at endpoint or first measurement (very low certainty evidence), compared with massage in pregnant women with a diagnosis of MDD.

Acupuncture appears to have no effect on depression diagnosis at short follow-up (9-16 weeks post-intervention) (very low certainty evidence), and appears to have no effect on depression mean scores at endpoint or first measurement (very low certainty evidence), or at short follow-up (9-16 weeks post-intervention) (very low certainty evidence), compared with massage in pregnant women with a diagnosis of MDD.

Footnotes:

* The 'assumed risk' for the *study population* is calculated using the mean baseline risk from the studies in the meta-analysis (i.e. total number of events in the control/comparison group divided by the total number of patients in the control/comparison group). The *moderate* risk scenario is calculated using the median control/comparison group risk from the studies in the meta-analysis. The 'corresponding risk' (and its 95% CI) is based on the assumed risk in the control/comparison group and the relative effect of the intervention (and its 95% CI).

a. Risk of bias in several domains

b. Optimal information size (for dichotomous outcomes, OIS=300 events; for continuous outcomes, OIS=400 participants) not met

Source: NICE 2015, Table 346, Table 351

Abbreviations: CI, confidence interval; MDD, major depressive disorder; RR, relative risk; SMD, standardised mean difference.

C3.6.3.2 Depression-specific acupuncture versus non-depression-specific acupuncture

There was very low certainty evidence from two studies for a moderate beneficial effect of depression-specific acupuncture post-treatment; however, the confidence in this estimate was very low due to serious imprecision and risk of bias in several domains (**Table C3-45**).

There was no statistically or clinically significant difference between depression-specific acupuncture and non-depression-specific acupuncture on mean depression scores at post-treatment or short-term follow-up. There was very low quality, single-study evidence for a moderate-to-large effect in the favour of depression-specific acupuncture on depression diagnosis at the end of intervention and at short term follow-up; however, these effects were not statistically significant and confidence in this estimate is very low due to very serious imprecision.

Table C3-45 Summary of findings (treatment) – depression-specific acupuncture versus non-depression-specific acupuncture

Outcomes (follow-up)	Illustrative comparative risks*		Relative effect (95% CI)	No. of participants (studies)	Certainty of the evidence (GRADE)
	Assumed risk Control	Corresponding risk Intervention			
Treatment non-response					
HRSD >=14 and >=50% reduction from baseline	*Study population*		**RR 0.59 (0.4, 0.88)**	121 (2 studies)	●○○○ Very low (a,b)
	593 per 1000	350 per 1000 (237, 522)			
	Moderate				
	576 per 1000	340 per 1000 (230, 507)			
Depression diagnosis					
Post-treatment (0-8 weeks) – available case	*Study population*		RR 0.47 (0.11, 2.13)	35 (1 study)	●○○○ Very low (a,b)
	263 per 1000	124 per 1000 (29, 561)			
	Moderate				
	263 per 1000	124 per 1000 (29, 560)			
Short term follow-up (9-16 weeks) – available case	*Study population*		RR 0.64 (0.06, 6.39)	32 (1 study)	●○○○ Very low (a,b)
	111 per 1000	71 per 1000 (7, 710)			
	Moderate				
	111 per 1000	71 per 1000 (7, 709)			
Depression mean scores					
Post-treatment (0-8 weeks) – available case	SMD -0.38 (-1.06, 0.29)		-	35 (1 study)	●○○○ Very low (a,b)
Short term follow-up (9-16 weeks) – available case	SMD -0.12 (-0.82, 0.57)		-	32 (1 study)	●○○○ Very low (a,b)

Evidence Statements:

Depression-specific acupuncture may improve response to treatment (measured using the HRSD) at endpoint or first measurement (very low certainty evidence) compared with non-depression-specific acupuncture in pregnant women with a diagnosis of MDD.

Depression-specific acupuncture appears to have no effect on depression diagnosis (very low certainty evidence) or depression mean scores (very low certainty evidence) at endpoint or first measurement, or at short follow-up (9-16 weeks post-intervention) compared with non-depression-specific acupuncture in pregnant women with a diagnosis of MDD.

Outcomes (follow-up)	Illustrative comparative risks*		Relative effect (95% CI)	No. of participants (studies)	Certainty of the evidence (GRADE)
	Assumed risk Control	Corresponding risk Intervention			
Footnotes: * The 'assumed risk' for the *study population* is calculated using the mean baseline risk from the studies in the meta-analysis (i.e. total number of events in the control/comparison group divided by the total number of patients in the control/comparison group). The *moderate* risk scenario is calculated using the median control/comparison group risk from the studies in the meta-analysis. The 'corresponding risk' (and its 95% CI) is based on the assumed risk in the control/comparison group and the relative effect of the intervention (and its 95% CI). a. Risk of bias in several domains b. Optimal information size (for dichotomous outcomes, OIS=300 events; for continuous outcomes, OIS=400 participants) not met.					

Source: NICE 2015, Table 347, Table 352

Abbreviations: CI, confidence interval; HRSD, Hamilton Rating Scale for Depression; MDD, major depressive disorder; RR, relative risk; SMD, standardised mean difference.

C3.6.3.3 Electroacupuncture versus non-invasive sham acupuncture

There was no statistically or clinically significant effect for electroacupuncture on mean depression scores or mean anxiety scores at post-treatment (**Table C3-46**).

Table C3-46 Summary of findings (treatment) – electroacupuncture versus non-invasive sham acupuncture

Outcomes (follow-up)	Illustrative comparative risks*		Relative effect (95% CI)	No. of participants (studies)	Certainty of the evidence (GRADE)
	Assumed risk Control	Corresponding risk Intervention			
Depression mean scores					
Post-treatment (0-8 weeks) – available case analysis	SMD -0.21 (-1.09, 0.67)			20 (1 study)	●○○○ Very low (a,b)
Anxiety mean scores					
Available case analysis	SMD -0.02 (-0.9, 0.85)			20 (1 study)	●○○○ Very low (a,b)
Evidence Statement: *Electroacupuncture appears to have no effect on depression mean scores at endpoint or first measurement (very low certainty evidence) compared with non-invasive sham acupuncture in postpartum women with a diagnosis of MDD.*					
Footnotes: * The 'assumed risk' for the *study population* is calculated using the mean baseline risk from the studies in the meta-analysis (i.e. total number of events in the control/comparison group divided by the total number of patients in the control/comparison group). The *moderate* risk scenario is calculated using the median control/comparison group risk from the studies in the meta-analysis. The 'corresponding risk' (and its 95% CI) is based on the assumed risk in the control/comparison group and the relative effect of the intervention (and its 95% CI). a. Risk of bias in several domains b. Optimal information size (for dichotomous outcomes, OIS=300 events; for continuous outcomes, OIS=400 participants) not met.					

Source: NICE 2015, Table 353, Table 358

Abbreviations: CI, confidence interval; MDD, major depressive disorder; SMD, standardised mean difference.

C3.6.4 Electroconvulsive therapy

No SRs or individual RCTs were identified that assessed the effect of ECT on the treatment of antenatal or postnatal mental health problems or maternal side effects.

Table C3-47 Summary of findings (treatment) – electroconvulsive therapy

Evidence Statement: *There is no RCT evidence for ECT as an intervention for women with mental health problems in the perinatal period.*

C3.6.5 Transcranial magnetic stimulation

No SRs or individual RCTs were identified that assessed the effect of TMS on the treatment of antenatal or postnatal mental health problems or maternal side effects.

Table C3-48 Summary of findings (treatment) – transcranial magnetic stimulation

Evidence Statement: *There is no RCT evidence for TMS as an intervention for women with mental health problems in the perinatal period.*

C4 RESULTS – PREVENTION

For the majority of psychosocial, psychological, physical and pharmacological interventions, the National Institute for Health and Care Excellence Clinical Guideline Number 192 (NICE 2015) was chosen as the foundation review, primarily due to its currency, comprehensiveness, and high quality. The EWG agreed that the current Review would reproduce the Summary of Findings (SoF) tables from NICE 2015 and that replication of data extraction tables, risk-of-bias assessment, or Evidence Profile (EP) tables was not required. Readers are referred to the NICE guideline CG192 and appendices for this information.

NICE 2015 did not specifically assess evidence relating to online (web-based or computer-based) interventions. As such, the current Evidence Review relied on other published SRs, together with a literature search update to identify recent RCTs not included in the published reviews. For all relevant RCTs relating to online interventions, a full assessment of the evidence was required, including data extraction, risk-of-bias assessment, and EP tables; these are available in the **Part C Appendix**. Evidence from additional SRs was used for cognitive behaviour and interpersonal therapies (CBT/IPT; prevention) and omega-3 fatty acids (prevention); the quality of the SR was assessed, the SR evidence was transcribed directly into an SoF table, and the certainty of the body of evidence was informed by the SR assessment of risk of bias of the individual studies.

C4.1 PREVENTION WITH PSYCHOSOCIAL INTERVENTIONS

C4.1.1 Psychoeducation

Of the three SRs of prevention using psychoeducation identified in the literature search, NICE 2015 was chosen as the foundation review due to its currency, high quality and comprehensiveness. NICE 2015 included three RCTs that compared psychologically informed psychoeducation interventions with treatment as usual or enhanced treatment as usual[55]. The intervention was administered antenatally in two RCTs, and both antenatally and postnatally in one RCT. In all RCTs, the intervention involved five or six sessions of face-to-face psychoeducation delivered to individuals (one RCT; setting not reported), a hospital group setting (one RCT), or both individuals and groups (one RCT; setting not reported).

Although the other SRs included several additional RCTs, these studies mainly assessed education on preparing for parenting and are captured in the section on non-mental-health-focused education and support (**Section C4.1.5**).

C4.1.1.1 Psychologically (CBT/IPT) informed psychoeducation versus treatment as usual or enhanced treatment as usual

NICE 2015 did not consider the timing of the intervention, format or mode of delivery in their analyses.

The evidence for psychologically (CBT/IPT) informed psychoeducation as a preventive intervention for women at-risk of developing postnatal depression was inconsistent (**Table C4-1**). There was evidence from three studies for moderate-to-large effects of psychoeducation on preventing depression diagnosis (P=0.08); however, the confidence in this effect estimate is low due to serious imprecision. This effect was also not maintained at intermediate follow-up. In addition, no

[55] Enhanced treatment as usual involved non-mental health-focused education and support in the form of a booklet.

clinically or statistically significant preventive effects were observed on depression symptomatology or depression mean symptoms at endpoint or intermediate follow-up.

Although there was evidence of higher attrition at endpoint (follow-up 26-27 weeks) in the intervention group relative to treatment as usual or enhanced treatment as usual, this effect was not statistically significant due to very serious imprecision.

Table C4-1 Summary of findings (prevention) – psychologically (CBT/IPT) informed psychoeducation versus treatment as usual or enhanced treatment as usual

Outcomes (follow-up)	Illustrative comparative risks*		Relative effect (95% CI)	No. of participants (studies)	Certainty of the evidence (GRADE)
	Assumed risk Control	Corresponding risk Intervention			
Depression diagnosis					
Post-treatment – ITT analysis (at-risk populations) SCAN, SCID or Structured Clinical Interview for Childhood Diagnoses (KID-SCID) (mean 27 weeks)	*Study population*		RR 0.69 (0.45, 1.05)	360 (3 studies)	⨁⨁◯◯ Low (a,b)
	229 per 1000	158 per 1000 (103, 241)			
	Moderate				
	333 per 1000	230 per 1000 (150, 350)			
Post-treatment – available case analysis (at-risk populations) SCAN, SCID or KIDSCID (mean 27 weeks)	*Study population*		RR 0.48 (0.23, 1.01)	320 (3 studies)	⨁⨁◯◯ Low (a,b)
	132 per 1000	63 per 1000 (30, 133)			
	Moderate				
	227 per 1000	109 per 1000 (52, 229)			
Intermediate follow-up (17-24 weeks post-intervention) – ITT analysis (at-risk populations) SCID (mean 20 weeks)	*Study population*		RR 0.77 (0.33, 1.75)	45 (1 study)	⨁⨁◯◯ Low (a,b)
	381 per 1000	293 per 1000 (126, 667)			
	Moderate				
	381 per 1000	293 per 1000 (126, 667)			
Intermediate follow-up (17-24 weeks post-intervention) – available case analysis (at-risk populations) SCID (mean 20 weeks)	*Study population*		RR 0.64 (0.17, 2.46)	37 (1 study)	⨁⨁◯◯ Low (a,b)
	235 per 1000	151 per 1000 (40, 579)			
	Moderate				
	235 per 1000	150 per 1000 (40, 578)			
Depression symptomatology					
Post-treatment – ITT analysis (at-risk populations) EPDS ≥11/12 (mean 27 weeks)	*Study population*		RR 0.85 (0.58, 1.25)	254 (2 studies)	⨁⨁◯◯ Low (a,b)
	299 per 1000	254 per 1000 (174, 374)			
	Moderate				
	370 per 1000	315 per 1000 (215, 462)			
Post-treatment – available case analysis (at-risk populations) EPDS ≥11/12 (mean 27 weeks)	*Study population*		RR 0.88 (0.49, 1.57)	221 (2 studies)	⨁⨁◯◯ Low (a,b)
	183 per 1000	161 per 1000 (90, 288)			
	Moderate				
	171 per 1000	150 per 1000 (84, 268)			
Intermediate follow-up (17-24 weeks post-intervention) – ITT analysis (at-risk populations) EPDS >12	*Study population*		RR 1.17 (0.62, 2.2)	45 (1 study)	⨁⨁◯◯ Low (a,b)
	429 per 1000	501 per 1000 (266, 943)			
	Moderate				

Outcomes (follow-up)	Illustrative comparative risks*		Relative effect (95% CI)	No. of participants (studies)	Certainty of the evidence (GRADE)
	Assumed risk Control	Corresponding risk Intervention			
(mean 20 weeks)	429 per 1000	502 per 1000 (266, 944)			
Intermediate follow-up (17-24 weeks post-intervention) – available case analysis (at-risk populations) EPDS >12 (mean 20 weeks)	*Study population*		RR 1 (0.24, 4.18)	30 (1 study)	●●○○ Low (a,b)
	200 per 1000	200 per 1000 (48, 836)			
	Moderate				
	200 per 1000	200 per 1000 (48, 836)			
Depression mean scores					
Post-treatment – available case analysis (at-risk populations) EPDS	SMD -0.06 (-0.75, 0.62)		-	33 (1 study)	●●○○ Low (a)
Intermediate follow-up (17-24 weeks post-intervention) – available case analysis (at-risk populations) EPDS (mean 20 weeks)	SMD -0.02 (-0.74, 0.7)		-	30 (1 study)	●●○○ Low (a,b)
Evidence Statements: ***CBT/IPT-informed psychoeducation*** *Psychologically (CBT/IPT) informed psychoeducation (individual, face-to-face) may have an effect[56] on depression diagnosis (low certainty evidence) but does not change depression symptomatology (low certainty evidence) at endpoint or first measurement compared with treatment as usual or enhanced treatment as usual in women who are considered to be 'at risk' of developing mental health problems in the perinatal period.* ***IPT-informed psychoeducation*** *IPT-informed psychoeducation (individual, face-to-face) appears to have no effect on depression diagnosis (low certainty evidence) or depression symptomatology (low certainty evidence) at intermediate follow-up (17-24 weeks post-intervention) compared with treatment as usual in women who are considered to be 'at risk' of developing mental health problems in the perinatal period.* *IPT-informed psychoeducation (individual, face-to-face) appears to have no effect on depression mean scores at endpoint or first measurement (low certainty evidence), or at intermediate follow-up (17-24 weeks post-intervention) (low certainty evidence), compared with treatment as usual in women who are considered to be 'at risk' of developing mental health problems in the perinatal period.*					
Footnotes: * The 'assumed risk' for the *study population* is calculated using the mean baseline risk from the studies in the meta-analysis (i.e. total number of events in the control/comparison group divided by the total number of patients in the control/comparison group). The *moderate* risk scenario is calculated using the median control/comparison group risk from the studies in the meta-analysis. The 'corresponding risk' (and its 95% CI) is based on the assumed risk in the control/comparison group and the relative effect of the intervention (and its 95% CI). a. Total number of events is less than 300 (a threshold rule-of-thumb) b. 95% CI crosses both line of no effect and measure of appreciable benefit or harm (SMD -0.5/0.5 or RR 0.75/1.25)					

Source: NICE 2015, Table 40

Abbreviations: CBT, cognitive behaviour therapy; CI, confidence interval; EPDS, Edinburgh Postnatal Depression Scale; IPT, interpersonal psychotherapy; ITT, intention-to-treat; KID-SCID, Structured Clinical Interview for Childhood Diagnoses; RR, relative risk; SCAN, Schedules for Clinical Assessment in Neuropsychiatry; SCID, Structured Clinical Interview for DSM Disorders; SMD, standardised mean difference.

C4.1.2 Psychoeducational booklet

Of the two SRs of prevention using psychoeducational booklet interventions identified in the literature search, NICE 2015 was chosen as the foundation review because individual study data was extracted and a meta-analysis was undertaken. NICE 2015 included two large RCTs from Australia and the United States that

[56] RR 0.69 (95% CI 0.45, 1.05); P=0.08

compared a psychoeducational booklet on PND with treatment as usual or enhanced treatment as usual[57]. In the Australian RCT the psychoeducational booklet was provided in hospital to pregnant women with psychosocial risk factors and a family history of mental health problems. In the RCT from the US, the intervention was a psychoeducational booklet and telephone support given to postpartum women with psychosocial risk factors.

One additional RCT from Taiwan was not included in NICE 2015 but the study was relatively small in terms of sample size (N=70). The authors of this study concluded that informational support given to women in the postnatal period may contribute to psychological wellbeing.

C4.1.2.1 Psychoeducational booklet versus treatment as usual or enhanced treatment as usual

NICE 2015 did not consider the timing of the intervention in their analyses.

Moderate-to-low certainty evidence from up to two studies does not provide convincing evidence that a psychoeducational booklet prevents depression symptomatology (**Table C4-2**).

Table C4-2 Summary of findings (prevention) – psychoeducational booklet versus treatment as usual or enhanced treatment as usual

Outcomes (follow-up)	Illustrative comparative risks*		Relative effect (95% CI)	No. of participants (studies)	Certainty of the evidence (GRADE)
	Assumed risk Control	Corresponding risk Intervention			
Depression symptomatology					
Post-treatment – ITT analysis (at-risk populations) EPDS ≥10/12 (mean 3 weeks)	*Study population*		RR 0.9 (0.79, 1.03)	1,140 (2 studies)	●●●○ Moderate (a)
	419 per 1000	377 per 1000 (331, 431)			
	Moderate				
	409 per 1000	368 per 1000 (323, 421)			
Post-treatment – available case analysis (at-risk populations) EPDS ≥10/12 (mean 3 weeks)	*Study population*		RR 0.73 (0.51, 1.06)	838 (2 studies)	●○○○ Very low (a,b,c)
	208 per 1000	152 per 1000 (106, 220)			
	Moderate				
	218 per 1000	159 per 1000 (111, 231)			
Short Follow-up (9-16 weeks post-intervention) – ITT analysis (at-risk populations) EPDS ≥10 (mean 13 weeks)	*Study population*		RR 0.88 (0.64, 1.23)	540 (1 study)	●●○○ Low (a,b)
	222 per 1000	196 per 1000 (142, 273)			
	Moderate				
	222 per 1000	195 per 1000 (142, 273)			
Short Follow-up (9-16 weeks post-intervention) – available case analysis (at-risk populations) EPDS ≥10 (mean 13 weeks)	*Study population*		RR 0.64 (0.38, 1.08)	479 (1 study)	●●○○ Low (b,c)
	132 per 1000	85 per 1000 (50, 143)			
	Moderate				
	132 per 1000	84 per 1000 (50, 143)			
Intermediate follow-up (17-24 weeks post-intervention) – ITT analysis (at-risk populations) EPDS ≥10 (mean 26 weeks)	*Study population*		RR 0.83 (0.65, 1.08)	540 (1 study)	●●○○ Low (b,c)
	333 per 1000	277 per 1000 (217, 360)			
	Moderate				
	333 per 1000	276 per 1000 (216, 360)			
	Study population		RR 0.64 (0.37, 1.1)	423 (1 study)	●●○○

[57] Enhanced treatment as usual involved non-mental health-focused education and support in the form of a booklet.

Outcomes (follow-up)	**Illustrative comparative risks***		**Relative effect (95% CI)**	**No. of participants (studies)**	**Certainty of the evidence (GRADE)**
	Assumed risk Control	**Corresponding risk Intervention**			
Intermediate follow-up (17-24 weeks post-intervention) – available case analysis (at-risk populations)	139 per 1000	89 per 1000 (51, 153)			Low (b,c)
	Moderate				
EPDS ≥10 (mean 26 weeks)	139 per 1000	89 per 1000 (51, 153)			
Evidence Statements: *A psychoeducational booklet has no effect on depression symptomatology at endpoint or first measurement (moderate certainty evidence) compared with treatment as usual or enhanced treatment as usual in pregnant or postpartum women who are considered to be 'at risk' of developing mental health problems in the perinatal period (psychosocial risk factors and/or a history of mental health problems).* *A psychoeducational booklet and telephone support appears to have no effect on depression symptomatology at short follow-up (9-16 weeks post-intervention) (low certainty evidence), or at intermediate follow-up (17-24 weeks post-intervention) (low certainty evidence), compared with enhanced treatment as usual (non-mental-health-focused education and support booklet) in postpartum women who are considered to be 'at risk' of developing mental health problems in the perinatal period (psychosocial risk factors).*					
Footnotes: * The 'assumed risk' for the study population is calculated using the mean baseline risk from the studies in the meta-analysis (i.e. total number of events in the control/comparison group divided by the total number of patients in the control/comparison group). The moderate risk scenario is calculated using the median control/comparison group risk from the studies in the meta-analysis. The 'corresponding risk' (and its 95% CI) is based on the assumed risk in the control/comparison group and the relative effect of the intervention (and its 95% CI). a. Risk of bias due to statistically significant group differences at baseline b. Total number of events is less than 300 (a threshold rule-of-thumb) c. 95% CI crosses both line of no effect and measure of appreciable benefit or harm (SMD -0.5/0.5 or RR 0.75/1.25)					

Source: NICE 2015, Table 41

Abbreviations: CI, confidence interval; EPDS, Edinburgh Postnatal Depression Scale; ITT, intention-to-treat; RR, relative risk; SMD, standardised mean difference.

C4.1.3 Social/peer support

Of the two SRs of prevention using social/peer support identified in the literature search, NICE 2015 was chosen as the foundation review because the eligibility criteria were clearer. NICE 2015 included one RCT from the United Kingdom that compared social support with treatment as usual in women at risk of depression. The intervention involved antenatal and postnatal peer-mediated support, which included one-to-one befriending and psychoeducational group meetings.

The other SR included studies that were specifically excluded from NICE 2015 due to methodological reasons, or were classified as treatment rather than prevention studies, or are not generalisable to Australia. Of the three additional RCTs that were not included in NICE 2015, one focused on peer mentor support given to pregnant women living with human immunodeficiency virus (HIV) in South Africa, another assessed the effectiveness of a booklet and video provided by a nurse to pregnant adolescents in the United States, and the third assessed the impact of a supportive labour companion doula for low risk pregnant women from a low income, multi-cultural urban population in South Africa. As these three studies focus on very specific populations, the findings may not be sufficiently generalisable to the target population in Australia.

C4.1.3.1 Social support versus treatment as usual

Very low quality, single-study evidence revealed no preventive benefit of social support on depression diagnosis in women at risk of developing PND, when using an ITT approach (**Table C4-3**). Moreover, there are risk-of-bias concerns with this study due to non-blind outcome assessment. There was higher attrition in the intervention group relative to treatment as usual; however, this effect estimate was not statistically significant due to serious imprecision.

Table C4-3 Summary of findings (prevention) – social support versus treatment as usual

Outcomes (follow-up)	**Illustrative comparative risks***		**Relative effect (95% CI)**	**No. of participants (studies)**	**Certainty of the evidence (GRADE)**
	Assumed risk Control	**Corresponding risk Intervention**			
Depression diagnosis					
Post-treatment – ITT analysis (at-risk populations) Schedules for Clinical Assessment in Neuropsychiatry (SCAN) (mean 12 weeks)	*Study population*		RR 0.85 (0.65, 1.1)	117 (1 study)	●○○○ Very low (a,b,c)
	714 per 1000	607 per 1000 (464, 786)			
	Moderate				
	714 per 1000	607 per 1000 (464, 785)			
Post-treatment – available case analysis (at-risk populations) SCAN (mean 12 weeks)	*Study population*		**RR 0.37 (0.17, 0.8)**	65 (1 study)	●○○○ Very low (a,b)
	543 per 1000	201 per 1000 (92, 434)			
	Moderate				
	543 per 1000	201 per 1000 (92, 434)			
Evidence Statement: *Peer-mediated social support (one-to-one befriending and psychoeducational group meetings) appears to have no effect on depression diagnosis at endpoint or first measurement (very low certainty evidence) compared with treatment as usual in pregnant and postpartum women who are considered to be 'at risk' of developing mental health problems in the perinatal period.*					
Footnotes: * The 'assumed risk' for the *study population* is calculated using the mean baseline risk from the studies in the meta-analysis (i.e. total number of events in the control/comparison group divided by the total number of patients in the control/comparison group). The *moderate* risk scenario is calculated using the median control/comparison group risk from the studies in the meta-analysis. The 'corresponding risk' (and its 95% CI) is based on the assumed risk in the control/comparison group and the relative effect of the intervention (and its 95% CI). a. Risk of bias due to non-blind outcome assessment b. Total number of events is less than 300 (a threshold rule-of-thumb) c. 95% CI crosses both line of no effect and measure of appreciable benefit or harm (SMD -0.5/0.5 or RR 0.75/1.25)					

Source: NICE 2015, Table 39

Abbreviations: CI, confidence interval; ITT, intention-to-treat; RR, relative risk; SCAN, Schedules for Clinical Assessment in Neuropsychiatry; SMD, standardised mean difference.

Note: Statistically significant differences are shown in bold.

C4.1.4 Home visits

Of the two SRs of prevention using home visits identified in the literature search, NICE 2015 was chosen as the foundation review due to its currency, high quality and comprehensiveness. NICE 2015 included five RCTs, one of which was from Australia. The five RCTs assessed home visits to provide emotional and practical support and information, predominantly for women with psychosocial risk factors, but also including adolescent mothers (three RCTs). The Australian RCT (N=120) assessed home visits provided by a physiotherapist and psychologist to women at risk of mental health problems due to preterm delivery. The Australian

intervention involved a psychological component directed at the mother and family, and a physiotherapy component directed at the infant. Of the remaining four RCTs, one involved antenatal home visits and three involved both antenatal and postnatal home visits.

C4.1.4.1 Home visits versus treatment as usual

NICE 2015 did not consider the timing of the intervention in their analyses.

Very low certainty evidence from up to two studies suggests that home visits are no more effective than treatment as usual at preventing depression symptomatology at endpoint or first measurement, or at very long follow-up (>104 weeks post-intervention), using an ITT approach (**Table C4-4**). However, confidence in this effect estimate is low due to risk-of-bias concerns and very serious imprecision. The two RCTs in the analysis were targeted at very different populations. One study involved home visitation, mentoring and case management delivered to adolescent mothers from an economically disadvantaged background in the United States, while the other (from Australia) involved an intervention with a physiotherapy and psychological component that was designed for families with a preterm infant (born at <30 weeks' gestational age).

Very low certainty evidence from one Australian study showed moderate-to-large effects of home visits on mean anxiety symptoms and on preventing anxiety symptomatology at endpoint and long-term follow-up in women who had a preterm delivery. However, confidence in these effect estimates is very low due to risk-of-bias concerns and imprecision.

A single study (very low certainty evidence) found a borderline statistically significant benefit of home visits relative to treatment as usual for preventing poor maternal sensitivity assessed using the CARE index (P=0.05) for women with psychosocial risk factors and (family) history of mental health problems; however, these estimates did not meet the criteria for clinically appreciable benefits. The intervention involved 18 months of weekly visits from a health visitor trained in understanding the processes of helping, skills of relating to parents effectively and methods of promoting parent–infant interaction using the Family Partnership Model.

Table C4-4 Summary of findings (prevention) – home visits versus treatment as usual

Outcomes (follow-up)	Illustrative comparative risks*		Relative effect (95% CI)	No. of participants (studies)	Certainty of the evidence (GRADE)
	Assumed risk Control	Corresponding risk Intervention			
Depression symptomatology					
Post-treatment– ITT analysis (at-risk populations) CES-D ≥21 or HADS– Depression >7 (52-117 weeks)	*Study population*		RR 0.94 (0.45, 1.96)	204 (2 studies)	⨁◯◯◯ Very low (a,b,c,d,e)
	434 per 1000	408 per 1000 (195, 851)			
	Moderate				
	429 per 1000	403 per 1000 (193, 841)			
Post-treatment– available case analysis (at-risk populations) CES-D ≥16/21 or HADS– Depression >7 (52-117 weeks)	*Study population*		RR 0.78 (0.44, 1.41)	684 (3 studies)	⨁◯◯◯ Very low (a,c,d,f)
	332 per 1000	259 per 1000 (146, 468)			
	Moderate				
	256 per 1000	200 per 1000 (113, 361)			
Very long Follow-up (>104 weeks post-intervention) – ITT analysis (at-risk populations) HADS– Depression ≥8 (mean 104 weeks)	*Study population*		RR 0.90 (0.59, 1.35)	120 (1 study)	⨁◯◯◯ Very low (a,c,d,e)
	458 per 1000	412 per 1000 (270, 618)			
	Moderate				
	158 per 1000	142 per 1000 (93, 213)			
Very long Follow-up (>104 weeks post-intervention) – available case analysis (at-risk populations) HADS– Depression ≥8 (mean 104 weeks)	*Study population*		RR 0.49 (0.13, 1.81)	77 (1 study)	⨁◯◯◯ Very low (a,c,d,e)
	158 per 1000	77 per 1000 (21, 286)			
	Moderate				
	158 per 1000	77 per 1000 (21, 286)			
Depression mean scores					
Post-treatment – available case analysis (at-risk populations) CES-D or HADS – Depression (mean 52 weeks)	SMD -0.38 (-0.75, -0.01)		-	621 (2 studies)	⨁◯◯◯ Very low (a,g)
Very long Follow-up (>104 weeks post-intervention) – available case analysis (at-risk populations) HADS – Depression (mean 104 weeks)	SMD -0.37 (-0.82, 0.08)		-	77 (1 study)	⨁◯◯◯ Very low (a,d,e,h)
Anxiety symptomatology					
Post-treatment – ITT analysis (at-risk populations) HADS – Anxiety >7 (mean 52 weeks)	*Study population*		**RR 0.63 (0.43, 0.91)**	120 (1 study)	⨁◯◯◯ Very low (a,c,e)
	627 per 1000	395 per 1000 (270, 571)			
	Moderate				
	627 per 1000	395 per 1000 (270, 571)			
Post-treatment – available case analysis (at-risk populations) HADS – Anxiety >7 (mean 52 weeks)	*Study population*		**RR 0.44 (0.23, 0.82)**	90 (1 study)	⨁◯◯◯ Very low (a,c,e)
	488 per 1000	215 per 1000 (112, 400)			
	Moderate				
	488 per 1000	215 per 1000 (112, 400)			
Long Follow-up (25-103 weeks post-intervention) – ITT analysis (at-risk populations) HADS– Anxiety ≥8 (mean 104 weeks)	*Study population*		**RR 0.74 (0.55, 0.98)**	120 (1 study)	⨁◯◯◯ Very low (a,c,e)
	712 per 1000	527 per 1000 (392, 698)			
	Moderate				
	712 per 1000	527 per 1000 (392, 698)			
Long Follow-up (25-103 weeks post-intervention) – available case analysis (at-risk populations) HADS– Anxiety ≥8 (mean 104 weeks)	*Study population*		**RR 0.46 (0.25, 0.85)**	77 (1 study)	⨁◯◯◯ Very low (a,c,e)
	553 per 1000	254 per 1000 (138, 470)			
	Moderate				
	553 per 1000	254 per 1000 (138, 470)			

Outcomes (follow-up)	Illustrative comparative risks*		Relative effect (95% CI)	No. of participants (studies)	Certainty of the evidence (GRADE)
	Assumed risk Control	Corresponding risk Intervention			
Anxiety mean scores					
Post-treatment – available case analysis (at-risk populations) HADS – Anxiety (mean 52 weeks)	SMD -0.89 (-1.33, -0.46)		-	90 (1 study)	●○○○ Very low (a,e,h)
Long Follow-up (25-103 weeks post-intervention) – available case analysis (at-risk populations) HADS – Anxiety (mean 104 weeks)	SMD -0.61 (-1.06, -0.15)		-	77 (1 study)	●○○○ Very low (a,e,h)
Maternal sensitivity mean scores					
Post-treatment – available case analysis (at-risk populations) CARE Index scale – Maternal sensitivity (mean 78 weeks)	SMD 0.36 (0, 0.72)		-	121 (1 study)	●○○○ Very low (d,e,h)

Evidence Statements:

Home visits appear to have no effect on depression symptomatology (very low certainty evidence) at endpoint or first measurement compared with treatment as usual in pregnant and postpartum women who are considered to be 'at risk' of developing mental health problems in the perinatal period (adolescence and psychosocial risk factors or preterm delivery)

Home visits appear to have no effect on depression symptomatology at very long follow-up (>104 weeks) (very low certainty evidence) compared with treatment as usual in postpartum women who are considered to be 'at risk' of developing mental health problems due to preterm delivery.

Home visits may improve depression mean scores at endpoint or first measurement (very low certainty evidence) compared with treatment as usual in pregnant and postpartum women who are considered to be 'at risk' of developing mental health problems in the perinatal period (adolescence and psychosocial risk factors or preterm delivery); however, the magnitude of the benefit may not be clinically significant.

Home visits may improve depression mean scores at very long follow-up (>104 weeks) (very low certainty evidence) compared with treatment as usual in postpartum women who are considered to be 'at risk' of developing mental health problems due to preterm delivery; however, the magnitude of the benefit may not be clinically significant.

Home visits may improve anxiety mean scores at endpoint or first measurement (very low certainty evidence), and at long follow-up (25-103 weeks post-intervention) (very low certainty evidence), compared with treatment as usual in postpartum women who are considered to be 'at risk' of developing mental health problems due to preterm delivery.

Home visits may improve anxiety symptomatology at endpoint or first measurement (very low certainty evidence), and at long follow-up (25-103 weeks post-intervention) (very low certainty evidence), compared with treatment as usual in postpartum women who are considered to be 'at risk' of developing mental health problems due to preterm delivery; however, the magnitude of the benefit may not be clinically significant.

Home visits may improve maternal sensitivity mean scores at endpoint or first measurement (very low certainty evidence) compared with treatment as usual in pregnant and postpartum women who are considered to be 'at risk' of developing mental health problems in the perinatal period (multiple psychosocial risk factors); however, the magnitude of the benefit may not be clinically significant.

Footnotes:

* The 'assumed risk' for the *Study population* is calculated using the mean baseline risk from the studies in the meta-analysis (i.e. total number of events in the control/comparison group divided by the total number of patients in the control/comparison group). The moderate risk scenario is calculated using the median control/comparison group risk from the studies in the meta-analysis. The 'corresponding risk' (and its 95% CI) is based on the assumed risk in the control/comparison group and the relative effect of the intervention (and its 95% CI).

a. Risk of bias due to statistically significant group differences at baseline
b. There is evidence of considerable heterogeneity of study effect sizes
c. Total number of events is less than 300 (a threshold rule-of-thumb)
d. 95% CI crosses both line of no effect and measure of appreciable benefit or harm (SMD -0.5/0.5 or RR 0.75/1.25)
e. Paper omits data
f. There is evidence of moderate heterogeneity of study effect sizes
g. There is evidence of substantial heterogeneity of study effect sizes
h. Total population size is less than 400 (a threshold rule-of-thumb)

Source: NICE 2015, Table 43, Table 49, Table 52, Table 56

Abbreviations: CES-D, Center for Epidemiologic Studies Depression Scale; CI, confidence interval; HADS, Hospital Anxiety and Depression Scale; ITT, intention-to-treat; RR, relative risk; SD, standard deviation; SMD, standardised mean difference.

Note: Statistically significant differences are shown in bold.

C4.1.5 Non-mental-health-focused education/support

Of the two SRs of prevention using non-mental-health-focused education or support identified in the literature search, NICE 2015 was chosen as the foundation review due to its currency, high quality and comprehensiveness. NICE 2015 included four RCTs, one of which was from Australia. The included studies compared non-mental-health-focused education and support with treatment as usual or enhanced treatment as usual[58] for women with a range of risk factors including psychosocial risk factors, preterm delivery and low birthweight baby, and multiple (twin) pregnancy. In one RCT the intervention involved written and audiotaped education provided individually to postpartum women at hospital. In the other three RCTs the intervention involved face-to-face education and support provided antenatally and postnatally to women in a group format (one RCT) or in an individual and group format (two RCTs that also included home visits as part of the intervention). The setting varied within and across studies, and involved community, home, hospital and clinic.

NICE 2015 missed an RCT from the United States (N=167) that assessed a paraprofessional-delivered in-home intervention for young reservation-based American Indian mothers, and an Australian RCT (N=44) that assessed an educational intervention focusing on parenting and coping strategies delivered in an individual and group format to pregnant and postpartum women. The SR that included these additional studies found that education on preparing for parenting had a positive effect on depression compared with usual care; however, the effects were not statistically significant.

C4.1.5.1 Non-mental-health-focused education/support versus treatment as usual or enhanced treatment as usual

NICE 2015 did not consider the timing of the intervention, format or mode of delivery in their analyses.

Low certainty evidence from up to two studies suggests that non-mental-health-focused education and support may be more effective than treatment as usual or enhanced treatment as usual at preventing depression symptomatology for women with multiple births or at risk of developing postnatal depression (no further details reported). However, effects were not maintained at intermediate or long-term follow-ups, and there was no evidence for statistically or clinically significant preventive benefits for depression mean symptoms at any time point (**Table C4-5**).

There was single-study evidence for a moderate effect of non-mental-health-focused education and support for preventing anxiety symptomatology (at endpoint and short-term follow-up) in women with multiple births when an ITT analysis approach was used. However, confidence in these effect estimates was very low due to serious imprecision and selective reporting bias. In addition, there was no evidence for statistically or clinically significant effects on anxiety mean scores at endpoint, short-term or intermediate follow-up, or on anxiety symptomatology at intermediate follow-up.

A single study found no evidence at any time point for a clinically or statistically significant effect on mother-infant attachment problems for non-mental-health-focused education and support group and home visits relative to treatment as usual for women with an uncomplicated twin pregnancy, using an ITT approach. However, confidence in this effect estimate was very low due to very serious imprecision and risk of selective reporting bias.

[58] Enhanced treatment as usual involved non-mental health-focused education (one RCT) and non-mental health-focused education and support without the focus on healthy eating and exercise (one RCT).

Table C4-5 Summary of findings (prevention) – non-mental health-focused education and support versus treatment as usual or enhanced treatment as usual

Outcomes (follow-up)	Illustrative comparative risks*		Relative effect (95% CI)	No. of participants (studies)	Certainty of the evidence (GRADE)
	Assumed risk Control	Corresponding risk Intervention			
Depression symptomatology					
Post-treatment – ITT analysis (at-risk populations) EPDS >12 (6-13 weeks)	*Study population*		RR 0.7 (0.44, 1.14)	306 (2 studies)	●●○○ Low (a,b)
	320 per 1000	224 per 1000 (141, 365)			
	Moderate				
	316 per 1000	221 per 1000 (139, 360)			
Post-treatment – available case analysis (at-risk populations) EPDS >12 (6-13 weeks)	*Study population*		RR 0.57 (0.31, 1.05)	261 (2 studies)	●●○○ Low (a,b)
	188 per 1000	107 per 1000 (58, 197)			
	Moderate				
	188 per 1000	107 per 1000 (58, 197)			
Short Follow-up (9-16 weeks post-intervention) – ITT analysis (at-risk populations) EPDS >12 (mean 6 weeks)	*Study population*		RR 0.68 (0.44, 1.06)	162 (1 study)	●●○○ Low (a,b)
	402 per 1000	274 per 1000 (177, 427)			
	Moderate				
	402 per 1000	273 per 1000 (177, 426)			
Short Follow-up (9-16 weeks post-intervention) – available case analysis (at-risk populations) – Non-mental-health-focused education and support EPDS >12 (mean 12 weeks)	*Study population*		RR 0.48 (0.21, 1.12)	128 (1 study)	●●○○ Low (a,b)
	222 per 1000	107 per 1000 (47, 249)			
	Moderate				
	222 per 1000	107 per 1000 (47, 249)			
Intermediate follow-up (17-24 weeks post-intervention) – ITT analysis (at-risk populations) EPDS >12 (20-24 weeks)	*Study population*		RR 0.91 (0.44, 1.89)	306 (2 studies)	●○○○ Very low (a,b,e)
	294 per 1000	268 per 1000 (129, 556)			
	Moderate				
	290 per 1000	264 per 1000 (128, 548)			
Intermediate follow-up (17-24 weeks post-intervention) - available case analysis (at-risk populations) EPDS >12 (20-24 weeks)	*Study population*		RR 0.84 (0.27, 2.63)	254 (2 studies)	●○○○ Very low (a,b,e)
	143 per 1000	120 per 1000 (39, 376)			
	Moderate				
	142 per 1000	119 per 1000 (38, 373)			
Long Follow-up (25-103 weeks post-intervention) – ITT analysis (at-risk populations) EPDS >12 (mean 52 weeks)	*Study population*		RR 0.84 (0.57, 1.25)	162 (1 study)	●●○○ Low (a,b)
	415 per 1000	348 per 1000 (236, 518)			
	Moderate				
	415 per 1000	349 per 1000 (237, 519)			
Long Follow-up (25-103 weeks post-intervention) – available case analysis (at-risk populations) EPDS >12 (mean 52 weeks)	*Study population*		RR 0.87 (0.42, 1.83)	123 (1 study)	●●○○ Low (a,b)
	200 per 1000	174 per 1000 (84, 366)			
	Moderate				
	200 per 1000	174 per 1000 (84, 366)			
Depression mean scores					
Post-treatment – ITT analysis (at-risk populations) CES-D (mean 28 weeks)	SMD -0.13 (-0.37, 0.1)		-	275 (1 study)	●●○○ Low (c,d)
Post-treatment – available case analysis (at-risk populations) BDI or EPDS	SMD -0.14 (-0.34, 0.07)		-	370 (2 studies)	●●●○ Moderate (c)
Short Follow-up (9-16 weeks post-intervention) – available case analysis (at-risk populations) EPDS (mean 12 weeks)	SMD -0.21 (-0.56, 0.13)		-	128 (1 study)	●●○○ Low (b,c)

Outcomes (follow-up)	Illustrative comparative risks*		Relative effect (95% CI)	No. of participants (studies)	Certainty of the evidence (GRADE)
	Assumed risk Control	Corresponding risk Intervention			
Intermediate follow-up (17-24 weeks post-intervention) – available case analysis (at-risk populations) EPDS (mean 24 weeks)	SMD -0.3 (-0.64, 0.04)		-	133 (1 study)	●●○○ Low (b,c)
Long Follow-up (25-103 weeks post-intervention) -Available case analysis (at-risk populations) EPDS (mean 52 weeks)	SMD -0.08 (-0.44, 0.27)		-	123 (1 study)	●●○○ Low (c)
Anxiety symptomatology					
Post-treatment – ITT analysis (at-risk populations) HADS – Anxiety (above unspecified threshold) (mean 6 weeks)	*Study population*		RR 0.74 (0.44, 1.24)	162 (1 study)	●○○○ Very low (a,b,d)
	305 per 1000	226 per 1000 (134, 378)			
	Moderate				
	305 per 1000	226 per 1000 (134, 378)			
Post-treatment – available case analysis (at-risk populations) HADS – Anxiety (above unspecified threshold) (mean 6 weeks)	*Study population*		RR 0.93 (0.32, 2.72)	131 (1 study)	●○○○ Very low (a,b,d)
	95 per 1000	89 per 1000 (30, 259)			
	Moderate				
	95 per 1000	88 per 1000 (30, 258)			
Short Follow-up (9-16 weeks post-intervention) – ITT analysis (at-risk populations) HADS – Anxiety (above unspecified threshold) (mean 12 weeks)	*Study population*		RR 0.67 (0.38, 1.19)	162 (1 study)	●○○○ Very low (a,b,d)
	280 per 1000	188 per 1000 (107, 334)			
	Moderate				
	281 per 1000	188 per 1000 (107, 334)			
Short Follow-up (9-16 weeks post-intervention) – available case analysis (at-risk populations) HADS – Anxiety (above unspecified threshold) (mean 12 weeks)	*Study population*		RR 0.11 (0.01, 1.96)	128 (1 study)	●○○○ Very low (a,b,d)
	63 per 1000	7 per 1000 (1, 124)			
	Moderate				
	64 per 1000	7 per 1000 (1, 125)			
Intermediate follow-up (17-24 weeks post-intervention) – ITT analysis (at-risk populations) HADS – Anxiety (above unspecified threshold) (mean 24 weeks)	*Study population*		RR 0.76 (0.44, 1.31)	162 (1 study)	●○○○ Very low (a,b,d)
	280 per 1000	213 per 1000 (123, 367)			
	Moderate				
	281 per 1000	214 per 1000 (124, 368)			
Intermediate follow-up (17-24 weeks post-intervention) – available case analysis (at-risk populations) HADS – Anxiety (above unspecified threshold) (mean 24 weeks)	*Study population*		RR 0.94 (0.25, 3.6)	130 (1 study)	●○○○ Very low (a,b,d)
	63 per 1000	60 per 1000 (16, 229)			
	Moderate				
	64 per 1000	60 per 1000 (16, 230)			
Anxiety mean scores					
Post-treatment – available case analysis (at-risk populations) STAI-S or HADS –Anxiety (mean 6 weeks)	SMD -0.1 (-0.3, 0.11)		-	370 (2 studies)	●●●○ Moderate (c)
Short Follow-up (9-16 weeks post-intervention) – available case analysis (at-risk populations) HADS – Anxiety (mean 12 weeks)	SMD -0.2 (-0.54, 0.15)		-	128 (1 study)	●○○○ Very low (b,c,d)
Intermediate follow-up (17-24 weeks post-intervention) – available case analysis (at-risk populations) HADS – Anxiety (mean 24 weeks)	SMD -0.26 (-0.6, 0.09)		-	130 (1 study)	●○○○ Very low (b,c,d)

Outcomes (follow-up)	Illustrative comparative risks*		Relative effect (95% CI)	No. of participants (studies)	Certainty of the evidence (GRADE)
	Assumed risk Control	Corresponding risk Intervention			
Mother-infant attachment problems					
Post-treatment – ITT analysis (at-risk populations) Green scale: Mother-infant attachment problems (above unspecified threshold) (mean 6 weeks)	*Study population*		RR 0.9 (0.65, 1.25)	162 (1 study)	⨁◯◯◯ Very low (a,b,d)
	500 per 1000	450 per 1000 (325, 625)			
	Moderate				
	500 per 1000	450 per 1000 (325, 625)			
Post-treatment – available case analysis (at-risk populations) Green scale: Mother-infant attachment problems (above unspecified threshold) (mean 6 weeks)	*Study population*		RR 1.01 (0.64, 1.59)	133 (1 study)	⨁◯◯◯ Very low (a,b,d)
	359 per 1000	363 per 1000 (230, 571)			
	Moderate				
	359 per 1000	363 per 1000 (230, 571)			
Short Follow-up (9-16 weeks post-intervention) – ITT analysis (at-risk populations) Green scale: Mother-infant attachment problems (above unspecified threshold) (mean 12 weeks)	*Study population*		RR 1.08 (0.78, 1.49)	162 (1 study)	⨁◯◯◯ Very low (a,b,d)
	463 per 1000	500 per 1000 (361, 690)			
	Moderate				
	463 per 1000	500 per 1000 (361, 690)			
Short Follow-up (9-16 weeks post-intervention) – available case analysis (at-risk populations) Green scale: Mother-infant attachment problems (above unspecified threshold) (mean 12 weeks)	Study population		RR 1.29 (0.78, 2.13)	126 (1 study)	⨁◯◯◯ Very low (a,b,d)
	290 per 1000	375 per 1000 (226, 618)			
	Moderate				
	290 per 1000	374 per 1000 (226, 618)			
Intermediate follow-up (17-24 weeks post-intervention) – ITT analysis (at-risk populations) Green scale: Mother-infant attachment problems (above unspecified threshold) (mean 24 weeks)	*Study population*		RR 0.85 (0.64, 1.14)	162 (1 study)	⨁◯◯◯ Very low (a,b,d)
	585 per 1000	498 per 1000 (375, 667)			
	Moderate				
	585 per 1000	497 per 1000 (374, 667)			
Intermediate follow-up (17-24 weeks post-intervention) – available case analysis (at-risk populations) Green scale: Mother-infant attachment problems (above unspecified threshold) (mean 24 weeks)	*Study population*		RR 0.89 (0.59, 1.34)	127 (1 study)	⨁◯◯◯ Very low (a,b,d)
	443 per 1000	394 per 1000 (261, 593)			
	Moderate				
	443 per 1000	394 per 1000 (261, 594)			
Positive mother-infant interaction mean scores					
Post-treatment – available case analysis (at-risk populations) Index of Parental Behavior in the NICU: Positive interaction with quiet alert infant	**SMD 0.57 (0.29, 0.85)**		-	211 (1 study)	⨁⨁◯◯ Low (c,d)

Evidence Statements:

Non-mental-health-focused education and support (individual and group, face-to-face, with or without home visits) appears to have no effect on depression symptomatology at endpoint or first measurement (low certainty evidence), or at short follow-up (9-16 weeks post-intervention) (low certainty evidence), or at intermediate follow-up (17-24 weeks post-intervention) (very low certainty evidence), compared with treatment as usual in pregnant and postpartum women who are considered to be 'at risk' of developing mental health problems in the perinatal period.

Non-mental-health-focused education and support (individual and group, face-to-face, with home visits) appears to have no effect on depression symptomatology (low certainty evidence) at long follow-up (25-103 weeks post-intervention) compared with treatment as usual in pregnant and postpartum women who are considered to be 'at risk' of developing mental health problems due to multiple (twin) pregnancy

Non-mental-health-focused education and support (individual and group, face-to-face, with home visits) appears to have no effect on depression mean scores (low certainty evidence) at endpoint or first measurement compared with enhanced treatment as usual (non-mental-health-focused education and support without the focus on healthy eating and exercise) in pregnant and postpartum women who are considered to be 'at risk' of developing mental health problems in the perinatal period (psychosocial risk factors).

Non-mental-health-focused education and support (individual and group, face-to-face, with home visits) appears to have no effect on depression mean scores (low certainty evidence) at short (9-16 weeks post-intervention), intermediate (17-24 weeks post-intervention), or long (25-103 weeks post-intervention) follow-up compared with treatment as usual in pregnant and postpartum women who are considered to be 'at risk' of developing mental health problems due to multiple (twin) pregnancy

Outcomes (follow-up)	Illustrative comparative risks*		Relative effect (95% CI)	No. of participants (studies)	Certainty of the evidence (GRADE)
	Assumed risk Control	Corresponding risk Intervention			
Non-mental-health-focused education and support (individual and group, face-to-face, with home visits) appears to have no effect on anxiety symptomatology (very low certainty evidence) at endpoint or first measurement, or at short follow-up (9-16 weeks post-intervention), or at intermediate follow-up (17-24 weeks post-intervention) compared with treatment as usual in pregnant and postpartum women who are considered to be 'at risk' of developing mental health problems due to multiple (twin) pregnancy. *Non-mental-health-focused education and support (individual and group, with or without home visits) has no effect on anxiety mean scores at endpoint or first measurement (moderate certainty evidence), and appears to have no effect on anxiety mean scores at short follow-up (9-16 weeks post-intervention) (very low certainty evidence), or at intermediate follow-up (17-24 weeks post-intervention) (very low certainty evidence) compared with treatment as usual in pregnant and postpartum women who are considered to be 'at risk' of developing mental health problems due to preterm delivery and low birthweight or multiple (twin) pregnancy.* *Non-mental-health-focused education and support (individual and group, with or without home visits) appears to have no effect on mother-infant attachment problems (very low certainty evidence) at endpoint or first measurement, at short follow-up (9-16 weeks post-intervention), or at intermediate follow-up (17-24 weeks post-intervention), compared with treatment as usual in pregnant and postpartum women who are considered to be 'at risk' of developing mental health problems due to multiple (twin) pregnancy* *Non-mental-health-focused education and support (individual, written and audiotaped) appears to have no effect on positive mother-infant interaction mean scores (low certainty evidence) at endpoint or first measurement compared with enhanced treatment as usual (non-mental-health-focused information) in postpartum women who are considered to be 'at risk' of developing mental health problems due to preterm delivery and low birthweight.*					
Footnotes: * The 'assumed risk' for the study population is calculated using the mean baseline risk from the studies in the meta-analysis (i.e. total number of events in the control/comparison group divided by the total number of patients in the control/comparison group). The moderate risk scenario is calculated using the median control/comparison group risk from the studies in the meta-analysis. The 'corresponding risk' (and its 95% CI) is based on the assumed risk in the control/comparison group and the relative effect of the intervention (and its 95% CI). a. Total number of events is less than 300 (a threshold rule-of-thumb) b. 95% CI crosses both line of no effect and measure of appreciable benefit or harm (SMD -0.5/0.5 or RR 0.75/1.25) c. Total population size is less than 400 (a threshold rule-of-thumb) d. Paper omits data e. There is evidence of substantial heterogeneity of study effect sizes					

Source: NICE 2015, Table 42, Table 48, Table 55

Abbreviations: BDI, Beck Depression Inventory; CES-D, Center for Epidemiologic Studies Depression Scale; CI, confidence interval; EPDS, Edinburgh Postnatal Depression Scale; HADS, Hospital Anxiety and Depression Scale; ITT, intention-to-treat; NICU, neonatal intensive care unit; RR, relative risk; SMD, standardised mean difference; STAI-S, State-Trait Anxiety Inventory-State.

C4.1.6 Pre-delivery discussion

The literature search identified no SRs that relate to this intervention.

Table C4-6 Summary of findings (prevention) – pre-delivery discussion

Evidence Statement: *There is no RCT evidence for pre-delivery discussion in pregnant women who are considered to be 'at risk' of developing mental health problems in the perinatal period.*

C4.1.7 Post-delivery discussion

Of the two SRs of post-delivery discussion identified in the literature search, NICE 2015 was chosen as the foundation review. NICE 2015 included one RCT from Australia (N=1,041) that assessed individual, face-to-face, midwife-led post-delivery discussion (single session) for women who had an operative delivery.

C4.1.7.1 Post-delivery discussion versus enhanced treatment as usual

A single study found no clinically or statistically significant benefits of a midwife-led post-delivery discussion relative to enhanced treatment as usual (a non-mental health-focused information booklet) on preventing depression or poor general mental health outcomes in women who had had an operative delivery (**Table C4-7**).

Table C4-7 Summary of findings (prevention) – post-delivery discussion versus enhanced treatment as usual

Outcomes (follow-up)	Illustrative comparative risks*		Relative effect (95% CI)	No. of participants (studies)	Certainty of the evidence (GRADE)
	Assumed risk Control	Corresponding risk Intervention			
Depression symptomatology					
Post-treatment – ITT analysis (at-risk populations) EPDS ≥13 (mean 26 weeks)	*Study population*		RR 0.98 (0.8, 1.2)	1,041 (1 study)	●●●○ Moderate (a)
	263 per 1000	258 per 1000 (210, 316)			
	Moderate				
	263 per 1000	258 per 1000 (210, 316)			
Post-treatment – available case analysis (at-risk populations) EPDS ≥13 (mean 26 weeks)	*Study population*		RR 1.2 (0.89, 1.62)	916 (1 study)	●●○○ Low (a,b)
	145 per 1000	174 per 1000 (129, 235)			
	Moderate				
	145 per 1000	174 per 1000 (129, 235)			
Very long Follow-up (>104 weeks post-intervention) – ITT analysis (at-risk populations) EPDS ≥13 (208-312 weeks)	*Study population*		RR 1.01 (0.91, 1.12)	1,041 (1 study)	●●●● High
	568 per 1000	574 per 1000 (517, 636)			
	Moderate				
	568 per 1000	574 per 1000 (517, 636)			
Very long Follow-up (>104 weeks post-intervention) – available case analysis (at-risk populations) EPDS ≥13 (208-312 weeks)	*Study population*		RR 0.95 (0.65, 1.4)	534 (1 study)	●●○○ Low (a,b)
	167 per 1000	158 per 1000 (108, 233)			
	Moderate				
	167 per 1000	159 per 1000 (109, 234)			
Depression mean scores					
Post-treatment – available case analysis (at-risk populations) EPDS (mean 26 weeks)	SMD 0.08 (-0.05, 0.21)			916 (1 study)	●●●● High
Very long Follow-up (>104 weeks post-intervention) – available case analysis (at-risk populations) EPDS (208-312 weeks)	SMD -0.08 (-0.25, 0.09)			534 (1 study)	●●●● High

Evidence Statement:

Individual, midwife-led post-delivery discussion has no effect on depression symptomatology at endpoint or first measurement (moderate certainty evidence) or at very long follow-up (>104 weeks post-intervention) (high certainty evidence) compared with a non-mental health-focused information booklet in women who are considered to be 'at risk' of developing mental health problems in the postnatal period due to an operative delivery.

Individual, midwife-led post-delivery discussion has no effect on depression mean scores at endpoint or first measurement (high certainty evidence), or at very long follow-up (>104 weeks post-intervention) (high certainty evidence), compared with a non-mental health-focused information booklet in women who are considered to be 'at risk' of developing mental health problems in the postnatal period due to an operative delivery

Outcomes (follow-up)	Illustrative comparative risks*		Relative effect (95% CI)	No. of participants (studies)	Certainty of the evidence (GRADE)
	Assumed risk Control	Corresponding risk Intervention			
Footnotes: * The 'assumed risk' for the *study population* is calculated using the mean baseline risk from the studies in the meta-analysis (i.e. total number of events in the control/comparison group divided by the total number of patients in the control/comparison group). The *moderate* risk scenario is calculated using the median control/comparison group risk from the studies in the meta-analysis. The 'corresponding risk' (and its 95% CI) is based on the assumed risk in the control/comparison group and the relative effect of the intervention (and its 95% CI). a. Total number of events is less than 300 (a threshold rule-of-thumb) b. 95% CI crosses both line of no effect and measure of appreciable benefit or harm (SMD -0.5/0.5 or RR 0.75/1.25)					

Source: NICE 2015, Table 44, Table 53

Abbreviations: CI, confidence interval; EPDS, Edinburgh Postnatal Depression Scale; ITT, intention-to-treat; RR, relative risk; SMD, standardised mean difference.

C4.1.8 Post-miscarriage self-help

Only one SR of prevention using post-miscarriage self-help (NICE 2015) was identified in the literature search. NICE 2015 included one RCT conducted in European German-speaking countries that compared post-miscarriage self-help with waitlist control. The intervention involved a five-week cognitive behaviour internet-based self-help therapy for parents after the loss of a child during pregnancy (due to miscarriage, termination due to fetal abnormality, or stillbirth). The self-help intervention was based on CBT principles and participants were assigned written tasks (10 x 45-minute assignments) which were personalised by the therapist for each participant. At baseline, 37% study participants had an IES score >35 (baseline IES-R mean score 31.1 [SD 8.6]).

C4.1.8.1 Post-miscarriage self-help versus treatment as usual

A single study showed large effects of post-miscarriage self-help on preventing PTSD symptomatology and reducing mean PTSD for women who had lost a child during pregnancy (**Table C4-8**). However, confidence in these effect estimates was very low due to risk-of-bias concerns and imprecision.

Table C4-8 Summary of findings (prevention) – post-miscarriage self-help versus treatment as usual

Outcomes (follow-up)	Illustrative comparative risks*		Relative effect (95% CI)	No. of participants (studies)	Certainty of the evidence (GRADE)
	Assumed risk Control	Corresponding risk Intervention			
PTSD symptomatology					
Post-treatment – ITT IES-R ≥35 (mean 5 weeks)	*Study population*		**RR 0.34 (0.18, 0.62)**	228 (1 study)	●○○○ Very low (a,c)
	310 per 1000	105 per 1000 (56, 192)			
	Moderate				
	310 per 1000	105 per 1000 (56, 192)			
PTSD mean scores					
Post-treatment – ITT IES-R (mean 5 weeks)	**SMD -0.88 (-1.15, -0.61)**		-	228 (1 study)	●○○○ Very low (a,b)

Outcomes (follow-up)	Illustrative comparative risks*		Relative effect (95% CI)	No. of participants (studies)	Certainty of the evidence (GRADE)
	Assumed risk Control	Corresponding risk Intervention			
Depression mean symptoms					
Post-treatment – ITT BSI: Depression[59] (mean 5 weeks)	**SMD -0.64 (-0.91, -0.37)**		-	228 (1 study)	●●○○ Low (a,b)
Anxiety mean scores					
Post-treatment – ITT BSI: Anxiety[60] (mean 5 weeks)	**SMD -0.47 (-0.73, -0.2)**		-	228 (1 study)	●●○○ Low (a,b)
Evidence Statement: *Internet-based cognitive behaviour self-help therapy appears to improve PTSD symptomatology (very low certainty evidence), PTSD mean scores (very low certainty evidence), depression mean symptoms (low certainty evidence), and anxiety mean scores (low certainty evidence), at endpoint or first measurement compared with waitlist control in women who are considered to be 'at risk' of developing mental health problems due to the loss of a child during pregnancy.*					
Footnotes: * The 'assumed risk' for the *study population* is calculated using the mean baseline risk from the studies in the meta-analysis (i.e. total number of events in the control/comparison group divided by the total number of patients in the control/comparison group). The *moderate* risk scenario is calculated using the median control/comparison group risk from the studies in the meta-analysis. The 'corresponding risk' (and its 95% CI) is based on the assumed risk in the control/comparison group and the relative effect of the intervention (and its 95% CI). a. Risk of bias due to statistically significant group differences at baseline b. Imprecision - Total population size is less than 400 (a threshold rule-of-thumb) c. Imprecision - Total number of events is less than 300 (a threshold rule-of-thumb)					

Source: NICE 2015, Table 38, Table 47, Table 50, Table 51

Abbreviations: BSI, Brief Symptom Inventory; CI, confidence interval; IES-R, Impact of Events Scale – Revised; ITT, intention-to-treat; PTSD, post-traumatic stress disorder; RR, relative risk; SMD, standardised mean difference.

Note: Statistically significant differences are shown in bold.

C4.1.9 Seeing and/or holding stillborn infant

Only one SR of prevention associated with seeing and/or holding stillborn infant was identified in the literature search (NICE 2015) but no RCTs were included. NICE 2015 included three retrospective cohort studies and one nested cohort within a case-control study. All included studies compared mental health outcomes in women who saw and/or held their stillborn infants compared with those who did not. The length of time since the stillbirth varied considerably within and between studies, ranging from less than one year to 18 years. One study only recruited women who had previously experienced a stillbirth and were pregnant with another child.

C4.1.9.1 Seeing and/or holding stillborn infant versus not seeing and/or holding the stillborn infant

The evidence for benefits or harms associated with seeing and/or holding the stillborn infant was contradictory with evidence from a single cohort study from the United Kingdom suggestive of harms associated with these protocols following stillbirth and evidence from a Swedish study and Norwegian study suggestive of benefits associated with spending as much time with the stillborn infant as women wished or holding the stillborn infant. Potential reasons for these differences

[59] Outcome is a subscale of a global severity measure – not depression-specific

[60] Outcome is a subscale of a global severity measure – not anxiety specific

could be differences in gestational age at the time of stillbirth (none of the papers report the mean gestational age at stillbirth) and pregnancy status at the time of participation in the studies.

Table C4-9 Summary of findings (prevention) – seeing and/or holding stillborn infant versus not seeing and/or holding stillborn infant

Evidence Statement: *There is no RCT evidence for seeing and/or holding the stillborn infant versus not seeing and/or holding the stillborn infant in women who are considered to be 'at risk' of developing mental health problems in the perinatal period.*

C4.1.10 Mother-infant relationship interventions

Of the two SRs of prevention associated with mother-infant relationship interventions identified in the literature search, NICE 2015 was chosen as the foundation review due to its currency, high quality and comprehensiveness. The four RCTs included in NICE 2015 compared face-to-face mother-infant relationship interventions with treatment as usual in women with psychosocial risk factors (one RCT) or with premature or low birthweight babies (three RCTs). One RCT was from Australia (assessing an intervention largely based on the Mother-Infant Transaction Program) while the others were from Norway (Mother-Infant Transaction Program), the Netherlands (Infant Behavioural Assessment and Intervention Program), and South Africa (a relationship/attachment based intervention that closely follows the principles of The Social Baby). The intervention was delivered antenatally and postnatally at home in one RCT, and postnatally (at home, or both at hospital and home) in the remaining three RCTs.

One additional RCT from the United Kingdom was not included in NICE 2015 but the study was relatively small in terms of sample size (N=35). The antenatal parenting support intervention, which was underpinned by attachment theory and aimed at women with additional health and social care needs, appeared to have positive effects on the women's mental health and well-being overall at 8-12 weeks postnatally.

C4.1.10.1 Mother-infant relationship interventions versus treatment as usual

NICE 2015 did not consider the timing or setting of the intervention in their analyses.

A single study in women living in socioeconomically deprived community in South Africa provided low certainty evidence that a mother-infant relationship intervention aimed at improving the quality of the mother-infant relationship and infant attachment had no clinically or statistically significant effect on preventing mother-infant attachment problems (assessed using the Ainsworth Strange Situation Procedure); however, a moderate benefit was seen when an available case analysis approach was used. There was also evidence from two studies (one from Australia and one from the Netherlands) for a small benefit of a mother-infant relationship intervention on preventing poor mother-infant interaction mean scores for women who had had a preterm delivery and/or a low birthweight baby; however, this effect estimate did not reach criteria for a clinically meaningful benefit (SMD<0.5). There was no statistically significant difference between study groups for any other observed outcome measures.

The evidence for mother-infant relationship interventions preventing depression in women with psychosocial risk factors or who had a preterm delivery and/or low birthweight baby was inconsistent (**Table C4-10**); however, the interventions were not specifically intended for this purpose. A single study showed no

statistically or clinically significant effects of a mother-infant relationship intervention on depression diagnosis in women living in a socioeconomically deprived community in South Africa, using an ITT approach. However, a single study in Norwegian women who had a preterm delivery showed large harms on depression symptomatology associated with mother-infant relationship interventions (one and a half times more likely to score CES-D ≥16); however, the confidence in this effect estimate is very low due to risk-of-bias concerns and very serious imprecision, and the effect was not maintained at long follow-up (25-103 weeks post-intervention). There was no evidence for statistically or clinically significant effects of mother-infant relationship interventions on mean depression symptoms at short-term or long-term follow-up, and no evidence for clinically significant effects on depression mean symptoms at endpoint.

Table C4-10 Summary of findings (prevention) – mother-infant relationship interventions versus treatment as usual

Outcomes (follow-up)	Illustrative comparative risks*		Relative effect (95% CI)	No. of participants (studies)	Certainty of the evidence (GRADE)
	Assumed risk Control	Corresponding risk Intervention			
Depression diagnosis					
Post-treatment – ITT analysis (at-risk populations) SCID (mean 26 weeks)	*Study population*		RR 1 (0.76, 1.31)	449 (1 study)	●●○○ Low (a,b)
	323 per 1000	323 per 1000 (246, 423)			
	Moderate				
	323 per 1000	323 per 1000 (245, 423)			
Post-treatment – available case analysis (at-risk populations) SCID (mean 26 weeks)	*Study population*		RR 0.78 (0.47, 1.32)	354 (1 study)	●●○○ Low (a,b)
	158 per 1000	123 per 1000 (74, 208)			
	Moderate				
	158 per 1000	123 per 1000 (74, 209)			
Long Follow-up (25-103 weeks post-intervention) – ITT analysis (at-risk populations) SCID (mean 52 weeks)	*Study population*		RR 1 (0.77, 1.3)	449 (1 study)	●●○○ Low (a,b)
	332 per 1000	332 per 1000 (256, 431)			
	Moderate				
	332 per 1000	332 per 1000 (256, 432)			
Long Follow-up (25-103 weeks post-intervention) – available case analysis (at-risk populations) SCID (mean 52 weeks)	*Study population*		RR 0.71 (0.41, 1.23)	346 (1 study)	●●○○ Low (a,b)
	155 per 1000	110 per 1000 (63, 190)			
	Moderate				
	155 per 1000	110 per 1000 (64, 191)			
Depression symptomatology					
Post-treatment – ITT analysis (at-risk populations) CES-D ≥16 (mean 27 weeks)	*Study population*		RR 1.52 (0.77, 3)	106 (1 study)	●○○○ Very low (a,d,g)
	200 per 1000	304 per 1000 (154, 600)			
	Moderate				
	200 per 1000	304 per 1000 (154, 600)			
Post-treatment – available case analysis (at-risk populations) CES-D ≥16 (mean 27 weeks)	*Study population*		RR 2.8 (0.6, 13.11)	87 (1 study)	●○○○ Very low (a,b,g)
	48 per 1000	133 per 1000 (29, 624)			
	Moderate				
	48 per 1000	134 per 1000 (29, 629			
Long Follow-up (25-103 weeks post-intervention) – ITT analysis (at-risk populations) CES-D ≥16 (mean 53 weeks)	*Study population*		RR 0.94 (0.56, 1.58)	106 (1 study)	●○○○ Very low (a,b,g)
	360 per 1000	338 per 1000 (202, 569)			
	Moderate				
	360 per 1000	338 per 1000 (202, 569)			

Outcomes (follow-up)	Illustrative comparative risks*		Relative effect (95% CI)	No. of participants (studies)	Certainty of the evidence (GRADE)
	Assumed risk Control	Corresponding risk Intervention			
Long Follow-up (25-103 weeks post-intervention) – available case analysis (at-risk populations) CES-D ≥16 (mean 53 weeks)	*Study population*		RR 0.75 (0.25, 2.27)	80 (1 study)	●○○○ Very low (a,b,g)
	158 per 1000	118 per 1000 (39, 358)			
	Moderate				
	158 per 1000	119 per 1000 (40, 359)			
Depression mean scores					
Post-treatment – available case analysis (at-risk populations) EPDS (15-26 weeks)	**SMD -0.22 (-0.41, -0.02)**		-	417 (2 studies)	●●●● High
Short Follow-up (9-16 weeks post-intervention) – available case analysis (at-risk populations) EPDS (mean 28 weeks)	SMD -0.3 (-0.8, 0.19)		-	63 (1 study)	●●○○ Low (b,c)
Long Follow-up (25-103 weeks post-intervention) – available case analysis (at-risk populations) EPDS (mean 52 weeks)	SMD -0.14 (-0.35, 0.06)		-	354 (1 study)	●●●○ Moderate (c)
Mother-infant attachment problems					
Post-treatment – ITT analysis (at-risk populations) Ainsworth Strange Situation: Insecure (mean 78 weeks)	*Study population*		RR 0.85 (0.71, 1.02)	449 (1 study)	●●○○ Low (a,b)
	555 per 1000	471 per 1000 (394, 566)			
	Moderate				
	555 per 1000	472 per 1000 (394, 566)			
Post-treatment – available case analysis (at-risk populations) Ainsworth Strange Situation: Insecure (mean 78 weeks)	*Study population*		**RR 0.69 (0.5, 0.97)**	318 (1 study)	●●○○ Low (a)
	370 per 1000	256 per 1000 (185, 359)			
	Moderate				
	370 per 1000	255 per 1000 (185, 359)			
Positive mother-infant interaction mean scores					
Post-treatment – available case analysis (at-risk populations) Infant and Caregiver Engagement Phases (ICEP): Maternal positive engagement (% of time during behavioural observation) or Synchrony Scale (Milgrom & Meitz, 1988): Reciprocity/Synchrony (15-26 weeks)	**SMD 0.46 (0.16, 0.76)**		-	175 (2 studies)	●●○○ Low (c)
Maternal sensitivity mean scores					
Post-treatment – available case analysis (at-risk populations) Maternal Sensitivity and Responsivity Scales: Maternal sensitivity or synchrony (Milgrom & Meitz, 1988): Maternal Respond (15-26 weeks)	SMD 0.62 (-0.11, 1.35)		-	172 (2 studies)	●○○○ Very low (b,c,d)

Evidence Statements:

An individual, face-to-face mother-infant relationship intervention appears to have no effect on mother-infant attachment problems at endpoint or first measurement (low certainty evidence) compared with treatment as usual in pregnant and postpartum women who are considered to be 'at risk' of developing mental health problems in the perinatal period due to psychosocial risk factors.

Individual, face-to-face mother-infant relationship interventions may improve positive mother-infant interaction mean scores at endpoint or first measurement (low certainty evidence) compared with treatment as usual in postpartum women who are considered to be 'at risk' of developing mental health problems due to preterm delivery and/or low birthweight; however, the magnitude of the benefit is not clinically significant.

Individual, face-to-face mother-infant relationship interventions appear to have no effect on maternal sensitivity mean scores at endpoint or first measurement (very low certainty evidence) compared with treatment as usual in postpartum women who are considered to be 'at risk' of developing mental health problems due to preterm delivery and/or low birthweight.

An individual, face-to-face mother-infant relationship intervention improves depression mean scores at endpoint or first measurement (high certainty evidence) compared with treatment as usual in pregnant and postpartum women who are considered to be 'at risk' of developing mental health problems in the perinatal period due to psychosocial risk factors or preterm delivery and/or low birthweight; however, the magnitude on the benefit is not clinically significant.

Outcomes (follow-up)	Illustrative comparative risks*		Relative effect (95% CI)	No. of participants (studies)	Certainty of the evidence (GRADE)
	Assumed risk Control	Corresponding risk Intervention			
An individual, face-to-face mother-infant relationship intervention has no effect on depression mean scores at long follow-up (25-103 weeks post-intervention) (moderate certainty evidence), and appears to have no effect on depression diagnosis at endpoint or first measurement (low certainty evidence), or at long follow-up (25-103 weeks post-intervention) (low certainty evidence), compared with treatment as usual in pregnant and postpartum women who are considered to be 'at risk' of developing mental health problems in the perinatal period due to psychosocial risk factors. *An individual, face-to-face mother-infant relationship intervention appears to have no effect on depression mean scores at short follow-up (9-16 weeks post-intervention) (low certainty evidence), and appears to have no effect (and may be harmful) on depression symptomatology at endpoint or first measurement (very low certainty evidence), or at long follow-up (25-103 weeks post-intervention) (very low certainty evidence), compared with treatment as usual in postpartum women who are considered to be 'at risk' of developing mental health problems due to preterm delivery and/or low birthweight.*					
Footnotes: * The 'assumed risk' for the *study population* is calculated using the mean baseline risk from the studies in the meta-analysis (i.e. total number of events in the control/comparison group divided by the total number of patients in the control/comparison group). The *moderate* risk scenario is calculated using the median control/comparison group risk from the studies in the meta-analysis. The 'corresponding risk' (and its 95% CI) is based on the assumed risk in the control/comparison group and the relative effect of the intervention (and its 95% CI). a. Total number of events is less than 300 (a threshold rule-of-thumb) b. 95% CI crosses both line of no effect and measure of appreciable benefit or harm (SMD -0.5/0.5 or RR 0.75/1.25) c. Total population size is less than 400 (a threshold rule-of-thumb) d. There is evidence of considerable heterogeneity of study effect sizes e. High risk of selection bias due to statistically significant baseline difference with the intervention group having more mothers with earlier preterm birth and non-Norwegian origin f. Paper omits data g. Risk of bias due to statistically significant group differences at baseline					

Source: NICE 2015, Table 45, Table 54, Table 57

Abbreviations: CES-D, Center for Epidemiologic Studies Depression Scale; CI, confidence interval; EPDS, Edinburgh Postnatal Depression Scale; HADS, Hospital Anxiety and Depression Scale; ICEP, Infant and Caregiver Engagement Phases; ITT, intention-to-treat; PICS, Pictoral Infant Communication Scales; RR, relative risk; SCID, Structured Clinical Interview for DSM Disorders; SMD, standardised mean difference; STSI, Short Temperament Scale for Infants.

Note: Statistically significant differences are shown in bold.

C4.1.11 Co-parenting interventions

The literature search identified no SRs that relate to this intervention.

Table C4-11 Summary of findings (prevention) – co-parenting interventions

Evidence Statement: *There is no RCT evidence for co-parenting interventions in women who are considered to be 'at risk' of developing mental health problems in the perinatal period.*

C4.1.12 Mindfulness

Three SRs of prevention using mindfulness interventions were identified in the literature search but only one RCT (identified in the Taylor 2016 SR) is considered relevant to the prevention of mental health problems in the perinatal period. The pilot RCT from the United States (N=55) assessed an adapted Mindfulness-Based Cognitive Therapy (MBCT) aimed at the prevention of depressive relapse/recurrence in pregnant women with a history of major depressive disorder but who were not currently clinically depressed. Although there was no significant difference in depressive symptoms between intervention and control participants at post-

intervention, the mindfulness intervention appeared to be protective against depressive relapse up to six months postpartum (estimated 18.4% for intervention participants compared with 50.2% for control participants; HR 3.87 [95% CI 1.39, 10.76]).

A SoF table has not been constructed for this outcome as it required data extraction, risk-of-bias assessment and formulation of comparative risks – all of which were out of scope for this PICO.

Table C4-12 Summary of findings (prevention) – mindfulness

Evidence Statement: *There is limited RCT evidence for mindfulness interventions in women who are considered to be 'at risk' of developing mental health problems in the perinatal period.*

C4.2 PREVENTION WITH PSYCHOLOGICAL INTERVENTIONS

C4.2.1 Structured psychological interventions (CBT or IPT)

Of the three SRs of prevention using structured psychological interventions identified in the literature search, Morrell 2016 was chosen as the foundation review. Of note, NICE 2015 did not include structured psychological interventions (CBT and IPT) as an explicit preventive intervention type for women considered to be 'at risk' of mental health problems in the perinatal period. However, all except one of the RCTs included in the three identified SRs were either excluded from NICE 2015 due to methodological reasons or were classified under alternative intervention types and are therefore accounted for in other sections of the current report (most often 'psychologically informed psychoeducation' or 'structured psychological interventions' for treatment rather than prevention). The only RCT that is not mentioned in the NICE 2015 SR was judged by Morrell 2016 to be at high risk of bias. Chabrol 2002 (N=258) assessed an individual CBT-based intervention that involved one cognitive behaviour prevention session during hospitalisation to pregnant women at risk of depression.

Morrell 2016 included five selective preventive intervention RCTs for structured psychological interventions, three of which were CBT-based and two were IPT-based. Comparisons were made with educational information in one RCT and usual care in the other four RCTs. One Australian RCT provided the intervention in a group format, while the other four RCTs incorporated individual sessions. None of the interventions were provided in the home setting. One RCT provided the intervention in the antenatal period only whereas two RCTs initiated the intervention postnatally and two RCTs provided the intervention across the perinatal period from pregnancy to after childbirth. Interventions were provided by a variety of service providers.

Morrell 2016 also included 13 indicated preventive intervention RCTs for structured psychological interventions, eight of which were CBT-based and five were IPT-based. Comparisons were made with educational information in two RCTs and with usual care in the other 11 RCTs. Five RCTs evaluated group sessions, seven evaluated individual sessions, and one evaluated both group and individual sessions. Three RCTs took place in the home setting. Two RCTs were undertaken in the antenatal period only, one in the postnatal period only, and the remainder were undertaken in both antenatal and postnatal periods. The interventions were provided by different health-care providers in all except one RCT where the intervention was provided by a group facilitator.

It should be noted that Morrell 2016 has several errors in referencing, but that best efforts have been used in the current Review to validate and cross-reference their reported data.

C4.2.1.1 Structured psychological interventions (CBT and IPT) versus usual care

Of the five preventive intervention RCTs, two were included in the network meta-analysis (NMA).[61] One RCT (Chabrol 2002) was included in an NMA that was used to compare the effects of a CBT-based intervention with thyroxine and midwife-led debriefing following childbirth, relative to usual care on EPDS threshold data. The NMA for EPDS threshold score at 6 weeks postnatally found that the CBT-based intervention had the biggest effect relative to usual care (although this was not statistically significant), and had the highest probability of being the best (probability 0.84). The authors concluded that, in general, the intervention effects were inconclusive.

Two selective preventive intervention RCTs (Zlotnick 2011 and Chabrol 2002) were included in an NMA that was used to compare the effects of a CBT-based intervention, IPT-based intervention, education on preparing for parenting, midwife-led debriefing after childbirth and peer support relative to usual care on EPDS mean scores. The NMA found that the interventions associated with the greatest reduction in EPDS mean score were the IPT-based intervention (at 3-4 months) and the CBT-based intervention (at 6-8 weeks). However, not all interventions provided information about intervention effects at each time, making it difficult to draw inferences across all interventions at each time. In general, the intervention effects were inconclusive and the CIs were wide. Although the structured psychological interventions appeared to be the most beneficial interventions, the evidence for the effect of CBT-based intervention came from one RCT (N=158) that was judged to be at high risk of bias, and the evidence for the effect of IPT-based interventions came from a small pilot RCT (N=163); as such, the results should be treated with caution.

Of the 13 indicated preventive intervention RCTs, six were included in the NMA.[62] One RCT (Morrell 2009a/2009b) was included in a NMA that was used to compare the effects of a CBT-based intervention, PCA-based intervention and education on preparing for parenting relative to usual care on EPDS threshold. The NMA for EPDS threshold score at 6 months postnatally found that the CBT-based intervention had reduced odds of high EPDS scores compared with usual care; however, the effect was not statistically significant. The authors concluded that the intervention effects were, in general, inconclusive.

Four indicated preventive intervention RCTs (Grote 2009; Morrell 2009a/2009b; Munoz 2007; Gorman 1997) were included in a NMA that was used to compare the effects of CBT-based intervention, IPT-based intervention, educational information, midwifery continuous care, peer support, PCA-based intervention and promoting parent–infant interaction relative to usual care on EPDS mean scores.[63] The NMA found that the interventions associated with the greatest reduction in EPDS mean scores were IPT-based interventions (at 6-7 months) and CBT-based interventions (at 12 months), although none of the effects were statistically significant. Not all interventions provided information about intervention effects at each time, making inferences across all treatments at each time difficult. In general, the intervention effects were inconclusive and the CIs were wide. The most beneficial treatments appeared to be IPT-based intervention, educational information, CBT-based intervention and PCA-based intervention.

[61] Two RCTs were excluded because of a lack of EPDS data, and one RCT was excluded because there was no usual care comparator.
[62] Six RCTs were excluded because of a lack of available EPDS data, and one RCT was excluded because it could not be connected to the main network of evidence.
[63] Austin 2008 and Ginsburg 2012 were also included in the NMA, providing data for the comparison of CBT-based interventions versus educational information interventions.

Table C4-13 Summary of findings (prevention) – structured psychological interventions versus usual care

Outcomes (follow-up)	Illustrative comparative risks*		Relative effect (95% CI)	No. of participants** (studies)	[Risk of bias]*** Certainty of the evidence (GRADE)
	Assumed risk Control	Corresponding risk Intervention			
Depression symptomatology					
CBT-based Selective preventive – 6 weeks postnatally EPDS threshold score	*Study population*		OR 0.46 (0.18, 1.10)	258 (1 study)	[High risk of bias] ●○○○ Very low
	NE	NE			
	Moderate				
	NE	NE			
CBT-based Indicated preventive – 6 months postnatally EPDS threshold score	*Study population*		OR 0.59 (0.26, 1.38)	595 (1 study)	[Low risk of bias] ●●●○ Moderate
	NE	NE			
	Moderate				
	NE	NE			
Depression mean scores					
CBT-based Selective preventive – 6 weeks postnatally EPDS	MD -1.75 (-4.25, 0.71)		-	258 (1 study)	[High risk of bias] ●○○○ Very low
CBT-based Indicated preventive – 3 months postnatally EPDS	MD -1.38 (-6.07, 3.87)		-	41 (1 study)	[Unclear risk of bias] ●○○○ Very low
IPT-based Selective preventive – 3 months postnatally EPDS	MD -1.85 (-5.60, 2.14)		-	54 (1 study)	[Unclear risk of bias] ●○○○ Very low
CBT-based Indicated preventive – 6 months postnatally EPDS	MD -0.34 (-3.06, 3.01)		-	595 (1 study)	[Low risk of bias] ●●●○ Moderate
IPT-based Indicated preventive – 6 months postnatally EPDS	MD -4.25 (-7.87, 0.43)		-	98 (2 studies)	[Unclear risk of bias] ●○○○ Very low
CBT-based Indicated preventive – 12 months postnatally EPDS	MD -2.18 (-5.39, 1.15)		-	636 (2 studies)	[Low risk of bias; unclear risk of bias] ●●○○ Low

Evidence Statements:

Therapies delivered to an individual

A single cognitive behaviour prevention session (individual) during hospitalisation appears to have no effect on depression symptomatology (very low certainty evidence) and appears to have no effect on depression mean scores (very low certainty evidence) at follow-up (6 weeks postnatally) compared with usual care, in pregnant women with significantly higher than average risk of PND due to one or more social risk factors.

A CBT-based intervention (individual with home visits) may have an effect on depression symptomatology (moderate certainty evidence) but has no effect on depression mean scores (moderate certainty evidence) at follow-up (6 months postnatally) compared with usual care, in postpartum women who scored 12 or more on the EPDS.

An IPT-based intervention (individual) for low-income pregnant women with intimate partner violence appears to have no effect on depression mean scores at follow-up (3 months postnatally) (very low certainty evidence) compared with usual care, in women with significantly higher than average risk of PND due to one or more social risk factors.

An IPT-based intervention (individual) appears to have no effect on depression mean scores at follow-up (6 months postnatally) (very low certainty evidence) compared with usual care, in pregnant and postpartum women at high risk of developing PND on the basis of psychological risk factors, above average scores on psychological measures or other indications of a predisposition to PND.

Therapies delivered to a group

Outcomes (follow-up)	Illustrative comparative risks*		Relative effect (95% CI)	No. of participants** (studies)	[Risk of bias]*** Certainty of the evidence (GRADE)
	Assumed risk Control	Corresponding risk Intervention			
A CBT-based intervention (group) appears to have no effect on depression mean scores) at follow-up (3 months postnatally) (very low certainty evidence) compared with usual care, in low-income predominantly Latina women who screened positive for a major depressive episode and/or who scored 16 or more on the CES-D.					
Therapies delivered to a group or individual					
A CBT-based intervention (group or individual) appears to have no effect on depression mean scores at follow-up (12 months postnatally) (low certainty evidence) compared with usual care, in pregnant and postpartum women at high risk of developing PND on the basis of psychological risk factors, above average scores on psychological measures or other indications of a predisposition to PND.					
Footnotes: * The 'assumed risk' for the *study population* is calculated using the mean baseline risk from the studies in the meta-analysis (i.e. total number of events in the control/comparison group divided by the total number of patients in the control/comparison group). The *moderate* risk scenario is calculated using the median control/comparison group risk from the studies in the meta-analysis. The 'corresponding risk' (and its 95% CI) is based on the assumed risk in the control/comparison group and the relative effect of the intervention (and its 95% CI). ** Refers to number randomised rather than analysed. Number analysed in the SR was not reported. *** Risk of bias as assessed in Morrell 2016. This was translated for the purposes of this report into a GRADE quality of the evidence rating using the following rules: Overall risk of bias low = GRADE high quality. Overall risk of bias low but only one study = GRADE moderate quality. Overall risk of bias high = GRADE very low quality. Overall risk of bias unclear = GRADE very low quality.					

Source: Morrell 2016, Table 36, Table 46

Abbreviations: CBT, cognitive behaviour therapy; CI, confidence interval; EPDS, Edinburgh Postnatal Depression Scale; IPT, interpersonal therapy; MD, mean difference; NE, not estimable (from data in SR); OR, odds ratio; PND, postnatal depression; SR, systematic review.

C4.2.2 Directive counselling

The literature search identified no SRs that relate to this intervention.

Table C4-14 Summary of findings (prevention) – directive counselling

Evidence Statement:
There is no RCT evidence for directive counselling in women who are considered to be 'at risk' of developing mental health problems in the perinatal period.

C4.2.3 Non-directive counselling

The literature search identified no SRs with RCTs that relate to non-directive counselling for the prevention of mental health problems in the perinatal period.

Table C4-15 Summary of findings (prevention) – non-directive counselling

Evidence Statement:
There is no RCT evidence for non-directive counselling in women who are considered to be 'at risk' of developing mental health problems in the perinatal period.

C4.2.4 Case management/individual treatment

Only one SR of prevention using case management or individual treatment (NICE 2015) was identified in the literature search. NICE 2015 included one RCT from the United States (N=34) that assessed in-hospital case management and individualised treatment in women who had preterm delivery and low birthweight babies. The intervention was coordinated by one clinician (care manager) from an interdisciplinary team which included pediatrics, psychology, nursing, and physical therapy. The intervention addressed four major domains including: infant behaviour and characteristics; family organisation and functioning; caregiving environment; and home discharge and community resources.

C4.2.4.1 Case management and individualised treatment versus treatment as usual

A single study provided very low certainty evidence for a large effect of case management and individualised treatment on preventing depression symptomatology for women who had a preterm delivery or low birthweight baby (**Table C4-16**), with women in the intervention group showing a 75% risk reduction for scoring above threshold on a depression scale (BDI ≥9). However, confidence in this effect estimate is very low due to risk-of-bias concerns (statistically significant group differences in maternal age at baseline with older mean age in the intervention group) and very serious imprecision.

Table C4-16 Summary of findings (prevention) – case-management and individualised treatment versus treatment as usual

Outcomes (follow-up)	Illustrative comparative risks*		Relative effect (95% CI)	No. of participants (studies)	Certainty of the evidence (GRADE)
	Assumed risk Control	Corresponding risk Intervention			
Depression symptomatology					
Post-treatment – ITT analysis (at-risk populations) BDI ≥9 (mean 5 weeks)	*Study population*		RR 0.25 (0.06, 1.05)	34 (1 study)	●○○○ Very low (a,b,c)
	438 per 1000	109 per 1000 (26, 459)			
	Moderate				
	438 per 1000	109 per 1000 (26, 460)			
Post-treatment – Available case analysis (at-risk populations) BDI ≥9 (mean 5 weeks)	*Study population*		RR 0.25 (0.06, 1.05)	34 (1 study)	●○○○ Very low (a,b,c)
	438 per 1000	109 per 1000 (26, 459)			
	Moderate				
	438 per 1000	109 per 1000 (26, 460)			
Maternal sensitivity					
Post-treatment – ITT analysis (at-risk populations) Behavioural observation: Maternal sensitivity (mean 5 weeks)	*Study population*		RR 1.4 (0.95, 2.05)	30 (1 study)	●○○○ Very low (b,c,d)
	667 per 1000	933 per 1000 (633, 1000)			
	Moderate				
	667 per 1000	934 per 1000 (634, 1000)			
Post-treatment – available case analysis (at-risk populations) Behavioural observation: Maternal sensitivity (mean 5 weeks)	*Study population*		RR 1.4 (0.95, 2.05)	30 (1 study)	●○○○ Very low (b,c,d)
	667 per 1000	933 per 1000 (633, 1000)			
	Moderate				
	667 per 1000	934 per 1000 (634, 1000)			

Outcomes (follow-up)	Illustrative comparative risks*		Relative effect (95% CI)	No. of participants (studies)	Certainty of the evidence (GRADE)
	Assumed risk Control	Corresponding risk Intervention			
Evidence Statement: *In-hospital case management and individualised treatment may have an effect[64] on depression symptomatology at endpoint or first measurement (very low certainty evidence) compared with treatment as usual in women who are considered to be 'at risk' of developing mental health problems due to preterm delivery.* *In-hospital case management and individualised treatment appears to have no effect on maternal sensitivity at endpoint or first measurement (very low certainty evidence) compared with treatment as usual in women who are considered to be 'at risk' of developing mental health problems due to preterm delivery.*					
Footnotes: * The 'assumed risk' for the *study population* is calculated using the mean baseline risk from the studies in the meta-analysis (i.e. total number of events in the control/comparison group divided by the total number of patients in the control/comparison group). The *moderate* risk scenario is calculated using the median control/comparison group risk from the studies in the meta-analysis. The 'corresponding risk' (and its 95% CI) is based on the assumed risk in the control/comparison group and the relative effect of the intervention (and its 95% CI). a. Risk of bias due to statistically significant group differences at baseline b. Total number of events is less than 300 (a threshold rule-of-thumb) c. 95% CI crosses both line of no effect and measure of appreciable benefit or harm (SMD -0.5/0.5 or RR 0.75/1.25) d. High risk of selection bias due to unclear allocation concealment and statistically significant baseline difference in maternal age (29.7 in intervention group and 25.9 in control group)					

Source: NICE 2015, Table 46, Table 58

Abbreviations: BDI, Beck Depression Inventory; CI, confidence interval; ITT, intention-to-treat; RR, relative risk; SMD, standardised mean difference.

C4.2.5 Self-help and facilitated self-help

The literature search identified no SRs that relate to this intervention.

Table C4-17 Summary of findings (prevention) – self-help

Evidence Statement: *There is no RCT evidence for self-help and facilitated self-help in women who are considered to be 'at risk' of developing mental health problems in the perinatal period.*

C4.2.6 Post-traumatic birth counselling

The literature search identified no SRs that relate to this intervention.

Table C4-18 Summary of findings (prevention) – post-traumatic birth counselling

Evidence Statement: *There is no RCT evidence for post-traumatic birth counselling in women who are considered to be 'at risk' of developing mental health problems in the perinatal period.*

[64] RR 0.25 (95% CI 0.06, 1.05); P=0.06

C4.2.7 Post-miscarriage counselling

The literature search identified no SRs that relate to this intervention.

Table C4-19 Summary of findings (prevention) – post-miscarriage counselling

Evidence Statement: *There is no RCT evidence for post-miscarriage counselling in women who are considered to be 'at risk' of developing mental health problems in the perinatal period.*

C4.3 PREVENTION WITH ONLINE INTERVENTIONS

Only one SR of prevention using online interventions (Ashford 2016) was identified in the literature search. Ashford 2016 included four studies of web- or computer-based interventions for the prevention of mental health problems. No additional studies of web- or computer-based interventions were identified by the other SRs included in the current report.

Of the four prevention studies included in Ashford 2016, two were RCTs, one was a modified partially randomised patient preference trial, and one was a quasi-experimental pre-test/post-test study without a control group. The preventive interventions varied in the mental health issue and timeframe for which they were developed. For pregnant women, web- and computer-based interventions were developed for stress and anxiety and mental health of women diagnosed with preterm labour. For the postpartum period, web-based interventions were developed for stress and for overall psychological health of women and their partners following miscarriage. Due to the small number of studies and their heterogeneous methodological designs and quality, the authors of the Ashford 2016 SR considered that data synthesis in the form of a meta-analysis would be inappropriate and therefore information was synthesised and reported narratively.

Only one of the RCTs identified in the Ashford 2016 SR compared an online intervention with an offline intervention. The RCT (reported in a doctoral dissertation) compared the web-based 'LivingSMART' intervention from the United States with a face-to-face version of the same program. 'LivingSMART' was a postpartum stress management program based on Herbert Benson's theory of relaxation responses and stress management techniques. The web-based program offered audio instruction of the techniques and weekly emails. The educational information, handouts, additional resources, and relaxation training, was the same for each group. Four treatment sections were covered over a four-week period, with each week divided into three areas: information, relaxation, and exercises. Exercises and homework assignments were recommended for practice during the week. Social support was provided to each of the two groups. In the Internet-based program, participants were able to email or call the researcher with questions, comments and concerns, for the duration of the study. Individuals in the face-to-face program were able to have direct contact with the researcher as well as with other participants. Although the study did not recruit women with specific risk factors for mental health problems, 47.4% of study participants reported being diagnosed with depression or anxiety at some point in their lives, and 19% were currently taking medication for the treatment of depression or anxiety.

A literature search was conducted to identify RCTs of online interventions published after the literature search date of the Ashford 2016 SR. Only those studies that compared an online intervention with an offline version of the same intervention were considered eligible. No additional studies, published in full, were identified in the literature search update.

C4.3.1.1 Online intervention versus offline (face-to-face) intervention

On the basis of a single RCT, there was no significant reduction in mean depression scores in women who received a web-based postpartum stress management intervention or in women who received a face-to-face version of the same intervention. Post-intervention stress and anxiety mean scores were significantly lower than pre-intervention scores in the web-based intervention group, whereas the face-to-face control group showed no significant improvement post-intervention.[65] However, there was no significant between-group differences in post-intervention stress, anxiety or depression mean scores, and no significant differences between groups in mean change from baseline scores.[66] Attrition in the intervention group was 41.1% versus 33.3% in the control group.

Table C4-20 Summary of findings (prevention) – online intervention versus offline (face-to-face) intervention

Outcomes (follow-up)	Illustrative comparative risks*		Relative effect (95% CI)	No. of participants (studies)	Certainty of the evidence (GRADE)
	Assumed risk Control	Corresponding risk Intervention			
Depression mean scores					
One week post-treatment – available case analysis BDI-II	MD 2.05 (-1.67, 5.77)		-	38 (1 study)	●○○○ Very low (a,b,c)
Anxiety mean scores					
One week post-treatment – available case analysis STAI	MD 0.73 (-3.52, 4.98)		-	38 (1 study)	●○○○ Very low (a,b,c)
Perceived stress mean scores					
One week post-treatment – available case analysis PSS	MD -0.43 (-3.85, 2.99)		-	38 (1 study)	●○○○ Very low (a,b,c)
Evidence Statement: *A web-based postpartum stress management intervention appears to have no effect on depression mean scores (very low certainty evidence), anxiety mean scores (very low certainty evidence), or perceived stress mean scores (very low certainty evidence), at one week post-intervention compared with a face-to-face version of the program in postpartum women (with no specific risk factors for developing mental health problems in the perinatal period).*					

Footnotes:

* The 'assumed risk' for the *study population* is calculated using the mean baseline risk from the studies in the meta-analysis (i.e. total number of events in the control/comparison group divided by the total number of patients in the control/comparison group). The *moderate* risk scenario is calculated using the median control/comparison group risk from the studies in the meta-analysis. The 'corresponding risk' (and its 95% CI) is based on the assumed risk in the control/comparison group and the relative effect of the intervention (and its 95% CI).

a. High risk of bias due to unclear allocation concealment and high rate of attrition

b. Study not targeted to women at risk of mental health problems in the perinatal period

c. 95% CI crosses both line of no effect and measure of appreciable benefit or harm (SMD -0.5/0.5)

Source: Raw data (mean and SD) taken from King 2009, Table 1. Post-intervention between-group difference calculated post hoc using Review Manager 5.3.

Abbreviations: BDI, Beck Depression Inventory; CI, confidence interval; MD, mean difference; PSS, Perceived Stress Scale; STAI, State Trait Anxiety Inventory.

[65] Post hoc tests showed a 24% reduction in stress and a 25% reduction in anxiety in the online group, both of which were statistically significant. The control group findings showed a 10% reduction in anxiety and a 7% reduction in stress, which were not statistically significant. Both groups experienced a reduction in depression that was not statistically significant (16% reduction in the online group and 7% reduction in the control group).

[66] Between-group differences not reported in King 2009 thesis dissertation but was calculated for the purposes of the current Review using Review Manager 5.3.

C4.4 PREVENTION WITH PHARMACOLOGICAL INTERVENTIONS

C4.4.1 Antidepressants

Of the two SRs identified in the scoping and updated searches, NICE 2015 was chosen as the foundation review due to its assessment of the evidence using SoF tables. Both SRs included the same two RCTs – one comparing SSRIs (sertraline) with placebo and one comparing TCAs (nortriptyline).

C4.4.1.1 SSRIs

The NICE 2015 SR provided data for one comparison involving an SSRI: sertraline versus placebo.

Table C4-21 summarises the evidence and provides Evidence Statements relating to the comparison between sertraline and placebo. There was very low certainty evidence that prophylaxis with sertraline does not appear to prevent recurrence of postnatal depression; however, the reduction in risk was very substantial (RR 0.14) and the upper 95% CI only just crosses 1.0, indicating that there may be a significant effect, but the analysis is underpowered. In terms of adverse events, there was very low certainty evidence of no difference in dizziness between sertraline and placebo, and a significantly increased risk of drowsiness.

Table C4-21 Summary of findings (prevention) – SSRIs (sertraline) versus placebo

Outcomes (follow-up)	Illustrative comparative risks*		Relative effect (95% CI)	No. of participants (studies)	Certainty of the evidence (GRADE) Comments
	Assumed risk Control	Corresponding risk Intervention			
Recurrence					
Recurrence of depression	*Study population*		RR 0.14	22	●○○○
Post-treatment	500 per 1000	70 per 1000 (10, 535)	(0.02, 1.07)	(1 RCT)[67]	Very low (a,b)
HRSD ≥ 15 on two occasions and DSM-IV	*Moderate*				
(17 weeks)	500 per 1000	70 per 1000 (10, 535)			
Adverse events					
Dizziness	*Study population*		RR 4.57	22	●○○○
Post-treatment	125 per 1000	571 per 1000 (86, 1000)	(0.69, 30.2)	(1 RCT)[68]	Very low (a,b)
(17 weeks)	*Moderate*				
	125 per 1000	571 per 1000 (86, 1000)			
Drowsiness	*Study population*		**RR 1.93**	22	●○○○
Post-treatment	500 per 1000	965 per 1000 (500, 1000)	**(1.00, 3.74)**	(1 RCT)[69]	Very low (a,b)
(17 weeks)	*Moderate*				
	500 per 1000	965 per 1000 (500, 1000)			

[67] NICE 2015 (Wisner 2004).
[68] NICE 2015 (Wisner 2004).
[69] NICE 2015 (Wisner 2004).

Outcomes (follow-up)	Illustrative comparative risks*		Relative effect (95% CI)	No. of participants (studies)	Certainty of the evidence (GRADE) Comments
	Assumed risk Control	Corresponding risk Intervention			
Evidence Statements: *Prophylaxis with sertraline appears to have no effect on (but may reduce) the risk of recurrence of depression at 17 weeks post-treatment compared with placebo, in women with one or more psychological risk factors for the development of postnatal depression (very low certainty evidence).* *Prophylaxis with sertraline appears to have no effect on the risk of dizziness at 17 weeks post-treatment compared with placebo, in women with one or more psychological risk factors for the development of postnatal depression (very low certainty evidence).* *Prophylaxis with sertraline may increase the risk of drowsiness at 17 weeks post-treatment compared with placebo, in women with one or more psychological risk factors for the development of postnatal depression, from an absolute risk of 50% to 97% (very low certainty evidence).*					
Footnotes: * The 'assumed risk' for the study population is calculated using the mean baseline risk from the studies in the meta-analysis (i.e. total number of events in the control/comparison group divided by the total number of patients in the control/comparison group). The moderate risk scenario is calculated using the median control/comparison group risk from the studies in the meta-analysis. The 'corresponding risk' (and its 95% CI) is based on the assumed risk in the control/comparison group and the relative effect of the intervention (and its 95% CI). a. Unclear attrition bias and independence of data assumption contravened. b. Total population size is less than 400 (a threshold rule-of-thumb) and 95% CI crosses both line of no effect and measure of appreciable benefit or harm (SMD -0.5/0.5 or RR 0.75/1.25).					

Source: NICE 2015 – Table 281 and Table 283.

Abbreviations: CI, confidence interval; DSM-IV, Diagnostic and Statistical Manual of Mental Disorders, 4th Edition; HRSD, Hamilton Rating Scale for Depression; PND, postnatal depression; RCT, randomised controlled trial; RR, relative risk; SMD, standardised mean difference.

C4.4.1.2 TCAs

The NICE 2015 SR provided data for one comparison involving a TCA: nortriptyline versus placebo.

Table C4-22 summarises the evidence and provides Evidence Statements relating to the comparison between nortriptyline and placebo. There was very low certainty evidence that prophylaxis with nortriptyline does not appear to prevent recurrence of postnatal depression. In terms of adverse events, there was very low certainty evidence of no difference in discontinuation due to adverse events, but the 95% CI was very wide, indicating a lack of power in the analysis. There was moderate certainty evidence that use of nortriptyline results in an increased risk of constipation compared with placebo.

Table C4-22 Summary of findings (prevention) – TCAs (nortriptyline) versus placebo

Outcomes (follow-up)	Illustrative comparative risks*		Relative effect (95% CI)	No. of participants (studies)	Certainty of the evidence (GRADE)
	Assumed risk Control	Corresponding risk Intervention			
Recurrence of depression					
Recurrence of major depression	*Study population*		RR 0.96	51	●●○○
Post-treatment	240 per 1000	230 per 1000 (86, 622)	(0.36, 2.59)	(1 RCT)[70]	Low (a)
HRSD ≥ 15 and RDC for major depression	*Moderate*				
(22 weeks)	240 per 1000	230 per 1000 (86, 622)			

[70] NICE 2015 (Wisner 2001).

Outcomes (follow-up)	**Illustrative comparative risks***		**Relative effect (95% CI)**	**No. of participants (studies)**	**Certainty of the evidence (GRADE)**
	Assumed risk Control	**Corresponding risk Intervention**			
Recurrence of major depression postpartum	*Study population*		RR 1.20 (0.57, 2.55)	51 (1 RCT)[70]	●●○○ Low (a)
Long-term follow-up – 25-103 weeks post intervention	320 per 1000	384 per 1000 (182, 816)			
HRSD ≥ 15 and RDC for major depression	*Moderate*				
(26 weeks)	320 per 1000	384 per 1000 (182, 816)			
Side effects					
Discontinuation due to adverse events	*Study population*		RR 0.32 (0.01, 7.53)	51 (1 RCT)[70]	●●○○ Low (a)
Post-treatment	40 per 1000	13 per 1000 (0, 301)			
(20 weeks)	*Moderate*				
	40 per 1000	13 per 1000 (0, 301)			
Constipation	*Study population*		**RR 3.21 (1.55, 6.64)**	51 (1 RCT)[70]	●●●○ Moderate (b)
Post-treatment	240 per 1000	770 per 1000 (372, 1000)			
(20 weeks)	*Moderate*				
	NR	NR			

Evidence Statements:

Prophylaxis with nortriptyline appears to have no effect on the risk of recurrence of depression at 22 weeks post-treatment, or 26 weeks post-intervention, compared with placebo, in women with one or more psychological risk factors for the development of postnatal depression (low certainty evidence).

Prophylaxis with nortriptyline increases the risk of constipation at 22 weeks post-treatment compared with placebo, in women with one or more psychological risk factors for the development of postnatal depression, from an absolute risk of 24% to 77% (moderate certainty evidence).

Footnotes:

* The 'assumed risk' for the study population is calculated using the mean baseline risk from the studies in the meta-analysis (i.e. total number of events in the control/comparison group divided by the total number of patients in the control/comparison group). The moderate risk scenario is calculated using the median control/comparison group risk from the studies in the meta-analysis. The 'corresponding risk' (and its 95% CI) is based on the assumed risk in the control/comparison group and the relative effect of the intervention (and its 95% CI).

a. Total population size is less than 400 (a threshold rule-of-thumb) and 95% CI crosses both line of no effect and measure of appreciable benefit or harm (SMD -0.5/0.5 or RR 0.75/1.25).

b. Total population size is less than 400 (a threshold rule-of-thumb).

Source: NICE 2015 – Table 282 and Table 284.

Abbreviations: CI, confidence interval; HRSD, Hamilton Rating Scale for Depression; PND, postnatal depression; RCT, randomised controlled trial; RDC, Research Diagnostic Criteria; RR, relative risk; SMD, standardised mean difference.

C4.4.2 Antipsychotics

No SRs or individual RCTs were identified that assessed the effect of antipsychotics on the prevention of antenatal or postnatal mental health problems in women who are considered to be 'at risk', or maternal side effects.

Table C4-23 Summary of findings (prevention) – antipsychotics

Evidence Statement: *There is no RCT evidence for antipsychotics as an intervention for pregnant women who are considered to be 'at risk' of developing mental health problems in the perinatal period.*

C4.4.3 Anticonvulsants

No SRs or individual RCTs were identified that assessed the effectiveness of anticonvulsants on the prevention of antenatal or postnatal mental health problems in women who are considered to be 'at risk'.

Table C4-24 Summary of findings (prevention) – anticonvulsants

Evidence Statement: *There is no RCT evidence for anticonvulsants as an intervention for pregnant women who are considered to be 'at risk' of developing mental health problems in the perinatal period.*

C4.4.4 Benzodiazepines and z-drugs

No SRs or individual RCTs were identified that assessed the effectiveness of benzodiazepines and z-drugs on the prevention of antenatal or postnatal mental health problems in women who are considered to be 'at risk'.

Table C4-25 Summary of findings (prevention) – benzodiazepines and z-drugs

Evidence Statement: *There is no RCT evidence for benzodiazepines and z-drugs as an intervention for pregnant women who are considered to be 'at risk' of developing mental health problems in the perinatal period.*

C4.4.5 Lithium

No SRs or individual RCTs were identified that assessed the effectiveness of lithium on the prevention of antenatal or postnatal mental health problems in women who are considered to be 'at risk'.

Table C4-26 Summary of findings (prevention) – lithium

Evidence Statement: *There is no RCT evidence for lithium as an intervention for pregnant women who are considered to be 'at risk' of developing mental health problems in the perinatal period.*

C4.5 PREVENTION WITH COMPLEMENTARY INTERVENTIONS

C4.5.1 Omega-3 fatty acids

One SR was identified in the scoping and updated searches that assessed the use of omega-3 fatty acids compared with placebo to prevent postnatal depression (Miller 2013). The single included study (Mozurkewich 2013) examined separately two types of omega-3 fatty acids: eicosapentaenoic acid (EPA)-rich fish oil supplements and docosahexaenoic acid (DHA)-rich fish oil supplements. Each will be considered separately.

C4.5.1.1 Eicosapentaenoic acid (EPA)

Table C4-27 summarises the evidence and provides Evidence Statements relating to the comparison between EPA and placebo. There was moderate certainty evidence that prophylaxis with EPA compared with placebo does not reduce depression mean score or prevent diagnosis with MDD at 6-8 weeks postnatal in women at risk of developing postnatal depression.

Table C4-27 Summary of findings (prevention) – omega-3 fatty acids (EPA) versus placebo

Outcomes (follow-up)	Illustrative comparative risks*		Relative effect (95% CI)	No. of participants (studies)	Certainty of the evidence (GRADE)
	Assumed risk Control	Corresponding risk Intervention			
Diagnosis of MDD					
Presence of MDD	*Study population*		RR 1.58	80	●●●○
Post-treatment - ITT analysis	49 per 1000	77 per 1000 (14, 438)	(0.28, 8.94)	(1 RCT)[71]	Moderate(a)
MINI	*Moderate*				
(6-8 weeks post-partum)	NR	NR			
Mean depression score					
Mean depression score	MD 0.70		-	80	●●●○
Post-treatment – ITT analysis	(-1.78, 3.18)			(1 RCT)[72]	Moderate(a)
BDI					
(6-8 weeks post-partum)					
Evidence Statements:					
Prophylaxis with EPA has no effect on the risk of being diagnosed with major depressive disorder at 6-8 weeks postpartum compared with placebo, in women at risk of developing postnatal depression (moderate certainty evidence).					
Prophylaxis with EPA has no effect on depression mean score at 6-8 weeks postpartum compared with placebo, in women at risk of developing postnatal depression (moderate certainty evidence).					

Footnotes:

* The 'assumed risk' for the study population is calculated using the mean baseline risk from the studies in the meta-analysis (i.e. total number of events in the control/comparison group divided by the total number of patients in the control/comparison group). The moderate risk scenario is calculated using the median control/comparison group risk from the studies in the meta-analysis. The 'corresponding risk' (and its 95% CI) is based on the assumed risk in the control/comparison group and the relative effect of the intervention (and its 95% CI).

a. Total population size is less than 400 (a threshold rule-of-thumb) and 95% CI crosses both line of no effect and measure of appreciable benefit or harm (SMD -0.5/0.5 or RR 0.75/1.25).

Source: Miller 2013 – Analysis 2.1 and 2.2.

Abbreviations: CI, confidence interval; BDI, Beck Depression Inventory; EPDS, Edinburgh Postnatal Depression Scale; HRSD, Hamilton Rating Scale for Depression; MDD, major depressive disorder; RCT, randomised controlled trial; RR, relative risk; SMD, standardised mean difference.

C4.5.1.2 Docosahexaenoic acid (DHA)

Table C4-28 summarises the evidence and provides Evidence Statements relating to the comparison between DHA and placebo. There was moderate certainty evidence that prophylaxis with EPA compared with placebo does not reduce depression mean score or prevent diagnosis with MDD at 6-8 weeks postnatal in women at risk of developing postnatal depression.

[71] Miller 2013 (Mozurkewich 2013).

[72] Miller 2013 (Mozurkewich 2013).

Table C4-28 Summary of findings (prevention) – omega-3 fatty acid (DHA) versus placebo

Outcomes (follow-up)	Illustrative comparative risks*		Relative effect (95% CI)	No. of participants (studies)	Certainty of the evidence (GRADE)
	Assumed risk Control	Corresponding risk Intervention			
Diagnosis of MDD					
Presence of MDD	*Study population*		RR 1.08	79	●●●○
Post-treatment - ITT analysis	49 per 1000	53 per 1000 (8, 357)	(0.16, 7.28)	(1 RCT)[73]	Moderate(a)
MINI	*Moderate*				
(6-8 weeks post-partum)	NR	NR			
Mean depression score					
Mean depression score	MD -0.20		-	79	●●●○
Post-treatment – ITT analysis	(-2.61, 2.21)			(1 RCT)[74]	Moderate(a)
BDI					
(6-8 weeks post-partum)					
Evidence Statements:					
Prophylaxis with DHA has no effect on the risk of being diagnosed with major depressive disorder at 6-8 weeks postpartum compared with placebo, in women at risk of developing postnatal depression (moderate certainty evidence).					
Prophylaxis with DHA has no effect on depression mean score at 6-8 weeks postpartum compared with placebo, in women at risk of developing postnatal depression (moderate certainty evidence).					

Footnotes:

* The 'assumed risk' for the study population is calculated using the mean baseline risk from the studies in the meta-analysis (i.e. total number of events in the control/comparison group divided by the total number of patients in the control/comparison group). The moderate risk scenario is calculated using the median control/comparison group risk from the studies in the meta-analysis. The 'corresponding risk' (and its 95% CI) is based on the assumed risk in the control/comparison group and the relative effect of the intervention (and its 95% CI).

a. Total population size is less than 400 (a threshold rule-of-thumb) and 95% CI crosses both line of no effect and measure of appreciable benefit or harm (SMD -0.5/0.5 or RR 0.75/1.25).

Source: NICE 2015 – Analysis 3.1 and 3.2.

Abbreviations: CI, confidence interval; BDI, Beck Depression Inventory; EPDS, Edinburgh Postnatal Depression Scale; HRSD, Hamilton Rating Scale for Depression; MDD, major depressive disorder; PND, postnatal depression; RCT, randomised controlled trial; RR, relative risk; SMD, standardised mean difference.

[73] Miller 2013 (Mozurkewich 2013).

[74] Miller 2013 (Mozurkewich 2013).

C4.5.2 St John's wort

No SRs or individual RCTs were identified that assessed the effectiveness of St John's wort on the prevention of antenatal or postnatal mental health problems in women who are considered to be 'at risk'.

Table C4-29 Summary of findings (prevention) – St John's wort

Evidence Statement: *There is no RCT evidence for St John's wort as an intervention for pregnant women who are considered to be 'at risk' of developing mental health problems in the perinatal period.*

C4.5.3 Gingko biloba

No SRs or individual RCTs were identified that assessed the effectiveness of gingko biloba on the prevention of antenatal or postnatal mental health problems in women who are considered to be 'at risk',.

Table C4-30 Summary of findings (prevention) – gingko biloba

Evidence Statement: *There is no RCT evidence for Gingko biloba as an intervention for pregnant women who are considered to be 'at risk' of developing mental health problems in the perinatal period.*

C4.6 PREVENTION WITH PHYSICAL INTERVENTIONS

C4.6.1 Exercise

Only one SR of prevention using physical interventions (Daley 2015) was identified in the literature search. The SR identified one RCT (N=34) that assessed experiential exercise as part of a mindfulness intervention in women at risk of antenatal depression. However, on the basis of participant baseline symptoms, the RCT was considered to have recruited depressed women and the intervention was therefore classified as a treatment rather than preventive intervention.

Table C4-31 Summary of findings (prevention) – exercise

Evidence Statement:
There is no RCT evidence for exercise as an intervention for pregnant women who are considered to be 'at risk' of developing mental health problems in the perinatal period.

C4.6.2 Yoga

The literature search identified no SRs that relate to this intervention.

Table C4-32 Summary of findings (prevention) – yoga

Evidence Statement:
There is no RCT evidence for yoga as an intervention for pregnant women who are considered to be 'at risk' of developing mental health problems in the perinatal period.

C4.6.3 Acupuncture

Only one SR of prevention using acupuncture (NICE 2015) was identified in the literature search. The RCT from Brazil (N=29) assessed acupuncture delivered over a 12-week period to postpartum women with preterm infants with very low birthweight. Placebo acupuncture was applied using the same needles customised to not perforate skin, and a toothpick to create the sensation of needle perforation.

C4.6.3.1 Acupuncture versus placebo acupuncture

There was no statistically or clinically significant effect of acupuncture on mean anxiety scores at the end of intervention (**Table C4-33**).

Table C4-33 Summary of findings (prevention) – acupuncture versus placebo acupuncture

Outcomes (follow-up)	Illustrative comparative risks*		Relative effect (95% CI)	No. of participants (studies)	Certainty of the evidence (GRADE)
	Assumed risk Control	Corresponding risk Intervention			
Anxiety mean scores					
Post intervention- Available case analysis STAI (12 weeks)	SMD 0.56 (-0.19, 1.3)		-	29 (1 study)	●○○○ Very low (a,b)
Evidence Statement: *Acupuncture (delivered over 12 weeks) appears to have no effect on anxiety mean scores at endpoint or first measurement (very low certainty evidence) compared to placebo acupuncture, in women who are considered to be 'at risk' of developing mental health problems due to preterm delivery and low birthweight.*					
Footnotes: *The basis for the assumed risk (for example the median control group risk across studies) is provided in footnotes. The corresponding risk (and its 95% CI) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI). a. High risk of bias in several domains b. Total population size is less than 400 (a threshold rule-of-thumb) and 95% CI crosses both line of no effect and measure of appreciable benefit or harm (SMD -0.5/0.5 or RR 0.75/1.25)					

Source: NICE 2015, Table 341

Abbreviations: CI, confidence interval; RR relative risk; SMD, standardised mean difference; STAI, State-Trait Anxiety Inventory.

C4.6.4 Electroconvulsive therapy

No SRs or individual RCTs were identified that assessed the effectiveness of ECT on the prevention of mental health problems during pregnancy.

Table C4-34 Summary of findings (prevention) – electroconvulsive therapy

Evidence Statement: *There is no RCT evidence for ECT as an intervention for pregnant women who are considered to be 'at risk' of developing mental health problems in the perinatal period.*

C4.6.5 Transcranial magnetic stimulation

No SRs or individual RCTs were identified that assessed the effectiveness of TMS on the prevention of mental health problems during pregnancy.

Table C4-35 Summary of findings (prevention) – transcranial magnetic stimulation

Evidence Statement: *There is no RCT evidence for TMS as an intervention for pregnant women who are considered to be 'at risk' of developing mental health problems in the perinatal period.*

C4.7 ECONOMIC EVIDENCE

No relevant Australian economic evaluations of interventions for the treatment or prevention of perinatal mental health problems were identified in the literature search. Although there are existing economic evaluations from other countries, they have limited local context applicability, since the design, delivery, and cost of healthcare systems around the world very greatly.

An Australian economic analysis has been published of the psychoeducational intervention 'What Were We Thinking (WWWT)', which recruited English-speaking first-time mothers who had recently given birth and attended participating Maternal and Child Health Centres (MCHCs) in Victoria (Ride 2016). The intervention focused on parental partner relationships, management of infant behaviour and parental fatigue. Participants did not strictly meet the criteria for this Review because they did not necessarily have risk factors for mental health problems or mental health symptomatology.

A community-based before and after controlled study found that WWWT reduced postnatal mental health problems among women with no history of psychiatric disorders. The Sleep, Parenting and Relationships in a Community Setting (SPARCS) cluster-randomised trial was subsequently conducted to examine the clinical and cost-effectiveness of WWWT for the prevention of depression, anxiety and adjustment disorders in women at six months postpartum. Participants at intervention centres received WWWT-informed care during MCH visits, and both parents were invited to attend an extra six-hour first-time-parent group session on a Saturday, during which the WWWT intervention was delivered, and received printed materials to take home. Participants at control MCHCs were provided usual MCH care. At follow-up, the unadjusted 30-day prevalence of DSM-IV diagnoses of depression, anxiety and adjustment disorders was 8.57% in the control group, and 8.70% in the intervention group.

The economic evaluation took a public-sector perspective (incorporating healthcare, early childhood and social service costs), plus the participant's out-of-pocket costs. There was no statistically significant difference in either effectiveness or costs; however, the authors claimed that the point estimate of cost-effectiveness suggested WWWT might be a cost-effective intervention for the prevention of postnatal mental health problems in first-time mothers, albeit with a high degree of uncertainty surrounding the result.

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