Development of a Core Outcome Set (COS) for treatment of depression during or after pregnancy (antenatal and postpartum depression)

SBU POLICY SUPPORT

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Summary

Swedish Agency for Health Technology Assessment and Assessment of Social Services (SBU) has enabled relevant interested parties (particularly patients, researchers, and healthcare personnel), from Sweden and other countries, to agree on which outcomes should be included in a Core Outcome Set (COS) for future research studies in the treatment of antenatal and postpartum depression. In total, the COS included nine outcomes (Table 1).

Background

A core outcome set (COS) is an agreed standardised set of outcomes that should be assessed and reported, as a minimum, in all clinical trials in specific areas of health or health care. The outcomes that are to be included in different COS are selected by a consensus process, in which healthcare personnel, researchers, and patients should be included. By developing and implementing COS, the aim is to enable the results from various studies to be more readily comparable and synthesised, and that the basis for decisions, for patients and healthcare personnel, will therefore be strengthened (Figure 1).

Table 1 Outcomes included in the core outcome set.

Self-assessed symptoms of depression, assessed with a scale that captures differences in sleep*
Diagnosis of depression as assessed by a clinician should include a structured interview
Parent to infant bonding
Self-assessed symptoms of anxiety
Quality of life
Satisfaction with the study intervention
Suicidal thoughts, attempts or completed suicide*
Thoughts of harming the baby, including thoughts of extended suicide*
Adverse events including spontaneous or induced abortion, miscarriage, fetal death and neonatal death

** Outcomes which are included in the COS, based on the results of survey 2 the remaining outcomes were included after discussions during the consensus meeting.*

Aim

Development of a COS for future research studies in the treatment of antenatal and postpartum depression.

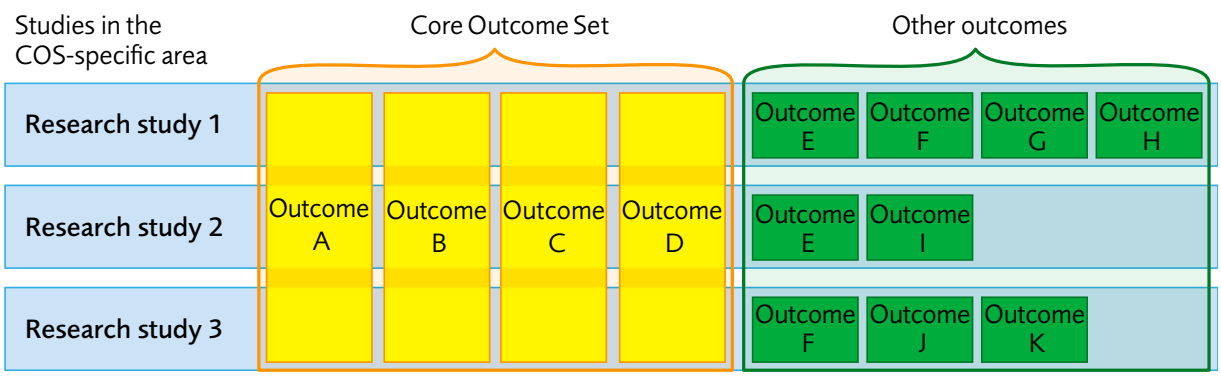

Figure 1 Schematic illustration showing the intended use of COS.

The primary target groups for this report are researchers and research funders. The project has been commissioned by the Swedish government as part of its efforts for the promotion of women's health. This is the first time SBU has facilitated the development of a COS.

The area of antenatal and postpartum depression was chosen based on the results from an overview of existing and ongoing COS within the field of maternal health [1].

Method

The project was registered in the COMET initiative registry [2] and is developed according to the-COS-STAD Recommendations [3]. The project followed an a priori established protocol (Appendix 1).

The study consisted of three parts: (1) a systematic overview of the outcomes reported in systematic reviews and randomised controlled trials (RCTs) published 2018–2019, as well as in ongoing RCT on the topic, (2) a two-round Delphi survey with relevant stakeholders to prioritise the outcomes used in the studies, and (3) a consensus meeting where the final COS is decided (Figure 2). The project does not address the questions of which method should be applied to assess the outcomes, or when the outcomes should be assessed.

Identifying outcomes in research

In order to identify outcomes used in current research, a literature search for relevant randomised controlled trials (RCT) and systematic reviews published 2018–2019 as well as study protocols for RCT (no time limit) was undertaken (search strategy presented in Appendix 2).

Inclusion criteria

Population

- Pregnant women, or their partners suffering from depression
- New mothers or their partners suffering from depressions

Intervention

Any intervention given for depression

Control

Any type of control was accepted

Outcome

Outcomes relating to the effect of the treatment given

Study design

Randomised controlled trials or systematic reviews. Both protocols and published studies were included.

Limitations

Conference abstracts, studies investigating prevention of depression and studies investigating treatments given to persons suffering from a combination of depression and other chronic conditions such as HIV infection, were excluded.

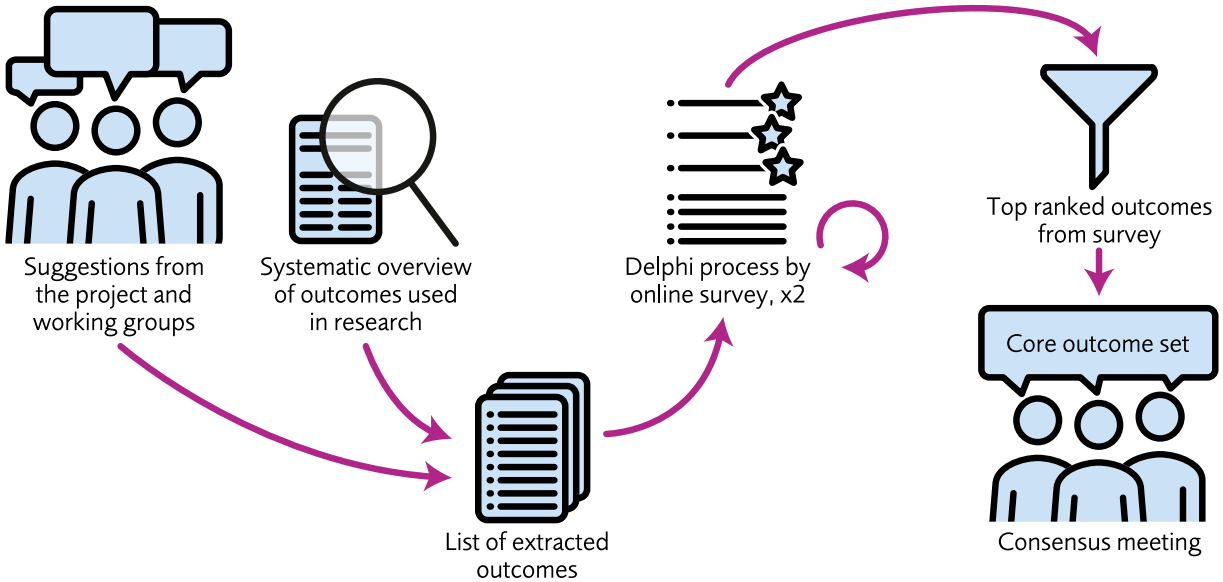

Figure 2 Flow chart of the project.

Language

No language restriction applied to the search strategy, but the final inclusion was only for studies in English or Scandinavian languages

Search period

From 2018 to 2019 (clinicaltrials.gov no time restriction). Final search September–October 2019 (full search strategy presented in Appendix 2)

Databases searched

Medline (OVID), Cochrane library (Wiley), PsycINFO (EBSCO), Cinahl (EBSCO) and ClinicalTrials.gov

Client/patient involvement

Yes

All identified studies were screened for relevance independently by two members of the study management. Data were extracted by one review author and checked by another review author.

Following data were extracted from the studies:

- Reference
- Study design
- Year for publication
- Intervention/s used
- Outcomes, with notification if outcomes are stated as primary or secondary
- Tool for outcome measure
- Time for outcome measure

After extraction, the identified outcomes were analysed and all outcomes that are unique were listed. Some very similar outcomes in that list were brought together, for example outcomes measuring different hormonal or pharmaceutical levels were combined as under biological parameters.

Development of a Core Outcome Set

This process comprises a two-round Delphi survey and a consensus meeting. Relevant stakeholders (the working group) participated in the entire process, giving their perspectives on which outcomes are so important that they should be included in the COS. To allow international participation, all material was translated into English and information about the project was disseminated both within Sweden and internationally. In all, 222 people expressed an interest in participating, of whom 24 were international participants (Table 3). All participants belonged to one of the following four stakeholder group:

- Patient- or relative
- Researcher within the field
- Health professional
- HTA-agencies policy makers and others

In the Delphi study, all participants independently ranked the various outcomes in terms of importance and relevance, in two consecutive surveys. The information sent to the participants are presented in Appendix 3. Before they answered the second survey, they were shown how the different s takeholder groups, had ranked the outcomes in the first survey. In the first survey there was also an opportunity to suggest additional outcomes which were not identified in the actual research. The results of the surveys were analysed according to previously determined criteria, as to whether the outcome should be included in the COS. One exception from the pre-set protocol was made after the Delphi process. This to enable all outcomes included in the consensus meeting to be properly discussed. In total 23 outcomes were passed forward to the consensus meeting. Based on the results from the second survey three outcomes (marked with * in Table 1) were classified as consensus in, and thereby included in the COS. In addition, outcomes fulfilling either of the two the below specified criteria where discussed during meeting:

- Any outcome for which at least 70% of participants in either one of the stakeholder group scored as critically important (7–9)

- The ten outcomes given the highest scores by each stakeholder group

The entire process concluded with a meeting at which a selection of the participants who had been in the Delphi study reached consensus about which further outcomes, over and above those which had already met the inclusion criteria, should be included in the COS. After the consensus meeting, all those who had completed the second questionnaire were given access to, and the option of making comments on, the final COS.

Results

Identifying outcomes in research

A total of 165 studies (Figure 3) were included and are described in further detail in Appendix 4. Excluded studies with reason for exclusion are presented in Appendix 5. On the basis of the included studies, a list was made of 93 different outcomes which were used in the research. As well, a further 13 outcomes were added by the project participants. Thus, in all,

Table 2 Summary of results from the systematic overview of outcomes.

	Number of studies	Antenatal depression	Postpartum depression	Both antenatal samt postpartum depression	Number of outcomes in the studies, Median; Mean (min–max)
RCT-protocol	104	33	60	11	5; 6 (1–24)
RCT-published (2018–2019)	27	12	12	3	5; 6 (1–19)
Systematic reviews published (2018–2019)	34	8	16	10	2; 3 (1–13)
Total	165	53	88	24	5; 6 (1–24

105 outcomes were included in the consensus process. On average, the RCTs contained six outcomes and the systematic reviews four outcomes (Table 2). The three most common outcomes in the included studies were self-assessed symptoms of depression, clinical diagnosis of depression and self-assessed symptoms of anxiety.

Development of a Core Outcome Set

A flow chart describing the different steps of the development of the COS are presented in Figure 4.

Out of the 222 people who expressed an interest to partake in the project, 151 completed survey 1 and 123 completed survey 2 (Table 3). All outcomes included in the survey and a summary of the results are presented in Table 4. A more detailed presentation of the results from survey 1 and survey 2 are available in Appendix 6 and Appendix 7.

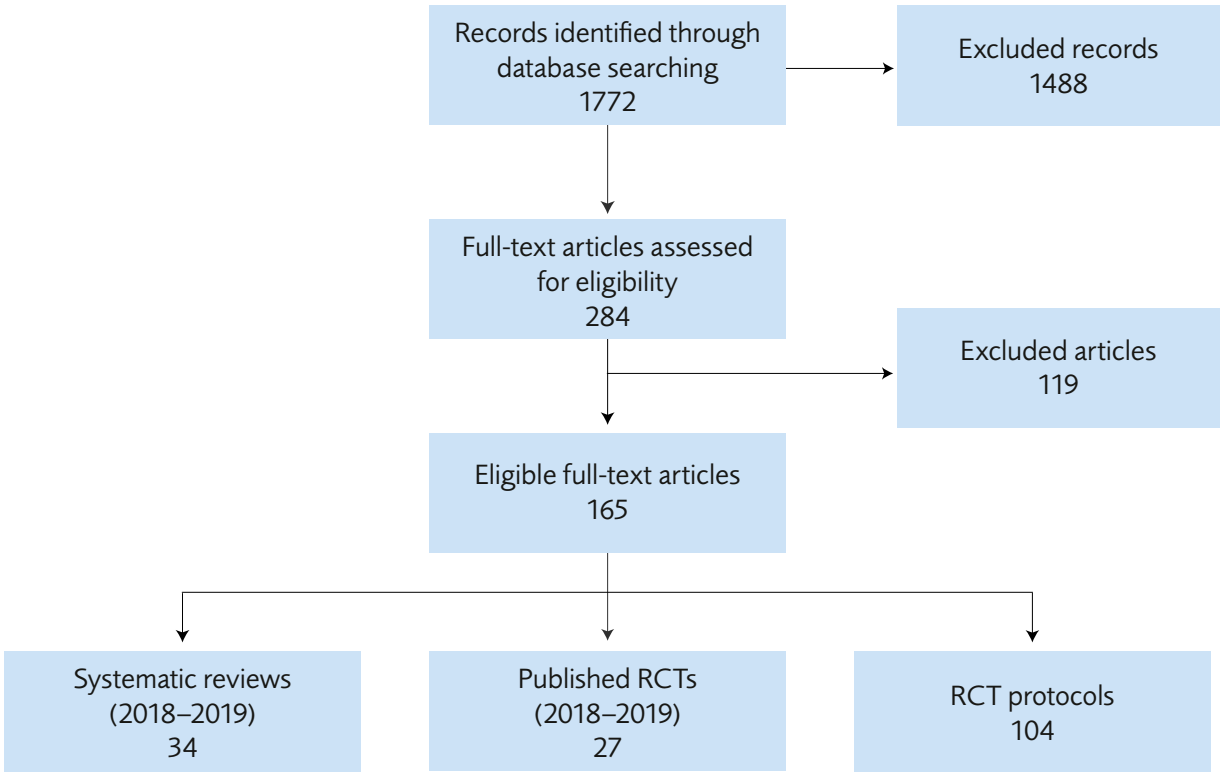

Figure 3 Flow Chart.

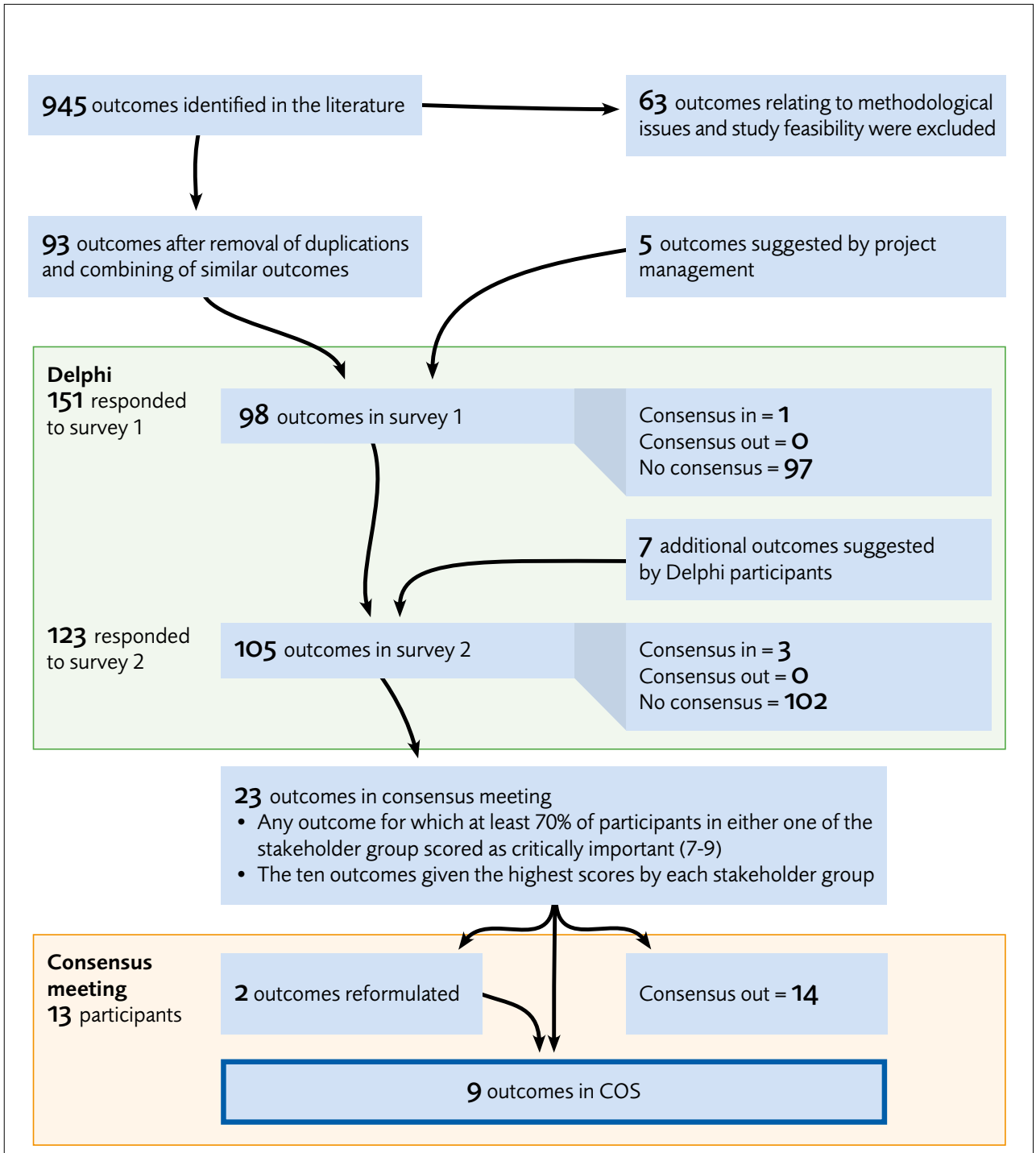

Figure 4 Flow chart of the different steps in the development of the Core outcome set.

Table 3 Characteristics of participants in the Delphi online survey.

	Signed up for participation	Completed survey 1	Completed survey 2	Participated in consensus-meeting
Researcher within the field	41	30	31	3
HTA-agencies, policy makers and others	13	11	9	2
Patient- or relative	69	43	33	4
Health professional	99	67	50	4
Total (from countries other than Sweden)	222 (24*)	151 (20)	123 (18)	13 (0)

** Brazil (n=1), Norway (n=1), United kingdom (n=4), Ireland (n=7), Finland (n=1), Germany (n=2), China (n=2), Nigeria (n=1), France (n=1), Holland (n=1), Portugal (n=1), India (n=1), Israel (n=1)*

After analysing the result of both surveys, three outcomes met the criteria for inclusion in the COS (marked * in Table 1). As well as these three outcomes, a further 20 were discussed during the consensus meeting.

Thirteen people participated in the consensus meeting: all four stakeholder groups were represented. During the meeting the group agreed on inclusion of a further six outcomes in the COS and also to amend the formulation of some of the included outcomes. No further comments were received from other participants with respect to the COS which was developed during the consensus meeting. The outcomes which are included in the final COS are described in Table 1.

Discussion

The aim is that the outcomes included in this COS are to be measured in future studies and systematic reviews of treatment of antenatal and postnatal depression (intervention studies). If this is achieved it will result in improved potential to synthesise the results from different studies. In the long term this will lead to a stronger evidence. This can be important for some of the outcomes which occur less frequently, for example suicide, and where a large patient material is necessary in order to discern differences between various treatment methods. Most of the outcomes in the agreed COS are currently used in research (Figure 5). However, only one of the selected outcomes, self-assessed symptoms of depression, is used in more than 50% of the identified studies. The second most commonly used outcome, diagnosis of depression as assessed by a clinician only occurred in 33%.

In the protocol for the present study the maximum number of outcomes to be included in the COS had already been limited to ten. We believe that a greater number is not practical. After going thru the actual studies in this field, we can state that generally they contain around six outcomes, i.e. fewer than the number included in this COS. Thus, despite our ambition to try to limit the number of outcomes, the nine outcomes included in this COS, may be to many. This might lead to difficulties for researchers to include further outcomes specific to the research question. This project has not addressed how and when these outcomes should be measured, directives that should be included in a comprehensive COS. We intend, however, to pursue these questions in a future project.

This COS included an outcome which has not been identified in any study, namely ”thoughts about harming the child”. This highlights the need to involve patients, healthcare personnel and researchers in the process of selecting which outcome to include in a COS, and also to encourage the project participants to suggest outcomes over and above those which are already used in research.

SBU would like to thank all those who have been involved in, or assisted in dissemination of information about, the project, especially all those who participated in the development of the COS.

Table 4 Summary of results from survey 1 and 2. Highlighted in Bold are outcomes discussed during the consensus meeting.

Outcome	Survey 1		Survey 2		Number of studies including this outcome (av 165)
	Number of replys	Median (IQR1-IQR3)	Number of replys	Median (IQR1-IQR3)	
Depressive symptoms	149	7 (6–9)	123	8 (7–9)	133[a]
Depression in partner	144	6 (4–7)	123	5 (4–6,5)	1
Psychiatric diagnosis of depression	147	7 (6–8)	119	8 (6–9)	57[a]
Recovery from depression (remission)	146	7 (6–8)	121	7 (5–8)	17[a]
Depression relapse	144	7 (6–8)	121	7 (6–8)	4[a]
Time to remission from depression	143	6 (5–8)	122	6 (5–7)	1[a,c]
Was depression treatment initiated	145	7 (6–9)	122	7 (6–9)	6[a]
Change in antidepressant medication	141	6 (4–7)	120	6 (4–7)	3
Expert rating of overall disease burden	137	6 (4–8)	118	6 (4–7)	17[a]
Anxiety symptoms	141	7 (6–8)	119	7 (5–8)	51[a]
Fear of childbirth	142	6 (4,25–8)	119	6 (4,5–8)	0[d]
Psychiatric diagnosis of anxiety	141	7 (5–8)	118	6 (5–7)	8[a]
Other psychiatric or neuropsychiatric diagnoses	138	6 (5–7)	117	6 (5–8)	2[b]
Mood	139	6 (5–8)	119	6 (5–8)	5
Self-harm	141	7 (6–8)	118	7 (6–9)	0[d]
Suicidal thoughts or attempts or completed suicide	140	9 (7–9)	114	9 (8–9)	10[a]
Cognitive ability	143	6 (4–7)	117	5 (4–7)	4
Eating disorder symptoms	138	6 (4–7)	118	5 (4–6)	2
Visit to clinic for fear of childbirth	141	6 (4–8)	118	5 (4–7)	0[d]
Post-traumatic stress symptoms	141	7 (6–8)	119	7 (4,5–8)	1[b]
Psychiatric diagnosis of postpartum stress syndrome in relation with childbirth	141	7 (5–9)	117	7 (5–8)	0[d]
Psychiatric diagnosis of postpartum psychosis	138	7 (6–9)	115	7 (6–9)	0[d]
Domestic/intimate partner violence	136	8 (5–9)	118	7 (6–9)	1[c]
Family functioning	137	6 (5–8)	119	6 (5–7)	4
Quality of relationship	139	5 (4–7)	119	5 (4–6)	9[a]
Parent to infant bonding	140	7 (6–9)	119	7 (6–8)	18
Attachment	139	8 (6–9)	118	7 (5,25–8)	2[a,c]
Parenting Sense of Competency	139	6 (5–8)	119	6 (5–8)	13[a]
Parental stress	139	6 (5–7)	118	6 (5–7)	15[a]
General stress	139	6 (4–7)	118	6 (4–6)	5
Parent-infant interaction	138	7 (6–9)	116	7 (5–8)	11[a]
Attitudes about parenting	137	6 (4–7)	117	5 (3–6)	4
Family planning	141	5 (4–7)	118	4 (3–6)	1[b]
Daily functioning level/activities of daily living	137	6 (5–8)	119	6 (5–7)	23
Sleep	138	7 (6–9)	119	7 (5,5–8)	8[a]
Fatigue	137	6 (5–8)	119	6 (5–8)	2[c]
Quality of life	140	6 (5–8)	117	6 (5–8)	26[a]

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Table 4 continued

Outcome	Survey 1		Survey 2		Number of studies including this outcome (av 165)
	Number of replys	Median (IQR1-IQR3)	Number of replys	Median (IQR1-IQR3)	
Sexual desire/function	135	5 (3–6)	119	4 (3–6)	1[c]
Stigma	138	6 (4–8)	117	6 (4–7)	2[b]
Social relationships	138	6 (5–7)	119	6 (4–7)	9
Perceived ability to cope with life challenges	136	6 (4,75–7)	117	6 (4–7)	1[c]
Effort-based decision-making	135	6 (4–7)	118	5 (4–6)	4[b]
Self-compassion	135	5 (4–7)	117	5 (3–6)	1[b]
Lifestyle	134	6 (4–7)	116	5 (4–6)	1[b]
Verbal fluency	122	3 (2–4)	108	3 (2–5)	1
Personality	128	4 (3–6)	112	3 (3–5)	2
Perceived social support/Help-Seeking	137	7 (5–8)	117	6 (5–7)	12
Socio-emotional competence	131	6 (4–7)	117	5 (4–6)	4
Confidence to self-help	133	6 (4–7)	116	5 (3–7)	3
Mentalizing, reflective functioning and level of mindfulness	133	5 (4–7)	116	5 (3–6,25)	5[a,c]
Self-esteem	135	6 (4–8)	117	6 (4–7)	3
Adverse event	133	7 (5–8)	116	6 (5–8)	29[a]
Spontaneous abortion or stillbirth	127	7 (6–9)	112	8 (5–9)	1[b]
Perinatal mortality	126	8 (6–9)	111	8 (6–9)	1[b]
Infections during pregnancy	119	5 (3–6)	108	4 (3–6)	1[b]
Residual physical problems after delivery	133	7 (6–9)	115	7 (5–8)	4[a,b]
Birth injury	130	6 (5–9)	115	7 (5–8)	5
Pain	131	6 (4–7)	115	6 (4–8)	1[b]
Gestational hypertension or preeclampsia	124	6 (4–7)	103	5 (4–7)	3[b]
Gestational age at delivery	130	6 (5–8)	111	6 (4–7)	5[b]
Gestational diabetes	121	5 (3–7)	107	5 (3–7)	1[b]
Estimated blood loss	121	6 (4–7)	105	5 (3–7)	2[b]
Induction of labour	126	6 (4–7)	110	5 (4–7)	1[b]
Mode of delivery	132	6 (5–8)	114	6 (4–8)	6[a]
Fetal growth assessment by ultrasound	124	5 (4–7)	108	5 (3–6)	1[b]
Complications associated with the placenta	117	5 (3–7)	108	5 (3–7)	1[b]
Vaginal and/or faecal microbiota	107	3 (3–6)	102	3 (3–5)	1[b]
Transition of care from pregnancy to postpartum	133	7 (6–9)	115	7 (5–9)	1[a,b]
Breastfeeding	131	6 (4–8)	114	6 (4–7)	8
Child attention	126	5 (4–7)	109	5 (4–6)	3[c]
Duration of crying episodes	127	6 (4–7)	109	5 (3–6)	1[b]
Child development	133	7 (5–8)	112	6 (5–8)	19[a]
Neurodevelopmental and neurobehavioral outcomes	128	7 (5,75–8)	111	7 (5–8)	2[a,c]
Infant sleep	131	6 (5–7)	112	6 (4–8)	1[b]
Vaccinations received/Immunization status	123	4 (2–6)	109	3 (2–6)	4

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Table 4 continued

Outcome	Survey 1		Survey 2		Number of studies including this outcome (av 165)
	Number of replys	Median (IQR1-IQR3)	Number of replys	Median (IQR1-IQR3)	
Infant or child's temperament	132	5 (4–7)	112	4 (3–6)	6[a]
Biological parameters in the infant	110	5 (3–7)	96	4 (3–6)	6
Well-baby check-up status	132	6 (4–7)	111	5 (3–7)	2
Congenital malformations	125	6 (4–8)	104	6 (4–7)	1[b]
Infant antibiotic use	117	4 (3–6)	100	3 (3–5,25)	1[b]
Birth weight, height and head circumference	126	5,5 (4–6)	106	5 (3–6)	8[a]
Small for gestational age (SGA)	123	6 (4–7)	105	5 (4–7)	3[b]
Apgar score	123	5 (4–7)	106	5 (3–7)	4[a]
Neonatal intensive care unit admission	126	6 (5–8)	106	6 (5–8)	4
Cost-effectiveness	130	6 (4–7)	106	5 (4–7)	9[a]
Use of health services	131	6 (4–7)	110	5 (4–6)	16
Engagement and retention with health services	133	6 (4–7)	109	5 (4–6)	3
Sick-leave	133	6 (4–7)	113	6 (4–7)	3
Satisfaction with intervention	136	7 (6–8)	114	7 (6–8)	31[a]
Therapeutic alliance	135	7 (6–9)	113	7 (6–9)	2
Quality of care	136	6 (5–8)	114	7 (5–8)	5
Parent experience	133	7 (6–8)	114	7 (5–8)	2[a]
Pregnancy/delivery experience	135	7 (5–9)	114	7 (6–9)	2[a,b]
Biological parameters	112	5 (4–7)	99	4 (3–6)	15[a]
Maternal vital signs/physical examination	116	4 (3–6)	101	4 (3–6)	6[a]
Knowledge about anti-depressant treatment in pregnancy	128	5 (4–7)	110	5 (4–7)	2[b]
Partner's attendance	135	6 (5–7)	114	6 (4–7)	2
Coping strategies among relatives	126	5,5 (4–7)	112	5 (4–6,25)	1[b]
Separation or divorce	–	–	112	5 (3–7)	0[e]
Ability to return to work/change of work	–	–	113	5 (4–7)	0[e]
Obsessive thoughts or intrusive thoughts	–	–	110	6 (4–7)	0[e]
Fear of something bad happening to the baby	–	–	113	6 (4–8)	0[e]
Thoughts of harming the baby, (including thoughts of extended suicide)	–	–	113	8 (7–9)	0[e]
Level of compliance with the given treatment	–	–	112	7 (6–8)	0[e]
Mental health literacy	–	–	113	6 (4–8)	0[e]

[a] *Indicates that the outcome has been listed as primary in at least one study*
[b] *The outcome has only been identified in studies on antenatal depressionn*
[c] *The outcome has only been identified in studies on postpartum depression*
[d] *The outcome has been added by the project management*
[e] *The outcome has been added by participants in the delphi survey*

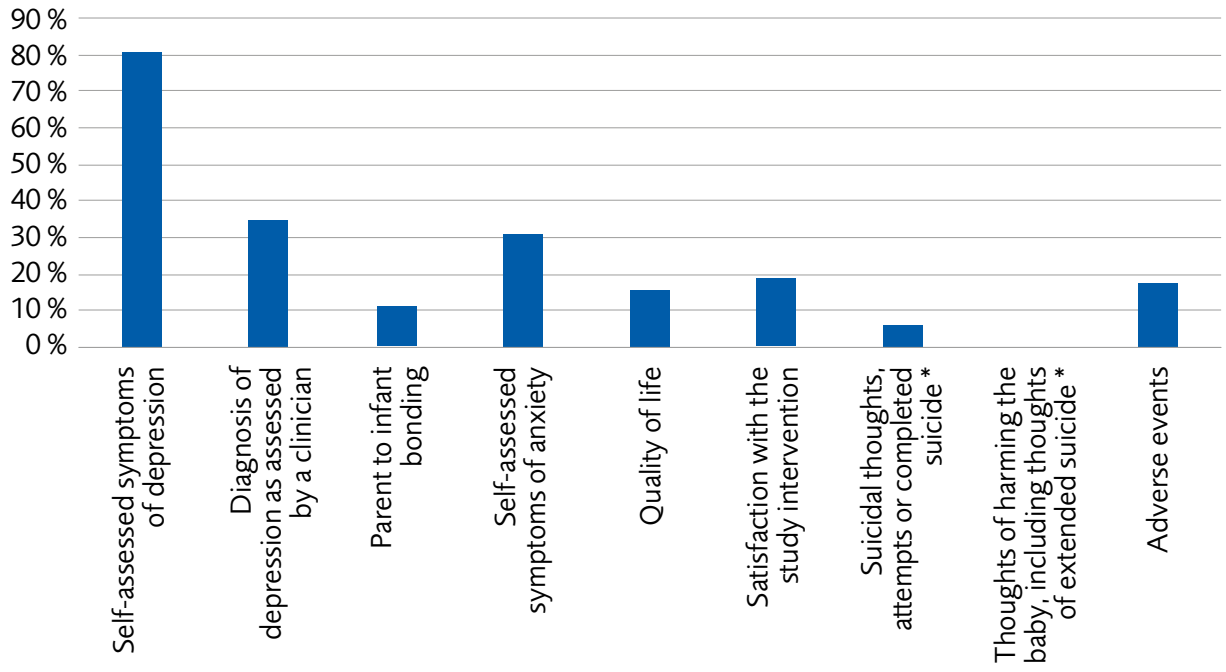

Figure 5 Frequency of the COS included outcomes in the identified studies.

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The full report in Swedish

The full report ”Vad är viktigt att mäta i forskning som undersöker behandling av depression under och efter graviditet” (in Swedish), www.sbu.se/314

Appendices

1. Protocol
2. Search strategies
3. Information to the participants
4. Included articles
5. Excluded studies
6. Results survey 1
7. Results survey 2

Project group

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