Depressione in gravidanza e nel post-partum

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La gravidanza nelle pazienti con Disturbi Psichici

- programmare una gravidanza durante la terapia farmacologica di mantenimento
- episodio di malattia durante la gravidanza
- gravidanza inattesa durante la terapia farmacologica
- allattamento in una paziente che assume psicofarmaci

UNIVERSITA' DEGLI STUDI DI PARMA
ISTITUTO DI CLINICA PSICHIATRICA

Corso di aggiornamento

I DISTURBI PSICHICI GRAVIDICO-PUERPERALI E LORO TRATTAMENTO

Parma, 20 giugno 2002

Centro "S. Elisabetta"
CAMPUS UNIVERSITARIO
Viale delle Scienze

PROGRAMMA

ore 9.00 Apertura dei lavori
L. Benassi

ore 9.10 ***I disturbi psichici gravidico-puerperali***
C. Maggini

ore 9.55 ***L'impiego degli psicofarmaci in gravidanza e nel puerperio***
C. Marchesi

ore 10.40 Pausa caffè

ore 11.00 ***Dibattito con l'esperto***
L. Benassi, C. Maggini, C. Marchesi

ore 12.00 ***Presentazione delle scale di valutazione per la depressione e dimostrazione del loro utilizzo***
C. Marchesi

ore 13.30 Chiusura dei lavori

INFORMAZIONI GENERALI

Iscrizione al Corso di aggiornamento
L'iscrizione al Corso è gratuita.
E' obbligatorio inviare alla Segreteria Organizzativa la scheda di iscrizione debitamente compilata **entro e non oltre il 14 giugno 2002** al fine di poter rispettare gli obblighi E.C.M.
L'iscrizione è limitata (max 90 persone).

Segreteria Congressuale
La Segreteria Congressuale sarà funzionante presso il Centro S. Elisabetta con il seguente orario:
Giovedì 20 giugno 2002 dalle ore 8.00 alle ore 13.30.

Educazione continua in medicina - ECM
Crediti assegnati n°5.

Attestato di Frequenza
Al termine del Corso di aggiornamento sarà rilasciato un attestato di frequenza.

Variazioni
La Segreteria Scientifica e la Segreteria Organizzativa si riservano il diritto di apportare al programma tutte le variazioni che si rendessero necessarie per ragioni tecniche e/o scientifiche.

UNIVERSITÀ DEGLI STUDI DI PARMA

SERVIZIO SANITARIO REGIONALE
EMILIA-ROMAGNA
Azienda Unità Sanitaria Locale di Parma

Disturbi dell'umore in gravidanza: rischi e benefici del trattamento farmacologico

Parma, 22 Ottobre 2010

Centro Congressi
Starhotel Du Parc
V.le Piacenza 12/c

"Sorrow". Vincent Van Gogh, 1882

PROGRAMMA

Ore 8.30 **Registrazione Partecipanti**

Ore 9.00 **Presentazione del Corso**
Carlo Marchesi
Università degli Studi di Parma

Ore 9.10 **Saluto delle Autorità Accademiche e Sanitarie**

Moderatori:
Alberto Bacchi Modena
Università degli Studi di Parma
Daniela Viviani
Azienda Ospedaliero - Universitaria di Parma

Ore 9.20 **Depressione Maggiore e Disturbi d'Ansia in gravidanza**
Carlo Marchesi
Università degli Studi di Parma

Ore 10.00 **Disturbo Bipolare in gravidanza**
Mauro Mauri
Università degli Studi di Pisa

Ore 10.40 **L'uso degli antidepressivi in gravidanza: rischi e benefici**
Cesario Bellantuono
Università degli Studi di Ancona

Ore 11.20 Pausa Caffè

Ore 11.40 **L'uso degli antipsicotici e degli stabilizzatori dell'umore in gravidanza: rischi e benefici**
Salvatore Gentile
Dipartimento di Salute Mentale, Salerno

Ore 12.20 **Il consenso informato nel trattamento dei disturbi dell'umore in gravidanza**
Stefano Ferracuti
Università degli Studi di Roma

Ore 13.00 Pausa Pranzo

Ore 14.30 **Lavoro di gruppo: "Discussione di casi clinici"**

Ore 16.00 **Discussione in Plenaria del Lavoro di Gruppo**

Ore 17.00 **Test di apprendimento**

Ore 17.30 **Conclusione del Corso**
Carlo Marchesi
Università degli Studi di Parma

Pharmacologic Treatment of Depression During Pregnancy

REVIEW

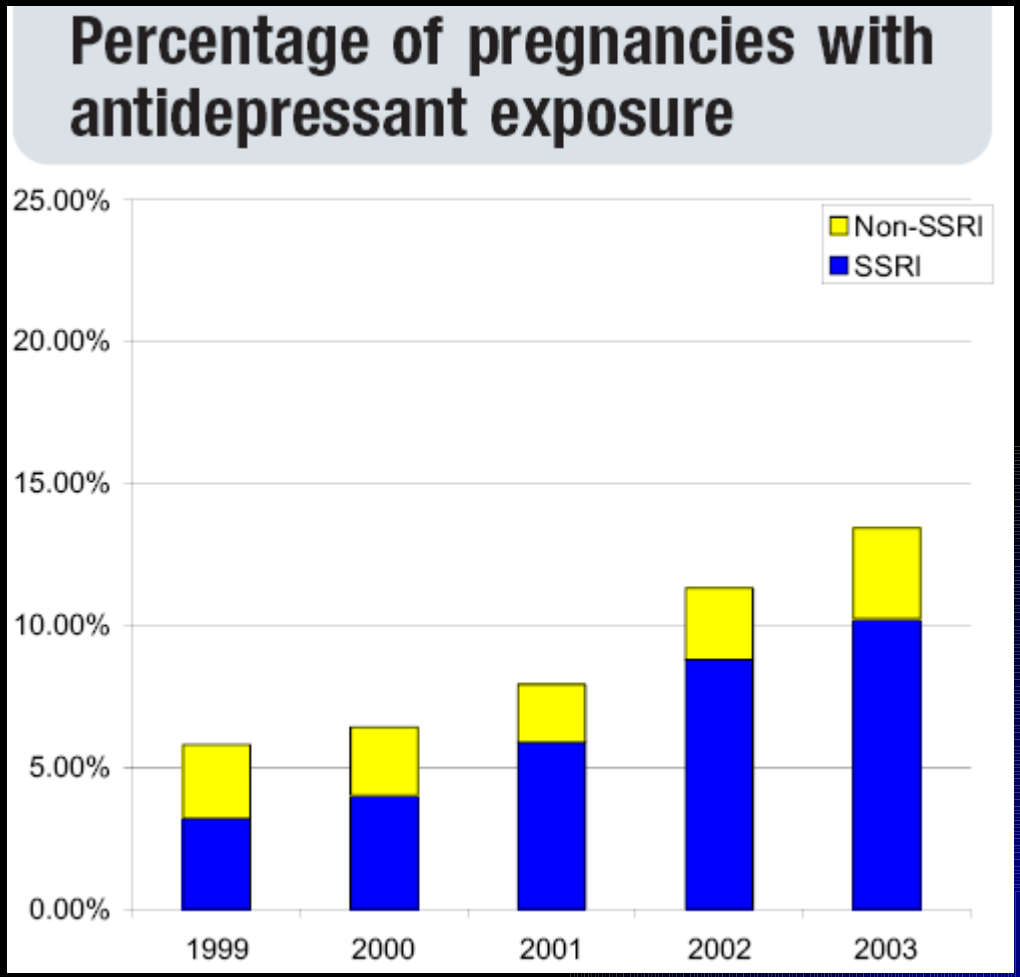
JAMA. 1999;282:1264-1269

Katherine L. Wisner, MD, MS
Alan J. Gelenberg, MD
Henrietta Leonard, MD
Deborah Zarin, MD
Ellen Frank, PhD

Data Synthesis Data were available for tricyclic antidepressants (collectively), fluoxetine, and newer selective serotonin reuptake inhibitors (collectively). Exposure to these agents did not increase risk for intrauterine death or major birth defects. Decreased birth weights of infants exposed to fluoxetine in the third trimester were identified in 1 study. The development of children whose mothers took tricyclics or fluoxetine during gestation did not differ from that of controls. Direct drug effects and withdrawal syndromes occurred in some neonates whose mothers were treated with antidepressants near term.

Increasing use of antidepressants in pregnancy

Am J Obstet Gynecol 2007;196;544.e1-544.e5.



Delivery outcome after maternal use of antidepressant drugs in pregnancy: an update using Swedish data

Table 1. *Number of women using specific antidepressant drugs either before the first antenatal visit ('Early') or prescribed the drugs during pregnancy ('Later')*

Drug name	ATC code	Early	Later
TCAs	*N06AA*	*1662*	*784*
Imipramine	N06AA02	10	3
Clomipramine	N06AA04	1208	592
Lofepramine	N06AA07	6	1
Amitriptyline	N06AA09	379	158
Nortriptyline	N06AA10	33	23
Protryptyline	N06AA11	1	0
Maprotiline	N06AA21	9	1
SSRIs	*N06AB*	*10 170*	*4809*
Fluoxetine	N06AB03	1522	892
Citalopram	N06AB04	3950	1648
Paroxetine	N06AB05	1208	405
Sertraline	N06AB06	3297	1825
Fluvoxamine	N06AB08	42	17
Escitalopram	N06AB10	153	56
Unspecified	N06AB00	86	39
MOAIs	*N06AG*	37	18
Moclobemide	N06AG02	37	18
SNRIs	*N06AX*	*1351*	*538*
Mianserin	N06AX03	85	33
Nefazodone	N06AX06	44	7
Mirtazapine	N06AX11	277	123
Bupropion	N06AX12	37	9
Venlafaxine	N06AX16	859	363
Reboxetine	N06AX18	28	6
Duloxetine	N06AX21	37	4
Unspecified antidepressants	*N06A*	*10*	*0*

Reis and Kallen, Psychol Med 2010; 40: 1723-33

The Ethics of Randomized Placebo-Controlled Trials of Antidepressants With Pregnant Women

Obstet Gynecol 2008;112:1361–8,

CONCLUSION: Randomized placebo-controlled trials of antidepressant medications during pregnancy are ethically justified. Well-conducted and ethically justified trials of antidepressants should improve the quality of care provided to depressed pregnant women and thus address a major public health problem.

Depressione in gravidanza:
premesse metodologiche

La stima della prevalenza della depressione in gravidanza varia dall'8 al 51%.

Le diverse modalità di valutazione possono spiegare la variabilità dei risultati.

Infatti, la prevalenza di depressione è maggiore :

1- se i sintomi, anziché i disturbi, sono valutati;

2- se le scale di autosomministrate, anziché le interviste strutturate, sono utilizzate;

3- se la gravità dei sintomi, anziché i criteri diagnostici operazionali, è impiegata;

4- se i sintomi somatici, frequenti in gravidanza, sono inclusi nella valutazione;

5- se il numero delle valutazioni è maggiore.

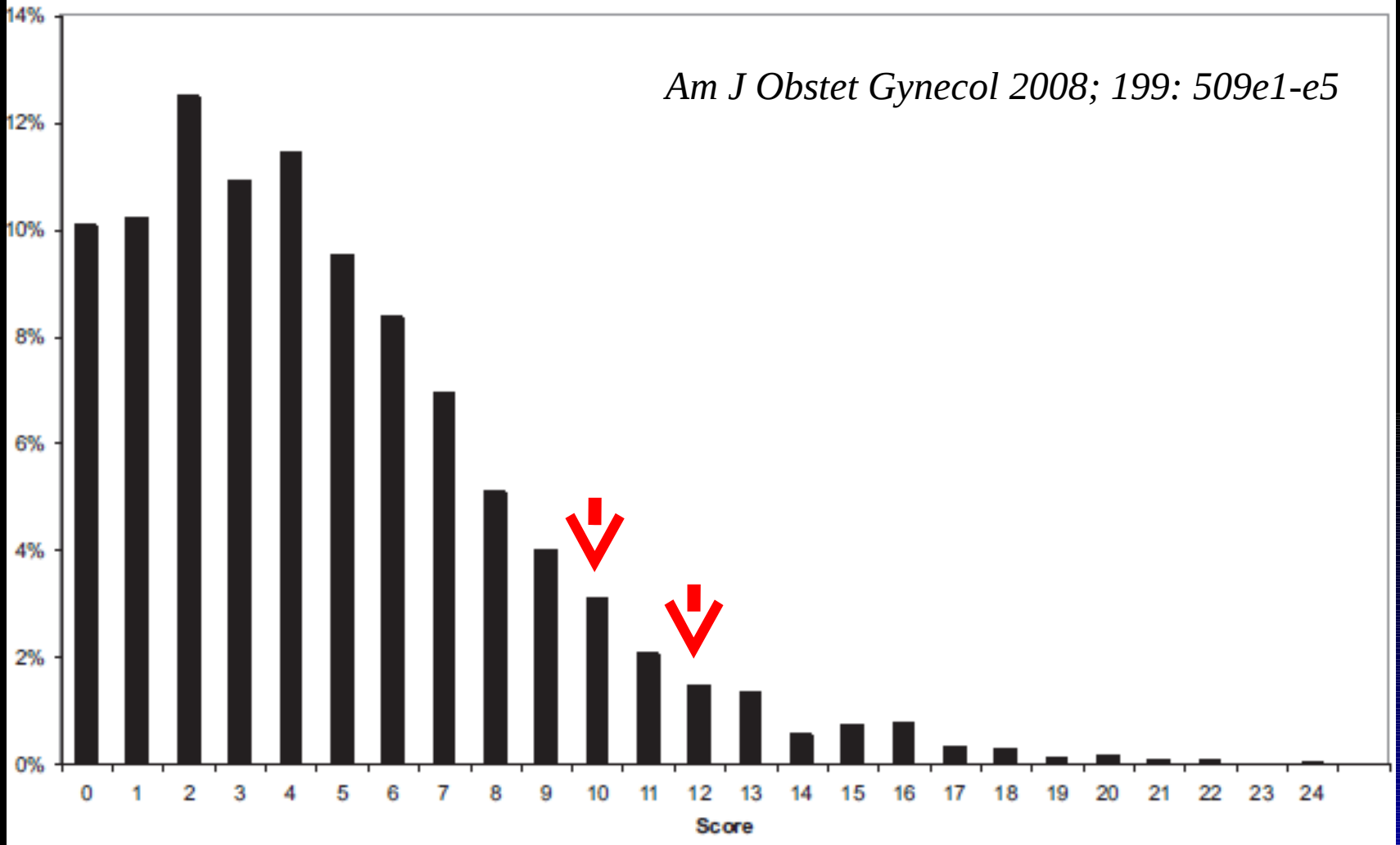
Marchesi et al., *Obstet Gynecol 2009; 113: 1292-8*

Screening for Depression During and After Pregnancy

Obstest Gynecol 2010; 115;394-95

Screening Tool	Number of Items	Time to Complete	Sensitivity/ specificity
Edinburgh Postnatal Depression Scale (EPDS)	10	Less than 5 min	Sensitivity: 59–100% Specificity: 49–100%
Postpartum Depression Screening Scale (PDSS)	35	5–10 min	Sensitivity: 91–94% Specificity: 72–98%
Patient Health Questionnaire-9 (PHQ-9)	9	Less than 5 min	Sensitivity: 75% Specificity: 90%
Beck Depression Inventory (BDI)	21	5–10 min	Sensitivity: 47.6–82% Specificity: 85.9–89%
Beck Depression Inventory-II (BDI-II)	21	5–10 min	Sensitivity: 56–57% Specificity: 97–100%
Center for Epidemiologic Studies Depression Scale (CES-D)	20	5–10 min	Sensitivity: 60% Specificity: 92%
Zung Self-Rating Depression Scale (Zung SDS)	20	5–10 min	Sensitivity: 45–89% Specificity: 77–88%

Distribution of antepartum and postpartum Edinburgh Postnatal Depression Scale Scores



Am J Obstet Gynecol 2008; 199: 509e1-e5

Distribution of EPDS scores in the cohort of 1548 women who were screened from 24-28 weeks of gestation and again after delivery (total of 3168 completed screens).

Major and Minor Depression in Pregnancy

Marchesi et al Obstet Gynecol 2009; 113: 1292-8

Major depression was diagnosed in 19 women (12.3%) and minor depression in 28 (18.1%), whereas the remaining 107 women did not show any depressive symptoms (controls). In five women, minor depression symptoms preceded (n=3) or followed (n=2) major depression.

Table 2. Onset and Duration of Depressive Episodes in Pregnant Women

	Major Depression (n=19)	Minor Depression (n=28)
Onset of depression (trimester)		
First*	7 (36.8)	17 (60.7)
Second	4 (21.1)	7 (25.0)
Third	8 (42.1)	4 (14.3)
Duration of depression* (mo)		
1	5 (26.3)	16 (57.1)
2	7 (36.8)	7 (25.0)
3–4	3 (15.8)	5 (17.9)
5 or more	4 (21.1)	–

PHQ-9

NAME: _____ **DATE:** _____

Over the *last 2 weeks*, how often have you been bothered by any of the following problems?
(use "✓" to indicate your answer)

	Not at all	Several days	More than half the days	Nearly every day
1. Little interest or pleasure in doing things	0	1	2	3
2. Feeling down, depressed, or hopeless	0	1	2	3
3. Trouble falling or staying asleep, or sleeping too much	0	1	2	3
4. Feeling tired or having little energy	0	1	2	3
5. Poor appetite or overeating	0	1	2	3
6. Feeling bad about yourself—or that you are a failure or have let yourself or your family down	0	1	2	3
7. Trouble concentrating on things, such as reading the newspaper or watching television	0	1	2	3
8. Moving or speaking so slowly that other people could have noticed. Or the opposite—being so fidgety or restless that you have been moving around a lot more than usual	0	1	2	3
9. Thoughts that you would be better off dead, or of hurting yourself in some way	0	1	2	3
add columns:		+	+	
TOTAL:				

10. If you checked off *any* problems, how *difficult* have these problems made it for you to do your work, take care of things at home, or get along with other people?

- **Not difficult at all** _____
- **Somewhat difficult** _____
- **Very difficult** _____
- **Extremely difficult** _____

Spitzer et al, JAMA 1994; 272: 1749-56

Depression during pregnancy

BMJ 2007:334:1003-5

SUMMARY POINTS

- Rates of depression are higher during pregnancy than at any other point during a woman's life
- About half of "postnatal" depression starts during pregnancy
- Two thirds of women with a history of recurrent depression will relapse during pregnancy if they discontinue their medications after conception
- Depression during pregnancy is associated with poorer obstetric outcomes, particularly preterm delivery
- Women who are depressed during pregnancy are more likely to smoke and drink alcohol and less likely to attend for antenatal obstetric care than women who are not depressed
- The treatment of depression during pregnancy must be considered individually for each woman, with the possibility of relapse and poorer obstetric outcomes balanced against the possible risks associated with taking antidepressant medication

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Psychiatric Disorders in Pregnant and Postpartum Women in the United States

Arch Gen Psychiatry. 2008;65(7):805-815

Table 2. Twelve-Month Prevalence and ORs of *DSM-IV* Axis I Psychiatric Disorders by

Disorder	% (SE) Nonpregnant Women (n=13 025)	% (SE) Past-Year Pregnant Women[a] (n=1524)	OR (95% CI)	AOR[b] (95% CI)
Any psychiatric disorder	30.1 (0.8)	25.3 (1.3)	0.78 (0.69-0.90)	0.75 (0.62-0.90)
Any new-onset psychiatric disorder (current but not before past 12 mo)	7.0 (0.3)	8.0 (0.8)	1.16 (0.92-1.46)	0.97 (0.75-1.25)
Any substance use disorder	19.9 (0.7)	14.6 (1.2)	0.68 (0.57-0.82)	0.56 (0.44-0.71)
Any alcohol use disorder	7.6 (0.4)	3.6 (0.5)	0.45 (0.34-0.60)	0.49 (0.36-0.67)
Any drug use disorder	2.0 (0.2)	1.6 (0.4)	0.82 (0.49-1.37)	0.52 (0.29-0.94)
Nicotine dependence	14.6 (0.6)	12.5 (1.1)	0.84 (0.68-1.02)	0.79 (0.64-0.97)
Any mood disorder	13.7 (0.5)	13.3 (1.1)	0.96 (0.80-1.16)	1.04 (0.83-1.32)
MDD	8.1 (0.9)	8.4 (0.4)	0.95 (0.75-1.20)	1.24 (0.94-1.64)
Dysthymia	2.0 (0.2)	0.9 (0.4)	0.46 (0.21-1.00)	0.51 (0.22-1.18)
Bipolar disorder	2.3 (0.2)	2.8 (0.5)	1.26 (0.86-1.84)	1.09 (0.70-1.70)
Any anxiety disorder	14.9 (0.6)	13.0 (1.1)	0.85 (0.70-1.03)	0.99 (0.68-1.43)
Panic disorder	3.0 (0.2)	2.2 (0.5)	0.73 (0.46-1.15)	0.91 (0.53-1.56)
Social anxiety disorder	2.8 (0.2)	1.8 (0.4)	0.65 (0.41-1.02)	0.66 (0.33-1.31)
Specific phobia	10.2 (0.5)	9.2 (0.9)	0.89 (0.72-1.11)	0.93 (0.53-1.61)
Generalized anxiety	1.8 (0.2)	1.3 (0.4)	0.73 (0.42-1.29)	1.57 (0.82-3.02)
Any psychotic disorder	0.3 (0.1)	0.4 (0.2)	1.14 (0.44-2.94)	1.50 (0.54-4.18)
Any substance use	73.8 (1.0)	63.0 (1.8)	0.60 (0.53-0.69)	0.66 (0.57-0.77)
Any alcohol use	68.5 (0.9)	59.0 (1.7)	0.66 (0.58-0.75)	0.71 (0.61-0.81)
Any tobacco use	26.6 (0.8)	21.9 (1.5)	0.77 (0.66-0.91)	0.76 (0.64-0.89)
Any illicit drug use	6.8 (0.3)	6.2 (0.7)	0.91 (0.72-1.17)	0.87 (0.66-1.15)
Mean No. of cigarettes a day in past 12 mo (only among smokers)	15.9 (0.3)	16.6 (1.4)	$t=0.52$ $P=.60$	$\beta=0.05$ SE=0.04 $P=.29$[d]

Is pregnancy associated with mood and anxiety disorders? A cross-sectional study

General Hospital Psychiatry 32 (2010) 213–215

Mood and anxiety disorders in the pregnant and nonpregnant women

	Pregnant women (n=309)	Nonpregnant women (n=107)	Odds ratio (95% CI)	P value[a]
Axis I diagnoses				
Major depression	17 (5.5)	5 (4.7)	1.17 (0.44–3.11)	1.000
Dysthymic disorder	8 (2.6)	1 (0.9)	2.77 (0.35–21.89)	0.458
Bipolar disorder	– (–)	– (–)	–	–
Panic disorder	6 (1.9)	1 (0.9)	2.07 (0.25–17.06)	.683
Obsessive-compulsive disorder	16 (5.2)	3 (2.8)	1.84 (0.55–6.21)	.425
Social phobia	10 (3.2)	3 (2.8)	1.15 (0.32–2.92)	1.000
Specific phobia	10 (3.2)	5 (4.7)	0.68 (0.24–1.96)	.547
Posttraumatic stress disorder	– (–)	– (–)	–	–
Generalized anxiety disorder	11 (3.6)	4 (3.7)	0.95 (0.31–2.92)	1.000
Any mood disorder	25 (8.1)	8 (7.5)	1.04 (0.66–1.64)	1.000
Any anxiety disorder	48 (15.5)	16 (15.0)	1.04 (0.62–1.75)	1.000
Any mood or anxiety disorder	60 (19.4)	20 (18.7)	1.08 (0.50–2.33)	1.000

[a] Fisher's Exact Test.

Risk factors for depressive symptoms during pregnancy: a systematic review

Am J Obstet Gynecol 2010.

Factor	Total no. of studies	Total no. of subjects	Bivariate trend of association[a]	Multivariate trend of association[a]
Anxiety[18-28]	11	4696	++++	[b]
Life stress, composite[20,24,29-32,43,47-49,52,55-57,68,69,72,73]	18	9973	+++	+++
Life events, total (positive and negative)	15	9645	+++	Inconsistent
Negative life events			++++	+++
Daily hassles	5	1134	[c]	[b]
Personal history of depression[24,32,54,62,69,74]	6	3566	+++	[b]
Social support[20,22,24,27,28,30-35,43,48,49,52,53,55-57,60,64,68,69,73]				
Lack of social support, any source	17	5752	+++	+
Lack of social support, partner	9	7139	++++	++++
Domestic violence[24,29,30,46,54,57,67]	7	3738	+	++
Unintended pregnancy[24,60,61,63,64,68]	6	11,470	+++	[b]
Relationships[20,22,24,27,32-38,43,46,48,50,52,59,60,62,64,65,68-73]				
Cohabitation	19	12,483	++	Inconsistent
Poor relationship quality	11	4005	+++	[c]
Demographics				
Public insurance/uninsured[29,30,34,50,57,58]	6	2008	+++	[b]
Medicaid (US studies only)			+++	[b]
Socioeconomic status[56,59,64,69,73]	5	2805	[c]	[c]
Lower income[20,31,32,37-39,46,48,49,56,64]	11	6285	+	[b]
Unemployment[20,27,32,35,38,39,47,49,50,64,68,71-73]	14	9417	[c]	Inconsistent
Lower education[20,21,30,32-39,43,49,50,56,62,68,71-73]	20	11,529	+	[c]
Maternal age[20,22,30,32-39,43,46,48,49,59,62,64,67,68,71,73]	22	13,837	Inconsistent	[c]
Maternal race/ethnicity[29-42]	14	6671	Inconsistent	[c]
Substance abuse				
Smoking[30,32,33,36,38,41,54,56,57,59,71]	11	6641	+	[c]
Alcohol use[32,33,36,44,45,54,56,57,66,71]	10	10,621	Inconsistent	[c]
Illicit drug use[30,32,33,38,46,49,57,64]	8	3010	[c]	Inconsistent
Nulliparity[22,24,34-37,39,46-48,51,59,62,64,66,68,72,73]	18	9786	[c]	Inconsistent
Poor obstetric history[19,24,32,34,39,47,49,59,64,68]	10	6888	[c]	[c]

lack of sample size

No effect.

Major and Minor Depression in Pregnancy

Marchesi et al Obstet Gynecol 2009; 113: 1292-8

Table 3. Risk Factors for Developing Major Depression, Minor Depression, or No Depression in Pregnant Women

	Depression Groups							
	Major Depression vs Control				Minor Depression vs Control			
	β	χ^2	P	OR (95% CI)	β	χ^2	P	OR (95% CI)
No. of sons		1.62	.20			0.25	.61	
Housewife (yes)		2.21	.13		1.9	12.16	<.001	7.2 (2.3–22.1)
Unwanted pregnancy (yes)		1.59	.20		0.9	4.09	.04	2.4 (1.0–5.7)
Problems with the husband/partner (yes)	2.0	3.78	.04	7.8 (1.0–62.7)		0.28	.59	
Problems with family (yes)		0.02	.87			0.03	.85	
Problems with job (yes)		1.37	.24			0.14	.70	
Family support (yes)		1.63	.20			0.04	.83	
Previous depressive episodes (yes)	2.2	14.05	<.001	9.5 (2.9–30.8)	1.5	6.70	.01	4.7 (1.4–15.3)

Depression symptoms during pregnancy

Arch Womens Ment Health (2008) 11: 43–48

Item	Scale range	PD ($n=61$) mean score (SD)	P ($n=41$) mean score (SD)	PD vs. P		D ($n=53$) mean score (SD)	PD vs. D	
				U (p)	AUC[a]		U (p)	AUC
1. Depressed mood	0–4	2.3 (0.9)	0.2 (0.5)	137.5 (0.000)	0.95*	2.3 (0.8)	1561.0 (0.735)	0.52
2. Guilt	0–4	1.2 (0.7)	0.2 (0.2)	295.0 (0.000)	0.89*	1.7 (0.7)	1014.0 (0.000)	0.33*
3. Suicidality	0–4	0.2 (0.5)	0[b]	1100.0 (0.003)	NA[c]	0.6 (0.8)	1255.0 (0.009)	0.39*
4. Insomnia early	0–2	0.7 (0.9)	0.4 (0.7)	1108.0 (0.064)	0.59	1.3 (0.8)	1046.5 (0.000)	0.33*
5. Insomnia middle	0–2	1.5 (0.7)	1.2 (0.6)	914.5 (0.002)	0.66*	1.2 (0.9)	1361.0 (0.103)	0.58
6. Insomnia late	0–2	0.7 (0.9)	0.2 (0.5)	934.0 (0.001)	0.65*	0.8 (0.9)	1453.5 (0.308)	0.45
7. Work and activities (anhedonia)	0–4	3.1 (0.9)	0.2 (0.6)	95.0 (0.000)	0.96*	3.1 (0.9)	1589.0 (0.865)	0.52
8. Psychomotor retardation	0–4	0.9 (0.8)	0.3 (0.5)	723.5 (0.000)	0.73*	0.4 (0.7)	980.0 (0.000)	0.69*
9. Agitation	0–4	0.4 (0.8)	0.1 (0.3)	1146.5 (0.053)	0.57	0.5 (0.8)	1443.5 (0.218)	0.45
10. Psychological anxiety	0–4	2.8 (0.7)	0.98 (1.2)	354.5 (0.000)	0.87*	2.6 (0.9)	1397.5 (0.171)	0.58
11. Somatic anxiety	0–4	1.7 (1.3)	0.3 (0.7)	494.5 (0.000)	0.82*	1.9 (1.2)	1532.0 (0.621)	0.47
12. Gastrointestinal (appetite)	0–2	0.8 (0.7)	0.2 (0.5)	677.0 (0.000)	0.75*	0.6 (0.7)	1341.5 (0.090)	0.58
13. Somatic general (energy)	0–2	1.7 (0.5)	0.8 (0.6)	401.5 (0.000)	0.85*	1.8 (0.4)	1599.5 (0.895)	0.50
14. Genital symptoms (libido)	0–2	1.5 (.7)	0.7 (0.9)	792.0 (0.000)	0.70**	1.3 (0.7)	1468.5 (0.346)	0.55
15. Hypochondriasis (somatic complaints)	0–4	1.3 (1.0)	0.8 (0.8)	1024.0 (0.024)	0.62*	1.0 (1.1)	1346.0 (0.102)	0.59
16. Weight loss[d]	0–2	0.2 (0.5)	0.1 (0.3)	1207.5 (0.100)	0.55	0.3 (0.6)	1596.5 (0.854)	0.49
17. Insight	0–2	0.02 (0.1)	0[b]		NA	0.04 (0.2)		0.49
18. Diurnal variation	0–3	1.4 (1.2)	0.5 (0.8)	809.5 (0.000)	0.70*	1.0 (1.1)	1399.5 (0.249)	0.58
19. Depersonalization/derealization	0–4	0.1 (0.4)	0 (0.2)	1255.0 (0.314)	0.53	0.3 (0.8)	1412.5 (0.042)	0.44
20. Paranoid symptoms	0–3	0.03 (0.2)	0[b]	1298.0 (0.227)	NA	0.2 (0.4)	1364.5 (0.007)	0.44**
21. Obsessive and compulsive	0–2	0.1 (0.3)	0.1 (0.2)	1249.0 (0.213)	0.53	0.1 (0.4)	1558.0 (0.570)	0.49
22. Helplessness	0–4	2.0 (0.9)	0.02 (0.2)	528.5 (0.000)	0.80*	1.1 (0.8)	1374.5 (0.145)	0.57
23. Hopelessness	0–3	1.5 (1.3)	0.1 (0.2)	452.0 (0.000)	0.83*	1.5 (1.0)	1538.5 (0.647)	0.51
24. Worthlessness	0–4	1.3 (1.0)	0.1 (0.3)	355.5 (0.000)	0.87*	1.5 (1.3)	1432.0 (0.345)	0.45

Typical somatic symptoms of pregnancy and their impact on a diagnosis of major depressive disorder☆,☆☆

General Hospital Psychiatry 31 (2009) 327–333

Odds ratios of depression and medication use for behavioral and cognitive symptoms

Symptom	Depression stem positive vs. negative			Medication use vs. no medication use		
	OR	95% CI	*P*	OR	95% CI	*P*
1-Appetite decrease	2.95	1.98–4.41	<.0001	1.28	0.91–1.81	.16
2-Appetite increase	1.05	0.69–1.59	.84	1.10	0.78–1.55	.58
3-Trouble sleeping	2.72	1.88–3.93	<.0001	1.09	0.80–1.50	.58
4-Oversleeping	1.32	0.86–2.04	.20	2.11	1.44–3.07	<.001
5-Decrease in energy	2.73	1.79–4.15	<.0001	1.54	1.08–2.20	.02
6-Increase in energy	0.57	0.25–1.33	.19	1.19	0.58–2.43	.63
7-Moving slowly	2.29	1.58–3.34	<.0001	1.07	0.72–1.60	.73
8-Feeling jittery	3.25	1.67–6.31	<.001	1.97	0.93–4.18	.08
9-Thinking slowly	3.50	2.19–5.59	<.0001	1.23	0.75–2.01	.42
10-Racing thoughts	2.39	1.45–3.95	<.001	1.71	1.03–2.83	.04
11-Trouble concentrating	3.94	2.63–5.88	<.0001	1.97	1.34–2.89	<.001
12-Indecisive	3.54	2.03–6.19	<.0001	1.28	0.66–2.46	.46
13-Feeling guilty/worthless	6.89	3.82–12.42	<.0001	1.61	0.82–3.20	.17

Depression during pregnancy

BMJ 2007:334:1003-5

No

SUMMARY POINTS

Rates of depression are higher during pregnancy than at any other point during a woman's life

About half of "postnatal" depression starts during pregnancy

Two thirds of women with a history of recurrent depression will relapse during pregnancy if they discontinue their medications after conception

Depression during pregnancy is associated with poorer obstetric outcomes, particularly preterm delivery

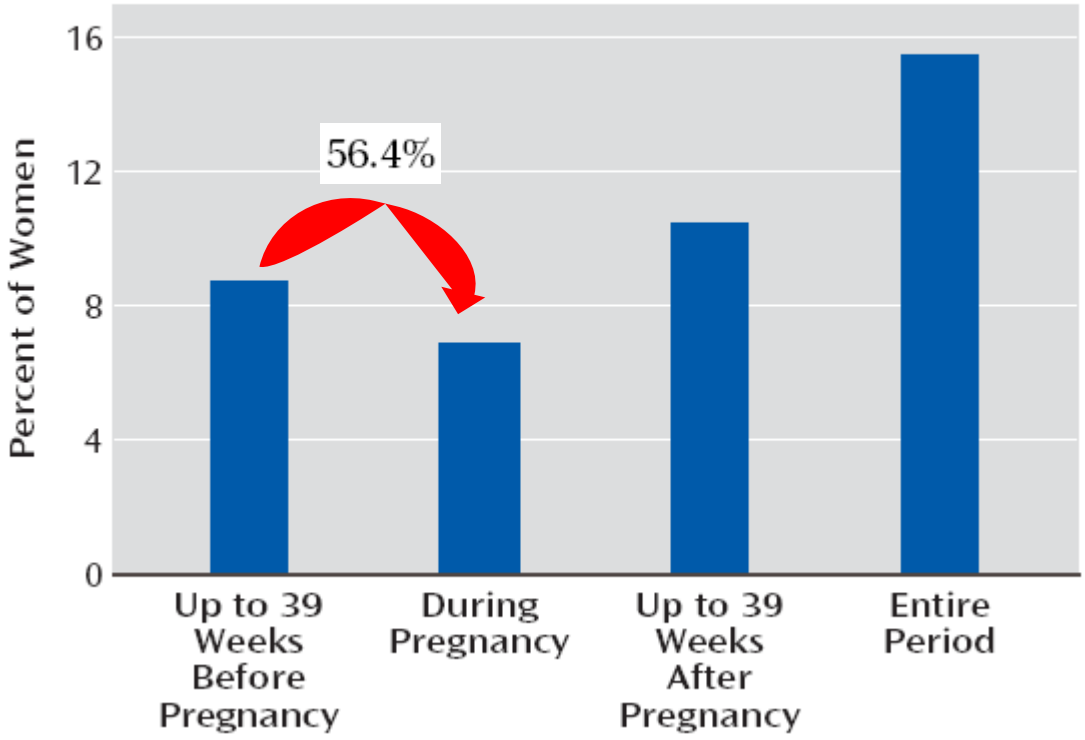
Women who are depressed during pregnancy are more likely to smoke and drink alcohol and less likely to attend for antenatal obstetric care than women who are not depressed

The treatment of depression during pregnancy must be considered individually for each woman, with the possibility of relapse and poorer obstetric outcomes balanced against the possible risks associated with taking antidepressant medication

Clinically Identified Maternal Depression Before, During, and After Pregnancies Ending in Live Births

Am J Psychiatry 2007; 164:1515–1520

FIGURE 1. Percent of Women With Diagnosed Depression Before, During, and After Pregnancy



Depression symptoms during pregnancy

Arch Womens Ment Health (2008) 11: 43–48

Sample characteristic	Value for sample		
	P	PD	D
N	41	61	53
Mean age (years)	33 (5)[a]	33 (5)	34 (8)
Mean nr. of weeks pregnant	20.7 (6.1)	20.2 (5.5)	NA[b]
Caucasians (%)	67	72	92[c]
Mean HAMD-24 total	7.3 (5.1)	26.2 (5.6)	27.1 (5.3)
Mean BDI total	5.7 (3.9)	24.9 (7.1)	27.0 (5.3)
History of past MDD (% of sample)	9.3	78.7	86.6
Duration of current episode (months)	NA	4.3 ± 3.4	8.6 ± 6.3

Relapse of Major Depression During Pregnancy in Women Who Maintain or Discontinue Antidepressant Treatment

JAMA. 2006;295:499-507

Table 3. Relapse of Major Depression During Pregnancy

Relapse Status	All Women	Medication Status			
		Maintained	Increased	Decreased	Discontinued
No relapse	115 (57.2)	61 (74.4)	11 (55.0)	22 (64.7)	21 (32.3)
Relapse by trimester					
All	86 (42.8)	21 (25.6)	9 (45.0)	12 (35.3)	44 (67.7)
First	44 (51.2)	11 (52.4)	7 (77.8)	5 (41.7)	21 (47.7)
Second	31 (36.0)	9 (42.9)	2 (22.2)	3 (25.0)	19 (43.2)
Third	11 (12.8)	1 (4.8)	0 (0.0)	4 (33.3)	4 (9.1)

Table 2. Clinical Characteristics of Pregnant Women With Histories of Major Depression Across Different Medication Treatment Conditions*

Variable	All (N = 201)	Maintained (n = 82)	Increased (n = 20)	Decreased (n = 34)	Discontinued (n = 65)
Age at onset, y					
<14	44 (23.2)	19 (24.0)	3 (16.7)	7 (21.9)	15 (24.6)
14-17	45 (23.7)	19 (24.0)	5 (27.8)	4 (12.5)	17 (27.9)
18-25	50 (26.3)	19 (24.0)	7 (38.9)	11 (34.4)	13 (21.3)
>25	51 (26.8)	22 (28.0)	3 (16.7)	10 (31.2)	16 (26.2)
Duration of illness, y					
<5	24 (12.6)	9 (11.4)	2 (11.1)	4 (12.5)	9 (14.8)
5-14	67 (35.3)	27 (34.2)	9 (50.0)	14 (43.8)	17 (27.9)
15-20	61 (32.1)	28 (35.4)	4 (22.2)	10 (31.2)	19 (31.2)
>20	38 (20.0)	15 (19.0)	3 (16.7)	4 (12.5)	16 (26.2)
No. of prior episodes					
<3	46 (23.4)	18 (22.2)	4 (20.0)	8 (23.5)	16 (25.8)
3-4	64 (32.5)	31 (38.3)	5 (25.0)	9 (26.5)	19 (30.6)
5-6	45 (22.8)	16 (19.8)	5 (25.0)	9 (26.5)	15 (24.2)
>6	42 (21.3)	16 (19.8)	6 (30.0)	8 (23.5)	12 (19.4)
No. of episodes in prior pregnancies					
Never pregnant	49 (25.3)	20 (25.3)	4 (21.0)	12 (36.4)	13 (20.6)
None	96 (49.5)	37 (46.8)	11 (57.9)	11 (33.3)	37 (58.7)
>1	49 (25.3)	22 (27.8)	4 (21.0)	10 (30.3)	13 (20.6)
No. of prior postpartum episodes					
Never pregnant	49 (26.1)	20 (26.3)	4 (22.2)	12 (36.4)	13 (21.3)
None	84 (44.7)	38 (50.0)	6 (33.3)	11 (33.3)	29 (47.5)
>1	55 (29.3)	18 (23.7)	8 (44.4)	10 (30.3)	19 (31.2)
Duration of prior episode, wk					
1-6	43 (23.1)	13 (16.9)	5 (26.3)	9 (29.0)	16 (27.1)
7-12	48 (25.8)	21 (27.3)	4 (21.0)	7 (22.6)	16 (27.1)
13-36	49 (26.3)	22 (28.6)	7 (36.8)	8 (25.8)	12 (20.3)
>36	46 (24.7)	21 (27.3)	3 (15.8)	7 (22.6)	15 (25.4)
Time since onset of most recent episode, wk					
0-24	28 (15.3)	10 (13.0)	4 (21.0)	5 (16.1)	9 (16.1)
25-72	54 (29.5)	16 (20.8)	9 (47.4)	12 (38.7)	17 (30.4)
73-144	47 (25.7)	19 (24.7)	4 (21.0)	7 (22.6)	17 (30.4)
>144	54 (29.5)	32 (41.6)	2 (10.5)	7 (22.6)	13 (23.2)
No. of attempts to discontinue antidepressant medication					
0	49 (26.5)	21 (28.0)	3 (16.7)	13 (40.6)	12 (20.0)
1	57 (30.8)	23 (30.7)	3 (16.7)	9 (28.1)	22 (36.7)
2	35 (18.9)	17 (22.7)	5 (27.8)	5 (15.6)	8 (13.3)
>2	44 (23.8)	14 (18.7)	7 (38.9)	5 (15.6)	18 (30.0)

JAMA. 2006;295:499-507

Pregnancy as a major determinant for discontinuation of antidepressants: an analysis of data from The Health Improvement Network.

J Clin Psychiatry. 2011 Mar 8.

114,999 pregnant women who had a live birth between 1992 and 2006

RESULTS: Antidepressant prescribing in pregnancy increased nearly 4-fold from 1992 to 2006 (RR= 3.87; 95% CI, 1.73-8.66; P < .001).

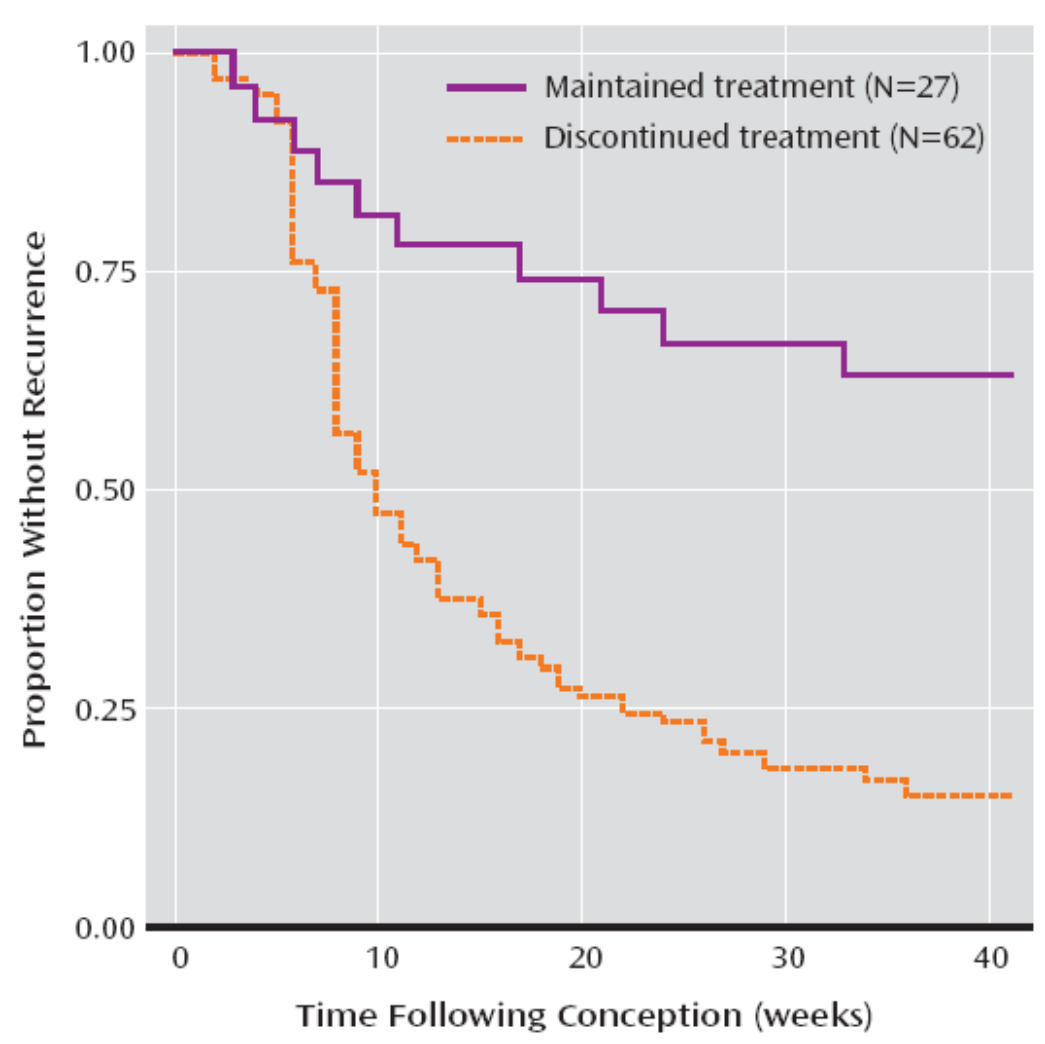
Since 2001, approximately 3% of the cohort received antidepressants at some stage during pregnancy. Selective serotonin reuptake inhibitors accounted for approximately 80% of the prescribed antidepressants. Antidepressants were more likely to be stopped in pregnant than in nonpregnant women, in particular during the first 6 weeks of pregnancy (HR= 5.19; 95% CI, 4.85-5.56; p < .001).

Only 10% of women treated before pregnancy still received antidepressants at the start of the third trimester. In contrast, 35% of nonpregnant women were still treated after a similar time period.

Article

Risk of Recurrence in Women With Bipolar Disorder During Pregnancy: Prospective Study of Mood Stabilizer Discontinuation

Viguera et al, *Am J Psychiatry 2007; 164: 1817-1824*



Conclusions: Discontinuation of mood stabilizer, particularly abruptly during pregnancy carries a high risk for new morbidity in women with bipolar disorder, especially for early depressive and dysphoric states. However, this risk is reduced markedly by continued mood stabilizer treatment. Treatment planning for pregnant women with bipolar disorder should consider not only the relative risks of fetal exposure to mood stabilizers but also the high risk of recurrence and morbidity associated with stopping maintenance mood stabilizer treatment.

Article

Risk of Recurrence in Women With Bipolar Disorder During Pregnancy: Prospective Study of Mood Stabilizer Discontinuation

TABLE 2. Morbidity During Pregnancy Versus Treatment Status

Variable	All Subjects (N=89)		Subjects Who Maintained Treatment (N=27)		Subjects Who Discontinued Treatment (N=62)	
	N	%	N	%	N	%
Risk of at least one recurrence[a]	63/89	70.8	10/27	37.0	53/62	85.5
First recurrence risk by trimester						
First	42/89	47.2	6/27	22.2	36/62	58.1
Second	15/47	31.9	3/21	14.3	12/26	46.2
Third	6/32	18.8	1/18	5.6	5/14	35.7
Recurrence polarity (all recurrences)[b]						
Depression	34/89	38.2	5/27	18.5	29/62	46.8
Mixed state	26/89	29.2	0/27	0.0	26/62	41.9
Hypomania	15/89	16.8	7/27	25.9	8/62	12.9
Mania	6/89	6.7	2/27	7.4	4/62	6.5
Percent of pregnancy weeks ill						
	Mean	SD	Mean	SD	Mean	SD
All cases[c]	32.8	31.5	8.8	21.3	43.3	29.6
	N	%	N	%	N	%
Stable subjects (%)[d]	26/89	29.2	17/27	63.0	9/62	14.5

Viguera et al, *Am J Psychiatry 2007; 164: 1817-1824*

Depression during pregnancy

BMJ 2007:334:1003-5

No

Si

SUMMARY POINTS

Rates of depression are higher during pregnancy than at any other point during a woman's life

About half of "postnatal" depression starts during pregnancy

Two thirds of women with a history of recurrent depression will relapse during pregnancy if they discontinue their medications after conception

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Women who are depressed during pregnancy are more likely to smoke and drink alcohol and less likely to attend for antenatal obstetric care than women who are not depressed

The treatment of depression during pregnancy must be considered individually for each woman, with the possibility of relapse and poorer obstetric outcomes balanced against the possible risks associated with taking antidepressant medication

Psychiatric Disorders in Pregnant and Postpartum Women in the United States

Arch Gen Psychiatry. 2008;65(7):805-815

Table 2. Twelve-Month Prevalence and ORs of *DSM-IV* Axis I Psychiatric Disorders by

Disorder	% (SE) Nonpregnant Women (n=13 025)	% (SE) Past-Year Pregnant Women[a] (n=1524)	OR (95% CI)	AOR[b] (95% CI)
Any psychiatric disorder	30.1 (0.8)	25.3 (1.3)	0.78 (0.69-0.90)	0.75 (0.62-0.90)
Any new-onset psychiatric disorder (current but not before past 12 mo)	7.0 (0.3)	8.0 (0.8)	1.16 (0.92-1.46)	0.97 (0.75-1.25)
Any substance use disorder	19.9 (0.7)	14.6 (1.2)	0.68 (0.57-0.82)	0.56 (0.44-0.71)
Any alcohol use disorder	7.6 (0.4)	3.6 (0.5)	0.45 (0.34-0.60)	0.49 (0.36-0.67)
Any drug use disorder	2.0 (0.2)	1.6 (0.4)	0.82 (0.49-1.37)	0.52 (0.29-0.94)
Nicotine dependence	14.6 (0.6)	12.5 (1.1)	0.84 (0.68-1.02)	0.79 (0.64-0.97)
Any mood disorder	13.7 (0.5)	13.3 (1.1)	0.96 (0.80-1.16)	1.04 (0.83-1.32)
MDD	8.1 (0.9)	8.4 (0.4)	0.95 (0.75-1.20)	1.24 (0.94-1.64)
Dysthymia	2.0 (0.2)	0.9 (0.4)	0.46 (0.21-1.00)	0.51 (0.22-1.18)
Bipolar disorder	2.3 (0.2)	2.8 (0.5)	1.26 (0.86-1.84)	1.09 (0.70-1.70)
Any anxiety disorder	14.9 (0.6)	13.0 (1.1)	0.85 (0.70-1.03)	0.99 (0.68-1.43)
Panic disorder	3.0 (0.2)	2.2 (0.5)	0.73 (0.46-1.15)	0.91 (0.53-1.56)
Social anxiety disorder	2.8 (0.2)	1.8 (0.4)	0.65 (0.41-1.02)	0.66 (0.33-1.31)
Specific phobia	10.2 (0.5)	9.2 (0.9)	0.89 (0.72-1.11)	0.93 (0.53-1.61)
Generalized anxiety	1.8 (0.2)	1.3 (0.4)	0.73 (0.42-1.29)	1.57 (0.82-3.02)
Any psychotic disorder	0.3 (0.1)	0.4 (0.2)	1.14 (0.44-2.94)	1.50 (0.54-4.18)
Any substance use	73.8 (1.0)	63.0 (1.8)	0.60 (0.53-0.69)	0.66 (0.57-0.77)
Any alcohol use	68.5 (0.9)	59.0 (1.7)	0.66 (0.58-0.75)	0.71 (0.61-0.81)
Any tobacco use	26.6 (0.8)	21.9 (1.5)	0.77 (0.66-0.91)	0.76 (0.64-0.89)
Any illicit drug use	6.8 (0.3)	6.2 (0.7)	0.91 (0.72-1.17)	0.87 (0.66-1.15)
Mean No. of cigarettes a day in past 12 mo (only among smokers)	15.9 (0.3)	16.6 (1.4)	$t=0.52$ $P=.60$	$\beta=0.05$ SE=0.04 $P=.29$[d]

Antenatal care

routine care for the healthy pregnant woman

National Collaborating Centre for Women's and Children's Health

Clinical Guideline
March 2008

Commissioned by the National Institute for Health and Clinical Excellence

Recommendations on alcohol consumption

Pregnant women and women planning a pregnancy should be advised to avoid drinking alcohol in the first 3 months of pregnancy if possible because it may be associated with an increased risk of miscarriage.

If women choose to drink alcohol during pregnancy they should be advised to drink no more than 1 to 2 UK units once or twice a week (1 unit equals half a pint of ordinary strength lager or beer, or one shot [25 ml] of spirits. One small [125 ml] glass of wine is equal to 1.5 UK units). Although there is uncertainty regarding a safe level of alcohol consumption in pregnancy, at this low level there is no evidence of harm to the unborn baby.

Women should be informed that getting drunk or binge drinking during pregnancy (defined as more than 5 standard drinks or 7.5 UK units on a single occasion) may be harmful to the unborn baby.

Effetti dell'esposizione prenatale all'alcol

Diagnosis	FAS Facial Features	Confirmed Prenatal Alcohol Exposure	Additional Criteria
Fetal Alcohol Syndrome (FAS) with confirmed maternal alcohol exposure	Yes	Yes	
FAS without confirmed maternal alcohol exposure	Yes	No	Growth retardation; central nervous system (CNS) abnormality; or evidence of a behavioral or cognitive disorder inconsistent with the expected developmental level, with hereditary factors, or with the environment
Partial FAS with confirmed maternal alcohol exposure	Some	Yes	
Alcohol-related birth defects (ARBD)	No	Yes	Any of a number of anomalies (e.g., heart or kidney defects) present at birth that are associated with maternal alcohol consumption during pregnancy
Alcohol-related neurodevelopmental disorder (ARND)	No	Yes	Evidence of CNS abnormality (e.g., abnormally small head, abnormal brain structures, and specific neurological signs); evidence of a behavioral or cognitive disorder inconsistent with the expected developmental level, with hereditary factors, or with the environment; or evidence of both

SOURCE:Stratton et al. 1996. Reprinted with permission from *Fetal Alcohol Syndrome: Diagnosis, Epidemiology, Prevention, and Treatment.* Copyright 1996, National Academy of Sciences, Washington, DC.

Neurobehavioural outcomes of children with fetal alcohol spectrum disorders

Summary of outcomes associated with prenatal alcohol exposure

Behavioural	Mental health	Adaptive and executive functioning
Antisocial behaviour	Alcohol problems	Socialization
Delinquent behaviour	Mood disorder	Employment difficulties
Classroom/school behaviours	Bipolar disorder	Independent living difficulties
Learning behaviours	Depression	Inhibitory control
Externalizing behaviour	Panic disorder	Cause and effect reasoning
Aggressive behaviour	Hyperkinetic disorders	Planning and organizing
Criminal activity	Emotional disorders	Learning from mistakes
Maladaptive behaviour	Conduct disorders	
Impulsivity	Sleep disorders	
Teasing/bullying	Abnormal habits	
Dishonesty	Stereotypical behaviour	
Avoiding work/school	Other psychiatric disorders	
Sexual inappropriateness	(post-traumatic stress disorder,	
Self-injury	obsessive-compulsive disorder and	
Alcohol/drug use	oppositional defiant disorder)	

Rasmussen et al, *Paediatr Child Health 2008; 13: 185-191*

Antenatal care

routine care for the healthy pregnant woman

National Collaborating Centre for Women's and Children's Health

Clinical Guideline
March 2008

Commissioned by the National Institute for Health and Clinical Excellence

Recommendations on smoking

At the first contact with the woman, discuss her smoking status, provide information about the risks of smoking to the unborn child and the hazards of exposure to secondhand smoke. Address any concerns she and her partner or family may have about stopping smoking.*

Pregnant women should be informed about the specific risks of smoking during pregnancy (such as the risk of having a baby with low birthweight and preterm birth). The benefits of quitting at any stage should be emphasised.

Prenatal Care Visits and Associated Costs for Treatment-Seeking Women With Depressive Disorders

Lin et al Psychiatric Serv 2009; 60: 1261-64

Prenatal care visits and costs according to demographic characteristics and comorbid medical disorders for 23,290 pregnant women in Taiwan, 2004–2006

Variable	M	SD	p
Number of prenatal care visits			
Mental health care visits for depressive disorder ≤1 year before conception			<.001
Yes	8.50	4.10	
No	9.17	4.49	

Variable	M	SD	p
Prenatal care costs (NT$)[a]			
Mental health care visits for depressive disorder ≤1 year before conception			<.001
Yes	51,187	46,959	
No	27,998	30,259	

the higher cost, it might be related to obstetric complications or detrimental health behaviors aggravated by untreated depressive disorders

Depression during pregnancy

BMJ 2007:334:1003-5

No

Si

Si

SUMMARY POINTS

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The management of depression during pregnancy: a report from the American Psychiatric Association and the American College of Obstetricians and Gynecologists

Obstest Gynecol 2009; 114: 703-713

2. Maternal depression and adverse reproductive outcomes

2.1. Miscarriage

Reasons for miscarriage, especially early events, are difficult to obtain because prospective data collection must begin with pregnancy recognition. Fetal loss after recognition of pregnancy, typically after 6 weeks gestation, only occurs in about 8% of women and large sample sizes are needed to assess differences among exposures associated with this outcome. Accordingly, there is a paucity of information about depression and spontaneous pregnancy loss. We found existing studies problematic because of small sample sizes and other methodological limitations, which preclude definitive conclusions [5–7].

The management of depression during pregnancy: a report from the American Psychiatric Association and the American College of Obstetricians and Gynecologists

Obstest Gynecol 2009; 114: 703-713

2. Maternal depression and adverse reproductive outcomes

2.2. Growth effects

Fetal growth effects are typically manifested as delivery of low birth weight (LBW) (born <2500 g) or small for gestational age (SGA) (typically birth weight <10% of age-adjusted weight) infants. Depressive symptoms in the mother have been linked with an increased risk for delivery of a LBW [8] or SGA infant [9] in some but not all studies [10,11]. Only the latter negative reports included structured diagnostic assessments for depression but the numbers of women with major depressive disorder (MDD) were small in both studies. The current state of information does not support or refute an association between MDD and LBW or SGA delivery.

The management of depression during pregnancy: a report from the American Psychiatric Association and the American College of Obstetricians and Gynecologists

Obstest Gynecol 2009; 114: 703-713

2. Maternal depression and adverse reproductive outcomes

2.3. Preterm delivery

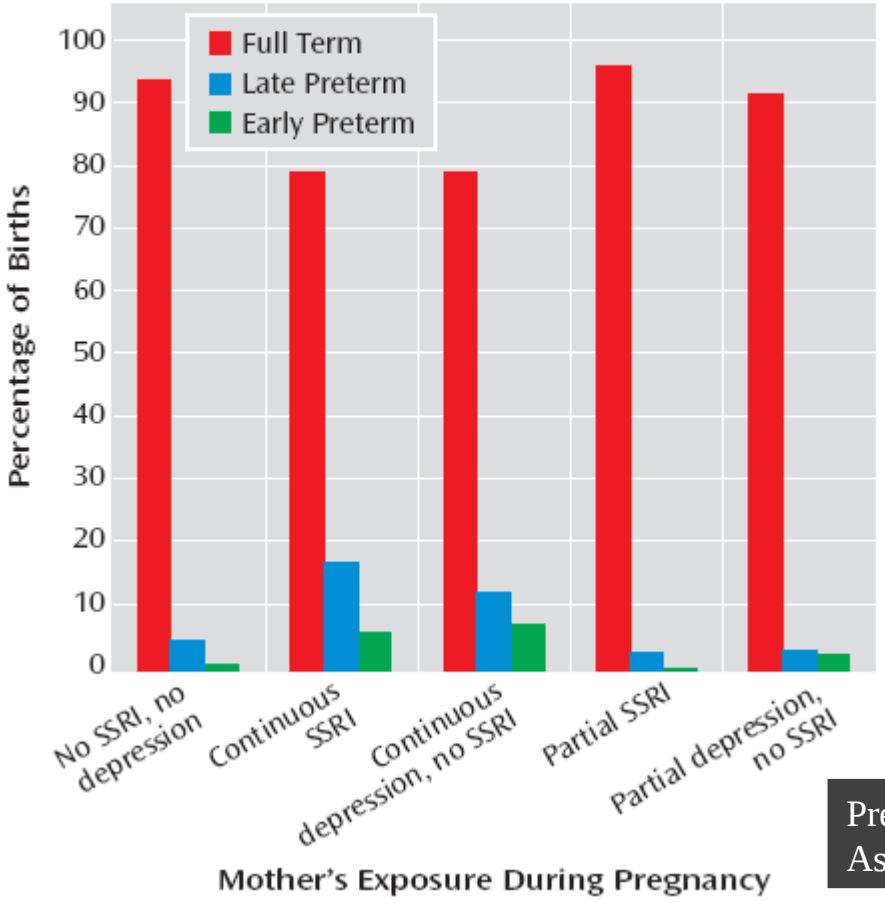
Preterm deliveries (PTD) are deliveries that occur prior to 37 completed weeks of gestation. Several studies report an association between depressive symptoms or a depressive disorder and shorter gestations, including PTD [8,9,12], although findings are not consistent [10,11]. The same limitations discussed above apply to the outcomes of PTD and gestational age, and thus, available data neither support nor refute a link between MDD and these outcomes.

Major Depression and Antidepressant Treatment: Impact on Pregnancy and Neonatal Outcomes

Am J Psychiatry 2009; 166:557–566

> 37
34-37
< 34

FIGURE 3. Relation of Infant's Gestational Age at Birth to Mother's Exposure to SSRI Antidepressants and Depression During Pregnancy



Presente per tutta o per la maggior parte
Assente per almeno un trimestre

The management of depression during pregnancy: a report from the American Psychiatric Association and the American College of Obstetricians and Gynecologists

Obstest Gynecol 2009; 114: 703-713

2. Maternal depression and adverse reproductive outcomes

2.4. Neonatal effects

We could identify no studies that link maternal depression to congenital anomalies in their infants. However, neonates born to mothers with a depressive disorder have increased risk for irritability, less activity and attentiveness, and fewer without depression [13]. This suggests that either genetic and/or other perinatal factors have an impact on infant behavior. In small studies, newborns of depressed women have physiologic profiles that parallel those of their mothers and include elevated cortisol, decreased peripheral levels of dopamine and serotonin, greater relative right frontal electroencephalogram activation and lower vagal tone [13].

The management of depression during pregnancy: a report from the American Psychiatric Association and the American College of Obstetricians and Gynecologists

2. Maternal depression and adverse reproductive outcomes

Obstest Gynecol 2009; 114: 703-713

2.5. Long-term effects on offspring

In this study, children exposed to maternal depressive symptoms at 18 and 32 weeks gestation, but not postnatally, showed greater developmental delay at 18 months than children with mothers who were not depressed in pregnancy. The odds ratio (OR) for developmental problems for offspring born to a mother with depressive symptoms according to a cutoff of 12 on the EPDS was 1.34 (95% CI=1.01–1.78; *P*=.043).The only study to use independent assessors found no effect of depression in pregnancy on child development [14], while the third study used maternal report of child development and found possible indirect effects of antenatal depression, particularly for couples who required infertility treatment [15]. The possibility of bias and existence of studies that do not agree support the need for more work to determine the degree of later developmental risk conferred to a child when mother is depressed in pregnancy.

Depression and anxiety during pregnancy: A risk factor for obstetric, fetal and neonatal outcome? A critical review of the literature

The Journal of Maternal-Fetal and Neonatal Medicine, March 2007; 20(3): 189–209

A question that arises in this context is the possibility of a dose–effect relationship with clinical levels of depression and anxiety possibly having a more negative impact on obstetric, fetal and neonatal outcome than the reported subclinical levels.

Effetto neonatale maggiore se

→disturbo depressivo vs sintomi depressivi

→ depressione cronica vs breve durata

→ comorbidità disturbi depressivi ed ansiosi

Major and Minor Depression in Pregnancy

Marchesi et al submitted Obstet Gynecol

	DM n. 19	ND n. 107	p
Età gestazionale	38.5±1.2	38.8±1.5	NS
Peso alla nascita	3132±461	3243±461	NS
Apgar 1° min	8.6±0.5	8.5±1.0	NS
Apgar 5° min	9.5±0.5	9.4±0.7	NS
→ HADS-D	12.4±2.9	3.2±2.7	<0.001
→ Durata (mesi)	2.3±1.7		

Comorbid depression and anxiety effects on pregnancy and neonatal outcome

Infant Behavior & Development 33 (2010) 23–29

	Non-depressed	Anxiety	Depressed	Comorbid	*F*	*p*
Measures						
Prematurity (%)	6.0[a]	10.2[b]	6.5[a]	14.5[c]	11.26	.01
Birthweight	3352.17[a] (448.26)	3195.76[b] (347.75)	3355.57[a] (404.14)	3224.29[b] (483.42)	4.80	.003
Birth length	50.66[a] (3.16)	50.40[ab] (1.40)	50.75[ab] (3.56)	49.56[b] (4.96)	2.64	.05

Depression during pregnancy

BMJ 2007:334:1003-5

No

Si

?

Si

SUMMARY POINTS

Rates of depression are higher during pregnancy than at any other point during a woman's life

About half of "postnatal" depression starts during pregnancy

Two thirds of women with a history of recurrent depression will relapse during pregnancy if they discontinue their medications after conception

Depression during pregnancy is associated with poorer obstetric outcomes, particularly preterm delivery

Women who are depressed during pregnancy are more likely to smoke and drink alcohol and less likely to attend for antenatal obstetric care than women who are not depressed

The treatment of depression during pregnancy must be considered individually for each woman, with the possibility of relapse and poorer obstetric outcomes balanced against the possible risks associated with taking antidepressant medication

Antenatal risk factors for postnatal depression: A large prospective study

Journal of Affective Disorders 108 (2008) 147–157

Adjusted odds ratios (ORs) from the multiple logistic regression model ($N = 7797$)

Risk factor	OR (95% CIs)	*p*-value
Antenatal EPDS score	1.18 (1.15–1.21)	<.0001
Previous psychiatric condition	1.70 (1.39–2.07)	<.0001
Antenatal emotional problems	1.39 (1.12–1.73)	<.01
Level of daily hassle	1.17 (0.89–1.55)	.26
High versus moderate		
Minimal versus moderate	0.79 (0.64–0.97)	<.05
Perfectionism	1.26 (1.04–1.52)	<.05
Partner support		
High versus moderate	0.68 (0.51–0.89)	<.01
Minimal versus moderate	0.99 (0.66–1.47)	.95
No partner versus moderate	0.62 (0.34–1.12)	.11

Antenatal risk factors for postpartum depression: a synthesis of recent literature

General Hospital Psychiatry 26 (2004) 289–295

Risk factors for postpartum depression

Antenatal predictor variable [study reference]	Total number of subjects	Cohen's effect size
Depression during pregnancy [18,28,30–32]	>3000	Strong/moderate Effect size = 0.75
Anxiety during pregnancy [18,24,28,31–33]	>1100	Strong/moderate Effect size = 0.68
Life events [18, 28, 38]	>2500	Strong/moderate Effect size = 0.61
Social support [18,28,43–45]	>3100	Strong/moderate Effect size = −0.64
Previous history of depression [18,28,30,31]	>3700	Strong/moderate Effect size = 0.58
Neuroticism [18,31,38]	>600	Moderate Effect size = 0.39
Marital relationship [5,18,28]	>1700	Moderate Effect size = 0.39
Socioeconomic status [18,26, 28,38,43,50]	>1700	Small Effect size = −0.14
Obstetric factors [18,26,28, 31,44,47,48]	>9500	Small Effect size = 0.26

Risk factors for postpartum depression: the role of the Postpartum Depression Predictors Inventory-Revised

Arch Womens Ment Health (2009) 12:239–249

PDPI-R Prenatal items	3rd month of pregnancy, RR (95% CI)	8th month of pregnancy, RR (95% CI)	1st month in postpartum, RR (95% CI)
F1 Being single	1.92 (0.77–4.82)	0.45 (0.06–3.4)	0.72 (0.17–3.1)
F2 Low socioeconomic status	3.3 (0.69–15.8)	4.9 (0.95–25.1)	2.29 (0.27–19.5)
F3 Low self-esteem	2.39 (1.54–3.7)	1.6 (0.95–2.7)	2.9 (1.9–4.6)
F4 Prenatal depression	6.12 (3.1–12.1)	5.2 (2.6–10.3)	9.97 (5.1–19.7)
F5 Prenatal anxiety	2.2 (1.2–4.4)	9.5 (3.3–27.2)	5.5 (2.6–11.9)
F6 Pregnancy intendedness	0.49 (0.21–1.1)	0.86 (0.44–1.7)	1.1 (0.61–2.0)
F7 Prior depression	3.14 (1.6–6.1)	3.8 (1.9–7.4)	4.6 (2.36–8.9)
F8 Lack of social support	1.31 (1.14–1.5)	1.5 (1.3–1.8)	1.4 (1.2–1.7)
F9 Marital dissatisfaction	1.12 (0.71–2.1)	1.4 (0.89–2.3)	1.6 (1.02–2.4)
F10 Life stress	1.36 (0.98–1.88)	1.62 (1.2–2.2)	1.5 (1.1–2.0)
Postnatal items			
F11 Childcare stress			2.8 (1.8–4.2)
F12 Infant temperament			1.6 (1.1–2.3)
F13 Maternity blues			4.9 (2.2–11.1)

Depression during pregnancy

BMJ 2007:334:1003-5

No

Si

Si

?

Si

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Women who are depressed during pregnancy are more likely to smoke and drink alcohol and less likely to attend for antenatal obstetric care than women who are not depressed

The treatment of depression during pregnancy must be considered individually for each woman, with the possibility of relapse and poorer obstetric outcomes balanced against the possible risks associated with taking antidepressant medication

Delivery outcome after maternal use of antidepressant drugs in pregnancy: an update using Swedish data

Table 1. *Number of women using specific antidepressant drugs either before the first antenatal visit ('Early') or prescribed the drugs during pregnancy ('Later')*

Drug name	ATC code	Early	Later
TCAs	*N06AA*	*1662*	*784*
Imipramine	N06AA02	10	3
Clomipramine	N06AA04	1208	592
Lofepramine	N06AA07	6	1
Amitriptyline	N06AA09	379	158
Nortriptyline	N06AA10	33	23
Protryptyline	N06AA11	1	0
Maprotiline	N06AA21	9	1
SSRIs	*N06AB*	*10 170*	*4809*
Fluoxetine	N06AB03	1522	892
Citalopram	N06AB04	3950	1648
Paroxetine	N06AB05	1208	405
Sertraline	N06AB06	3297	1825
Fluvoxamine	N06AB08	42	17
Escitalopram	N06AB10	153	56
Unspecified	N06AB00	86	39
MOAIs	*N06AG*	37	18
Moclobemide	N06AG02	37	18
SNRIs	*N06AX*	*1351*	*538*
Mianserin	N06AX03	85	33
Nefazodone	N06AX06	44	7
Mirtazapine	N06AX11	277	123
Bupropion	N06AX12	37	9
Venlafaxine	N06AX16	859	363
Reboxetine	N06AX18	28	6
Duloxetine	N06AX21	37	4
Unspecified antidepressants	*N06A*	*10*	*0*

Reis and Kallen, Psychol Med 2010; 40: 1723-33

Delivery outcome after maternal use of antidepressant drugs in pregnancy: an update using Swedish data

Method

The study is based on data from the Swedish Medical Birth Register (MBR; National Board of Health and Welfare, 2003) from 1 July 1995 up to 2007. This register contains information on almost all deliveries in Sweden (1–2% missing), with data collected during prenatal care (nearly every pregnant woman attends the free prenatal care system), delivery, and the paediatric examination of the newborn infant. Information on drug use is based partly on an interview conducted by the midwife at the first antenatal visit (in 90% of cases before the end of the first trimester, with the majority being between weeks 10 and 12) ('early use') and partly on information from the antenatal care with respect to drugs prescribed later during the pregnancy by the attending doctor ('later

Reis and Kallen, Psychol Med 2010; 40: 1723-33

Delivery outcome after maternal use of antidepressant drugs in pregnancy: an update using Swedish data

Table 2. *Some maternal delivery diagnoses after use of antidepressants (ADs) early in pregnancy, later in pregnancy, and both early and later in pregnancy. Odds ratios (ORs) with 95% confidence intervals (CIs) after adjustment for year of birth, maternal age, parity, smoking and body mass index (BMI)*

		Early use			Later use			Both early and later use		
Maternal diagnosis	Number in population	No. taking ADs	OR	95% CI	No. taking ADs	OR	95% CI	No. taking ADs	OR	95% CI
Pre-existing diabetes	5987	287	1.35	1.19–1.52	137	1.32	1.11–1.58			
Chronic hypertension	12 351	261	1.34	1.18–1.52	119	1.25	1.04–1.51			
Gestational diabetes	9724	202	1.37	1.18–1.58	81	1.16	0.93–1.45	68	1.37	1.08–1.75
Pre-eclampsia	48 361	222	1.28	1.19–1.37	413	1.38	1.25–1.53	309	1.50	1.33–1.69
Hyperemesis	10 535	234	1.45	1.27–1.66	102	1.31	1.07–1.60	87	1.59	1.28–1.96
Placenta previa	11 856	252	1.36	1.20–1.55	107	1.21	1.00–1.47	86	1.38	1.11–1.72
Placenta abruption	12 860	263	1.29	1.14–1.47	102	1.05	0.86–1.29	84	1.23	0.99–1.53
Premature rupture of membranes	25 175	475	1.30	1.18–1.43	233	1.36	1.19–1.56	174	1.47	1.26–1.72
Bleeding before partus	14 544	263	1.25	1.10–1.42	112	1.15	0.95–1.39	92	1.34	1.09–1.66
Bleeding during partus	21 918	441	1.33	1.20–1.46	238	1.45	1.27–1.65	180	1.58	1.36–1.84
Bleeding after partus	61 155	822	1.11	1.03–1.19	355	1.02	0.92–1.14	257	1.08	0.95–1.22
Induction of delivery[a]	11 407	1900	1.29	1.22–1.35	900	1.29	1.19–1.38	617	1.29	1.18–1.41
Caesarean section	168 867	3009	1.38	1.32–1.44	1418	1.35	1.27–1.44	1008	1.74	1.30–1.51

Reis and Kallen, Psychol Med 2010; 40: 1723-33

Delivery outcome after maternal use of antidepressant drugs in pregnancy: an update using Swedish data

Table 3. *Effect of preterm birth and birthweight in singletons according to antidepressant (AD) use later in pregnancy. Odds ratios (ORs) with 95% confidence interval (CIs) adjusted for year of birth, maternal age, parity, smoking and body mass index (BMI)*

		TCA			SSRI			SNRI		
Infant characteristics	Number in population	No. with AD	OR	95% CI	No. with AD	OR	95% CI	No. with AD	OR	95% CI
Preterm birth (<37 weeks)	57 946	87	2.36	1.89–2.94	356	1.46	1.31–1.63	54	1.98	1.49–2.63
Low birthweight (<2500 g)	37 105	37	1.39	1.00–1.95	190	1.13	0.97–1.31	36	1.87	1.33–2.64
High birthweight (>4500 g)	46 050	21	0.62	0.40–0.95	165	0.89	0.70–1.04	18	0.80	0.53–1.38
SGA (<2 S.D. from expected weight)	24 802	14	0.77	0.45–1.32	122	1.01	0.84–1.22	24	1.84	1.20–2.81
LGA (>2 S.D. from expected weight)	68 814	58	1.12	0.85–1.48	292	1.06	0.93–1.19	38	1.23	0.88–1.72

SGA, Small for gestational age; LGA, large for gestational age; AD, antidepressant; TCA, tricyclic antidepressant; SSRI, selective serotonin reuptake inhibitor; SNRI, serotonin-norepinephrine reuptake inhibitor; S.D., standard deviation.

Reis and Kallen, Psychol Med 2010; 40: 1723-33

Delivery outcome after maternal use of antidepressant drugs in pregnancy: an update using Swedish data

Table 4. *Six neonatal diagnoses in infants born after maternal antidepressant (AD) use. Odds ratios (ORs) with 95% confidence intervals (CIs) adjusted for year of birth, maternal age, parity, smoking and body mass index (BMI)*

		Early use			Later use			Both early and later use		
Infant diagnosis	Number in population	No. with AD	OR	95% CI	No. with AD	OR	95% CI	No. with AD	OR	95% CI
Hypoglycaemia	34794	585	1.33	1.22–1.45	311	1.43	1.31–1.65	221	1.56	1.36–1.79
Respiratory diagnoses	57487	811	1.34	1.25–1.44	437	1.62	1.47–1.79	305	1.65	1.46–1.85
Low Apgar score when known	15541	276	1.55	1.38–1.77	159	1.99	1.70–2.33	128	2.34	1.96–2.79
CNS diagnoses	8226	136	1.31	1.11–1.56	77	1.50	1.19–1.88	53	1.49	1.13–1.97
Jaundice	52004	643	1.09	1.01–1.19	318	1.13	1.01–1.27	230	1.22	1.06–1.39
Intracerebral haemorrhage	1635	23	1.17	0.77–1.78	12	1.28	0.66–2.23	8	1.20	0.52–2.37

CNS, Central nervous system; AD, antidepressant.

Reis and Kallen, Psychol Med 2010; 40: 1723-33

Delivery outcome after maternal use of antidepressant drugs in pregnancy: an update using Swedish data

Table 5. *Five groups of congenital malformations where risks seemed to differ with the group of antidepressant used. Odds ratios (ORs) with 95% confidence interval (CIs) adjusted for year of birth, maternal age, parity, smoking and body mass index (BMI)*

	TCA			SSRI			SNRI		
Congenital malformation	Number with malformation	OR	95% CI	Number with malformation	OR	95% CI	Number with malformation	OR	95% CI
Relatively severe malformation	77	1.36	1.07–1.72	345	1.08	0.97–1.21	43	1.00	0.73–1.37
Any cardiovascular defect	30	1.63	1.12–2.36	109	0.99	0.82–1.20	20	1.33	0.84–2.09
VSD and/or ASD	17	1.84	1.13–2.97	61	1.00	0.77–1.29	11	1.26	0.63–2.26[a]
Hypospadias	9	1.93	0.88–3.67	38	1.30	0.94–1.80	6	1.47	0.54–3.19[a]
Cystic kidney	0	0.00	0.00–4.34[a]	9	2.39	1.09–4.54	0	0.00	0.00–8.02[a]

TCA, Tricyclic antidepressant; SSRI, selective serotonin reuptake inhibitor; SNRI, serotonin-norepinephrine reuptake inhibitor; VSD, ventricular septal defect; ASD, atrial septal defect.
[a] Risk ratio (observed/expected number) with exact 95% CI based on Poisson distributions.

Reis and Kallen, Psychol Med 2010; 40: 1723-33

Delivery outcome after maternal use of antidepressant drugs in pregnancy: an update using Swedish data

Table 6. *Three groups of congenital malformations where risks seemed to differ with the SSRI used. Odds ratios (ORs) with 95% confidence intervals (CIs) adjusted for year of birth, maternal age, parity, smoking and body mass index (BMI)*

	Relatively severe malformation			Any cardiovascular defect			Hypospadias		
	n	OR	95% CI	*n*	OR	95% CI	*n*	OR	95% CI
Fluoxetine	60	1.29	1.00–1.67	21	1.31	0.85–2.02	5	1.10	0.36–2.57[a]
Citalopram	133	1.06	0.88–1.26	37	0.86	0.62–1.20	38	1.30	0.94–1.80
Paroxetine	49	1.20	0.90–1.61	24	1.66	1.09–2.53	9	2.45	1.12–4.64[a]
Sertraline	100	0.99	0.81–1.21	26	0.74	0.50–1.09	8	0.89	0.38–1.75[a]
χ^2 (3 df)	4.32			12.5			17.9		
p	0.23			<0.01			<0.001		

Reis and Kallen, Psychol Med 2010; 40: 1723-33

NHS

National Institute for Health and Clinical Excellence

Issue date: July 2006

Bipolar disorder

The management of bipolar disorder in adults, children and adolescents, in primary and secondary care

www.nice.org.uk

Sali di litio in gravidanza

Registro Internationale “Lithium Babies” (1968-76)

neonati --> 11% anomalie congenite

8% difetti cardiaci

3% cardiopatia di Ebstein

Studi prospettici con litio 148 --> 2.7% malformazioni (0.6%Ebstein)

senza litio 148 --> 2.0%

Studi caso-controllo --> 208 anomalia di Ebstein : 0 esposti al Li

398 senza malformazioni: 2 esposti

--> 11 con difetti cardiaci: 3 (27%) esposti

20 nessuna anomalia : 4 (20%) esposti

Llewellyn et al, 1998

Sali di litio in gravidanza

Effetto teratogeno

aumenta di 10-20 volte il rischio di difetti cardiaci (0.05-0.1% vs 0.005%)

Tossicità neonatale

Aritmia (bradicardia, irregolarità), ipotiroidismo (gozzo non tossico?), diabete insipido, cianosi e ipotonia (floppy baby syndrome).

Teratogenesi comportamentale

60 lithium babies --> 83% sviluppo psicomotorio normale
57 fratelli --> 89%

(Llewellyn et al, 1998; Eberhard-Gran et al 2005)

Teratogenicity and Anticonvulsants: Lessons From Neurology to Psychiatry

J Clin Psychiatry 2007;68[suppl 9]:29–33

Table 1. Malformation Rates With Anticonvulsant Treatment: Pregnancy Registries

Registry	Patients (No.)	Type of AED Therapy	Malformation Rate (%)
International Registry of Antiepileptic Drugs and Pregnancy (EURAP)[10]	> 5000 enrolled pregnancies	Monotherapy	5.0
		Polytherapy	8.0
North American Antiepileptic Pregnancy Registry[11,15]	3633 women	Monotherapy:	
		lamotrigine	2.7
		phenobarbital	6.5
		valproate	10.7
International Lamotrigine Pregnancy Registry[18]	680 infants	Monotherapy:	
		lamotrigine	2.8
		Polytherapy:	
		lamotrigine + valproic acid	10.5
United Kingdom Epilepsy and Pregnancy Register[9]	3607 cases	No AED exposure	3.5
		Monotherapy:	
		carbamazepine	2.2
		valproate	6.2
		Polytherapy	6.0
Australian Pregnancy Registry[14]	≥ 450 women with 396 birth outcomes	No AED exposure	3.6
		Monotherapy:	
		carbamazepine	4.5
		lamotrigine	5.6
		valproate	16.0

Antiepilettici in gravidanza

UK Epilepsy and Pregnancy Register 1996-2005

Table 3 Types of major congenital malformation by antiepileptic drug

Drug	Cases (n)	NTD	Facial cleft	Cardiac	Hypospadias/GUT	GIT	Skeletal	Other
Carbamazepine	900	2 (0.2%)	4 (0.4%)	6 (0.7%)	2 (0.2%)	2 (0.2%)	3 (0.3%)	1 (0.1%)
Valproate	715	7 (1.0%)	11 (1.5%)	5 (0.7%)	9 (1.3%)	2 (0.3%)	8 (1.1%)	2 (0.3%)
Lamotrigine	647	1 (0.2%)	1 (0.2%)	4 (0.6%)	6 (0.9%)	3 (0.5%)	2 (0.3%)	4 (0.6%)
Phenytoin	82	0 (0.0%)	1 (1.2%)	1 (1.2%)	0 (0.0%)	1 (1.2%)	0 (0.0%)	0 (0.0%)

GIT, gastrointestinal tract defects; GUT, genitourinary tract defects; NTD, neural tube defects.

Table 4 Major congenital malformation rate for monotherapy exposure to carbamazepine, valproate, and lamotrigine by dose

AED	Maximum daily dose (mg)	Total informative exposures (n)	MCMs (n)	MCM rate, % (95% CI)
Carbamazepine	<400	401	7	1.7 (0.8 to 3.6)
	400 to 1000	385	10	2.6 (1.4 to 4.7)
	>1000	92	3	3.3 (1.1 to 9.2)
Valproate	<600	266	11	4.1 (2.3 to 7.3)
	600 to 1000	247	15	6.1 (3.7 to 9.8)
	>1000	186	17	9.1 (5.8 to 14.1)
Lamotrigine	<100	151	2	1.3 (0.4 to 4.7)
	100 to 200	208	4	1.9 (0.8 to 4.8)
	>200	279	15	5.4 (3.3 to 8.7)

AED, antiepileptic drug; CI, confidence interval; MCM, major congenital malformation.

(Morrow et al, *J Neurol Neurosurg Psychiatry 2006;77: 193-198*)

1.7.1.5 The following drugs should not be routinely prescribed for pregnant women with bipolar disorder:

- valproate – because of risk to the fetus and subsequent child development
- carbamazepine – because of its limited efficacy and risk of harm to the fetus
- lithium – because of risk of harm to the fetus, such as cardiac problems
- lamotrigine* – because of the risk of harm to the fetus
- paroxetine – because of the risk of cardiovascular malformations in the fetus
- long-term treatment with benzodiazepines – because of risks during pregnancy and the immediate postnatal period, such as cleft palate and floppy baby syndrome.

1.7.2 Women planning a pregnancy

1.7.2.1 Women with bipolar disorder who are considering pregnancy should normally be advised to stop taking valproate, carbamazepine, lithium and lamotrigine*, and alternative prophylactic drugs (such as an antipsychotic) should be considered.

1.7.2.2 Women taking antipsychotics who are planning a pregnancy should be advised that the raised prolactin levels associated with some antipsychotics reduce the chances of conception. If prolactin levels are raised, an alternative drug should be considered.

1.7.2.3 If a woman who needs antimanic medication plans to become pregnant, a low-dose typical or atypical antipsychotic should be considered, because they are of least known risk.

1.7.2.4 If a woman taking lithium plans to become pregnant, the following options should be considered:

- if the patient is well and not at high risk of relapse – gradually stopping lithium
- if the patient is not well or is at high risk of relapse:
  - switching gradually to an antipsychotic, or
  - stopping lithium and restarting it in the second trimester if the woman is not planning to breastfeed and her symptoms have responded better to lithium than to other drugs in the past, or
  - continuing with lithium, after full discussion of the risks, while trying to conceive and throughout the pregnancy, if manic episodes have complicated the woman's previous pregnancies, and her symptoms have responded well to lithium.

1.7.2.5 If a woman remains on lithium during pregnancy, serum lithium levels should be monitored every 4 weeks, then weekly from the 36th week, and less than 24 hours after childbirth. The dose should be adjusted to keep serum levels within the therapeutic range. The woman should maintain adequate fluid intake.

1.7.2.6 If a woman planning a pregnancy becomes depressed after stopping prophylactic medication, psychological therapy (CBT) should be offered in preference to an antidepressant because of the risk of switching associated with antidepressants. If an antidepressant is used, it should usually be an SSRI (but not paroxetine because of the risk of cardiovascular malformations in the fetus) and the woman should be monitored closely.

1.7.3 Women with an unplanned pregnancy

1.7.3.1 If a woman with bipolar disorder has an unplanned pregnancy:

- the pregnancy should be confirmed as quickly as possible
- the woman should be advised to stop taking valproate, carbamazepine and lamotrigine*
- if the pregnancy is confirmed in the first trimester, and the woman is stable, lithium should be stopped gradually over 4 weeks, and the woman informed that this may not remove the risk of cardiac defects in the fetus
- if the woman remains on lithium during pregnancy serum lithium levels should be checked every 4 weeks, then weekly from the 36th week, and less than 24 hours after childbirth; the dose should be adjusted to keep serum levels within the therapeutic range, and the woman should maintain adequate fluid intake
- an antipsychotic should be offered as prophylactic medication

Antipsicotici atipici in gravidanza

Clozapina

Teratogenesi

- 200 casi segnalati alla Novartis → 6% malformazioni
- 61 casi → 5 (8%) malformazioni
- 6 case reports → nessuna malformazione

Nguyen e Lalonde. *Encephale 2003; 29: 119-124*

Ernst e Goldberg. *J Clin Psychiatry 2002; 63(suppl 4): 42- 55*

Tossicità neonatale

- floppy baby syndrome, epilessia

Teratogenesi comportamentale

- bambini 2-3 a. e uno a 6 a: nessuna anomalia

Antipsicotici atipici in gravidanza

Olanzapina

Teratogenesi

casi segnalati alla Lilly → 1% malformazioni

- 7 case reports (8 donne) → nessuna malformazione

Ernst e Goldberg. *J Clin Psychiatry 2002; 63(suppl 4): 42- 55*

Antipsicotici atipici in gravidanza

Quetiapina

Teratogenesi

- 2 case reports → nessuna malformazione

Tény et al. *Am J Psychiatry 2002; 159: 674*

Taylor et al. *Am J Psychiatry 2003; 160: 589-560*

Risperidone

Teratogenesi

7 casi segnalati alla Janssen → nessuna malformazione

- 2 case reports → - agenesia del corpo calloso;
  - nessuna malformazione in 2 neonati,

Ratnayake e Libretto. *J Clin Psychiatry 2002; 63: 76-77*

Ernst e Goldberg. *J Clin Psychiatry 2002; 63(suppl 4): 42- 55*

Pregnancy Outcome of Women Using Atypical Antipsychotic Drugs: A Prospective Comparative Study

Kate McKenna, M.Sc.; Gideon Koren, M.D.; Maria Tetelbaum, M.D.; Lynda Wilton, Ph.D.; Saad Shakir, M.D.; Orna Diav-Citrin, M.D.; Andrea Levinson, M.D.; Robert B. Zipursky, M.D.; and Adrienne Einarson, R.N.

(J Clin Psychiatry 2005;66:444–449)

women exposed to olanzapine (N = 60), risperidone (N = 49), quetiapine (N = 36), and clozapine (N = 6). We

Table 2. Comparison of Pregnancy Outcome Between Women Exposed to Atypical Antipsychotics and Non-Teratogenic Agents

Outcome	Atypical Antipsychotic (N = 151)	Non-Teratogenic Agent (N = 151)	p Value
Live birth, N	110	135	< .001
Spontaneous abortion, N (%)	22 (14.5)	13 (8.6)	.15
Stillbirth, N (%)	4 (2.6)	4 (2.6)	1.0
Therapeutic abortion, N (%)	15 (9.9)	2 (1.3)	.003
Major malformation, N (%)	1 (0.9)	2 (1.5)	1.0
Birth weight, mean (SD), g	3341 (685)	3411 (534)	.38
Gestational age at birth, mean (SD), wk	39 (1)	39 (1)	1.0

Maternal Use of Antipsychotics in Early Pregnancy and Delivery Outcome

Abstract: The effect of various antipsychotics during pregnancy has repeatedly been studied, but for most atypical antipsychotics, only little information is available. We identified from the Swedish Medical Birth Register 2908 women who had reported the use of any antipsychotic or lithium in early pregnancy and studied malformation rates with data also from the Register of Congenital Malformations and the Hospital Discharge Register. Comparisons were made with all births (n = 958,729) after adjustment for some confounders. Risks were expressed as odds ratios (ORs).

Most women had used dixyrazine or prochlorperazine mainly because of nausea and vomiting in early pregnancy. Seventy-nine women had used lithium, and these outcomes are reported separately. Hence, the main analysis was restricted to 570 women (576 infants) using other antipsychotics. There was a statistically significant increase in the risk for a congenital malformation—after exclusion of some common and minor conditions, the OR was 1.52 (95% confidence interval, 1.05–2.19). Exclusion of infants exposed to anticonvulsants reduced the OR only slightly. Most of the increased risk was caused by cardiovascular defects, mainly atrium or ventricular septum defect. No certain drug specificity was found. Except for an increased risk for congenital malformations, a nearly doubling of the risk for gestational diabetes and a 40% increased risk for cesarean delivery was noted. Because there seems to be little drug specificity, it is possible that underlying pathology or unidentified confounding explains the excess risk.

(*J Clin Psychopharmacol* 2008;28:279–288

Swedish Medical Birth Register

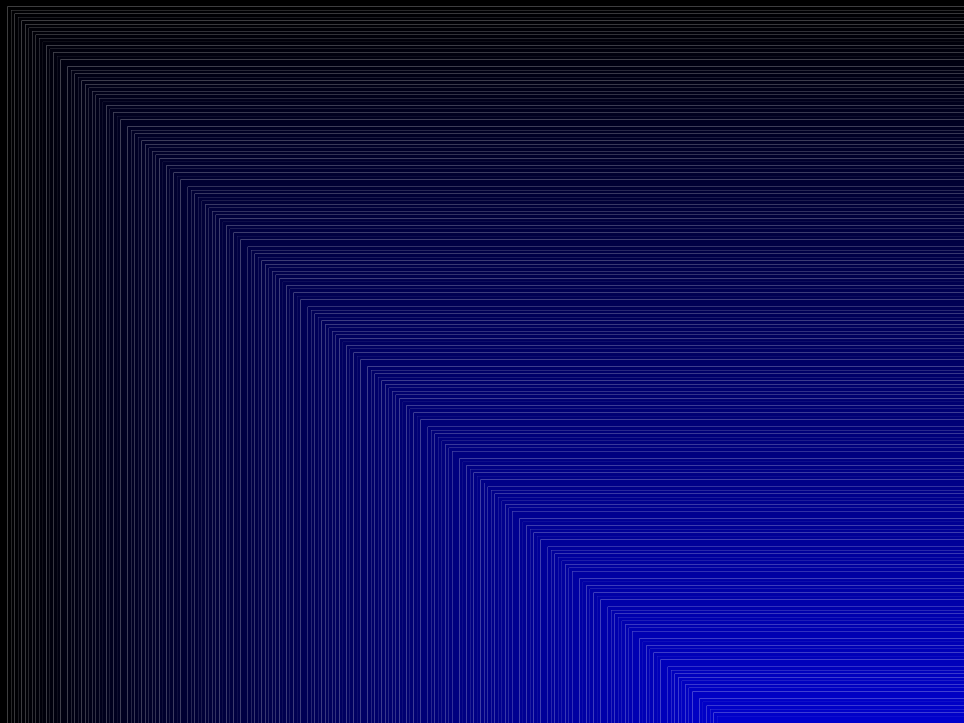
2908 used AP in early pregancy

Most women used prochlorperazina or dixyrazine

570 women used other AP

Malformation OR 1.52 (1.05-2.19)
Diabetes OR 1.78(1.04-3.01)
Cesarean del. OR 1.43 (1.17-1.74)

No drug specificity



Post-partum Depression

Disorder	Onset and Duration	Symptoms	Treatment
Postpartum Blues	Onset is 3-4 d postpartum and can last 12 h to 2 wk	Rapid but mild mood swings, irritability, tearfulness, anxiety, and insomnia	No treatment required, except support and reassurance
Postpartum Depression	Onset is within 6-12 mo postpartum and can last weeks to months	More extreme disturbances in appetite, sleep, and libido; intense anxiety, fatigue, and/or feelings of guilt	Counseling, therapy, medication, or combination usually required by health care professional
Postpartum Psychosis	Onset is up to 2 wk postpartum and can last weeks to months	Symptoms are severe and include disorganized behavior, rapid mood swings, delusions, and hallucinations	Hospitalization usually required

The Journal for Nurse Practitioners April 2006

Postpartum depression: a disorder in search of a definition

Arch Womens Ment Health (2010) 13:37–40

Time considerations

The DSM-IV sets 4 weeks post-birth as the delimiter for *with postpartum onset*; in contrast, the ICD-10 classifies mental disorders as *associated with the puerperium* if they begin within 6 weeks after birth. An international expert panel convened at Satra Bruk, Sweden, recommended 3 months as the time frame for specifying postpartum

Postpartum depression: a disorder in search of a definition

Arch Womens Ment Health (2010) 13:37–40

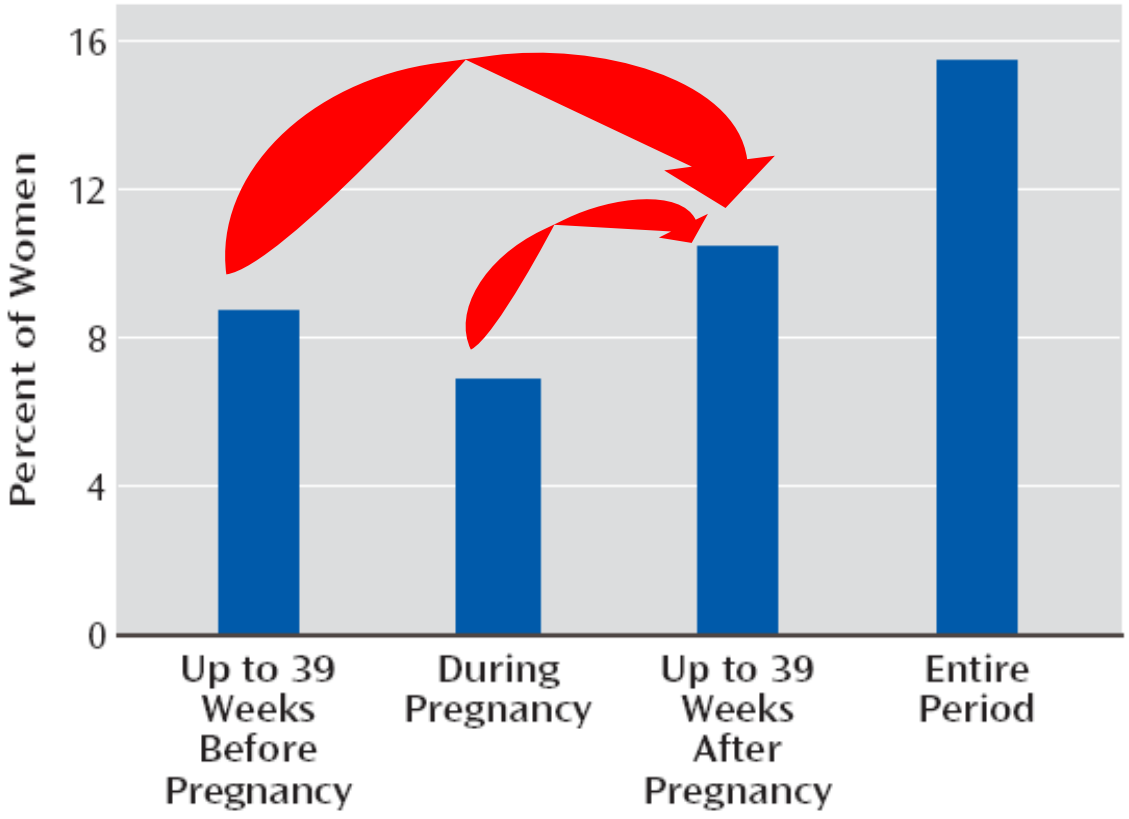
Diagnostic considerations

The diagnostic entities most frequently observed after birth in both the Kendell et al. (1987) and Munk-Olsen et al. (2006) studies were major mood disorders, with a particular risk for bipolar disorder. Munk-Olsen et al observed highly significant relative risks of 23.33 in the first 30 days and 6.30 in the 31–60 days after birth for bipolar disorder. Kendell et al reported an RR of 21.7 for admission with psychosis (primarily bipolar disorder) within 30 days of

Clinically Identified Maternal Depression Before, During, and After Pregnancies Ending in Live Births

Am J Psychiatry 2007; 164:1515–1520

FIGURE 1. Percent of Women With Diagnosed Depression Before, During, and After Pregnancy



Impact of Antenatal and Postpartum Maternal Mental Illness: How are the Children?

Brand and Brennan, *Clin Obstet Gynecol 2009; 52: 441-455*

Età valutazione: 8 mesi-16 anni

Esito: funzioni cognitive, comportamento, psicopatologia

	Gravidanza	**Post-partum**	Infanzia
Ansia/stress	+++	**+**	?
Depressione	+	**+**	++

Postpartum depression effects on early interactions, parenting, and safety practices: A review

Infant Behavior & Development 33 (2010) 1–6

In this paper studies are reviewed from the last decade on postpartum depression effects on early interactions, parenting, safety practices and on early interventions. The interaction disturbances of depressed mothers and their infants appear to be universal, across different cultures and socioeconomic status groups and, include less sensitivity of the mothers and responsivity of the infants. Several caregiving activities also appear to be compromised by postpartum depression including feeding practices, most especially breastfeeding, sleep routines and well-child visits, vaccinations and safety practices. These data highlight the need for universal screening of maternal and paternal depression during the postpartum period. Early interventions reviewed here include psychotherapy and interaction coaching for the mothers, and infant massage for their infants.

Postpartum depression effects on early interactions, parenting, and safety practices: A review

Infant Behavior & Development 33 (2010) 1–6

La relazione con il neonato (3-6 mesi) si caratterizza per:

-intrusività, ansia, controllo, iperstimolazione

oppure

- passività, distacco, scarsa stimolazione

Il contatto fisico: meno frequente, meno “affettivo”, “negativo”

(i neonati si toccano maggiormente la pelle)

Il contatto verbale: meno frequente, meno stimolante, meno “affettivo”

(da bambini, linguaggio povero e peggior funzionamento cognitivo-verbale)

Attività “ludiche”: ridotte (giocare, leggere, cantare...)

Postpartum depression effects on early interactions, parenting, and safety practices: A review

Infant Behavior & Development 33 (2010) 1–6

Compromissioni cure parentali

allattamento, sonno, salute, visite mediche

Il sonno del neonato

- posizione prona anziché supina
- dormire nel letto dei genitori
- essere accudito nella fase di addormentamento
- fase di addormentamento più lunga
- risvegli notturni più frequenti e più lunghi
- pianti notturni più frequenti

Postnatal depression: A global public health perspective

Perspectives in Public Health 2009 129: 221

It is recommended that all women should have their mental and emotional health assessed postnatally so that the presence of PND can be ascertained.

?

Antidepressant Drugs and Breastfeeding: A Review of the Literature

BREASTFEEDING MEDICINE
Volume 00, Number 00, 2010

TABLE 1. SUMMARY OF BASIC PHARMACOKINETIC PARAMETERS OF ANTIDEPRESSANT DRUGS DURING BREASTFEEDING[37]

	Half-life	T_{max}	*M/P*	*PB*	*Oral bioavailability*
SSRI					
Citalopram	36 hours	2–4 hours	1.16–3	80%	80%
Escitalopram	27–32 hours	5 hours	2.2	56%	80%
Fluoxetine	2–3 days	1.5–12 hours	0.28–0.67	94.5%	100%
Fluvoxamine	15.6 hours	3–8 hours	1.34	80%	53%
Paroxetine	21 hours	5–8 hours	0.056–1.3	95%	Complete
Sertraline	26 hours	7–8 hours	0.89	98%	Complete
NRI					
Reboxetine	NR	NR	NR	NR	NR
SNRI					
Venlafaxine	5 hours	2.25 hours	2.75	27%	92%
Duloxetine	12 hours	6 hours	0.267–1.29	>90%	>70%
Tricyclic antidepressant					
Amitriptyline	31–46 hours	2–4 hours	1	94.8%	Complete
Nortriptyline	16–90 hours	7–8.5 hours	0.87–3.71	92%	51 %
Clomipramine	19–37 hours	—	0.84–1.62	96%	Complete
Desipramine	7–60 hours	4–6 hours	0.4–0.9	82%	90%
Imipramine	8–16 hours	1–2 hours	0.5–1.5	90%	90%
Dothiepin	14.4–23.4 hours	3 hours	0.3	—	30%
Doxepine	8–24 hours	2 hours	1.08–1.66	80–85%	Complete
Protriptyline	NR	NR	NR	NR	NR
Trimipramine	NR	NR	NR	NR	NR
Tetracyclic antidepressant					
Amoxapine	8 hours	2 hours	0.21	15–25%	18–54%
Maprotiline	27–58 hours	12 hours	1.5	88%	100%
Mianserine	NR	NR	NR	NR	NR
MAOIs	NR	NR	NR	NR	NR
Atypical					
Bupropion	8–24 hours	2 hours	2.51–8.58	75–88%	85%
St. John's wort	26.5 hours	5.9 hours	NR	NR	NR
Nefazodone	1–4 hours	1 hour	0.1–0.27	>99%	20%
Mirtazapine	20–40 hours	2 hours	0.76	85%	50%
Quetiapine*	6 hours	1.5 hours	0.29	83%	100%
Trazodone	4–9 hours	1–2 hours	0.142	85–95%	65%
Lithium*	17–24 hours	2–4 hours	0.24–0.66	0%	Complete

Antidepressant Drugs and Breastfeeding: A Review of the Literature

BREASTFEEDING MEDICINE
Volume 00, Number 00, 2010

TABLE 2. SAFETY ASSESSMENT OF ANTIDEPRESSANT DRUGS DURING BREASTFEEDING

Drug	Reference: Briggs et al.[36] (2008)[a]	Reference: Hale[37] (2010)[b]	Reference: LactMed[38] (2010)
SSRI[40–47]			
Citalopram[48–51]	L-PT	L2	Agents with lower excretion into breastmilk may be preferred, especially while nursing a newborn or preterm infant. The breastfed infant should be monitored for behavioral side effects such as sedation or fussiness.
Escitalopram[52]	N-PT	L2	Escitalopram would not be expected to cause any adverse effects during breastfeeding. Monitor the infant for drowsiness if the infant is older than 2 months, exclusively breastfed infants, and when using combinations of psychotropic drugs.
Fluoxetine[53–60]	L-PT	L2	Agents with lower excretion into breastmilk may be preferred, especially while nursing a newborn or preterm infant. The breastfed infant should be monitored for behavioral side effects such as colic, fussiness, or sedation and for adequate weight gain.
Fluvoxamine[61–64]	L-PT	L2	Maternal fluvoxamine doses of up to 300 mg daily produce low levels in breastmilk and would not be expected to cause any adverse effects in breastfed infants, especially if the infant is older than 2 months.
Paroxetine[62,65–66]	L-PT	L2	Paroxetine has not been detected in the serum of most infants tested and should be considered one of the preferred antidepressants during breastfeeding.
Sertraline[62,67–70]	L-PT	L2	Sertraline is usually not detected in the serum of the infant and should be considered one of the preferred antidepressants during breastfeeding.

L-PT, limited human data—potential toxicity
N-PT, no human data—potential toxicity
L1, safest; L2, safer; L3, moderately safe; L4, possibly hazardous;

Antidepressant Drugs and Breastfeeding: A Review of the Literature

BREASTFEEDING MEDICINE
Volume 00, Number 00, 2010

NRI			
Reboxetine	NR	NR	NR
SNRI			
Venlafaxine[71,72]	L-PT	L3	Breastfed infants, especially newborn or preterm infants, should be monitored for excessive sedation and adequate weight gain. Include measurement of serum desvenlafaxine to rule out toxicity. Newborn infants of mothers who took the drug during pregnancy may experience poor neonatal adaptation syndrome; it has been proposed the use of venlafaxine during breastfeeding as a method of mitigating infant venlafaxine withdrawal symptoms.
Duloxetine[73]	N-PT	L3	An alternate drug that has been better studied may be preferred, especially while nursing a newborn or preterm infant. Monitor the infant for drowsiness, adequate weight gain, and developmental milestones, especially in younger, exclusively breastfed infants and when using combinations of psychotropic drugs.
Tricyclic antidepressant			
Amitriptyline	L-PT	L2	Amitriptyline use during breastfeeding would usually not be expected to cause any adverse effects in breastfed infants, especially if the infant is older than 2 months. Other agents with fewer active metabolites may be preferred when large doses are required or while nursing a newborn or preterm infant.
Nortriptyline	L-PT	L2	Most authoritative reviewers consider nortriptyline one of the preferred antidepressants during breastfeeding.
Clomipramine[74,75]	L-PT	L2	The use of clomipramine during breastfeeding is acceptable but may be less desirable than other tricyclic antidepressants that have been studied more thoroughly.
Desipramine	L-PT	L2	Desipramine use during breastfeeding would usually not be expected to cause any adverse effects in breastfed infants, especially if the infant is older than 2 months.
Imipramine	L-PT	L2	Imipramine use during breastfeeding would usually not be expected to cause any adverse effects in breastfed infants, especially if the infant is older than 2 months. Other agents may be preferred when large doses are required or while nursing a newborn or preterm infant.

Antidepressant Drugs and Breastfeeding: A Review of the Literature

BREASTFEEDING MEDICINE
Volume 00, Number 00, 2010

Atypical			
Bupropion[83–87]	L-PT	L3	Another drug may be preferred, especially while nursing a newborn or preterm infant. Exclusively breastfed infants should be monitored if this drug is used during lactation, possibly including measurement of serum levels.
St. John's wort[88-92]	L-PT	L2	NR
Nefazodone[93]	L-PT	L4	Nefazodone produce low but variable levels in milk that would not be expected to cause adverse effects in a breastfed infant, especially if the infant is older than 2 months. Until more data become available, other drugs may be preferred, especially while nursing a newborn or preterm infant.
Mirtazapine[94–97]	L-PT	L3	Maternal doses of up to 120 mg daily produce low levels in milk and would not be expected to cause any adverse effects in breastfed infants, especially if the infant is older than 2 months. Exclusively breastfed infants should be monitored for behavioral side effects and adequate growth if this drug is used during lactation.
Quetiapine[72,98–100]*	L-PT	L2	Limited information indicates that maternal quetiapine oral doses of up to 400 mg daily produce low levels in milk. Other agents may be preferred, especially while nursing a newborn or preterm infant.
Trazodone[101]	L-PT	L2	Trazodone would not be expected to cause any adverse effects in breastfed infants, especially if the infant is older than 2 months or when doses of 100 mg or less are used at bedtime for sleep.
Lithium[102,103]*	L-PT	L3	Limited data suggest that lithium in milk can adversely affect the infant when its elimination is impaired, as in dehydration or in newborn or premature infants.

Psychotropic Drug Use During Breastfeeding: A Review of the Evidence

Pediatrics 2009;124;e547-e556

Drug	Dosage, mg/d	No. of Pairs (Mother–Infant)	M/P	% Dose	Compatibility Level With Breastfeeding
Antipsychotics					
Haloperidol	3–30	11	0.6–8.1	0.2–9.6	Yes
Chlorpromazine	40–120	3	0.4–0.9	0.1–0.2	Yes
Clozapine	50–100	2	2.8–4.3	1.0–1.1	No
Lithium	600–1500	30	0.2–1.3	3.5–69.0	No
Olanzapine	2.5–20.0	14	0.1–0.8	<0.1–4.0	Yes
Perphenazine	16–24	2	0.7–1.1	0.1–0.2	Caution
Quetiapine	25–400	8	0.3	0.1–0.5	Caution
Risperidone	1.5–4.0	3	0.1–0.5	2.8–4.7	Caution
Sulpiride	100	65	—	2.3–17.7	No
Zuclopenthixol	4–50	7	0.1–0.7	<0.1–0.5	Caution
Aripiprazole	15	1	0.9	0.8	Caution
Antiepileptics					
Valproic acid	500–2400	24	<0.1–0.1	0.1–3.9	Yes
Carbamazepine	500–1300	33	0.2–2.6	1.1–7.3	Yes
Clonazepam	4	2	0.3–0.4	1.3–2.4	Caution
Ethosuximide	250–1420	18	0.7–1.0	31.0–99.0	No
Phenytoin	100–600	27	<0.1–0.5	0.5–8.9	Yes
Phenobarbital	30–120	34	0.1–0.8	33.6–297.0	No
Gabapentin	600–2400	8	0.7–1.3	1.3–6.5	Caution
Lamotrigine	100–800	42	0.1–1.1	1.8–21.1	No
Levetiracetam	1000–3500	33	0.8–3.1	0.5–16.0	No
Oxcarbazepine	600–900	2	0.5–5.0	0.1	Caution

NHS

National Institute for Health and Clinical Excellence

Issue date: July 2006

Bipolar disorder

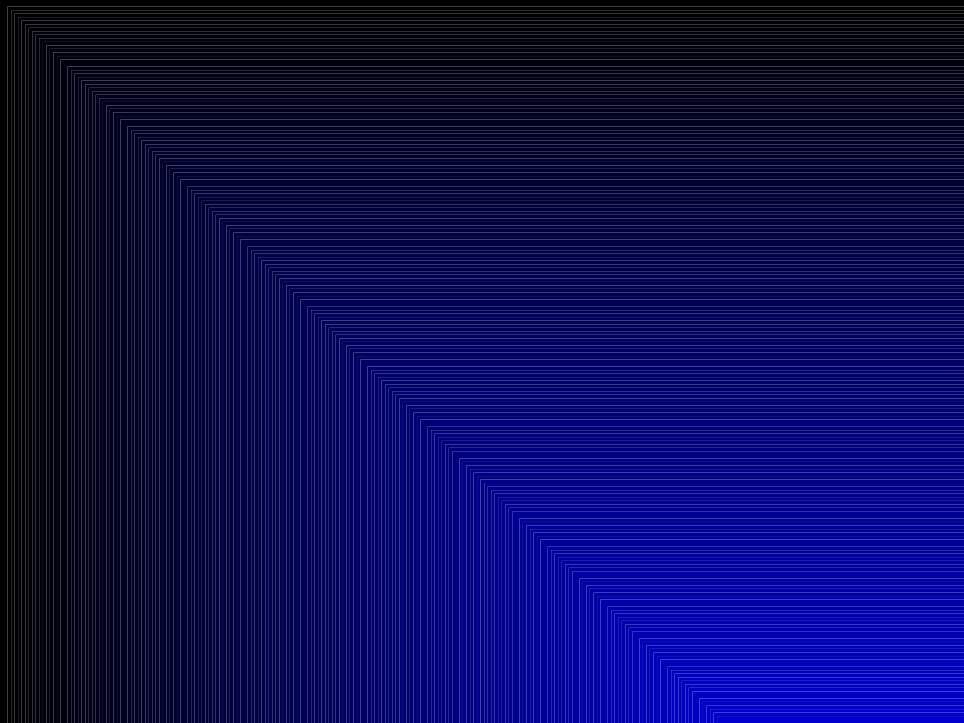
The management of bipolar disorder in adults, children and adolescents, in primary and secondary care

www.nice.org.uk

1.7.6 Breastfeeding

1.7.6.1 Women with bipolar disorder who are taking psychotropic medication and wish to breastfeed should:

- have advice on the risks and benefits of breastfeeding
- be advised not to breastfeed if taking lithium, benzodiazepines or lamotrigine*, and offered a prophylactic agent that can be used when breastfeeding – an antipsychotic should be the first choice (but not clozapine*)
- be prescribed an SSRI if an antidepressant is used (but not fluoxetine or citalopram).



Disturbi d’Ansia in gravidanza

Psychiatric Disorders in Pregnant and Postpartum Women in the United States

Arch Gen Psychiatry. 2008;65(7):805-815

Table 2. Twelve-Month Prevalence and ORs of *DSM-IV* Axis I Psychiatric Disorders by

Disorder	% (SE) Nonpregnant Women (n=13 025)	% (SE) Past-Year Pregnant Women[a] (n=1524)	OR (95% CI)	AOR[b] (95% CI)
Any psychiatric disorder	30.1 (0.8)	25.3 (1.3)	0.78 (0.69-0.90)	0.75 (0.62-0.90)
Any new-onset psychiatric disorder (current but not before past 12 mo)	7.0 (0.3)	8.0 (0.8)	1.16 (0.92-1.46)	0.97 (0.75-1.25)
Any substance use disorder	19.9 (0.7)	14.6 (1.2)	0.68 (0.57-0.82)	0.56 (0.44-0.71)
Any alcohol use disorder	7.6 (0.4)	3.6 (0.5)	0.45 (0.34-0.60)	0.49 (0.36-0.67)
Any drug use disorder	2.0 (0.2)	1.6 (0.4)	0.82 (0.49-1.37)	0.52 (0.29-0.94)
Nicotine dependence	14.6 (0.6)	12.5 (1.1)	0.84 (0.68-1.02)	0.79 (0.64-0.97)
Any mood disorder	13.7 (0.5)	13.3 (1.1)	0.96 (0.80-1.16)	1.04 (0.83-1.32)
MDD	8.1 (0.9)	8.4 (0.4)	0.95 (0.75-1.20)	1.24 (0.94-1.64)
Dysthymia	2.0 (0.2)	0.9 (0.4)	0.46 (0.21-1.00)	0.51 (0.22-1.18)
Bipolar disorder	2.3 (0.2)	2.8 (0.5)	1.26 (0.86-1.84)	1.09 (0.70-1.70)
Any anxiety disorder	14.9 (0.6)	13.0 (1.1)	0.85 (0.70-1.03)	0.99 (0.68-1.43)
Panic disorder	3.0 (0.2)	2.2 (0.5)	0.73 (0.46-1.15)	0.91 (0.53-1.56)
Social anxiety disorder	2.8 (0.2)	1.8 (0.4)	0.65 (0.41-1.02)	0.66 (0.33-1.31)
Specific phobia	10.2 (0.5)	9.2 (0.9)	0.89 (0.72-1.11)	0.93 (0.53-1.61)
Generalized anxiety	1.8 (0.2)	1.3 (0.4)	0.73 (0.42-1.29)	1.57 (0.82-3.02)
Any psychotic disorder	0.3 (0.1)	0.4 (0.2)	1.14 (0.44-2.94)	1.50 (0.54-4.18)
Any substance use	73.8 (1.0)	63.0 (1.8)	0.60 (0.53-0.69)	0.66 (0.57-0.77)
Any alcohol use	68.5 (0.9)	59.0 (1.7)	0.66 (0.58-0.75)	0.71 (0.61-0.81)
Any tobacco use	26.6 (0.8)	21.9 (1.5)	0.77 (0.66-0.91)	0.76 (0.64-0.89)
Any illicit drug use	6.8 (0.3)	6.2 (0.7)	0.91 (0.72-1.17)	0.87 (0.66-1.15)
Mean No. of cigarettes a day in past 12 mo (only among smokers)	15.9 (0.3)	16.6 (1.4)	$t=0.52$ $P=.60$	$\beta=0.05$ SE=0.04 $P=.29$[d]

Is pregnancy associated with mood and anxiety disorders? A cross-sectional study

General Hospital Psychiatry 32 (2010) 213–215

Mood and anxiety disorders in the pregnant and nonpregnant women

	Pregnant women (n=309)	Nonpregnant women (n=107)	Odds ratio (95% CI)	P value[a]
Axis I diagnoses				
Major depression	17 (5.5)	5 (4.7)	1.17 (0.44–3.11)	1.000
Dysthymic disorder	8 (2.6)	1 (0.9)	2.77 (0.35–21.89)	0.458
Bipolar disorder	– (–)	– (–)	–	–
Panic disorder	6 (1.9)	1 (0.9)	2.07 (0.25–17.06)	.683
Obsessive-compulsive disorder	16 (5.2)	3 (2.8)	1.84 (0.55–6.21)	.425
Social phobia	10 (3.2)	3 (2.8)	1.15 (0.32–2.92)	1.000
Specific phobia	10 (3.2)	5 (4.7)	0.68 (0.24–1.96)	.547
Posttraumatic stress disorder	– (–)	– (–)	–	–
Generalized anxiety disorder	11 (3.6)	4 (3.7)	0.95 (0.31–2.92)	1.000
Any mood disorder	25 (8.1)	8 (7.5)	1.04 (0.66–1.64)	1.000
Any anxiety disorder	48 (15.5)	16 (15.0)	1.04 (0.62–1.75)	1.000
Any mood or anxiety disorder	60 (19.4)	20 (18.7)	1.08 (0.50–2.33)	1.000

[a] Fisher's Exact Test.

Panic disorder during pregnancy and postpartum period

European Psychiatry 21 (2006) 495–500

Main results of studies on the course of panic disorder during pregnancy and postpartum period in women with preexisting panic disorder (N = number of pregnancies, + = improvement, = no change, – = deterioration)

Authors	N	Pregnancy			Post-partum period		
		+	=	–	+	=	–
Cohen et al., 1994 [11]	48	10 (21%)	28 (58%)	10 (21%)	–	–	–
Cohen et al., 1994 [12]	40	–	–	–	3 (8%)	23 (57%)	14 (35%)
Cohen et al., 1996 [13]	10	1 (10%)	6 (60%)	3 (30%)	–	1 (10%)	9 (90%)
Cowley and Roy-Byrne, 1989 [14]	11	8 (73%)	1 (9%)	2 (18%)	1 (9%)	1 (9%)	9 (82%)
Fisch, 1989 [17]	5	5	–	–	–	–	5
George et al., 1987 [18]	3	3	–	–	–	–	3
Klein et al., 1994 [31]	33	14 (74%)	4 (21%)	1 (21%)	–	–	–
Kraus, 1989 [32]	2	2	–	–	–	–	2
Metz et al., 1988 [34]	3	3	–	–	–	–	3
Northcott and Stein, 1994 [36]	67	19 (43%)	16 (24%)	22 (33%)	12 (18%)	13 (19%)	42 (67%)
Sholomskas et al., 1993 [42]	64	–	–	–	7 (11%)	–	–
Verburg et al., 1994 [47]	4			3			
Villeponteaux et al., 1992 [48]	22	14 (64%)	5 (23%)	3 (13%)	–	–	–
Wisner et al., 1996 [51]	45	12 (27%)	31 (69%)	2 (4%)	–	31 (69%)	14 (31%)

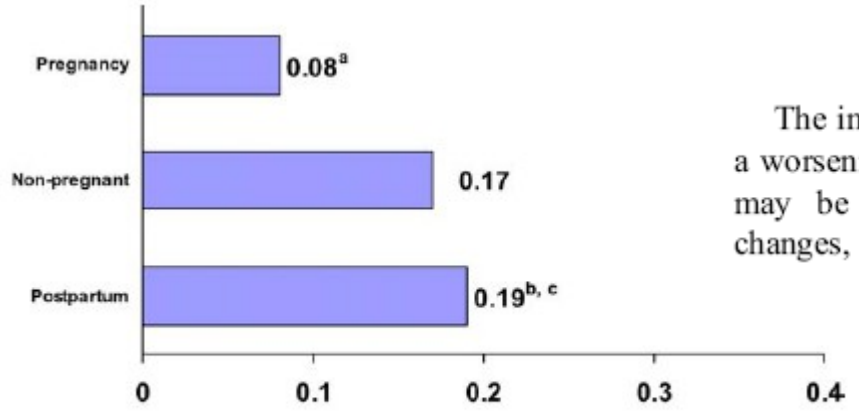


Fig. 1. Panic manifestation quotients during pregnancy, non-pregnancy and postpartum period (PMQ; means). Non-pregnant = non-pregnancy period in women who had been pregnant.

The improvement of panic symptoms during pregnancy and a worsening of panic symptoms during the postpartum period may be explained by psychosocial influences, hormonal changes, and the 'false suffocation alarm hypothesis'.

Recurrence of Panic Disorder During Pregnancy: A 7-Year Naturalistic Follow-up Study

Clin Neuropharmacol 2006;29:132–137

TABLE 1. Demographics and Baseline Measurements (N = 68)

	PD-P (n = 34)	PD-NP (n = 34)	*P*
Age (y, mean ± SD)	24.7 ± 9.6	23.1 ± 9.9	NS
Diagnosis (PD/PDA)	20/14	19/15	NS
Relapse after pregnancy	15/26	8/18	0.001
PSQ (number of panic attacks/wk)	4.9 + 2.3	4.2 + 3.9	NS
Total risk of relapse	18/34	12/34	0.001

Conclusions:

Our naturalistic follow-up study demonstrated that pregnancy might confer an increased risk of relapse in PD. Moreover, when compared with patients who develop PD while not pregnant (PD-NP), patients who develop PD during pregnancy (PD-P) appear to have a higher risk of relapse at the time of a subsequent pregnancy ($P < 0.001$).

Pregnancy outcomes among women with panic disorder — Do panic attacks during pregnancy matter?

Journal of Affective Disorders 120 (2010) 258–262

Crude and adjusted odds ratios (OR) for low birth weight (LBW), preterm birth, and small for gestational age (SGA) between mothers without a history of the chronic disease and mothers with panic disorder during pregnancy, 2001–2003 ($n = 1{,}902$).

Variable	Mothers with no history of this chronic disease		Mothers with panic disorder			
			Mothers without a panic attack during pregnancy		Mothers who experienced a panic attack during pregnancy	
	$n = 1585$		$n = 273$		$n = 44$	
	No.	Percent (%)	No.	Percent (%)	No.	Percent (%)
Low birth weight						
Yes	83	5.2	19	7.0	3	6.8
No	1502	94.8	254	93.0	41	93.2
Crude OR (95% CI)	1.00		1.35 (0.81–2.27)		1.32 (0.40–4.37)	
Adjusted[a] OR (95% CI)	1.00		1.27 (0.75–2.15)		1.30 (0.39–4.38)	
Preterm birth						
Yes	113	7.1	24	8.8	7	15.9
No	1472	92.9	249	91.2	37	84.1
Crude OR (95% CI)	1.00		1.26 (0.79–1.99)		2.47* (1.08–5.66)	
Adjusted[a] OR (95% CI)	1.00		1.27 (0.80–2.03)		2.54* (1.09–5.93)	
Small for gestational age						
Yes	223	14.1	51	18.7	12	27.3
No	1362	85.9	222	81.3	32	72.7
Crude OR (95% CI)	1.00		1.40* (1.10–1.96)		2.29* (1.16–4.51)	
Adjusted[a] OR (95% CI)	1.00		1.45* (1.03–2.04)		2.29* (1.14–4.60)	

*$p < 0.05$.

CI, confidence interval.

[a] Adjusted for infant's gender, parity, maternal age, highest maternal and paternal education level (separately), parental age difference, mothers' marital status, and family monthly income, as well as gestational hypertension, diabetes, hyperlipidemia, renal disease, and coronary heart disease.

Association between maternal panic disorders and pregnancy complications and delivery outcomes

European Journal of Obstetrics & Gynecology and Reproductive Biology 124 (2006) 47–52

Differentiation of effect of panic disorders and related drug treatments for gestational age and preterm birth

	Antipanic disorder drugs[a]	
	Yes	No
Panic disorders		
Yes		
N	151	59
Gestational age (mean, S.D.)	38.9 ± 2.4	39.0 ± 2.3
t-test, *p*-value	$t = 2.3$, $p = 0.03$	$t = 1.5$, $p = 0.14$
Preterm birth (%)	14.8	22.0
χ^2 test, *p*-value	$\chi^2_1 = 6.9$, $p = 0.009$	$\chi^2_1 = 14.2$, $p = 0.0002$
No		
N	4686	33,278
Gestational age (mean, S.D.)	38.9 ± 2.2	39.4 ± 2.0
t-test, *p*-value	$t = 14.6$, $p < 0.0001$	Reference
Preterm birth (%)	14.3	8.4
χ^2 test, *p*-value	$\chi^2_1 = 172.6$, $p < 0.0001$	Reference

[a] Diazepam, Chlordiazepoxide, Phenobarbitals, Meprobamate, Tofisopam, Nitrazepam, Medazepam and Alprazolum.

Maternal panic disorder: Infant prematurity and low birth weight

Anxiety Disorders 20 (2006) 342–352

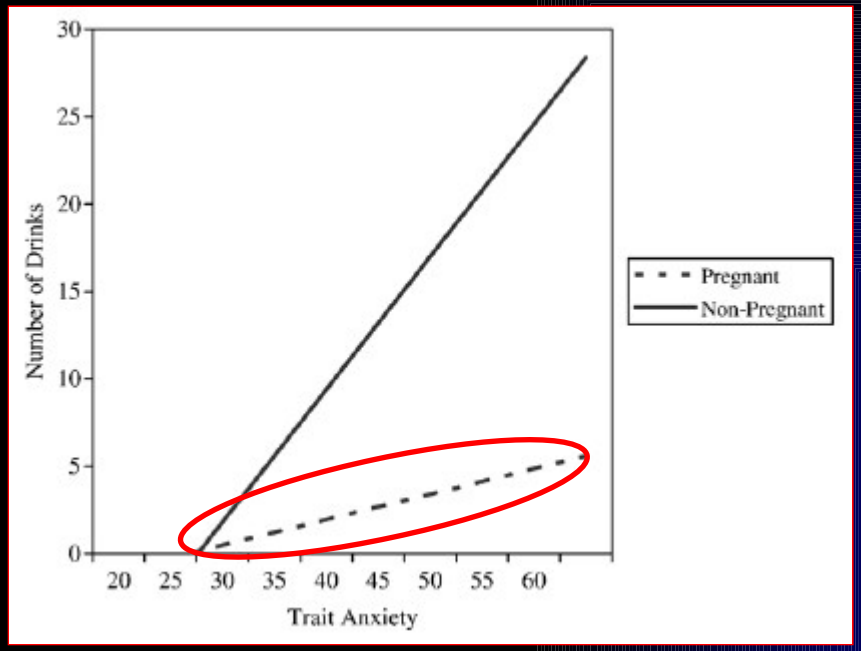
Previous research has suggested that maternal stress might induce a catecholamine response, leading to increased maternal blood pressure, and decreased uterine blood flow (Ascher, 1978). Research has shown maternal anxiety to be associated with abnormal patterns of blood flow through the uterine arteries (Teixeira, Fisk, & Glover, 1999). Vasoconstriction could reduce placental perfusion, which might contribute to reduced oxygen and calorie transfer to the fetus and thus intrauterine growth restriction (Meyers, 1975). Another possible mechanism could involve the elevation of opiate or β-endorphin levels in maternal blood and release of placental opiates along with hypothalamic–pituitary–adrenal activation: this cascade might contribute to hypoxia and/or cause disruption in the growth of the developing fetus (Sandman et al., 1990). Other proposed mechanisms for maternal stress could include: (1) an indirect impact as a result of unhealthy lifestyles and poor coping behaviors (Sheehan, 1998), or (2) a direct impact through stress-dependent hormones (Gitau, Fisk, Teixeira, Cameron, & Glover, 2001; Sandman et al., 1999).

Panic disorder, trait anxiety, and alcohol use in pregnant and nonpregnant women

Comprehensive Psychiatry 48 (2007) 504 – 510

Summary of hierarchical regression analysis with quantity/frequency of past 30-day alcohol use as a dependent variable and pregnancy status as a moderator (n = 496)

Variable	*R*	*B*	SE *B*	*β*	*P*
Step 1					
Age	0.14	0.38	0.12	.15	<.001
Status (unemployed)	0.08	3.38	1.80	.09	ns
Step 2					
Panic disorder	0.16	8.03	4.07	.09	<.05
Mean-centered trait anxiety	0.18	0.29	0.08	.15	<.001
Pregnancy status (nonpregnant)	0.17	6.20	2.26	.13	<.006
Step 3					
Panic disorder × pregnancy (nonpregnant)	0.18	1.98	8.22	.02	ns
Trait anxiety × pregnancy (nonpregnant)	0.24	0.64	0.20	.17	<.001



Maternal Panic Disorder and Congenital Abnormalities: A Population-Based Case-Control Study

Birth Defects Research (Part A) 76:253–261 (2006)

Study groups	All No.	All Adjusted POR[b] (95% CI)	With antipanic disorder drugs[a] No.	With antipanic disorder drugs[a] Adjusted POR[b] (95% CI)	Without antipanic disorder drugs No.	Without antipanic disorder drugs Adjusted POR[b] (95% CI)
Controls	187	Reference	128	Reference	59	Reference
Cleft lip ± palate	15	**2.1 (1.2–3.5)**	8	1.5 (0.7–3.2)	7	**3.1 (1.4–6.9)**
Multiple CAs	19	**2.6 (1.6–4.2)**	13	1.7 (0.9–3.1)	6	**2.9 (1.2–6.7)**

*Bold numbers refer to significant differences.

[a]Including Alprazolam, Chlordiazepoxide, Diazepam, Medazepam, Meprobamate, Nitrazepam, Phenobarbital and Tofisopam.

[b]Prevalence odds ratio (POR) with 95% confidence intervals (CIs) adjusted for maternal age, birth order, maternal employment status, influenza and/or the common cold, and use of folic acid in an unconditional logistic regression model.

CA congenital abnormalities

. **CONCLUSIONS:** A higher rate of isolated CL/P and multiple congenital abnormalities may be caused by the direct biological effect of panic disorder or by the interaction of maternal panic disorder and lifestyle factors. Antipanic drug treatment seems to have a protective effect for isolated CL/P and multiple congenital abnormalities.

Anxiety Disorders During Pregnancy and the Postpartum Period: A Systematic Review

J Clin Psychiatry 2006;67:1285–1298

Study	N	Inclusion Criteria and Design	Pregnancy[b]			Postpartum[b]			Notes
			Symptom Decrease	No Change	Symptom Increase	Symptom Decrease	No Change	Symptom Increase	
Obsessive-compulsive disorder									
Williams and Koran (1997)[42]	29 (24 with at least 1 live birth)	Standardized telephone interview regarding clinical course of OCD during and after pregnancy with OCD outpatients	14% (4)	69% (20)	17% (5)			29% (7)	No information about medication use provided. 37% (N = 9) of women also reported a postpartum depression
Labad et al (2005)[44]	46 (12 with preexisting OCD and at least 1 live birth)	Semistructured interview regarding relationship between reproductive cycle events and OCD with female outpatients	8.0% (1)	83.3% (10)	8.0% (1)	0% (0)	50% (6)	50% (6)	No patients used antiobsessive treatment during pregnancy

Female Reproductive Cycle and Obsessive-Compulsive Disorder

J Clin Psychiatry 2005;66:428–435

Table 2. Onset of Obsessive-Compulsive Disorder at Reproductive Events

Reproductive Event	N/N	%
Menarche (within the following 12 months)	10/46	22
Pregnancy		
All patients	1/46	2
Patients with children[a]	1/17	6
Postpartum		
All patients	3/46	7
Patients with children[a]	3/17	18
Menopause		
All patients	1/46	2
Postmenopausal patients[b]	1/11	9

[a]Patients who delivered at least 1 live-born child.
[b]Patients with natural menopause (N – 9) or surgical menopause (N – 2) following a hysterectomy with removal of both ovaries.

Table 3. Worsening of Preexisting Obsessive-Compulsive Disorder (OCD) at Reproductive Events

Reproductive Event	N/N[a]	%
Premenstruum	9/45	20
Abortion or miscarriage	0/6	0
Pregnancy	1/12	8
Postpartum	6/12	50
Perimenopause/menopause	1/12	8

[a]Sample sizes are compounded by the number of patients with preexisting OCD at each reproductive event.

Table 4. Results of Stepwise Logistic Regression for Premenstrual and Postpartum Exacerbations of Obsessive-Compulsive Disorder (OCD) and Their Association With Premenstrual Symptoms

	Model 1 Premenstrual Worsening of OCD[a]			Model 2 Onset or Worsening of OCD at Postpartum[a]		
Covariate	OR	95% CI	p	OR	95% CI	p
Number of premenstrual mood symptoms[b]	5.1	1.6 to 16.1	.006	2.7	1.1 to 6.8	.039
Premenstrual worsening of OCD[b]	NA	NA	NA	NS	NS	NS

Onset and Exacerbation of Obsessive-Compulsive Disorder in Pregnancy and the Postpartum Period

J Clin Psychiatry 2010;71(8):1061–1068

Table 3. OCD Symptoms Most Frequently Reported by Women in the Ever Pregnant and Never Pregnant Groups

		Ever Pregnant Group		
Symptom, n (%)	Never Pregnant Group (n = 48)	All Pregnant Women (n = 77)[a]	Perinatal-Related OCD Onset (n = 24)	Nonperinatal-Related OCD Onset (n = 53)[b]
Aggressive	18 (37.5)	22 (28.6)	5 (20.8)	17 (32.1)
Contamination	23 (47.9)	35 (45.5)	16 (66.7)[c]	19 (35.9)[c]
Sexual	7 (14.6)	4 (5.2)	1 (4.2)	3 (5.7)
Hoarding/saving	6 (12.5)	5 (6.5)	0 (0)	5 (9.4)
Religious/scrupulosity	8 (16.7)[c]	3 (3.9)[c]	1 (4.2)	2 (3.8)
Symmetry/exactness	13 (27.1)	17 (22.1)	6 (25.0)	11 (20.8)
Somatic/illness	4 (8.3)	5 (6.5)	2 (8.3)	3 (5.7)
Miscellaneous obsessions	15 (31.3)	23 (29.9)	6 (25.0)	17 (32.1)
Cleaning/washing	23 (47.9)	45 (58.4)	17 (10.8)	28 (52.8)
Checking	27 (56.3)	38 (49.4)	12 (50.0)	26 (49.1)
Repeating	18 (37.5)	24 (31.2)	8 (33.3)	16 (30.2)
Counting	11 (22.9)	12 (15.6)	1 (4.2)	11 (20.8)
Ordering/arranging	3 (6.3)[d]	17 (22.1)[d]	6 (25.0)	11 (20.8)
Collecting	8 (16.7)	5 (6.5)	0 (0)	5 (9.4)
Miscellaneous compulsions	16 (33.3)[c]	11 (14.3)[c]	2 (8.3)	9 (17.0)
Worry—aggression or harm to babies	NA	16 (20.8)	6 (25.0)	10 (18.9)
Total, mean ± SD	4.2 ± 2.0	3.7 ± 1.4	3.7 ± 1.3	3.6 ± 1.5

[c] $P = .01$.
[d] $P = .02$.

Correlates of ante- and postnatal depression in fathers: A systematic review

Journal of Affective Disorders xxx (2010) xxx–xxx

reviewed studies, having a depressed partner, poor quality relationship between the father and the mother, and low social support are the most common correlates of depression in men both during their partners' pregnancy and in the postpartum period.

Acute Onset of Obsessive-Compulsive Disorder in Males Following Childbirth

(Psychosomatics 2001; 42:429–431

Psicofarmaci in gravidanza

Effetti teratogeni

uno psicofarmaco è teratogeno se aumenta l'incidenza di malformazioni maggiori

(compromissione funzionale o correzione chirurgica)

(Cohen e Rosembaum, 1998; Wisner, 1999; Boska, 2001)

Incidenza di malformazioni

Gravidanze accertate -----> 84.5% neonato vivo

Neonati vivi

-----> 2-4% malformazioni maggiori

-----> 12% malformazioni minori

Stowe et al, 1999

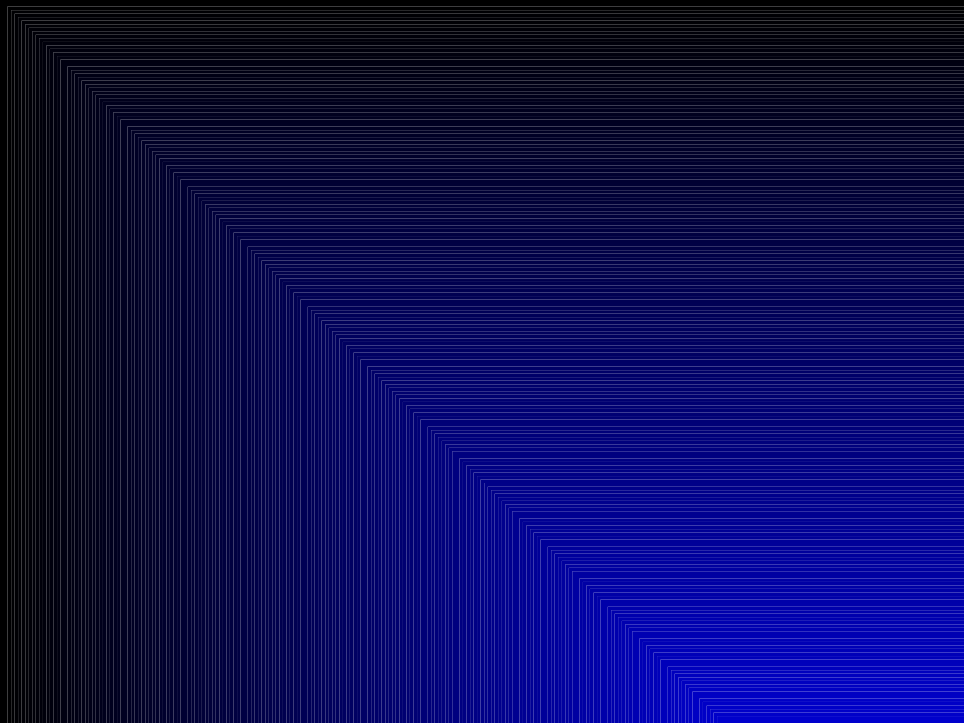
Malformazioni
fattori di rischio

- età materna
- fumo
- farmaci

prescritti nell'80% delle gestanti; il 30% ha assunto psicofarmaci

- assunzione di alcool o di altre sostanze
- tossine
- igiene della gravidanza
- nel 65%-70% dei casi la causa è sconosciuta

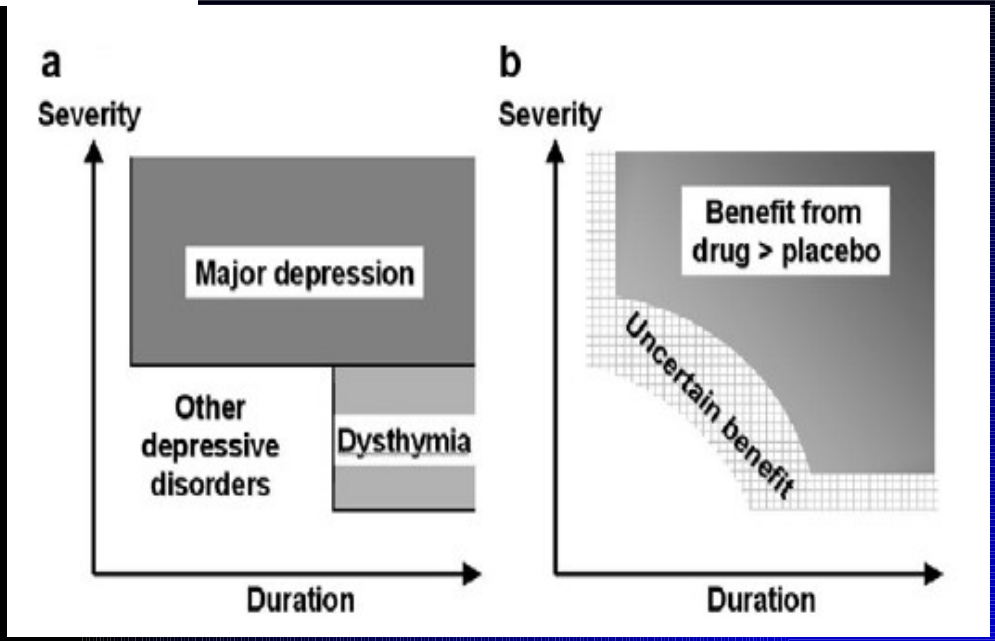
(Stowe et al, 1999, Wisner et al, 1999)



2.1 Indications for antidepressants

- Determine the duration and severity of depression to guide treatment choice (A).
- Antidepressants are a first line treatment for:
  - moderate and severe major depression in adults irrespective of environmental factors and depression type (A),
  - subthreshold depression that has persisted for 2 years or more (A).
- Antidepressants are a treatment option in short duration mild major depression in adults (B) and should be considered if there is a prior history of moderate to severe recurrent depression (D) or the depression persists for more than 2–3 months (D).

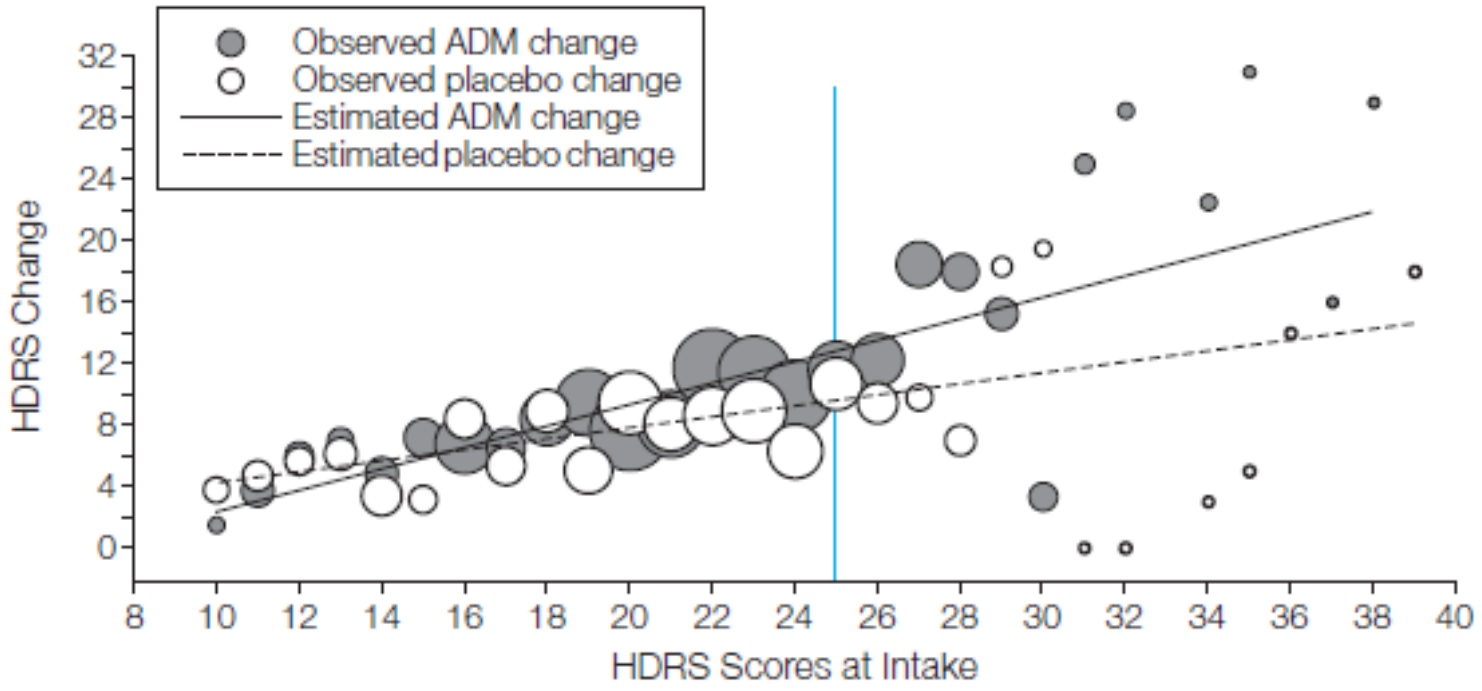
Evidence-based guidelines for treating depressive disorders with antidepressants: A revision of the 2000 British Association for Psychopharmacology guidelines
J Psychopharmacol 2008; 22: 343-396



Antidepressant Drug Effects and Depression Severity: A Patient-Level Meta-analysis

JAMA. 2010;303(1):47-53

Figure 2. Observed and Estimated Change in HDRS Scores Following Treatment With ADM and Placebo



Evidence-based guidelines for treating depressive disorders with antidepressants: A revision of the 2000 British Association for Psychopharmacology guidelines
J Psychopharmacol 2008; 22: 343-396

Psychological and behavioural treatments

- Psychological and behavioural treatments should be administered by appropriately trained practitioners with fidelity to techniques showing evidence-based efficacy (S).
- For major depression of mild to moderate severity:
  - cognitive behaviour therapy (CBT) (A), behaviour therapy/activity scheduling (BT/AS) (A) and interpersonal psychotherapy (IPT) (A) are alternatives to antidepressants in acute treatment,
  - CBT is recommended if psychological treatment is used as monotherapy for recurrent depression (B).
- For severe major depression:
  - psychological or behavioural treatment is not recommended as sole therapy (B) but routinely consider adding CBT (A) or BT/AS (B) to antidepressant treatment,
  - therapists using psychological and behavioural techniques should be experienced in treating depression (B).