Disturbi Depressivi nel periodo perinatale

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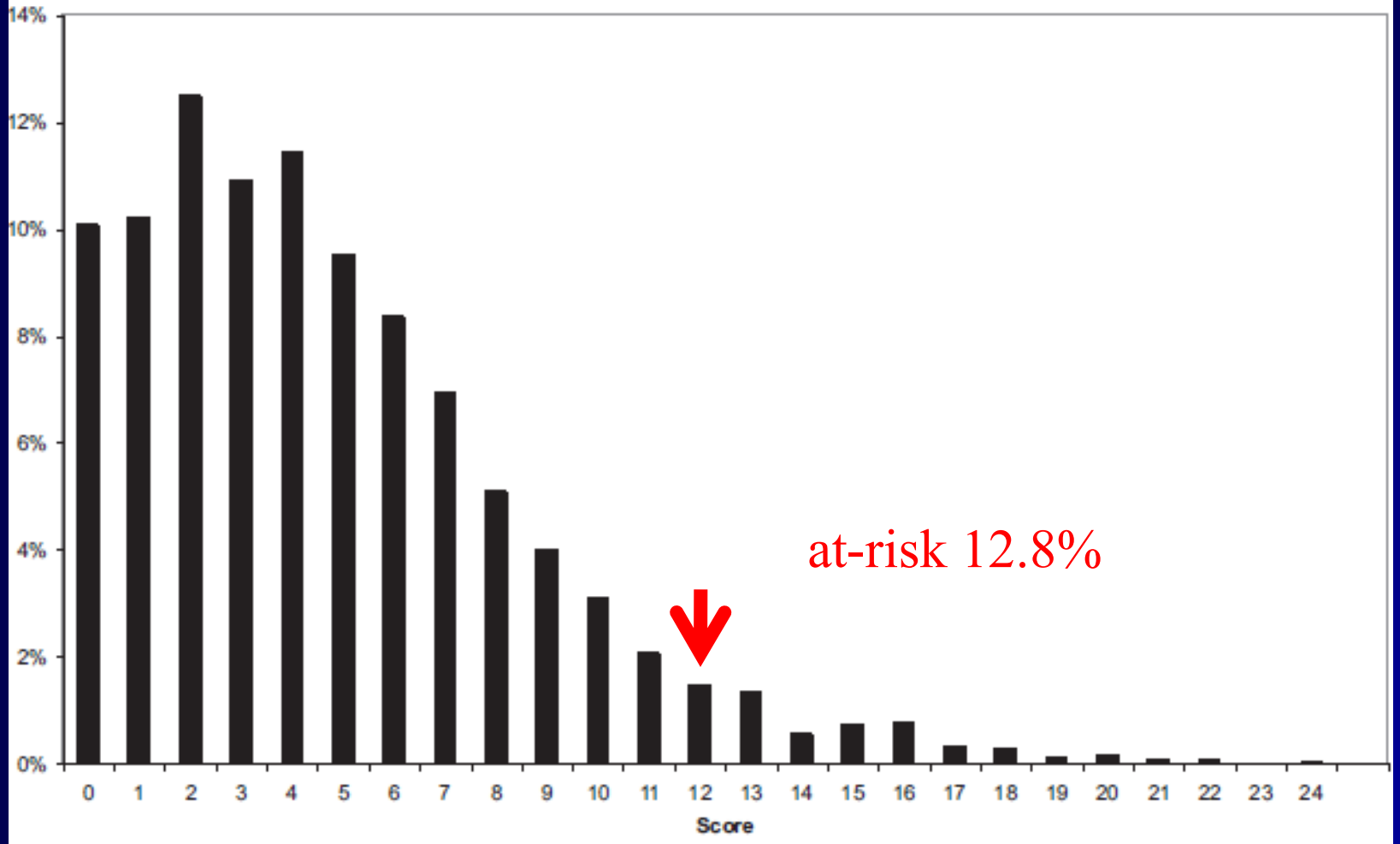
Punti in discussione

1. Nel periodo perinatale la donna *si può ammalare più frequentemente di depressione*
2. Quando *esordisce* la depressione *post-partum*
3. Quanto è *grave* la depressione perinatale
4. Qual'è *l'impatto della depressione* sulla vita della donna e del neonato
5. Chi sono le *donne a rischio* di ammalarsi di depressione perinatale
6. Il *trattamento della depressione perinatale è diverso* dal trattamento in altri periodi della vita della donna

La gravidanza non è una malattia

Preoccupazioni “fisiologiche”
riferite alla gravidanza
e alla futura nascita

Distribution of antepartum and postpartum Edinburgh Postnatal Depression Scale Scores



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).

Kim et al. *Am J Obstet Gynecol 2008; 199: 509e1-e5*

Maternity Blues

- Prevalenza: 50-85% donne.

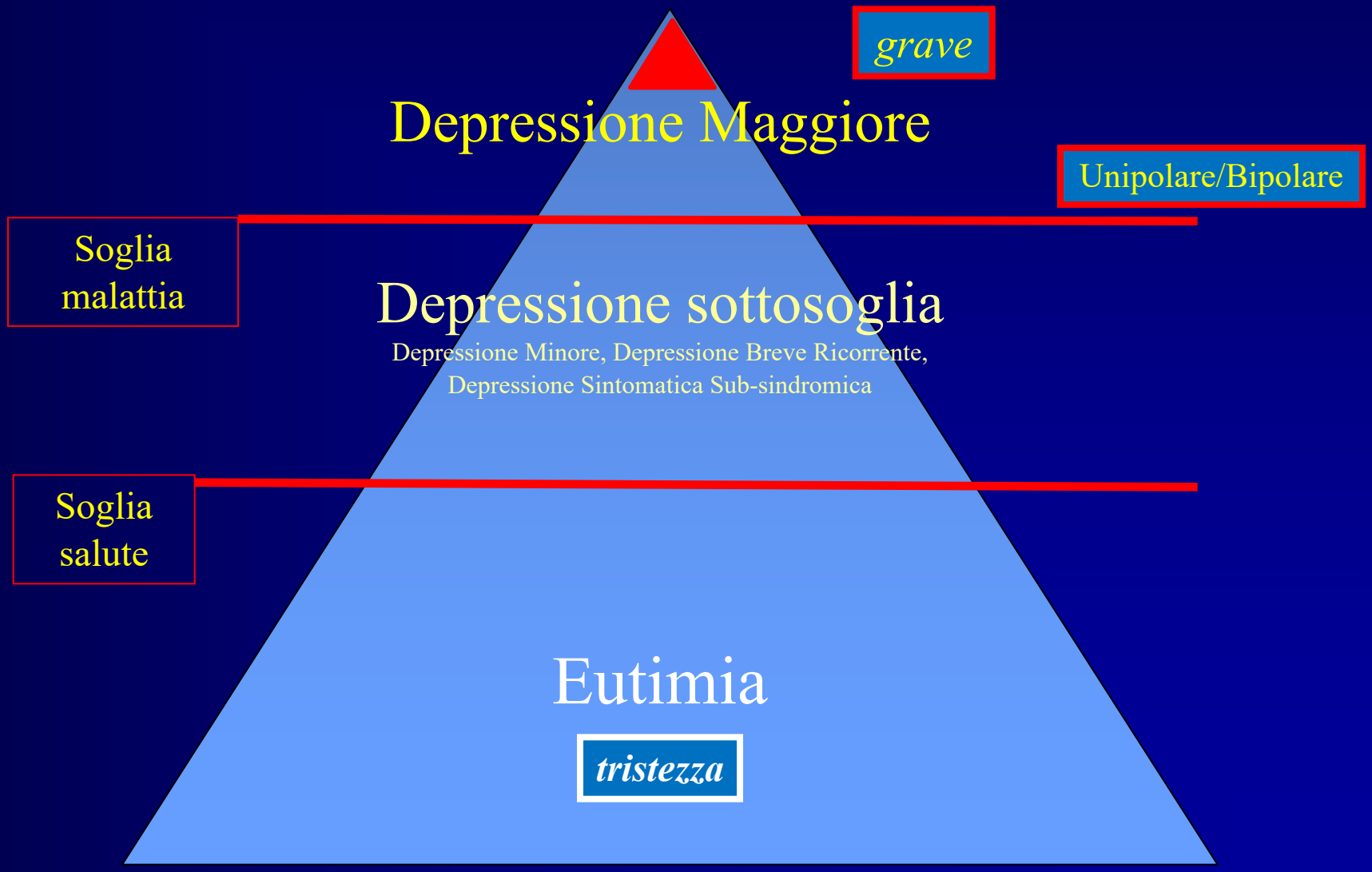
- Esordio: entro pochi giorni dal parto (48 ore).

- Sintomi: tristezza, tendenza al pianto, sentimenti di insufficienza e di incapacità, irritabilità, ansia, difficoltà di concentrazione e di memoria, disturbi del sonno e dell'appetito, cefalea, astenia.

- Remissione: entro 2 settimane. Durata protratta: comparsa di depressione postpartum.

Burt e Stein, J Clin Psychiatry 2002; 63 (suppl 7): 9-15
Steiner et al. J Affect Disord 2003;74:67-83

Disturbo Depressivo perinatale



Psychiatric Disorders in Pregnant and Postpartum Women in the United States

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

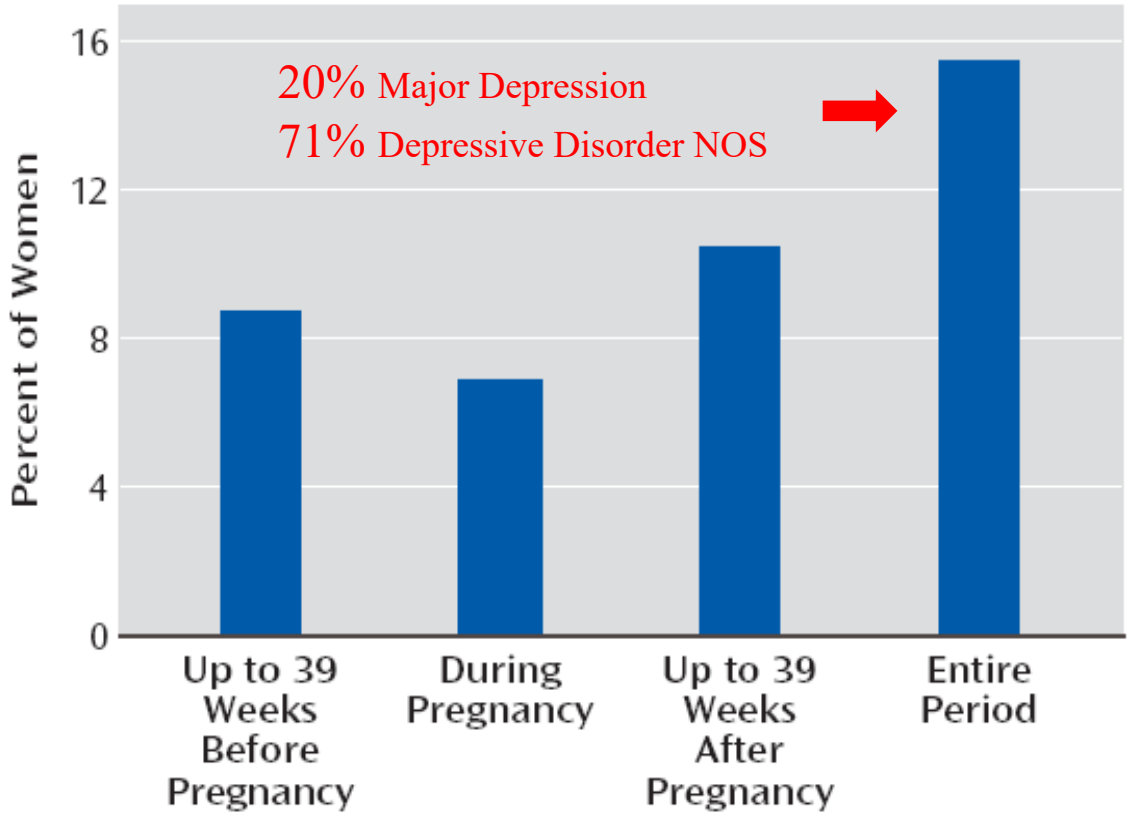
Table 2. Twelve-Month Prevalence and ORs of *DSM-IV* Axis I Psychiatric Disorders by

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]

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



Major and Minor Depression in Pregnancy

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

154 women, assessed monthly during pregnancy

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)	–

La gravidanza non è una malattia

Expanding the international conversation with fathers' mental health: toward an era of inclusion in perinatal research and practice

Fisher et al. *Arch Womens Ment Health 2021; 24: 841-848*

1. Depression occurs in *8–10%* of men between the first trimester of pregnancy and the first year postpartum, with the highest rate occurring 3 to 6 months post- partum.

2. This rate is *higher than* the rate of the *general* public (~ 5%) who are of parenting age.

Prevalence of Perinatal Depression and Anxiety in Both Parents
A Systematic Review and Meta-analysis

Smithe et al. *JAMA Psychiatry 2022;5:e2218969*

RESULTS

Twenty-three studies were included, with data from 29286 couples.

The pooled prevalence of depression in *both parents* was

- *antenatal 1.72%*
- *early postnatal* (up to 12 weeks) *2.37%*
- *late postnatal* (3-12 months) 3.18%

CONCLUSIONS AND RELEVANCE

Perinatal health care must consider the mental health needs of parents, both as individuals and as a parental dyad.

Postpartum depression: a disorder in search of a definition

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

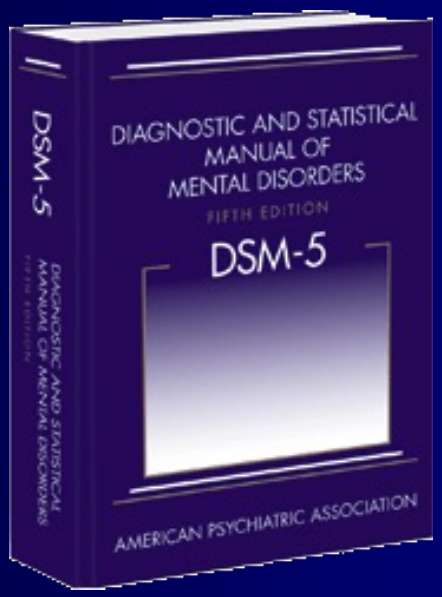
Time considerations

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

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.



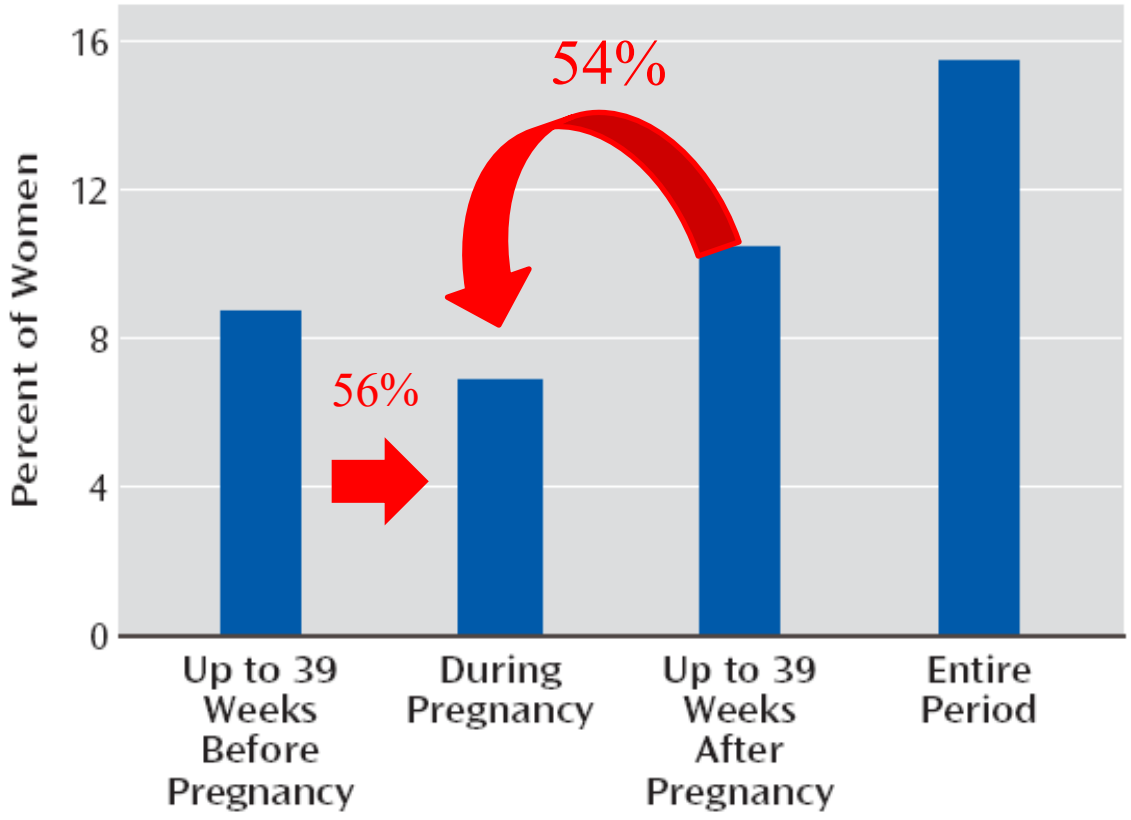
Depressive Disorders with peripartum onset

This specifier can be applied to the current or most recent episode of major de pression if onset of mood symptoms occurs *during pregnancy* or in the 4 weeks following delivery.

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



Lifetime prevalence and correlates of perinatal depression in a case-cohort study of depression

Kiewa et al. *BMJ Open 2022; 12: e059300*

Table 1 Reported timing of symptoms of perinatal depression among women with PND

	During pregnancy only	After delivery only	Both during pregnancy and after delivery	Missing
All PND cases (N=5058)	295 (6%)	1627 (32%)	3073 (61%)	63 (1%)
PND_priorDep (N=2261)	144 (6%)	592 (26%)	1507 (67%)	18 (1%)
PND_firstDep (N=878)	28 (3%)	325 (37%)	510 (58%)	15 (2%)

Results are shown for all those meeting PND criteria and separately for those with a prior history of major depression (PND_priorDep) and those whose first onset of major depression was perinatal (PND_firstDep).
PND, perinatal depression.

Gravità della depressione perinatale

Major and Minor Depression in Pregnancy

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

154 women, assessed monthly during pregnancy

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.

Concerning treatments, no depressed women were treated with antidepressants or other psychotropic drugs. Only two women with major depression received psychological support.

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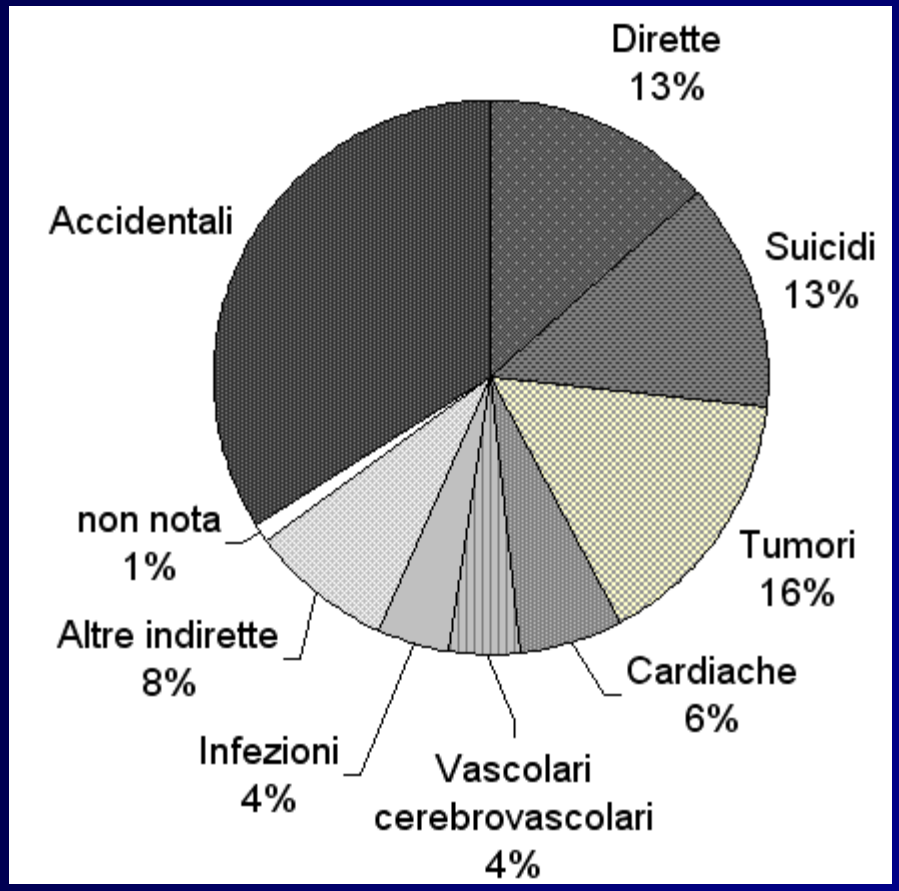
DOSSIER
Agenzia sanitaria e sociale regionale
RegioneEmilia-Romagna
SERVIZIO SANITARIO REGIONALE EMILIA-ROMAGNA

Mortalità e morbosità materna in Emilia-Romagna. Rapporto 2001-2007

Distribuzione per causa di 97 casi di morti materne



Agli iniziali 13 casi di suicidio, 5 casi sono stati aggiunti in seguito all'analisi della documentazione clinica.

Suicidi → 18%

L'età media al decesso: 29,2 anni

Le morti sono avvenute:
- in *gravidanza* 11%
- *dopo il parto* 44%;
- dopo un aborto volontario 33%
- dopo un aborto spontaneo 11%

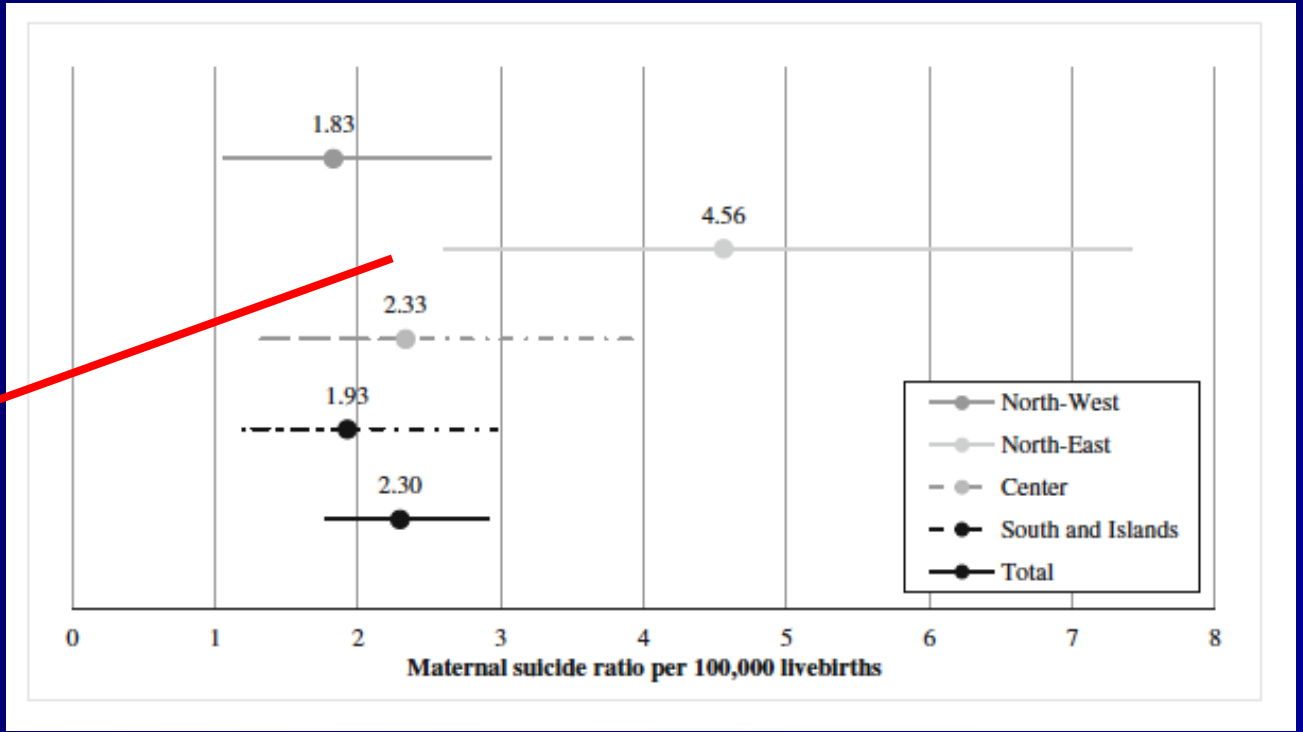
Maternal suicide in Italy

Lega et al. *Arch Women Mental Health 2020; 23: 199-206*

Neonati vivi in Italia 408.892 (ISTAT 2020)

Periodo 2006-2012 in 10 regioni italiane
67 suicidi su 549 madri morte (12%)

- 4 in gravidanza
- 34 entro un anno dal parto
- 18 dopo IVG
- 11 dopo aborto spontaneo



Emilia Romagna 2020
neonati 30321 = 1.4

Tasso di suicidio popolazione generale 6.7/100000 (ISTAT 2019)

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

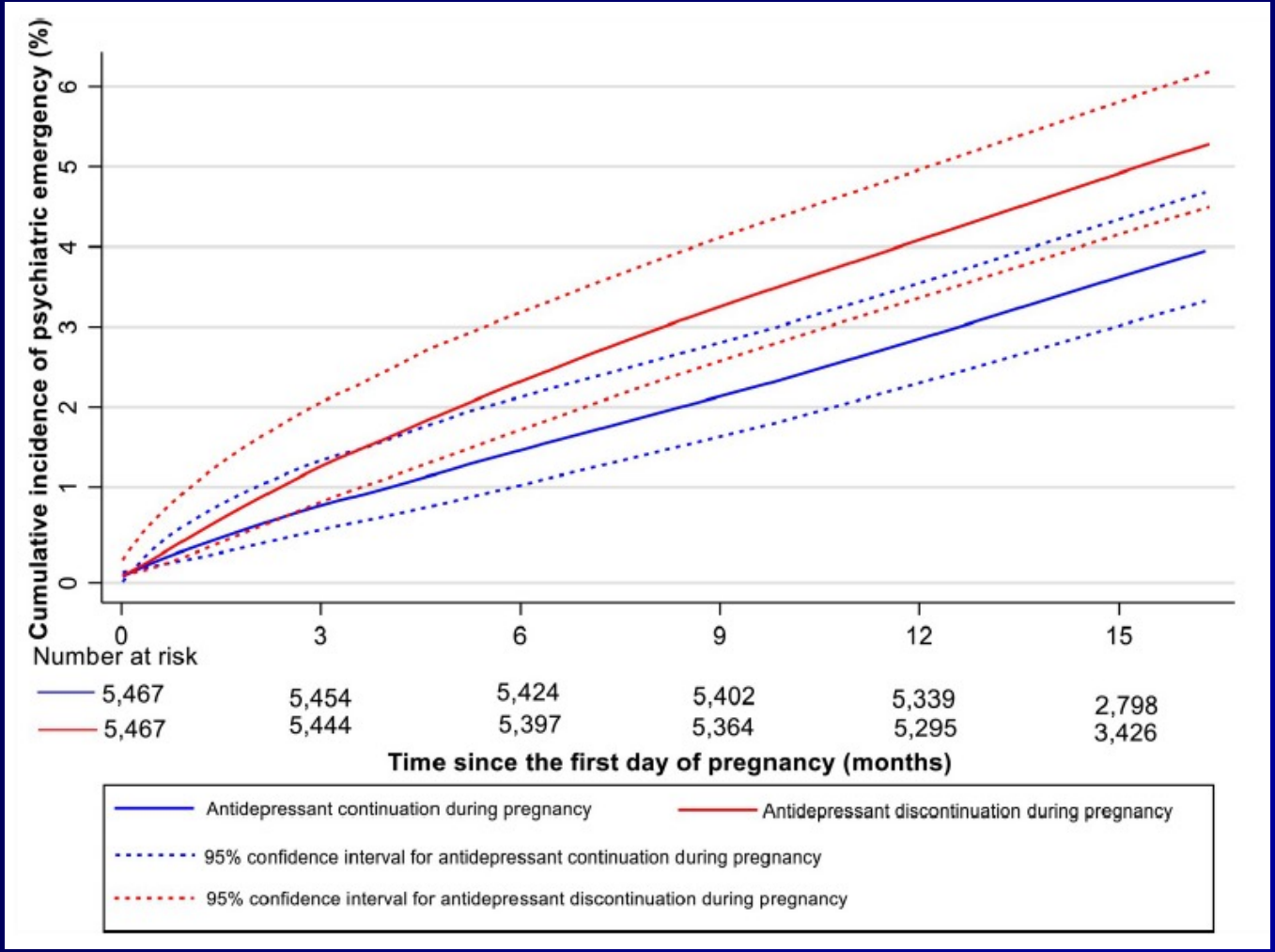
Variable	M	SD	p
Number of prenatal care visits			
Mental health care visits for depressive disorder ≤1 year before conception			<.001
Yes	8.50	4.10	
No	9.17	4.49	

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	

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

Antidepressant discontinuation before or during pregnancy and risk of psychiatric emergency in Denmark: A population-based propensity score–matched cohort study

Liu et al. *PloS Med 2022; 19: e1003895*



Effect of Depressive Disorders and Their Pharmacological Treatment during Pregnancy on Maternal and Neonatal Outcome

Parpinel et al. *J Clin Med 2022; 11: 1486*

	DG-Tr (n = 199)	DG-Untr (n = 82)	χ^2/F	p
Age (years)	35.04 (±4.890)	33.34 (±5.51)	6.499	0.011
BMI, mean ± SD	26.30 ± 6.70	26.50 (±6.90)	0.876	0.395
Parity, n (%)				
• nulliparous	111 (50.80)	38 (46.30)	0.452	0.501
• multiparous	98 (49.20)	44 (53.70)		
Smoking habit, n (%)				
• yes	61 (30.70)	30 (36.60)	0.933	0.334
• no	138 (69.30)	52 (63.40)		
Gestational age at delivery (weeks)	40.00 ± 3.02	38.94 ± 2.59	0.320	0.572
Preterm birth, n (%)				
• yes	20 (10.10)	9 (11.00)	0.048	0.827
• no	178 (89.90)	73 (89.00)		
Induction of labor, n (%)				
• yes	102 (51.30)	62 (75.60)	17.062	0.072
• no	97 (48.70)	20 (24.40)		
Delivery, n (%)				
• spontaneous	104 (52.30)	30 (36.60)	5.720	0.017
• cesarean section	95 (52.30)	52 (63.40)		
Neonatal weight (grams)	3025.72 ± 523.46	2996.28 ± 528.58	0.182	0.670
SGA, n (%)				
• yes	25 (12.60)	12 (14.60)	0.218	0.641
• no	174 (87.40)	70 (85.40)		
APGAR score at 5 min	8.69 ± 0.96	8.93 ± 0.49	4.638	0.032

BMI: body mass index, SGA: small for gestational age.

Association between high levels of comorbid anxiety and depressive symptoms and decreased likelihood of birth without intervention: A longitudinal prospective cohort study

Hulsbosch et al. *BJOG 2022;0:1-11*

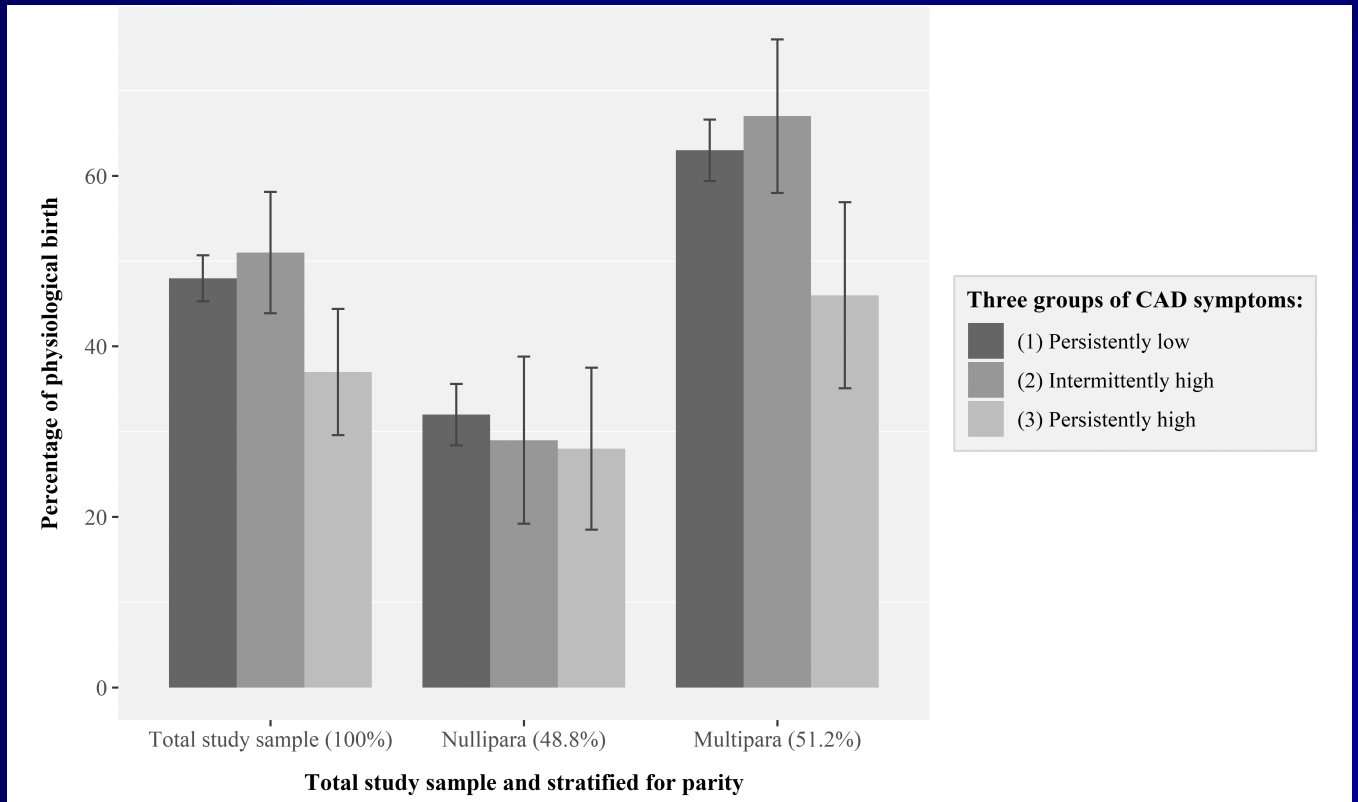


FIGURE 1 Physiological birth for three groups of comorbid anxiety and depressive (CAD) symptoms: total study sample and stratified for parity (n = 1682). The error bars represent the 95% confidence intervals of the estimated percentages.

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 è maggiore se

1. disturbo depressivo vs sintomi depressivi
2. depressione cronica vs breve durata
3. comorbidità disturbi depressivi ed ansiosi

Neonatal Outcomes in Women With Untreated Antenatal Depression Compared With Women Without Depression

A Systematic Review and Meta-analysis

Jarde et al. *JAMA Psychiatry 2016; 73: 826-837*

Table 2. Results of the Meta-analyses of Our Primary and Secondary Outcomes

Outcomes	No. of Studies	No. of Women Included	Crude OR/MD (95% CI)	*P* Value	I^2, %
Primary outcomes					
PTB, wk					
<37	14	21 048	1.56 (1.25 to 1.94)[a]	<.001[a]	39
<32	No study reported data				
LBW (<2500 g)	8	3262	1.96 (1.24 to 3.10)[a]	.004[a]	48
SGA (<10%)	1	4044	1.37 (1.10 to 1.70)[a]	.005[a]	NA
LGA (>90%)	No study reported data				
NICU admission	2	200	1.12 (0.40 to 3.15)	.83	0

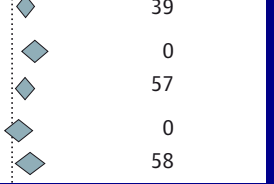
Neonatal Outcomes in Women With Untreated Antenatal Depression Compared With Women Without Depression

A Systematic Review and Meta-analysis

Jarde et al. *JAMA Psychiatry 2016; 73: 826-837*

Figure 2. Results of Subgroup Analyses for Preterm Birth and Low Birth Weight

Variables	Groups	No. of Studies	No. of Women Included	Crude OR (95% CI)	*P* Value	I^2, %
Primary outcomes						
Preterm birth	All studies	14	21 048	1.56 (1.25-1.94)	–	39
Assessment of depression	Clinical diagnostic or interview	7	2104	1.91 (1.35-2.69)	.23	0
	Self-administered questionnaire	7	18 974	1.45 (1.09-1.92)		57
Depression severity	Moderate	3	4474	1.30 (0.94-1.82)	.36	0
	Severe	8	7830	1.66 (1.11-2.49)		58
Low birth weight (<2.5 kg)	All studies	8	3262	1.96 (1.24-3.10)	–	48
Infants included	Not limited to term infants	6	2305	1.72 (0.88-3.37)	.23	57
	Limited to term infants only	2	981	2.54 (1.59-4.09)		0
Assessment of depression	Clinical diagnostic or interview	4	762	1.94 (0.71-5.32)	.89	69
	Self-administered questionnaire	4	2524	2.09 (1.28-3.40)		24
Depression severity	Moderate	2	1220	1.98 (1.30-3.02)	.92	10
	Severe	4	1216	2.10 (0.67-6.63)		69



Anxiety, depression, and birth outcomes in a cohort of unmedicated women

Ossola et al. *J Maternal-Fetal Neonatal Med 2019;*

Table 2. Regression coefficients of anxious and depressive symptoms expressed as area under the curve in 299 pregnant women.

	Dependent variables			
	Gestational age	Birth weight	Apgar 1′	Apgar 5′
AUC anxiety	−0.001 (−0.02, 0.008)	−5.76 (−10.96, −2.81)*	0.004 (−0.005, 0.013)	0.000 (−0.004, 0.004)
AUC depression	−0.01 (−0.02, 0.01)	3.44 (−2.33, 9.22)	−0.001 (−0.010, 0.008)	0.000 (−0.004, 0.004)

Association of Persistent and Severe Postnatal Depression With Child Outcomes

Netsi et al. *JAMA Psychiatry 2018; 75: 247: 247-253*

Table 3. Logistic and Ordinal Logistic Regressions Investigating the Association Between Postnatal Depression and Adverse Child Outcomes, Controlling for Maternal Education

	Behavioral Problems at 3.5 y (n = 7917)[a]		Low GCSE Mathematics Grades at 16 y (n = 4941)		Offspring Depression at 18 y (n = 3486)	
Level of PND Severity	OR (95% CI)	*P* Value	OR (95% CI)	*P* Value	OR (95% CI)	*P* Value
Below threshold[b]	1 [Reference]	NA	1 [Reference]	NA	1 [Reference]	NA
Moderate but not persistent[c]	2.22 (1.74-2.83)	<.001	1.14 (0.77-1.68)	.51	1.11 (0.51-2.44)	.79
Marked but not persistent[d]	1.91 (1.36-2.68)	<.001	1.53 (0.89-2.63)	.13	2.34 (1.03-5.29)	.04
Severe but not persistent[e]	2.39 (1.78-3.22)	<.001	1.40 (0.89-2.22)	.15	1.72 (0.77-3.82)	.18
Moderate persistent[f]	3.04 (2.10-4.38)	<.001	1.65 (0.89-3.05)	.11	1.05 (0.32-3.42)	.94
Marked persistent[g]	2.84 (1.71-4.71)	<.001	1.32 (0.60-2.90)	.46	2.30 (0.67-7.90)	.19
Severe persistent[h]	4.84 (2.94-7.98)	<.001	2.65 (1.26-5.57)	.01	7.44 (2.89-19.11)	<.001

Abbreviations; EPDS, Edinburgh Postnatal Depression Scale; GCSE, General Certificate of Secondary Education; NA, not applicable; OR, odds ratio; PND, postnatal depression.

[a] Using the Rutter revised total problems scale.

[b] EPDS score of less than 13 points in the postnatal year.

[c] EPDS score of 13 to 14 points at 2 months and less than 13 points at 8 months.

[d] EPDS score of 15 to 16 points at 2 months and less than 15 points at 8 months.

[e] EPDS score of 17 or more points at 2 months and less than 17 points at 8 months.

[f] EPDS score of 13 to 14 points at 2 months and 13 or more points at 8 months.

[g] EPDS score of 15 to 16 points at 2 months and 15 or more points at 8 months.

[h] EPDS score of 17 or more points at 2 and 8 months.

Fattori di rischio per la depressione perinatale

- se li conosci, puoi intervenire precocemente.

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.

Perinatal mental illness: Definition, description and aetiology

O'Hara et al. *Best Pract Res Clin Obstet Gynaecol 2014; 28: 3–12*

Risk factors include past *history of depression*, *anxiety*, or *bipolar disorder*, as well psychosocial factors, such as ongoing *conflict with the partner*, *poor social support*, and ongoing *stressful life events*.

Heterogeneity in perinatal depression: how far have we come? A systematic review

Hudson et al, *Arch Womens Ment Health. 2017; 20: 11–23*

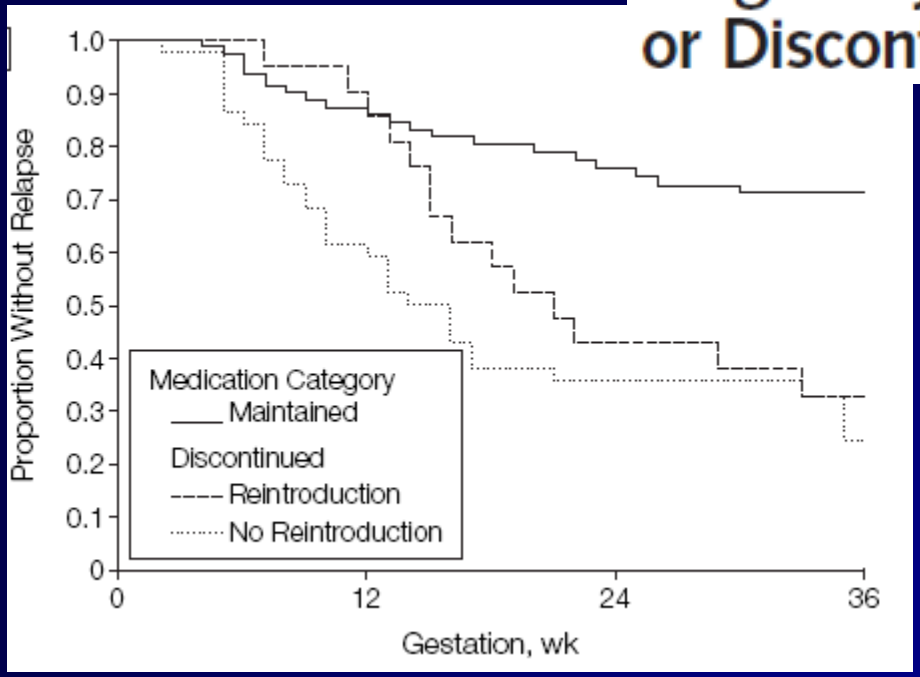
predictors related to a higher burden (high sum of score) of depressive symptoms: *low education, negative life events, ethnic-minority status, unintended pregnancy, mood or anxiety symptoms during pregnancy, and prior history of psychopathology*

Risk factors of perinatal depression in women: a systematic review and meta-analysis

Yang *et al. BMC Psychiatry 2022;22:63*

We found evidence supporting *lower educational level, poor economic status of families, history of mental illness, domestic violence perinatal smoking or drinking*, and *multiparity* were associated with depression in perinatal women, regardless of the subgroup confounding variables.

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



Cohen et al. *JAMA 2006; 295: 499-507*

Table 3. Relapse of Major Depression During Pregnancy

		Medication Status			
Relapse Status	All Women	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)

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DOSSIER
Agenzia sanitaria e sociale regionale
RegioneEmilia-Romagna
SERVIZIO SANITARIO REGIONALE EMILIA-ROMAGNA

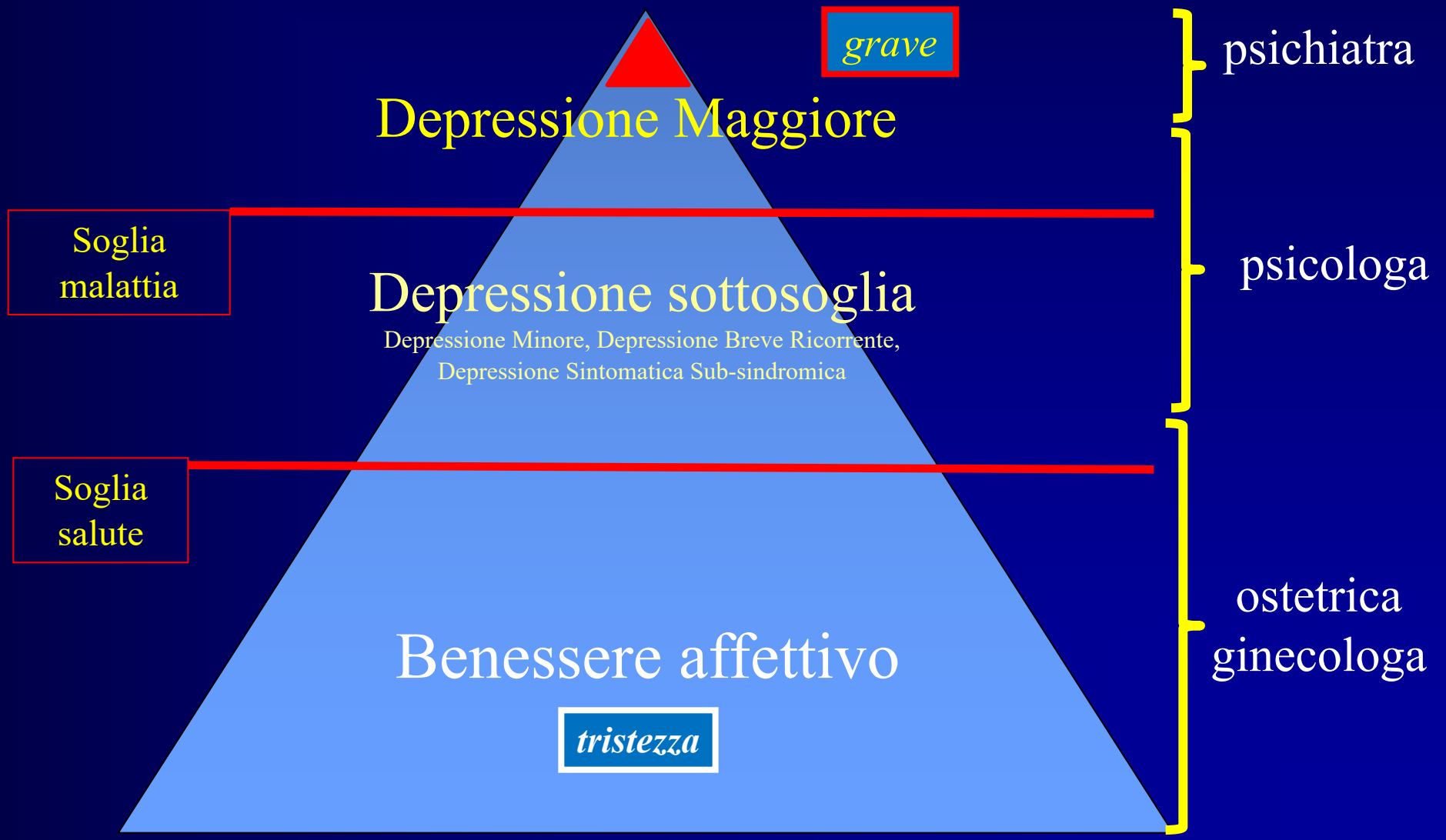
Mortalità e morbosità materna in Emilia-Romagna. Rapporto 2001-2007

Per i casi in cui è stata possibile una valutazione della qualità del percorso assistenziale, i fattori di substandard care rilevati sono stati:

- la mancata attivazione e presa in carico dei servizi territoriali psichiatrici alla dimissione di donne sintomatiche

- la sospensione inappropriata della terapia con psicofarmaci durante la gravidanza.

Depressione in gravidanza e nel puerperio



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.

45 references: 18 concerning drugs in pregnancy

Il *trattamento della depressione perinatale non è differente* dal trattamento in altri periodi della vita della donna

Se necessario, è possibile utilizzare i farmaci nel trattamento della depressione perinatale ?

No: non ci sono dati sufficienti

Depression in pregnancy: time to stop terrifying pregnant women.

J Popul Ther Clin Pharmacol. 2012;19(3):e369-70.

Yet, physicians and epidemiologists continue to terrify women who are at serious life threatening risks if not treated pharmacologically, with *non evidence-based information*.

This paper calls for *immediate stop of such practice*.

Prevalence of Antidepressant Use during Pregnancy in Denmark, a Nation-Wide Cohort Study

Jimenez-Solem et al. *Plos One April 2013; 8: e63034*

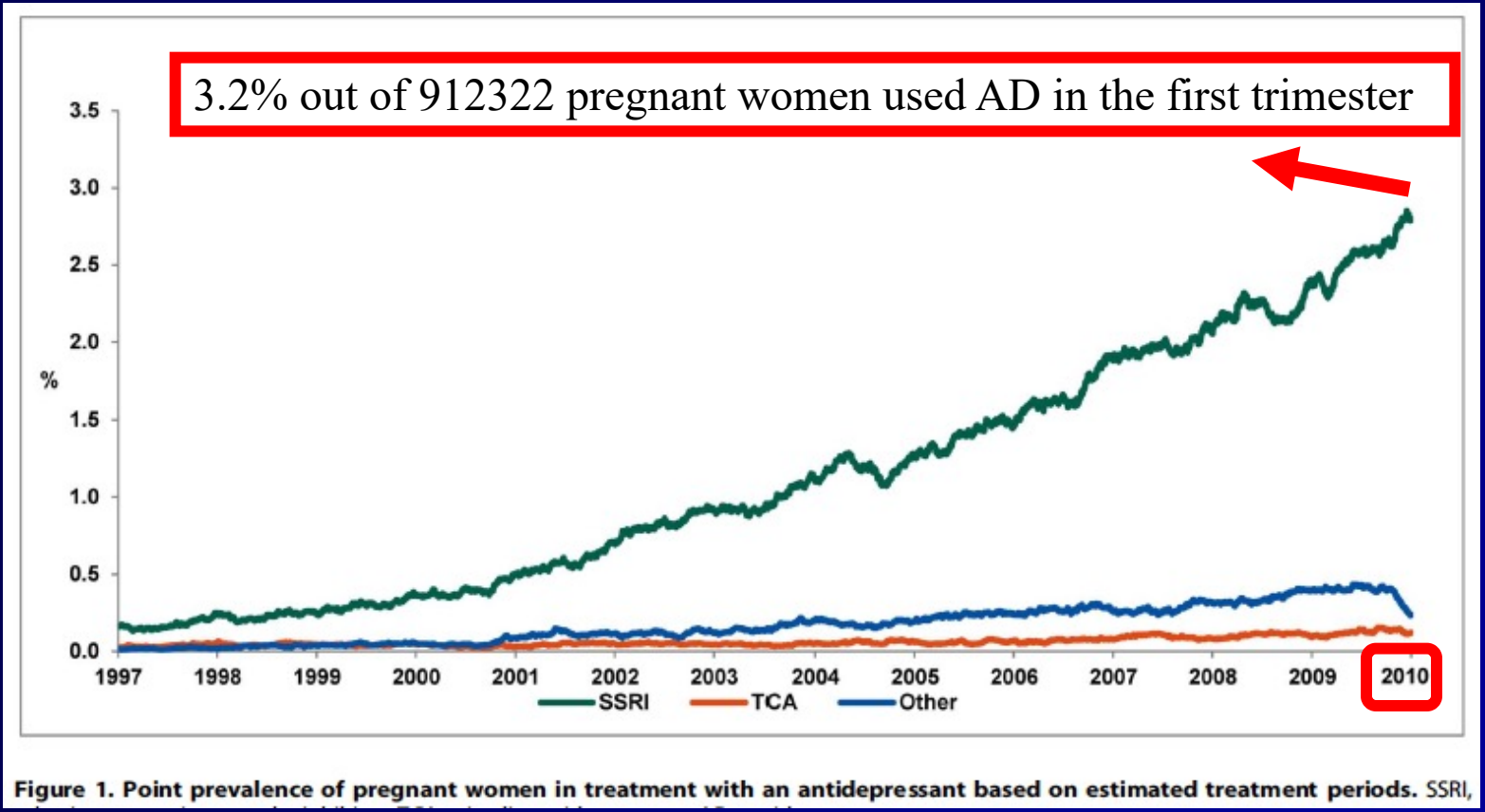


Figure 1. Point prevalence of pregnant women in treatment with an antidepressant based on estimated treatment periods. SSRI,

Huybrechts et al. *N Engl J Med 2014; 370: 2397-2407*

6.8% out of 949504 pregnant women used AD in the first trimester

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

Prevalence of Antidepressant Use during Pregnancy in Denmark, a Nation-Wide Cohort Study

Table 3. Number of women exposed to an antidepressant during pregnancy.

	Trimester		
	First	**Second**	**Third**
Any antidepressant	18273	13039	9721
SSRI	15403 (84.29)	11370 (87.20)	8641 (88.89)
Citalopram	6657 (36.43)	4306 (33.02)	2850 (29.32)
Escitalopram	1539 (8.42)	722 (5.54)	344 (3.54)
Fluoxetine	3898 (21.33)	3618 (27.75)	2927 (30.11)
Paroxetine	1779 (9.74)	1164 (8.93)	816 (8.39)
Sertraline	3059 (16.74)	2565 (19.67)	2328 (23.95)
TCA	1101 (6.03)	748 (5.74)	479 (4.93)
Amitriptyline	578 (3.16)	292 (2.24)	120 (1.23)
Clomipramin	125 (0.68)	89 (0.68)	57 (0.59)
Dosulepin	40 (0.22)	42 (0.32)	36 (0.37)
Imipramin	61 (0.33)	32 (0.25)	15 (0.15)
Nortriptyiline	327 (1.79)	308 (2.36)	254 (2.61)
Other	3039 (16.63)	1655 (12.69)	934 (9.61)
Mianserin	270 (1.48)	113 (0.87)	57 (0.59)
Mirtazapine	876 (4.79)	348 (2.67)	142 (1.46)
Venlafaxine	1687 (9.23)	1109 (8.51)	703 (7.23)

Jimenez-Solem et al.
Plos One April 2013; 8: e63034

Il *trattamento farmacologico della depressione in gravidanza*

Valutati i seguenti effetti:

-teratogeno (incidenza > 3-5% malformazioni spontanee)

-esito gravidanza (aborto spontaneo, nascita pretermine, difetto di crescita fetale)

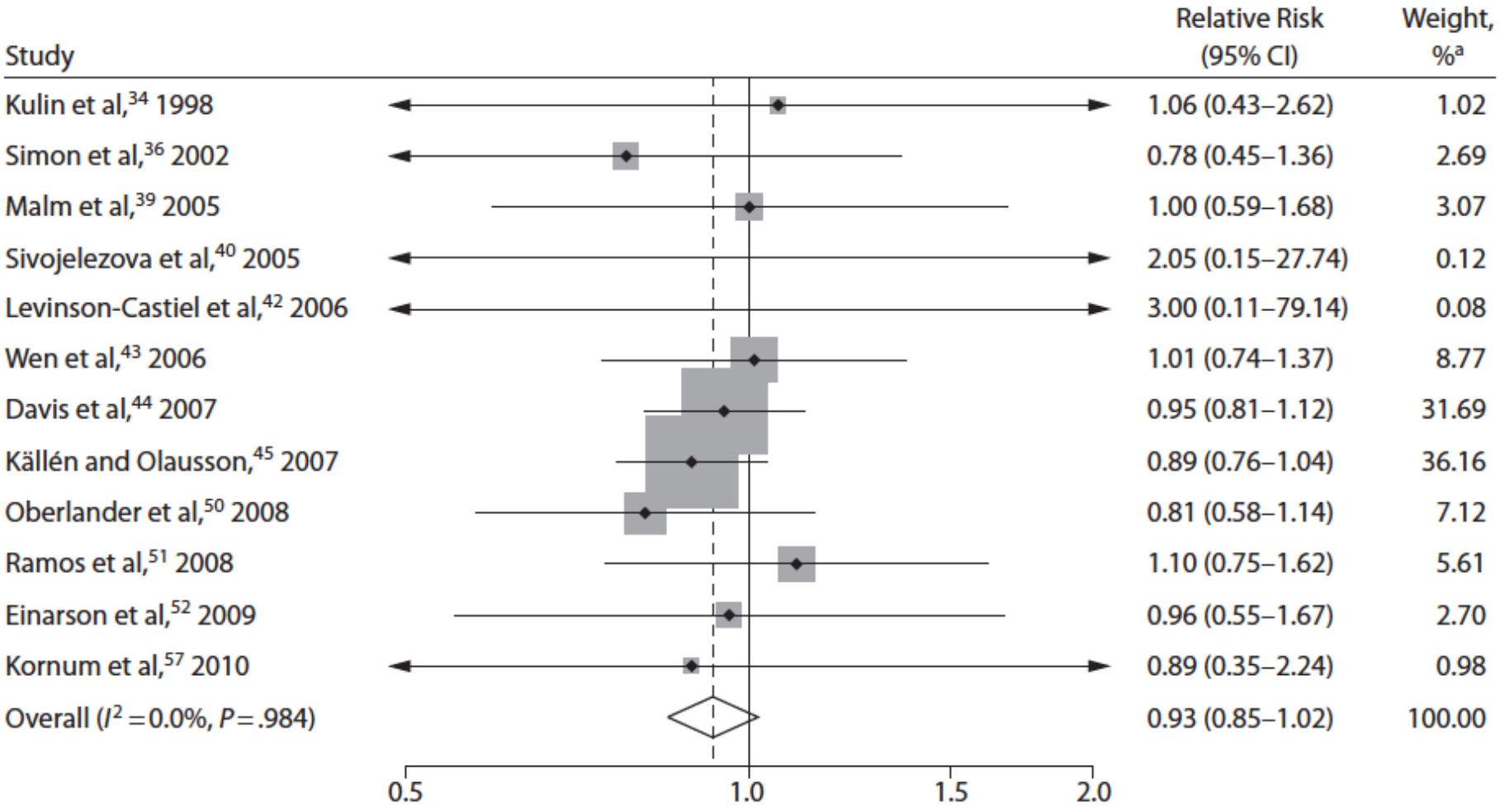
-esito neonato (sindrome da adattamento neonatale)

-esiti comportamentali a lungo termine (sviluppo mentale, linguaggio, problemi comportamentali, autismo)

Antidepressant Exposure During Pregnancy and Congenital Malformations: Is There an Association? A Systematic Review and Meta-Analysis of the Best Evidence

J Clin Psychiatry 2013;74(4):e293–e308

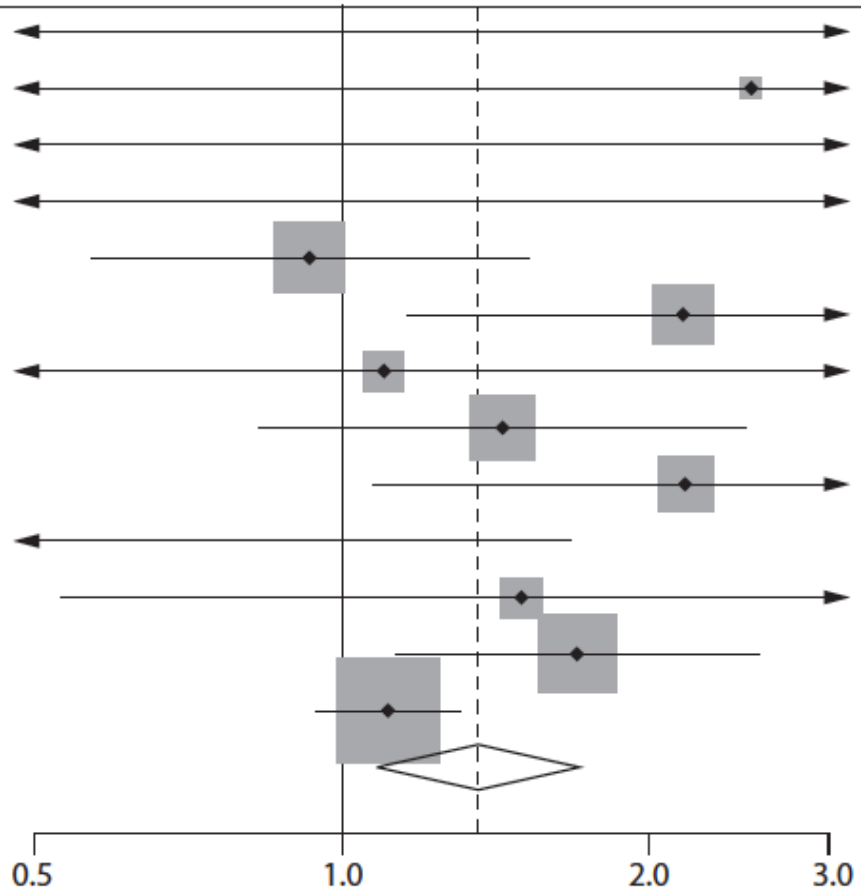
Figure 2. Exposure to Any Antidepressant and the Risk of Congenital Malformations: Meta-Analysis Results for Studies Above the Quality Threshold



Antidepressant Exposure During Pregnancy and Congenital Malformations: Is There an Association? A Systematic Review and Meta-Analysis of the Best Evidence

J Clin Psychiatry 2013;74(4):e293–e308

Figure 3. Exposure to Any Antidepressant and the Risk of Cardiovascular Malformations: Meta-Analysis Results for Studies Above the Quality Threshold



Antidepressant Exposure During Pregnancy and Congenital Malformations: Is There an Association? A Systematic Review and Meta-Analysis of the Best Evidence

J Clin Psychiatry 2013;74(4):e293–e308

Conclusions: Overall, antidepressants do not appear to be associated with an increased risk of congenital malformations, but statistical significance was found for cardiovascular malformations. Results were robust in several sensitivity analyses. Given that the RRs are marginal, they may be the result of uncontrolled confounders. Although the RRs were statistically significant, none reached clinically significant levels.

Gestational Exposure to Serotonin Reuptake Inhibitors and Pregnancy Outcome; Exploring the Role of Bias and Confounders

Koren and Ornoy. *Curr Neuropharmacol 2021;19: 2227-2232*

The present study highlights sources of bias that may explain why children exposed in utero to SRI exhibit higher rates of congenital malformations, mostly cardiovascular and other complications.

It appears that *pregnant women treated for depression and anxiety are distinctively different from healthy women in numerous covariates, which may confound pregnancy outcomes.*

Acknowledging and adjusting for these sources of bias are critical before one selects to withhold therapy for moderate or severe cases of depression and anxiety in pregnancy.

Exposure to selective serotonin reuptake inhibitors and the risk of congenital malformations: a nationwide cohort study

Jimenez-Solem et al.
BMJ Open 2012;2:e001148

Table 2 Risk of congenital malformations among women exposed to an SSRI versus women with no exposure

	Exposed to any SSRI					
			Paused during pregnancy			

Conclusions: The apparent association between SSRI use and congenital malformations of the heart may be confounded by indications. The moderate absolute risk increase combined with uncertainty for causality still requires the risk versus benefit to be evaluated in each individual case.

Congenital malformations of the limbs	53 (1.27)	0.93 (0.71 to 1.23)	14 (1.74)	1.37 (0.80 to 2.32)	0.18	11 785 (1.40)

Estimates are presented as ORs with 95% CIs.
*p Value for comparison of ORs between pregnancies exposed throughout the first trimester and pregnancies with paused exposure during pregnancy.
†Multivariable logistic regressions are adjusted for mother's age, parity, income, education, smoking and year of conception.
SSRI, selective serotonin reuptake inhibitor.

Antidepressant Use in Pregnancy and the Risk of Cardiac Defects

Huybrechts et al. *N Engl J Med 2014; 370: 2397-2407*

Results

64,389 women (6.8%) used antidepressants during the first trimester.

Infants born with a cardiac defect:

- *not exposed* to antidepressants *72.3 per 10,000*
- *exposed* to antidepressants *90.1 per 10,000*.

Associations between antidepressant use and cardiac defects were attenuated with increasing levels of adjustment for confounding.

For SSRIs, relative risks for any cardiac defect were :

- *1.25 (95%CI, 1.13–1.38) unadjusted*,
- 1.12 (1.00–1.26) depression-restricted,
- *1.06 (0.93–1.22) depression-restricted and fully-adjusted*.

Conclusions

Results of this large population-based cohort study suggest *no substantial increased risk of cardiac malformations* attributable to SSRIs.

Guidelines on treatment of perinatal depression with antidepressants: an international review

Molenaar et al. *ANZJP 2018; 52: 320–327*

Table 1. Summary of guideline recommendations pre-, during and post-pregnancy and perinatal medication recommendations.

				Pre-pregnancy					Pregnancy				Postpartum					Medication recommendations	
	Country of origin	Year of publi-cation	Perinatal specific	Pregnancy planning	Continue AD	Switch AD	Psycho-therapy for new depression	Medi-cation for new depres-sion	Continue AD	Switch AD	Psycho-therapy for new depres-sion	Medi-cation for new depres-sion	Continue AD	Switch AD	Breast-feeding	Psycho-therapy for new depres-sion	Medi-cation for new depres-sion	Preferred medication	Non-preferred medication
ACOG	USA	2008	√								0	+							Paroxetine
APA	USA	2010		+			+	0	0		+	+			+	0	0		Paroxetine
BC	Canada	2014	√	+		–			0	–	+	+	+		+				Paroxetine
BMU	China	2015									+	+							
CANMAT	Canada	2016		+							+	+			+	+	+	Sertraline, (es) citalopram	Paroxetine, fluoxetine
COPE	Australia	2017	√				+	+			+	+			+	+	+		
Danish	Denmark	2014	√						+	+	+				0			Sertraline, citalopram	Paroxetine, fluoxetine
DGPPN	Germany	2017							+		0	0							Paroxetine, fluoxetine
NFOG	Norway	2015	√				–		+	–	+			+	+				Paroxetine
NHS	Spain	2014																Fluoxetine	Paroxetine
NICE	UK	2014	√	+			+	+	0	0	+	+	0	0	+	+	+		
NVOG	Netherlands	2012	√		+	–			0				+		+				Paroxetine
MOH	Singapore	2012							0		+	+				+	+		
RANZCP	Australia and New Zealand	2015		+							+					+	+		Paroxetine, fluoxetine, venlafaxine
SIGN	UK	2012	√						+	–	+	+			+	+	+		Paroxetine
VA/DoD	USA	2016									+					+		Sertraline	Paroxetine, fluoxetine

√: yes; +: advised by guideline; –: discouraged by guideline; 0: mentioned but no steering recommendation; ACOG: American College of Obstetricians and Gynaecologists; APA: American Psychiatric Association; VA/DoD: Department of Veterans Affairs/Department of Defense; BC: British Columbia Reproductive Mental Health Program & Perinatal Services British Columbia; BMU: Beijing Medical University; CANMAT: Canadian Network for Mood and Anxiety Treatments; COPE: Centre of Perinatal Excellence; RANZCP: Royal Australian and New Zealand College of Psychiatrists; NICE: National Institute for Health and Care Excellence; SIGN: Scottish Intercollegiate Guidelines Network; Danish: Danish Psychiatric Society, Danish Society for Obstetrics and Gynaecology, Danish Paediatric Society and Danish Company for Clinical Pharmacology; DGPPN: German Society for Psychiatry and Psychotherapy, Psychosomatics and Neurology; NVOG: Dutch Society of Obstetrics and Gynaecology; NFOG: Nordic Federation of Societies of Obstetrics and Gynaecology; NHS: Spanish ministry of health, social services and equality; MOH: Ministry of Health, Singapore.

Treatment of Peripartum Depression with Antidepressants and Other Psychotropic Medications: A Synthesis of Clinical Practice Guidelines in Europe

Kittel-Schneider et al. *Int J Environ Res Public Health 2022, 19, 1973*

Table 1. Overview of recommendations in the CPGs in women with *antenatal depression*.

Country, Publication Year, Type	New Depression, Initiate AD	Preexisting Depression, Continue AD	AD Dose Adjustment and Monitoring	Switching AD	Preferred or Not Preferred AD	AD Use before vs during Pregnancy (%)	Most Common ADs Used during Pregnancy	Treatment of Co-Morbid Anxiety	Other Psychotropics during Pregnancy (%)
Germany [26] N-PPD	Yes, after individual risk benefit evaluation, individual disease history, preference and availability of alternative treatments	Yes, in moderate-to-severe cases. Abrupt discontinuation is discouraged. Psychotherapy first line	Monotherapy if possible, lowest effective dose Continuous measurement of plasma levels	NS	Sertraline, citalopram / Paroxetine, fluoxetine	4.0 [27] vs. 0.4 (unpublished data)	Amitriptyline, (es)citalopram, sertraline (unpublished data)	NS	BZD: 3.3 [25] AP: 0.3 [21] Quetiapine: 0.2 [21]
Italy [28] PMH-S	Yes, after individual risk–benefit assessment	Yes, after individual risk–benefit assessment	NS	NS	NS	3.3–4.4 [29] vs. 1.2–1.6 [29]	Paroxetine, sertraline, citalopram [29]	Yes, BZD can be used	BZD: 1.4 [30] AP: 0.8 [31] Quetiapine: NA SAH: 0.4* [24]
United Kingdom [44,45] PMH-S	Yes, particularly for moderate-to-severe depression, after discussing with the woman the risk–benefit assessment of AD; drug choice based on lowest risk, monotherapy if possible and at the lowest effective dose	Yes, particularly for moderate-to-severe depression, after discussing with the woman the risk–benefit assessment of AD; monotherapy if possible and at the lowest effective dose	Yes, dosages may need to be adjusted in pregnancy	Option to be discussed with the woman but aim is to expose fetus to as few drugs as possible	Unspecified, choice based on prior drug response and its safety profile	8.8–9.6 vs. 3.7 [29]	Fluoxetine, citalopram [29]	Yes, with ADs. Do not offer BZD except for the short-term treatment of severe anxiety and agitation.	BZD: 1.2 * [25] AP: 0.3–4.6 [21,46] Quetiapine: 0.4 [21]

Anniverno, R.; Bramante, A.; Petrilli, G.; Mencacci, C. Prevenzione, Diagnosi E Trattamento Della Psicopatologia Perinatale: Linee Guida Per Professionisti Della Salute; Osservatorio Nazionale sulla Salute della Donna: Milano, Italy, 2010.

Charlton, R.A.; Jordan, S.; Pierini, A.; Garne, E.; Neville, A.J.; Hansen, A.V.; Gini, R.; Thayer, D.; Tingay, K.; Puccini, A.; et al. Selective serotonin reuptake inhibitor prescribing before, during and after pregnancy: A population-based study in six European regions. BJOG 2015, 122, 1010–1020

Treatment of Peripartum Depression with Antidepressants and Other Psychotropic Medications: A Synthesis of Clinical Practice Guidelines in Europe

Kittel-Schneider et al. *Int J Environ Res Public Health 2022, 19, 1973*

Table 2. Overview of recommendations in the CPGs in women with *postnatal depression*.

Country, Publication Year, Type	Depression, Initiate or Continue AD	AD Intake by Time of BF	Switching AD	Preferred or Not Preferred AD	AD Use Postpartum (%)	Most Common ADs Postpartum	Treatment Co-Morbid Anxiety	Other Psychotropic Postpartum (%)
Germany [26] N-PPD	Yes, after risk–benefit analysis for mother and child and individual disease history, preference, and availability of alternative treatments	Yes, after risk–benefit analysis for mother and child	NS	SSRIs, tricyclics / NS	NA	NA	NS	BZD: NA AP: NA Quetiapine: NA
Italy [28] PMH-S	Yes, after risk–benefit analysis for mother and child	No, use of SSRI does not prevent BF	NS	NS / Fluoxetine	2.5–3.4 [29]	NA	Yes, short-term acting BZD	BZD: NA AP: NA Quetiapine: NA
United Kingdom [44,45] PMH-S	Yes, particularly for moderate-to-severe depression after discussing with the woman of the risk–benefit assessment of AD; drug choice based on lowest risk, monotherapy if possible and at the lowest effective dose.	Consider risks and benefits of BF, which should generally be encouraged, but monitor baby for any adverse effects.	Option to be discussed with the woman, but aim is to expose the breastfed infant to as few drugs as possible.	Unspecified, choice based on prior drug response and its safety profile in breastfeeding.	5.5–12.9 [29,46]	SSRI [49]	Yes, but do not offer BZD except for the short-term treatment of severe anxiety. BZD best avoided in BF if possible; use drug with shortest half-life.	BZD: NA AP: 0.4 [46] Quetiapine: NA

Anniverno, R.; Bramante, A.; Petrilli, G.; Mencacci, C. Prevenzione, Diagnosi E Trattamento Della Psicopatologia Perinatale: Linee Guida Per Professionisti Della Salute; Osservatorio Nazionale sulla Salute della Donna: Milano, Italy, 2010.

Charlton, R.A.; Jordan, S.; Pierini, A.; Garne, E.; Neville, A.J.; Hansen, A.V.; Gini, R.; Thayer, D.; Tingay, K.; Puccini, A.; et al. Selective serotonin reuptake inhibitor prescribing before, during and after pregnancy: A population-based study in six European regions. BJOG 2015, 122, 1010–1020

Conclusioni

1. La gravidanza *non è una malattia ma ci si può ammalare* di depressione nel periodo perinatale
2. La depressione *post-partum è esordita in gravidanza* nella maggioranza delle donne
3. La depressione perinatale è *grave in un'esigua minoranza* di donne
4. La depressione *ha un impatto negativo* sulla vita della donna e del neonato
5. Chi sono le *donne a rischio* di ammalarsi di depressione perinatale
6. Il *trattamento della depressione perinatale non è diverso* dal trattamento in altri periodi della vita della donna

Depression in pregnancy: time to stop terrifying pregnant women.

J Popul Ther Clin Pharmacol. 2012;19(3):e369-70.

Soffrire di depressione non è una colpa né è segno di debolezza

Non avere paura

Vieni, ti posso aiutare

Buon lavoro !!!!