



Managing antidepressants during pregnancy

Guidance to support the multidisciplinary team manage a patient on antidepressants during pregnancy

Empowering decision-making in mental health



Psychotropic Drug Directory

Available through



**Medicines
Complete**



Guidance for a patient on antidepressants during pregnancy

Empowering decision-making in mental health



Doris is a 38-year-old woman with a diagnosis of chronic depression. She has been treated for this condition since her late twenties and has in the past attempted suicide by taking an overdose of a tricyclic antidepressant from which she recovered. She is now well-established on high-dose Fluoxetine 60 mg once daily and has been on this medication for the past two years.

During a follow-up appointment with the CMHT psychiatrist, Doris presented high-spirited, and looking forward to the future. Doris asked about stopping her medication as she is now feeling “great”, and she is planning for a pregnancy.

Doris’ psychiatrist considers her proposal and brings her case to the multidisciplinary team meeting where the team discuss whether stopping fluoxetine at this point is the best course of action for her.

The psychiatric nurse consults Psychotropic Drug Directory to find out about the risks of untreated depression in pregnancy and the latest recommendations on how to manage depression during pregnancy.

3.9 Perinatal

Psychotropic Drug Directory

Subsections	Related Content
Psychotropic effects on fertility, pregnancy, and breastfeeding	
3.9.1 Antipsychotics	
3.9.2 Antidepressants	
3.9.3 Mood and bipolar	
3.9.4 Anxiolytics and hypnotics	
3.9.5 Anticonvulsants	
3.9.6 Others	

3.9.2 Antidepressants

The risks of untreated depression in pregnancy

- A higher incidence of SIDS, poor engagement and poor self-care, and slower rates of fetal body and head growth (n = 7 696, El Marroun *et al*, *Arch Gen Psychiatry* 2012; **69**: 706–14)
- Increased ICU admissions, pre-eclampsia, premature delivery [OR = 2.4] and decreased breastfeeding initiation (s = 30, Grigoriadis *et al*, *J Clin Psychiatry* 2013; **74**: 321–41)
- Increased risk of vaginal bleeding in early pregnancy [OR = 1.22] and midpregnancy [OR = 1.28] but not postpartum (1.02% of 57 279 pregnancies, Lupattelli *et al*, *J Clin Psychopharmacol* 2014; **34**: 143–8), although a later study suggests a 1.6–1.9-fold increased risk of postpartum hemorrhage (n = 322 224, Hanley *et al*, *Obstet Gynecol* 2016; **127**: 553–61)
- Increased risk of preterm (<37/52) birth [25% vs 7–10%; OR = 1.56] and low birth weight [OR = 1.96], greater with more severe depression and unaffected by antidepressants (s = 23, n = 25 663, Jarde *et al*, *JAMA Psychiatry* 2016; **73**: 826–37).



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Management of depression during pregnancy

The 2009 US report (Yonkers *et al*, *Gen Hosp Psychiatry* 2009; **31**: 403–13; Yonkers *et al*, *Obstet Gynecol* 2009; **114**: 703–13) recommends:

1. In women thinking of getting pregnant:
 - a. If mild or asymptomatic for 6/12 or longer, consider tapering and discontinuing pre-pregnancy unless if the depression was severe or recurrent (e.g. psychotic, bipolar and history of suicide).
2. In pregnant women currently taking antidepressants:
 - a. If stable and want to stay on medication may be able to after discussion with a psychiatrist/obstetrician
 - b. Who want to discontinue may attempt tapering, and stopping if no symptoms recur
 - c. Who have recurrent depression, or residual symptoms despite antidepressants, may be helped by psychological therapies as a replacement or augmentation
 - d. Who had severe/psychotic depression (e.g. suicidal attempts, weight loss) should remain on antidepressants and/or be referred to a specialist for 'aggressive' treatment.
3. Pregnant women who are depressed, but not currently on antidepressants:
 - a. Psychotherapy may be helpful if the woman prefers to avoid antidepressants
 - b. If preferring antidepressants, choose carefully based on, e.g. trimester, PMH, comorbidity.
4. All pregnant women should:
 - a. Seek psychiatric help urgently if suicidal or psychotic symptoms develop.

These recommendations present a wide range of clinical scenarios; including women already taking antidepressants who had suicidal attempts like Doris.

Doris has been asymptomatic for the last 2 years, but since she had several episodes of relapse and a suicide attempt in the past, her psychiatrist is considering the option to continue fluoxetine during her future pregnancy. The psychiatrist searches on Psychotropic Drug Directory for the current recommendations regarding treatment duration with antidepressants and finds that after several episodes of depression, an antidepressant should be taken for at least 5 years or longer.



The screenshot shows the Medicines Complete website interface. At the top, there is a search bar containing '1.14 Depression' and a search icon. To the right of the search bar are several utility icons: a link icon, a refresh icon, a share icon, a print icon, and a user profile icon. Below the search bar, the page title is 'Psychotropic Drug Directory' with a 'Highlight search' toggle. On the left side, there is a navigation menu with 'Subsections' and 'Related Content' tabs. Under 'Subsections', '1.14.1 Unipolar depression' is selected and highlighted. Other options include 'BNF listed', 'Combinations (of medicines with some intrinsic antidepressant activity)', 'Adjuncts/unlicensed/some efficacy', 'Unlicensed/possible efficacy', 'Case reports', 'No efficacy', '1.14.2 Postpartum depression (PPD)', and another 'BNF listed' option. The main content area on the right displays text under the heading 'c. Maintenance or relapse prevention'. The text discusses maintenance therapy for chronic depression, citing studies by Solomon et al (2000) and Wilkinson and Izmeth (2016). It mentions that relapse risk increases with successive episodes and that continuing antidepressants in the elderly for 12 months is helpful. It also notes that relapse has been significantly lower with antidepressants in every study over the last 25 years, with an average relapse reduction of 52% compared to placebo. Below this text is a section titled 'Minimum treatment duration recommendations' with four numbered points: i. First episode – six months post-recovery; ii. Second episode – 1–3 years; iii. Third episode – five years or longer (n = 128, RCT, d/b, p/c, three years, Frank et al, Arch Gen Psychiatry 1990; 47: 1093–9; two-year follow-up, Kupfer et al, Arch Gen Psychiatry 1992; 49: 769–73); iv. Fourth and subsequent episodes – the person should have a very good reason to stop.

Therefore, the psychiatrist determines that to minimise the risk of a potentially devastating relapse, Doris should continue taking an antidepressant as it has only been two years from her initial recovery.

To inform this decision, the psychiatrist also searches Psychotropic Drug Directory to find out the latest research available about the safety of antidepressants during pregnancy in general, and that of fluoxetine in particular.

The **Perinatal** section on Psychotropic Drug Directory includes evidence-based information on the safety of psychotropic drugs from the first trimester of pregnancy to birth and breastfeeding, including pregnancy-related conditions such as gestational diabetes or maternal hypertension. For this case, the psychiatrist looks at the dedicated section for the SSRIs, specifically, fluoxetine.



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12b. Fluoxetine

Fertility

See introduction.

T1

- A major review concludes there is a slight but statistically significant increase in the risk of CV defects, but that the absolute risks are low (SR&M-A, s = 16, Gao *et al*, *Br J Clin Pharmacol* 2017; **83** : 2134–47). The risks are:
 - MCMS RR = 1.18
 - CV malformations RR = 1.36
 - Septal defects RR = 1.38
 - Non-septal defects RR = 1.39.

T2–3 *

- Fluoxetine plasma levels are unchanged in T3 (n = 54 393; mbp = 281, Westin *et al*, *PLoS One* 2017; **12** : e0181082; FFT)
- There is little or no increase in the rates of low birth weight and preterm births, although high-dose fluoxetine (40–80 mg/d) may be associated with a risk of lower birth weight (n = 138, Hendrick *et al*, *Am J Obstet Gynaecol* 2003; **188** : 812–15; FFT).

Birth

- See introduction for PPHN
- Fluoxetine withdrawal symptoms are unusual but can include irritability, increased tonus, jitteriness and poor feeding, usually only lasting a few days (n = 1, Anbu and Theodore, *Indian Pediatr* 2006; **43** : 66–9), but rarely up to six weeks (n = 1, Alehan *et al*, *J Matern Fetal Neonatal Med* 2008; **21** : 921–3).

Breastfeeding

- Fluoxetine up to 20 mg/d produces low infant peak serum levels at 8 hours (n = 19, Hendrick *et al*, *Biol Psychiatry* 2001; **15** : 775–82), mostly less than 10%, the notional level of concern (e.g. mbp = 10, Suri *et al*, *Biol Psychiatry* 2002; **52** : 446–51) but some can be up to 22% (s = 67, Weissman *et al*, *Am J Psychiatry* 2004; **161** : 1066–78) with the risk of accumulation (mbp = 14, Kristensen *et al*, *Br J Clin Pharmacol* 1999; **48** : 521–7)
- Infant plasma levels (s = 11, n = 190, Burt *et al*, *Am J Psychiatry* 2001; **158** : 1001–9) have no clear association with maternal dose, age or plasma levels, so there is clearly significant interpatient variability.

PND (postnatal development)

- There is no effect on global IQ, language development or behavioural development (n = 139, 18–86/12, Nulman *et al*, *NEJM* 1997; **336** : 258–62; FFT), cognition or temperament. In contrast untreated depression is associated with poorer cognitive and language achievement (TCA n = 46, fluoxetine n = 40, controls n = 36;

Some studies suggest that there is a small risk of cardiovascular defects during the first trimester of pregnancy with fluoxetine. The psychiatrist also finds on Psychotropic Drug Directory an informative table about the risk of psychotropic drugs on fertility, pregnancy, and breastfeeding that helps him inform his decision by comparing the risk of fluoxetine with other antidepressants.



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Supports the optimal and rational use of medicines, to improve the quality of life for people with mental health needs.

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Access other publications for further information:

Psychotropic effects on fertility, pregnancy, and breastfeeding

Swipe or scroll within the table to navigate

Antidepressants								
SSRIs ¹²								
(Es)citalopram ^{12a}	L?	C	C	L	L	M	L	L?
Fluoxetine ^{12b}	L?	C	C	L/M	L/M	M	M	L
Fluvoxamine ^{12c}	L?	C	C	M	M	M	L	L
Paroxetine ^{12d}	M	D	D	M/H	M	M/H	M	L?
Sertraline ^{12e}	L?	C	C	M	L/M	M	L	L?

NK = not known; L = lower risk; M = medium risk/known but manageable; H = higher risk; ? = some data, e.g. animal studies, cases, lack of negative reports suggests this is the grade

Based on what is known about the reproductive safety of fluoxetine, the psychiatrist is now confident that continuing the treatment is the right approach to best help Doris. She is then counselled about the importance of continuing with the treatment, given her chronic condition and the increased risk of pregnancy complications if depression is left untreated.



Psychotropic Drug Directory

Psychotropic Drug Directory supports the optimal and rational use of medicines, to improve the quality of life for people with mental health needs.

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