

## ONLINE SUPPLEMENTARY MATERIALS

### COLLEGE OF OBSTETRICIANS AND GYNECOLOGISTS SINGAPORE INTEGRATED PERINATAL MENTAL HEALTH GUIDELINES FOR DEPRESSION AND ANXIETY GRADE EVIDENCE TO DECISION FRAMEWORK

#### QUESTION

What are the recommendations to provide a holistic approach towards caring for women with depression and anxiety during preconception, antepartum and postpartum periods?

#### Question details

Problem: To improve the care of women with perinatal depression and anxiety in Singapore

Option: A set of recommendations that provide holistic recommendations towards good perinatal mental health outcomes

Comparison: NA

Main outcomes:

- Recommendations for preconception management of perinatal depression and anxiety
- Recommendations for antenatal management of depression and anxiety
- Recommendations for postnatal management of depression and anxiety
- Recommendations for special populations – women who have experienced maternal adverse events, women with special needs, pregnant adolescents.

Setting: Singapore community

Perspective: Healthcare providers

#### Background

Perinatal depression and anxiety are a public health concern with implications on maternal and child health outcomes. The neurodevelopmental impact of depression and anxiety on the growing foetus has been clearly evidenced in the Singapore population (GUSTO birth cohort study), with changes in microstructure, functional connectivity as well as epigenetic footprint. The adverse impact extends into the postpartum period, during which maternal depression and anxiety have been found to be associated with infant negative temperament, reduced maternal sensitivity, child behavioural problems, and decreased school readiness ([www.gusto.sg](http://www.gusto.sg)). Given that preconception mental health has been found to be closely related to antenatal mental health, which in turn predicts postnatal mental health, there is a crucial need for early identification and intervention to ensure the best health outcomes for women and children. These guidelines have been developed to provide guidance on

addressing depression and anxiety, during the preconception, antepartum and postpartum phases, with an aim to enhance population health for mothers and children.

### ***Problem – is it a priority?***

#### Research Evidence

The lifetime prevalence of major depression and generalised anxiety disorder have respectively been found to be 7.7-9.2% and 1.9-2.2% amongst women of childbearing age (Subramaniam et al 2020, Singapore Mental Health Study), whilst antepartum depressive states (both major and minor) occur in 12.2% and postpartum depressive states in 6.8% (Chee et al 2006).

### ***Target audience for developing Perinatal Mental Health Guidelines for Depression and Anxiety***

Target audience: General Practitioners, Family Medicine Physicians, Primary Health Practitioners, Obstetricians & Gynaecologists, Paediatricians, Nursing, Social Workers and Counsellors, Psychiatrists, and other mental health professionals, We aim to make this document readable to the wider public and non-healthcare lay community, as awareness and public education are key to addressing maternal mental health at the population level.

This guideline does not include severe mental disorders such as schizophrenia and bipolar disorders, which will be covered in subsequent editions.

### **Methodology**

Literature review of evidence pertaining to recommendations at each stage in childbearing.

Expert consensus review of recommendations to arrive at final statement

### ***Desirable effects***

How substantial are the desirable anticipated effects?

## Research evidence: Preconception management

Type of outcome	Author	Type of study	No of studies/Participants	Summary of Findings	Certainty of Evidence
Preconception management	Biaggi 2016	Systematic review	97 studies reviewed	Review identifies the main risk factors involved in the onset of antenatal anxiety and depression. The most relevant factors associated with antenatal depression or anxiety were: lack of partner or of social support; history of abuse or of domestic violence; personal history of mental illness; unplanned or unwanted pregnancy; adverse events in life and high perceived stress; present/past pregnancy complications; and pregnancy loss. The results show the complex aetiology of antenatal depression and anxiety. The administration of a screening tool to identify women at risk of anxiety and depression during pregnancy should be universal practice in order to promote the long-term wellbeing of mothers and babies, and the knowledge of specific risk factors may help create such screening tool targeting women at higher risk.	⊕⊕○○
	Abajobir et al, 2016	Systematic review and meta-analyses	512 studies reviewed	Systematic review based on PRISMA guidelines and meta-analysed studies reporting an association between unintended pregnancy and maternal depression. Meta-bias and funnel plot of inverse variance detected no publication bias. Overall prevalence of maternal depression in unintended pregnancy was 21%. Unintended pregnancy was significantly associated with maternal depression. Despite statistically significant heterogeneities of included studies, sub-group analyses revealed positive and significant associations by types of unintended pregnancies, timing of measurements with respect to pregnancy and childbirth, study designs and settings. The prevalence of perinatal depression is two-fold in women with unintended pregnancy. Perinatal care settings may screen pregnancy intention and depression of women backed by integrating family planning and mental health services.	⊕⊕⊕○
			44 studies reviewed	Review of publications on the management of contraception for women with mental illness. The majority of women chose	⊕⊕○○

Type of outcome	Author	Type of study	No of studies/Participants	Summary of Findings	Certainty of Evidence
	McCloskey et al, 2021	Narrative review		combined oral contraceptives, with 14% choosing long-acting reversible contraceptives. The impact of hormonal contraceptives on the risk for depression is unclear: similar or lower rates of mood symptoms in hormonal contraceptive users compared with nonusers. Proactive management of mental illness, contraception, and pregnancy improves a woman's capacity to function and optimises her mental and reproductive health.	
	Dennis et al, 2022	Cross sectional study	621 participants	Nationwide Canadian survey, demonstrating that individuals with a lifetime or current mental illness were significantly more likely to have several risk factors for suboptimal reproductive and perinatal outcomes, including increased rates of obesity, stress, fatigue, loneliness, number of chronic health conditions, and medication use. Further, they were more likely to have high-risk health behaviours including increased substance use, internet addiction, poorer eating habits, and decreased physical activity. There are many important reproductive and perinatal risk factors that are modifiable via preconception interventions which could have a significant positive impact on women's health trajectories and those of their future children.	⊕⊕○○
	Kee et al, 2020	Cohort study	280 participants	Prospective analysis of anxiety and depressive symptom profiles from preconception through to parturition. Symptoms of depression or anxiety in the preconception phase strongly predicted those across pregnancy and into the early postnatal period. The symptom network analysis revealed that the symptom profiles remained largely unchanged from preconception into the second trimester, and for a significant portion of women, maternal mental health remains consistent from preconception into pregnancy.	⊕⊕○○
	Westdhal et al, 2007	Cohort study	1047 participants	Thirty-three percent of the sample reported elevated levels of depressive symptoms predicted from sociodemographic factors, social support, and social conflict. Social support and	⊕⊕○○

Type of outcome	Author	Type of study	No of studies/Participants	Summary of Findings	Certainty of Evidence
				<p>conflict had independent effects on depressive symptoms although social conflict was a stronger predictor. There was a "dose-response," with each increase in interpersonal risk factor resulting in consequent risk for probable depression based on symptom reports (CES-D<math>\geq</math>16). Seventy-six percent of women with a composite score of three or more high-risk responses reported depressive symptoms.</p>	
	<p>van Lee et al, 2020</p>	<p>Cohort study</p>	<p>535 participants</p>	<p>Six factors studied in pregnancy: poor diet quality (Healthy eating index for Singapore pregnant women &lt; median), poor sleep quality (global Pittsburgh sleep quality index score &gt; 5), physical inactivity (&lt; 600 MET-minutes/week), vitamin D insufficiency (&lt; 50 nmol/l), smoking before or during pregnancy, and the perceived need for social support. These six lifestyle habits contributed to 32% of the variance in depressive symptoms during pregnancy. The prevalence of being probably depressed was 6.4 (95% CI 2.1, 19.8; p trend &lt; 0.001) for expecting women who had <math>\geq</math>4 risk factors compared to women who had <math>\leq</math>1 risk factor. No association was observed between the number of risk factors and depressive symptoms at 3 months postpartum.</p>	<p><math>\oplus\oplus\circ\circ</math></p>

## Research evidence: Antenatal management

Type of outcome	Author	Type of study	No of studies/Participants	Summary of Findings	Certainty of Evidence
Antenatal management	Marcus et al, 2003	Cross-sectional study	3472 participants	Pregnant women aged 18 and above were screened while waiting for their prenatal care visits in 10 obstetrics clinics using a brief (10 minute) screening questionnaire. This screen measured demographics, tobacco and alcohol (TWEAK problem alcohol use screening measure), and depression measures, including the Centre for Epidemiological Studies-Depression scale (CES-D), use of antidepressant medications, past history of depression, and current treatment (i.e., medications, psychotherapy, or counselling) for depression. 20% of the women screened (n = 689) scored above the cut-off score on the CES-D, and only 13.8% of those women reported receiving any formal treatment for depression. Past history of depression, poorer overall health, greater alcohol use consequences, smoking, being unmarried, unemployment, and lower educational attainment were significantly associated with symptoms of depression during pregnancy.	⊕⊕○○
	Norhayati et al, 2015	Systematic review	203 studies	A literature search conducted between 2005 and 2014 identified 203 studies, of which 191 used self-reported questionnaires and 21 used structured clinical interviews. Nine studies used a combination of self-reported questionnaires and clinical interviews. The prevalence of postpartum depression varied from 1.9% to 82.1% in developing countries and from 5.2% to 74.0% in developed countries when self-reported questionnaires were used. Structured clinical interviews showed a lower prevalence of postpartum depression, ranging from 0.1% in Finland to 26.3% in India. Antenatal depression and anxiety, previous psychiatric illness, poor marital relationship, stressful life events, negative attitude towards pregnancy, and lack of social support were significant contributors to postpartum depression.	⊕⊕○○
	Pedersen et al, 2009	Cohort study	496881 singleton liveborn children	Data was collected from four Danish nationwide registries (medical birth registry, national register of medicinal product statistics, fertility database and the national hospital registry) which were	⊕⊕○○

Type of outcome	Author	Type of study	No of studies/Participants	Summary of Findings	Certainty of Evidence
				<p>linked by a unique personal identifier assigned to all citizens at birth. Exposure was defined as two or more redemptions (filling of a prescription) of an SSRI from 28 days before to 112 days after the beginning of gestation. Women with any redemption of insulin or antihypertensive medications in a period of three months before the estimated beginning of gestation and those with any redemption during the exposure window to other psychotropic medications, such as antiepileptic medication, antipsychotics, and anxiolytics, were excluded. A cohort consisting of all liveborn children in Denmark between 1 January 1996 and 31 December 2003 was constructed based on information from the medical birth registry (n=553 689). From these 1213 children were excluded because of coding errors, 22 045 because of emigration, 8388 because of exposure to other psychoactive or antidiabetic drugs as described above, and 21 653 multiple births and 3509 stillbirths. The final study population comprised 496 881 singleton liveborn children. Multiple logistical regressions were conducted on dichotomous outcomes adjusted for maternal age, calendar time, marital status, income and smoking. Women taking an SSRI were more likely to be older, living alone, unmarried, and smokers. Redemptions for SSRIs were not associated with major malformations overall but were associated with septal heart defects (odds ratio 1.99, 95% confidence interval 1.13 to 3.53). For individual SSRIs, the odds ratio for septal heart defects was 3.25 (1.21 to 8.75) for sertraline, 2.52 (1.04 to 6.10) for citalopram, and 1.34 (0.33 to 5.41) for fluoxetine. Redemptions for more than one type of SSRI were associated with septal heart defects (4.70, 1.74 to 12.7)). The absolute increase in the prevalence of malformations was low—the prevalence of septal heart defects was 0.5% (2315/493 113) among unexposed children, 0.9% (12/1370) among children whose mothers were prescribed any SSRI, and 2.1% (4/193) among children whose mothers were prescribed more than one type of SSRI.</p>	
	Yonkers et al, 2017	Cohort study	2654 participants	Between July 2005 and July 2009, women at 137 obstetric practices in Connecticut and Massachusetts were recruited before 17 weeks	⊕⊕○○

Type of outcome	Author	Type of study	No of studies/Participants	Summary of Findings	Certainty of Evidence
				<p>of pregnancy and reassessed at 28 (<math>\pm</math>4) weeks of pregnancy and 8 (<math>\pm</math>4) weeks postpartum. Psychiatric diagnoses were determined by answers to the World Mental Health Composite International Diagnostic Interview. Assessments also gathered information on treatment with medications and confounding factors, such as substance use, previous adverse birth outcomes, and demographic factors. Of the 2654 women in the final analysis (mean [SD] age, 31.0 [5.7] years), most were non-Hispanic white (1957 [73.7%]), 98 had panic disorder, 252 had GAD, 67 were treated with a benzodiazepine, and 293 were treated with a serotonin reuptake inhibitor during pregnancy. In adjusted models, neither panic disorder nor GAD was associated with maternal or neonatal complications of interest. Most medication exposures occurred early in pregnancy. Maternal benzodiazepine use was associated with caesarean delivery (odds ratio [OR], 2.45; 95% CI, 1.36-4.40), low birth weight (OR, 3.41; 95% CI, 1.61-7.26), and use of ventilatory support for the newborn (OR, 2.85; 95% CI, 1.2-6.9). Maternal serotonin reuptake inhibitor use was associated with hypertensive diseases of pregnancy (OR, 2.82; 95% CI, 1.58-5.04), preterm birth (OR, 1.56; 95% CI, 1.02-2.38), and use of minor respiratory interventions (OR, 1.81; 95% CI, 1.39-2.37). With maternal benzodiazepine treatment, rates of ventilatory support increased by 61 of 1000 neonates and duration of gestation was shortened by 3.6 days; with maternal serotonin reuptake inhibitor use, gestation was shortened by 1.8 days, 152 of 1000 additional newborns required minor respiratory interventions, and 53 of 1000 additional women experienced hypertensive diseases of pregnancy.</p>	
	van Lee et al, 2020	Cohort study	535 participants	<p>Six factors studied in pregnancy: poor diet quality (Healthy eating index for Singapore pregnant women &lt;median), poor sleep quality (global Pittsburgh sleep quality index score &gt; 5), physical inactivity (&lt;600 MET-minutes/week), vitamin D insufficiency (&lt;50 nmol/l), smoking before or during pregnancy, and the perceived need for social support. These six lifestyle habits contributed to 32% of the</p>	⊕⊕○○



Type of outcome	Author	Type of study	No of studies/Participants	Summary of Findings	Certainty of Evidence
				variance in depressive symptoms during pregnancy. The prevalence of being probably depressed was 6.4 (95% CI 2.1, 19.8; p trend < 0.001) for expecting women who had ≥4 risk factors compared to women who had ≤1 risk factor. No association was observed between the number of risk factors and depressive symptoms at 3 months postpartum.	
	Bowen et al, 2014	Case control study	38 participants	Women between 15-28 weeks of gestation were recruited to antenatal psychotherapy groups using either interpersonal or mindfulness-based therapy. Data regarding symptoms of depression, anxiety, worry and stress, medication use, other therapies used, sociodemographic and obstetrical information were collected upon intake to the Psychotherapy Group. Women completed their second questionnaire when the group ended, approximately six weeks after they completed their initial assessment. Lastly, women completed a telephone interview at approximately four weeks postpartum. The Edinburgh Postpartum Depression Scale (EPDS), Cambridge Worry Scale (CWS) and State Trait Anxiety Inventory (STAI) were used to assess depressive symptoms, worry and anxiety respectively. Descriptive, Chi-square, and GEE analyses were used to compare depression and worry symptoms with a matched control group of pregnant women (N=68). Group therapy participants reported significant reductions in worry and depression symptoms antenatally and postnatally, compared to controls. There was no difference in symptom reduction when different types of therapy groups were compared.	⊕⊕○○

Type of outcome	Author	Type of study	No of studies/Participants	Summary of Findings	Certainty of Evidence
Postnatal Management	Beck et al. 2001	Systematic view and Meta-analysis	84 studies reviewed	This review is an update to an earlier meta-analysis done in the 1980s which looked at the magnitude of the relationships between postpartum depression and various risk factors. 13 significant predictors of postpartum depression were identified of which 10 had moderate effect sizes and 3 had small effect sizes. The mean effect size indicator ranges for each risk factor were as follows: prenatal depression (.44 to .46), self-esteem (.45 to .47), childcare stress (.45 to .46), prenatal anxiety (.41 to .45), life stress (.38 to .40), social support (.36 to .41), marital relationship (.38 to .39), history of previous depression (.38 to .39), infant temperament (.33 to .34), maternity blues (.25 to .31), marital status (.21 to .35), socioeconomic status (.19 to .22), and unplanned/unwanted pregnancy (.14 to .17)	⊕⊕⊕○
	Brown et al. 2021	Systematic review and Meta-analysis	11 studies reviewed	This review assessed the effectiveness and safety of antidepressant drugs in comparison with any other treatment. Meta-analysis showed that there may be a benefit of SSRIs over placebo in response (55% versus 43%; pooled risk ratio (RR) 1.27, 95% confidence interval (CI) 0.97 to 1.66); remission (42% versus 27%; RR 1.54, 95% CI 0.99 to 2.41); and reduced depressive symptoms (standardised mean difference (SMD) -0.30, 95% CI -0.55 to -0.05; 4 studies, 251 women), at 5 to 12 weeks' follow-up. However, it was hard to determine adverse events of SSRI administration due to limited data.	⊕⊕⊕○
	Donker et al. 2009	Systematic review and Meta-analysis	4 studies reviewed	This review assessed the effectiveness of passive psychoeducation in reducing symptoms of depression, anxiety or psychological distress. The pooled standardised-effect size (four studies, four comparisons) for reduced symptoms of depression and psychological distress at post-intervention was $d = 0.20$ (95% confidence interval: 0.01-0.40; $Z = 2.04$ ; $P = 0.04$ ; the number needed to treat: 9). Heterogeneity was not significant among the studies ( $I^2 = 32.77$ , $Q:4.46$ ; $P = 0.22$ ). Hence this review showed that brief passive psychoeducational interventions for depression and psychological distress can reduce symptoms.	⊕⊕⊕○

Type of outcome	Author	Type of study	No of studies/Participants	Summary of Findings	Certainty of Evidence
	Sloman et al. 2019	Systematic review	122 studies reviewed	This review evaluated both the infant and the maternal consequences of untreated maternal postpartum depression. The results of the studies were synthesised into three categories: (a) the maternal consequences of postpartum depression, including physical health, psychological health, relationship, and risky behaviours; (b) the infant consequences of postpartum depression, including anthropometry, physical health, sleep, and motor, cognitive, language, emotional, social, and behavioural development; and (c) mother–child interactions, including bonding, breastfeeding, and the maternal role. The results suggest that postpartum depression creates an environment that is not conducive to the personal development of mothers or the optimal development of a child.	⊕⊕○○
	Machado et al. 2020	Narrative review	55 studies reviewed	This article considers first-time mothers' perceptions of the effectiveness of social supports and perceived barriers to accessing support and provides recommendations for best practice. Much of the research around postnatal support fails to distinguish the specific type of support, meaning creating support solutions for the postpartum period may not be effectively targeted.	⊕⊕○○

### Research evidence: Special considerations

Type of outcome	Author	Type of study	No of studies/Participants	Summary of Findings	Certainty of Evidence
	Furuta et al, 2014	Cohort study	1824 participants	Prospective cohort study of women who gave birth over six months in 2010 in an inner city maternity unit in England. Primary outcomes were prevalence of PTSD	⊕⊕○○

Type of outcome	Author	Type of study	No of studies/Participants	Summary of Findings	Certainty of Evidence
<p><b>Special considerations for severe obstetric events</b></p>				<p>symptoms namely: 1) intrusion and 2) avoidance as measured using the Impact of Event Scale at 6 – 8 weeks postpartum via a self-administered postal questionnaire. Secondary outcomes included probable depression. Prevalence of a clinically significant level of intrusion and avoidance were 6.4% (n=114) and 8.4% (n=150) respectively. There was a higher risk of PTSD symptoms among women who experienced severe maternal morbidity compared with women who did not (adjusted OR = 2.11, 95%CI = 1.17-3.78 for intrusion; adjusted OR = 3.28, 95%CI = 2.01-5.36 for avoidance). Higher ratings of reported sense of control during labour/birth partially mediated the risk of PTSD symptoms. There were no statistically significant differences in the prevalence or severity of symptoms of depression. Individually tailored care that increases women’s sense of control during labour may be a protective factor with further work required to promote effective interventions to prevent these symptoms.</p>	
	<p>Morton et al, 2021</p>	<p>Expert opinion</p>	<p>512 studies reviewed</p>	<p>Systematic review based on PRISMA guidelines and meta-analysed studies reporting an association between unintended pregnancy and maternal depression. Meta-bias and funnel plot of inverse variance detected no publication bias. Overall prevalence of maternal depression in unintended pregnancy was 21%. Unintended pregnancy was significantly associated with maternal depression. Despite statistically significant heterogeneities of included studies, sub-group analyses revealed positive and significant associations by types of unintended pregnancies, timing of measurements with respect to pregnancy and childbirth, study designs and settings. The prevalence of perinatal depression is two-fold in women with unintended pregnancy. Perinatal care settings may screen pregnancy intention and depression</p>	<p>⊕⊕⊕○</p>

Type of outcome	Author	Type of study	No of studies/Participants	Summary of Findings	Certainty of Evidence
				of women backed by integrating family planning and mental health services.	
<b>Special considerations for adolescents and women with special needs</b>	D'Angelo et al, 2020	Narrative review	76 studies reviewed	This review found that women with disabilities feel the desire for motherhood as much as women without special clinical needs. Their fertility is often not impacted by disability and they can have children. However, several issues must be considered, depending on the physical, mental or developmental disability. Women with a physical disability often experience higher risks of caesarean section, preterm birth, growth restriction and low birth weight when compared to controls. Women with intellectual or developmental disabilities are often young, unmarried, unemployed and have limited access to care. They often struggle following instructions or recognizing the conditions that require medical help. They are more likely to experience preeclampsia, diabetes, venous thromboembolism, caesarean delivery, infant low birth weight, preterm birth, neonatal intensive care unit admission, and perinatal death. It is important that both women and men with disabilities could be provided with accurate, accessible, and understandable information about sexual health and options regarding contraception and reproduction; also to have the chance to discuss sexual matters, pregnancy desires and concerns with healthcare providers so they can provide appropriate screenings, contraceptive services, preconception, and prenatal care.	⊕⊕○○
	Siegel et al 2014	Narrative review	40 studies reviewed	This review looks at the intersection of psychopathology and adolescent pregnancy and the postpartum period. Existing literature shows that pregnant and parenting adolescents are at greater risk for experiencing depressive symptoms than pregnant and postpartum adult women. Depression in the perinatal period is also a	⊕⊕○○

Type of outcome	Author	Type of study	No of studies/Participants	Summary of Findings	Certainty of Evidence
				risk factor for substance and alcohol abuse and a harsher parenting style in adolescents.	

<b>Special considerations for infant health and neurodevelopment and caregiving needs</b>	Hudak & Tan, 2012	Review paper	10 studies	The clinical report by the Committee on Drugs and the Committee on foetus and Newborn, The American Academy of Pediatrics reviewed in impact of late pregnancy use of SSRIs. There is evidence of neonatal poor adaptation syndrome characterised by crying, irritability, tremors, poor suck, feeding difficulty, hypertonia, tachypnea, sleep disturbances, hypoglycemia and seizures. There effects have an onset within hours, and typically last up to one week, although may persist till 4 week.	⊕⊕○○
	Rifkin-Graboi et al. 2015	Cohort study	20 mother-infant dyads	This study explored whether maternal sensitivity predicts human limbic system development and functional connectivity patterns. There were indirect associations between maternal sensitivity and the amygdala demonstrating similar indirect but not significant results. Functional analyses revealed direct associations between maternal sensitivity and connectivity between the hippocampus and areas important for emotional regulation and socio-emotional functioning. There may also be indirect associations between limbic structures and regions related to autobiographical memory.	⊕⊕○○
	Bigelow et al. 2018	Cohort study	87 mother-infant dyads	This study explored relations among maternal depression risk, maternal mind-mindedness, and infants' attachment behaviour. Mothers who are at risk for depression in their infants' early lives may be hampered in their capacity to respond appropriately to their infants' mental states. Infants with mothers who have difficulty responding appropriately to their mental states, as suggested by low appropriate mind-mindedness, may feel less known and recognised by their mothers, a key theme in the origins of disorganised attachment.	⊕⊕○○
	Bakermans-Kranenburg et al. 2003	Systematic review and Meta-analysis	70 studies reviewed	This review explored whether early preventive intervention is effective in enhancing parental sensitivity and infant attachment security. Randomised interventions appeared rather effective in changing insensitive parenting and infant attachment insecurity.	⊕⊕⊕○

				<p>The most effective interventions used a moderate number of sessions and a clear-cut behavioural focus in families with, as well as without, multiple problems. Interventions that were more effective in enhancing parental sensitivity were also more effective in enhancing attachment security, which supports the notion of a causal role of sensitivity in shaping attachment.</p>	
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**Undesirable effects**

How substantial are the undesirable anticipated effects?

**Research evidence: Antenatal and postnatal management**

Type of outcome	Author	Type of study	No of studies/Participants	Summary of Findings	Certainty of Evidence
<b>Antenatal and Postnatal management</b>	Soe et al, 2015	Cohort study	174 participants	<p>GUSTO birth cohort study followed up mothers and children from 26 weeks gestation to 24 months age. After controlling for postnatal maternal depressive symptoms, infants born to mothers with higher prenatal maternal depressive symptoms showed greater functional connectivity of the amygdala with the left temporal cortex and insula, as well as the bilateral anterior cingulate, medial orbitofrontal and ventromedial prefrontal cortices, which are largely consistent with patterns of connectivity observed in adolescents and adults with major depressive disorder. Novel evidence that prenatal maternal depressive symptomatology alters the amygdala's functional connectivity in early postnatal life, which reveals that the neuroimaging correlates of the familial transmission</p>	⊕⊕○○



Type of outcome	Author	Type of study	No of studies/Participants	Summary of Findings	Certainty of Evidence
				of phenotypes associated with maternal mood are apparent in infants at 6 months of age.	
	Law et al , 2021	Cohort study	512 studies reviewed	Prospective data from 505 mother–child dyads from GUSTO birth cohort, from pregnancy to 2-years postpartum, analysed with child behavioural, socio-emotional and cognitive outcomes from 2 to 6 years of age. Household income found to be a robust predictor of antenatal maternal mental health and all child outcomes. Between children from the bottom and top household income quartiles, four dimensions of school readiness skills differed by a range of 0.52 (95% CI: 0.23, 0.67) to 1.21S.D. (95% CI: 1.02, 1.40). Thirty-eight percent of pregnant mothers in this cohort were found to have perinatal depressive and anxiety symptoms in the subclinical and clinical ranges. Poorer school readiness skills were found in children of these mothers when compared to those of mothers with little or no symptoms. After adjustment of unmeasured confounding on the indirect effect, antenatal maternal mental health provided a robust mediating path between household income and multiple school readiness outcomes ( $\chi^2$ 126.05, df 63, $p < 0.001$ ; RMSEA = 0.031, CFI = 0.980, SRMR = 0.034). Pregnant mothers with mental health symptoms, particularly those from economically-challenged households, are potential targets for intervention to level the playing field of their children.	⊕⊕⊕○
	Qiu et al, 2013	Cohort study	175 participants	Study aimed to examine the consequences of antenatal and postnatal exposure to maternal anxiety upon early infant development of the hippocampus, a key structure for stress regulation. 175 neonates underwent magnetic resonance imaging (MRI) at birth and among them 35 had repeated scans at 6 months of age. Maternal anxiety was assessed using the State-Trait Anxiety Inventory (STAI) at week 26 of pregnancy and 3 months after delivery. Regression analyses showed that antenatal maternal anxiety did	⊕⊕○○

Type of outcome	Author	Type of study	No of studies/Participants	Summary of Findings	Certainty of Evidence
				<p>not influence bilateral hippocampal volume at birth. However, children of mothers reporting increased anxiety during pregnancy showed slower growth of both the left and right hippocampus over the first 6 months of life. This effect of antenatal maternal anxiety upon right hippocampal growth became statistically stronger when controlling for postnatal maternal anxiety. Furthermore, a strong positive association between postnatal maternal anxiety and right hippocampal growth was detected, whereas a strong negative association between postnatal maternal anxiety and the left hippocampal volume at 6 months of life was found. Hence, the postnatal growth of bilateral hippocampi shows distinct responses to postnatal maternal anxiety. The size of the left hippocampus during early development is likely to reflect the influence of the exposure to perinatal maternal anxiety, whereas right hippocampal growth is constrained by antenatal maternal anxiety, but enhanced in response to increased postnatal maternal anxiety.</p>	

***Certainty of the evidence***

What is the overall certainty of the evidence of effects?

**Research evidence: Certainty of evidence**

Type of outcome	Author	Type of study	No of studies/Participants	Overall Certainty of Evidence
<b>Preconception management</b>	Biaggi 2016	Systematic review	97 studies reviewed	⊕⊕○○
	Abajobir et al, 2016	Systematic review and meta-analyses	512 studies reviewed	
	McCloskey et el, 2021	Narrative review	44 studies reviewed	
	Dennis et al, 2022	Cross sectional study	621 participants	
	Kee et al, 2020	Cohort study	280 participants	
	Westdhal et al, 2007	Cohort study	1047 participants	
	van Lee et al, 2020	Cohort study	535 participants	
<b>Antenatal management</b>	Marcus et al, 2003	Cross-sectional study	3472 participants	⊕⊕○○
	Norhayati et al, 2015	Systematic review	203 studies	
	Pedersen et al, 2009	Cohort study	496881 singleton liveborn children	
	Yonkers et al, 2017	Cohort study	2654 participants	
	van Lee et al, 2020	Cohort study	535 participants	
	Bowen et al, 2014	Case control study	38 participants	
<b>Postnatal management</b>	Beck et al. 2001	Systematic view and Meta-analysis	84 studies reviewed	⊕⊕○○
	Brown et al. 2021	Systematic review and Meta-analysis	11 studies reviewed	
	Donker et al. 2009	Systematic review and Meta-analysis	4 studies reviewed	
	Sloman et al. 2019	Systematic review	122 studies reviewed	
	Machado et al. 2020	Narrative review	55 studies reviewed	
<b>Special considerations</b>	Furuta et al. 2014	Cohort study	1824 participants	⊕⊕○○
	Morton et al, 2021	Expert opinion	512 studies reviewed	
	D'Angelo 2020	Narrative review	76 studies reviewed	
	Siegel et al 2014	Narrative review	40 studies reviewed	
	Hudak & Tan, 2012	Narrative review	40 studies reviewed	
	Rifkin-Graboi et al. 2015	Cohort study	20 mother-infant dyads	
	Bigelow et al. 2018	Cohort study	87 mother-infant dyads	
Bakermans-Kranenburg et al. 2003	Systematic review and Meta-analysis	70 studies reviewed		

### **Values**

Is there important uncertainty about, or variability in, how much people value the main outcomes?

### **Research evidence**

Based on the findings of two surveys conducted in 2022, I-MUM (Integrated Maternal Perinatal Mental Health Care) and I-Doc (Doctor's Knowledge, Attitudes and Perceptions of Perinatal Mental Health), there is evidence of gaps in the perinatal mental health literacy among perinatal women and doctors in terms of their knowledge, attitudes, and practices. Additionally, most participants value the outcomes, viz recommendations for care of women during the childbearing period.

### **Balance of effects**

Does the balance between desirable and undesirable effects favour the option or the comparison?

### **Research evidence**

Based on the findings of I-MUM and I-DOC, most participants will benefit from recommendations.

### **Resources required**

How large are the resource requirements (costs)?

### **Research evidence**

Public will benefit from educational and outreach efforts to build awareness and easy understanding and reference.

Healthcare providers will require scientific report and educational lectures or workshops to improve skills in delivering the recommendations. To meet these needs, publication of the guidelines will follow, and ongoing educational efforts to disseminate knowledge and understanding, beginning with the IPRAMHO Conference on Feb 2023, when the guidelines will be launched.

Long-term improvement in maternal and child health and wellbeing will result in considerable savings in healthcare expenditure.

### **Certainty of evidence of required resources**

What is the certainty of the evidence of resource requirements (costs)?

### **Research evidence**

Long-term improvement in maternal and child health and wellbeing result in considerable savings in healthcare expenditure.

This is assumed to be similar to existing lifestyle-related campaigns (e.g. War on Diabetes)

### ***Cost-effectiveness***

Does the cost-effectiveness of the option favour the option or the comparison?

### **Research evidence**

The investment in the public and healthcare provider education of these recommendations likely will reduce the overall healthcare costs considerably. This is similar to existing lifestyle-related campaigns.

### ***Equity***

What would be the impact on health equity?

### **Local and Research evidence**

These recommendations are available to all mothers and mothers-to-be in the community.

Already, collaborative efforts are ongoing with Health Promotion Board to enable the outreach to public. The validated screening tool EPDS is available on the national health promotion site HealthHub.

These recommendations can be delivered to primary care, tertiary care and related organisations.

Already, dissemination of these guidelines is slowly being effected through the various professional bodies, namely Singapore Psychiatric Association, College of Psychiatrists, College of Obstetrician and Gynaecologists, Perinatal Society, College of Family Physicians

### ***Acceptability***

Is the option acceptable to key stakeholders?

### **Research evidence**

The option is acceptable to key stakeholders as there are existing lifestyle-related recommendations and practice especially amongst professional groups with more experience.

Consensus was sought from an interprofessional group in Nov 2022, with the guidelines largely acceptable, with minor amendments which have been incorporated, and reviewed by the various professional bodies endorsing the guidelines

### ***Feasibility***

Is the option feasible to implement?

### **Research evidence**

The option is likely feasible to implement as this approach is similar to existing lifestyle-related programmes and campaigns. Already, initial steps are underway to communicate and share the guidelines.

## CONCLUSIONS

### Summary of judgements

Problem	- Don't know	- Varies		- No	- Probably No	- Probably Yes	- Yes
Desirable effects	- Don't know	- Varies		- Trivial	- Small	- Moderate	- Large
Undesirable effects	- Don't know	- Varies		- Large	- Moderate	- Small	- Trivial
Certainty of evidence	- Don't know			- Very low	- Low	- Moderate	- High
Values				- Important uncertainty or variability	- Possible important uncertainty or variability	- Probably no Important uncertainty or variability	- No important uncertainty or variability
Balance of effects	- Don't know	- Varies	- Favours the comparison	- Probably favours the comparison	- Does not favour either the option or the comparison	- Probably favours the option	- Favours the option

Resources required	- Don't know	- Varies	- Large costs	- Moderate costs	- Negligible costs of savings	- Moderate savings	- Large savings
Certainty of evidence of required resources	- No included studies			- Very Low	- Small	- Moderate	- High
Cost-effectiveness	- Don't know	- Varies	- Favours the comparison	- Probably favours the comparison	- Does not favour either the option or comparison	- Probably favours the option	- Favours the option
Equity	- Don't know	- Varies	- Reduced	- Probably reduced	- Probably no impact	- Probably increased	- Increased
Acceptability	- Don't know	- Varies		- No	- Probably No	- Probably Yes	- Yes
Feasibility	- Don't know	- Varies		- No	- Probably No	- Probably Yes	- Yes





### ***Type of recommendation***

#### ***Recommendation***

1. Increase Awareness and Provide Advice of Preconception Mental Health
  - A. Provide advice on pregnancy planning
  - B. Have preconception counselling on impact of maternal mental illness and treatment
  
2. Optimise Preconception Mental Health
  - A. Make lifestyle adjustments to optimise preconception mental health
  - B. Evaluate medication use in consideration of childbearing. Have a holistic approach to preconception mental health
  
3. Have Screening and Assessment for Antenatal Depression/ Anxiety
  - A. Provide screening for antenatal depression/anxiety
  - B. Have assessment of antenatal depression/anxiety
  
4. Optimise care, treatment & support for antenatal depression/ anxiety
  - A. Counsel on medication use in antenatal depression/ anxiety
  - B. Provide holistic approach to care for patients with antenatal depression/ anxiety
  - C. Provide monitoring and support for women receiving care for antenatal depression/anxiety
  
5. Have Screening and assessment for postnatal depression/ anxiety
  - A. Provide screening for postnatal depression and anxiety
  - B. Have assessment of postnatal depression and anxiety:
  
6. Optimise care, treatment and support for postnatal depression/ anxiety
  - A. Evaluate medication use in postnatal depression/ anxiety
  - B. Have a holistic approach towards care for patients with postnatal depression/ anxiety
  - C. Provide monitoring and support for women receiving care for postnatal depression/ anxiety
  
7. Provide mental health support in severe maternal events and those with mental health needs
  
8. Tailor perinatal mental healthcare for adolescents and women with special needs
  
9. Promote higher caregiving quality for perinatal and infant physical and mental health needs

10. Aim to integrate the above recommendations into healthcare framework for the best results.

***Justification***

The guidelines document recommendations to improve the maternal and child health outcomes in Singapore, by adopting a holistic approach towards integrating care during the preconception, antenatal and postnatal periods. The early recognition of women at risk in the perinatal period and provision of care by addressing medical and psychosocial aspects, as well as attending to healthy lifestyle adjustments, with relevant attention to special populations and vulnerable groups, can help to achieve optimal population health.

## Detailed Justification

<ul style="list-style-type: none"> <li>*Problem</li> <li>*Desirable effects</li> <li>Undesirable effects</li> <li>*Certainty of evidence</li> <li>Values</li> <li>Balance of effects</li> <li>Resources required</li> <li>Certainty of evidence off required resources</li> <li>*Cost-effectiveness</li> <li>Equity</li> <li>*Acceptability</li> <li>Feasibility</li> </ul>	<p><b>Problem</b></p> <p>Perinatal mental health, along with preconception mental health, which is correlated with antenatal mental health, has adverse impact on maternal and child health outcomes. Lifestyle adjustments and early detection and intervention, targeting medical and psychosocial needs can improve population health outcomes.</p> <p><b>Desirable effects</b></p> <p>There is at least moderately certain evidence to support the incorporation of recommended strategies to promote preconception, antenatal and postnatal mental health.</p> <p><b>Certainty of evidence</b></p> <p>There is at least moderately certain evidence to support the recommendations, and the evidence consisted of many systematic reviews with good number of studies or participants</p> <p><b>Cost-effectiveness</b></p> <p>Lifestyle adjustments and early intervention will likely reduce overall healthcare costs in the future</p> <p><b>Acceptability</b></p> <p>Recent surveys of mothers (I-MUM) and care providers(I-DOC) have evidenced value in greater understanding, and need for perinatal mental health literacy</p> <p>These guidelines have been reviewed in consensus, and have been endorsed by the College of Obstetricians and Gynaecologists, College of Family Physicians, Perinatal Society, Singapore Psychiatric Association, College of Psychiatrists, Health Promotion Board</p>
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