

Multiple modifiable lifestyle factors and the risk of perinatal depression during pregnancy: Findings from the GUSTO cohort

Linde van Lee^{a,1}, Airu Chia^{b,c,a,1}, Desiree Phua^a, Marjorelee Colega^a, Natarajan Padmapriya^b, Jonathan Y. Bernard^{a,d}, Shirong Cai^{a,b}, Elaine K.H. Tham^a, Oon Hoe Teoh^e, Daniel Goh^f, Joshua J. Gooley^g, Peter D. Gluckman^{a,h}, Fabian Yap^{e,i,j}, Lynette P.C. Shek^{a,f}, Keith M. Godfrey^k, Kok Hian Tan^{i,l}, Yap-Seng Chong^{a,b}, Falk Müller-Riemenschneider^{c,m}, Birit Broekman^{a,n,o}, Michael Meaney^{a,p}, Helen Chen^q, Mary F.F. Chong^{a,c,r,*}

^a Singapore Institute for Clinical Sciences, Agency for Science, Technology and Research, Singapore

^b Department of Obstetrics and Gynaecology, Yong Loo Lin School of Medicine, National University of Singapore, Singapore

^c Saw Swee Hock School of Public Health, National University of Singapore, Singapore

^d Early Life Research On Later Health Unit, Centre for Research in Epidemiology and Statistics Sorbonne Paris Cité (CRESS), National Institute of Health and Medical Research (Inserm), Villejuif, France

^e Department of Paediatrics, KK Women's and Children's Hospital, Singapore

^f Department of Pediatrics, Yong Loo Lin School of Medicine, National University of Singapore, Singapore

^g Center for Cognitive Neuroscience, Program in Neuroscience and behavioural disorders, Duke-NUS Medical School, Singapore

^h Liggins Institute, University of Auckland, Auckland, New Zealand

ⁱ Duke-NUS Medical School, Singapore, Singapore

^j Lee Kong Chian School of Medicine, Nanyang Technological University, Singapore, Singapore

^k MRC Lifecourse Epidemiology Unit and NIHR Southampton Biomedical Research Centre, University of Southampton and University Hospital Southampton NHS Foundation Trust, Southampton, UK

^l Department of Maternal Fetal Medicine, KK Women's and Children's Hospital, Singapore

^m Institute for Social Medicine, Epidemiology and Health Economics, Charité University Medical Centre, Berlin, Germany

ⁿ Department of Psychiatry, Amsterdam UMC, location VUmc, VU University, Amsterdam, the Netherlands

^o Department of Psychiatry, Onze Lieve Vrouwe Gasthuis, Amsterdam, the Netherlands

^p Departments of Psychiatry and Neurology and Neurosurgery, McGill University, Montreal, Canada

^q Department of Psychological Medicine, KK Women's and Children's hospital, Singapore

^r Clinical Nutrition Research Centre, Agency for Science, Technology and Research, Singapore

ARTICLE INFO

Available online xxxx

Keywords:

Perinatal Depression
Pregnancy
Lifestyle Behaviours
Diet
Physical Activity
Smoking
Sleep Quality

ABSTRACT

Background: Studies have identified lifestyle risk factors for perinatal depression, but none have examined the cumulative effect of these risk factors in pregnant women.

Methods: We considered the following six factors during pregnancy: poor diet quality (Healthy eating index for Singapore pregnant women < median), poor sleep quality (global Pittsburgh sleep quality index score > 5), physical inactivity (< 600 MET-minutes/week), vitamin D insufficiency (< 50 nmol/l), smoking before or during pregnancy, and the perceived need for social support. Probable depression was assessed using the Edinburgh postnatal depression scale during pregnancy (> 15) and at three months postpartum (≥ 13). Prevalence risk ratios were calculated with Poisson regressions while adjusting for potential confounders.

Results: Of 535 pregnant women, 207 (39%) had zero or one risk factor, 146 (27%) had two, 119 (22%) had three, 48 (9%) had four, and 15 (3%) had ≥ 5 risk factors at 26–28 weeks' gestation. 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; $p_{\text{trend}} < 0.001$) 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 ($p_{\text{trend}} = 0.746$).

Conclusion: Pregnant women with ≥ 4 lifestyle risk factors showed a higher prevalence of depression during pregnancy, while no associations were observed for postpartum depression.

Clinical trial registration: This cohort is registered under the Clinical Trials identifier NCT01174875; <http://www.clinicaltrials.gov/ct2/show/NCT01174875?term=GUSTO&rank=2>

* Corresponding author at: Saw Swee Hock School of Public Health, National University of Singapore, Tahir Foundation Building, 12 Science Drive 2, #09-01Q, 117549, Singapore.
E-mail address: Mary_Chong@nus.edu.sg (M.F.F. Chong).

¹ contributed equally to this work

1. Introduction

Maternal mental well-being during and after pregnancy is of great importance for the overall health of mothers and their offspring. Previous studies have reported higher risks of pre-eclampsia, loss of productivity, unfavourable parenting practices, family repercussion, and impaired mother-infant bonding in women with depression at 20 weeks gestation and 3 months postpartum [1]. Moreover, antepartum depression (between 12 and 36 weeks of gestation) has been associated with higher risk of depression and obesity in the offspring during childhood [2]. Estimations suggest that 10 to 20% of women experience depressive symptoms during pregnancy or after delivery [3], making perinatal depression a substantial public health problem [4].

Multiple lifestyle factors have been associated with the risk of depression in general; including substance abuse, smoking, nutrition, sleep, physical activity, vitamin D and social support [5], whereas changes in social, psychological and hormonal levels during pregnancy are risk factors more specifically for perinatal depression [6]. Previously, we demonstrated that higher physical activity level, good sleep quality, and better nutritional status were independently associated with lower risk of depressive symptoms in pregnant women [7–11], which is consistent with findings in the literature [12–14]. These lifestyle behaviours are interrelated and may have synergistic effects on the risk of mental disorders [15–17]. Examination of behavioural patterns may therefore be useful to formulate effective integrated prevention or treatment approaches for depression [18].

To date, four cross-sectional studies have examined the combination of multiple lifestyle factors on the risk of depression in adults and showed mixed results. Pronk et al. have shown that adherence to three to four optimal lifestyle behaviour was associated with a 1.5 times lower likelihood of feeling depressed as compared to adherence to none or one optimal behaviour in 34,603 predominantly white employees [15]. Secondly, American adults who only adhered to zero to three health practices had a 3.3 times higher risk of depression as compared to participants adhering to six to seven health practices [19]. Moreover, middle-aged men and women who adhered to zero or one protective lifestyle behaviours had a 2.2 times higher risk of depression as compared to those adhering to four behaviours [20]. However, no association was found between the combination of seven health-related lifestyle practices and the risk of severe depression in 254 Japanese factory workers [21]. None of these studies or others have specifically studied the cumulative associations of multiple health behaviours and perinatal depression: a vulnerable period in which mood disorders may have a significant impact on both mother and child health in later life [1,2].

To fill this gap in literature, we aimed to investigate the cumulative risk of the lifestyle behaviours on depressive symptoms during pregnancy and after delivery. We selected the following six modifiable lifestyle factors based on previous findings from our cohort [7–11] and the literature [22–26]: poor diet quality, insufficient vitamin D status, smoking habits, insufficient physical activity, poor sleep quality, and perceived need for social support. We hypothesized that there would be a positive linear association between the number of poor lifestyle behaviours assessed during pregnancy and depressive symptoms assessed in the late second trimester of pregnancy and at 3 months postpartum.

2. Methods

2.1. Study design and participants

The Growing Up in Singapore Towards healthy Outcomes (GUSTO) cohort study recruited 1247 pregnant Singapore citizens or permanent

residents in their first trimester during the period between June 2009 and September 2010. They were two major public hospitals in Singapore. Inclusion criteria included women of Chinese, Malay or Indian descent and participant's parents and spouse's parents of the same ethnic origin, ages 18 to 50 years with the intention to live in Singapore for the following 5 years and intention to deliver in one of the two major maternity units in Singapore; and willing to donate cord, cord blood and placenta. Persons with pre-existing serious health conditions including psychoses and type I diabetes or who were receiving chemotherapy or psychotropic drugs were excluded from participation. Further detailed information on recruitment and eligibility criteria has been reported previously [27]. The study was approved by the National Healthcare Group Domain Specific Review Board (reference number D/09/021) and the Sing Health Centralised Institutional Review Board (reference number 2009/280/D) and written informed consent was obtained from all participants at inclusion.

2.2. Depressive symptoms

Depressive symptoms were self-reported using the Edinburgh Postnatal Depression Scale (EPDS) at 26–28 weeks' gestation and 3 months postpartum. The EPDS is a 10-item screening tool that rates the intensity of depressive symptoms in the preceding seven days [28]. It is a well-known and validated instrument for use in the perinatal period [29] and showed good reliability of 0.82 by means of Cronbach's analyses in our cohort [30]. Participants were considered at high risk for probable depression when having EPDS scores ≥ 15 during pregnancy or EPDS scores ≥ 13 postpartum based on previously published normative values [29].

2.3. Lifestyle risk factors

In this study, we selected behavioural risk factors that have been independently associated with depression during and after pregnancy within the GUSTO cohort; sleep quality and physical activity [7,8]. We chose to include diet quality to reflect the dietary components (omega-3 and omega-6 fatty acids, choline, and folate) that were previously demonstrated to be associated with antepartum depression in the GUSTO cohort [9–11]. Moreover, diet quality has consistently shown inverse associations with depression in literature [22,23]. In addition, on the basis of previous literature, we included smoking habits, vitamin D, and social support [24–26], which we observed to be significantly associated with depression in additional unpublished analyses on the GUSTO cohort (Supplemental table 1). Although alcohol use was suggested an important risk factor for depression [5], we did not include it, because the rate of self-reported habitual alcohol intake during pregnancy was low in our study sample (<2%).

2.4. Diet quality

Dietary intake at 26–28 weeks gestation was assessed by a face-to-face 24-h recall using the validated five-step multiple pass interviewing technique to increase accuracy [31]. Visual aids were used to increase the accuracy of reported food portions. Energy and nutrient intakes were, thereafter, calculated using a local food composition database [32], the USDA food composition database [33] and information from food labels. The dietary intake was used to calculate diet quality as defined by the Healthy Eating Index for pregnant women in Singapore (HEI-SGP) that reflects the Singapore dietary guidelines for pregnant women [34]. Briefly, the HEI-SGP comprises 11 components: total fruit, whole fruit, total vegetables, dark green, leafy, and orange

vegetables, total rice and alternatives, whole grains, dairy, total protein foods, use of antepartum supplements, total fat, and saturated fat. Total fruit, whole fruit, total vegetables, and dark green, leafy, and orange vegetables were scored between 0 and 5 and the remaining seven components were scored between 0 and 10 resulting in a total summed score of 0–90, which was converted to a 0–100 scale for easier interpretation. Higher scores on the HEI-SGP correspond to greater adherence to the dietary recommendations. Within the GUSTO study sample, the HEI-SGP was able to rank participants based on their macro- and micronutrient intakes [34] and to date, has been related to sleep quality [35], infant birth outcomes [36], and retinal microvasculature abnormalities [37]. We used scores below the median of the HEI-SGP score (52.2 points) to define poor diet quality, as no standard cut-off value is yet available.

2.5. Lifestyle questionnaires (sleep, need for emotional support, smoking habits, physical activity)

At 26–28 weeks gestation, participants were asked to complete multiple questionnaires during the clinic visit. Sleep quality was assessed using the validated Pittsburgh Sleep Quality Index [38] in a random subsample of the study population. This questionnaire contains 19 items used to derive 7 components on a 0–3 scale (subjective sleep quality, sleep latency, sleep duration, sleep efficiency, sleep disturbances, use of sleep medications, and daytime dysfunction) resulting in a summed global score ranging from 0 to 21; higher scores represent poorer subjective sleep quality. Poor sleep quality was defined as having a global PSQI score higher than five [38] based on previous published normative values [38,39].

Need for emotional support was assessed in another random subsample of the study population by the question “During the last two weeks, did you feel that you needed someone to give you feedback, that is, to approve you or tell you that you have made the right choice or right decision?”. Response options for the question were ‘yes’ or ‘no’.

Smoking habits were assessed before and during pregnancy in all participants. Women who smoked before or during pregnancy were considered smokers.

Questions on physical activity level included light-moderate, moderate and vigorous intensity activities during the first 6 months of pregnancy. Frequency and duration for each intensity level were obtained, then converted into total weekly durations and finally into Metabolic Equivalent Task (MET) values (3.3, 4.0 and 8.0 MET-hour for light-moderate, moderate, and vigorous intensities, respectively) in line with the International Physical Activity Questionnaire short form as described in a previous publication [40]. Total MET was calculated and being insufficiently active was defined as less than 600 MET-minutes/week as per the WHO recommendations [41].

2.6. Vitamin D status

A venepuncture was drawn during the clinic visit at 26–28 weeks’ gestation. Plasma blood samples were analysed for 25(OH)D2 and 25(OH)D3 by isotope-dilution liquid chromatography-tandem mass spectrometry (Applied Biosystems, California, US). The intra- and inter-assay coefficient of variation for both metabolites were < 10.3%. Detailed information on extraction and assessment methods have been published previously [42]. Insufficient vitamin D was defined as plasma concentrations <50 nmol/l according to the standards of the Endocrine Society clinical practice guidelines [43] and was previously used within the GUSTO cohort [44].

2.7. Covariates

Questions on demographics including age, ethnicity, marital status, education level, household income, employment status, and parity were administered during the clinic visit at 26–28 weeks gestation or during the recruitment phase. Anxiety was assessed during pregnancy

using the State-Trait Anxiety Inventory [45]. Probable anxiety was defined as a STAI-state antenatal score ≥ 41 , which was the top 75th percentile of the population under study. Perceived stress was asked during the clinic visit at 26–28 weeks’ gestation as follows: “In general how much stress or pressure have you experienced in your daily living in the last 4 weeks?” and recorded on a 4-point Likert scale, where four points indicated the most stress.

2.8. Statistical analyses

In total, 1247 pregnant women were recruited, of whom those with missing values for the lifestyle risk factors ($n = 709$; Fig. 1) or missing data for the EPDS (antepartum $n = 3$, postpartum $n = 179$) were excluded, resulting in an analytical antepartum sample of 535 participants and postpartum sample of 356 participants. A comparison between the included and excluded participants can be found in Supplemental table 2. The participants in the analytical antepartum sample had higher education levels and household income as compared to the excluded participants. No differences between included and excluded participants were observed for age, pre-pregnancy BMI, ethnicity and probable antepartum depression, and probable anxiety. These were similar for the analytical postpartum sample (results not shown).

Characteristics of the sample were presented according to having probable antepartum depression or not. Differences between groups were computed using independent samples *t*-test, Mann-Whitney *U* test for non-normal distributed variables or chi-square for categorical variables.

The lifestyle risk factors were dichotomized into high versus low risk as described earlier (also see: Table 1) and the number of high-risk lifestyle factors was summed. Women with 4 or more risk factors were combined due to low number of persons with depressive symptoms, and those with one or no risk factor were combined due to the lack of depression cases in the lowest category.

Poisson regression analyses with robust variance were used to calculate the relative risk of being probably depressed during pregnancy (outcome) for each number of lifestyle risk factors (exposure). Statistical models were adjusted for ethnicity (Chinese, Malay, Indian), education level (primary/secondary, postsecondary, university), age (years), household income (S\$ 0–1999, S\$ 2000–5999, S\$ ≥ 6000), employment status (unemployed/employed), and parity (first/>1 children). The analyses for postpartum depression were additionally adjusted for

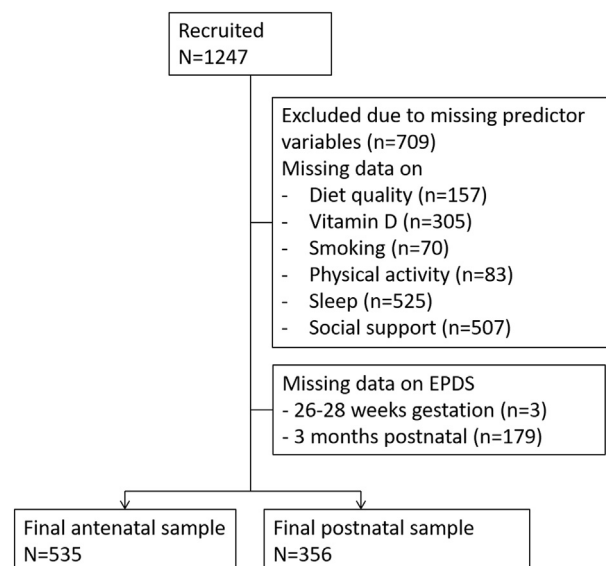


Fig. 1. Flow chart of study participants.

Table 1
Prevalence and criteria of lifestyle risk factors in 535 expecting women.

Risk factors	Criteria	Prevalence (n, %)	95% CI
Smoking habits	Smoking pre-pregnancy or during pregnancy	69, 12.8%	0.10, 0.16
Insufficient plasma vitamin D	< 50 nmol/l	71, 13.2%	0.11, 0.16
Physical inactive	< 600 MET-minutes/week	197, 36.6%	0.33, 0.41
Poor sleep quality	Global PSQI score > 5	234, 43.5%	0.39, 0.48
emotional support	The perceived need for feedback, approval or reassurance from someone	249, 46.3%	0.42, 0.51
Poor diet quality	HEI-SGP < median (HEI SGP score < 52.2)	257, 47.8%	0.44, 0.52

HEI-SGP, healthy eating index for pregnant women in Singapore; MET, Metabolic equivalents of task; PSQI, Pittsburgh sleep quality index.

antepartum depression assessed at 26–28 weeks gestation. The explained variance (*r*-squared) was obtained for each of the single lifestyle risk factors and combinations of these factors in the relation with depressive symptoms using linear regression.

To explore the robustness of our results, we additionally examined the poor diet quality definition by using the <75th percentiles as the cut-off value (HEI < 61.6) and antenatal minor depression definition (EPDS score > 10) in sensitivity analyses. Also, we further examined the potential confounding effect of marital status and perceived stress in daily life and the possibility of effect modification of ethnicity by including an interaction term between ethnicity and lifestyle risk factors. To distinguish poor sleep due to depressive symptoms from sleep disturbance due to pregnancy, we further excluded those that mentioned having difficulties sleeping most of the time in the EPDS questionnaire (*n* = 19). Lastly, we examined multicollinearity of our statistical model by computing the variance inflation factor.

Missing values for the covariates (i.e. education (*n* = 21), household income (*n* = 34), employment status (*n* = 9) and parity (*n* = 1)) were imputed by chained equations on 20 imputed datasets. These regression models additionally included the lifestyle risk factors and depression status and all covariates for better prediction [46]. The results of the 20 datasets were pooled. Sensitivity analyses showed only minor changes in results while using imputed data as compared to omitting participants who had missing values in the covariates. Stata SE version 14.2 (StataCorp LP, Chicago, USA) was used for all analyses and *p*-value < 0.05 was used to define statistical significance.

3. Results

The prevalence of the single lifestyle risk factors was 59 (11%) for none of the risk factors, 148 (28%) for one risk factor, 146 (27%) for two, 119 (22%) for three, 48 (9%) for four, and 11 (2%) for 5, and 4 (1%) for all risk factors at 26–28 weeks gestation (Table 1). We observed the lowest prevalence for smoking before and during pregnancy (13%) and vitamin D insufficiency (13%); whereas almost half of the sample reporting poor sleep quality (44%), poor diet quality (48%) and the perceived need for emotional support from someone (46%). About a third of the sample (37%) reported being insufficiently active according to the WHO recommendations.

Pregnant women who were categorised as having probable antepartum depression (*n* = 38) had a median of three risk factors (25–75th percentiles: 2–4), whereas non-depressed women reported a significantly lower median of two risk factors (25–75th percentiles: 1–3, *p* < 0.001) (Table 2). These probable-depressed women were, furthermore, more likely to have poorer diet quality, sleep quality, to be a smoker, in need of emotional support, younger, less educated, anxious, of Malay descent and reported a lower household income as compared to women without antepartum depression. There were no differences detected between women with and without probable depression for pre-pregnancy BMI, energy intake, employment status, pre-pregnancy alcohol intake, parity, physical activity, and vitamin D concentrations.

For every increase of one risk factor, we observed and a higher prevalence of antepartum depression (Table 3) in the adjusted model. Compared to those with zero or 1 risk factor, participants with ≥4 risk factors

Table 2
Baseline characteristics* of 535 study participants according to having antepartum probable depression.

	Probable depression	No depression	
	EPDS ≥ 15 (<i>n</i> = 38)	EPDS < 15 (<i>n</i> = 497)	<i>p</i> for difference
Age (y)	28.4 (1.1)	30.8 (0.2)	0.008
Pre-pregnancy BMI (kg/m ²)	23.2 (0.8)	22.6 (0.2)	0.471
Energy intake (kcal)	1738.5 (108.5)	1888.3 (25.4)	0.122
Employed	65.7%	75.2%	0.229
Education			0.001
Primary/secondary	47.1%	23.1%	
Postsecondary	14.7%	10.8%	
University	38.2%	66.0%	
Household income			<0.001
S\$ 0–1999	28.6%	10.9%	
S\$ 2000–5999	34.3%	25.5%	
S\$ ≥ 6000	37.1%	63.5%	
Ethnicity			0.002
Chinese	26.3%	55.3%	
Malay	42.1%	26.0%	
Indian	31.6%	18.5%	
pre-pregnancy alcohol intake	36.8%	38.1%	0.877
First child	60.5%	55.9%	0.572
Probable anxiety	83.8%	19.3%	<0.001
HEI-SGP	46.0 (2.1)	53.4 (0.6)	0.002
Vitamin D (nmol/l)	73.2 (3.8)	81.7 (1.2)	0.066
Smoking (y/n)	29.0%	11.7%	0.011
Physical activity (MET-minutes/week)	1039 (297–2772)	891 (329–2079)	0.604
PSQI global score	8.8 (0.6)	5.2 (0.12)	<0.001
need for emotional support (y/n)	65.8%	44.5%	0.002
Number of risk factors	3 (2–4)	2 (1–3)	<0.001

*Mean (SE), median (25–75th percentile) or % from pooled analyses.

EPDS: Edinburgh postnatal depression scale; HEI-SGP: Healthy Eating Index - Singapore. Probable Anxiety was defined as STAI-state antenatal score ≥ 41.

had a 6-fold [PR 6.4 (95%CI 2.1, 19.8)] higher prevalence of antepartum depression, as compared to those with 0 or 1 risk factor. The linear trend was highly significant (*p*_{trend} < 0.001). We observed no linear association between the number of lifestyle risk factors and depressive symptoms at three months postpartum (≥4 factors: *p*_{trend} = 0.715; Table 3).

Next, we examined which lifestyle risk factors were driving the association with depression by explaining the most variance in our analytical sample. We observed that sleep quality was the most important predictor (*r*² = 0.28; Table 4), whereas vitamin D concentrations and MET-minutes of physical activity contributed the least to the variance explained. The explained variance increased from 10% (including only the covariates) to 32% by combining all lifestyle risk factors.

Sensitivity analyses showed that defining poor diet quality using the 75th percentile gave similar results when examining the number of lifestyle factors on perinatal depressive symptoms (Supplemental Table 3). Additional adjustment for marital status or perceived daily stress did not alter our results meaningfully (data not shown) and no effect modification by ethnicity was observed (interaction term for antenatal depression *P* = 0.728). Excluding those who reported severe

Table 3

Prevalence ratios (PR)* between depressive symptoms as assessed by EPDS and the number of lifestyle risk factor score.

		Probable depression at 26–28 weeks' gestation							Probable depression at 3 months postpartum						
		Crude			Multivariate adjusted				Crude			Multivariate adjusted†			
	n	PR	95% CI	p	PR	95% CI	p	n	PR	95% CI	p	PR	95% CI	p	
0–1	207	0.00	Ref	–	0.00	Ref	–	141	0.00	Ref	–	0.00	Ref	–	
2	146	1.98	0.64, 6.14	0.234	1.82	0.59, 5.61	0.298	100	1.69	0.76, 3.77	0.198	1.38	0.62, 3.07	0.425	
3	119	4.52	1.65, 12.39	0.003	3.44	1.12, 10.59	0.032	72	0.98	0.35, 2.76	0.968	0.61	0.22, 1.73	0.353	
4–6	63	8.54	3.16, 23.06	<0.001	6.43	2.09, 19.77	0.001	43	2.62	1.10, 6.23	0.029	1.72	0.68, 4.31	0.250	
B trend‡	535	2.06	1.51, 2.75	<0.001	1.87	1.32, 2.63	<0.001	356	1.26	0.94, 1.69	0.116	1.06	0.78, 1.43	0.715	

* Adjusted for age, ethnicity, educational level, household income, employment status, and parity.

† Additionally adjusted for depressive symptoms at 26–28 weeks' gestation.

‡ Determined by linear regression of probable depression on a continuous lifestyle factor score.

Table 4

The cumulative explained variance of single lifestyle factors on depressive symptoms in 535 expecting women*.

Lifestyle risk factors	R ²
0.	0.103
1. HEI-SGP	0.112
2. Vitamin D	0.103
3. Smoking	0.119
4. Sleep	0.278
5. Physical activity level	0.104
6. Social support	0.135
4 & 6	0.307
1 & 4 & 6	0.310
1 & 4 & 5 & 6	0.311
1 & 3 & 4 & 5 & 6	0.316
All	0.318

* Including the covariates: age, ethnicity, educational level, household income, employment status and parity.

sleeping difficulties did not change our results (**Supplemental Table 4**). No issues with multicollinearity were observed showing by the mean variance inflation factor of 1.65 and none of the correlations between the lifestyle behaviours were greater than 0.13.

4. Discussion

We observed that pregnant women with ≥ 4 risk factors had at least a 6-fold higher prevalence of having antepartum probable depression compared to those having zero or one risk factor, while no association was observed for postpartum depression. This combination of six lifestyle factors accounted for over a third of the variance in antepartum depressive symptoms. To the best of our knowledge, we are the first to study the relationships of a combination of multiple, modifiable lifestyle risk factors (diet quality, vitamin D concentrations, smoking, physical activity, sleep quality, and need for emotional support) with mental well-being during the perinatal period.

Our findings are consistent with previous findings from non-pregnant adults, showing that being exposed to multiple lifestyle risk factors is related to an increased prevalence of depression, ranging from a 1.5- to 3.3-fold increased prevalence comparing the persons with the highest to the lowest number of risk factors [15,19,20]. Another study did not show an association between the combination of lifestyle behaviours and reported severe depression in Japanese factory male workers, but observed a significant inverse relationship with depression as assessed with the Self-rating Depression Scale and overall mental health in those older than 40 years [21]. Most of the lifestyle risk factors examined in these studies (e.g., smoking, alcohol drinking, breakfast consumption, sleep duration, work hours, physical activity, subjective stress, and diet) were similar to our selected risk factors.

Sleep appeared to be the strongest contributor to depressive symptoms according to the variance explained in our statistical model. This

might not be surprising, as women during pregnancy may experience difficulty sleeping due to normal changes of pregnancy in her body such as hormonal changes, need to urinate more frequently, abdominal discomfort, leg cramps, back pain and anxiety for labour and delivery. Women with multiple symptoms may face greater difficulties sleeping [47]. However, poor sleep is a hallmark feature of mood disorders [48] and might have common causes [49]. It was reported in a meta-analysis of 17 studies that non-depressed subjects with insomnia had a twofold higher prevalence to develop depression compared to subjects without sleep difficulties. These suggest that programs on mental well-being during pregnancy could include emphasis on sleep habits and improvement of sleep hygiene practices through environmental changes, or behavioural therapies [47], alongside other lifestyle changes. However, we acknowledge that the directionality of this association cannot be made from this study, and more research is needed.

The six lifestyle habits contributed 32% to the variance of depressive symptoms in our study population, meaning that 68% of the variance was still unaccounted for. When compared to another study conducted in older persons, our finding was higher than a reported explained variance of 17.6% in psychological stress ratings by social support and sleep, but similar to the 35% explained variance in quality of life ratings by psychological stress and functional limitations [50]. We only considered modifiable behaviours for prevention or co-treatment purposes and may have excluded important risk factors that are not easily modifiable. For example life stress (i.e. important psychologically life events such as death or divorce), childhood adversities, satisfaction at work, unintended pregnancy, and insurance status have been suggested as important risk factors for antepartum depression [51]. Moreover, longer duration of depressive episode, and family history of mood disorders appeared to be important risk factors in previously published studies in non-pregnant populations [52].

Similar to our previous findings in the GUSTO cohort in which lifestyle factors were examined individually [7,9–11], we observed no linear association between the combination of risk factors with postpartum depression. In our prior work, however, poor sleep quality during pregnancy showed an association with depressive symptoms at 3 months postpartum in the GUSTO cohort [8]. Our null findings for postpartum depressive symptoms might be explained by the major changes in lifestyle habits (i.e. dietary intake and physical activity) after the delivery, potentially caused by coping with a newborn and higher nutritional needs for recovery from the delivery and breastfeeding, that might be stronger predictors for postpartum mental well-being [53,54]. In addition, a third of our study sample did not complete the postpartum depression questionnaires (3 months postpartum $n = 179$), which may have resulted in selection bias and loss of statistical power.

Lifestyle factors are often clustered and intertwined in multidimensional behavioural patterns. For example, people who adhere to the physical activity recommendations are more likely to also consume healthy diets [17]. Prior studies have reported 'healthy' clusters comprising persons who reported a physically active life, healthy diet, and no smoking [55], or inversely high-risk clusters of poor health behaviours

for sleep, fruit and vegetable intake, physical activity, sexual behaviour, drug use, and alcoholic beverages [56]. In addition, lifestyle habits are known to be patterned among demographical variables; healthy lifestyles are commonly found in those who are older, and have a higher socio-economic status [55], which agrees with our study. We observed that those that had none, or one risk factor were more likely to be older, of Chinese descent, had university or higher degree, and higher household income as compared to those having multiple risk factors.

There are a number of plausible mechanisms underlying the relationship between lifestyle behaviours and depression. It was suggested that diet, vitamin D, and sleep may have an impact on neurotransmitter imbalances, HPA-axis disturbances, oxidative stress, neuro-progression, mitochondrial disturbances, and immune inflammation [24,57]. Physical activity has been associated with increases in β -endorphins release, neurotransmitter availability, and blood flow to the brain [57]. Lastly, the need for emotional support may contribute to lower stress levels [58].

A strength of the present study is the use of multiple modifiable lifestyle risk factors that may provide important information for future behavioural change interventions aimed at prevention or co-treatment of mental mood disorders during the perinatal period. Furthermore, we provided extensive information on multiple lifestyle habits, depression during the perinatal period and important confounders.

5. Limitations

This study has some limitations that merit attention. Our associations are largely cross-sectional and no conclusion on causality can be drawn. It is recognized that most lifestyle factors have bidirectional relationships with mental well-being [57], such that having a high likelihood of depression can in turn lead to poorer adoption of healthy lifestyles [59]. A randomized controlled trial has previously shown that lifestyle recommendations on sleep, exercise, diet and sunlight exposure significantly decreased depressive symptoms and lowered remission rates in 80 Spanish outpatients with major depression [60]. However, these findings are yet to be replicated. The value of modifying lifestyle behaviours as an approach to preventing or treating depressive symptoms will need to be further investigated using intervention studies. Secondly, the lifestyle habits were measured at 26–28 weeks gestation and may not accurately reflect late pregnancy or postpartum habits. Repeated measurements performed longitudinally would have strengthened our analyses and could have given insight into lifestyle changes during the perinatal period and its cumulative effect on the development of depression. Thirdly, we excluded persons who reported taking psychotropic drugs or having pre-existing mental disorders, thus generalizability to populations with more severe depression might be limited. Moreover, misclassification in depression status during the perinatal period is possible and may have attenuated our results. In the current study, 43% of the original sample of participants were included because the sleep and emotional support questionnaires were administered in a random subsample of the study population. Consequently, this led to a smaller study sample and low prevalence of depression, which could have under-powered our study, leading to underestimation of our results. Moreover, we acknowledge that using a single question to indicate emotional support and stress is not comprehensive and may be subjected to measurement error. Lastly, while our statistical models included many covariates known for their association between mood and lifestyle habits, our findings may be subject to residual confounding from unmeasured confounders. For example, need for emotional support from specifically the partner has been strongly related to depression during pregnancy and the first postpartum year [51,61], but this was not assessed in our cohort.

6. Conclusion

This study demonstrates that pregnant women with more lifestyle risk factors as compared to those having 1 or zero risk factors have an

increased prevalence of probable antepartum depression. No associations were observed between lifestyle factors and postpartum depression. These lifestyle risk factors are modifiable, suggesting that multi-component lifestyle behavioural interventions could provide a more holistic and comprehensive strategy for prevention or co-treatment of depressive symptoms in pregnant women and therefore possibly also postpartum depression. Our research should be replicated in longitudinal studies and the effectiveness of behavioural programs should be further examined in intervention studies.

Funding

This research is supported by the Singapore National Research Foundation under its Translational and Clinical Research (TCR) Flagship Programme and administered by the Singapore Ministry of Health's National Medical Research Council (NMRC), Singapore- NMRC/TCR/004-NUS/2008; NMRC/TCR/012-NUHS/2014. Additional funding is provided by the Singapore Institute for Clinical Sciences, Agency for Science Technology and Research (A*STAR), Singapore.

Acknowledgements

We would like to thank the participants and the GUSTO study group including: Allan Sheppard, Amutha Chinnadurai, Anne Eng Neo Goh, Anne Rifkin-Graboi, Anqi Qiu, Arijit Biswas, Bee Wah Lee, Birit F.P. Broekman, Boon Long Quah, Borys Shuter, Chai Kiat Chng, Cheryl Ngo, Choon Looi Bong, Christiani Jeyakumar Henry, Cornelia Yin Ing Chee, Yam Thiam Daniel Goh, Doris Fok, Fabian Yap, George Seow Heong Yeo, Helen Chen, Hugo P S van Bever, Iliana Magiati, Inez Bik Yun Wong, Ivy Yee-Man Lau, Jeevesh Kapur, Jenny L. Richmond, Jerry Kok Yen Chan, Joanna D. Holbrook, Joshua J. Gooley, Keith M. Godfrey, Kenneth Kwek, Kok Hian Tan, Krishnamoorthy Niduvaje, Leher Singh, Lin Su, Lourdes Mary Daniel, Lynette P Shek, Marielle V. Fortier, Mark Hanson, Mary Rauff, Mei Chien Chua, Michael Meaney, Mya Thway Tint, Neerja Karnani, Ngee Lek, Oon Hoe Teoh, P. C. Wong, Peter D. Gluckman, Pratibha Agarwal, Rob M. van Dam, Salome A. Rebello, Seang-Mei Saw, Shang Chee Chong, Shirong Cai, Shu-E Soh, Sok Bee Lim, Chin-Ying Stephen Hsu, Victor Samuel Rajadurai, Walter Stunkel, Wee Meng Han, Wei Pang, Yap-Seng Chong, Yin Bun Cheung, Yiong Huak Chan and Yung Seng Lee.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.comppsy.2020.152210>.

References

- [1] Andersson L, Sundstrom-Poromaa I, Wulff M, Astrom M, Bixo M. Implications of antenatal depression and anxiety for obstetric outcome. *Obstet Gynecol.* 2004;104: 467–76.
- [2] Gentile S. Untreated depression during pregnancy: short- and long-term effects in offspring. A systematic review. *Neuroscience.* 2017;342:154–66.
- [3] Tripathy P. A public health approach to perinatal mental health: improving health and wellbeing of mothers and babies. *J Gynecol Obstet Hum Reprod.* 2020;49: 101747.
- [4] Cuijpers P, Beekman AF, Reynolds CF. Preventing depression: a global priority. *JAMA.* 2012;307:1033–4.
- [5] Hidaka BH. Depression as a disease of modernity: explanations for increasing prevalence. *J Affect Disord.* 2012;140:205–14.
- [6] Gelaye B, Rondon MB, Araya R, Williams MA. Epidemiology of maternal depression, risk factors, and child outcomes in low-income and middle-income countries. *Lancet Psychiatry.* 2016;3:973–82.
- [7] Padmapriya N, Bernard JY, Liang S, Loy SL, Shen Z, Kwek K, et al. Association of physical activity and sedentary behavior with depression and anxiety symptoms during pregnancy in a multiethnic cohort of Asian women. *Arch Womens Ment Health.* 2016;19:1119–28.
- [8] Tham EK, Tan J, Chong YS, Kwek K, Saw SM, Teoh OH, et al. Associations between poor subjective prenatal sleep quality and postnatal depression and anxiety symptoms. *J Affect Disord.* 2016;202:91–4.

- [9] Chong MF, Ong YL, Calder PC, Colega M, Wong JX, Tan CS, et al. Long-chain polyunsaturated fatty acid status during pregnancy and maternal mental health in pregnancy and the postpartum period: results from the GUSTO study. *J Clin Psychiatry*. 2015;76:e848–56.
- [10] Chong MF, Wong JX, Colega M, Chen LW, van Dam RM, Tan CS, et al. Relationships of maternal folate and vitamin B12 status during pregnancy with perinatal depression: the GUSTO study. *J Psychiatr Res*. 2014;55:110–6.
- [11] Van Lee L, Quah EPL, Saw S-M, Yap F, Godfrey KM, Chong YS, et al. Maternal choline status during pregnancy, but not that of betaine, is related to antenatal mental well-being: the growing up in Singapore towards healthy outcomes cohort. *Depress Anxiety*. 2017;34:877–87.
- [12] Bei B, Coo S, Trinder J. Sleep and mood during pregnancy and the postpartum period. *Sleep Med Clin*. 2015;10:25–33.
- [13] Shivakumar G, Brandon AR, Snell PG, Santiago-Munoz P, Johnson NL, Trivedi MH, et al. Antenatal depression: a rationale for studying exercise. *Depress Anxiety*. 2011;28:234–42.
- [14] Sparling TM, Henschke N, Nesbitt RC, Gabrys S. The role of diet and nutritional supplementation in perinatal depression: a systematic review. *Matern Child Nutr*. 2016;13(1).
- [15] Pronk NP, Katz AS, Gallagher J, Austin E, Mullen D, Lowry M, et al. Adherence to optimal lifestyle behaviors is related to emotional health indicators among employees. *Popul Health Manag*. 2011;14:59–67.
- [16] RMv Dam, Li T, Spiegelman D, Franco OH, Hu FB. Combined impact of lifestyle factors on mortality: prospective cohort study in US women. *BMJ*. 2008;337.
- [17] Berrigan D, Dodd K, Troiano RP, Krebs-Smith SM, Barbash RB. Patterns of health behavior in U.S. adults. *Prev Med*. 2003;36:615–23.
- [18] Jacka FN, Mykletun A, Berk M. Moving towards a population health approach to the primary prevention of common mental disorders. *BMC Med*. 2012;10:149.
- [19] Frederick T, Frerichs RR, Clark VA. Personal health habits and symptoms of depression at the community level. *Prev Med*. 1988;17:173–82.
- [20] Maher GM, Perry CP, Perry JJ, Harrington JM. Protective lifestyle behaviours and depression in middle-aged Irish men and women: a secondary analysis. *Public Health Nutr*. 2016;19:2999–3006.
- [21] Suda M, Nakayama K, Morimoto K. Relationship between behavioral lifestyle and mental health status evaluated using the GHQ-28 and SDS questionnaires in Japanese factory workers. *Ind Health*. 2007;45:467–73.
- [22] Baskin R, Hill B, Jacka FN, O'Neil A, Skouteris H. The association between diet quality and mental health during the perinatal period. A systematic review. *Appetite*. 2015;91:41–7.
- [23] Baskin R, Hill B, Jacka FN, O'Neil A, Skouteris H. Antenatal dietary patterns and depressive symptoms during pregnancy and early post-partum. *Matern Child Nutr*. 2017;13.
- [24] Spedding S. Vitamin D and depression: a systematic review and meta-analysis comparing studies with and without biological flaws. *Nutrients*. 2014;6:1501.
- [25] Garipey G, Honkaniemi H, Quesnel-Vallee A. Social support and protection from depression: systematic review of current findings in Western countries. *Br J psychiatry J ment sci*. 2016;209:284–93.
- [26] Kim TH, Connolly JA, Tamim H. The effect of social support around pregnancy on postpartum depression among Canadian teen mothers and adult mothers in the maternity experiences survey. *BMC Pregnancy Childbirth*. 2014;14:162.
- [27] Soh SE, Tint MT, Gluckman PD, Godfrey KM, Rifkin-Graboi A, Chan YH, et al. Cohort profile: growing up in Singapore towards healthy outcomes (GUSTO) birth cohort study. *Int J Epidemiol*. 2014;43:1401–9.
- [28] Cox JL, Holden JM, Sagovsky R. Detection of postnatal depression. Development of the 10-item Edinburgh postnatal depression scale. *Br J psychiatry J ment sci*. 1987;150:782–6.
- [29] Gibson J, McKenzie-McHarg K, Shakespeare J, Price J, Gray R. A systematic review of studies validating the Edinburgh postnatal depression scale in antepartum and postpartum women. *Acta Psychiatr Scand*. 2009;119:350–64.
- [30] Rifkin-Graboi A, Bai J, Chen H, WBr Hameed, Sim LW, Tint MT, et al. Prenatal maternal depression associates with microstructure of right amygdala in neonates at birth. *Biol Psychiatry*. 2013;74:837–44.
- [31] Conway JM, Ingwersen LA, Vinyard BT, Moshfegh AJ. Effectiveness of the US Department of Agriculture 5-step multiple-pass method in assessing food intake in obese and nonobese women. *Am J Clin Nutr*. 2003;77:1171–8.
- [32] Health Promotion Board. Energy and nutrient composition of food Singapore ; 2011.
- [33] United States Department of Agriculture. USDA food composition database Baltimore, USA ; 2011.
- [34] Han CY, Colega M, Quah EPL, Chan YH, Godfrey KM, Kwek K, et al. A healthy eating index to measure diet quality in pregnant women in Singapore: a cross-sectional study. *BMC Nutr*. 2015;1:39.
- [35] van Lee L, Chia AR, Loy SL, Colega M, Tham EKH, Cai S, et al. Sleep and dietary patterns in pregnancy: findings from the GUSTO cohort. *Int J Environ Res Public Health*. 2017;14.
- [36] Chia AR, Tint MT, Han CY, Chen LW, Colega M, Aris IM, et al. Adherence to a healthy eating index for pregnant women is associated with lower neonatal adiposity in a multiethnic Asian cohort: the growing up in Singapore towards healthy outcomes (GUSTO) study. *Am J Clin Nutr*. 2018;107:71–9.
- [37] Li LJ, Ong PG, Colega MT, Han CY, Chen LW, Man Eyn Kidd R, et al. Correction: the impact of macronutrients on retinal microvasculature among Singapore pregnant women during the mid-late gestation. *PLoS One*. 2016;11:e0165218.
- [38] Buysse DJ, Reynolds 3rd CF, Monk TH, Berman SR, Kupfer DJ. The Pittsburgh sleep quality index: a new instrument for psychiatric practice and research. *Psychiatry Res*. 1989;28:193–213.
- [39] Backhaus J, Junghanns K, Broocks A, Riemann D, Hohagen F. Retest reliability and validity of the Pittsburgh sleep quality index in primary insomnia. *J Psychosom Res*. 2002;53:737–40.
- [40] Padmapriya N, Shen L, Soh S-E, Shen Z, Kwek K, Godfrey KM, et al. Physical activity and sedentary behavior patterns before and during pregnancy in a multi-ethnic sample of Asian women in Singapore. *Matern Child Health J*. 2015;19:2523–35.
- [41] World Health Organization. Global recommendations on physical activity for health; 2010.
- [42] Maunsell Z, Wright DJ, Rainbow SJ. Routine isotope-dilution liquid chromatography-tandem mass spectrometry assay for simultaneous measurement of the 25-Hydroxy metabolites of vitamins D₂ and D₃. *Clin Chem*. 2005;51:1683–90.
- [43] Holick MF, Binkley NC, Bischoff-Ferrari HA, Gordon CM, Hanley DA, Heaney RP, et al. Evaluation, treatment, and prevention of vitamin D deficiency: an Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab*. 2011;96:1911–30.
- [44] Ong YL, Quah PL, Tint MT, Aris IM, Chen LW, van Dam RM, et al. The association of maternal vitamin D status with infant birth outcomes, postnatal growth and adiposity in the first 2 years of life in a multi-ethnic Asian population: the growing up in Singapore towards healthy outcomes (GUSTO) cohort study. *Br J Nutr*. 2016;116:621–31.
- [45] Spielberger CD, Gorsuch RL, Lushene R, Vagg PR, Jacobs GA. Manual for the state-trait anxiety inventory. Palo Alto, CA: Consulting Psychologists Press; 1983.
- [46] White IR, Royston P, Wood AM. Multiple imputation using chained equations: issues and guidance for practice. *Stat Med*. 2011;30:377–99.
- [47] Hashmi AM, Bhatia SK, Bhatia SK, Khawaja IS. Insomnia during pregnancy: diagnosis and rational interventions. *Pak J med sci*. 2016;32:1030–7.
- [48] American Psychiatric Association. Diagnostic and statistical manual of mental disorders. (Fifth Ed.). 5 ed. Arlington VA: American Psychiatric Publishing; 2013.
- [49] Staner L. Comorbidity of insomnia and depression. *Sleep Med Rev*. 2010;14:35–46.
- [50] Atkins J, Naismith SL, Luscombe GM, Hickie IB. Psychological distress and quality of life in older persons: relative contributions of fixed and modifiable risk factors. *BMC Psychiatry*. 2013;13:249.
- [51] Lancaster CA, Gold KJ, Flynn HA, Yoo H, Marcus SM, Davis MM. Risk factors for depressive symptoms during pregnancy: a systematic review. *Am J Obstet Gynecol*. 2010;202:5–14.
- [52] Hölzel L, Härter M, Reese C, Kriston L. Risk factors for chronic depression — a systematic review. *J Affect Disord*. 2011;129:1–13.
- [53] Chen LW, Low YL, Fok D, Han WM, Chong YS, Gluckman P, et al. Dietary changes during pregnancy and the postpartum period in Singaporean Chinese, Malay and Indian women: the GUSTO birth cohort study. *Public Health Nutr*. 2014;17:1930–8.
- [54] Pereira MA, Rifas-Shiman SL, Kleinman KP, Rich-Edwards JW, Peterson KE, Gillman MW. Predictors of change in physical activity during and after pregnancy: project viva. *Am J Prev Med*. 2007;32:312–9.
- [55] Conry MC, Morgan K, Curry P, McGee H, Harrington J, Ward M, et al. The clustering of health behaviours in Ireland and their relationship with mental health, self-rated health and quality of life. *BMC Public Health*. 2011;11:692.
- [56] Kwan MY, Arbour-Nicitopoulos KP, Duku E, Faulkner G. Patterns of multiple health risk-behaviours in university students and their association with mental health: application of latent class analysis. *Health Promot Chron Dis Prev Can Res Policy Prac*. 2016;36:163–70.
- [57] Lopresti AL, Hood SD, Drummond PD. A review of lifestyle factors that contribute to important pathways associated with major depression: diet, sleep and exercise. *J Affect Disord*. 2013;148:12–27.
- [58] Elsenbruch S, Benson S, Rücke M, Rose M, Dudenhausen J, Pincus-Knackstedt MK, et al. Social support during pregnancy: effects on maternal depressive symptoms, smoking and pregnancy outcome. *Hum Reprod*. 2007;22:869–77.
- [59] Sin NL, Kumar AD, Gehi AK, Whooley MA. Direction of association between depressive symptoms and lifestyle behaviors in patients with coronary heart disease: the heart and soul study. *Ann Behav Med*. 2016;50:523–32.
- [60] García-Toro M, Ibarra O, Gili M, Serrano MJ, Oliván B, Vicens E, et al. Four hygienic-dietary recommendations as add-on treatment in depression: a randomized-controlled trial. *J Affect Disord*. 2012;140:200–3.
- [61] O'Hara MW, Swain AM. Rates and risk of postpartum depression - a meta-analysis. *Int Rev Psychiatry*. 1996;8:37–54.