Psychological Medicine

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Maternal adherence to healthy lifestyle and risk of depressive symptoms in the offspring: mediation by offspring lifestyle

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Original Article

Cite this article: Wang W-C, Ding M, Strohmaier S, Schernhammer E, Sun Q, Chavarro JE, Tiemeier H (2023). Maternal adherence to healthy lifestyle and risk of depressive symptoms in the offspring: mediation by offspring lifestyle. *Psychological Medicine* **53**, 6068–6076. https://doi.org/10.1017/S0033291722003257

Received: 22 February 2022
Revised: 21 September 2022
Accepted: 28 September 2022
First published online: 15 November 2022

Key words:
Depressive symptoms; healthy lifestyle; mother–child pairs

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Abstract

Background. Adherence to healthy lifestyles can be beneficial for depression among adults, but the intergenerational impact of maternal healthy lifestyles on offspring depressive symptoms is unknown.

Methods. In total, 10 368 mothers in Nurses' Health Study II and 13 478 offspring in the Growing Up Today Study were paired. Maternal and offspring healthy lifestyles were defined as a composite score including a healthy diet, normal body mass index (BMI), never-smoking, light-to-moderate consumption of alcohol, and regular moderate-to-vigorous physical activity. Maternal lifestyles were assessed during their offspring's childhood. Offspring depressive symptoms were repeatedly assessed five times using the Center for Epidemiological Studies Depression Scale-10 (CESD-10); the offspring were between the ages of 14 and 30 when the first CESD-10 was assessed. Covariates included maternal variables (age at baseline, race/ethnicity, antidepressant use, pregnancy complications, etc.) and offspring age and sex.

Results. Children of mothers with the healthiest lifestyle had significantly fewer depressive symptoms (a 0.30 lower CESD-10 score, 95% confidence interval (CI) 0.09–0.50) in comparison with children of mothers with the least healthy lifestyle. The association was only found significant in female offspring but not in males. For individual maternal lifestyle factors, a normal BMI, never-smoking, and adherence to regular physical activity were independently associated with fewer depressive symptoms among the offspring. The association between maternal healthy lifestyles and offspring depressive symptoms was mediated by offspring's healthy lifestyles (mediation effect: 53.2%, 95% CI 15.8–87.3).

Conclusions. Our finding indicates the potential mechanism of intergenerational transmission of healthy lifestyles to reduce the risk of depressive symptoms in offspring.

Introduction

Depression is one of the leading causes of disability and mortality worldwide. While major depressive disorder (MDD) studies have primarily focused on depression among adults, early-onset depression among adolescents is increasingly recognized as a public health challenge. In the USA, the 12-month prevalence of major depressive episodes among adolescents aged 12–17 has increased from 8.7% to 11.3% between 2005 and 2014 (Mojtabai, Olfson, & Han, 2016). Further, about half of adolescents diagnosed with MDD suffer from comorbid psychiatric disorders (Hauenstein, 2003; Lewinsohn, Rohde, & Seeley, 1998).

Explanations for the occurrence of depressive disorders include biological and psychosocial risk factors (Bernaras, Jaureguizar, & Garaigordobil, 2019; Garber, 2006). While biological (e.g. genetics, sex) and psychosocial (e.g. social support, stress events, family structures) factors are implicated in depression risk, growing evidence suggests that modifiable healthy lifestyle behaviors including a healthy diet, non-smoking, being physically active, having a normal body mass index (BMI), and light-to-moderate alcohol consumption are independently associated with less depressive symptoms among adults (Adjibade et al., 2018; Loprinzi & Mahoney, 2014). Previous studies showed that maternal exposures could be associated with children's mental health due to 'fetal programming' with potential long-term effects of intrauterine exposures (Faa et al., 2016; Lewinsohn et al., 1998; Thapar, Collishaw, Pine, & Thapar, 2012). The beneficial impact of maternal healthy lifestyle behaviors such as non-smoking and regular exercise on their mental well-being was shown to potentially be transmitted to the offspring

via reduced intrauterine exposure to inflammatory markers independently (Chatterton et al., 2017; Indredavik, Brubakk, Romundstad, & Vik, 2007). In addition, mothers' lifestyle behaviors could influence their offspring's lifestyle choices. Children with mothers who have a healthier lifestyle may adhere better to a healthier lifestyle themselves, which could be related to the offspring's mental health (Larsen et al., 2015; Moore et al., 1991). However, the possible association of maternal overall healthy lifestyle during their offspring's early and middle childhood with offspring's healthy lifestyle and the subsequent risk of depression is unexplored.

In this study, we aimed to examine the association of maternal overall healthy lifestyle (comprising a healthy diet, non-smoking, being physically active, normal BMI, and light-to-moderate alcohol consumption) during their offspring's childhood and adolescence with offspring depression, using mother–child dyads in the Nurses' Health Study II and Growing Up Today Study. We explored the possible mediation effect of offspring's healthy lifestyle on the association between maternal healthy lifestyle and offspring depression. We hypothesize that a healthier maternal lifestyle is associated with less offspring depressive symptoms and that this association is mediated by the offspring's healthy lifestyle.

Methods

Study population

The Nurses' Health Study II (NHSII) was established in 1989 with a population of 116 430 women. The target population of NHSII was all nurses aged 25–42 years who reside in 1 of 14 states (California, Connecticut, Indiana, Iowa, Kentucky, Massachusetts, Michigan, Missouri, New York, North Carolina, Ohio, Pennsylvania, South Carolina, and Texas). The participant completed a questionnaire about lifestyle factors, anthropometric variables, and medical history at the baseline (Colditz & Hankinson, 2005). Follow-up questionnaires are sent biennially to collect updated information. A validated food-frequency questionnaire (FFQ) was first collected in 1991 and was updated every 4 years.

For the children of women in the NHSII, baseline questionnaires were mailed to potential participants between the ages of 9 and 14 – the Growing Up Today Study (GUTS) recruited 16 882 children of NHSII participants in 1996 (GUTSI). Furthermore, in 2004, the study expanded with an additional 10 923 children (GUTSII) between the ages of 10 and 17. Participants completed follow-up questionnaires every 1–3 years. The two cohorts were merged into one cohort in 2013.

We excluded NHSII participants who had missing data on exposure assessment, i.e. BMI, smoking history, physical activity, alcohol consumption, or the FFQ at baseline. We also excluded GUTS participants with no single Center for Epidemiological Studies Depression Scale-10 (CESD-10) score. In addition, we excluded GUTS participants who had missing data on BMI, smoking history, physical activity, alcohol consumption, or the FFQ. After merging the two cohorts, our final study included 13 478 offspring in GUTS born to 10 368 mothers (online Supplementary Fig. S1). The study's follow-up period was from 1989 for NHSII participants' exposure assessment until five offspring outcome measures (single CESD-10 scores assessments) between 2010 and 2016. In 2010 when the first outcome was assessed, the offspring were between the ages of 14 and 30, with an average age of 19.

This study was approved by the Committees on the Use of Human Subjects in Research at the Brigham and Women's Hospital and the Harvard T.H. Chan School of Public. Mothers and the offspring were informed of the multigeneration linkages, and the return of the baseline questionnaire by NHSII and GUTS participants was considered informed consent in both cohorts. GUTS participants were informed about data linkage with maternal data.

Maternal lifestyle factors

NHSII participants' baseline assessments were conducted between 1989 and 1991, when participants were between 25 and 45 years old, with an average of 30; their offspring was between 0 and 9, with a mean age of 2. The body height, weight, and smoking were asked in biennial questionnaires. We then calculated participants' BMI by dividing the weight (kg) by height squared (m^2). Smoking status was categorized as current, past, or never smokers. Diet was assessed by a 131-item FFQ to obtain information on the usual intake of food and beverages. In FFQs, participants were asked how often (from 'never or less than once per month' to '6 or more times per day'), on average, they consumed a standard portion size of each food item during the previous year. The FFQ has shown reasonable validity and reproducibility (Feskanich et al., 1993; Rimm et al., 1992; Salvini et al., 1989; Willett et al., 1985). Questions about the consumption of alcoholic beverages (including beer, wine, and liquor) were included in each questionnaire. Overall diet quality was calculated using the Alternate Healthy Eating Index 2010 diet score (AHEI) without alcohol, which consists of the information on vegetables, fruit, whole grains, nuts and legumes, long-chain omega-3 fatty acids, polyunsaturated fatty acids, sugar-sweetened drinks, and fruit juice, red and processed meat, trans-fats, and sodium consumption. The AHEI has been significantly associated with an altered risk of chronic diseases (Chiuve et al., 2012). AHEI-2010 items have a minimum score of 0 and a maximum score of 10, adding up to a total score ranging from 0 (non-adherence) to 110 (perfect adherence). Mothers' physical activity was assessed by a validated self-reported questionnaire. Participants were asked about the amount of time they spent on each of the following physical activities: walking, jogging, running, bicycling, calisthenics, aerobics, aerobic dance, rowing machine use, lap swimming, playing tennis, and playing squash or racquetball. From the information, we estimated the weekly average time spent on any moderate-to-vigorous activities over the past year, as reported previously by Wolf et al. (1994).

Definition of healthy lifestyle scores

Previous studies have shown that adherence to a combination of healthy lifestyle factors is positively associated with disease-free life expectancy (Dhana et al., 2018; Stenholm et al., 2016; van Dam, Li, Spiegelman, Franco, & Hu, 2008). The lifestyle factors were dichotomized using the cut-offs developed previously for healthy lifestyle factors, which included a healthy diet as an AHEI score in the top 40%, a normal BMI as BMI between 18.5 and 24.9 kg/m^2, non-smoking as a never or former smoker, light-to-moderate consumption ($\geqslant$1 and <15 g/day) of alcohol, and an average of at least 150 min a week of regular moderate-to-vigorous physical activity (Dhana et al., 2018; van Dam et al., 2008). Each of the five items was coded 1 for adherence and 0 if not. The sum of the scores is the final healthy

https://doi.org/10.1017/S0033291722003257 Published online by Cambridge University Press

lifestyle score ranging from 0 to 5; higher scores indicate a healthier lifestyle.

Outcome assessment

Depressive symptoms of the offspring were assessed using the CESD-10 in 2010, 2011, 2013, 2014, and 2016. We then combined CESD-10 scores in 2010 and in 2011 as one measure since CESD-10 was only assessed in GUTSI in 2010 and GUTSII in 2011 before GUTSI and GUTSII merged.

The 10-item scale is a well-validated tool for detecting depressive symptoms in the general population for use in adolescents (Baron, Davies, & Lund, 2017; Boey, 1999; Bradley, Bagnell, & Brannen, 2010).

Covariate and mediator assessment

We considered several possible confounders, including maternal and offspring variables. Baseline maternal characteristics of NHSII, including age, race/ethnicity, antidepressant use (any lifetime use occurring before or at study baseline), household income, chronic disease (diabetes, cardiovascular disease, or cancer), and pregnancy complications for the offspring included in the study (gestational diabetes, pre-eclampsia, and pregnant-induced hypertension), were obtained from NHSII questionnaires. As all mothers worked as nurses at baseline, we controlled for socioeconomic status by adjusting for the education of the spouse/partner. We adjusted for offspring age and sex.

To assess potential mediators of offspring's healthy lifestyle, we obtained information on offspring's height, weight, physical activity, diet, and smoking in 1996 for GUTSI when they were between 9 and 14 years old; and in 2004 for GUTSII when they were 10–17 years old (on average, 10 years before the first CESD-10 assessment, range 4 years). The offspring's alcohol consumption was not included since the information was incomplete due to the offspring's young age when the assessment was done. The quality of the offspring's diet was again assessed using the AHEI-2010 diet score, excluding scoring for alcohol intake. Physical activity was calculated by hours per week spent on physical activity of moderate-to-vigorous intensity over the past year. We then applied the exact definition of healthy lifestyle scores for mothers to calculate their offspring's healthy lifestyle scores except for the definition of normal BMI among offspring. We used the age and sex-specific cutoff values of BMI from the World Health Organization's child growth standards.

Statistical analysis

Maternal healthy lifestyle scores and offspring healthy lifestyle scores

To explore the association between maternal healthy lifestyle scores and offspring healthy lifestyle scores, we used generalized estimating equations (GEEs) to account for sibling clusters, adjusting for maternal age at baseline, maternal antidepressant use, race/ethnicity, annual household income, education of spouse/partner, chronic diseases, pregnancy complications, and offspring sex.

Maternal healthy lifestyle scores and offspring depressive symptoms

We also used GEEs to evaluate the association between categorical maternal healthy lifestyle scores and offspring depressive symptoms. In these analyses, we accounted for sibling clusters and repeated measures of CESD-10 scores across four time points; we adjusted for maternal covariates as mentioned above and offspring characteristics (age and sex). The potential effect of moderation by child age was tested by dichotomizing child age (<18 or ⩾18 years) and adding an interaction term. Likewise, the potential effect of moderation by offspring sex and the possible change in the association with follow-up duration were tested by adding interaction terms to the GEE model of depressive symptoms. Sex-specific associations were examined by conducting analysis in male and female offspring. Next, we assessed the association between categories of each of the five maternal lifestyle factors and offspring CESD-10 scores. We calculated the mediation proportion and 95% confidence interval (CI) of offspring lifestyle factors on offspring depressive symptoms using % Mediate macro in SAS based on the methods of Lin, Fleming, and De Gruttola (1997) and Nevo, Liao, and Spiegelman (2017).

Although GEE can analyze incomplete data with missingness for the repeated outcomes (CESD-10 scores), it requires a strong assumption of missing completely at random (Little & Rubin, 2019). Multiple imputation is one of the alternatives to account for missingness that only requires missing at random assumption and reduces biased estimates (Ditlhong, Ngesa, & Kombo, 2018). We used multiple imputation (SAS PROC MI procedure) for the missing values of the repeated CESD-10 scores in 2010/2011, 2013, 2014, and 2016. The predictive model included variables such as offspring sex and age, CESD-10 scores from other assessment waves, healthy lifestyle scores, and maternal covariates. We used the PROC MIANALYZE to estimate the pooled effect of 20 imputed datasets to calculate the estimated CESD-10 scores and 95% CIs by categories of healthy lifestyle scores and each of the five lifestyle factors after adjusting for maternal and offspring covariates. All statistical tests were two-sided, with statistical significance considered at $p < 0.05$. All statistical analyses were conducted using SAS version 9.4 (SAS Institute, Cary, NC, USA).

Results

Our study included 10 368 mothers and 13 478 offspring (Table 1). Mothers were, on average, 30 years old at baseline. The mean BMI for mothers was 23.78 kg/m^2, and most (71%) of the mothers were never smokers. The average time spent on moderate-to-vigorous physical activity was 2.4 h per week. Mothers reported having a mean AHEI diet score of 24.49 and a mean alcohol intake of 2.71 g per day. As less than 1% of mothers had a score of 0, we combined total scores of 0 and 1 into scores of 1 to define the least healthy lifestyle score. In our study, 11% of mothers had a healthy lifestyle score of 1, and 8% had an optimal healthy lifestyle score of 5. In total, 22% of mothers reported having antidepressant use at baseline. The offspring were, on average, 19 years old at the first CESD-10 assessment in 2010. More girls than boys were included in the study (64% girls and 36% boys).

We have compared the characteristics of included and excluded offspring and their mother's lifestyle factors (online Supplementary Table S1). Excluded offspring were shown to have more males than females (59%, 41%). The mothers of excluded offspring had a higher average BMI (24.04 kg/m^2) and fewer never smokers (68%) than the mothers of included offspring had (23.78 kg/m^2, 71%). We further calculated the correlation coefficients between the CESD-10 assessments at four different time points (online Supplementary Table S2). The

https://doi.org/10.1017/S0033291722003257 Published online by Cambridge University Press

Table 1. Characteristics of NHSII and GUTS participants (baseline 1989 for NHSII, and 2010 for GUTS)

Characteristics	Value
Maternal characteristics at baseline	
No. of mothers	10 368
Age, year, mean (s.d.)	30.01 (3.94)
White race or ethnicity (%)	97
Lifestyle factors	
Alternate healthy eating index 2010, diet score, mean (s.d.)	24.49 (6.67)
BMI, kg/m^2, mean (s.d.)	23.78 (4.53)
Moderate/vigorous-intensity exercise, hour/week, mean (s.d.)	2.36 (3.32)
Alcohol intake, g/day, mean (s.d.)	2.71 (5.23)
Smoking status (%)	
Never smoker	71
Former smoker	22
Current smoker	7
Healthy lifestyle score (%)	
1, poor health score	11
2	27
3	32
4	22
5, optimal health score	8
Maternal antidepressant use at baseline, yes (%)	22
Pregnancy complications (%)	
Gestational diabetes, yes	3
Pre-eclampsia, yes	4
Pregnancy-induced hypertension, yes	5
Household income (%)	
<$74 000	30
$75 000–149 000	56
⩾$150 000	13
Missing value (%)	1
Education of spouse/partner (%)	
High school or less	30
College graduate	30
Graduate degree	33
Missing value	7
Offspring characteristics	
No of children	13 478
Male sex (%)	36
CESD-10, mean (s.d.), missingness (%)	
First assessment in 2010/2011	7.37 (4.71), 20%
Second assessment in 2013	6.70 (4.42), 36%
Third assessment in 2014	7.01 (4.59), 32%
Fourth assessment in 2016	6.81 (4.83), 21%
Healthy lifestyle score (%)	
0, poor health score	1
1	12
2	45
3	39
4, optimal health score	3
Age in 2010[a], years, mean (s.d.), range	18.98 (1.87), 14–30

[a]First CESD-10 assessment.

table shows positive correlations between the CESD-10 scores at different time points.

Maternal healthy lifestyle scores and offspring depressive symptoms

We evaluated the association between maternal healthy lifestyle scores and offspring depressive symptoms in adolescence and adulthood (Table 2). A higher maternal healthy lifestyle score was associated with a lower depression score in offspring after controlling for maternal and offspring covariates. Compared to children of mothers with the least healthy lifestyle (score 1), children of mothers with the healthiest lifestyle (score 5) had a 0.30 (95% CI 0.09–0.50) lower depression score. The association between maternal healthy lifestyle scores and offspring depressive symptoms was stronger among offspring of older age (>18 years, interaction term: p value <0.001, see details in online Supplementary Table S3) and differed by sex (interaction term: p value: 0.004, see details in online Supplementary Table S4). The association between maternal healthy lifestyle scores and CESD-10 scores in the offspring did not change across follow-up time [0.02 (95% CI −0.02 to 0.05, the interaction with follow-up time), p value: 0.29].

We further examined associations of individual maternal lifestyle factors in relation to offspring depressive symptoms (Table 2). BMI, smoking status, and physical activity were independently significantly associated with offspring depression scores. Children of mothers with normal BMI (BMI 18.5–24.9) had lower depression scores than children of overweight mothers (BMI 25.0–29.9) and lower depression scores than children of obese mothers (BMI ⩾ 30). Compared to offspring whose mothers were past or current smokers, offspring whose mothers were never smokers had lower depression scores, respectively. Adherence to regular physical activity of more than 150 min per week of moderate/vigorous exercise in mothers was associated with lower depression scores in offspring than in physically inactive mothers. Maternal AHEI score and maternal alcohol intake were not significantly associated with offspring depression scores.

Next, we examined whether the association between maternal healthy lifestyle scores and offspring depressive symptoms is specific for offspring sex (Table 3). Female offspring of mothers with the healthiest lifestyle (score 5) had a 0.47 (0.20–0.74) lower depression score compared to female offspring of mothers with

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Table 2. Association of maternal lifestyle factors with offspring depression score (CESD-10[a])

		Offspring depression score (CESD-10)			
		Unadjusted model		Adjusted model	
		Estimate (95% CI)	*p* value	Estimate (95% CI)	*p* value
Maternal healthy lifestyle score					
Healthy lifestyle score	1	0 (Ref.)	–	0 (Ref.)	–
	2	−0.23 (−0.39 to −0.07)	0.006	−0.20 (−0.36 to −0.03)	0.02
	3	−0.36 (−0.51 to −0.21)	<0.001	−0.30 (−0.45 to −0.15)	<0.001
	4	−0.29 (−0.46 to −0.12)	0.001	−0.26 (−0.43 to −0.08)	0.004
	5 (most healthy)	−0.34 (−0.55 to −0.14)	0.001	−0.30 (−0.50 to −0.09)	0.005
Individual maternal lifestyle factors					
Alternate Healthy Eating Index 2010 diet score	Quintiles 1 (most healthy)	0 (Ref.)	–	0 (Ref.)	–
	Quintiles 2	−0.16 (−0.30 to −0.02)	0.03	−0.11 (−0.25 to 0.03)	0.13
	Quintiles 3	−0.09 (−0.23 to 0.05)	0.19	−0.04 (−0.18 to 0.10)	0.55
	Quintiles 4	−0.22 (−0.36 to −0.08)	0.002	−0.16 (−0.30 to −0.02)	0.03
	Quintiles 5	−0.18 (−0.33 to −0.03)	0.02	−0.09 (−0.24 to 0.07)	0.27
BMI	<18.5	−0.11 (−0.36 to 0.13)	0.37	−0.12 (−0.36 to 0.13)	0.35
	18.5–24.9	0 (Ref.)	–	0 (Ref.)	–
	25.0–29.9	0.33 (0.23–0.46)	<0.001	0.30 (0.18–0.42)	<0.001
	⩾30.0	0.69 (0.53–0.85)	<0.001	0.59 (0.43–0.76)	<0.001
Smoking status	Never smoker	0 (Ref.)	–	0 (Ref.)	–
	Former smoker	0.33 (0.22–0.44)	<0.001	0.26 (0.15–0.38)	<0.001
	Current smoker	0.67 (0.48–0.86)	<0.001	0.62 (0.43–0.81)	<0.001
Alcohol intake (g/day)	0	−0.05 (−0.16 to 0.05)	0.32	−0.08 (−0.18 to 0.03)	0.15
	1.0–4.9	0 (Ref.)	–	0 (Ref.)	–
	5.0–14.9	−0.002 (−0.14 to 0.07)	0.98	−0.004 (−0.15 to 0.06)	0.13
	⩾15.0	−0.14 (−0.41 to 0.14)	0.34	−0.22 (−0.49 to 0.14)	0.96
Moderate/vigorous intensity exercise (min/week)	0	0.21 (0.05–0.38)	0.01	0.19 (0.03–0.35)	0.02
	1–149	0.01 (−0.09 to 0.11)	0.85	0.02 (−0.08 to 0.12)	0.65
	⩾150	0 (Ref.)	–	0 (Ref.)	–

The adjusted model adjusted for mothers' age at baseline, race/ethnicity, annual household income, education of spouse/partner, pregnancy complications, antidepressant use at baseline, chronic diseases, and offspring age and sex (boy/girl).
[a]Center for Epidemiological Studies Depression Scale-10 (CESD-10).

the least healthy lifestyle (score 1). In contrast, there was no significant association of maternal lifestyle scores with offspring depression scores among male offspring.

Maternal healthy lifestyle scores and offspring's healthy lifestyle scores

The maternal healthy lifestyle scores were associated with the offspring's healthy lifestyle scores (Table 4). Children of mothers with the highest healthy lifestyle scores had a 0.23 (0.17–0.29) higher healthy lifestyle score than children of mothers with a score of 1, after controlling for maternal and offspring covariates.

Next, we examined the association between offspring healthy lifestyle scores and offspring depressive symptoms and found that higher offspring healthy scores were associated with fewer offspring depressive symptoms (online Supplementary Table S5). We then examined the potential mediation effect of offspring lifestyle factors on the association between maternal healthy lifestyle scores and offspring depressive symptoms. The association was mediated by overall continuous offspring healthy lifestyle scores [overall mediation effect: 53.2% (15.8–87.3)] (Table 5). Offspring lifestyle factors such as healthy diet, normal BMI, never-smoking, and regular physical activity were significant mediators of the effect of maternal healthy lifestyle scores on offspring depressive symptoms when examined separately.

https://doi.org/10.1017/S0033291722003257 Published online by Cambridge University Press

Table 3. Sex-specific analysis: association of maternal lifestyle factors with offspring depression score (CESD-10[a])

		Offspring depression score (CESD-10)			
		Unadjusted model		Adjusted model	
The maternal healthy lifestyle score		Estimate (95% CI)	*p* value	Estimate (95% CI)	*p* value
Male offspring					
Healthy lifestyle score	1	0 (Ref.)	–	0 (Ref.)	–
	2	−0.10 (−0.39 to 0.19)	0.48	−0.09 (−0.39 to 0.20)	0.51
	3	0.11 (−0.18 to 0.42)	0.43	0.11 (−0.19 to 0.41)	0.45
	4	0.18 (−0.20 to 0.56)	0.34	0.13 (−0.25 to 0.51)	0.48
	5 (most healthy)	0.16 (−0.23 to 0.56)	0.40	0.14 (−0.27 to 0.54)	0.50
Female offspring					
Healthy lifestyle score	1	0 (Ref.)	–	0 (Ref.)	–
	2	−0.25 (−0.45 to −0.04)	0.02	−0.19 (−0.39 to 0.01)	0.06
	3	−0.57 (−0.78 to −0.36)	<0.001	−0.49 (−0.68 to −0.29)	<0.001
	4	−0.50 (−0.71 to −0.30)	<0.001	−0.41 (−0.61 to −0.22)	<0.001
	5 (most healthy)	−0.58 (−0.85 to −0.31)	<0.001	−0.47 (−0.74 to −0.20)	<0.001

The adjusted model adjusted for mothers' age at baseline, race/ethnicity, annual household income, education of spouse/partner, pregnancy complications, antidepressant use at baseline, chronic diseases, and offspring age.
[a]Center for Epidemiological Studies Depression Scale-10 (CESD-10).

Table 4. Association of offspring healthy lifestyle score with maternal healthy lifestyle score

		Estimate	95% CI	*p* value
Offspring healthy lifestyle score				
Maternal healthy lifestyle score	1 (lowest)	0 (Ref.)		–
	2	0.02	(−0.02 to 0.07)	0.31
	3	0.09	(0.04–0.14)	<0.001
	4	0.15	(0.10–0.20)	<0.001
	5 (highest)	0.23	(0.17–0.29)	<0.001

The model adjusted for mother's age at baseline, race/ethnicity (white, yes/no), household income (<US$74 000, $75 000–149 000, ⩾$150 000), pregnancy complications, antidepressant use at baseline, educational attainment of spouse/partner (high school, college, graduate school), chronic diseases, and offspring age and sex (boy/girl).

Discussion

In our study, including 10 368 mothers and 13 478 of their offspring, we found that an overall healthier lifestyle of mothers was associated with less depressive symptoms (CESD-10) in the offspring in adolescence and adulthood. This finding was explained by a strong association among female offspring. Of the individual maternal healthy lifestyle factors assessed during their offspring's early and middle childhood, a normal BMI, being physically active, and non-smoking were independently associated with less depressive symptoms in the offspring. Offspring healthy lifestyles explained a substantial proportion of the association between maternal healthy lifestyles and offspring depressive symptoms.

With growing evidence of the protective impact of modifiable healthy lifestyle behaviors on reducing the risk of depression, several studies further investigated if this benefit is transmitted intergenerationally to the offspring (Adjibade et al., 2018; Ashford, van Lier, Timmermans, Cuijpers, & Koot, 2008; Buttery, Mensink, & Busch, 2014; D'Onofrio et al., 2008; Indredavik et al., 2007; Jantsch et al., 2022; Loprinzi & Mahoney, 2014; Moylan et al., 2015). In a mother–child pairs study, maternal smoking during pregnancy was associated with a higher risk of internalizing psychiatric symptoms such as anxiety and depression in the offspring (Moylan et al., 2015). Maternal obesity was associated with a higher risk of depressive and internalizing problems for offspring (Edlow, 2017; Jantsch et al., 2022). In addition, research on maternal alcohol consumption showed that no moderate alcohol intake during pregnancy was associated with a lower risk of depression in the offspring (Easey, Timpson, & Munafò, 2020). However, no study has examined the effect of the combined healthy lifestyle of mothers on offspring depression. Furthermore, little is known about whether offspring healthy lifestyles mediate the association between maternal healthy lifestyles and offspring depression.

Our study extended the knowledge of the role of individual maternal lifestyle factors in the overall maternal healthy lifestyles during their offspring's early and middle childhood in reducing offspring depressive symptoms. Consistent with previous studies, we found that maternal obesity and smoking were associated with increased offspring depressive symptoms. We also found that children born to women who had regular physical activities with moderate intensity had fewer depressive symptoms than children whose mothers did not. The finding showed the importance of a composite healthy lifestyle that has a protective association with depressive symptoms in the next generation. It is worth noting that maternal alcohol consumption and dietary patterns were

https://doi.org/10.1017/S0033291722003257 Published online by Cambridge University Press

Table 5. Offspring lifestyle factors mediated the effect of maternal healthy lifestyle scores on offspring depressive symptoms

Mediation variables	Total effect	Direct effect	Proportion mediation	*p* value
Outcome offspring depressive symptoms				
Categorical indicators				
Offspring healthy diet	−0.08 (−0.14 to −0.01)	−0.07 (−0.13 to 0.00)	13.2% (4.0–35.6)	0.005
Offspring normal BMI	−0.08 (−0.14 to −0.01)	−0.07 (−0.13 to 0.02)	13.9% (5.2–32.4)	<0.001
Offspring never-smoking	−0.08 (−0.14 to −0.01)	−0.05 (−0.12 to 0.02)	38.1% (10.4–76.6)	0.003
Offspring regular physical activity	−0.08 (−0.14 to −0.01)	−0.07 (−0.13 to 0.00)	16.5% (6.1–37.4)	<0.001
Continuous indicator				
Overall offspring healthy lifestyle scores	−0.08 (−0.14 to −0.01)	−0.04 (−0.10 to 0.03)	53.2% (15.8–87.3)	<0.001

The model adjusted for mother's age at baseline, race/ethnicity (white, yes/no), household income (<US$74 000, $75 000–149 000, ⩾$150 000), pregnancy complications, antidepressant use at baseline, educational attainment of spouse/partner (high school, college, graduate school), chronic diseases, and offspring age and sex (boy/girl).

not associated with offspring depressive symptoms. The protective effect of light-to-moderate alcohol consumption on health is controversial given the potential of confounding by poor health in the non-drinkers (i.e. abstinence reflects poor health) (Davey Smith, Holmes, Davies, & Ebrahim, 2020).

Mechanisms

Mothers' lifestyles and behaviors are strongly related to their offspring's lifestyles. Offspring of mothers with a healthier lifestyle adhere to a healthier lifestyle later in (Larsen et al., 2015; Moore et al., 1991). There are several mechanisms potentially underlying this long-term impact of maternal lifestyles. One is through the role modeling process; that is, children adopt their parents' lifestyle behaviors when establishing their behaviors (Herman & Polivy, 2005; White, Johnson, & Buyske, 2000). Another theory is the mimicry effect; children copy their parents' behaviors unwittingly and turn them into their norms (Hermans et al., 2012). Apart from parents passively influencing their children's behaviors, parenting style, monitoring, and content could also considerably impact offspring's healthy lifestyles throughout childhood, adolescence, and even adulthood through guidance and joint activities (Larsen et al., 2015; Yao & Rhodes, 2015). The association between maternal healthy lifestyle scores and offspring depressive symptoms was stronger among offspring over 18 years old. This age interaction may be explained by environmental risks and adverse experiences that accumulate with age. Our results suggest that healthier behaviors may have a stronger protective effect on older ages, which may be when more adversity has been experienced over time. Alternatively, older children may simply have been exposed longer to maternal modeling and monitoring during their adolescent development and thus have internalized the protective effects better. Our study showed that the association between maternal healthy lifestyles and offspring depressive symptoms could be partially explained by the mediation effect of offspring healthy lifestyles in pre-adolescence and adolescence.

Several other possible pathways could also serve as explanations for our observations. The first is the intrauterine mechanism. In our study, we assessed mothers' healthy lifestyles during their offspring's early and middle childhood; however, intrauterine transmission cannot be ruled out as maternal lifestyle patterns tend to be stable and may have been present during pregnancy. Studies have shown that pro-inflammatory cytokines (such as interleukin-6) induced by maternal obesity and smoking could cross the placental barrier and impact neurodevelopment in the fetus, as well as alter the hypothalamic–pituitary–adrenal axis (Howell & Powell, 2017; Sullivan, Riper, Lockard, & Valleau, 2015). Also, intrauterine exposure to nicotine may disrupt offspring's brain development due to DNA methylation and gene expression alteration (Chatterton et al., 2017). Previous studies found that the offspring of mothers who exercise during pregnancy regularly had increased neurogenesis and neuronal activity that could improve their mental health and cognitive function in animals and humans (Rahimi et al., 2020; Robinson & Bucci, 2012).

The intergenerational association of maternal lifestyles to offspring mental health could also reflect confounding by family socioeconomic status, parental education level, genetic heredity, and maternal depression (Scaglioni et al., 2018; Yao & Rhodes, 2015). Maternal depression may be a consequence of an unhealthy lifestyle but may also contribute independently to the intergenerational transmission of poor maternal health. In the current study, we controlled for family socioeconomic status, parental education level, and baseline maternal antidepressant use; however, we could not rule out that untreated maternal depression or depression diagnosed later in life impacted the offspring.

In the sex-specific analysis, we only found that the protective impact of the maternal lifestyle scores on offspring depressive symptoms was explained by the association in female offspring. Two possible pathways could explain this sex interaction. First, previous studies showed that girls experience more parental monitoring than boys because of double standards in expectations and social influences (Axinn, Young-Demarco, & Ro, 2011; Seedall & Anthony, 2015). Therefore, girls are more likely to adopt their parents' healthy lifestyle behaviors and may therefore experience more protective or risk-increasing effects. Second, after excluding offspring without lifestyle or CESD-10 assessment, the remaining population included more female participants (70%), which implies that we had more power to detect associations in females.

Our findings need to be interpreted with caution, as we cannot establish the causality of the association between maternal healthy lifestyles and offspring depressive symptoms. However, our study provides evidence that the mother's healthy lifestyle is significantly associated with the mental health of their offspring. The relationship between maternal healthy lifestyles and offspring depressive symptoms highlights the importance of the heritable environmental or genetic risk for mental health that could not be easily explained by socioeconomic status in this study.

https://doi.org/10.1017/S0033291722003257 Published online by Cambridge University Press

Strengths and limitations

The strengths of our study include the large sample size and the prospective design with mothers and their offspring from two ongoing cohorts. A design with all mothers recruited as nurses reduced confounding bias caused by socio-demographics. The detailed information on the mothers' household income and the education of their spouses/partners allowed us to further control for potential confounding by socioeconomic status.

Several limitations should be considered. First, the lifestyle factors and outcome of depressive symptoms were self-reported, which might introduce measurement errors and misclassifications. However, previous validation studies of self-reported body weight/height, physical activity, and CESD-10 scale in the NHS showed that these measures were reliable and valid in both mothers and offspring cohorts (Baron et al., 2017; Field, Aneja, & Rosner, 2007; Rimm et al., 1990; Sanchez-Villegas et al., 2008; Wolf et al., 1994). Second, most NHSII participants are nurses of Caucasian ancestry and relatively homogeneous socioeconomic status, which limits the generalizability of our results to the general population. Third, the possibility of confounding by unmeasured covariates remains. Our data could not sufficiently capture maternal mental health, and we have no knowledge of paternal health. In the near future, it warrants further investigation of whether genetic risk factors or paternal lifestyle factors play a role in developing offspring depression. Fourth, there are potential problems with BMI as a marker of lifestyle (Gutin, 2018). BMI is not only a marker of lifestyle, but BMI is partly genetically determined. Moreover, defining overweight according to BMI classification can be inaccurate (Karchynskaya et al., 2020). The formula to calculate BMI does not account for race and maternal age. Also, the BMI equation does not consider the body fat content, the proportion of muscle mass, and bone density. Fifth, potential selection bias could be introduced by the characteristic difference between included and excluded offspring in our study. More boys than girls were excluded due to the lack of information on lifestyle factors and the CESD-10 assessment. Since healthier participants are more likely to participate and provide their health information, our sex-specific analysis must be interpreted with caution as results could be influenced by selected effects in the male offspring population.

Conclusion

In conclusion, we found that a healthier maternal lifestyle during their offspring's early and middle childhood was associated with less depressive symptoms (CESD-10) in female offspring. This association was largely mediated through offspring's healthy lifestyles during pre-adolescence and adolescence. The association between healthy lifestyle factors and fewer offspring depressive symptoms includes a normal BMI, non-smoking history, and regular exercise. This putative intergeneration transmission of maternal lifestyles to the offspring likely has broad health implications, including a reduced risk of depressive symptoms.

Supplementary material. The supplementary material for this article can be found at https://doi.org/10.1017/S0033291722003257

Financial support. This work was supported by the National Institutes of Health (U01HL145386, P30DK046200, and U01CA176726); and the Center for Disease Control and Prevention/The National Institute for Occupational Safety and Health (5R01OH009803).

Conflict of interest. None.

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