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7 **Association of maternal depression with dietary intake, growth**
8 **and development in preterm infants: a cohort study in Beijing of**
9 **China**

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15 Running title: Association between maternal depression and development of preterm
16 infants

Abstract: This study aimed to explore the association of maternal depression with nutrient intake, growth and development of preterm infants. A cohort study including 201 infants was conducted in Beijing. Based on an infant's gestational age and mother's status, the infants were divided into four groups: non-depression-fullterm (64), non-depression-preterm (70), depression-fullterm (36) and depression- preterm (31). Data on sociodemographic characteristics, nutritional intake, growth and developmental status of children at 8 months(corrected ages) were collected using quantitative questionnaire, 24-Hour Dietary Recall, anthropometric measurements and the Bayley-III scale. A multivariate analysis was used to evaluate the effects of both maternal depression and preterm birth on growth and development. The intake of energy, protein and carbohydrates in the depression group was lower than the amounts recommended. Specifically, the depression preterm groups had the lowest Z-scores for length and weight and the lowest Bayley-III scores. Preterm infants of depressed mothers are at higher risk of poor growth and development delay.

Keywords: maternal depression; preterm; infant; nutrition; growth; development.

33 **Introduction**

34 Mothers are highly vulnerable to depression in the first year after childbirth. Indeed,
35 worldwide, approximately 10–20% of mothers suffer from depression during this
36 period[1, 2]. In China, the results of a meta-analysis showed that the prevalence of
37 postpartum depression was ranging from 13.1–16.3% [3]. Maternal depression has
38 detrimental effect on child growth and development outcomes, including
39 malnutrition[4], developmental delay [5] and behavioural and emotional problems[6].
40 Studies have shown that depression among mothers is associated with disrupted
41 mother-infant interactions[7], less positive interactions between mothers and infants.
42 Further, depressed mother provide less cognitive stimulation to infants and infants
43 show less secure attachment to depressed than non-depressed mothers[7, 8].
44 Depression characteristics may limit the ability of mothers to respond appropriately
45 when feeding their children[9].

46 According to estimates by World Health Organization (WHO), approximately 15
47 million premature babies (more than 1 in 10 babies) are born every year[10]. Preterm
48 infants often display poor growth rates and development delays[11]. Studies have also
49 suggested that growth is ‘pre-programmed’ to occur at certain times that if missed,
50 may not be recoverable[12]. A clear association exists between under-nutrition and
51 poor growth and development in preterm infants[13]. Preterm infants need higher
52 nutrition intake to ‘catch-up’ their growth in the first year after birth[14]. Nutritional
53 supplements [15]and feeding strategies[16] for preterm infants have been widely
54 studied. Infant feeding practices not only involve the transfer of nutrients, but also

represent a complex activity, as infant's neuro-motor, cognitive, social and communicative capacities develop during their first year[17].

Previous studies have indicated that maternal depression or preterm birth affects children's health [4, 6, 11]. Thus, the preterm infants of depressed mothers may be at high risk of experiencing serious feeding problems, malnutrition and poor growth and development. However, the issue of whether a history of maternal depression is also associated with prematurity and affects dietary intake, growth and development remains underexplored. This study sought to explore whether maternal depression and preterm birth are associated with the nutrition intake, body growth and development of premature infants of depressed mothers. Specifically, this study aimed to explore whether the preterm infants with depressed mothers are more vulnerable than either fullterm birth with a depressed mother or preterm birth alone.

Materials and Methods

Participants and Study Design

A cohort study was used to investigate the association between maternal depression and the growth and development of preterm infants. The cohort study was conducted at Haidian Maternal & Child Health Hospital and Peking University Third Hospital from December 2012 to November 2014. A total of 130 preterm infants (born at 30^{0/7} to 36^{6/7} weeks' gestational age) comprised the exposed group and a total of 130 fullterm infants (born at 37^{0/7} to 41^{6/7} weeks' gestational age) from the same maternity ward comprised the non-exposed group. Mothers' depression status was measured within three days of delivery. Based on maternal depression and delivery status, the

77 infants were divided into four subgroups: non-depression-fullterm,
78 non-depression-preterm, depression-fullterm and depression-preterm. The study
79 procedures were explained to each pregnant woman when she was admitted to the
80 delivery room and written informed consent was obtained for all of the infants
81 involved in the study.

82 Within three days of delivery, physical and neuro-motor examinations were performed
83 on all infants by developmental paediatricians. The exclusion criteria for the study
84 included medical complications in the perinatal period, intra-partum infection,
85 hypoxic-ischemic encephalopathy, genetic metabolic diseases, any disability, cerebral
86 palsy and hearing impairment.

87 The baseline survey within three days of delivery was conducted using a standardised
88 questionnaire. The socio-economic characteristics of mothers and households were
89 collected, including their age, ethnicity, education and income. The Edinburgh
90 Postnatal Depression Scale (EPDS) was used to screening postpartum depression.
91 EPDS is a self-administered questionnaire which has been translated and validated in
92 Chinese women [18]. Women were asked to complete the EPDS by themselves.
93 Neonatal information (e.g., sex, Apgar scores, gestational age at birth, delivery
94 method, birth weight and birth length) was collected from medical records.

95 At 8 months of age, after adjusting for an infant's expected date of delivery for
96 preterm infants, a follow-up face-to-face survey was administered. At the follow-up,
97 201 pairs of mothers and infants were interviewed (59 participant pairs were missing).

98 Two observers who were blinded to the birth and hospital information of participants

have assessed the infants' neurodevelopment. The observers included trained developmental pediatricians and medical students who had bachelor degree or above. Inter observer agreement between the two observers has achieved the high level of 95%. Using the Length Meter with Model WB-B Horizontal Type for baby, each infant's length was measured to the nearest 0.1 cm (Wujin Weighing Apparatus Factory, Changzhou, China). A scale was used to measure weight to the nearest 0.1 kg (Bailida electronic scale HD-305; Wuxi Measurement Factory, Wuxi, China). The third Edition of the Bayley scales of Infant and Toddler Development (Bayley-III)(Pearson) was used to evaluate infants' developmental status. Finally, a 24-Hour Dietary Recall (HDR) survey on food intake was used to collect information about infants' food consumption. Approval for the study was obtained from the Ethics Committee of Peking University's Health Science Centre (No. IRB00001052 - 13001).

Measurements

Status of Maternal Depression

The Chinese version of the EPDS, comprising 10 items, was used in the study. Its psychometric performance is comparable to the original scale[18]. For each item, mothers were invited to score their postpartum status over the past 7 days across different levels (i.e., 0–3). Thus, total scores ranged from 0–30. A cut-off score of 9 was used in the study to balance sensitivity and specificity. A score over 9 was taken to be a positive indication of depression symptoms[19, 20].

Nutritional Intake

The 24-Hour Dietary Recall (HDR) survey was administered during a face-to-face interview with the caregiver who had fed the infant the previous day. All of the researchers were trained on the process for administering a standardised dietary survey, the requirements and methods of the auxiliary measuring atlas and the process for completing the HDR survey. All of the foods and liquids consumed by the infant in the last 24 hours were recorded. The survey included questions about the number of meals, food names, food textures and the amount consumed by the infant in the previous day (i.e., in the last 24 hours). The foods included breast milk, infant formula milk, staple foods, vegetables, legumes, fruits, meat and fish, eggs and dairy. An auxiliary food atlas was used to measure food quantity. Records of infants' food consumption at 8 months were used to calculate infants' intakes of energy and nutrients. Based on the 2004 China Food Composition[21], the energy and nutrients consumed were analysed and converted into percentage of Recommended Nutrient Intakes (RNIs) or Adequate Intakes (AIs) for energy and nutrients based on age- and gender-normalised Dietary Reference Intake (DRIs). For each dietary element, adequate intake was defined as greater or equal to 100% DRI.

Anthropometric Measurements

The body weight and length of each infant were measured twice and mean values were used. Infants were weighed without shoes, wearing light indoor clothing. Infants' length was measured without shoes and socks. The SAS macro recommended by the WHO (<http://www.who.int/childgrowth/software/en/>) was used to calculate infants' Z-scores for weight and length at 8 months (corrected age).

Developmental Assessments

The infants' general development at 8 months of age was assessed using the Bayley-III scale in our study[22]. The Bayley-III scale comprises five major developmental domains: cognitive, language, motor, social-emotional and adaptive behaviour. Cognitive and motor scales were conducted in the present study. Each item was scored as 1 (passed) or 0 (not passed) for the cognitive (91 items) and motor (66 fine and 72 gross motor items) scales. The progression or regression of the tests for all scales adhered to the reversal and discontinue rules. Under the reversal rule, a participant must obtain 'passed' scores for the first three consecutive items following an age-specific start point in the examination to progress. If participant receives a 'not passed' score on any of these items, the assessment score reverts to the previous age range until the rule is met. Conversely, under the discontinue rule, the examination is terminated when 'not passed' scores are recorded for five consecutive items. Finally, the total composite scores for Cognitive scale and Motor scale were calculated, a higher domain score represented a better development.

Statistical analysis

Chi-square tests were used to compare differences among the four subgroups across categorical variables (i.e., infant gender, delivery method and family income). A univariate analysis of variance (ANOVA) was conducted to compare differences in four groups across numerical variables (i.e., the Apgar score, gestational age, birth weight, birth length, maternal age, maternal education and EPDS score). The

Bonferroni test was used to perform pairwise comparisons between group mean. Where significant differences were found for any of variables, they were subsequently considered in a Multivariate Variate Analysis of Variance (MANOVA) that compared the differences of the dietary nutrients consumed, growth and development of infants in four groups. A p-value < 0.05 was considered statistically significant. All the data were analysed using SPSS 23.0 (SPSS Inc., Chicago, IL, USA).

Results

Demographic and Anthropometric Measurements

Table 1 shows the characteristics of the 201 infants (followed-up at age of 8 months) involved in this cohort study. It should be noted there was an attrition rate of 22.7% (i.e., 59) infants. In relation to gender, gestational age, Apgar score, birth length, birth weight, the proportion of preterm, mother's age, education, mental status and income, the characteristics of the 201 infants did not differ significantly from those of the 59 infants who did not participate in the follow-up part of the study.

Table 1. Characteristics of the followed sample and missing sample.

	Follow up	Missing	x2 or t	P
Sample size	201	59		
Gestational term				
Preterm	101(50.25)	29(49.15)	0.02	0.88
Fullterm	100(49.75)	30(50.85)		
Infant gender			0.44	0.5
Male	106(52.74)	34(57.63)		
Female	95(47.26)	25(42.37)		
1-minute Apgar score,x±s	9.90 ± 0.41	9.84 ± 0.44	0.85	0.39
5-minute Apgar score,x±s	9.98 ± 0.14	9.95 ± 0.22	1.01	0.31
10-minute Apgar score,x±s	9.99 ± 0.12	9.95 ± 0.22	1.19	0.23
Gestational age, weeks,x±s	36.26 ± 2.60	36.34 ± 3.09	-0.17	0.86
Delivery way				
Vaginal delivery	67 (33.33)	19 (32.2)	0.026	0.87
Cesarean delivery	134 (66.67)	40 (67.8)		
Birth weight, g,x±s	2755.6 ± 762.6	2811.5 ± 849.5	-0.48	0.62
Birth length, cm,x±s	47.40 ± 4.59	47.40 ± 4.59	0.01	0.99
Maternal age,years,x±s	30.84 ± 3.85	31.08 ± 3.96	-0.43	0.6
Maternal education, years,x±s	16.27 ± 2.19	15.84 ± 2.45	1.26	0.2
Family income (RMB,yuan),n(%)			1.79	0.4
~100000	81 (40.3)	29(49.15)		
100001~200000	103(51.24)	27(45.76)		
>200000	17(8.46)	3(5.08)		
Total score of EPDS	7.69 ± 2.61	7.79 ± 2.99	-0.26	0.8
<9	134(66.67)	38(64.41)		
9-10	34(16.92)	13(22.03)		
11-12	27(13.43)	6(10.17)		
>=13	6(2.99)	2(3.39)		

Table 2 sets out participants' demographic and anthropometric measurements. There were no statistically significant differences between fullterm infants in the depression and non-depression group ($p > 0.05$) and preterm infants ($p > 0.05$) in relation to gender, Apgar score, gestational age, birth weight, birth length, maternal age, maternal education and family income. However, depressed mothers had significantly higher

187 EPDS scores than non-depressed mothers in both the fullterm and preterm groups. No
188 significant differences were found in four groups in relation to infant gender, maternal
189 age, education and family income, except in relation to delivery method ($p = 0.03$).
190 Thus, the variable of delivery method was controlled for in the subsequent
191 multivariate analyses.
192

193 Table 2. Demographic and anthropometric measurements of infants.

Variables		Fullterm(100/130)*		preterm (101/130) *		x2 or F	P
		non-depression	Depression	non-depression	Depression		
		(64/82) *	(36/48) *	(70/90) *	(31/40) *		
Infant gender,n(%)							
Male		33(51.56)	19(52.78)	37(52.86)	17(54.84)	x2=0.09	0.99
Female		31(48.44)	17(47.22)	33(47.14)	14(45.16)		
1-minute Apgar score,x±s		9.98±0.13	9.97±0.17	9.81±0.55	9.84±0.58	F=2.56	0.06
5-minute Apgar score,x±s		10.00±0.00	10.00±0.00	9.97±0.17	9.94±0.25	F=1.83	0.14
10-minute Apgar score,x±s		10.00±0.00	10.00±0.00	9.99±0.12	9.94±0.25	F=2.27	0.08
Gestational weeks,x±s	age,	38.86±1.00	38.92±1.02	34.59±1.64 ^{ab}	34.29±1.82 ^{ab}	x2=83.64	<0.01
Delivery way							
Vaginal delivery		25(39.06)	17(47.22)	20(28.57)	5(16.13) ^{ab}	x2=8.91	0.03
Cesarean delivery		39(60.94)	19(52.78)	50(71.43)	26(83.87)		
Birth weight, g,x±s		3375.94 ± 421.13	3317.78 ± 367.77	2195.57 ± 528.06 ^{ab}	2086.45 ± 557.84 ^{ab}	F=106.05	<0.01
Birth length, cm,x±s		50.67 ± 1.48	50.14 ± 1.17	44.46 ± 4.83 ^{ab}	43.84 ± 4.12 ^{ab}	F=55.68	<0.01
Maternal age,years,x±s		31.23 ± 3.41	30.12 ± 3.12	31.13 ± 4.63	30.26 ± 3.55	F=1.00	0.39
Maternal education, years,x±s		16.60±1.68	16.06±2.29	16.05±2.21	16.29±2.95	F=0.58	0.56
Family income (RMB,yuan),n(%)							
~100000		18(32.14)	8(25.81)	22(31.88)	7(22.58)	x2=7.09	0.31
100001~200000		20(35.71)	16(51.61)	28(40.58)	9(29.03)		
>200000		18(32.14)	7(22.58)	19(27.54)	15(48.39)		
EPDS score within postpartum 3 days (x±s)							
<9		64(100)	0	70(100)	0		
9-10		0	20(55.56)	0	14(45.16)		
11-12		0	12(33.33)	0	15(48.39)		
>=13		0	4(11.11)	0	2(6.45)		

194 Note: a: compared with non-depression-fullterm group, P<0.05; b: compared with
195 depression-fullterm group, P<0.05; c: compared with non-depression-preterm group,
196 P<0.05. *: followed samples to original samples.

24 Hour Diet Recall

The intake of most nutrients (e.g., energy, protein, fat, vitamin A, thiamine, riboflavin, niacin, vitamin C, vitamin E, calcium, phosphorus, potassium, sodium, iron, zinc, selenium, copper and retinol) in the non-depression-preterm group was higher than that in the other three groups. In relation to fullterm infants, the energy, protein and fat intake in the depression group was lower than that in the non-depression group ($p < 0.05$). The intake of other nutrients (e.g., carbohydrate, thiamin, riboflavin, niacin, vitamin C, vitamin E, calcium, phosphorus, potassium, magnesium, iron, zinc, selenium) in the depression group for fullterm infants was lower than that in the non-depression group although there were no statistical differences between groups ($p > 0.05$). The intake of energy, protein, carbohydrate and most other nutrients was lower among preterm infants with depressed mothers than other infants without depressed mothers ($p < 0.05$ and see in Table 3).

Table 3. Energy and nutrient intake among four groups at 8 corrected monthsage(%).

Variables	Fullterm(100)		preterm (101)	
	non-depression (64)	depression (36)	non-depression (70)	depression(31)
Energy(kJ)	3040.64 ±794.28	2685.25 ±967.18 ^a	3109.25 ±1040.57 ^b	2649.80 ±1162.85 ^{ac}
Protein(g)	20.57 ±7.95	17.39 ±7.33 ^a	22.55 ±8.28 ^b	17.85 ±8.50 ^c
Fat(g)	31.33 ±9.36	27.14 ±11.85 ^a	32.67 ±12.20 ^b	28.81 ±14.49
Carbohydrate(g)	91.95 ±28.15	83.58 ±29.63	90.30 ±30.94	76.57 ±34.11 ^{ac}
Diet fiber(g)	1.42 ±1.41	1.55 ±1.24	1.38 ±1.24	1.32 ±1.10
Cholesterol(g)	282.56 ±228.29	289.92 ±224.31	221.54 ±185.72	236.62 ±171.87
Ash(g)	2.45 ±1.13	2.44 ±1.29	1.77 ±1.20 ^{ab}	1.71 ±0.97 ^{ab}
Vitamin A(ugRE)	431.12 ±296.82	456.03 ±399.30	500.09 ±236.20	443.71 ±240.70
Tot carotene (ug)	406.45 ±655.13	437.12 ±709.63	307.32 ±402.33	278.12 ±293.12
Thiamin(mg)	0.41 ±0.27	0.34 ±0.23	0.55 ±0.29 ^{ab}	0.43 ±0.26 ^c
Riboflavin(mg)	0.71 ±0.34	0.63 ±0.33	0.84 ±0.39 ^{ab}	0.68 ±0.36 ^c
Niacin(ug)	4.69 ±2.67	3.77 ±2.35	5.96 ±2.94 ^{ab}	4.47 ±2.66 ^c
Vitamin C(mg)	60.67 ±26.56	57.80 ±28.54	69.27 ±30.51 ^{ab}	55.36 ±29.06 ^c
Vitamin E(mg)	9.43 ±10.29	7.93 ±8.30	16.18 ±11.02 ^{ab}	12.33 ±10.22 ^{b^c}
Calcium(mg)	530.82 ±318.26	488.32 ±285.05	680.18 ±325.28 ^{ab}	588.04 ±236.54
Phosphorus(mg)	467.28 ±347.91	375.88 ±285.57	664.61 ±372.77 ^{ab}	492.86 ±321.22 ^c
Potassium(mg)	531.69 ±458.17	426.28 ±337.40	784.08 ±469.20 ^{ab}	549.72 ±409.60 ^c
Sodium(mg)	119.31 ±120.08	133.20 ±173.83	233.30 ±206.28 ^{ab}	131.48 ±111.93 ^c
Magnesium(mg)	202.78 ±88.21	179.33 ±89.62	133.96 ±64.71 ^{ab}	140.09 ±80.96 ^{ab}
Iron(mg)	7.07 ±4.87	6.98 ±4.55	9.76 ±4.77 ^{ab}	9.07 ±4.72 ^{ab}
Zinc(mg)	4.49 ±1.78	4.22 ±2.42	5.48 ±2.59 ^{ab}	4.47 ±2.54 ^c
Selenium(ug)	12.95 ±10.38	10.42 ±8.24	17.47 ±8.58 ^{ab}	13.03 ±8.54 ^c
Copper(mg)	0.51 ±0.28	0.60 ±0.51	0.64 ±0.27 ^a	0.52 ±0.29 ^c
Manganese(mg)	0.47 ±0.51	0.49 ±0.47	0.45 ±0.35	0.47 ±0.68
Retinol(mg)	298.76 ±256.56	310.56 ±389.21	390.03 ±231.37 ^a	349.16 ±217.96

Note:

a: compared with non-depression-fullterm group, P<0.05; b: compared with depression-fullterm group, P<0.05; c: compared with non-depression-preterm group, P<0.05

Further, the mean dietary consumption of energy, protein and carbohydrate in the depression group was lower than 100% of RNI both in fullterm and preterm infants (see Table 4). In the non-depression-preterm group, the mean intakes of energy, protein and carbohydrate were adequate and were higher than 100% of RNI.

Table 4. The mean intake of energy and nutrients compared with the RNI in infants at 8 months corrected age among four groups(%).

Variables	Fullterm (100)		Preterm (101)	
	non-depression(64)	depression(36)	non-depression(64)	depression(36)
Energy	99.04±31.81	87.11±34.16	101.61±36.25 ^b	93.01±38.43
Protein	102.86±39.75	86.96±36.66 ^a	112.73±41.40 ^b	89.27±42.48 ^{ac}
Carbohydrate	108.18±33.12	98.33±34.85	106.23±36.40	90.08±40.13 ^{ac}
Vitamin A	123.18±84.80	130.30±114.08	142.88±67.48	126.77±68.77
Thiamin	135.40±90.59	114.88±77.65	181.76±96.86 ^{ab}	142.26±87.25 ^c
Riboflavin	142.03±68.22	126.16±65.43	168.43±77.51 ^{ab}	136.56±71.48 ^c
Niacin	156.44±89.05	125.51±78.42	198.55±98.09 ^{ab}	149.11±88.63 ^c
Vitamin C	151.67±66.39	144.51±71.36	173.18±76.28 ^b	138.39±72.66 ^c
Vitamin E	235.66±257.26	198.31±207.51	404.46±275.49 ^{ab}	308.32±255.44 ^{bc}
Calcium	212.33±127.30	195.33±114.02	272.07±130.11 ^{ab}	235.21±94.62
Phosphorus	259.60±193.28	208.82±158.65	369.23±207.10 ^{ab}	273.81±178.46 ^c
Potassium	96.67±83.30	77.51±61.35	142.56±85.31 ^{ab}	99.95±74.47 ^c
Sodium	34.09±34.31	38.06±49.66	66.66±58.94 ^{ab}	37.57±31.98 ^c
Magnesium	311.97±135.71	275.89±137.87	206.09±99.56 ^{ab}	215.52±124.56 ^{ab}
Iron	70.70±48.70	69.81±45.54	97.58±47.74 ^{ab}	90.65±47.18 ^{ab}
Zinc	128.27±50.94	120.55±69.27	156.57±74.01 ^{ab}	127.81±72.44 ^c
Selenium	64.77±51.88	52.08±41.19	87.37±42.90 ^{ab}	65.15±42.68 ^c
Copper	170.40±92.02	201.65±170.76	214.67±90.84 ^a	172.77±97.22 ^c
Manganese	67.01±72.43	70.19±67.51	63.58±49.57	67.54±96.66

Note:

RNI: Recommended Nutrient Intakes;a: compared with nondepression-fullterm group,P<0.05; b: compared with depression-fullterm group,P<0.05; c: compared with nondepression-preterm group, P<0.05

Impact on Growth and Development

Z-scores for weight, length, Bayley-III composite scores for cognitive scale and motor scale were lower among preterm infants in the depression group than those in the fullterm group ($p < 0.05$ and see Table 5). The Z-scores for weight, Bayley-III composite scores for cognitive scale and motor scale of preterm infants in the

depression group were lower than those of preterm infants in the non-depression group ($p < 0.05$). The Z-scores for length of preterm infants in the depression group were lower than those in the non-depression group although there were no statistical differences between groups ($p > 0.05$). No significant differences were present between preterm non-depression group and fullterm group ($p > 0.05$).

Table 5. Comparison of growth and development in infants at 8 months corrected age among four groups.

Variables	Fullterm (100)		Preterm (101)	
	non-depression(64)	depression (36)	non-depression(70)	depression (31)
Weight Z-score	1.14 $\pm$ 0.93	1.16 $\pm$ 1.00	1.04 $\pm$ 1.07	0.31 $\pm$ 1.20 ^{abc}
Length Z-score	0.86 $\pm$ 1.05	0.93 $\pm$ 1.01	0.66 $\pm$ 1.17	0.35 $\pm$ 1.13 ^{ab}
Cognitive composite score	105.82 $\pm$ 9.87	105.21 $\pm$ 8.36	105.83 $\pm$ 9.60	101.61 $\pm$ 8.10 ^{abc}
Motor composite score	102.41 $\pm$ 8.99	100.01 $\pm$ 9.39	100.92 $\pm$ 7.59	96.52 $\pm$ 9.75 ^{abc}

Note:

a: compared with non-depression fullterm group, $P < 0.05$; b: compared with depression fullterm group, $P < 0.05$; c: compared with non-depression-preterm group, $P < 0.05$

Discussion

In our study, the dietary intake of energy, protein and carbohydrates in the depression group was lower than the recommended intake. Further, the preterm infants of depressed mothers do not have sufficient nutrient intake for 'catch-up growth' and had poorer growth and development than infants of fullterm groups, more importantly, lower than preterm infants of non-depressed mothers. The results of this study are consistent with previous studies; infants of mothers with depression had poor growth[4, 23]. This may be because mothers with depression have low maternal responses to infant's needs[24]. For example, it has been shown that mothers with elevated depression symptoms demonstrate less responsive feeding practices than

264 mothers with lower levels of depression symptoms[25]. Further, mothers with more
265 depression symptoms are less interactive and show less encouragement to engage
266 infants in feeding[26]. Other studies [24, 27] have suggested that depressed mothers
267 display negative maternal feeding behaviours over the first year of an infant's life.

268 Preterm infants often have nutrient deficits and display poor growth[13]. Further, they
269 need higher nutrition intake for 'catch-up growth' in the first year after their births[14,
270 28]. Our study demonstrated that preterm infants of mothers without depression had
271 the highest nutrient intake of the four groups. This may be attributable to the careful
272 feeding practices[29, 30] of mothers without depression. Usually, mothers without
273 depression are aware of the functional immaturity of the gastrointestinal system[30]
274 and show adequate sensitivity and involvement in the nutritional management of their
275 preterm infants[29]. Further, our results showed that the preterm infants with
276 depressed mothers did not have sufficient nutrient intake for 'catch-up growth'. This
277 is probably due to the poor feeding competency of mothers with depression.
278 Consequently, preterm infants of depressed mothers displayed poorer growth than
279 preterm infants of non-depressed mothers. A previous study[31]showed that
280 interventions among mothers experiencing depressive symptom may improve their
281 responsiveness to child feeding.

282 Our study indicated that the preterm infants of depressed mothers performed more
283 poorly on cognitive development tests than infants in the other three groups. These
284 findings are consistent with previous studies and suggested that the preterm infants of
285 depressed mothers are an at-risk population. For example, previous studies[8, 32]

have shown that depressed mothers provide less cognitive stimulation and less interaction to their infants than non-depressed mothers. Aktar et al.[33] suggested that maternal depression might affect infants' attention to emotion-object associations in social learning contexts. Perra et al.[34] found an association between maternal postnatal depression and later cognitive development. Further, it has been pointed out that early maternal depression and environmental risk factors directly affect children's cognitive and social functioning later in life[6, 35].

In the present study, both maternal depression and preterm births were found to be associated with delayed motor development. A previous study[36] suggested that delayed gross motor development was associated with smaller body sizes throughout infancy (i.e., poor 'catch-up' growth) and that nutrition is the material basis for infant growth and development. Our study indicated that both maternal depression and preterm births were associated with the nutrition of infants. Depressed mothers with poor feeding practices may not provide sufficient nutrition for the 'catch-up' growth of preterm infants and consequently preterm infants experience delayed motor development. Additionally, nutrient intake deficiencies can lead to brain and metabolic abnormalities[37] that may affect motor function. Further, depressed mothers display less positive interactions with and provide less motor stimulation to their infants[7, 8]. This is probably another reason for delayed motor development.

Furthermore, deficient postnatal 'catch-up' growth was associated with poor neurologic outcome for preterm infants[12, 38, 39], gross motor development information was associated with child cognitive performance[40]. Pina-Camacho et

al.[41] conducted a path analysis and indicated that maternal depression and unhealthy nutrition in early life periods are inter-related and independent risk factors for abnormal child emotional–behavioural development. Thus, supporting individuals with maternal depression and nutrition interventions may be especially important for preterm infants.

This study has a number of strengths compared to previous studies. First, this is the first time the dual effects of maternal depression and preterm birth on infants’ growth and development were examined. Previous studies have only looked at effects of maternal depression [4, 23] or preterm birth [11, 42] alone on infants’ growth and development. Our study discovered that the preterm infants with depressed mothers had poorer nutrition intake, growth and development, and were more vulnerable than either fullterm birth with a depressed mother or preterm birth alone. The finding is important as it will inform future intervention practice to focus on the more vulnerable group of preterm born infants with depressed mothers. Second, this is the first study to investigate the nutrition intake of infants with depressed mothers using the 24-HDR method. This approach provided novel insights into the effects of both maternal depression and preterm birth on infants’ growth and development.

This study also has some limitations. First, the attrition of approximately 22.7% of the infants at the follow-up time of 8 months maybe have had a small impact on the results. However, it should be noted that the remaining 201 infants did not differ significantly from the 59 infants that did not take part in the follow-up part of the study in terms of their demographics and anthropometric measurements. Second,

mothers' depression status was measured within three days of delivery in our study and its predictive value to infant development may be over estimated. Although previous studies found the positive correlation between the EPDS scores at 2 to 3 days postpartum and at 4 to 6 weeks postpartum ($r = 0.59$, $P < 0.0001$) [43], the EPDS scores at 3 days postpartum only may not fully represent mothers' mental status in later postpartum. Maternal mental status may be associated with many other factors such as mode of delivery[44, 45], newborn sex[46], family status [47], etc. Misclassification of mothers' depression status may be confounded by these factors in our study. Future study should measure mothers depression at different postnatal time to provide predictive value of mothers mental status at 2 to 3 days postpartum. Third, as we did not obtain sufficient samples of mothers with severe depression symptoms ($EPDS \geq 13$), the association between depression symptoms and outcomes may have been underestimated. Thus, future studies may be needed with a sufficient sample of participants with severe depression symptoms. Fourth, the disruption of mother-infant interactions and stimulation of infants have not been considered as independent variables and not included in the multivariable models.

For the implications and future research, the cognitive and motor development of infants is based on their physical growth. Further, 'catch-up' growth during infancy is directly related to improved neurodevelopment[39]. A previous study[40] found that gross motor development is associated with cognitive performance. Further, disrupted interactions between depressed mothers and infants may affect infants' motor development. Consequently adequate nutritional support and healthy mother–infant

interactions may contribute to the ‘catch-up’ growth of preterm infants and their motor and cognitive development. The preterm infants of depressed mothers require special attention to ensure their ‘catch-up’ growth and improve their development as soon as possible. It is important to support mothers with maternal depression and nutrition intervention. In conclusion, the preterm infants with depressed mothers are more vulnerable than either fullterm birth with a depressed mother or preterm birth alone, the preterm infants of depressed mothers are at high risk of poor nutrition intake, poor growth and developmental delay and thus require special attention. Intervention approaches should seek to support mothers with maternal depression, improve mother-infant interactions and consider the necessity of nutrition interventions.

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379 **Compliance with ethics guidelines**

380 Han Wang, Hong Zhou, Yan Zhang, Yan Wang, Jing Sun declare that they have no
381 conflict of interest. All procedures related to human samples were approved by the
382 Ethics Committee of Peking University's Health Science Centre (No. IRB00001052 -
383 13001). Informed consent was obtained from all parents for inclusion in the study.

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