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Does tea consumption during early pregnancy have an adverse effect on birth outcomes?

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1 2

3 Abstract

Background Tea, a common beverage, has been suggested to exhibit a number of health
benefits. However, one of its active ingredients, caffeine, has been associated with preterm
birth and low birthweight. We investigated whether tea consumption during early pregnancy is
associated with an increased risk of preterm birth and abnormal foetal growth.

Does tea consumption during early pregnancy have an adverse effect on birth outcomes?

8 Methods A total of 8775 pregnant women were included from the Born in Guangzhou Cohort

9 Study. Tea consumption (type, frequency and strength) during their first trimester and social

10 and demographic factors were obtained via questionnaires administered during pregnancy.

11 Information on birth outcomes and complications during pregnancy was obtained from hospital

12 medical records.

13 **Results** Overall habitual tea drinking (≥ 1 serving/week) prevalence among pregnant women

14 was low, at 16%. After adjustment for potential confounding factors (e.g. maternal age,

15 educational level, monthly income) tea drinking during early pregnancy was not associated

16 with an increased risk of preterm birth, small or large for gestational age (p>0.05).

17 **Conclusions** We did not identify a consistent association between frequency of tea

18 consumption or tea strength and adverse birth outcomes among Chinese pregnant women with

19 low tea consumption. Our findings suggest that occasional tea drinking during pregnancy is not

20 associated with increased risk of preterm birth or abnormal foetal growth. Given the high

21 overall number of annual births in China, our findings have important public health

22 significance.

23 Keywords: Tea: Preterm birth: Abnormal foetal growth: Chinese: Birth cohort

24 Introduction

25 Preterm birth and abnormal foetal growth (including small for gestational age [SGA] and large for gestational age [LGA]) are important predictors of neonatal morbidity and mortality 26 27 as well as adverse health outcomes in childhood and adulthood (1-3). A recent study in seven regions in China suggests a preterm birth rate of 7.1% in 2011 (4), and data from Guangzhou, 28 29 the largest city in southern China, indicate the prevalence of SGA and LGA being 8.6% and 30 8.5%, respectively (5). Whilst the rates are not particularly high compared to those of south 31 Asia (13.3%) and sub-Saharan Africa (12.3%) (6), given the large absolute number of live 32 births in China (12% of global total in 2010) (6), identification of risk factors associated with 33 preterm birth and abnormal foetal growth is of particular public health importance. 34 Tea is a beverage prepared from the leaves of the plant Camellia sinensis, and contains a number of biologically active constituents, including polyphenols (e.g. catechins) and 35 36 alkaloids (e.g. caffeine). Tea is broadly classified into green, oolong and black tea according 37 to the degree of enzyme-mediated oxidation (known as fermentation) (7). There has been some conflicting evidence on the health benefits of tea⁽⁸⁻¹⁰⁾, but much less 38 39 is known about the potential effects of tea drinking during pregnancy on foetal growth and 40 development. In vivo studies in rats suggested black tea(11) or green tea catechin(12) had no 41 effect on the weight of pups, but to our knowledge, no human studies have investigated the 42 effects of tea on preterm birth and birthweight. On the other hand, reports have suggested that 43 one of the active ingredients in tea, caffeine, is negatively associated with birthweight (13-17). 44 This relationship was confirmed in a recent meta-analysis (18), although there was no 45 association with preterm birth (18, 19). It should be noted, however, that tea consumption has a lesser contribution than coffee for total caffeine intake in the Western populations studied 46 47 (13-17), whereas in China tea remains the most popular beverage (20).

The current Chinese dietary guidelines (21) do not comment on the frequency of intake and the type of tea. As a substantial number of tea drinkers in China are of child-bearing age, clarifying the potential association of tea consumption on gestational age and birthweight is of public health importance. Using data from a large prospective birth cohort in China, we investigated the effect of tea drinking during early pregnancy on foetal growth and preterm birth.

54

57

55 Methods

56 Recruitment

the Guangzhou Women and Children's Medical Center (GWCMC), China, which

59 commenced in February 2012. Details of the recruitment can be found elsewhere (22). Briefly,

The Born in Guangzhou Cohort Study (BIGCS) is an ongoing prospective study conducted by

all pregnant women residing within Guangzhou who attended their first routine antenatal

61 examination (usually around week 16) at two campuses of GWCMC, and who intended to

for remain in Guangzhou with their child for ≥ 3 years were invited to participate in BIGCS. At

63 baseline recruitment, demographic and socio-economic information were obtained via self-

64 completed questionnaires, as well as data on workplace and home exposures, lifestyle,

65 medical histories, and health status before and during pregnancy. BIGCS has received

66 approval from the Institutional Ethics Committee of GWCMC. All participants gave written

- 67 informed consent.
- 68 For this analysis, data from pregnant women recruited between February 2012 and

69 December 2014 (n = 10277; 73.6% of those eligible) were used. We excluded those who

dropped out before delivery (n = 435), or terminated their pregnancies or had stillbirths (n =

111), or had multiple gestation (n = 212), or who had missing delivery data (n = 155),

resulting in 9364 singleton births in this report (Figure 1).

73 Tea consumption

74 Participants were asked at baseline (around 16 weeks of gestation) whether they regularly consumed tea during pregnancy. Subsequently, participants were asked to specify the type of 75 76 tea they drank (green, oolong, black [known as "red tea" in China], and dark [a variety of post-fermented tea in China]), how many servings they consumed each type in a typical week 77 78 (one serving was defined as 150 mL of tea), and the strength of tea (defined subjectively: 79 weak, moderate, strong) they preferred. We grouped the types of teas into green 80 (unfermented), oolong (semi-fermented) and black and dark tea (fermented) teas. Frequency was categorised into <1, 1–3, and >3 servings/week, and tea strength was dichotomised into 81 82 weak and moderate/strong. 83 84 Birth outcomes 85 Birthweight among other birth outcomes (gestational age, parity, mode of delivery, and foetal 86 sex) were obtained from the Guangzhou Perinatal Health Care and Delivery Surveillance 87 System which records all births within the municipality. Gestational age at birth was 88 determined based on ultrasound examination within the first- or early second-trimester. 89 Preterm birth was defined as delivery before 37 weeks gestation. Those births with gestational 90 age 37 weeks or above were considered as term. SGA and LGA were defined as a gestational 91 age-adjusted birthweight below the 10th and above the 90th percentile, respectively, derived 92 from a local population-based birthweight reference (23). The remaining births were 93 considered as appropriate for gestational age (AGA). 94 95 **Covariates** 96 From the questionnaire, we derived maternal age (continuous), highest education level and

97 maternal monthly income. Both education level and monthly income category were used as

98 proxies for socio-economic status. Maternal smoking three months before pregnancy and 99 during pregnancy (number of cigarettes per day) was assessed. Participants were considered 100 to have environmental tobacco smoke exposure if they were either exposed to second-hand 101 smoke at home or at work during early pregnancy. Folic acid supplement use was recorded in 102 the questionnaire. Pre-pregnancy maternal height (cm) and weight (kg) were self-reported at 103 recruitment, from which body mass index (BMI; kg/m2) was derived. Information on 104 complications during the current pregnancy, including pre-eclampsia, pregnancy-induced 105 hypertension, pre-pregnancy hypertension, gestational diabetes and pre-pregnancy diabetes, 106 was obtained from medical records after delivery.

107

108 Statistical analysis

109 Differences in characteristics by frequency of tea consumption during early pregnancy were 110 evaluated using Student's t-test, χ^2 test or Mann-Whitney U test where appropriate. Logistic 111 regression models were constructed in order to assess the relationship between tea 112 consumption during early pregnancy (frequency and strength) and birth outcomes, adjusting 113 for known determinants of foetal growth (maternal age, complications during pregnancy, 114 parity, and foetal sex), as well as potential confounders relating to tea consumption (socio-115 economic status, exposure to tobacco smoke, and folic acid supplement use) based on 116 evidence from the literature. We also explored the dose-response relationship between tea 117 consumption and risk of adverse pregnancy outcomes, by including frequency of tea drinking 118 as continuous variable into the regression models. We examined the effects of individual 119 types of tea in two ways: (i) we included additional variables indicating other types of tea to 120 take into account the total tea intake, and (ii) we restricted the analysis to those who only 121 consumed one type of tea to avoid contamination bias. We compared distributions of Z-score

122 of birthweight and gestational age at birth (both continuous) using the Kruskal-Wallis test, 123 among women with different levels of tea consumption (<1, 1–3, and >3 servings/week). 124 We also examined whether any relationships were modified by maternal pre-pregnancy 125 BMI by including interaction terms in the models. Although previous studies have suggested 126 that caffeine intake is associated with adverse birth outcomes (13-16), the prevalence of 127 habitual coffee drinking (≥ 1 serving/week) was extremely low in this cohort (0.9%), and 128 hence we did not include coffee consumption as a confounding factor. However, we 129 conducted a sensitivity analysis restricting those included in the analyses to non-coffee 130 drinking participants. All analyses were performed using SAS statistical software version 9.2 131 (SAS Institute Inc., Cary, NC, USA). A two-tailed p-value of less than 0.05 was considered statistically significant in all statistical analyses. 132

133

134 Results

135 Of the 9364 eligible singleton pregnancies, 8775 (93.7%) had available information on tea 136 consumption during early pregnancy and were included in the analysis. Those who were 137 excluded were more likely to have a higher educational level and income compared to those 138 included in the final analyses (Supplementary Table 1). Table 1 presents the characteristics of 139 pregnant women at enrolment and selected pregnancy outcomes. In this sample, 1420 women 140 (16.2%) reported drinking tea at least once per week (median 3, interquartile range 2-5) 141 during early pregnancy. Most of the tea-drinking participants (71.8%) consumed only one 142 type of tea (median 2 servings/week), 22.7% two types (4 servings/week), and 4.2% three 143 types (6 servings/week). Those who consumed tea habitually (at least 1 serving per week) 144 were more likely to be slightly older, have a higher educational level, be exposed to second 145 hand tobacco smoke (34.8 vs. 29.7%), have a higher mean (\pm SD) pre-pregnancy BMI (20.6 \pm 146 2.8 vs. 20.3 ± 2.6 kg/m²) and to be multiparous (14.9 vs. 10.8%) compared to those mothers

who did not consume tea regularly. Overall, there were no significant difference in
birthweight and the proportions of SGA and LGA between children whose mothers did or did
not consume tea regularly at baseline.

150 Results of logistic regression of birth outcomes on tea consumption during early pregnancy 151 are presented in Table 2. There was no association between tea consumption during early 152 pregnancy and the birth outcomes we measured (preterm birth, SGA and LGA), after 153 adjustment for potential confounding factors (maternal age, educational level, monthly 154 income, exposure to environmental tobacco smoke and folic intake during early pregnancy, 155 pre-pregnancy BMI, parity, complications during pregnancy and foetal sex). Among the three 156 types of tea examined, frequent green tea consumption was significantly associated with LGA 157 (fully adjusted OR = 1.67; 95% CI, 1.01, 2.75; p=0.045), but non-significant risk estimates 158 were found for preterm birth (0.54; 0.18, 1.63) and SGA (0.57; 0.21, 1.51). We did not 159 observe any statistically meaningful relationship between oolong tea and dark/black tea 160 consumption and birth outcomes. When we included frequency of tea drinking as continuous 161 variable into the regression models, there was also no apparent dose-response relationship 162 between tea consumption and risk of adverse pregnancy outcomes. When we used Z-score of 163 birthweight instead of the binary SGA and LGA variables, we did not see a positive 164 association between green tea consumption and birthweight, although there was a decreasing 165 trend in gestational age at birth among Oolong tea-drinking women (Supplementary Table 2). 166 Among the regular tea drinkers at baseline, 22.7% and 4.2% consumed two and three or 167 more types of tea, respectively. To avoid potential attenuation of observed effect sizes due to 168 consumption of multiple tea types, we repeated the analysis by restricting to those who 169 reported to drink only one specific type. Overall, the risk estimates for preterm birth, SGA, 170 and LGA were very similar to those obtained from the analysis using the full sample although 171 the confidence intervals were slightly wider (Supplementary Table 3).

We also investigated the possible effects of tea strength (Table 3). Consumption of weak
Oolong tea was associated with reduced risk of preterm birth (OR: 0.21; 95% CI: 0.06, 0.76).
We did not find significant association between adverse birth outcomes and strength of green
or dark/black tea in multivariate analysis.

As tea drinking may be favoured by women who intend to lose weight, we also tested for potential interaction between pre-pregnancy BMI and tea consumption by including an interaction term in the regression model. This, however, did not change the risk estimates (results not shown). Restricting the analysis to non-coffee drinking participants also did not alter the conclusion (results not shown).

181

182 Discussion

183 In a contemporary sample of Chinese pregnant women with low consumption of tea, we did 184 not find evidence suggesting an adverse effect of tea consumption on gestational age or 185 birthweight of offspring after adjusting for potential confounding factors. Although higher 186 consumption of unfermented tea (green tea) was associated with an increased risk of LGA, 187 this finding was of borderline significance, and may be a result of multiple comparisons. As 188 the official Chinese dietary guidelines do not comment on tea intake during gestation (21), 189 pregnant women are likely to consult internet-based information for dietary advice, which 190 often delivers mixed messages without any scientific evidence, and many women might opt to 191 avoid tea drinking altogether. Our findings do not support the need for pregnant women to 192 abstain from tea drinking during early pregnancy, at least when it is consumed at a low to 193 moderate level.

To our knowledge, our study is the first to investigate the effects of tea consumption on birthweight in an Asian setting with a large prospective birth cohort study. Surprisingly, we observed a low prevalence (only 16%) of tea drinking in the study population. In fact, results 197 from the China Health and Nutrition Survey (CHNS) suggest the prevalence of tea drinking 198 had fallen by 10% between 1993 and 2009 (from 44% to 34%), and that the most prominent 199 decline has occurred in the 18–29 years age group (by about 20%) (20). Another study of 200 5133 adults from the three largest Chinese cities (Beijing, Shanghai, and Guangzhou) also 201 found a lower prevalence of tea drinking among those 20–29 years (27%) compared to 30-39 202 years (46%) (24). These figures support our observation that tea drinking is less popular 203 among the younger generation (particularly those of child-bearing age).

Whilst previous studies have attempted to assess the effect of tea consumption in relation to birthweight (13-17), the focus was generally on caffeine intake and not the beverage per se. A small case-control study of 155 women in Beijing, China found an increased risk of SGA associated with tea consumption at least twice a week during pregnancy (25). Potential recall bias and the lack of adjustment for SGA risk factors (e.g., complications during pregnancy, parity) in the analyses may explain the inconsistency with our own findings.

210 To date there has been no definitive conclusion on whether tea consumption in pregnant 211 women could affect offspring. It is proposed that excessive caffeine intake might be 212 teratogenic (26). However, a recent review by Brent et al. concluded that results from both 213 epidemiological and animal studies suggest caffeine intake is "unlikely to have reproductive 214 and developmental effects" (27). On the other hand, accumulating findings from animal and 215 human studies have pointed to a possible weight reduction effect by tea. Green tea extracts or 216 (-)-epigallocatechin-3-gallate (EGCG), one of the tea catechins, have been shown to reduce 217 weight gain, blood glucose or insulin levels in obese/diabetic animals or those on high-fat 218 diets (28). In humans, a number of small randomised-controlled trials have been conducted, as 219 summarised by two recent meta-analyses (29, 30). Most of the studies included administered 220 green tea or green tea extracts with caffeine in normal weight or overweight individuals and 221 showed weight reduction compared with caffeine-free controls, hence leading to a question of

222 whether weight loss was an effect of caffeine in tea, or due to a combined effect of caffeine 223 and tea catechins. A meta-analysis demonstrated that while both caffeine alone and the 224 combination of catechins and caffeine increased daily energy expenditure, only the latter 225 could significantly increase fat oxidation (31). A recent Cochrane review further supported 226 this concept, concluding that green tea preparations may induce little loss of weight in obese 227 or overweight adults (9). As maternal glucose and lipid metabolism during pregnancy is 228 highly relevant to the fetal nutrient supply (32, 33), it is entirely plausible that tea (or 229 catechins in combination with caffeine) could have an adverse impact on birthweight. 230 Nevertheless, after adjusting for confounders we did not find compelling evidence that tea 231 consumption was associated with birthweight Z-score, SGA or LGA. 232 Results from analyses using tea strength as an exposure measure are somewhat inconsistent 233 with those using the frequency of consumption. Firstly it should be noted that the strength of 234 tea is a subjective indicator in this study and could not precisely represent the dose of tea. 235 Additionally, longer steeping time may not only strengthen the flavour, but may also 236 encourage the release of other components as well as contaminants in tea leaves, such as 237 heavy metals (34). This may introduce toxic effects in addition to the potential weight 238 reducing capacity of catechins and caffeine. For example, a recent case-control study in China 239 found an association between drinking strong tea and congenital birth defect (35). 240 Strengths of this study include the prospective design, which to some extent reduced recall 241 bias. Our population has a low incidence of coffee drinking and this may avoid potential for 242 confounding due to the high caffeine content of coffee. There are also some limitations that 243 should be considered. Tea consumption was investigated only at baseline during early 244 gestation. It is possible that pregnant women could have changed their exposure during later 245 stages of pregnancy, leading to misclassification and regression dilution bias. Despite the 246 relatively large sample size, only 16% of our sample reported drinking tea at least once a

247 week. The small number of frequent tea drinkers renders the estimates unstable with wide confidence intervals, and we might not have sufficient statistical power to detect a true 248 249 association. Nevertheless, the opposing directions in the risk estimates for SGA and LGA 250 lend credibility to the findings. Furthermore, tea drinking in China is a social norm and any 251 misclassification is most likely random (rather than systematic or deliberate under- or over-252 reporting), diluting the effect size towards the null. Although we have controlled for a range 253 of confounders, we acknowledge the possibility of residual and unmeasured confounding due 254 to other potentially relevant variables such as sleep duration and diet during pregnancy. We 255 were unable to specify whether the observed effect was due to components unique to tea, 256 caffeine in tea or caffeine from other sources such as coffee, and to a lesser extent soft drinks 257 and pain killers. However, the prevalence of regular coffee drinking in our sample was 258 extremely low, and given the lower caffeine content in tea (36), we hypothesised that tea 259 drinking should be responsible for the majority of caffeine (and catechin) intake, and 260 therefore our risk estimates were less likely to be confounded by other dietary factors.

261

262 Conclusions

Our results do not suggest an adverse effect of tea consumption at a low to moderate level during early pregnancy on preterm birth or abnormal foetal growth among Chinese women. Given the high overall number of annual births (~17 million in 2014) and the relatively low prevalence of tea drinking among pregnant women in China, our findings have important public health significance in the context of other potential health benefits of tea. Future studies are warranted to confirm our findings and to re-examine the dietary guidelines, which currently do not provide guidance to pregnant women about tea drinking.

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Table 1 Characteristics of the mothers and their children by frequency of tea drinking at

| | Weekly tea | | |
|--|--------------------------|----------------------|---------|
| | <1 serving | ≥ 1 serving | P-value |
| | Mean \pm SD or No. (%) | Mean ± SD or No. (%) | |
| n | 7355 | 1420 | |
| Demographic and lifestyle | | | |
| Maternal age at enrollment (years) | 28.8 ± 3.3 | 29.1 ± 3.5 | < 0.01 |
| Educational level | | | |
| Middle school or below | 824 (11.2) | 117 (8.2) | |
| College | 1904 (25.9) | 333 (23.5) | |
| Undergraduate | 3803 (51.7) | 804 (56.6) | |
| Postgraduate | 824 (11.2) | 166 (11.7) | < 0.01 |
| Monthly income (Yuan [*]) | | | |
| ≤1500 | 733 (10.2) | 143 (10.4) | |
| 1501-4500 | 2365 (33.0) | 414 (30.0) | |
| 4501-9000 | 2967 (41.3) | 591 (42.8) | |
| ≥9001 | 1111 (15.5) | 234 (16.9) | 0.15 |
| Missing | 179 | 38 | |
| Pre-pregnancy BMI (kg/m ²) | 20.3 ± 2.6 | 20.6 ± 2.8 | < 0.01 |
| Missing | 121 | 21 | |
| Environmental tobacco smoke | | | 0.01 |
| exposure in early pregnancy | 2185 (29.7) | 493 (34.8) | <0.01 |
| Missing | 6 | 5 | |
| Folic acid intake in early pregnancy | 6721 (91.5) | 1300 (91.7) | 0.79 |

enrollment in the Born in Guangzhou Cohort Study, 2012-2014 (n=8775)

| Missing | 7 | 2 | |
|---|----------------|--------------|--------|
| Pregnancy-related | | | |
| Parity | | | |
| Primiparous | 6562 (89.2) | 1208 (85.1) | |
| Multiparous | 791 (10.8) | 212 (14.9) | < 0.01 |
| Missing | 2 | 0 | |
| Mode of delivery | | | |
| Vaginal delivery | 4805 (65.5) | 888 (62.8) | |
| Caesarean section | 2535 (34.5) | 527 (37.2) | 0.05 |
| Missing | 15 | 5 | |
| Gestational age at birth (weeks) | | | |
| Median [25 th , 75 th percentile] | 39 [38, 40] | 39 [38, 40] | 0.47 |
| Preterm birth | 364 (5.0) | 65 (4.6) | 0.55 |
| Missing | 41 | 6 | |
| Birthweight (g) | 3188 ± 432 | 3187 ± 422 | 0.95 |
| Missing | 27 | 5 | |
| Birthweight for gestational age | | | |
| SGA | 528 (7.2) | 96 (6.8) | |
| AGA | 5995 (81.8) | 1170 (82.7) | |
| LGA | 791 (10.8) | 148 (10.5) | 0.77 |
| Missing | 41 | 6 | |

Data presented as mean \pm SD or n (%) unless otherwise specified.

AGA: appropriate for gestational age; BMI: body mass index; LGA: large for gestational age; SGA: small for gestational age.

375 *: 1 Yuan ≈ US \$0.16 (May 2014).

| Weekly tea | Preterm birth Weekly tea | | | SGA | | | LGA | | |
|--------------------|--------------------------|-------------------|-------------------|----------|-------------------|-------------------|----------|-------------------|-------------------|
| consumption | n | OR (95% CI) | | Ν | OR (95% CI) | | n | OR (95% CI) | |
| (serving/week) | (Preterm | Crude | Adjusted * | (SGA | Crude | Adjusted * | (LGA | Crude | Adjusted * |
| | /term) | | | /AGA) | | | /AGA) | | |
| Any tea | | | | | | | | | |
| <1 | 364/6965 | 1.00 (Ref.) | 1.00 (Ref.) | 541/5995 | 1.00 (Ref.) | 1.00 (Ref.) | 791/5995 | 1.00 (Ref.) | 1.00 (Ref.) |
| 1-3 | 36/799 | 0.86 (0.61, 1.22) | 0.86 (0.59, 1.25) | 53/697 | 0.86 (0.64, 1.16) | 0.94 (0.70, 1.28) | 84/697 | 0.91 (0.72, 1.16) | 0.88 (0.68, 1.13) |
| >3 | 27/526 | 0.98 (0.66, 1.47) | 0.88 (0.57, 1.38) | 40/451 | 1.01 (0.72, 1.41) | 1.07 (0.75, 1.53) | 62/451 | 1.04 (0.79, 1.37) | 0.97 (0.72, 1.30) |
| <i>p</i> for trend | | 0.65 | 0.41 | | 0.67 | 0.90 | | 0.92 | 0.51 |
| Green tea | | | | | | | | | |
| 1-3 | 18/363 | 0.95 (0.58, 1.54) | 0.80 (0.44, 1.45) | 17/328 | 0.59 (0.36, 0.97) | 0.59 (0.33, 1.05) | 36/328 | 0.83 (0.59, 1.18) | 0.89 (0.60, 1.34) |
| >3 | 5/132 | 0.73 (0.30, 1.78) | 0.54 (0.18, 1.63) | 6/108 | 0.63 (0.28, 1.44) | 0.57 (0.21, 1.51) | 23/108 | 1.61 (1.02, 2.55) | 1.67 (1.01, 2.75) |
| <i>p</i> for trend | | 0.50 | 0.23 | | 0.03 | 0.07 | | 0.34 | 0.19 |
| Oolong tea | | | | | | | | | |
| 1-3 | 13/410 | 0.61 (0.35, 1.06) | 0.61 (0.33, 1.14) | 28/347 | 0.92 (0.62, 1.36) | 0.92 (0.58, 1.47) | 47/347 | 1.03 (0.75, 1.41) | 0.97 (0.66, 1.41) |

Table 2 Relationship between frequency of tea drinking and birth outcomes in the Born in Guangzhou Cohort Study, 2012-2014 (n=8775)

| >3 | 12/136 | 1.69 (0.93, 3.08) | 1.30 (0.58, 2.89) | 14/122 | 1.30 (0.74, 2.2 | 8) 1.38 (0.71, 2.66) | 12/122 | 0.75 (0.41, 1.36 | 5) 0.63 (0.29, 1.36) |
|--------------------|--------|-------------------|-------------------|--------|-----------------|----------------------|--------|------------------|----------------------|
| <i>p</i> for trend | | 0.81 | 0.73 | | 0.66 | 0.59 | | 0.53 | 0.35 |
| Dark/black tea | | | | | | | | | |
| 1-3 | 28/505 | 1.06 (0.72, 1.58) | 0.98 (0.62, 1.55) | 41/448 | 1.04 (0.75, 1.4 | 5) 1.20 (0.82, 1.76) | 44/448 | 0.75 (0.54, 1.02 | 2) 0.82 (0.58, 1.16) |
| >3 | 9/182 | 0.95 (0.48, 1.86) | 1.03 (0.49, 2.13) | 16/156 | 1.17 (0.69, 1.9 | 6) 1.61 (0.92, 2.80) | 19/156 | 0.92 (0.57, 1.50 |)) 0.75 (0.41, 1.35) |
| p for trend | | 0.95 | 0.99 | | 0.57 | 0.07 | | 0.17 | 0.18 |

377 AGA: appropriate for gestational age; CI: confidence interval; SGA: small for gestational age; LGA: large for gestational age; OR: odds ratio.

378 *: Model adjusted for maternal age, educational level, monthly income, exposure to environmental tobacco smoke and folic intake during early

379 pregnancy, pre-pregnancy BMI, previous history of complications during pregnancy, parity, sex of offspring, and where appropriate, frequency of

380 other types of tea consumed.

381

| | Preterm birth | | | SGA | | | | | |
|-----------------------|---------------|-------------------|-------------------|----------|-------------------|-------------------|----------|-------------------|-------------------|
| Strength of tea | n | OR (9. | 5% CI) | n | OR (95% CI) | | n | OR (95% CI) | |
| | (Preterm | Crude | Adjusted * | (SGA | Crude | Adjusted * | (LGA | Crude | Adjusted * |
| | /term) | | | /AGA) | | | /AGA) | | |
| Non-habitual drinkers | 364/6965 | 1.00 (Ref.) | 1.00 (Ref.) | 511/5659 | 1.00 (Ref.) | 1.00 (Ref.) | 760/5659 | 1.00 (Ref.) | 1.00 (Ref.) |
| (<1 serving/week) | | 1100 (11011) | | 011,0003 | | | 100/2023 | | 1100 (11011) |
| Green tea | | | | | | | | | |
| Weak | 6/156 | 0.74 (0.32, 1.68) | 0.89 (0.32, 2.50) | 9/137 | 0.75 (0.38, 1.47) | 0.89 (0.36, 2.17) | 16/137 | 0.89 (0.53, 1.49) | 0.76 (0.39, 1.49) |
| Moderate/strong | 16/336 | 0.91 (0.55, 1.52) | 0.89 (0.42, 1.90) | 14/295 | 0.54 (0.31, 0.93) | 0.53 (0.24, 1.13) | 43/295 | 1.11 (0.80, 1.53) | 1.02 (0.63, 1.63) |
| <i>p</i> for trend | | 0.58 | 0.77 | | 0.02 | 0.10 | | 0.67 | 0.91 |
| Oolong tea | | | | | | | | | |
| Weak | 5/204 | 0.47 (0.19, 1.15) | 0.21 (0.06, 0.76) | 17/170 | 1.14 (0.68, 1.88) | 1.07 (0.53, 2.17) | 22/170 | 0.98 (0.63, 1.54) | 0.85 (0.44, 1.66) |
| Moderate/strong | 19/340 | 1.07 (0.67, 1.72) | 0.79 (0.40, 1.58) | 25/296 | 0.96 (0.63, 1.46) | 0.88 (0.49, 1.59) | 37/296 | 0.95 (0.67, 1.34) | 1.09 (0.66, 1.79) |
| p for trend | | 0.76 | 0.64 | | 0.98 | 0.66 | | 0.76 | 0.71 |

382 Table 3 Relationship between strength of tea and birth outcomes in the Born in Guangzhou Cohort Study, 2012-2014 (n=8775)

| Dark/black tea | | | | | | |
|--------------------|--------------------------|-------------------|--------------------------|-------------------|--------------------------|-------------------|
| Weak | 14/313 0.86 (0.50, 1.48) | 0.87 (0.43, 1.76) | 23/272 0.96 (0.62, 1.48) | 1.02 (0.58, 1.81) | 32/272 0.89 (0.61, 1.30) | 1.05 (0.61, 1.80) |
| Moderate/strong | 22/372 1.13 (0.73, 1.76) | 1.04 (0.57, 1.89) | 34/329 1.17 (0.82, 1.69) | 1.12 (0.69, 1.84) | 31/329 0.72 (0.49, 1.04) | 0.84 (0.51, 1.38) |
| <i>p</i> for trend | 0.78 | 0.92 | 0.48 | 0.65 | 0.07 | 0.49 |

383 AGA: appropriate for gestational age; CI: confidence interval; SGA: small for gestational age; LGA: large for gestational age; OR: odds ratio.

384 *: Model adjusted for maternal age, educational level, monthly income, exposure to environmental tobacco smoke and folic intake during early

385 pregnancy, pre-pregnancy BMI, previous history of complications during pregnancy, parity, sex of offspring, and total tea consumption frequency.

386

387



- 389 Figure legends
- 390 Figure 1 Flowchart of participant recruitment in the Born in Guangzhou Cohort Study, 2012-
- 391 2014 (n=8775).