

## Article

# Impacts of Maternal Diet and Alcohol Consumption during Pregnancy on Maternal and Infant Gut Microbiota

Ying Wang <sup>1</sup>, Tianqu Xie <sup>2</sup> , Yinyin Wu <sup>2</sup>, Yanqun Liu <sup>2,\*</sup>, Zhijie Zou <sup>2</sup> and Jinbing Bai <sup>3</sup> 

<sup>1</sup> Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, 1095 Jiefang Avenue, Wuhan 430030, China; wangying9398@163.com

<sup>2</sup> Wuhan University School of Health Sciences, Wuhan University, 169 Donghu Road, Wuhan 430071, China; 2015302280014@whu.edu.cn (T.X.); 2019283050068@whu.edu.cn (Y.W.); zouzhijie@whu.edu.cn (Z.Z.)

<sup>3</sup> Nell Hodgson Woodruff School of Nursing, Emory University, 1520 Clifton Road, Atlanta, GA 30322, USA; jinbing.bai@emory.edu

\* Correspondence: liuyanqun@whu.edu.cn; Tel.: +86-027-68759710

**Abstract:** (1) Background: Maternal diet and alcohol consumption can influence both maternal and infant's gut microbiota. These relationships are still not examined in the Chinese population. The purpose of this study was to explore the effect of alcohol consumption and maternal diet during pregnancy on maternal and infant's gut microbiota. (2) Methods: Twenty-nine mother-child dyads were enrolled in central China. Fecal samples of mothers during late pregnancy and of newborns within 48 h were collected. The V3–V4 regions of 16S rRNA sequences were analyzed. A self-administrated questionnaire about simple diet frequency in the past week was completed by mothers before childbirth. The demographic information was finished by mothers at 24 h after childbirth. (3) Results: Among these 29 mothers, 10 mothers reported alcohol consumption during pregnancy. The PCoA ( $\beta$ -diversity) showed significant difference in maternal gut microbiota between the alcohol consumption group vs. the non-alcohol consumption group (abund-Jaccard,  $r = 0.2$ ,  $p = 0.006$ ). The same phenomenon was observed in newborns (unweighted-UniFrac full tree,  $r = 0.174$ ,  $p = 0.031$ ). Maternal alcohol consumption frequency showed positive associations with maternal *Phascolarctobacterium* ( $p = 0.032$ ) and *Blautia* ( $p = 0.019$ ); maternal *Faecalibacterium* ( $p = 0.013$ ) was negatively correlated with frequency of alcohol consumption. As for newborns, a positive relationship showed between *Megamonas* ( $p = 0.035$ ) and newborns with maternal alcohol consumption. The diet was not associated with both maternal and infant's gut microbiota. (4) Conclusions: Maternal alcohol consumption during pregnancy influenced the gut microbiota on both mothers and the newborns. Future research is needed to explore these relationships in a larger birth cohort. Understanding the long-term effect of alcohol consumption on maternal and newborns' gut microbiota is needed.

**Keywords:** gut microbiota; infant; alcohol consumption; maternal diet; pregnancy



**Citation:** Wang, Y.; Xie, T.; Wu, Y.; Liu, Y.; Zou, Z.; Bai, J. Impacts of Maternal Diet and Alcohol Consumption during Pregnancy on Maternal and Infant Gut Microbiota. *Biomolecules* **2021**, *11*, 369. <https://doi.org/10.3390/biom11030369>

Academic Editor: Natalia Osna

Received: 4 January 2021

Accepted: 24 February 2021

Published: 1 March 2021

**Publisher's Note:** MDPI stays neutral with regard to jurisdictional claims in published maps and institutional affiliations.



**Copyright:** © 2021 by the authors. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (<https://creativecommons.org/licenses/by/4.0/>).

## 1. Introduction

A variety of endogenous and exogenous factors can impact the gut microbiome [1,2]. The Human Microbiome Project (HMP) [3] and the American Gut Project [4] are two initiatives that focus on studying the characteristics of the human microbiome that are associated with both healthy and diseased humans [5]. According to their work, a series of factors can contribute to changes of the human gut microbiome such as demographic factors (e.g., sex, age, ethnicity, geography) [6] and health history (e.g., use of antibiotics) [7]. Importantly, lifestyles, including diet and alcohol consumption are primary factors that influence the development of the gut microbiota in early life [8]. Studies have suggested the existence of mother to child gut microbiota transmission during the neonatal period [9,10] and diet is another most important factor in modifying the composition and diversity of human gut microbiota other than geography and season changes [11]. The impact of both short-term and long-term intakes of different dietary components on changes of gut microbiota have been demonstrated [6,12].

Long-term habitual diet primarily refers diet patterns such as the Mediterranean diet and Western diet. Studies found that the Western diet was associated with high abundance of *Bacteroides* and *Firmicutes* while a plant-based habitual diet showed an increase of beneficial *Bifidobacteria* [6,13]. Additionally, recent epidemiological evidence in a large scale global population reported that dietary patterns can significantly affect gut microbiota composition, richness, and diversity [6,14,15]. Specific food composition-based interventions among certain human populations (e.g., obesity, diabetes, fatty liver, and elevated cholesterol) and animal models suggested that even short-term dietary consumption could significantly affect the composition of gut microbiota [14,16,17].

Besides the effect of diet consumption on gut microbiota, maternal prenatal diet could influence the abundance of infant's gut microbiota. In an American trial, maternal vitamin D supplementation during pregnancy was associated with lower abundance of *Clostridium difficile* and *Bifidobacterium* but higher abundance of *Bacteroides fragilis* in infants aged 3–6 months [18]. In a New Hampshire birth cohort study, higher abundance of *Streptococcus* and *Clostridium* of infants aged 6 weeks was associated with maternal fruit intake during pregnancy [19]. Another birth-cohort study in Spain [20] showed that maternal fat intake was positively related with neonatal *Firmicute* members and negatively associated with proteins and fiber intake. Similarly, one animal study about Japanese macaque [21] demonstrated that maternal high-fat intake could decrease infants' gut microbiota diversity at the age of 12 months. Compared with Western countries, Chinese people prefer vegetables and fruits and have different eating habits [22,23]. Until now, the effect of maternal Chinese diet during pregnancy on gut microbiota of newborn is rarely studied, and that from the first feces is needed to be proved urgently.

Women are more likely to drink alcohol during stressful and difficult situations [24,25]. A large number of women who have an unintended pregnancy may consume alcohol prior to the confirmation of pregnancy [26]. Evidence showed that pregnant women have drinking behaviors despite repeated warnings against alcohol consumption during pregnancy [27]. Maternal alcohol consumption has negative consequences on fetal and infant health, including fetal alcohol spectrum disorder [26], sudden infant death syndrome [28], and abnormalities [29]. Association between changes in the gut microbiota and alcohol consumption have been investigated extensively in the last few decades. Sufficient evidence suggested that both acute and chronic exposure to alcohol may lead to specific shift of the microbiota composition [30]. Bull-Otterson et al. [31] found that alcohol leads to a decreased abundance in *Firmicutes* and an increased number of *Actinobacteria* and *Proteobacteria* at phylum level. Evidence in humans also suggested that chronic alcohol consumption caused a decreased *Bacteroidetes* but increased *Proteobacteria*, as well as increased permeability of gastrointestinal tract [32]. However, changes of the gut microbiota in offspring born into alcohol consumption mothers during pregnancy are rarely investigated.

Both alcohol consumption and diet seem to have significant effects on the composition of the human gut microbiota [13,33,34]. However, whether alcohol consumption and diet habits during pregnancy were associated with the gut microbiota in mothers and newborns needs to be further investigated. Therefore, a population-based birth cohort study was performed to assess the influence of maternal alcohol consumption and diet during pregnancy on the gut microbiota of mothers and newborns. The results will confirm the relationship between maternal alcohol consumption, diet habits, and gut microbiota in both mothers and its offspring, which will provide a new angle to improve infants' health.

## 2. Materials and Methods

Between March 2017 and July 2017, 29 women during late pregnancy were recruited from an obstetric outpatient clinic in a tertiary hospital in central China (Table 1). The inclusion criteria were: (1) women in late pregnancy ( $\geq 28$  gestational weeks) who planned to deliver a baby in the hospital; and (2) the habitual residence is Wuhan, Hubei Province, China. The exclusion criteria included: pregnant women (1) with complications (e.g., gestational diabetes,

hypertensive disorders); (2) receiving antibiotic treatment during pregnancy; or (3) with cognitive impairment.

**Table 1.** Characteristics of maternal and infant birth cohort (N = 29).

Variable	Maternal Alcohol Consumption		p Value
	Yes (10, 34.38%)	No (19, 65.52%)	
Maternal age	29.8 ± 2.04	30.9 ± 4.15	0.44
Pre-BMI	20.77 ± 3.02	21.15 ± 2.63	0.73
GWG	15.95 ± 1.63	15.53 ± 4.52	0.82
Gestational week	40.13 ± 1.08	39.55 ± 4.15	0.15
Mode of delivery	C-section	7 (24.14%)	8 (27.59%)
	Vaginal delivery	3 (10.34%)	11 (37.93%)
Infant gender	Male	5 (17.24%)	5 (17.24%)
	Female	5 (17.24%)	14 (48.28%)
Newborns' alpha diversity	Shannon	4.01 ± 1.07	2.62 ± 1.70
Maternal alpha diversity	Shannon	3.66 ± 0.50	3.19 ± 0.49

Values listed are total for the variable (percent of total value n) or means ± SD. Across rows (\*) indicate means that are significantly different ( $p < 0.05$ ). Pre-BMI: pre-pregnancy body mass index; GWG: gestational weight gain.

### 2.1. Data Collection

After admission, a self-designed questionnaire was used to evaluate the 7-day frequency and structure of maternal diet prior to delivery, as well as alcohol consumption during pregnancy. As recommended by the Chinese Society of Nutrition [35], eight common domains of foods for Chinese women during pregnancy were collected, including meat, eggs, fish, vegetables, fruit, milk, nut, and soybean productions. We assessed the diet frequency which involved every day, 5/6 day a week, 3/4 day a week, 1/2 day a week, and never. Alcohol consumption was measured by consumption frequency, categorized as never, rarely, some of the time, and most of the time. Maternal demographic characteristics were collected in the hospital based on maternal self-report at 24 h after childbirth. Fecal samples from women at late pregnancy and their infants after birth within 48 h were collected in the hospital based on the Human Microbiome Project (HMP) protocol [21]. For sequencing and microbial composition analysis, we used Silva (SSU123) 16S rRNA database and the average sequencing depth was 50,000 reads/samples with a minimum of 30,000 reads. Our previous study [36] had elaborated details on DNA extraction, amplification of polymerase chain reaction (PCR), and Illumina MiSeq sequencing.

### 2.2. Statistical Methods

Before the analysis, data of genera relative abundance were transformed into the centered log ratio (CLR). Maternal alcohol consumption was further combined into the following: without alcohol consumption (n = 19) vs. with alcohol consumption (n = 10). For maternal diet, we translated the frequency data into numerical variables, which included: every day = 5, 5/6 day a week = 4, 3/4 day a week = 3, 1/2 day a week = 2, never = 1.

The difference of  $\alpha$ -diversity (Shannon index) in alcohol consumption was tested by Student's t-test at the operational taxonomic unit (OTU) level. To explore  $\beta$ -diversity of alcohol consumption in mothers and infants, principal coordinates analysis (PCoA) was conducted based on abund-Jaccard and unweighted-Unifrac full tree distance matrix and calculated using OTU information from each sample. Analysis of similarities (ANOSIM) was used to check whether these differences were significant. Community heatmap was used to visualize microbiota composition of the two alcohol consumption groups.

The heatmap was used to display the relationships among maternal alcohol consumption, diet frequency, and dominant bacterial communities (genus relative abundance  $\geq 1\%$ , based on Spearman correlation test). After adjusting confounders (e.g., gender [male vs. female], delivery mode [natural vs. C-section]), multivariate analysis of general liner model (GLM) was used to analyze significant factors on the mother and infant's gut microbiota. We set  $\alpha < 0.05$  as the significance level. All the analyses were adjusted using the Benjamini–

Hochberg false discovery rate (FDR, < 0.05) in multiple hypothesis tests. These analyses were performed using SPSS version 21 (IBM, Chicago, IL, USA) and R software [37].

### 3. Results

#### 3.1. Taxonomies of the Gut Microbiota

The values of Good's coverage were 99.7% in mothers and 99.6% in newborns. In total, 733 OTUs were acquired in maternal fecal samples. We found 98 families and 259 genera were revealed from 29 maternal samples. Among infants, 1480 OTUs were revealed from 29 newborns' meconium (i.e., the first feces), with 270 families and 579 genera profiled. Figure 1 shows taxonomic compositions of the dominant bacteria (relative abundance > 1%) at genus level. Based on the cutoff point of 1%, 18 genera were identified. The most abundant genera included *Bacteroides* (24.33%), *Faecalibacterium* (10.48%), *Prevotella-9* (7.77%), *[Eubacterium]\_rectale\_group* (4.89%), *Phascolarctobacterium* (3.79%), and *Megamonas* (3.71%) for mothers. Eighteen genera were identified in newborns and *Prevotella\_9* (11.74%), *Bacteroides* (11.21%), *Escherichia-Shigella* (10.92%), *Streptococcus* (6.78%), *Staphylococcus* (5.58%), and *Clostridium sensu stricto1* (5.11%) were primarily identified.

#### 3.2. Microbial Diversity

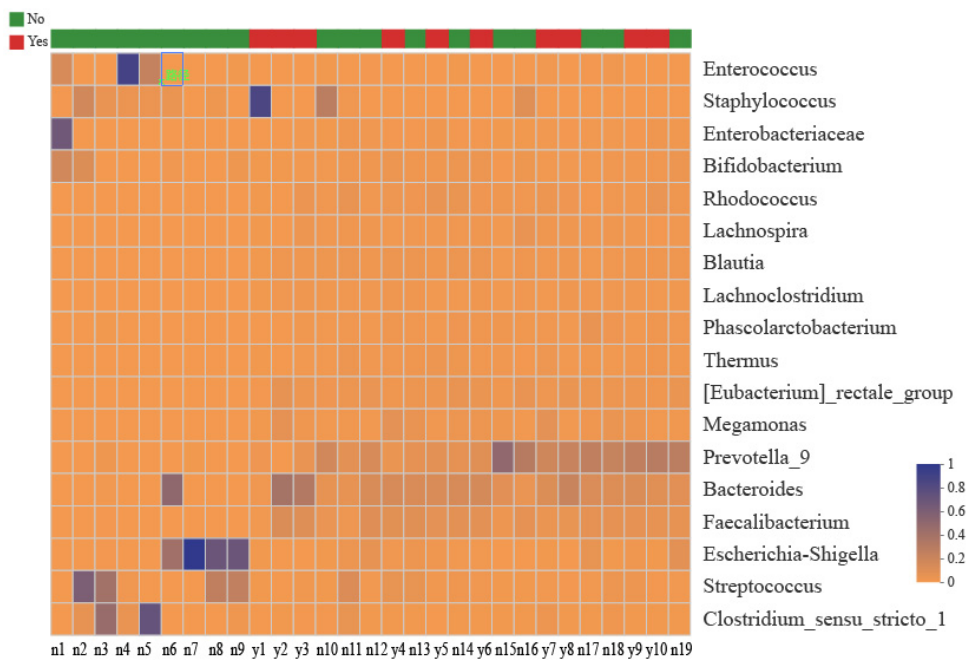
A significant difference in  $\alpha$ -diversity was found between alcohol consumption and without alcohol consumption groups in mothers ( $p = 0.02$ ) and in infants ( $p = 0.03$ ). Mothers with alcohol consumption showed a higher diversity compared with those without alcohol consumption during pregnancy, and similar results had been identified in newborns (Table 1). The  $\beta$ -diversity through PCoA shows that the bacterial structure was separated based on maternal alcohol consumption (Abund-Jaccard,  $r = 0.2$ ,  $p = 0.006$ ) (Figure 2a). For newborns, the first two principal component scores, accounting for 52.82% of the total variations (unweighted-UniFrac full tree,  $r = 0.174$ ,  $p = 0.031$ ) suggested that alcohol consumption was one of the important factors in the change of microbiota composition structure (Figure 2b).

#### 3.3. Associations between the Maternal Alcohol Consumption, Diet and Gut Microbiota Changes in Mothers and Infants

The heatmap shows relationships between gut microbiota changes and maternal diet and alcohol consumption (Figure 3). Significant relationships existed among maternal gut microbiota with intake frequency of fruit (*Lachnospiraceae*:  $r = 0.369$ ,  $p = 0.048$ ), egg (*Lachnospira*:  $r = -0.373$ ,  $p = 0.046$ ), fish (*Blautia*:  $r = -0.443$ ,  $p = 0.016$ ; *Prevotella\_9*:  $r = 0.379$ ,  $p = 0.042$ ), nut (*Blautia*:  $r = -0.448$ ,  $p = 0.015$ ), and soyabean products (*Lachnospira*:  $r = -0.443$ ,  $p = 0.011$ ). Moreover, maternal alcohol consumption during pregnancy had a strong relationship with maternal gut microbiota, including *Faecalibacterium* ( $r = -0.659$ ,  $p = 0.001$ ), *Prevotella\_9* ( $r = -0.407$ ,  $p = 0.029$ ), *Phascolarctobacterium* ( $r = 0.451$ ,  $p = 0.014$ ), and *Blautia* ( $r = 0.442$ ,  $p = 0.016$ ). Infants born in mothers who have had alcohol consumption during pregnancy revealed a similar impact on *Bacteroides* ( $r = 0.512$ ,  $p = 0.005$ ), *Faecalibacterium* ( $r = 0.460$ ,  $p = 0.012$ ), *Megamonas* ( $r = 0.521$ ,  $p = 0.004$ ), *Rhodococcus* ( $r = 0.495$ ,  $p = 0.006$ ), *Lachnoclostridium* ( $r = 0.483$ ,  $p = 0.008$ ), and *Thermus* ( $r = 0.426$ ,  $p = 0.021$ ). Maternal dietary intake of meat (*Enterococcus*:  $r = 0.376$ ,  $p = 0.044$ ), eggs (*Lachnospira*:  $r = -0.374$ ,  $p = 0.046$ ), nut (*Escherichia-Shigella*:  $r = -0.454$ ,  $p = 0.013$ ) and soybean products (*Enterobacteriaceae*:  $r = -0.373$ ,  $p = 0.046$ ) during pregnancy were related with their offspring's gut microbiota.

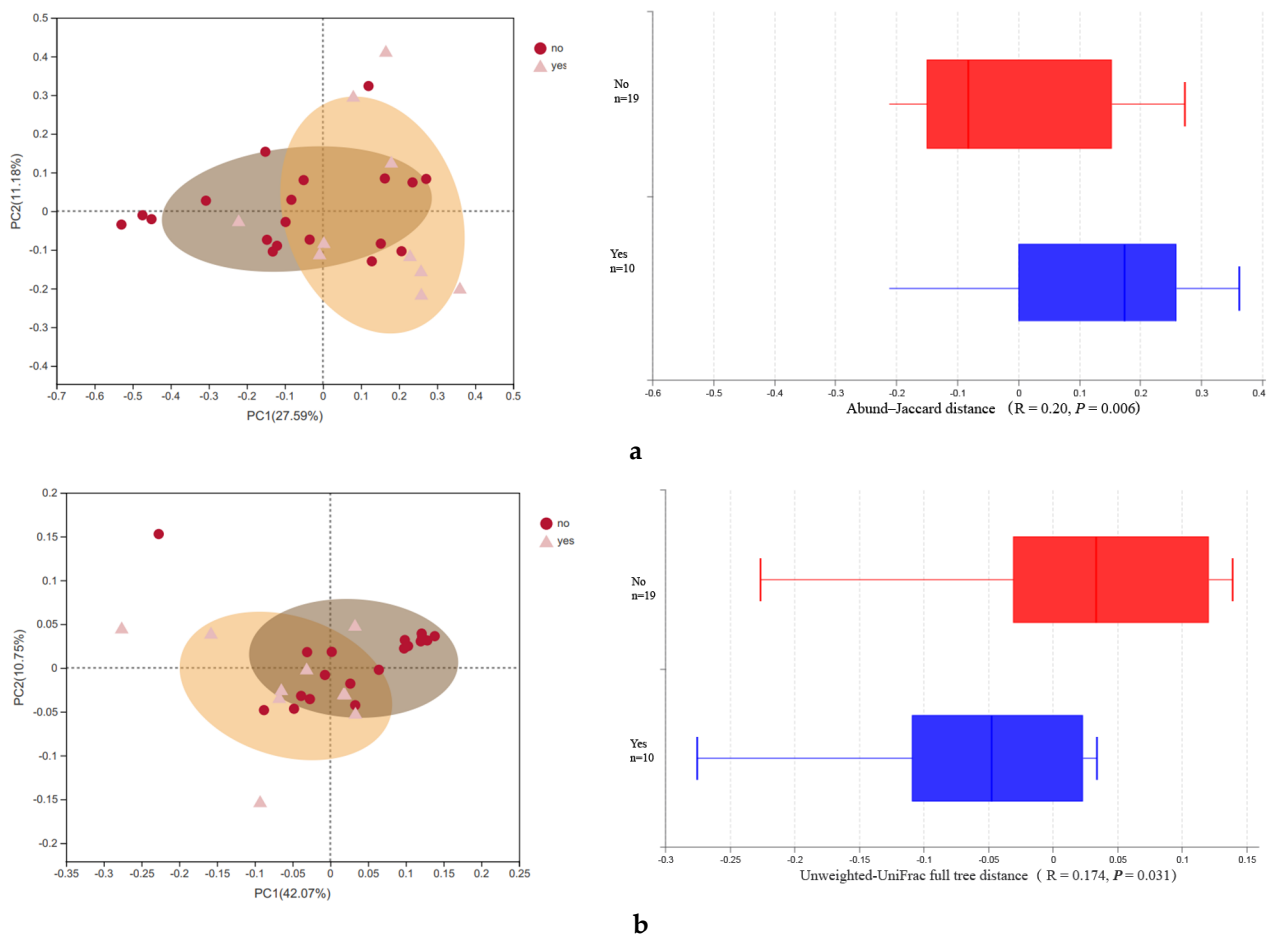


a



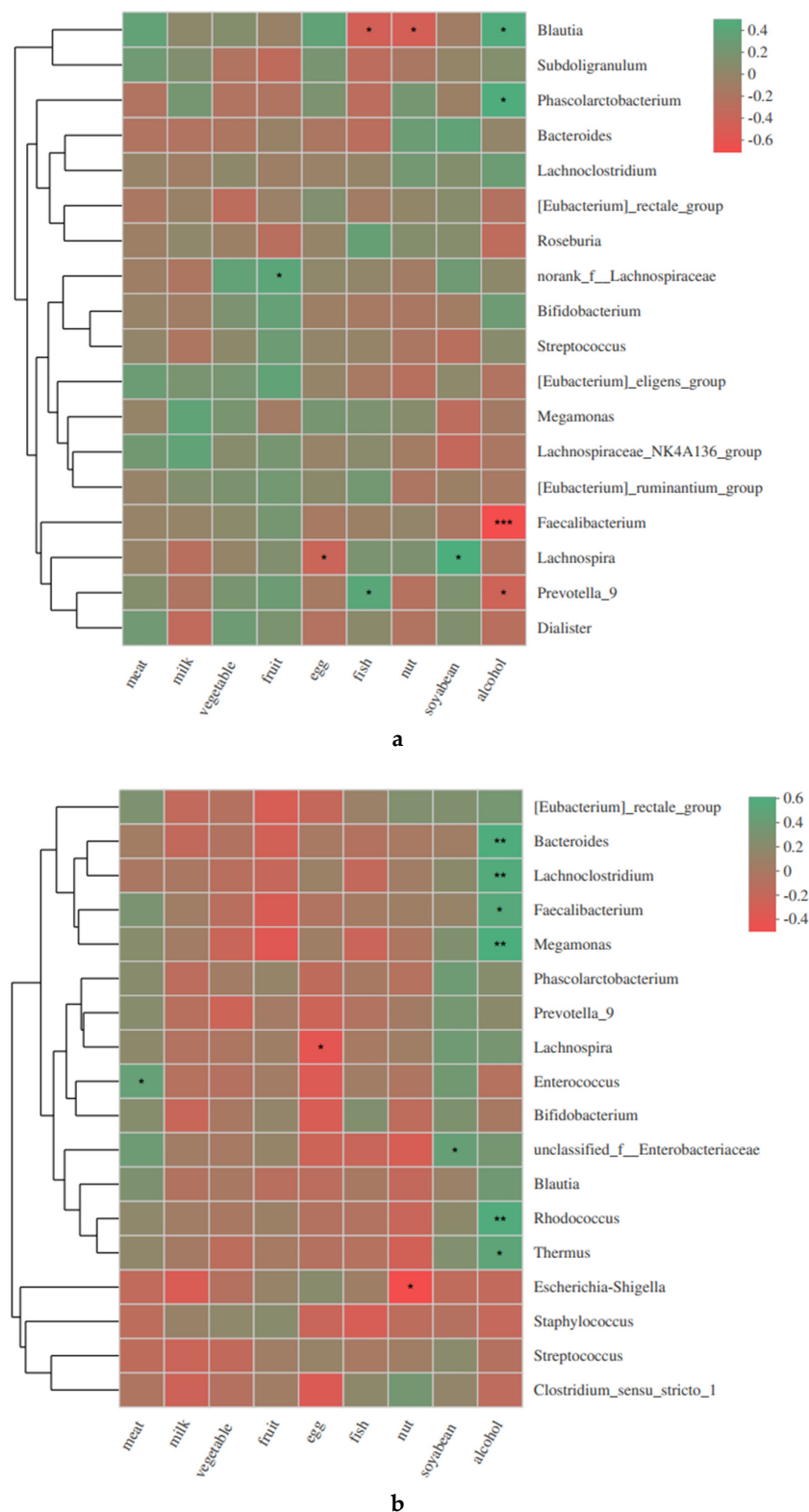
b

**Figure 1.** Distribution of microbial community for alcohol consumption group (Yes) vs. without alcohol consumption group (No) at genus level were visualized by community heatmap ( $\geq 1\%$  relative abundance). The abundance of different samples reflects through color changes: (a) indicates maternal gut microbiota composition; (b) indicates newborns' gut microbiota composition.



**Figure 2.** Principal co-ordinates analysis (PCoA) was conducted to display gut microbiota structure difference of the two alcohol consumption status on OTU level (distance matrix: mothers: abund-Jaccard; infants: unweighted-UniFrac full tree). The statistics of analysis of similarities (ANOSIM) are R and p. If R is closer to 1, it means that the difference between groups is greater than the difference within groups. The Box-plot represented the distribution of different groups of samples on the PC1 axis. **(a)** Indicates the maternal gut microbiota structure difference between with alcohol consumption and without alcohol consumption group; **(b)** indicates newborns' gut microbiota structure born into mothers with different alcohol consumption.

To further investigate the effects of maternal diet and alcohol consumption on maternal and infant's gut microbiota, GLM was performed to control possible confounders. Results showed that maternal alcohol consumption frequency was significantly related with maternal gut microbiota, including *Phascolarctobacterium* ( $\beta = 1771.10$ ,  $p = 0.034$ , adjust  $p = 0.032$ ) and *Blautia* ( $\beta = 538.60$ ,  $p = 0.020$ , adjust  $p = 0.019$ ). *Faecalibacterium* ( $\beta = -3055.7$ ,  $p = 0.001$ , adjust  $p = 0.013$ ) were negatively correlated with frequency of alcohol consumption. A positive relationship between *Megamonas* in infants and maternal alcohol consumption frequency ( $\beta = 1066.53$ ,  $p = 0.030$ , adjust  $p = 0.035$ ). The  $\alpha$ -diversity was not associated with alcohol consumption both in mothers and infants.



**Figure 3.** Relationship heatmap was performed to show the association between maternal/newborns' bacterial abundance and maternal diet intake frequency as well as alcohol consumption before delivery. The coefficient appeared color-coded based on under (red) or over-representation (green) in the analysis (\*  $0.01 < p \leq 0.05$ , \*\*  $0.001 < p \leq 0.01$ , \*\*\*  $p \leq 0.001$ ). **(a)** Indicates relationships among maternal gut microbiota with diet and alcohol consumption; **(b)** indicates relationships among newborns' gut microbiota with maternal diet and alcohol consumption.

#### 4. Discussion

In this study, alcohol consumption has significant impact on both maternal and offspring's gut microbiota. Mothers, who had alcohol consumption during pregnancy, had a significantly lower abundance in *Faecalibacterium* genus and a higher abundance in *Phascolarctobacterium*, *Blautia* genera compared with those without alcohol drinking groups. These findings were consistent with previous studies [31,32,38,39]. In a study with a pregnant animal model, reduced *Bacillus* was observed in pregnant mice exposure in ethanol [40]. Interestingly, plenty of research studies have proved the transmission of gut microbiota between mothers and offspring in utero. Studies [39,41,42] involving maternal diet, gestational weight gain (GWG), and antibiotic treatment have reinforced that point of view. Accordingly, several hypotheses [42] were proposed about transmission routes (e.g., vagina, placenta, amniotic fluid, cord blood, and fetal membranes) which means that maternal prenatal factors can alter the initial newborns' gut microbiota. In the study, for newborns with mothers who have consumed alcohol during pregnancy, we observed higher abundance in *Megamonas* genus. The over-growth of *Megamonas* in newborns further indicated that alcohol consumption during pregnancy might affect offspring's gut microbiota colonization in early life [43].

The negative effect of maternal alcohol consumption during pregnancy is undoubted, both on mothers and newborns. In this study, mothers with alcohol consumption during pregnancy had a lower-level abundance of *Faecalibacterium*. *Faecalibacterium* was shown to involved in intestinal anti-inflammatory [44] and play a role in preventing alcohol-induced gastrointestinal and extra-intestinal diseases [45,46] by blocking nuclear factor  $\kappa$ B (NF- $\kappa$ B) [47]. High intestinal permeability (IP) was positively related to the abundance of *Blautia* genus [48]. Additionally, the prevalence of *Phascolarctobacterium* was believed to associated with hepatic diseases including nonalcoholic steatohepatitis (NASH) [49] and hepatocellular carcinoma (HCC) [50]. In addition, *Blautia* was known to be elevated in people with depressive symptoms [51]. Furthermore, a number of studies in animals about the effect of alcohol on the gut microbiota also showed that alcohol consumption caused a decreased abundance of *Firmicutes* and increased numbers of *Verrucomicrobia* and *Bacteroidetes*, and *Firmicutes* have been confirmed, which was associated with anti-inflammatory activity in human body [38]. Canesso et al. [52] transplanted fecal samples of mice fed with alcohol into germ-free mice, and there was an increase of gut and hepatic inflammation which suggested that gut microbiota can mediate alcohol proinflammatory effect. Besides, in this study, *Megamonas* was abundant in infants exposed to alcohol consumption mothers. Additionally, increased *Megamonas* was proved to be associated with major depressive disorder [53]. Moreover, prenatal alcohol exposure was linked to changes in newborns' cognitive and behavioral development including depression, mood diseases, and autism [54,55]. In utero, MRI also demonstrated [56] that maternal ethanol exposure in gestation could perturb brain development associated motor control. According to Kakiyama's study, infants born into mothers who have alcohol consumption during pregnancy may result in hepatic damage, along with an increased number of *Bacteroides* [30]. Further, long-effect on offspring existed even low-level alcohol exposure during pregnancy [55]. In summary, alcohol consumption mediated mothers' gut microbiota composition and passed the effect on infants. However, their gut microbiota composition showed different changes. The inter-generational transmission of *Faecalibacterium*, *Phascolarctobacterium*, *Blautia*, and *Megamonas* genera were not found in this study. Other cohort study [57] has pointed out that excessive *Lachnospiraceae* genus transmission was observed in overweight mothers and overweight infants aged 1 and 3 years old. Nevertheless, plenty of factors were associated with the transmission process, including infants' gestational age, delivery mode, antibiotic usage, and the operating room microbes [58]. It may be the possible cause that different gut microbiota change patterns occurring in mothers and infants in this study. Besides that, further long-term clinical studies were strongly recommended, taking factors into account such as alcohol categories, specific levels of alcohol consumption during pregnancy. It would



help investigate roles of alcohol consumption in maternal and infants' gut microbiota more accurately.

In our study, we explored the effect of meat, eggs, fish, vegetables, fruit, milk, nut, and soybean productions on maternal and infants' gut microbiota. Although some maternal diet was associated with gut microbiota in mothers and infants, they were not significantly controlling confounder factors. However, studies have proved that [59] eggs intake was correlated with *Lachnospiraceae* and *Blautia*. Soybeans and grains as the main source of polyphenols including isoflavones and flavones were the primary dietary influencing factors on *Lactobacillus*, *Bifidobacterium*, and *Enterococcus avium* [60–64]. It also found [59] that pulses intake was negatively related to *clostridium*. In addition, the changes were translated significantly into gut microbiota of infants [65–67]. A previous study showed that high fat or oral probiotic supplement can drive gut microbiota changes in offspring [65]. Maternal *Lactobacillus rhamnosus* GG (LGG) consumption increased the abundance of *Bifidobacteria* colonization in infants [68]. The abundance of *Bacteroides* decreased in newborns exposure to maternal high-fat diet during pregnancy [69]. However, different duration and quantity of diet components intake may lead to various results in gut microbiota [70], based on the microbe–host co-metabolism [71]. Likewise, 35% of bacterial OTUs were related to eating time and frequency. Human gut microbiota changed throughout the day with a decreased concentration of butyrate, acetate, and propionate [72]. It seems to explain different findings in the relationships between diet and gut microbiota.

## 5. Conclusions

In conclusion, these results showed that maternal alcohol consumption during pregnancy induced changes of the gut microbiota in mothers and their offspring. In the area of maternal and infant health care, this study has provided compelling evidence that limiting maternal alcohol consumption is of benefit to both mothers and infants. Among limitations of our study, the dietary and alcohol assessment may be subjected to memory bias. Specific effects of different degrees and different kinds of alcohol consumption on the maternal and infant gut microbiota are still unclear. Future research should lay great stress on food/alcohol quantity or proportion and minimize bias as possible. Besides, a limited participant size results in less representative of the study. Thus, it is in urgent need to develop a large birth cohort and explore the long-term impact of alcohol consumption and diet on infant and mother's gut microbiota.

**Author Contributions:** Conceptualization, Y.L.; Data curation, Y.L.; Formal analysis, Y.W. (Ying Wang), T.X. and Y.W. (Yinyin Wu); Funding acquisition, Y.L.; Investigation, Y.W. (Ying Wang), T.X. and Y.W. (Yinyin Wu); Methodology, Y.L.; Project administration, Y.L.; Resources, Y.L.; Software, Y.W. (Ying Wang); Supervision, Y.L.; Validation, Y.L. and J.B.; Visualization, Y.L.; Writing—original draft, Y.W. (Ying Wang); Writing—review & editing, Y.W. (Ying Wang), Y.L., Z.Z. and J.B. All authors have read and agreed to the published version of the manuscript.

**Funding:** This research was funded by National Natural Science Foundation of China, grant number 81903334.

**Institutional Review Board Statement:** The research was approved by the Research Ethics Boards of Medical School of Wuhan University (JKHL2017-03-03).

**Informed Consent Statement:** Informed consent was obtained from all subjects involved in the study.

**Data Availability Statement:** The data presented in this study are openly available in Sequence Read Archive: SRA:SRP155310; BioProject: PRJNA482931.

**Acknowledgments:** We thank Shanghai Meiji biomedical technology co. LTD for help in sample management and sequence production.

**Conflicts of Interest:** The authors declare no conflict of interest.

## References

1. Bai, J.; Hu, Y.; Bruner, D.W. Composition of gut microbiota and its association with body mass index and lifestyle factors in a cohort of 7-18 years old children from the American Gut Project. *Pediatr. Obes.* **2019**, *14*, e12480. [[CrossRef](#)] [[PubMed](#)]
2. Wang, Y.; Chen, X.L.; Yu, Y.; Liu, Y.Q.; Zhang, Q.; Bai, J.B. Association between Gut Microbiota and Infant's Temperament in the First Year of Life in a Chinese Birth Cohort. *Microorganisms* **2020**, *8*, 753. [[CrossRef](#)] [[PubMed](#)]
3. The Human Microbiome Project Consortium. Structure, function and diversity of the healthy human microbiome. *Nature* **2012**, *486*, 207–214. [[CrossRef](#)]
4. McDonald, D.; Birmingham, A.; Knight, R. Context and the human microbiome. *Microbiome* **2015**, *3*, 52. [[CrossRef](#)] [[PubMed](#)]
5. Mayer, E.A.; Knight, R.; Mazmanian, S.K.; Cryan, J.F.; Tillisch, K. Gut microbes and the brain: Paradigm shift in neuroscience. *J. Neurosci.* **2014**, *34*, 15490–15496. [[CrossRef](#)] [[PubMed](#)]
6. Yatsunenkov, T.; Rey, F.E.; Manary, M.J.; Trehan, I.; Dominguez-Bello, M.G.; Contreras, M.; Magris, M.; Hidalgo, G.; Baldassano, R.N.; Anokhin, A.P.; et al. Human gut microbiome viewed across age and geography. *Nature* **2012**, *486*, 222–227. [[CrossRef](#)]
7. Lewis, J.D.; Chen, E.Z.; Baldassano, R.N.; Otley, A.R.; Griffiths, A.M.; Lee, D.; Bittinger, K.; Bailey, A.; Friedman, E.S.; Hoffmann, C.; et al. Inflammation, Antibiotics, and Diet as Environmental Stressors of the Gut Microbiome in Pediatric Crohn's Disease. *Cell Host Microbe* **2015**, *18*, 489–500. [[CrossRef](#)] [[PubMed](#)]
8. Clarke, S.F.; Murphy, E.F.; O'Sullivan, O.; Lucey, A.J.; Humphreys, M.; Hogan, A.; Hayes, P.; O'Reilly, M.; Jeffery, I.B.; Wood-Martin, R.; et al. Exercise and associated dietary extremes impact on gut microbial diversity. *Gut* **2014**, *63*, 1913–1920. [[CrossRef](#)]
9. Chang, J.Y.; Shin, S.M.; Chun, J.; Lee, J.H.; Seo, J.K. Pyrosequencing-based molecular monitoring of the intestinal bacterial colonization in preterm infants. *J. Pediatr. Gastroenterol. Nutr.* **2011**, *53*, 512–519. [[CrossRef](#)]
10. Gosalbes, M.J.; Llop, S.; Valles, Y.; Moya, A.; Ballester, F.; Francino, M.P. Meconium microbiota types dominated by lactic acid or enteric bacteria are differentially associated with maternal eczema and respiratory problems in infants. *Clin. Exp. Allergy* **2013**, *43*, 198–211. [[CrossRef](#)]
11. Jandhyala, S.M.; Talukdar, R.; Subramanyam, C.; Vuyyuru, H.; Sasikala, M.; Nageshwar Reddy, D. Role of the normal gut microbiota. *World J. Gastroenterol* **2015**, *21*, 8787–8803. [[CrossRef](#)] [[PubMed](#)]
12. Han, M.; Yang, K.; Yang, P.; Zhong, C.; Chen, C.; Wang, S.; Lu, Q.; Ning, K. Stratification of athletes' gut microbiota: The multifaceted hubs associated with dietary factors, physical characteristics and performance. *Gut Microbes* **2020**, *12*, 1–18. [[CrossRef](#)] [[PubMed](#)]
13. De Filippo, C.; Cavalieri, D.; Di Paola, M.; Ramazzotti, M.; Poullet, J.B.; Massart, S.; Collini, S.; Pieraccini, G.; Lionetti, P. Impact of diet in shaping gut microbiota revealed by a comparative study in children from Europe and rural Africa. *Proc. Natl. Acad. Sci. USA* **2010**, *107*, 14691–14696. [[CrossRef](#)]
14. Wu, G.D.; Chen, J.; Hoffmann, C.; Bittinger, K.; Chen, Y.Y.; Keilbaugh, S.A.; Bewtra, M.; Knights, D.; Walters, W.A.; Knight, R.; et al. Linking long-term dietary patterns with gut microbial enterotypes. *Science* **2011**, *334*, 105–108. [[CrossRef](#)]
15. Ou, J.; Carbonero, F.; Zoetendal, E.G.; DeLany, J.P.; Wang, M.; Newton, K.; Gaskins, H.R.; O'Keefe, S.J. Diet, microbiota, and microbial metabolites in colon cancer risk in rural Africans and African Americans. *Am. J. Clin. Nutr* **2013**, *98*, 111–120. [[CrossRef](#)]
16. David, L.A.; Maurice, C.F.; Carmody, R.N.; Gootenberg, D.B.; Button, J.E.; Wolfe, B.E.; Ling, A.V.; Devlin, A.S.; Varma, Y.; Fischbach, M.A.; et al. Diet rapidly and reproducibly alters the human gut microbiome. *Nature* **2014**, *505*, 559–563. [[CrossRef](#)] [[PubMed](#)]
17. Cotillard, A.; Kennedy, S.P.; Kong, L.C.; Prifti, E.; Pons, N.; Le Chatelier, E.; Almeida, M.; Quinquis, B.; Levenez, F.; Galleron, N.; et al. Dietary intervention impact on gut microbial gene richness. *Nature* **2013**, *500*, 585–588. [[CrossRef](#)] [[PubMed](#)]
18. Sordillo, J.E.; Zhou, Y.J.; McGeachie, M.J.; Ziniti, J.; Lange, N.; Laranjo, N.; Savage, J.R.; Carey, V.; O'Connor, G.; Sandel, M.; et al. Factors influencing the infant gut microbiome at age 3–6 months: Findings from the ethnically diverse Vitamin D Antenatal Asthma Reduction Trial (VDAART). *J. Allergy Clin. Immunol.* **2017**, *139*, 482–491.e14. [[CrossRef](#)] [[PubMed](#)]
19. Lundgren, S.N.; Madan, J.C.; Emond, J.A.; Morrison, H.G.; Christensen, B.C.; Karagas, M.R.; Hoen, A.G. Maternal diet during pregnancy is related with the infant stool microbiome in a delivery mode-dependent manner. *Microbiome* **2018**, *6*. [[CrossRef](#)]
20. Selma-Royo, M.; Garcia-Mantrana, I.; Calatayud, M.; Parra-Llorca, A.; Martinez-Costa, C.; Collado, M.C. Maternal diet during pregnancy and intestinal markers are associated with early gut microbiota. *Eur. J. Nutr.* **2020**. [[CrossRef](#)]
21. Ma, J.; Prince, A.L.; Bader, D.; Hu, M.; Ganu, R.; Baquero, K.; Blundell, P.; Harris, R.A.; Frias, A.E.; Grove, K.L.; et al. High-fat maternal diet during pregnancy persistently alters the offspring microbiome in a primate model. *Nat. Commun.* **2014**, *5*. [[CrossRef](#)] [[PubMed](#)]
22. Patil, B.S.; Jayaprakasha, G.K.; Vikram, A. Indigenous Crops of Asia and Southeast Asia: Exploring Health-promoting Properties. *Hortscience* **2012**, *47*, 821–827. [[CrossRef](#)]
23. Diep, C.S.; Leung, R.; Thompson, D.I.; Gor, B.J.; Baranowski, T. Culture and Diet Among Chinese American Children Aged 9–13 Years: A Qualitative Study. *J. Nutr. Educ. Behav.* **2017**, *49*, 275–284. [[CrossRef](#)]
24. Rodriguez, L.M.; Litt, D.M.; Stewart, S.H. Drinking to cope with the pandemic: The unique associations of COVID-19-related perceived threat and psychological distress to drinking behaviors in American men and women. *Addict. Behav.* **2020**, *110*, 106532. [[CrossRef](#)]
25. Peltier, M.R.; Verplaetse, T.L.; Mineur, Y.S.; Petrakis, I.L.; Cosgrove, K.P.; Picciotto, M.R.; McKee, S.A. Sex differences in stress-related alcohol use. *Neurobiol. Stress* **2019**, *10*. [[CrossRef](#)] [[PubMed](#)]

26. Akison, L.K.; Kuo, J.; Reid, N.; Boyd, R.N.; Moritz, K.M. Effect of Choline Supplementation on Neurological, Cognitive, and Behavioral Outcomes in Offspring Arising from Alcohol Exposure During Development: A Quantitative Systematic Review of Clinical and Preclinical Studies. *Alcohol. Clin. Exp. Res.* **2018**, *42*, 1591–1611. [CrossRef] [PubMed]
27. Muggl, E.; O’Leary, C.; Donath, S.; Orsini, F.; Forster, D.; Anderson, P.J.; Lewis, S.; Nagle, C.; Craig, J.M.; Elliott, E.J.B.P.H. “Did you ever drink more?” A detailed description of pregnant women’s drinking patterns. *BMC Public Health* **2016**, *16*, 1–13.
28. Isaacs, D. Maternal alcohol use and sudden infant death syndrome. *BMC Public Health* **2013**, *49*, 871. [CrossRef]
29. Sundermann, A.C.; Velez Edwards, D.R.; Slaughter, J.C.; Wu, P.; Jones, S.H.; Torstenson, E.S.; Hartmann, K.E. Week-by-week alcohol consumption in early pregnancy and spontaneous abortion risk: A prospective cohort study. *Am. J. Obstet Gynecol.* **2020**. [CrossRef]
30. Leung, C.; Rivera, L.; Furness, J.B.; Angus, P.W. The role of the gut microbiota in NAFLD. *Nat. Rev. Gastroenterol. Hepatol.* **2016**, *13*, 412–425. [CrossRef] [PubMed]
31. Bull-Otterson, L.; Feng, W.; Kirpich, I.; Wang, Y.; Qin, X.; Liu, Y.; Gobejishvili, L.; Joshi-Barve, S.; Ayvaz, T.; Petrosino, J.; et al. Metagenomic analyses of alcohol induced pathogenic alterations in the intestinal microbiome and the effect of *Lactobacillus rhamnosus* GG treatment. *PLoS ONE* **2013**, *8*, e53028. [CrossRef] [PubMed]
32. Rao, R.K.; Seth, A.; Sheth, P. Recent Advances in Alcoholic Liver Disease I. Role of intestinal permeability and endotoxemia in alcoholic liver disease. *Am. J. Physiol. Gastrointest Liver Physiol.* **2004**, *286*, G881–G884. [CrossRef]
33. Ames, N.J.; Barb, J.J.; Schuebel, K.; Mudra, S.; Meeks, B.K.; Tuason, R.T.S.; Brooks, A.T.; Kazmi, N.; Yang, S.; Ratteree, K.; et al. Longitudinal gut microbiome changes in alcohol use disorder are influenced by abstinence and drinking quantity. *Gut Microbes* **2020**, *11*, 1608–1631. [CrossRef]
34. Lowe, P.P.; Gyongyosi, B.; Satishchandran, A.; Iracheta-Vellve, A.; Ambade, A.; Kodys, K.; Catalano, D.; Ward, D.V.; Szabo, G. Alcohol-related changes in the intestinal microbiome influence neutrophil infiltration, inflammation and steatosis in early alcoholic hepatitis in mice. *PLoS ONE* **2017**, *12*, e0174544. [CrossRef]
35. Guo, Z. Interpretation of “Dietary Guidelines for Pregnant Women (2016)” by The Chinese Nutrition Society. *J. Pract. Obstetr. Gynecol.* **2018**, *34*.
36. Wang, Y.; Liu, Y.; Bai, J.; Chen, X. The Effect of Maternal Postpartum Practices on Infant Gut Microbiota: A Chinese Cohort Study. *Microorganisms* **2019**, *7*, 511. [CrossRef] [PubMed]
37. Team, R.C. A Language and Environment for Statistical Computing; R Foundation for Statistical Computing. Available online: <https://www.R-project.org/> (accessed on 22 February 2021).
38. Yan, A.W.; Fouts, D.E.; Brandl, J.; Starkel, P.; Torralba, M.; Schott, E.; Tsukamoto, H.; Nelson, K.E.; Brenner, D.A.; Schnabl, B. Enteric dysbiosis associated with a mouse model of alcoholic liver disease. *Hepatology* **2011**, *53*, 96–105. [CrossRef] [PubMed]
39. Kumbhare, S.V.; Patangia, D.V.V.; Patil, R.H.; Shouche, Y.S.; Patil, N.P. Factors influencing the gut microbiome in children: From infancy to childhood. *J. Biosci.* **2019**, *44*. [CrossRef]
40. Labrecque, M.T.; Malone, D.; Caldwell, K.E.; Allan, A.M. Impact of Ethanol and Saccharin on Fecal Microbiome in Pregnant and Non-Pregnant Mice. *J. Pregnancy Child. Health* **2015**, *2*. [CrossRef] [PubMed]
41. Vandenplas, Y.; Carnielli, V.P.; Ksiazzyk, J.; Luna, M.S.; Migacheva, N.; Mosselmans, J.M.; Picaud, J.C.; Possner, M.; Singhal, A.; Wabitsch, M. Factors affecting early-life intestinal microbiota development. *Nutrition* **2020**, *78*. [CrossRef]
42. Chu, D.M.; Meyer, K.M.; Prince, A.L.; Aagaard, K.M. Impact of maternal nutrition in pregnancy and lactation on offspring gut microbial composition and function (vol 7, pg 459, 2016). *Gut Microbes* **2017**, *8*. [CrossRef]
43. Capurso, G.; Lahner, E. The interaction between smoking, alcohol and the gut microbiome. *Best Pract. Res. Clin. Gastroenterol.* **2017**, *31*, 579–588. [CrossRef] [PubMed]
44. Sokol, H.; Pigneur, B.; Watterlot, L.; Lakhdari, O.; Bermudez-Humaran, L.G.; Gratadoux, J.J.; Blugeon, S.; Bridonneau, C.; Furet, J.P.; Corthier, G.; et al. Faecalibacterium prausnitzii is an anti-inflammatory commensal bacterium identified by gut microbiota analysis of Crohn disease patients. *Proc. Natl. Acad. Sci. USA* **2008**, *105*, 16731–16736. [CrossRef]
45. Cao, Y.; Shen, J.; Ran, Z.H. Association between Faecalibacterium prausnitzii Reduction and Inflammatory Bowel Disease: A Meta-Analysis and Systematic Review of the Literature. *Gastroent. Res. Pract.* **2014**, *2014*. [CrossRef]
46. Eppinga, H.; Weiland, C.J.S.; Thio, H.B.; van der Woude, C.J.; Nijsten, T.E.C.; Peppelenbosch, M.P.; Konstantinov, S.R. Similar Depletion of Protective Faecalibacterium prausnitzii in Psoriasis and Inflammatory Bowel Disease, but not in Hidradenitis Suppurativa. *J. Crohns Colitis* **2016**, *10*, 1067–1075. [CrossRef] [PubMed]
47. Banan, A.; Shaikh, M.; Zhang, L.J.; Forsythe, C.; Choudhary, S.; Farhadi, A.; Fields, J.Z.; Keshavarzian, A. NF-kappaB activation as a key mechanism in ethanol-induced disruption of the F-actin cytoskeleton and barrier integrity of intestinal epithelial monolayers. *Alcohol. Clin. Exp. Res.* **2005**, *29*, 139a.
48. Leclercq, S.; Matamoros, S.; Cani, P.D.; Neyrinck, A.M.; Jamar, F.; Starkel, P.; Windey, K.; Tremaroli, V.; Backhed, F.; Verbeke, K.; et al. Intestinal permeability, gut-bacterial dysbiosis, and behavioral markers of alcohol-dependence severity. *Proc. Natl. Acad. Sci. USA* **2014**, *111*, E4485–E4493. [CrossRef] [PubMed]
49. Sobhonslidsuk, A.; Chanprasertyothin, S.; Pongrujirkorn, T.; Kaewduang, P.; Promson, K.; Petraksa, S.; Ongphiphadhanakul, B. The Association of Gut Microbiota with Nonalcoholic Steatohepatitis in Thais. *Biomed. Res. Int.* **2018**, *2018*. [CrossRef] [PubMed]
50. Ponziani, F.R.; Bhoori, S.; Castelli, C.; Putignani, L.; Rivoltini, L.; Del Chierico, F.; Sanguinetti, M.; Morelli, D.; Sterbini, F.P.; Petito, V.; et al. Hepatocellular Carcinoma Is Associated With Gut Microbiota Profile and Inflammation in Nonalcoholic Fatty Liver Disease. *Hepatology* **2019**, *69*, 107–120. [CrossRef]

51. Cheung, S.G.; Goldenthal, A.R.; Uhlemann, A.C.; Mann, J.J.; Miller, J.M.; Sublette, M.E. Systematic Review of Gut Microbiota and Major Depression. *Front. Psychiatry* **2019**, *10*, 34. [[CrossRef](#)] [[PubMed](#)]
52. Canesso, M.C.C.; Queiroz, N.L.; Marcantonio, C.; Lauer, J.; Almeida, D.; Gamba, C.; Cassali, G.; Pedroso, S.H.; Moreira, C.; Martins, F.S.; et al. Comparing the effects of acute alcohol consumption in germ-free and conventional mice: The role of the gut microbiota. *BMC Microbiol.* **2014**, *14*, 240. [[CrossRef](#)]
53. Jiang, H.; Ling, Z.; Zhang, Y.; Mao, H.; Ma, Z.; Yin, Y.; Wang, W.; Tang, W.; Tan, Z.; Shi, J.; et al. Altered fecal microbiota composition in patients with major depressive disorder. *Brain Behav. Immun.* **2015**, *48*, 186–194. [[CrossRef](#)] [[PubMed](#)]
54. Ciafrè, S.; Ferraguti, G.; Greco, A.; Polimeni, A.; Ralli, M.; Ceci, F.M.; Ceccanti, M.; Fiore, M. Alcohol as an early life stressor: Epigenetics, metabolic, neuroendocrine and neurobehavioral implications. *Neuroscience Biobehav. Rev.* **2020**, *118*, 654–668. [[CrossRef](#)]
55. Lees, B.; Mewton, L.; Jacobus, J.; Valadez, E.A.; Stapinski, L.A.; Teesson, M.; Tapert, S.F.; Squeglia, L.M. Association of Prenatal Alcohol Exposure With Psychological, Behavioral, and Neurodevelopmental Outcomes in Children From the Adolescent Brain Cognitive Development Study. *Am. J. Psychiat* **2020**, *177*, 1060–1072. [[CrossRef](#)]
56. Wang, X.J.; Carlson, V.C.C.; Studholme, C.; Newman, N.; Ford, M.M.; Grant, K.A.; Kroenke, C.D. In utero MRI identifies consequences of early-gestation alcohol drinking on fetal brain development in rhesus macaques. *Proc. Natl. Acad. Sci. USA* **2020**, *117*, 10035–10044. [[CrossRef](#)]
57. Tun, H.M.; Bridgman, S.L.; Chari, R.; Field, C.J.; Guttman, D.S.; Becker, A.B.; Mandhane, P.J.; Turvey, S.E.; Subbarao, P.; Sears, M.R.; et al. Roles of Birth Mode and Infant Gut Microbiota in Intergenerational Transmission of Overweight and Obesity From Mother to Offspring. *JAMA Pediatr.* **2018**, *172*, 368–377. [[CrossRef](#)] [[PubMed](#)]
58. Ferretti, P.; Pasolli, E.; Tett, A.; Asnicar, F.; Gorfer, V.; Fedi, S.; Armanini, F.; Truong, D.T.; Manara, S.; Zolfo, M.; et al. Mother-to-Infant Microbial Transmission from Different Body Sites Shapes the Developing Infant Gut Microbiome. *Cell Host Microbe* **2018**, *24*, 133–145.e5. [[CrossRef](#)]
59. Zhernakova, A.; Kurilshikov, A.; Bonder, M.J.; Tigchelaar, E.F.; Schirmer, M.; Vatanen, T.; Mujagic, Z.; Vila, A.V.; Falony, G.; Vieira-Silva, S.; et al. Population-based metagenomics analysis reveals markers for gut microbiome composition and diversity. *Science* **2016**, *352*, 565–569. [[CrossRef](#)] [[PubMed](#)]
60. Odenyo, A.A.; Bishop, R.; Asefa, G.; Jamnadass, R.; Odongo, D.; Osuji, P. Characterization of tannin-tolerant bacterial isolates from East African ruminants. *Anaerobe* **2001**, *7*, 5–15. [[CrossRef](#)]
61. Wiseman, H.; Casey, K.; Bowey, E.A.; Duffy, R.; Davies, M.; Rowland, I.R.; Lloyd, A.S.; Murray, A.; Thompson, R.; Clarke, D.B. Influence of 10 wk of soy consumption on plasma concentrations and excretion of isoflavonoids and on gut microflora metabolism in healthy adults. *Am. J. Clin. Nutr.* **2004**, *80*, 692–699. [[CrossRef](#)] [[PubMed](#)]
62. Minamida, K.; Tanaka, M.; Abe, A.; Sone, T.; Tomita, F.; Hara, H.; Asano, K. Production of equol from daidzein by gram-positive rod-shaped bacterium isolated from rat intestine. *J. Biosci. Bioeng.* **2006**, *102*, 247–250. [[CrossRef](#)] [[PubMed](#)]
63. Heinonen, S.M.; Wahala, K.; Adlercreutz, H. Identification of urinary metabolites of the red clover isoflavones formononetin and biochanin A in human subjects. *J. Agric. Food Chem.* **2004**, *52*, 6802–6809. [[CrossRef](#)]
64. Coldham, N.G.; Darby, C.; Hows, M.; King, L.J.; Zhang, A.Q.; Sauer, M.J. Comparative metabolism of genistin by human and rat gut microflora: Detection and identification of the end-products of metabolism. *Xenobiotica* **2002**, *32*, 45–62. [[CrossRef](#)] [[PubMed](#)]
65. Paul, H.A.; Bomhof, M.R.; Vogel, H.J.; Reimer, R.A. Diet-induced changes in maternal gut microbiota and metabolomic profiles influence programming of offspring obesity risk in rats. *Sci. Rep.* **2016**, *6*, 20683. [[CrossRef](#)] [[PubMed](#)]
66. Parnell, J.A.; Reimer, R.A. Prebiotic fiber modulation of the gut microbiota improves risk factors for obesity and the metabolic syndrome. *Gut Microbes* **2012**, *3*, 29–34. [[CrossRef](#)] [[PubMed](#)]
67. Lopez-Legarrea, P.; Fuller, N.R.; Zulet, M.A.; Martinez, J.A.; Caterson, I.D. The influence of Mediterranean, carbohydrate and high protein diets on gut microbiota composition in the treatment of obesity and associated inflammatory state. *Asia Pac. J. Clin. Nutr.* **2014**, *23*, 360–368. [[CrossRef](#)] [[PubMed](#)]
68. Lahtinen, S.J.; Boyle, R.J.; Kivivuori, S.; Oppedisano, F.; Smith, K.R.; Robins-Browne, R.; Salminen, S.J.; Tang, M.L.K. Prenatal probiotic administration can influence Bifidobacterium microbiota development in infants at high risk of allergy. *J. Allergy Clin. Immun.* **2009**, *123*, 499–501. [[CrossRef](#)]
69. Chu, D.M.; Antony, K.M.; Ma, J.; Prince, A.L.; Showalter, L.; Moller, M.; Aagaard, K.M. The early infant gut microbiome varies in association with a maternal high-fat diet. *Genome Med.* **2016**, *8*, 77. [[CrossRef](#)] [[PubMed](#)]
70. Leeming, E.R.; Johnson, A.J.; Spector, T.D.; Le Roy, C.I. Effect of Diet on the Gut Microbiota: Rethinking Intervention Duration. *Nutrients* **2019**, *11*, 2862. [[CrossRef](#)]
71. Penney, N.; Barton, W.; Pasma, J.M.; Darzi, A.; Frost, G.; Cotter, P.D.; Holmes, E.; Shanahan, F.; O’Sullivan, O.; Garcia-Perez, I. Investigating the Role of Diet and Exercise in Gut Microbe-Host Cometalabolism. *mSystems* **2020**, *5*. [[CrossRef](#)]
72. Kaczmarek, J.L.; MUSAAD, S.M.A.; Holscher, H.D. Time of day and eating behaviors are associated with the composition and function of the human gastrointestinal microbiota. *Am. J. Clin. Nutr.* **2017**, *106*, 1220–1231. [[CrossRef](#)]