Reply to: Association between beverage consumption and liver fibrosis

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Reply to

Thank you for the opportunity to reply to the letter by Huang et al.[456] The authors of this letter posed two main questions, which we will address consecutively. First, they questioned why we categorised subtypes of tea (no vs any) differently from coffee consumption (no, moderate, and frequent). This is simply related to the small number of participants with frequent tea consumption, being N=91 with frequent green tea and

Table 1:

	log-transformed LSM		LSM≥8 kPa	
	beta (95%CI)	P-value	OR (95%CI)	P-value
		Model 1*		
Herbal Tea				
no	0 (ref)	**<0.001**	1 (ref)	**0.025**
moderate	**–0.097 (–0.128; –0.067)**		0.64 (0.41 – 1.01)	
frequent	**–0.109 (–0.163; –0.055)**		0.51 (0.21 – 1.20)	
Green Tea				
no	0 (ref)	0.093	1 (ref)	0.437
moderate	–0.028 (–0.060; 0.005)		0.87 (0.54 – 1.42)	
frequent	–0.029 (–0.098; 0.039)		0.73 (0.26 – 2.04)	
Black Tea				
no	0 (ref)	**0.006**	1 (ref)	0.273
moderate	–0.028 (–0.057; 0.001)		0.83 (0.55 – 1.24)	
frequent	**–0.051 (–0.089; –0.013)**		0.76 (0.45 – 1.30)	
		Model 3†		
Herbal Tea				
no	0 (ref)	**0.003**	1 (ref)	0.369
moderate	**–0.056 (–0.087; –0.026)**		0.74 (0.43 – 1.27)	
frequent	–0.040 (–0.093; 0.014)		0.86 (0.30 – 2.45)	
Green Tea				
no	0 (ref)	0.142	1 (ref)	0.579
moderate	0.017 (–0.016; 0.050)		1.31 (0.76 – 2.25)	
frequent	0.043 (–0.025; 0.111)		0.88 (0.23 – 3.29)	
Black Tea				
no	0 (ref)	0.502	1 (ref)	0.951
moderate	–0.012 (–0.041; 0.017)		0.90 (0.53 – 1.54)	
frequent	–0.011 (–0.049; 0.028)		1.20 (0.45 – 3.20)	

* Model 1: adjusted for coffee consumption, other subtypes of tea consumption, and energy intake. Significant results are marked in bold.

† Model 3 (i.e. full adjustment): adjusted for tea or coffee, energy intake, BMI, gender, age, steatosis, ALT, excessive alcohol intake, current or former smoking, HOMA-IR, soda consumption, cream and sugar use, DHDI, physical activity, lipid-lowering drugs and anti-diabetic drugs. Significant results are marked in bold.

N=162 with frequent herbal tea consumption, which would hamper the ability to perform robust multivariable analyses within subcategories. To illustrate this further, we show in *Table 1* the results of our multivariable models when using these subcategories. As can be seen, results of model 1 (adjusted only for coffee consumption, other subtypes of tea and energy intake) are very similar to our original dichotomised analyses.[130] However, results diminished (i.e. lower betas with a wide range of confidence intervals) after further adjustment for socio-demographic and lifestyle covariates in subsequent models and hence, we acknowledge that due to the low numbers, the results may not be extrapolated to populations with high herbal tea consumption. We therefore stand by our more stable, original analyses of dichotomised subtypes of tea.[130] For coffee intake, Huang et al. then conducted an unadjusted Chi-square test on our data and concluded that by dichotomising coffee intake into any vs. no, the association with significant liver fibrosis no longer existed. We cannot but disagree with using simple unadjusted Chi-square testing for making such strong inferences on complex data that can be subject to confounding. In either way, it is not surprising that pooling moderate and frequent consumption into one category with a wide range of consumption (from less than 1 up to 8.5 cups per day) would diminish the effect. There probably is a dose-effect relation which is supported by: a) our significant results for only frequent consumption, and b) a significant *P* for trend in all our coffee analyses. Also, although food and beverage categorisation reflect actual real life consumption more reliably than continuous data,[457] continuous coffee consumption *was* associated with LSM≥8kPa ($OR_{increase\ per\ cup}$ 0.84, 95%CI 0.72–0.96, *P*=0.014). This is further attested by a recent large umbrella-review of meta-analyses on coffee and human health which concluded that there was evidence of a non-linear association between coffee consumption and health outcomes with the largest relative risk reduction at three to four cups a day.[125]

Table 2

	log-transformed LSM		**LSM≥8 kPa**	
	beta (95%CI)	P-value	OR (95%CI)	P-value
		Model 3†		
Coffee				
no	0 (ref)	**0.001**	1 (ref)	**0.005**
moderate	–0.026 (–0.083; 0.032)		0.75 (0.34 – 1.68)	
frequent	**–0.066 (–0.120; –0.012)**		**0.39 (0.18 – 0.87)**	
Herbal Tea				
no	0 (ref)	**<0.001**	1 (ref)	0.274
any	**–0.053 (–0.082; –0.024)**		0.75 (0.45 – 1.26)	

†Model 3 (i.e. full adjustment): adjusted for tea or coffee, energy intake, BMI, gender, age, steatosis, ALT, excessive alcohol intake, current or former smoking, HOMA-IR, soda consumption, cream and sugar use, DHDI, physical activity, lipid-lowering drugs and anti-diabetic drugs. Significant results are marked in bold.

Secondly, the authors questioned whether we had accounted for the use of lipid-lowering and anti-diabetic drugs as potential confounders. In addition to the many other confounders we already adjusted for in our analysis, we agree that these drugs, could possibly additionally confound the relation between coffee, tea, and liver health. We therefore obtained detailed information on medication use from automated linkage to pharmacies with which 98% of the participants were registered. The most important results on the association of beverage consumption and liver stiffness additionally adjusted for lipid-lowering and anti-diabetic drugs, are depicted in *Table 2*. As can be seen, these results are nearly identical to the results from our original analyses, and hence, the abovementioned drugs do not seem to additionally confound the observed associations.

In conclusion, in this brief reply we demonstrated that (1) further categorisation of subtypes of tea led to comparable, but less stable results; we endorsed that (2) dichotomisation of coffee consumption was not associated with liver health, possibly because of a dose-responsive effect of coffee; and we showed that (3) both lipid-lowering and anti-diabetic drugs did not further confound our observed associations on coffee, tea, and liver stiffness.