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**Systematic differences among never, occasional, and moderate alcohol users in Southern China and its utility in alcohol research– a cross sectional study**

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## **ABSTRACT**

### Background

Western observational studies show moderate alcohol use, compared to never use, positively associated with health. Moderate users differ systematically from others, making these observations vulnerable to confounding. Observations from other contexts may help distinguish whether these associations are confounded. To assess whether Southern Chinese would provide a more suitable setting to examine the association of moderate alcohol use with health, we compared never alcohol users to moderate alcohol users and occasional users in this setting.

### Methods

We used age-adjusted multinomial regression to assess sex-stratified associations of alcohol use (never, occasional (<1 occasion /week), moderate ( $\leq 140$ g ethanol/week for women and  $\leq 210$ g for men)) with health attributes and indicators in the Guangzhou Biobank Cohort Study (2003-08) (n=26,361).

### Results

Among men, moderate alcohol users, when compared to never users, had slightly lower socioeconomic position and unhealthier lifestyle. Conversely, occasional alcohol users, when compared to never users, had higher socio-economic position and healthier lifestyle. Among women, when compared to never users, both occasional and moderate users had higher socioeconomic position and healthier lifestyle. However, all alcohol users for both sexes, when compared to never users, were more likely to be ever smokers and to be exposed to secondhand smoke.

### Conclusion

Observations in alcohol epidemiology may be affected by confounding due to contextually specific systematic differences. Results from a particular setting should not be interpreted as causal unless they are verified in different populations and preferably, in non-observational studies.

What is already known on this subject?

- In western populations moderate alcohol users usually have systematically healthier attributes than others making observations open to confounding. Whether these associations extend to non-western settings has not been examined.

What this study adds?

- Among Southern Chinese men moderate alcohol users did not have systematically healthier attributes. As the underlying confounding pattern associated with moderate alcohol use differs in Chinese and Western settings, Southern China may be a valuable setting to confirm associations of moderate alcohol use with health in men.

**Keywords:** Alcohol; confounding; Chinese; health; observational study; systematic differences

## INTRODUCTION

Many observational studies have shown that moderate alcohol use is related to better health, including less cardiovascular disease,<sup>1</sup> diabetes,<sup>2</sup> and cognitive decline.<sup>3,4</sup> However, moderate users have a myriad of positive health attributes, often not measured, which could be confounding the apparent protective effect of moderate alcohol use.<sup>5</sup> Randomized controlled trials (RCTs) of alcohol have been advocated to ascertain the causality of moderate alcohol use on health.<sup>6</sup> Alcohol trials are difficult to conduct due to the carcinogenicity of alcohol,<sup>7</sup> resources required for long-term follow-up, given the distant disease endpoints, such as cardiovascular mortality, and most likely low compliance with prolonged lifestyle modification. Consistency is one of Hill's considerations for causal inference but its usefulness is limited if most alcohol studies are done in western settings where the underlying confounding pattern associated with alcohol use is similar. Alternatively, it has been suggested that consistent effects in settings with a variety of confounding patterns may help confirm, or refute, causal effects for exposures where experimental studies are impractical,<sup>8</sup> which for moderate alcohol use requires information about confounding patterns in suitable non-Western settings.

In China, alcohol use is less prevalent compared to most Western countries or other East Asian countries such as Japan and South Korea. Within China, Southern Chinese drink less

than Northern Chinese.<sup>9</sup> Drinking is more acceptable in men than in women.<sup>10</sup> The main beverage consumed is distilled spirits.<sup>9</sup> Therefore, we hypothesized that the underlying confounding structure among moderate drinkers may be different from that in Western settings, and may provide an ideal setting in which to test the causality of moderate alcohol use on health. To establish if Southern China might be a suitable such setting, we compared various health-related attributes of moderate, never and occasional alcohol users in a large sample of Southern Chinese.

## **METHODS**

### **Participants**

The Guangzhou Biobank Cohort Study is a collaboration between the Guangzhou No.12 Hospital, the Universities of Hong Kong and Birmingham, and has been described in detail.<sup>11</sup> Recruitment of participants draws from “The Guangzhou Health and Happiness Association for the Respectable Elders”, a community social and welfare association unofficially aligned with the municipal government where membership is open to anyone aged 50+ years for a monthly, nominal fee of 4 Yuan (50 US cents). Recruitment for phase 1 took place from September 2003 to November 2004, for phase 2 from April 2005 to May 2006, and for phase 3 from September 2006 to January 2008. About 7% of permanent Guangzhou residents aged 50+ years are members of “The Guangzhou Health and Happiness Association for the

Respectable Elders”, of whom 33% enrolled for phase 1, 2 or 3 recruitment, and were included if they were capable of consenting, ambulatory, and not receiving treatment modalities which if omitted may result in immediate life threatening risk, such as chemotherapy or radiotherapy for cancer, or dialysis for renal failure. Participants underwent a detailed medical interview and physical examination at the Guangzhou No.12 Hospital, Guangzhou, China. A comprehensive face to face interview was conducted in the local dialect, using a standardized questionnaire and including detailed questions on socio-economic position, experiences throughout life, social relations and health behaviour. Specifically, participants were asked the following questions about alcohol use. We asked the participants how often they drank alcohol. We asked the type of alcohol usually consumed, and separately how much of each type of alcohol (beer, western table wine, spirits, Chinese rice wine or Chinese rice wine (high strength)) the participant usually consumed in a day. From this information we calculated the usual amount of alcohol consumed per week. Detailed description of these measurements have been previously reported.<sup>11</sup> The Guangzhou Medical Ethics Committee of the Chinese Medical Association approved the study and all participants gave written, informed consent before participation.

### **Independent variables**

We examined a range of health related attributes that may influence or indicate health.

Socio-demographic factors included age, sex and socio-economic position considered as job type, education and income. Lifestyle factors included smoking, secondhand smoke (SHS) exposure at home, work and during childhood,<sup>12</sup> physical activity,<sup>13</sup> consumption of one or more types of fruits per day (only in phases 1 and 2), sleeping hours per day in the last month, frequency of brushing teeth, frequency of seeing friends, and having someone to talk to in times of difficulties. Health conditions included self-related health, presence of own teeth, gum bleeding when brushing teeth and hearing ability (without hearing aid).

### **Dependent variable**

To reflect patterns of alcohol use in our setting, we categorized alcohol use as never, occasional, and moderate, based on the frequency of alcohol use and the usual amount per occasion. The definition of moderate alcohol use varies across countries. In the neighboring city of Hong Kong where the population shares a common ancestry with the participants in GBCS, alcohol use less than or equal to 2 units per day for women and 3 units per day for men, where one unit is 10g ethanol, has been considered as moderate.<sup>14</sup> Therefore, this definition was used in this analysis, and was consistent with other papers using the same sample.<sup>15 16</sup> Moderate alcohol users were defined as people using alcohol weekly with average consumption  $\leq 140$ g ethanol per week for women and  $\leq 210$ g for men. Occasional alcohol users were defined as people using alcohol less than once per week. Heavy alcohol

users (drinking more than moderate amounts) were excluded from the analysis as the effect of heavy use on health is less controversial and is seen in non-Western settings.<sup>17 18</sup> Moreover, the association of heavy drinking with ill health is less likely to be confounded by higher socioeconomic position and healthy lifestyles than the association of moderate drinking with good health. Former users were also excluded because the relationship of former users and health depends on their previous alcohol use status, and thus differences in the relationship between former use and health across settings could be a reflection of different composition of former alcohol users.<sup>19</sup> In this study, former users are likely to be former occasional users.

### **Statistical analysis**

Since we had three outcomes for alcohol use (never, moderate and occasional), we used age adjusted multinomial logistic regression to examine associations with the health related attributes. As the drinking pattern among men and women is different in our population,<sup>10</sup> we presented sex-stratified analysis. The reference group for each health related attribute was the group most likely to have better health, such as the highest income group or the highest education level.

### **RESULTS**

Of the 30,499 participants examined, 560 were heavy alcohol users and 1,071 were former



alcohol users, and hence were excluded, while 2,507 participants had missing information concerning one of the health-related attributes considered or alcohol use. The remaining 26,361 participants were used in the analysis.

Table 1 shows for men the adjusted odds ratio of each health related attribute in moderate and occasional alcohol users compared to never users. Among men, moderate alcohol users, when compared to never users, were more likely to have lower education (primary or < primary), to be widowed, to be ever smokers, to be exposed SHS (at home, at work), not to eat fruit daily, only to brush teeth once a day, but were more likely to see friends; other attributes were similar to never users. In contrast, occasional alcohol users, when compared to never users, were more likely to have higher income, higher physical activity, their own teeth, less gum bleeding although they were also more likely to be smokers , to be exposed SHS (at home, work, in childhood), and less likely to have someone to talk to in times of difficulties, and to have poorer hearing.

Table 1: Age-adjusted odds ratio for being an occasional or moderate alcohol user compared to a never users in 6,761 men in the Guangzhou Biobank Cohort Study (2003-08)

Sample size (n)		Never 4,173	Occasional 1,719	Moderate 869	Odds ratio of being an occasional user	95% CI	Odds ratio of being a moderate alcohol users	95% CI
<b>Demographic factors</b>								
Age group	50-54	7.4	12.0	9.0				
	55-59	18.2	23.2	17.4				
	60-64	25.3	25.4	23.7				
	65-69	25.8	21.6	24.4				
	70-74	17.6	13.8	19.9				
	75-79	4.9	3.0	4.0				
	80+	0.8	1.0	1.6				
<b>Socioeconomic factors</b>								
Marital status	Married	93.7	94.8	91.5	Reference		Reference	
	Separate	0.9	0.7	0.4	0.80	0.41 to 1.54	0.39	0.12 to 1.27
	Widowed	4.9	4.1	7.6	0.96	0.72 to 1.27	<b>1.55</b>	<b>1.15 to 2.09</b>
	Never married	0.3	0.4	0.6	1.35	0.53 to 3.44	2.03	0.71 to 5.79
€Job type	Non-manual	38.7	39.6	39.1	Reference		Reference	
	Manual	49.2	52.0	51.8	0.95	0.84 to 1.08	1.04	0.89 to 1.22
	Others	12.1	8.4	9.1	<b>0.60</b>	<b>0.49 to 0.74</b>	<b>0.74</b>	<b>0.56 to 0.96</b>
Education	College	8.4	8.0	6.6	Reference		Reference	
	Junior college	9.7	11.5	8.6	1.13	0.87 to 1.47	1.13	0.78 to 1.65
	Senior college	24.3	25.4	21.2	0.94	0.74 to 1.18	1.09	0.79 to 1.51
	Junior middle	29.7	29.9	29.8	0.93	0.74 to 1.17	1.27	0.93 to 1.74
	Primary	25.6	23.0	30.5	0.91	0.72 to 1.14	<b>1.52</b>	<b>1.10 to 2.07</b>
	<primary	2.3	2.3	3.3	1.13	0.74 to 1.73	<b>1.85</b>	<b>1.11 to 3.06</b>
Income	15,000+	33.0	37.9	32.3	Reference		Reference	
	10,000-15,000	41.2	36.0	42.4	<b>0.82</b>	<b>0.72 to 0.94</b>	1.04	0.88 to 1.24
	<10,000	20.7	21.4	20.3	<b>0.84</b>	<b>0.72 to 0.99</b>	0.97	0.79 to 1.20
	Unknown	5.2	4.8	5.1	<b>0.67</b>	<b>0.51 to 0.88</b>	0.97	0.68 to 1.39
<b>Lifestyle factors</b>								
Physical activity	§HEPA active	42.9	55.9	45.8	Reference		Reference	
	Minimally active	46.9	40.0	44.4	<b>0.64</b>	<b>0.57 to 0.72</b>	0.88	0.75 to 1.03
	Inactive	10.2	4.2	9.8	<b>0.27</b>	<b>0.20 to 0.35</b>	0.87	0.67 to 1.13
Smoking	Never smokers	47.9	38.9	28.1	Reference		Reference	
	Ex-smokers	26.7	28.4	32.5	<b>1.34</b>	<b>1.17 to 1.54</b>	<b>2.07</b>	<b>1.71 to 2.49</b>
	Current smokers	25.5	32.7	39.5	<b>1.49</b>	<b>1.30 to 1.71</b>	<b>2.68</b>	<b>2.23 to 3.21</b>
¶SHS at home	Yes	19.5	25.0	23.6	<b>1.41</b>	<b>1.23 to 1.61</b>	<b>1.28</b>	<b>1.08 to 1.53</b>
SHS at work	Yes	74.4	79.6	78.5	<b>1.32</b>	<b>1.15 to 1.52</b>	<b>1.27</b>	<b>1.07 to 1.52</b>
SHS in childhood	Yes	55.9	64.3	59.0	<b>1.34</b>	<b>1.19 to 1.51</b>	1.15	0.99 to 1.33
‡One or more types of fruits/day	No	53.9	54.4	58.9	1.01	0.87 to 1.18	<b>1.23</b>	<b>1.04 to 1.46</b>
Sleeping hours per day in last month (SD)		7.2 (1.4)	7.1 (1.4)	7.1 (1.4)	0.96	0.93 to 1.01	0.95	0.90 to 1.00

€Manual occupations are agricultural worker, factory work or sales and services; non-manual are administrator/manager, professional/technical and military/disciplined.

§HEPA: health-enhancing physical activity, i.e. vigorous activity at least 3 days a week achieving at least 1500 metabolic equivalent (MET) minutes per week or activity on 7 days of the week achieving at least 3000 MET minutes per week.

¶SHS: Secondhand smoke

‡Only for phases 1 and 2 (n=4,762)

Table 1: Age-adjusted odds ratio for being an occasional or moderate alcohol user compared to a never users in 6,761 men in the Guangzhou Biobank Cohort Study (2003-08) (continued)

Sample size (n)		Never	Occasional	Moderate	Odds ratio of being an occasional user	95% CI	Odds ratio of being a moderate alcohol user	95% CI
<b>Lifestyle factors</b>								
Frequency of brushing teeth	Twice a day	63.9	63.7	60.0	Reference		Reference	
	Once a day	35.5	35.7	39.0	1.02	0.91 to 1.15	<b>1.17</b>	<b>1.01 to 1.37</b>
	Less than once a day	0.6	0.6	1.0	1.14	0.54 to 2.40	1.93	0.89 to 4.19
Frequency of seeing friends	Almost daily	26.3	28.0	30.0	Reference		Reference	
	>=1/week	34.3	30.5	34.5	<b>0.80</b>	<b>0.69 to 0.93</b>	0.88	0.73 to 1.05
	>=1/month	25.4	25.5	21.8	0.90	0.77 to 1.06	<b>0.75</b>	<b>0.61 to 0.92</b>
	<1/month	14.0	16.0	13.7	1.08	0.90 to 1.29	0.86	0.67 to 1.09
Someone to talk to in times of difficulties	No	7.3	10.1	8.6	<b>1.40</b>	<b>1.15 to 1.71</b>	1.20	0.92 to 1.56
<b>Health conditions</b>								
Self rated health	Good/very good	84.5	86.5	85.3	Reference		Reference	
	Poor/very poor	15.6	13.5	14.7	0.87	0.74 to 1.02	0.94	0.76 to 1.15
Presence of own teeth	All	24.7	23.7	22.6	Reference		Reference	
	No, dentures	6.6	3.7	6.9	<b>0.72</b>	<b>0.53 to 0.97</b>	1.12	0.80 to 1.55
	Not all	68.8	72.7	70.5	1.19	1.04 to 1.36	1.12	0.94 to 1.34
Gum bleeding when brushing teeth	Rarely	75.5	74.8	76.0	Reference		Reference	
	Occasionally	16.0	18.9	16.3	1.14	0.99 to 1.33	1.01	0.83 to 1.24
	Sometimes	7.3	5.6	6.0	<b>0.74</b>	<b>0.58 to 0.94</b>	0.82	0.61 to 1.12
	Always	1.2	0.8	1.7	<b>0.54</b>	<b>0.29 to 0.99</b>	1.39	0.78 to 2.50
Hearing ability (without hearing aid)	Excellent/Good	30.1	27.7	29.3	Reference		Reference	
	Fair	61.4	64.3	62.4	<b>1.15</b>	<b>1.01 to 1.30</b>	1.03	0.87 to 1.21
	Poor/Unable to hear	8.5	8.0	8.3	1.20	0.95 to 1.50	0.98	0.73 to 1.31

Table 2: Age-adjusted odds ratio for being an occasional or moderate alcohol user compared to never users in 19,600 women in the Guangzhou Biobank Cohort Study (2003-08)

Sample size (n)		Never 16,036	Occasional 3,049	Moderate 515	Odds ratio of being an occasional user	95% CI	Odds ratio of being a moderate alcohol user	95% CI
<b>Demographic factors</b>								
Age group	50-54	21.2	33.5	20.0				
	55-59	26.8	27.7	24.9				
	60-64	19.5	16.6	19.4				
	65-69	18.9	12.5	20.4				
	70-74	10.6	7.5	12.0				
	75-79	2.4	1.5	2.5				
	80+	0.5	0.7	0.8				
<b>Socioeconomic factors</b>								
Marital status	Married	76.8	82.1	75.9	Reference		Reference	
	Separate	1.3	1.7	2.1	1.24	0.91 to 1.70	1.73	0.94 to 3.21
	Widowed	21.5	15.6	21.6	0.84	0.75 to 0.94	0.94	0.74 to 1.18
	Never married	0.5	0.6	0.4	1.00	0.60 to 1.68	0.81	0.20 to 3.31
€Job type	Non-manual	18.3	20.7	19.0	Reference		Reference	
	Manual	67.4	65.3	68.9	<b>0.86</b>	<b>0.78 to 0.95</b>	0.98	0.78 to 1.23
	Others	14.3	14.0	12.0	<b>0.79</b>	<b>0.69 to 0.91</b>	0.82	0.59 to 1.13
Education	College	1.7	1.7	2.3	Reference		Reference	
	Junior college	3.8	5.5	4.5	1.21	0.86 to 1.70	0.93	0.46 to 1.91
	Senior college	19.5	27.3	20.8	1.11	0.82 to 1.51	0.87	0.47 to 1.61
	Junior middle	24.9	27.9	28.7	0.93	0.69 to 1.26	0.93	0.51 to 1.70
	Primary	36.4	29.4	30.3	0.77	0.57 to 1.04	0.63	0.35 to 1.15
	<primary	13.7	8.2	13.4	<b>0.64</b>	<b>0.46 to 0.89</b>	0.67	0.36 to 1.27
Income	15,000+	11.8	17.6	15.7	Reference		Reference	
	10,000-15,000	43.4	51.0	43.1	<b>0.81</b>	<b>0.73 to 0.91</b>	<b>0.74</b>	<b>0.57 to 0.95</b>
	<10,000	40.0	28.0	36.5	<b>0.53</b>	<b>0.47 to 0.60</b>	<b>0.67</b>	<b>0.51 to 0.87</b>
	Unknown	4.8	3.4	4.7	<b>0.54</b>	<b>0.43 to 0.68</b>	0.72	0.45 to 1.15
<b>Lifestyle factors</b>								
Physical activity	§HEPA active	47.1	71.4	63.1	Reference		Reference	
	Minimally active	43.1	26.5	32.6	<b>0.40</b>	<b>0.37 to 0.44</b>	<b>0.56</b>	<b>0.47 to 0.68</b>
	Inactive	9.7	2.1	4.3	<b>0.13</b>	<b>0.10 to 0.16</b>	<b>0.33</b>	<b>0.21 to 0.51</b>
Smoking	Never smokers	96.9	96.3	91.5	Reference		Reference	
	Ex-smokers	1.5	1.7	3.3	<b>1.56</b>	<b>1.15 to 2.12</b>	<b>2.33</b>	<b>1.40 to 3.88</b>
	Current smokers	1.7	2.0	5.2	<b>1.54</b>	<b>1.16 to 2.05</b>	<b>3.21</b>	<b>2.13 to 4.85</b>
¶SHS at home	Yes	63.6	67.7	66.4	<b>1.19</b>	<b>1.10 to 1.30</b>	1.13	0.94 to 1.36
SHS at work	Yes	41.8	48.0	48.7	<b>1.21</b>	<b>1.12 to 1.31</b>	<b>1.34</b>	<b>1.13 to 1.60</b>
SHS in childhood	Yes	56.2	61.7	57.7	<b>1.14</b>	<b>1.05 to 1.23</b>	1.09	0.91 to 1.31
‡One or more types of fruits/day	No	50.4	46.2	49.2	<b>0.86</b>	<b>0.75 to 0.98</b>	0.95	0.76 to 1.20
Sleeping hours per day in last month (SD)		6.8 (1.4)	6.9 (1.4)	6.8 (1.4)	0.98	0.95 to 1.01	0.96	0.90 to 1.02

€Manual occupations are agricultural worker, factory work or sales and services; non-manual are administrator/manager, professional/technical and military/disciplined.

§HEPA: health-enhancing physical activity, i.e. vigorous activity at least 3 days a week achieving at least 1500 metabolic equivalent (MET) minutes per week or activity on 7 days of the week achieving at least 3000 MET minutes per week.

¶SHS: Secondhand smoke

‡Only for phases 1 and 2 (n=13,304)

Table 2: Age-adjusted odds ratio for being an occasional or moderate alcohol user compared to never users in 19,600 women in the Guangzhou Biobank Cohort Study (2003-08) (continued)

Sample size (n)		Never	Occasional	Moderate	Odds ratio of being an occasional user	95% CI	Odds ratio of being a moderate alcohol user	95% CI
<b>Lifestyle factors</b>								
Frequency of brushing teeth	Twice a day	71.8	76.8	74.8	Reference		Reference	
	Once a day	27.4	22.9	24.9	<b>0.84</b>	<b>0.77 to 0.92</b>	0.86	0.70 to 1.05
	Less than once a day	0.8	0.4	0.4	<b>0.49</b>	<b>0.26 to 0.91</b>	0.44	0.11 to 1.80
Frequency of seeing friends	Almost daily	30.6	32.1	34.8	Reference		Reference	
	>=1/week	36.3	34.1	32.8	<b>0.83</b>	<b>0.76 to 0.92</b>	0.80	0.65 to 1.00
	>=1/month	21.9	20.3	19.8	<b>0.83</b>	<b>0.74 to 0.92</b>	0.80	0.63 to 1.03
	<1/month	11.3	13.5	12.6	1.15	1.01 to 1.30	0.98	0.74 to 1.31
Someone to talk to in times of difficulties	No	5.5	7.6	6.4	<b>1.44</b>	<b>1.24 to 1.68</b>	1.15	0.80 to 1.64
<b>Health conditions</b>								
Self rated health	Good/very good	81.0	80.9	85.4	Reference		Reference	
	Poor/very poor	19.0	19.1	14.6	1.04	0.94 to 1.15	<b>0.72</b>	<b>0.56 to 0.92</b>
Presence of own teeth	All	24.8	26.4	25.6	Reference		Reference	
	No, dentures	6.1	3.9	6.0	0.86	0.69 to 1.06	0.86	0.57 to 1.31
	Not all	69.1	69.7	68.4	1.07	0.97 to 1.17	0.93	0.76 to 1.14
Gum bleeding when brushing teeth	Rarely	73.8	71.7	74.8	Reference		Reference	
	Occasionally	16.6	18.4	16.5	1.10	0.99 to 1.22	1.00	0.79 to 1.27
	Sometimes	7.9	8.3	7.2	1.01	0.88 to 1.17	0.91	0.65 to 1.28
	Always	1.7	1.7	1.6	0.93	0.69 to 1.27	0.93	0.46 to 1.89
Hearing ability (without hearing aid)	Excellent/Good	31.2	29.7	32.6	Reference		Reference	
	Fair	64.4	65.7	62.5	1.06	0.97 to 1.15	0.92	0.76 to 1.12
	Poor/Unable to hear	4.4	4.7	4.9	1.29	1.06 to 1.57	1.02	0.66 to 1.57

Table 2 shows that among women, moderate alcohol users, when compared to never users, were more likely to have higher income, higher physical activity, and better self-rated health although they were also more likely to be ever smokers, and to be exposed to SHS at work.

On the other hand, occasional alcohol users, when compared to never users, were more likely to have non-manual jobs, higher income, higher physical activity, daily fruit consumption, twice daily teeth brushing and a higher frequency of seeing friends although they were also more likely to be ever smokers, to be exposed to SHS (at home, work, in childhood), and less likely to have someone to talk to in times of difficulties.

## **DISCUSSION**

In this study we found systematic differences between never alcohol users compared to moderate alcohol users or occasional alcohol users in Southern Chinese, consistent with previous studies.<sup>5 20</sup> This study adds by showing that the underlying confounding pattern of alcohol use, as indicated by various socioeconomic, lifestyle and health-related factors, in Southern Chinese was different from that in western populations. Specifically, in Southern China, particularly among men, moderate alcohol users had fewer positive health-related attributes than never users, which is different to western populations where moderate alcohol users usually have more positive health-related attributes than never users. As such replicating associations of specifically moderate alcohol use with health in Southern Chinese

men, or similar settings, could provide a way of verify the causal role of moderate alcohol use.

Although statistical models usually carefully control for confounding, adjusted estimates remain vulnerable to residual confounding because confounders are difficult to measure precisely and identify comprehensively.<sup>21</sup> Moreover, we are not usually operating within a well-defined causal framework enabling clear distinction between confounders, mediators, colliders and markers of reverse causality, when adjustment for non-confounders may give invalid estimates.<sup>22</sup> Experimental designs investigating the long-term health effects of moderate alcohol use are unlikely to be feasible or ethical. Mendelian randomization designs require large sample sizes<sup>23</sup> and credible genetic instruments may only be present in some ethnic groups.<sup>24</sup> As such, observational studies in different contexts such as Sothern Chinese men, with justifiable statistical adjustments, appear to provide a useful alternative approach to verifying causality. In this study, we only adjusted for age. It is likely the attributes examined in this study are correlated. However, the main objective of this study was to demonstrate that never, occasional, and moderate users could be different in various ways instead of trying to quantify the independent contributions of each attribute to these differences. If consistent positive associations of moderate alcohol use with health were observed in this different non-Western context, it would imply that the positive associations seen in western

observational studies are insensitive to the underlying confounding pattern and add weight to the argument that moderate alcohol use is causally related to positive health outcomes, such as a lower risk of cardiovascular disease. However, if consistent positive associations of moderate alcohol use with health are less evident in this<sup>14 16</sup> and other non-western settings such as India,<sup>17</sup> it casts some doubt on the causal role of moderate alcohol use in better health. On the other hand, our study suggests that any positive associations of occasional alcohol use with health among Southern Chinese are likely to be susceptible to confounding by the associated positive health attributes.

Replication of associations in populations with different social patterning of moderate alcohol use, however, has caveats. First, among Chinese, ethnic specific genetic polymorphisms of alcohol metabolizing genes, such as aldehyde dehydrogenase 2 (*ALDH2*), may modify the effect of alcohol.<sup>25</sup> Observations about the effects of alcohol on health in Chinese could be ethnic specific. However, subgroup analyses by genotypes could be used to examine this possibility. Second, the main alcoholic drink in China is rice wine rather than grape wine or beer, so China would not be a good setting to investigate health effects of specific constituents of grape wine, such as resveratrol, although the effect of alcohol on factors such as HDL-cholesterol does not differ by beverage type.<sup>26</sup> Third, moderate alcohol use is less common in Southern Chinese, especially among women,<sup>9</sup> necessitating a large sample size to



obtain adequate power. Lastly, a study involving Southern Chinese women to replicate findings seen in western studies may not be feasible. For men, alcohol use is acceptable but not obligatory, however for women alcohol use is much less acceptable. Women alcohol users are likely to be those with higher socioeconomic position, as seen in other settings,<sup>27</sup> which all link to better health. Hence, any positive associations seen between moderate use and health outcomes among women could still be a consequence of residual confounding, due to healthier attributes in moderate users compared to never users. Different findings in different settings could be a potential indicator of differential confounding, which may help clarify whether an observed association is causal, although other factors such as genetics have also to be considered. Nevertheless, examination of the likely level and direction of confounding may help identify settings from which observations provide the best guide to causality, whilst non-observational study designs may also be required to confirm or refute causality convincingly.

Despite exploring a range of health-related attributes in a large sample in an understudied population, our study has some limitations. First, alcohol use was self-reported, but we have previously validated self-reported alcohol use against HDL-cholesterol and *ALDH2* polymorphisms.<sup>15 28</sup> Second, this cohort may not be representative of all Chinese. China encompasses 20% of the global population with hundreds of ethnic groups and a clear

north/south gradient in alcohol use exists.<sup>10 29</sup> Differences in ethnic-specific values and alcohol availability in each province, resulting from varying political and economic conditions throughout history, may also influence drinking patterns.<sup>30</sup> The prevalence of factors associated with alcohol use may be different in other parts of China. However, that would not invalidate the use of southern Chinese men to examine the health effects of moderate alcohol use. On the other hand, our sample might not be representative of the Southern Chinese population. The association of socio-economic and lifestyle factors with never, occasional and moderate alcohol use would be biased if we had excluded participants with different associations of socio-economic and lifestyle factors with alcohol user from our participants (for example excluding occasional alcohol users with poorer health), which is unlikely. Women were over-represented. However, the prevalence of diseases such as hypertension and diabetes among the participants was comparable to other population representative samples.<sup>11</sup> Third, GBCS consists of older Chinese; our results could be open to age bias as those who continue to use alcohol at older ages might have a healthier lifestyle and higher socio-position, thus exaggerating the difference between current and never alcohol users. However, the pattern was similar when we repeated the analyses with former users classified according to their earlier drinking habits (data not shown), suggesting little age bias.

## **CONCLUSIONS**

Our study shows few systematic differences between moderate alcohol users and never users in Southern Chinese, crucially these differences were such that moderate alcohol users, if anything, had lower socioeconomic position and unhealthier attributes than never users, unlike in Western settings, suggesting that Southern Chinese men could be used to assess the health effects of moderate alcohol use. Observations in alcohol epidemiology may be affected by confounding due to contextually specific systematic differences. Results from a particular setting should not be interpreted as causal unless they are verified in populations with a different pattern of health related attributes of moderate alcohol users, and if possible, in non-observational study designs such as Mendelian randomization studies.

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