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Associations between coffee consumption and all-cause and cause-specific mortality in a Japanese city: the Takayama study

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Abstract

Objective: Epidemiological studies suggest that coffee consumption is inversely associated with all-cause and cause-specific mortality. Evidence from studies targeting non-white, non-Western populations is still sparse, although coffee is popular and widely consumed in Asian countries.

Design: Population-based, prospective cohort study. We used Cox proportional hazards models with adjustment for dietary and lifestyle factors to estimate associations between coffee consumption and all-cause and cause-specific mortality. Dietary intake including coffee consumption was assessed only at baseline using a validated FFQ.

Setting: A Japanese city.

Participants: Individuals aged 35 years or older without cancer, CHD and stroke at baseline (*n* 29 079) and followed from 1992 to 2008.

Results: From 410 352 person-years, 5339 deaths were identified (mean follow-up = 14·1 years). Coffee consumption was inversely associated with mortality from all causes and CVD among all participants, but not from cancer. Compared with the category of 'none', the multivariate hazard ratio (95 % CI) for all-cause mortality was 0·93 (0·86, 1·00) for <1 cup/d, 0·84 (0·76, 0·93) for 1 cup/d and 0·81 (0·71, 0·92) for 2–3 cups/d. The multivariate hazard ratio (95 % CI) for cardiovascular mortality were 0·87 (0·77, 0·99) for <1 cup/d, 0·76 (0·63, 0·92) for 1 cup/d and 0·67 (0·50, 0·89) for 2–3 cups/d. Inverse associations were also observed for mortality from other causes, specifically infectious and digestive diseases.

Conclusion: Drinking coffee, even 1 cup/d, was inversely associated with all-cause mortality and mortality from cardiovascular, infectious and digestive diseases.

Keywords
Coffee
Mortality
Cohort studies
Prospective studies
Asia

Coffee may have a substantial impact on health because of its many bioactive compounds with potential therapeutic antioxidant, anti-inflammatory, antifibrotic or anticancer effects (e.g. the alkaloids, caffeine and trigonelline; chlorogenic acids; and the diterpenes, cafestol and kahweol)[1–3]. Four meta-analyses showed that coffee consumption was inversely associated with all-cause and CVD mortality[4–7]. Furthermore, a recent review of meta-analyses suggested that coffee consumption was more often associated with benefit than harm for a range of health outcomes, including all-cause and CVD mortality[8]. The evaluation was performed on existing studies, which were mainly from Western countries. However, evidence from studies targeting non-white, non-Western populations is still sparse, although lifestyles and disease risks can vary by ethnicity[9,10].

Recent studies targeting multi-ethnic, multinational populations reported that coffee consumption was inversely associated with all-cause mortality and such associations did not vary by ethnicity or country[11,12]. In two meta-analyses[4,6] (including three Japanese cohort studies[13–15]), coffee consumption was also inversely associated with all-cause mortality. A subsequent cohort study in Japan reported that coffee consumption was inversely associated with mortality from all causes, CVD and respiratory disease[16]. Coffee is popular and widely consumed in Asian countries, although the consumption seems to be lower than that in Western countries[17]. Past studies in Singapore and Korea reported that a little coffee consumption was inversely associated with hypertension and metabolic syndrome[18,19]. Thus, studying coffee use among Japanese community-dwelling people will

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aid in providing further insights into its associations with health.

In the present study, we examined the associations between coffee consumption and all-cause and cause-specific mortality with adjustment for important dietary and lifestyle factors using data from a population-based cohort in a Japanese city. We evaluated the health effects of fewer cups of coffee consumption than that in Western countries because the average consumption is lower in Japan (1–2 cups/person per d).

Methods

Study participants

The Takayama cohort study was initiated in 1992 and targeted all residents aged 35 years or older in Takayama city, Gifu Prefecture, Japan, to examine lifestyle and dietary factors associated with health. The study details were described previously[20]. In total, 31 552 residents (85·3 %) completed a self-administered questionnaire at baseline, including questions on demographic characteristics, body weight and height, smoking, alcohol drinking, diet and physical activities. We excluded participants who reported a prior diagnosis of cancer, CHD and stroke at baseline (*n* 2473), which left 29 079 participants (13 355 men and 15 724 women) in the analyses.

Follow-up and end point

The participants were followed from the baseline survey in 1992 to the date of death or the end of follow-up on 1 October 2008. The data on participants who died or moved out of Takayama city were obtained from basic resident or family registration databases. We identified the underlying causes of death using death certificates provided by the Legal Affairs Bureau, which were coded according to the International Classification of Disease, Tenth Revision (ICD-10). The main end points were all-cause mortality and mortality due to cancer (ICD-10: C00–D48), CVD (ICD-10: I00–I99; IHD: I20–I25; stroke: I60–I69) and other causes. Furthermore, respiratory disease (ICD-10: J10–J18 and J40–J47), injury (ICD-10: S00–T98), digestive disease (ICD-10: K00−K93) and infectious disease (ICD-10: A00−B99) were selected as additional end points.

Coffee consumption

Dietary intake including coffee consumption was assessed only at baseline by a validated 169-item semi-quantitative FFQ. The participants were asked to report how often and what amount they consumed for each food and beverage item during the past year. Nutrient intakes were estimated from the information on frequency and portion size using the fifth revised and enlarged edition of the Japanese Standard Tables of Food Composition. Details of the FFQ and the methods used for calculating nutrient intakes were described previously[21,22]. The frequency of coffee consumption during the past year was determined from the questionnaire at baseline and was originally grouped into nine categories: 'none', 'once per month', '2–3 times per month', 'once per week', '2–3 times per week', '4–6 times per week', 'once per day', '2–3 times per day' and '≥4 times per day'. Participants who drank coffee every day were presumed to answer with the number of coffees they drank in a day. We classified participants who drank coffee occasionally ('once per month', '2–3 times per month', 'once per week', '2–3 times per week' and '4–6 times per week') into a single category (<1 cup/d). Finally, the participants were categorized as follows: none, <1 cup/d, 1 cup/d, 2–3 cups/d and ≥4 cups/d. We utilized 12 d dietary records over a year to validate the estimated coffee consumption from the questionnaire. Spearman's correlation coefficients of estimated frequency (the number of cups) between the questionnaire and the records were 0·73 in men and 0·58 in women. We extrapolated the median frequency of coffee consumption using the results from all participants into the data for participants with missing information.

Covariates

We considered the following variables measured at baseline as potential *a priori* confounders: age; sex; marital status (married or not married (single, divorced/separated or widowed)); years of education (≤8, 9–11, 12–14 or ≥15 years); BMI (<18·5, 18·5–24·9, ≥25·0 kg/m^2 or missing); history of diabetes (no or yes); smoking status (never, former or current); alcohol intake (continuous); weekly vigorous exercise (never, 1, 2, 3, 4, 5, 6 or ≥7 times); use of any vitamin supplement (no or yes); total daily energy intake (continuous); daily intakes of vegetables and fruits, and red meat (continuous); and consumption of black tea, green tea, Chinese tea and soda (none, <1 or ≥1 times/d). Alcohol intake was categorized into five categories: non-drinkers or drinkers (<2·9, 2·9–<15·8, 15·8–<44·7 or ≥44·7 mg/d). In the stratified analyses by sex, alcohol intake was categorized into quartiles for men and into three categories for women (i.e. non-drinkers, or drinkers below or above the median for alcohol consumption). Daily intakes of vegetables and fruits, and red meat were adjusted for total energy intake using the residual method of energy adjustment[23].

Statistical analysis

Person-years for each study participant were counted from the date of the baseline survey to the date of death, date of censorship or the end of follow-up (1 October 2008), whichever occurred first. Using Cox proportional hazards models, we estimated age- and sex-adjusted hazard ratios (HR) and 95 % CI for associations of coffee consumption with all-cause and cause-specific mortality using the 'none'

Table 1 Baseline characteristics of total participants according to daily coffee consumption: Japanese adults aged ≥35 years (*n* 29 079) followed from 1992 to 2008, Takayama study

	Daily coffee consumption									
	None (*n* 6792)		<1 cup (*n* 11 338)		1 cup (*n* 6088)		2–3 cups (*n* 4378)		≥4 cups (*n* 483)	
	Mean, *n* or median	SD, % or IQR	Mean, *n* or median	SD, % or IQR	Mean, *n* or median	SD, % or IQR	Mean, *n* or median	SD, % or IQR	Mean, *n* or median	SD, % or IQR
Age (years), mean and SD	63·6	12·6	55·0	11·7	50·4	10·4	46·4	8·6	45·2	7·6
Men, *n* and %	2645	38·9	5183	45·7	2840	46·6	2414	55·1	273	56·5
Marital status, *n* and %										
Unmarried	1833	27·6	1746	15·6	802	13·3	516	11·9	74	15·5
Married	4797	72·4	9474	84·4	5218	86·7	3831	88·1	404	84·5
Education years, *n* and %										
≤8 years	3286	49·6	2629	23·5	779	12·9	257	5·9	20	4·2
9–11 years	2093	31·6	4476	39·9	2504	41·5	1572	36·3	162	34·0
12–14 years	1016	15·3	3307	29·5	2154	35·7	1911	44·2	217	45·6
≥15 years	230	3·5	796	7·1	598	9·9	587	13·6	77	16·2
BMI (kg/m^2), mean and SD	21·8	3·1	22·4	2·8	22·3	2·8	22·3	2·8	22·3	2·8
Diabetes, *n* and %										
No	6443	94·9	10 892	96·1	5924	97·3	4281	97·8	470	97·3
Yes	349	5·1	446	3·9	164	2·7	97	2·2	13	2·7
Smoking status, *n* and %										
Never	3520	51·8	5915	52·2	2810	46·2	1459	33·3	98	20·3
Former	1102	16·2	1855	16·4	808	13·3	477	10·9	31	6·4
Current	1292	19·0	2861	25·2	2178	35·8	2315	52·9	338	70·0
Missing	878	12·9	707	6·2	292	4·8	127	2·9	16	3·3
Alcohol intake (mg/d), median and IQR	1·9	0–27·9	6·3	0·9–34·7	8·1	1·1–37·8	12·5	1·5–40·6	8·3	0·9–36·7
Vigorous exercise ≥5 times/week, *n* and %	1089	17·9	2042	18·8	1111	19·0	771	18·0	105	22·1
Use of any vitamin supplement, *n* and %										
No	3945	58·1	7311	64·5	4024	66·1	3107	71·0	344	71·2
Yes	2030	29·9	3500	30·9	1765	29·0	1155	26·4	128	26·5
Missing	817	12·0	527	4·7	299	4·9	116	2·7	11	2·3
Dietary intake, mean and SD										
Total energy (kJ/d)	8796·4	3435·9	9854·2	3458·1	10 287·6	3587·8	10 782·6	3773·1	11 332·8	4301·2
Total energy (kcal/d)	2102·4	821·2	2355·2	826·5	2458·8	857·5	2577·1	901·8	2708·6	1028·0
Vegetables and fruits (g/d)	550·7	273·3	512·3	259·4	499·1	273·2	453·9	263·6	453·7	269·5
Red meat (g/d)	31·5	20·5	35·4	21·8	37·1	23·6	37·8	25·2	40·9	31·0
Beverage consumption, *n* and %										
Black tea										
None	5798	85·4	7082	62·5	4012	65·9	2839	64·9	326	67·5
<1 time/d	885	13·0	4075	35·9	1925	31·6	1459	33·3	142	29·4
≥1 time/d	109	1·6	181	1·6	151	2·5	80	1·8	15	3·1
Green tea										
None	2444	36·0	3109	27·4	1616	26·5	1186	27·1	128	26·5
<1 time/d	604	8·9	1825	16·1	839	13·8	738	16·9	104	21·5
≥1 time/d	3744	55·1	6404	56·5	3633	59·7	2454	56·1	251	52·0
Chinese tea										
None	4215	62·1	4149	36·6	2304	37·8	1429	32·6	166	34·4
<1 time/d	1892	27·9	5883	51·9	2773	45·6	2123	48·5	230	47·6
≥1 time/d	685	10·1	1306	11·5	1011	16·6	826	18·9	87	18·0
Soda										
None	4257	62·7	4002	35·3	2374	39·0	1471	33·6	165	34·2
<1 time/d	2387	35·1	7077	62·4	3442	56·5	2619	59·8	281	58·2
≥1 time/d	148	2·2	259	2·3	272	4·5	288	6·6	37	7·7

IQR, interquartile range.

category as a reference. Tests for linear trends in the associations were performed by assigning scores for the coffee-consumption categories, which started from 0 for the lowest category (none) to 4 for the highest category (≥4 cups/d). We then estimated multivariate HR after adjusting for all relevant confounding variables as mentioned above. We also conducted these analyses after stratifying by sex. In the analyses for cause-specific mortality (i.e. respiratory disease, injury, digestive disease and infectious disease), we collapsed the two higher categories into one category because of a small number of deaths in the category of ≥4 cups/d.

Table 2 Hazard ratios (HR) for mortality from all causes, cancer, CVD and other causes among total participants and participants stratified by sex, according to daily coffee consumption: Japanese adults aged ≥35 years (*n* 29 079) followed from 1992 to 2008, Takayama study

	Daily coffee consumption									
		<1 cup		1 cup		2–3 cups		≥4 cups		
	None	HR	95 % CI	HR	95 % CI	HR	95 % CI	HR	95 % CI	*P* for trend
Total										
Person-years	88 320	161 424		89 329		64 298		6981		
All-cause mortality										
Number of deaths	2346	1964		652		334		43		
Age- and sex-adjusted	1·00 (ref.)	0·86	0·81, 0·91	0·83	0·75, 0·91	0·92	0·81, 1·03	1·36	1·00, 1·85	0·003
Multivariate*	1·00 (ref.)	0·93	0·86, 1·00	0·84	0·76, 0·93	0·81	0·71, 0·92	1·09	0·80, 1·50	<0·001
Cancer mortality										
Number of deaths	568	646		237		154		15		
Age- and sex-adjusted	1·00 (ref.)	0·98	0·87, 1·10	0·91	0·78, 1·07	1·09	0·90, 1·32	1·13	0·67, 1·90	0·840
Multivariate*	1·00 (ref.)	1·03	0·90, 1·17	0·90	0·76, 1·07	0·99	0·80, 1·22	1·02	0·60, 1·73	0·541
CVD mortality										
Number of deaths	851	575		174		66		12		
Age- and sex-adjusted	1·00 (ref.)	0·80	0·72, 0·89	0·77	0·65, 0·91	0·72	0·56, 0·94	1·60	0·90, 2·84	<0·001
Multivariate*	1·00 (ref.)	0·87	0·77, 0·99	0·76	0·63, 0·92	0·67	0·50, 0·89	1·39	0·77, 2·49	0·002
Other cause mortality										
Number of deaths	926	742		241		27		5		
Age- and sex-adjusted	1·00 (ref.)	0·85	0·77, 0·94	0·82	0·71, 0·95	0·86	0·70, 1·06	1·46	0·89, 2·41	0·021
Multivariate*	1·00 (ref.)	0·91	0·81, 1·03	0·85	0·73, 1·00	0·72	0·57, 0·90	1·00	0·58, 1·72	0·005
Men										
Person-years	33 043	71 023		40 581		34 750		3903		
All-cause mortality										
Number of deaths	1049	1162		417		242		31		
Age-adjusted	1·00 (ref.)	0·85	0·78, 0·93	0·80	0·71, 0·90	0·82	0·71, 0·95	1·23	0·86, 1·77	0·002
Multivariate*	1·00 (ref.)	0·88	0·80, 0·97	0·77	0·67, 0·87	0·70	0·59, 0·82	0·99	0·68, 1·43	<0·001
Cancer mortality										
Number of deaths	309	400		146		108		11		
Age-adjusted	1·00 (ref.)	0·93	0·80, 1·08	0·84	0·69, 1·03	1·02	0·81, 1·29	1·15	0·62, 2·11	0·694
Multivariate*	1·00 (ref.)	0·95	0·80, 1·12	0·79	0·63, 0·98	0·88	0·69, 1·14	1·00	0·54, 1·86	0·120
CVD mortality										
Number of deaths	315	303		101		47		9		
Age-adjusted	1·00 (ref.)	0·77	0·66, 0·91	0·70	0·56, 0·89	0·61	0·44, 0·84	1·41	0·72, 2·77	0·001
Multivariate*	1·00 (ref.)	0·80	0·66, 0·96	0·68	0·53, 0·87	0·54	0·38, 0·76	1·21	0·61, 2·40	<0·001
Other cause mortality										
Number of deaths	425	458		170		86		11		
Age-adjusted	1·00 (ref.)	0·85	0·74, 0·97	0·85	0·71, 1·02	0·79	0·62, 1·00	1·21	0·66, 2·22	0·046
Multivariate*	1·00 (ref.)	0·88	0·75, 1·02	0·81	0·67, 1·00	0·63	0·48, 0·83	0·85	0·45, 1·62	0·001
Women										
Person-years	55 277	90 402		48 749		29 548		3078		
All-cause mortality										
Number of deaths	1297	802		235		92		12		
Age-adjusted	1·00 (ref.)	0·88	0·81, 0·97	0·88	0·76, 1·02	1·18	0·94, 1·48	1·63	0·92, 2·90	0·499
Multivariate*	1·00 (ref.)	0·98	0·88, 1·09	0·93	0·80, 1·10	1·04	0·80, 1·33	1·14	0·62, 2·10	0·928
Cancer mortality										
Number of deaths	259	246		91		46		4		
Age-adjusted	1·00 (ref.)	1·01	0·84, 1·21	0·99	0·77, 1·29	1·23	0·87, 1·73	1·10	0·41, 2·99	0·476
Multivariate*	1·00 (ref.)	1·08	0·87, 1·33	1·06	0·80, 1·40	1·21	0·83, 1·76	1·03	0·37, 2·84	0·517
CVD mortality										
Number of deaths	536	272		73		19		3		
Age-adjusted	1·00 (ref.)	0·85	0·73, 0·98	0·87	0·67, 1·12	0·97	0·60, 1·56	1·55	0·50, 4·86	0·162
Multivariate*	1·00 (ref.)	0·95	0·80, 1·14	0·86	0·65, 1·14	0·91	0·54, 1·53	1·24	0·39, 3·98	0·419
Other cause mortality										
Number of deaths	501	284		71		27		5		
Age-adjusted	1·00 (ref.)	0·87	0·75, 1·01	0·78	0·60, 1·01	1·14	0·76, 1·71	2·21	0·91, 5·38	0·294
Multivariate*	1·00 (ref.)	0·96	0·80, 1·15	0·91	0·69, 1·21	0·91	0·56, 1·47	1·17	0·43, 3·24	0·742

Ref., reference category.
*Marital status, years of education, BMI, diabetes, smoking status, alcohol intake, vigorous exercise, use of any vitamin supplement, dietary intake (total energy, vegetables and fruits, red meat) and beverage consumption (black tea, green tea, Chinese tea, soda) were also adjusted for.

In sensitivity analyses, we first estimated multivariate HR for all-cause mortality after excluding deaths within the first 3 years. To examine the impact of residual confounding from smoking status, we next conducted further analyses adjusting for smoking-years category (never, smoking <10, 11–20, 21–30, ≥30 years or smoking-years missing) instead of the smoking status category in the multivariate models. We also conducted the same analyses with smoking-cessation years category (currently smoking, <5, 6–10, >10 years of smoking cessation or never smoking).

Table 3 Hazard ratios (HR) for mortality from other specific causes among total participants, according to daily coffee consumption: Japanese adults aged ≥35 years (*n* 29 079) followed from 1992 to 2008, Takayama study

	Daily coffee consumption							
		<1 cup		1 cup		≥2 cups*		
	None	HR	95 % CI	HR	95 % CI	HR	95 % CI	*P* for trend
Respiratory disease								
Number of deaths (*n* 531)	261		186		52		32	
Multivariate†	1·00 (ref.)	0·95	0·76, 1·20	0·87	0·62, 1·21	0·94	0·61, 1·46	0·497
Injury								
Number of deaths (*n* 370)	129		131		70		40	
Multivariate†	1·00 (ref.)	0·82	0·61, 1·09	0·96	0·68, 1·36	0·74	0·48, 1·14	0·384
Digestive disease								
Number of deaths (*n* 163)	79		61		14		9	
Multivariate†	1·00 (ref.)	0·73	0·49, 1·09	0·34	0·17, 0·66	0·31	0·13, 0·71	0·001
Infectious disease								
Number of deaths (*n* 146)	73		53		12		8	
Multivariate†	1·00 (ref.)	0·60	0·38, 0·93	0·44	0·22, 0·88	0·52	0·23, 1·19	0·012
Urologic disease								
Number of deaths (*n* 112)	53		45		12		2	
Multivariate†	1·00 (ref.)	1·33	0·80, 2·21	1·04	0·50, 2·17	0·40	0·09, 1·78	0·540
Endocrine metabolic disease								
Number of deaths (*n* 79)	40		22		11		6	
Multivariate†	1·00 (ref.)	0·58	0·32, 1·08	0·71	0·33, 1·54	0·53	0·18, 1·52	0·227

Ref., reference category.
*The categories of 2–3 cups/d and ≥4 cups/d were collapsed into the single category of ≥2 cups/d because of a small number of deaths from the specific causes in the category of ≥4 cups/d.
†Age, sex, marital status, years of education, BMI, diabetes, smoking status, alcohol intake, vigorous exercise, use of any vitamin supplement, dietary intake (total energy, vegetables and fruits, red meat) and beverage consumption (black tea, green tea, Chinese tea, soda) were adjusted for.

Furthermore, considering dietary patterns which are potentially correlated with coffee consumption among Japanese adults[24,25], we additionally adjusted for intakes of fish, rice and dairy products. Statistical significance was defined as a two-sided *P* value of less than 0·05. The statistical software package Stata SE version 14.2 was used for all analyses.

Results

Table 1 shows the baseline characteristics of all participants according to coffee consumption category. Compared with participants who did not drank coffee, those who drank two or more cups of coffee daily tended to be younger, male, married and current smokers. They also tended to have a higher level of education, consume a larger amount of alcohol, have higher intakes of total energy and red meat, and have a lower intake of vegetables and fruits. In addition, they were more likely to drink black tea, green tea, Chinese tea and soda, and were less likely to have diabetes and use any vitamin supplement. After stratification by sex, men and women showed the same tendency except alcohol consumption in men; that is, men who drank two or more cups of coffee daily tended to consume a smaller amount of alcohol (see online supplementary material, Supplemental Table S1).

During 16 years of follow-up (mean = 14·1 years), 5339 deaths were identified among 410 352 total person-years. Table 2 shows the associations between coffee consumption and mortality from all causes, cancer, CVD and other causes among all participants and stratified by sex. Regarding all-cause mortality, coffee consumption was associated with reduced risk among all participants after adjusting for all potential confounders. Compared with the category of 'none', the HR (95 % CI) was 0·93 (0·86, 1·00) for <1 cup/d, 0·84 (0·76, 0·93) for 1 cup/d, 0·81 (0·71, 0·92) for 2–3 cups/d and 1·09 (0·80, 1·50) for ≥4 cups/d (*P* for trend <0·001). A similar pattern was observed for men, but not for women.

Coffee consumption was not associated with mortality from cancer among all participants or women, although drinking 1 cup coffee/d was associated with reduced risk in men (Table 2). Regarding mortality from CVD, coffee consumption was associated with reduced risk among all participants. Compared with the category of 'none', the HR (95 % CI) were 0·87 (0·77, 0·99) for <1 cup/d, 0·76 (0·63, 0·92) for 1 cup/d, 0·67 (0·50, 0·89) for 2–3 cups/d and 1·39 (0·77, 2·49) for ≥4 cups/d (*P* for trend = 0·002). A similar pattern was observed for men and women, although inverse associations among women across all categories did not reach statistical significance. Specifically, coffee consumption was associated with reduced risk for mortality from stroke and IHD among all participants. The HR (95 % CI) for the categories of <1 cup/d, 1 cup/d, 2–3 cups/d and ≥4 cups/d were 0·86 (0·70, 1·05), 0·64 (0·47, 0·87), 0·65 (0·41, 1·02) and 1·11 (0·41, 3·06) for stroke mortality, and 0·68 (0·50, 0·91), 0·69 (0·46, 1·04), 0·50 (0·27, 0·92) and 1·41 (0·50, 3·98) for IHD mortality, respectively. Regarding mortality from other causes, coffee consumption was associated with reduced risk among all participants.

Table 4 Sensitivity of hazard ratios (HR) for all-cause mortality among total participants, according to daily coffee consumption: Japanese adults aged ≥35 years (*n* 29 079) followed from 1992 to 2008, Takayama study

	Daily coffee consumption								
		<1 cup		1 cup		2–3 cups		≥4 cups	
	None	HR	95 % CI	HR	95 % CI	HR	95 % CI	HR	95 % CI	*P* for trend
Excluding deaths within the first 3 years (*n* 26 319)										
Multivariate*	1·00 (ref.)	0·91	0·84, 0·98	0·84	0·75, 0·93	0·81	0·70, 0·93	1·03	0·73, 1·45	0·001
Adjusting for the category of smoking-years instead of smoking status (*n* 25 562)										
Multivariate*	1·00 (ref.)	0·93	0·87, 1·01	0·85	0·76, 0·94	0·85	0·74, 0·97	1·13	0·74, 0·97	0·004
Adjusting for the category of smoking-cessation years instead of smoking status (*n* 25 510)										
Multivariate*	1·00 (ref.)	0·93	0·86, 1·00	0·83	0·75, 0·92	0·81	0·71, 0·93	1·04	0·71, 0·93	<0·001
Additionally adjusting for the categories of dietary intake (fish, rice, dairy products; *n* 26 943)										
Multivariate*	1·00 (ref.)	0·93	0·86, 1·00	0·83	0·75, 0·92	0·80	0·70, 0·92	1·08	0·78, 1·48	<0·001

Ref., reference category.
*Age, sex, marital status, years of education, BMI, diabetes, smoking status, alcohol intake, vigorous exercise, use of any vitamin supplement, dietary intake (total energy, vegetables and fruits, red meat) and dairy beverage consumption (black tea, green tea, Chinese tea, soda) were adjusted for.

The HR (95 % CI) were 0·91 (0·81, 1·03) for <1 cup/d, 0·85 (0·73, 1·00) for 1 cup/d, 0·72 (0·57, 0·90) for 2–3 cups/d and 1·00 (0·58, 1·72) for ≥4 cups/d (*P* for trend = 0·005). A similar pattern was observed for men, but not for women.

Table 3 shows the associations between coffee consumption and mortality from other specific causes among all participants. In the multivariate models, coffee consumption was significantly associated with reduced risk of mortality from digestive and infectious diseases. Coffee consumption was also inversely associated with mortality from the other specific causes, although the point estimates were not statistically significant.

In the sensitivity analyses (Table 4), even after excluding deaths within the first 3 years, the main findings for all-cause mortality among all participants did not change substantially. Furthermore, adjusting for the categories of smoking-years or smoking-cessation years instead of smoking status also did not change the findings substantially.

Discussion

We used data from a population-based prospective cohort study in a Japanese city (the Takayama study) to examine the associations of coffee consumption with all-cause and cause-specific mortality after adjusting for important dietary and lifestyle factors. The results showed that drinking coffee, even 1 cup/d, was associated with reduced risk of mortality from all causes, CVD and other causes among all participants, although the associations for ≥4 cups/d were no more significant. In the stratified analyses by sex, similar tendencies were observed for men, but not for women. Furthermore, coffee consumption was also inversely associated with mortality specifically from infectious and digestive diseases.

Although we found that drinking 1 cup coffee/d was associated with reduced risk for mortality from all and other specific causes, previous studies indicated that risks were lowest at 3–4 cups/d for all-cause and CVD mortality with no further reductions at >4 cups/d[5,7,26]. In the present study, there were few participants who drank ≥4 cups coffee/d (*n* 483, 1·7 %); therefore, we may have failed to observe a tendency in these associations.

The present finding of reduced risk for all-cause mortality is consistent with meta-analyses[4–7,26] and recent large-scale cohort studies in Western countries (targeting multi-ethnic populations)[11,12] and Japan[16]. In the present study, the risks decreased by 16 and 19 % for the categories of 1 cup/d and 2–3 cups/d, respectively, compared with the 'none' category. These findings are similar to those from large-scale cohort studies (15 % for 1 cup/d and 20 % for 2–3 cups/d in risk reductions among Japanese Americans compared with the 'none' category[11], and 15 % for the 1–2 cups/d category and 24 % for the 3–4 cups/d category in risk reductions compared with the 'almost-none' category[16]).

Coffee consumption was inversely associated with reduced risk for mortality from CVD, but not from cancer in the present study. This finding is consistent with three meta-analyses[5–7] and previous studies in Japan[14–16,27]. The protective associations on mortality from CVD are plausible because of the presence of various bioactive compounds in coffee, as mentioned above. By contrast, the association of coffee with cancer mortality may vary by cancer site (e.g. probable protective associations between coffee consumption and liver and endometrial cancers are suggested[3,28]). Further studies evaluating

coffee's associations with site-specific cancer mortality in non-Western countries are needed.

After stratification by sex, the inverse associations with mortality from all causes, CVD and other causes did not reach statistical significance in women. The potential reason is that women appeared to report coffee consumption less accurately than men. This may result in non-differential misclassifications, just making the estimates towards the null. It is also possible that caffeine, a coffee compound, could have sex-differentiated impacts on health[8,29]. For example, the CVD mortality risk in women is lower than that in men, which is influenced by the interactions between genetic, hormonal and environmental factors[30,31]. These factors could have sex-differentiated impacts on the associations between coffee consumption and CVD mortality.

In addition, coffee consumption seemed to be inversely associated with other specific-cause (non-CVD, non-cancer) mortality, although we found significant inverse associations only for mortality from infectious and digestive diseases. The bioactive compounds in coffee (e.g. polyphenol, caffeine and melanoidins) could exert such beneficial effects on liver function and chronic inflammation[1,2]. Past studies reported that coffee consumption was associated with lower levels of liver enzymes, C-reactive protein and adiponectin[12,32–34]. Therefore, it is likely that coffee consumption is also inversely associated with mortality from respiratory disease and endocrine/metabolic disease, as suggested by previous studies[8,11,12,16,35,36]. The non-significant inverse associations we observed could be due to a small number of cases. Future studies evaluating associations between coffee consumption and specific causes of death are thus awaited.

The major strengths of the present study are its prospective cohort design with 16 years of follow-up, its high participation rate (85·3 %), use of a valid dietary questionnaire and considering important potential confounding factors simultaneously. Therefore, the present findings provide further evidence for the protective effects of coffee consumption among non-white, non-Western populations.

The present study has several limitations. First, it did not provide strong evidence for high coffee consumption, despite the dose–response relationships in the inverse associations between coffee consumption and all-cause mortality and mortality specifically from CVD, infectious and digestive diseases. Second, coffee consumption was assessed at baseline only and may not reflect long-term coffee consumption, although a study of three prospective US cohorts indicated that a single assessment can capture coffee drinking habits over 10–20 years[36]. Indeed, participants with chronic disease may reduce their coffee consumption, but we excluded those participants from the analyses. Moreover, we conducted sensitivity analyses excluding deaths within the first 3 years, which did not change our findings substantially. However, the referent category of none could include those who had quit drinking coffee before baseline because of known or undiagnosed symptoms. Third, we did not collect information on how the participants prepared and served coffee, although its bioactive compounds vary depending on bean type, degree of roasting and preparation method, including quality of beans, grind settings and brewing methods[8,37]. Furthermore, we cannot differentiate between canned, instant or brewed coffee and cannot evaluate the associations of decaffeinated coffee because drinking decaffeinated coffee was likely to be rare in Japan[16]. These factors may result in moving the HR towards the null. Finally, we cannot rule out the possibility of residual confounding due to smoking status, which would be an important potential confounding factor. However, sensitivity analyses using two different smoking categories did not change the main findings substantially. In large-scale cohort studies, the results for the associations between coffee consumption and mortality were similar across smoking categories (i.e. never, former or current)[11,12,35].

Conclusion

In conclusion, after adjusting for important dietary and lifestyle confounders, we demonstrated that drinking coffee, even 1 cup/d, was associated with reduced risk of all-cause mortality and mortality specifically from CVD, infectious and digestive diseases. Thus, a little coffee consumption will contribute to increasing the health and long life of people in Asian countries, such as Japan.

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Supplementary material

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References

1. Nieber K (2017) The impact of coffee on health. *Planta Med* **83**, 1256–1263.
2. Ludwig IA, Clifford MN, Lean MEJ *et al.* (2014) Coffee: biochemistry and potential impact on health. *Food Funct* **5**, 1695–1717.
3. International Agency for Research on Cancer (2016) Q&A on Monographs Volume 116: Coffee, maté, and very hot beverages. https://www.iarc.fr/wp-content/uploads/2018/07/Monographs-QA_Vol116.pdf (accessed March 2019).
4. Je Y & Giovannucci E (2014) Coffee consumption and total mortality: a meta-analysis of twenty prospective cohort studies. *Br J Nutr* **111**, 1162–1173.
5. Crippa A, Discacciati A, Larsson SC *et al.* (2014) Coffee consumption and mortality from all causes, cardiovascular disease, and cancer: a dose–response meta-analysis. *Am J Epidemiol* **180**, 763–775.
6. Malerba S, Turati F, Galeone C *et al.* (2013) A meta-analysis of prospective studies of coffee consumption and mortality for all causes, cancers and cardiovascular diseases. *Eur J Epidemiol* **28**, 527–539.
7. Grosso G, Micek A, Godos J *et al.* (2016) Coffee consumption and risk of all-cause, cardiovascular, and cancer mortality in smokers and non-smokers: a dose–response meta-analysis. *Eur J Epidemiol* **31**, 1191–1205.
8. Poole R, Kennedy OJ, Roderick P *et al.* (2017) Coffee consumption and health: umbrella review of meta-analyses of multiple health outcomes. *BMJ* **359**, j5024.
9. Loftfield E, Freedman ND, Dodd KW *et al.* (2016) Coffee drinking is widespread in the United States, but usual intake varies by key demographic and lifestyle factors. *J Nutr* **146**, 1762–1768.
10. Loftfield E, Freedman ND, Graubard BI *et al.* (2015) Association of coffee consumption with overall and cause-specific mortality in a large US prospective cohort study. *Am J Epidemiol* **182**, 1010–1022.
11. Park S-Y, Freedman ND, Haiman CA *et al.* (2017) Association of coffee consumption with total and cause-specific mortality among nonwhite populations. *Ann Intern Med* **167**, 228–235.
12. Gunter MJ, Murphy N, Cross AJ *et al.* (2017) Coffee drinking and mortality in 10 European countries: a multinational cohort study. *Ann Intern Med* **167**, 236–247.
13. Iwai N, Ohshiro H, Kurozawa Y *et al.* (2002) Relationship between coffee and green tea consumption and all-cause mortality in a cohort of a rural Japanese population. *J Epidemiol* **12**, 191–198.
14. Sugiyama K, Kuriyama S, Akhter M *et al.* (2010) Coffee consumption and mortality due to all causes, cardiovascular disease, and cancer in Japanese women. *J Nutr* **140**, 1007–1013.
15. Tamakoshi A, Lin Y, Kawado M *et al.* (2011) Effect of coffee consumption on all-cause and total cancer mortality: findings from the JACC study. *Eur J Epidemiol* **26**, 285–293.
16. Saito E, Inoue M, Sawada N *et al.* (2015) Association of coffee intake with total and cause-specific mortality in a Japanese population: the Japan Public Health Center-based Prospective Study. *Am J Clin Nutr* **101**, 1029–1037.
17. All Japan Coffee Association (2017) Statistics: supply and demand of coffee in Japan (in Japanese). http://coffee.ajca.or.jp/data (accessed August 2018).
18. Chei C-L, Loh JK, Soh A *et al.* (2018) Coffee, tea, caffeine, and risk of hypertension: the Singapore Chinese Health Study. *Eur J Nutr* **57**, 1333–1342.
19. Kim K, Kim K & Park SM (2016) Association between the prevalence of metabolic syndrome and the level of coffee consumption among Korean women. *PLoS One* **11**, e0167007.
20. Shimizu H (1996) *The Basic Report on Takayama Study*. Gifu: Gifu University.
21. Nagata C, Takatsuka N, Shimizu N *et al.* (2004) Sodium intake and risk of death from stroke in Japanese men and women. *Stroke* **35**, 1543–1547.
22. Shimizu H, Ohwaki A, Kurisu Y *et al.* (1999) Validity and reproducibility of a quantitative food frequency questionnaire for a cohort study in Japan. *Jpn J Clin Oncol* **29**, 38–44.
23. Willett W (editor) (2012) Implications of total energy intake for epidemiologic analyses. In *Nutritional Epidemiology*, 3rd ed., pp. 260–286. New York: Oxford University Press.
24. Maruyama K, Iso H, Date C *et al.* (2013) Dietary patterns and risk of cardiovascular deaths among middle-aged Japanese: JACC Study. *Nutr Metab Cardiovasc Dis* **23**, 519–527.
25. Shimazu T, Kuriyama S, Hozawa A *et al.* (2007) Dietary patterns and cardiovascular disease mortality in Japan: a prospective cohort study. *Int J Epidemiol* **36**, 600–609.
26. Grosso G, Stepaniak U, Micek A *et al.* (2017) Coffee consumption and mortality in three Eastern European countries: results from the HAPIEE (Health, Alcohol and Psychosocial factors in Eastern Europe) study. *Public Health Nutr* **20**, 82–91.
27. Mineharu Y, Koizumi A, Wada Y *et al.* (2011) Coffee, green tea, black tea and oolong tea consumption and risk of mortality from cardiovascular disease in Japanese men and women. *J Epidemiol Community Health* **65**, 230–240.
28. World Cancer Research Fund & American Institute for Cancer Research (2018) Non-alcoholic drinks and the risk of cancer. In *Diet, Nutrition, Physical Activity and Cancer: A Global Perspective. Continuous Update Project Expert Report 2018*, pp. 1–62. London: WCRF International.
29. Temple JL & Ziegler AM (2011) Gender differences in subjective and physiological responses to caffeine and the role of steroid hormones. *J Caffeine Res* **1**, 41–48.
30. Winham SJ, de Andrade M & Miller VM (2014) Genetics of cardiovascular disease: importance of sex and ethnicity. *Atherosclerosis* **241**, 219–228.
31. Deo R & Albert CM (2012) Epidemiology and genetics of sudden cardiac death. *Circulation* **125**, 620–637.
32. Xiao Q, Sinha R, Graubard BI *et al.* (2014) Inverse associations of total and decaffeinated coffee with liver enzyme levels in National Health and Nutrition Examination Survey 1999-2010. *Hepatology* **60**, 2091–2098.
33. Zhang Y & Zhang D-Z (2018) Is coffee consumption associated with a lower level of serum C-reactive protein? A meta-analysis of observational studies. *Int J Food Sci Nutr* **69**, 985–994.
34. Zhang Y & Zhang D-Z (2018) Associations of coffee consumption with circulating level of adiponectin and leptin. A meta-analysis of observational studies. *Int J Food Sci Nutr* **69**, 1003–1012.
35. Freedman ND, Park Y, Abnet CC *et al.* (2012) Association of coffee drinking with total and cause-specific mortality. *N Engl J Med* **366**, 1891–1904.
36. Ding M, Satija A, Bhupathiraju SN *et al.* (2015) Association of coffee consumption with total and cause-specific mortality in 3 large prospective cohorts. *Circulation* **132**, 2305–2315.
37. Corrêa TAF, Monteiro MP, Mendes TMN *et al.* (2012) Medium light and medium roast paper-filtered coffee increased antioxidant capacity in healthy volunteers: results of a randomized trial. *Plant Foods Hum Nutr* **67**, 277–282.