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Consumption of Coffee, Tea, and Caffeine at Midlife, and the Risk of Physical Frailty in Late Life

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A B S T R A C T

Objectives: Our study evaluated the prospective association between the consumption of caffeine-containing beverages at midlife and the risk of physical frailty at late life within a population-based cohort of Chinese adults living in Singapore over a follow-up period of 20 years.
Design: Prospective cohort study.
Setting and Participants: We used data from 12,583 participants from the baseline and third follow-up interviews of the Singapore Chinese Health Study (SCHS). Participants had a mean age of 53 years at baseline (1993–1998), and a mean age of 73 years during the third follow-up (2014–2017).
Methods: At baseline, habitual consumption of caffeine-containing beverages was evaluated using a validated semi-quantitative food-frequency questionnaire. During the third follow-up, physical frailty was assessed using the modified Cardiovascular Health Study phenotype.
Results: Compared with non-daily drinkers, those who drank 4 or more cups of coffee daily had reduced odds of physical frailty [odds ratio (OR), 0.54; 95% CI, 0.38–0.76]. Similarly, compared with those who hardly drank tea, participants who drank tea everyday also had reduced odds (OR, 0.82; 95% CI, 0.71–0.95). Total daily caffeine intake at midlife was associated with reduced likelihood of frailty at late life in a dose-response relationship ($P_{trend} < .001$). Relative to their counterparts in the lowest quartile of daily caffeine intake (0–67.6 mg/d), participants in the highest quartile (223.0–910.4 mg/d) had an OR of 0.77 (95% CI, 0.66–0.91). Higher caffeine consumption was associated with lower likelihood of being in the slowest quintile for timed up-and-go (TUG) and weakest quintile for handgrip strength.
Conclusions and Implications: In this cohort of Chinese adults, higher consumption of caffeine at midlife, via coffee and tea, was associated with a reduced likelihood of physical frailty in late life.

Physical frailty is an age-related medical syndrome "characterized by diminished strength, endurance, and reduced physiologic function that increases an individual's vulnerability for developing increased dependency and/or death."[1] With global aging, there has been a rapid increase in the number of physically frail older adults, resulting in increased pressure on health care systems worldwide.[2] As such, there has been increasing international attention on the condition of physical frailty, and on interventions that might prevent or slow its progression in aging populations.[2,3]

In particular, an emerging body of evidence now supports the role of nutrition and diet in the prevention of physical frailty.[4-8] However, few studies have focused their investigations on the intake of caffeine-containing beverages like coffee and tea. This is of interest, as coffee and tea are not only among the most widely consumed beverages around the world,[9] but are also rich sources of bioactive compounds that include caffeine as well as polyphenols that possess antioxidant and anti-inflammatory properties.[10-12] Furthermore, findings from experimental and epidemiologic studies suggest that the

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consumption of these compounds may be associated with lower risks of comorbidities that could predispose one to physical frailty in aging, such as certain cancers, cardiovascular diseases, type 2 diabetes, obesity, neurodegenerative diseases, and sarcopenia.[12-14]

Among the studies that have included coffee and/or tea in their investigations with physical frailty, most were done as part of an overall dietary pattern or diversity score,[15-19] thus obscuring the individual association of coffee or tea with the adverse outcome. Few studies have specifically focused on coffee and/or tea, with most being cross-sectional in design.[20-26] These studies reported that the consumption of coffee[21-24] and/or tea[21,24-26] was associated with a reduced likelihood of physical frailty in older adults. In contrast, only 1 longitudinal study had specifically focused on coffee, and it did not find a statistically significant association with the risk of physical frailty.[27]

Thus, our study filled the gap by evaluating the prospective association between the consumption of caffeine-containing beverages (coffee, black tea, and green tea) at midlife and the risk of physical frailty at late life within a population-based cohort of Chinese adults living in Singapore over a follow-up period of 20 years. We hypothesized that after accounting for participants' sociodemographic characteristics, comorbidities, lifestyle factors, body mass index, physical activity, and usual diet, the consumption of caffeine at midlife, particularly via the drinking of coffee and tea, would be associated with a reduced likelihood of physical frailty at late life.

Methods

Study Population

This study was nested within a population-based prospective cohort known as the Singapore Chinese Health Study (SCHS).[28] The SCHS enrolled 63,257 participants (27,959 men and 35,298 women) who were 45 to 74 years old between April 1993 and December 1998. All participants were Chinese from the 2 major Chinese dialect groups in Singapore—the Hokkien and the Cantonese—who originated from the contiguous provinces of Fujian and Guangdong in the southern part of China, respectively. After recruitment, consenting survivors were re-contacted for follow-up interviews every 5 to 6 years: first follow-up interviews (1999–2004), second follow-up interviews (2006–2010), third follow-up interviews (2014–2017). In this study, we used data from 12,583 surviving participants who agreed to participate in the third follow-up interviews that were conducted in-person from July 2014 to December 2017. This study was approved by the institutional review board at the National University of Singapore, and written informed consent was obtained from all study participants.

As outlined in Figure 1, during the baseline interviews (1993–1998) at midlife, we evaluated the following characteristics in our participants: consumption of caffeine-containing beverages and food; sociodemographic characteristics; history of comorbidities, smoking, and alcohol consumption; hours of sleep per day; height and weight; physical activity; and usual dietary intake. Later, at the third follow-up interviews (2014–2017) in late life, we assessed participants for the presence of physical frailty criteria (weight loss, exhaustion, slowness, and weakness), where weight loss was computed from the difference in self-reported weight between the second (2006–2010) and third follow-up interviews. In this study, we only included participants who had complete data on all 4 criteria that defined physical frailty at the third follow-up (N = 12,583).

Assessment of Caffeine-containing Beverage Consumption at Midlife

At the baseline interviews (1993–1998), participants' usual dietary intake at midlife, including their consumption of caffeine-containing beverages, was assessed through the use of a 165-item semi-quantitative food-frequency questionnaire.[28] This questionnaire was specifically developed for our study population, and it was subsequently validated by interviewing 810 randomly chosen participants for their 24-hour dietary recalls on 2 separate occasions (covering a weekday and weekend approximately 2 months apart), and by readministering the food-frequency questionnaire to these chosen participants roughly 2 months after the second 24-hour recall interview. The correlation coefficients between these 2 methods for selected dietary components ranged between 0.24 and 0.79, and the differences between the mean values of most pairs for energy and selected nutrients were within 10%.[28]

In our food-frequency questionnaire, the frequencies of coffee, black tea, green tea, and soft drink consumption were asked for in separate questions, and participants were able to report their consumption of each beverage separately. For these beverages, participants selected their average intake frequency over the past year from 1 of 9 predefined categories (never or hardly ever, 1–3 cups/month, 1 cup/week, 2–3 cups/week, 4–6 cups/week, 1 cup/day, 2–3 cups/day, 4–5 cups/day, 6 or more cups/day), where a standard serving size of 1 cup was defined as 237 mL. Participants who did not drink tea at least once a month were categorized as never-drinkers. At the time of recruitment, decaffeinated coffee and tea were rarely consumed in our study population; as such, all coffee and tea consumed by the participants were assumed to be caffeinated. The total daily caffeine intake was estimated by summing the caffeine from all caffeine-containing beverages (including coffee, tea, and soft drinks) as well as caffeinated food items (such as chocolate).[28] The amount of caffeine (and other specific nutrients) in each beverage or food item was estimated using values from the Singapore Food Composition Database.[28]

Assessment of Other Covariates at Midlife

At the baseline interviews, trained interviewers used a structured questionnaire to obtain information on participants' sociodemographic characteristics, history of physician-diagnosed comorbidities (hypertension, angina/heart attack, stroke, diabetes, and cancer), lifestyle factors (history of smoking, and hours of sleep per day), height, weight, and physical activity (hours of strenuous sports, vigorous work, and moderate activity per week) at midlife. In addition, data from the food-frequency questionnaire was also used to assess the frequency of alcohol consumption, and usual dietary intake [amount of red meat, poultry, fish, shellfish, vegetables (and related juices), and fruit (and related juices) consumed, plus overall energy intake] at midlife.

Assessment of Physical Frailty in Late Life

During the third follow-up interviews (2014–2017), physical frailty was assessed using a modified version of the Cardiovascular Health Study (CHS) frailty phenotype[1,29,30] that included weight loss, exhaustion, slowness, and weakness.[31] The criterion of low activity was not included, as we did not collect relevant data for this measure. Body weight was self-reported, and participants met the criterion for weight loss if they had lost 10% or more of their weight since the second follow-up interviews (2006–2010).[31] All 12,583 participants included in this study had self-reported body weight in the second (2006–2010) and third (2014–2017) follow-up interviews, and the mean (SD) duration between these 2 interviews was 7.3 (1.0) years.[31] Weight data from the baseline (1993–1998) and first (1999–2004) follow-up interviews were not considered in the determination of this criterion. Participants met the criterion of exhaustion if they answered "No" to the question, "Do you feel full of energy?" The criterion of slowness was met if their timing for the

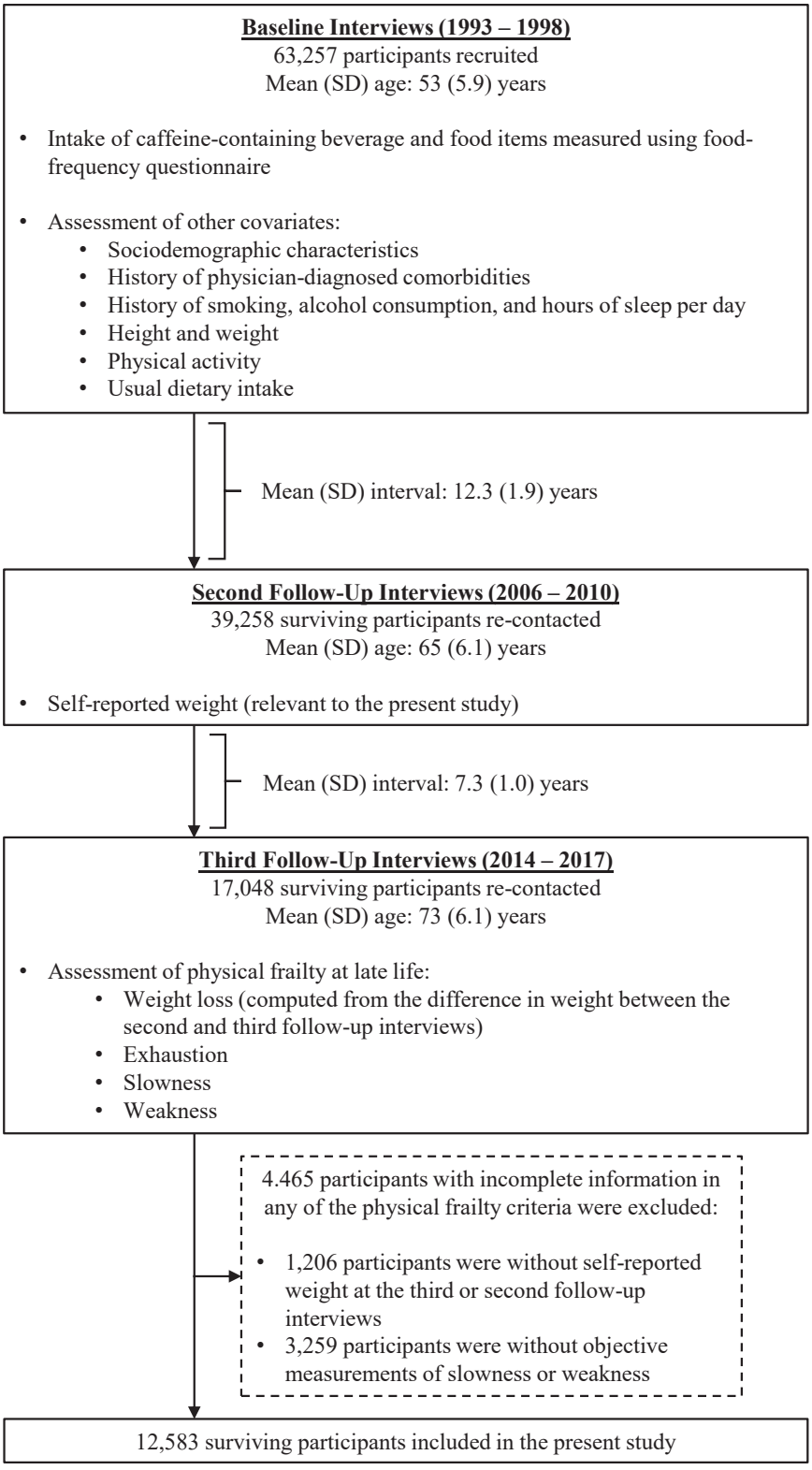

Fig. 1. Inclusion of participants for the study.

timed up-and-go (TUG) test[32] fell within the slowest sex-specific quintile, and they met the criterion of weakness if their handgrip strength was in the weakest sex-specific quintile. Participants who met 2 or more of these criteria were classified as being physically frail.[31]

Statistical Analyses

In descriptive analyses, we compared the means (SD) of continuous variables using 1-way analysis of variance, and we compared the proportions of categorical variables using Pearson's χ^2 test. We used

Table 1
Baseline Characteristics of the Participants, by Quartiles of Daily Caffeine Intake at Midlife

	Quartiles of Daily Caffeine Intake				*P* Value
	Q1 (Lowest)	Q2	Q3	Q4 (Highest)	
	n = 3151	n = 3141	n = 3149	n = 3142	
Mean caffeine intake (SD) [mg/d]	30.76 (21.34)	92.84 (11.04)	163.14 (37.24)	290.46 (83.16)	<.001
Mean age at assessment of frailty (SD) [y]	72.26 (6.16)	72.68 (6.20)	72.52 (6.01)	72.61 (5.90)	.037
Gender					<.001
Men	946 (30.0)	1054 (33.6)	1472 (46.7)	1748 (55.6)	
Women	2205 (70.0)	2087 (66.4)	1677 (53.3)	1394 (44.4)	
Dialect group					.73
Hokkien	1583 (50.2)	1609 (51.2)	1576 (50.0)	1569 (49.9)	
Cantonese	1568 (49.8)	1532 (48.8)	1573 (50.0)	1573 (50.1)	
Level of education					<.001
No formal education	528 (16.8)	559 (17.8)	414 (13.1)	486 (15.5)	
Primary school	1285 (40.8)	1389 (44.2)	1407 (44.7)	1433 (45.6)	
Secondary school	1033 (32.8)	955 (30.4)	1053 (33.4)	984 (31.3)	
Diploma/University	305 (9.7)	238 (7.6)	275 (8.7)	239 (7.6)	
Hypertension	555 (17.6)	648 (20.6)	620 (19.7)	538 (17.1)	<.001
Cardiovascular disease	71 (2.3)	72 (2.3)	61 (1.9)	84 (2.7)	.28
Diabetes	148 (4.7)	174 (5.5)	136 (4.3)	115 (3.7)	.004
Cancer	82 (2.6)	58 (1.8)	50 (1.6)	32 (1.0)	<.001
Frequency of alcohol consumption					<.001
Never	2721 (86.4)	2544 (81.0)	2435 (77.3)	2313 (73.6)	
Monthly	236 (7.5)	270 (8.6)	275 (8.7)	326 (10.4)	
Weekly	158 (5.0)	243 (7.7)	343 (10.9)	389 (12.4)	
Daily	36 (1.1)	84 (2.7)	96 (3.0)	114 (3.6)	
History of smoking					<.001
Never smoker	2796 (88.7)	2633 (83.8)	2423 (76.9)	2070 (65.9)	
Former smoker	222 (7.0)	217 (6.9)	316 (10.0)	360 (11.5)	
Current smoker	133 (4.2)	291 (9.3)	410 (13.0)	712 (22.7)	
Body mass index group					.016
Underweight [< 18.5 kg/m^2]	210 (6.7)	181 (5.8)	156 (5.0)	192 (6.1)	
Normal [18.5 to 22.9 kg/m^2]	1430 (45.4)	1403 (44.7)	1353 (43.0)	1368 (43.5)	
Overweight [23.0 to 27.4 kg/m^2]	1265 (40.1)	1286 (40.9)	1369 (43.5)	1286 (40.9)	
Obese [≥ 27.5 kg/m^2]	246 (7.8)	271 (8.6)	271 (8.6)	296 (9.4)	
Mean amount of sleep (SD) [h/d]	6.95 (1.07)	7.02 (1.03)	7.01 (1.06)	7.02 (1.08)	.039
Weekly participation in vigorous work or strenuous sports	530 (16.8)	513 (16.3)	606 (19.2)	686 (21.8)	<.001
Amount of moderate activity per week					<.001
None	2323 (73.7)	2419 (77.0)	2411 (76.6)	2462 (78.4)	
0.5 to 3 h	546 (17.3)	479 (15.2)	519 (16.5)	431 (13.7)	
≥4 h	282 (8.9)	243 (7.7)	219 (7.0)	249 (7.9)	
Mean intake of red meat (SD) [g/d]	27.43 (21.60)	29.54 (21.42)	33.10 (24.72)	35.80 (26.33)	<.001
Mean intake of poultry (SD) [g/d]	19.82 (18.31)	20.93 (18.14)	23.81 (21.14)	25.41 (21.85)	<.001
Mean intake of fish and shellfish (SD) [g/d]	54.35 (30.23)	56.09 (29.92)	59.69 (32.39)	60.62 (32.96)	<.001
Mean intake of vegetable and related juices (SD) [g/d]	119.61 (63.30)	118.07 (60.40)	126.31 (67.74)	121.71 (66.71)	<.001
Mean intake of fruit and related juices (SD) [g/d]	220.86 (164.85)	225.93 (158.62)	241.71 (174.42)	225.48 (170.53)	<.001
Mean total energy intake (SD) [kcal/d]	1477.94 (490.78)	1520.01 (493.63)	1667.48 (568.94)	1764.73 (587.70)	<.001

Continuous variables are presented as mean (SD), and categorical variables are presented as n (%).

binary logistic regression models to compute the odds ratios (OR) and 95% CIs for the associations between the consumption of the caffeine-containing beverages at midlife and physical frailty at late life. Orthogonal polynomial contrasts were used to test for the presence of linear trends. In Model 1, we adjusted for basic sociodemographic characteristics [age at physical tests; gender; dialect group (Hokkien, Cantonese); level of education (no formal education, primary, secondary, diploma/university)]. In Model 2, we additionally adjusted for history of physician-diagnosed comorbidities (hypertension, coronary artery disease, stroke, diabetes, cancer), smoking status (never smoker, former smoker, current smoker), alcohol consumption (never, monthly, weekly, daily), body mass index (<18.5, 18.5–22.9, 23.0–27.4, 27.5+ kg/m^2), hours of sleep per day (≤5, 6, 7, 8, 9+ hours)], physical activity (hours per week of strenuous sports, vigorous work, and moderate activity), and usual dietary intake [daily consumption of red meat, poultry, fish/shellfish, vegetables and related juices, and fruit and related juices (quartiles of intake as continuous variables) and total daily energy intake (kcal)] at midlife. In Model 3, we additionally adjusted for the frequency of consumption of other caffeine-containing beverages (coffee, black tea, green tea, soft drinks) as categorical variables.

In our analyses of caffeine intake and physical frailty, we further adjusted for coffee (number of cups per week) in Model 3A and for black and green tea (number of cups per month) in Model 3B to assess whether the main sources of caffeine (coffee or tea) affected the association between caffeine intake and frailty. We additionally assessed the association between caffeine intake and physical frailty after separate stratifications for age group at baseline interviews (<55, ≥55 years) and gender, and we tested for statistical significance by including a product term between caffeine and the factor (age group or gender) in the model. Finally, we evaluated the association between caffeine intake and each individual criterion of our physical frailty phenotype (weight loss, exhaustion, slowness, weakness) separately.

As sensitivity analyses, we excluded participants who met either of 2 criteria at the baseline interviews: (1) those who were 60 years and older; (2) those who had a history of hypertension, cardiovascular disease, diabetes, or cancer. All statistical analyses were conducted

Table 2
Associations Between the Consumption of Caffeine-containing Beverages at Midlife and Physical Frailty in Late Life

	Frequency of Coffee Consumption				P_{trend}
	Non-daily	1 Cup/day	2–3 Cups/day	4 + Cups/day	
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	
Cases/N	556/3960	725/4560	539/3640	47/423	
Model 1*	Ref.	1.05 (0.92–1.19)	0.97 (0.85–1.11)	0.63 (0.46–0.88)	.005
Model 2†	Ref.	1.04 (0.91–1.18)	0.93 (0.81–1.07)	0.56 (0.40–0.79)	<.001
Model 3‡	Ref.	1.01 (0.89–1.15)	0.90 (0.78–1.03)	0.54 (0.38–0.76)	<.001
	Frequency of Black Tea Consumption				P_{trend}
	Never	Monthly	Weekly	Daily	
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	
Cases/N	1236/7558	152/1090	277/2415	202/1520	
Model 1*	Ref.	0.96 (0.80–1.17)	0.79 (0.68–0.91)	0.89 (0.75–1.05)	.053
Model 2†	Ref.	0.98 (0.81–1.19)	0.80 (0.69–0.93)	0.89 (0.75–1.06)	.059
Model 3‡	Ref.	0.97 (0.79–1.18)	0.80 (0.68–0.93)	0.88 (0.73–1.04)	.044
	Frequency of Green Tea Consumption				P_{trend}
	Never	Monthly	Weekly	Daily	
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	
Cases/N	1068/6910	246/1614	331/2422	222/1637	
Model 1*	Ref.	1.05 (0.89–1.23)	0.92 (0.80–1.06)	0.84 (0.72–1.00)	.019
Model 2†	Ref.	1.04 (0.88–1.22)	0.91 (0.79–1.05)	0.82 (0.69–0.97)	.009
Model 3‡	Ref.	1.04 (0.88–1.23)	0.93 (0.80–1.08)	0.81 (0.68–0.96)	.008
	Frequency of Any Tea Consumption				P_{trend}
	Never	Monthly	Weekly	Daily	
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	
Cases/N	752/4623	262/1595	447/3367	406/2998	
Model 1*	Ref.	1.06 (0.90–1.25)	0.88 (0.77–1.00)	0.86 (0.75–0.99)	.007
Model 2†	Ref.	1.07 (0.91–1.26)	0.87 (0.76–1.00)	0.84 (0.73–0.98)	.003
Model 3‡	Ref.	1.07 (0.90–1.26)	0.87 (0.75–0.99)	0.82 (0.71–0.95)	.001

*Model 1: adjusted for age at physical tests (years), gender, dialect group (Hokkien, Cantonese), level of education (none, primary, secondary, diploma/university).
†Model 2: adjusted for Model 1 and hypertension, angina or heart attack, stroke, diabetes, cancer, alcohol consumption (none, monthly, weekly, daily), smoking history (never, former, current), body mass index (<18.5, 18.5–22.9, 23.0–27.4, 27.5+ kg/m^2), amount of sleep per day (≤5, 6, 7, 8, 9+ hours), amount of strenuous sports per week (0, 0.5–1, 2–3, 4+ hours), amount of vigorous work per week (0, 0.5–3, 4–6, 7+ hours), amount of moderate activity per week (0, 0.5–1, 2–3, 4–6, 7+ hours), red meat (quartiles), poultry (quartiles), fish and shellfish (quartiles), vegetable and related juices (quartiles), fruit and related juices (quartiles), daily energy intake (kcal).
‡Model 3: adjusted for Model 2 and frequency of soft drink consumption (almost never, 1–3 glasses/month, 1 glass/week, ≥2–3 glasses/week), plus frequency of coffee consumption (weekly or less, 1 cup/day, 2–3 cups/day, 4+ cups/day), frequency of black tea consumption (never, monthly, weekly, daily), frequency of green tea consumption (never, monthly, weekly, daily) (where applicable).

using Stata/SE 14.2 software (StataCorp LLC). All P values presented were 2-sided, and $P < .05$ was considered statistically significant.

Results

At the baseline interviews (1993–1998), the mean (SD) age of the 12,583 participants in this study was 53 (5.9) years, and their ages ranged from 45 to 74 years. At the time of the third follow-up interviews (2014–2017), after a mean (SD) follow-up time of 19.6 (1.9) years, the mean (SD) age of this same group of participants was 73 (6.1) years, and their ages ranged from 61 to 96 years.

Most of our participants (68.5%) drank coffee daily; among the daily drinkers, 52.9% of them drank 1 cup a day, 42.2% drank 2 to 3 cups per day, and 4.9% drank 4 or more cups per day. Hence, we categorized our participants into 4 groups for coffee intake: non-daily drinkers; 1 cup/day; 2 to 3 cups/day; and 4+ cups a day. In contrast, 36.7% of our participants were non-tea drinkers (less than once a month), and 39.4% reported drinking it on a monthly to weekly basis; only 23.8% drank tea daily, and among the daily drinkers, 62.4% drank 1 cup a day. Thus, for tea consumption, we categorized our participants into never, monthly, weekly, and daily drinkers instead.

Coffee and tea were the main sources of caffeine exposure in our cohort, accounting for 84% and 12% of total dietary caffeine intake, respectively. Other caffeinated food sources like soft drinks (0.7%), cocoa drinks, and other chocolate-related food items contributed to the remaining 4%. When compared with participants who had lower quartiles of daily caffeine intake at midlife, participants who had higher quartiles were more likely to be men, to drink alcohol, to smoke, and to participate in vigorous work or strenuous sports on a weekly basis (Table 1).

At the third follow-up (2014–2017), 1867 (14.8%) of the participants were classified as physically frail. Relative to their nonfrail counterparts, participants who were physically frail at the third follow-up were more likely to have been older at the point of assessment; they were also more likely to have had a history of comorbidities, to have smoked, and to have had a higher body mass index at midlife, and also less likely to have been physically active (Supplementary Table 1).

In the fully adjusted Model 3, coffee, black tea, and green tea consumption at midlife were independently associated with significantly reduced likelihood of physical frailty at late life (Table 2). Compared with participants who did not drink coffee daily, participants who drank 4 or more cups of coffee a day at midlife had a significantly reduced odds of physical frailty at late life (OR, 0.54; 95% CI, 0.38–0.76). When compared with non-drinkers, participants who drank black tea (OR, 0.88; 95% CI, 0.73–1.04), green tea (OR, 0.81; 95% CI, 0.68–0.96), or any tea (OR, 0.82; 95% CI, 0.71–0.95) daily at midlife had significantly reduced odds of physical frailty at late life.

Table 3
Associations Between Daily Caffeine Intake at Midlife and Physical Frailty in Late Life

	Quartiles of Daily Caffeine Intake				P_{trend}
	Q1	Q2	Q3	Q4	
	(0–67.6 mg/d)	(67.7–112.5 mg/d)	(112.6–222.4 mg/d)	(223.0–910.4 mg/d)	
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	
Cases/N	482/3151	508/3141	436/3149	441/3142	
Model 1*	Ref.	1.00 (0.87–1.16)	0.85 (0.73–0.98)	0.84 (0.72–0.97)	.004
Model 2†	Ref.	0.97 (0.84–1.13)	0.82 (0.70–0.96)	0.77 (0.66–0.91)	<.001
Model 3A‡	Ref.	0.97 (0.83–1.14)	0.82 (0.69–0.99)	0.78 (0.61–1.00)	.023
Model 3B§	Ref.	0.97 (0.84–1.13)	0.83 (0.71–0.97)	0.78 (0.66–0.92)	.001

*Model 1: adjusted for age at physical tests (years), gender, dialect group (Hokkien, Cantonese), level of education (none, primary, secondary, diploma/university).
†Model 2: adjusted for Model 1 and hypertension, angina or heart attack, stroke, diabetes, cancer, alcohol consumption (none, monthly, weekly, daily), smoking history (never, former, current), body mass index (<18.5, 18.5–22.9, 23.0–27.4, 27.5+ kg/m^2), amount of sleep per day (≤5, 6, 7, 8, 9+ hours), amount of strenuous sports per week (0, 0.5–1, 2–3, 4+ hours), amount of vigorous work per week (0, 0.5–3, 4–6, 7+ hours), amount of moderate activity per week (0, 0.5–1, 2–3, 4–6, 7+ hours), red meat (quartiles), poultry (quartiles), fish and shellfish (quartiles), vegetable and related juices (quartiles), fruit and related juices (quartiles), daily energy intake (kcal).
‡Model 3A: adjusted for Model 2 and frequency of coffee consumption (cups/week).
§Model 3B: adjusted for Model 2 and frequency of black tea consumption (cups/month), frequency of green tea consumption (cups/month).

After adjusting for sociodemographic characteristics, comorbidities, other lifestyle factors, and usual dietary intake (Model 2), total daily caffeine intake at midlife was associated with a reduced likelihood of frailty at late life in a dose-dependent manner ($P_{trend} < .001$) (Table 3). Compared with participants in the lowest quartile of daily caffeine intake [mean (SD) of 30.8 (21.3) mg/d; range of 0 to 67.6 mg/d], participants in the highest quartile [mean (SD) of 290.5 (83.2) mg/d; range of 223.0 to 910.4 mg/d] had significantly reduced odds of physical frailty at late life (OR, 0.77; 95% CI, 0.66–0.91). To further evaluate whether this association was different by the main source of caffeine, we further adjusted for coffee (in Model 3A) and tea (in Model 3B) separately. In both models, the associations between daily caffeine intake at midlife and physical frailty in late life remained essentially unchanged. In addition, the associations between caffeine intake and physical frailty did not significantly differ between those who were younger (<55 years) and those who were older (≥55 years) at the baseline interviews, or between men and women (Supplementary Table 2).

Finally, when we looked at the association between caffeine and the individual criteria of our physical frailty phenotype (Table 4), the results were robust and highly significant for the 2 objectively measured criteria of physical function: slowness (slow TUG time) ($P_{trend} = .003$), and weakness (weak handgrip strength) ($P_{trend} = .053$). Although the association of caffeine intake with the other 2 self-reported criteria (weight loss and exhaustion) did not reach statistical significance, higher caffeine intake was nonetheless associated with reduced risk.

As we did not assess our participants for physical frailty at the time of our baseline interviews, we could not ascertain whether they were all physically robust (free of physical frailty) at recruitment. As such, we conducted sensitivity analyses by excluding (n = 4108) participants who were more likely to have been physically frail at the baseline interviews (those 60 years and older at recruitment, or those with a baseline history of hypertension, cardiovascular disease, diabetes, or cancer). In these analyses, our findings remained unchanged (Supplementary Tables 3 and 4).

Discussion

Our study found that higher consumption of coffee, tea, and total caffeine at midlife was associated with a lower likelihood of physical frailty in late life. Specifically, higher caffeine consumption was associated with significantly lower likelihood of being in the slowest sex-specific quintile for the TUG test and the weakest sex-specific quintile for handgrip strength in the assessment of physical frailty.

Table 4
Associations Between Daily Caffeine Intake at Midlife and the Individual Physical Frailty Criteria in Late Life

	Quartiles of Daily Caffeine Intake				P_{trend}
	Q1 (0–67.6 mg/d)	Q2 (67.7–112.5 mg/d)	Q3 (112.6–222.4 mg/d)	Q4 (223.0–910.4 mg/d)	
Frailty criteria					
Slowness (TUG test time in the slowest sex-specific quintile)					
Cases/N	494/3151	515/3141	477/3149	484/3142	
OR (95% CI)*	Ref.	0.93 (0.80–1.08)	0.86 (0.74–1.00)	0.79 (0.68–0.93)	.003
Weakness (handgrip strength in the weakest sex-specific quintile)					
Cases/N	602/3151	610/3141	549/3149	597/3142	
OR (95% CI)*	Ref.	0.95 (0.84–1.09)	0.84 (0.74–0.97)	0.90 (0.79–1.04)	.053
Weight loss (lost ≥10% of self-reported body weight since the previous follow-up interview)					
Cases/N	348/3151	381/3141	354/3149	337/3142	
OR (95% CI)*	Ref.	1.07 (0.91–1.25)	0.99 (0.84–1.16)	0.90 (0.76–1.07)	.16
Exhaustion (answered “No” to the question: “Do you feel full of energy?”)					
Cases/N	576/3151	574/3141	528/3149	544/3142	
OR (95% CI)*	Ref.	0.98 (0.86–1.12)	0.91 (0.80–1.04)	0.94 (0.82–1.08)	.25

TUG, timed up-and-go.
*Model 2: adjusted for age at physical tests (years), gender, dialect group (Hokkien, Cantonese), level of education (none, primary, secondary, diploma/university), hypertension, angina or heart attack, stroke, diabetes, cancer, alcohol consumption (none, monthly, weekly, daily), smoking history (never, former, current), body mass index (<18.5, 18.5–22.9, 23.0–27.4, 27.5+ kg/m^2), amount of sleep per day (≤5, 6, 7, 8, 9+ hours), amount of strenuous sports per week (0, 0.5–1, 2–3, 4+ hours), amount of vigorous work per week (0, 0.5–3, 4–6, 7+ hours), amount of moderate activity per week (0, 0.5–1, 2–3, 4–6, 7+ hours), red meat (quartiles), poultry (quartiles), fish and shellfish (quartiles), vegetable and related juices (quartiles), fruit and related juices (quartiles), daily energy intake (kcal).

To our best knowledge, ours is the first longitudinal study to show a statistically significant association between coffee consumption and reduced likelihood of physical frailty.[20] Another longitudinal study was conducted among 3289 participants aged 60 years and older in the Seniors-ENRICA cohort from Spain. Although the authors did not find a significant association between coffee consumption and risk of physical frailty, they did report that participants who drank 2 or more cups of coffee a day had lower risk of impaired mobility compared with non-drinkers.[27] Our finding on the reduced risk of physical frailty with tea consumption concurred with 2 studies from the Chinese Longitudinal Healthy Longevity Survey, which both reported that, compared with non-tea drinkers, participants who consistently drank tea on a daily basis had significantly lower risks of having physical frailty.[33,34]

A cross-sectional study in the United States found that although the consumption of caffeinated coffee was associated with reduced frailty, the consumption of decaffeinated coffee did not have the same association[22]; this concurred with our finding that higher caffeine intake was associated with reduced risk of physical frailty. In addition, coffee and tea also contain a range of bioactive polyphenols that possess antioxidant and anti-inflammatory properties.[10-12] Studies have found that the consumption of both caffeine and polyphenols may be associated with lower risks of comorbidities that could predispose one to physical frailty in aging, such as certain cancers, cardiovascular diseases, type 2 diabetes, obesity, and neurodegenerative diseases[12,13]; this could explain the beneficial effects of caffeine, coffee, and tea on reducing the risk of physical frailty in our study.

Among the 4 criteria of physical frailty in our study, higher consumption of coffee, tea, and caffeine was significantly associated with better physical function: stronger handgrip strength and faster TUG time. Interestingly, in aged mice, coffee administration resulted in reduced progression of sarcopenia and increased skeletal muscle weight, and these effects were attributed to improved proliferation rate and DNA synthesis in the satellite cells of the muscle and maintenance of muscle integrity in an in vitro study.[14] Therefore, it is plausible that coffee could reduce the risk of physical frailty and improve physical function by improving muscle integrity and slowing the development of sarcopenia in aging.[27]

The strengths of our study included its prospective design, long follow-up period, and wide variation in coffee and tea intake. Although the validation for the intake of selected food and nutrient items in our food-frequency questionnaire did not include that of coffee, tea, and caffeine, we have previously published the associations between coffee/tea/caffeine and the risk of other disease outcomes in this cohort, including diabetes,[35] liver cancer[36] and cirrhosis mortality,[37] hypertension,[38] end-stage kidney disease,[39] and skin cancer.[40] This substantiates that the estimation for the intake of coffee/tea/caffeine in our cohort is robust. Another limitation was that we only used data on usual dietary intake at the baseline interviews (1993–1998). However, we repeated questions on coffee and tea consumption among a subset of 39,258 participants during the second follow-up interviews (2006–2010) conducted approximately 12 years after the baseline and found that the vast majority had retained their status as daily or non-daily drinkers of coffee (72.3%), black tea (85.6%), and green tea (85.2%).

A further limitation of our study was that we could not exclude participants who were already physically frail at baseline, because we did not conduct the relevant assessment. Nonetheless, in our sensitivity analyses that excluded 4108 (32.6%) of the participants who were more likely to have been physically frail at the baseline, our findings remained unchanged. Also, our modified 4-item version of the CHS frailty phenotype may have misclassified pre-frail subjects as frail[31], and this could have led to an underestimation in the associations of the exposures with the outcome. Finally, selection bias was possible because our study only involved a proportion of those recruited at the baseline interviews. As shown in previous analyses, participants who did not participate in the third follow-up interviews were generally older and more likely to have comorbidities and unhealthy lifestyles at recruitment,[41] and hence were likely to be at a higher risk for physical frailty. However, when we compared the caffeine intake at baseline between the 12,583 participants in this study and the 50,674 who were not included, after adjusting for age, gender, smoking, and physical activity, the intake levels were comparable (102.2 mg/d versus 103.9 mg/d; $P = .11$). Hence, the likelihood of selection bias was not high because study inclusion was related to the outcome but not to the exposure.

Conclusions and Implications

Our study showed that the consumption of coffee, tea, and caffeine at midlife may be associated with a reduced likelihood of physical frailty in late life. Coffee and tea have been cultivated and consumed for centuries, and they remain popular and widely available today. Therefore, interventions that encourage the consumption of these beverages alongside other dietary and lifestyle modifications may prove to be feasible and effective in reducing the risk of physical frailty in older adults. However, further studies are still needed to confirm these longitudinal associations, and to investigate if these effects on physical frailty are mediated by polyphenols or other chemical compounds.

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Supplementary Table 1
Midlife Characteristics of the Participants, by Status of Physical Frailty at Late Life

	Frail	Nonfrail	*P* Value
	n = 1867	n = 10,716	
Mean physical frailty score (SD) [0 to 4]	2.29 (0.51)	0.35 (0.48)	<.001
Weight loss	738 (39.5)	682 (6.4)	<.001
Exhaustion	937 (50.2)	1285 (12.0)	<.001
Slowness	1265 (67.8)	705 (6.6)	<.001
Weakness	1331 (71.3)	1027 (9.6)	<.001
Mean age at assessment of frailty (SD) [y]	76.92 (6.52)	71.75 (5.65)	<.001
Gender			.9
Men	772 (41.3)	4448 (41.5)	
Women	1095 (58.7)	6268 (58.5)	
Dialect group			.46
Hokkien	955 (51.2)	5382 (50.2)	
Cantonese	912 (48.8)	5334 (49.8)	
Level of education			<.001
No formal education	453 (24.3)	1534 (14.3)	
Primary school	916 (49.1)	4598 (42.9)	
Secondary school	407 (21.8)	3618 (33.8)	
Diploma/University	91 (4.9)	966 (9.0)	
Hypertension	509 (27.3)	1852 (17.3)	<.001
Cardiovascular disease	91 (4.9)	197 (1.8)	<.001
Diabetes	172 (9.2)	401 (3.7)	<.001
Cancer	50 (2.7)	172 (1.6)	.001
Frequency of alcohol consumption			.024
Never	1533 (82.1)	8480 (79.1)	
Monthly	137 (7.3)	970 (9.1)	
Weekly	150 (8.0)	983 (9.2)	
Daily	47 (2.5)	283 (2.6)	
History of smoking			<.001
Never smoker	1383 (74.1)	8539 (79.7)	
Former smoker	196 (10.5)	919 (8.6)	
Current smoker	288 (15.4)	1258 (11.7)	
Body mass index group			<.001
Underweight [< 18.5 kg/m^2]	110 (5.9)	629 (5.9)	
Normal [18.5 to 22.9 kg/m^2]	726 (38.9)	4828 (45.1)	
Overweight [23.0 to 27.4 kg/m^2]	826 (44.2)	4380 (40.9)	
Obese [≥ 27.5 kg/m^2]	205 (11.0)	879 (8.2)	
Mean amount of sleep (SD) [h/d]	6.98 (1.14)	7.01 (1.04)	.27
Weekly participation in vigorous work or strenuous sports	215 (11.5)	2120 (19.8)	<.001
Amount of moderate activity per week			<.001
None	1431 (76.6%)	8184 (76.4%)	
0.5 to 3 h	256 (13.7%)	1719 (16.0%)	
≥ 4 h	180 (9.6%)	813 (7.6%)	
Mean intake of red meat (SD) [g/d]	30.68 (24.81)	31.60 (23.65)	.12
Mean intake of poultry (SD) [g/d]	21.03 (19.25)	22.75 (20.17)	<.001
Mean intake of fish and shellfish (SD) [g/d]	55.83 (31.29)	58.01 (31.53)	.006
Mean intake of vegetable and related juices (SD) [g/d]	111.96 (58.28)	123.08 (65.58)	<.001
Mean intake of fruit and related juices (SD) [g/d]	206.05 (156.39)	232.41 (168.92)	<.001
Mean total energy intake (SD) [kcal/d]	1558.28 (551.86)	1616.06 (548.19)	<.001

Continuous variables are presented as mean (SD), and categorical variables are presented as n (%).

Supplementary Table 2
Associations Between Daily Caffeine Intake at Midlife and Physical Frailty in Late Life, Stratified by Age Group at Baseline Interviews and Gender Separately

	Quartiles of Daily Caffeine Intake				P_{trend}	$P_{interaction}$
	Q1 (0–67.6 mg/d)	Q2 (67.7–112.5 mg/d)	Q3 (112.6–222.4 mg/d)	Q4 (223.0–910.4 mg/d)		
Stratified by age group at baseline interviews						
<55 years						.55
Cases/N	181/2136	209/2089	167/2115	171/2097		
OR (95% CI)*	Ref.	1.07 (0.86–1.33)	0.83 (0.66–1.05)	0.80 (0.64–1.02)	.017	
≥55 years						
Cases/N	301/1015	299/1052	269/1034	270/1045		
OR (95% CI)*	Ref.	0.89 (0.73–1.09)	0.80 (0.65–0.99)	0.75 (0.61–0.93)	.006	
Stratified by gender						
Men						.80
Cases/N	140/946	179/1054	204/1472	249/1748		
OR (95% CI)*	Ref.	1.11 (0.85–1.44)	0.91 (0.70–1.17)	0.83 (0.65–1.07)	.065	
Women						
Cases/N	342/2205	329/2087	232/1677	192/1394		
OR (95% CI)*	Ref.	0.93 (0.78–1.11)	0.79 (0.65–0.96)	0.75 (0.61–0.93)	.003	

*Model 2: adjusted for age at physical tests (years), gender (where applicable), dialect group (Hokkien, Cantonese), level of education (none, primary, secondary, diploma/university), hypertension, angina or heart attack, stroke, diabetes, cancer, alcohol consumption (none, monthly, weekly, daily), smoking history (never, former, current), body mass index (<18.5, 18.5–22.9, 23.0–27.4, 27.5+ kg/m^2), amount of sleep per day (≤5, 6, 7, 8, 9+ hours), amount of strenuous sports per week (0, 0.5–1, 2–3, 4+ hours), amount of vigorous work per week (0, 0.5–3, 4–6, 7+ hours), amount of moderate activity per week (0, 0.5–1, 2–3, 4–6, 7+ hours), red meat (quartiles), poultry (quartiles), fish and shellfish (quartiles), vegetable and related juices (quartiles), fruit and related juices (quartiles), daily energy intake (kcal).

Supplementary Table 3
Associations Between the Consumption of Caffeine-containing Beverages at Midlife and Physical Frailty in Late Life, Among Participants Who Were <60 Years Old and Free From Hypertension, Cardiovascular Disease, Diabetes, and Cancer at the Baseline Interviews

	Frequency of Coffee Consumption				P_{trend}
	Non-daily	1 Cup/day	2–3 Cups/day	4 + Cups/day	
Cases/N	236/2655	315/2974	250/2547	20/299	
OR (95% CI)*	Ref.	1.05 (0.87–1.26)	0.84 (0.69–1.02)	0.45 (0.27–0.73)	.001
	Frequency of Black Tea Consumption				P_{trend}
	Never	Monthly	Weekly	Daily	
Cases/N	532/5014	78/787	138/1652	73/1022	
OR (95% CI)*	Ref.	1.03 (0.79–1.34)	0.88 (0.72–1.08)	0.68 (0.52–0.89)	.003
	Frequency of Green Tea Consumption				P_{trend}
	Never	Monthly	Weekly	Daily	
Cases/N	488/4751	113/1113	138/1590	82/1021	
OR (95% CI)*	Ref.	1.03 (0.82–1.30)	0.93 (0.75–1.15)	0.77 (0.60–0.99)	0.033
	Frequency of Any Tea Consumption				P_{trend}
	Never	Monthly	Weekly	Daily	
Cases/N	346/3148	123/1110	197/2279	155/1938	
OR (95% CI)*	Ref.	1.05 (0.83–1.31)	0.85 (0.70–1.03)	0.72 (0.58–0.89)	0.001

*Model 3: adjusted for age at physical tests (years), gender, dialect group (Hokkien, Cantonese), level of education (none, primary, secondary, diploma/university), alcohol consumption (none, monthly, weekly, daily), smoking history (never, former, current), body mass index (<18.5, 18.5–22.9, 23.0–27.4, 27.5+ kg/m^2), amount of sleep per day (≤5, 6, 7, 8, 9+ hours), amount of strenuous sports per week (0, 0.5–1, 2–3, 4+ hours), amount of vigorous work per week (0, 0.5–3, 4–6, 7+ hours), amount of moderate activity per week (0, 0.5–1, 2–3, 4–6, 7+ hours), red meat (quartiles), poultry (quartiles), fish and shellfish (quartiles), vegetable and related juices (quartiles), fruit and related juices (quartiles), daily energy intake (kcal), frequency of soft drink consumption (almost never, 1–3 glasses/month, 1 glass/week, ≥2–3 glasses/week), plus frequency of coffee consumption (weekly or less, 1 cup/day, 2–3 cups/day, 4+ cups/day), frequency of black tea consumption (never, monthly, weekly, daily), frequency of green tea consumption (never, monthly, weekly, daily) (where applicable).

Supplementary Table 4
Associations Between Daily Caffeine Intake at Midlife and Physical Frailty in Late Life, Among Participants Who Were <60 Years Old and Free From Hypertension, Cardiovascular Disease, Diabetes, and Cancer at the Baseline Interviews

	Quartiles of Daily Caffeine Intake				P_{trend}
	Q1 (0–67.6 mg/d)	Q2 (67.7–112.5 mg/d)	Q3 (112.6–222.4 mg/d)	Q4 (223.0–910.4 mg/d)	
Cases/N	211/2142	213/2028	202/2127	195/2178	
OR (95% CI)*	Ref.	0.98 (0.79–1.20)	0.85 (0.69–1.05)	0.71 (0.57–0.88)	.001

*Model 2: adjusted for age at physical tests (years), gender, dialect group (Hokkien, Cantonese), level of education (none, primary, secondary, diploma/university), alcohol consumption (none, monthly, weekly, daily), smoking history (never, former, current), body mass index (<18.5, 18.5–22.9, 23.0–27.4, 27.5+ kg/m^2), amount of sleep per day (≤5, 6, 7, 8, 9+ hours), amount of strenuous sports per week (0, 0.5–1, 2–3, 4+ hours), amount of vigorous work per week (0, 0.5–3, 4–6, 7+ hours), amount of moderate activity per week (0, 0.5–1, 2–3, 4–6, 7+ hours), red meat (quartiles), poultry (quartiles), fish and shellfish (quartiles), vegetable and related juices (quartiles), fruit and related juices (quartiles), daily energy intake (kcal).