## RESEARCH





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## Abstract

**Background** Previous observational studies have suggested diabetic patients should synchronize their foods and nutrient intake with their biological rhythm; however, the optimal intake time of coffee and tea for reducing all-cause and disease-specific mortality in diabetes is still unknown. This study aims to examine by investigating the association of timing for coffee and tea consumption with long-term survival in people with diabetes.

**Methods** A total of 5378 people with diabetes who enrolled in the National Health and Nutrition Examination Survey from 2003 to 2014 were recruited for this study. Coffee and tea intakes were measured by a 24-h dietary recall, which were divided by different time intervals across the day, including dawn to forenoon, forenoon to noon, noon to evening, and evening to dawn. Weighted cox proportional hazards regression models were developed to evaluate the survival-relationship of coffee and tea consumption with mortality of all-cause, cardiovascular disease (CVD), stroke, and diabetes.

**Results** During 47,361 person-year follow up, total 1639 death cases were documented, including 731 CVD deaths, 467 heart disease deaths, 99 stroke deaths, and 462 diabetes deaths. After adjustment for potential confounders, compared with participants without drinking coffee during dawn to forenoon, drinking coffee at this period was associated with increased mortality risk of all-cause (HR 1.25, 95% CI 1.05–1.50), CVD (HR 1.41, 95% CI 1.07–1.86), heart-disease (HR 1.47, 95% CI 1.05–2.07), and diabetes (HR 1.50, 95% CI 1.10–2.04). In contrast, drinking coffee during forenoon to noon had lower mortality risk of all-cause (HR 0.80, 95% CI 0.69–0.92), CVD (HR 0.79, 95% CI 0.63–0.99), and heart disease (HR 0.70, 95% CI 0.52–0.94). Similarly, drinking tea during forenoon to noon had lower risk of CVD mortality (HR = 0.62, 95% CI 0.44–0.87).

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**Conclusions** This study suggests that drinking coffee in dawn to forenoon is linked to a higher risk of death, but having coffee and tea from forenoon to noon is linked to a lower risk of overall mortality, CVD, and heart disease in individuals with diabetes.

Keywords Timing intake, Coffee, Tea, Diabetes, CVD, Mortality

## **Graphical Abstract**



Background

Diabetes mellitus poses a significant threat to global public health and is projected to affect up to 700 million individuals by 2045 [1]. As a crucial and cost-effective approach, dietary intervention plays a pivotal role in enhancing the long-term survival of people with diabetes [2-4]. Diabetic patients often experience a disrupted biological rhythm of glucose [5, 6], and rectifying this disruption is a promising target for improving blood glucose control [6, 7]. Because timing for dietary intake serves as an important zeitgeber that entrains biological rhythm [8], accumulating studies have suggested diabetic patients should synchronize their foods and nutrients intake with their biological rhythm of glucose homeostasis; otherwise, it may lead to poor blood glucose control [9–11]. Therefore, timing of consuming foods containing compounds capable of regulating biological clock is particularly important for diabetic patients.

Coffee and tea, two of the most commonly consumed beverages, have become part of people's dietary patterns. Although many studies have documented their beneficial health impacts in general population, their impacts on the health of diabetic patients has been a subject of controversy. Some studies suggest benefits [12, 13], while others find no impact [14] or even potential harm [15, 16]. In fact, there are abundant bioactive substances in coffee and tea, such as caffeine, catechin, chlorogenic acid, theobromine, lysine, and etc., and several animal studies indicated that these substances can entrain biological rhythm by regulating various circadian clock genes associated with blood glucose homeostasis [17, 18]. Therefore, compared with daily coffee and tea consumption, consumption timing may be a more important aspect in terms of long-term survival among diabetic patients. However, few studies have examined whether and how coffee and tea consumption timing influences the natural course of diabetes.

In this study, we hypothesized aligning the timing for coffee and tea consumption with biological clocks can lead to improved long-term survival of diabetic patients, while misalignment may have the opposite effect. To examine this hypothesis, this study investigated the association of coffee and tea consumption with all-cause and disease-specific mortality by different time periods among diabetic patients in a nationally representative sample of U.S. adults.

## Methods

## **Study population**

The National Health and Nutrition Examination Survey (NHANES) is a research program designed to assess the health and nutritional status of population in the USA. Data sources include individual structured interviews, telephone follow-up, health screening at mobile screening centers, and laboratory sample analysis [19]. It used a multistage stratified sampling approach that was

representative of broader U.S. population, and institutional review board approval and written informed consent from the National Center for Health Statistics were obtained before data collection.

This study recruited adults (age  $\geq$  18 years) with diabetes in NHANES (2003–2014). Diabetes was defined by a self-reported diagnosis, medication for hyperglycemia, hemoglobin Alc (HbA1c)  $\geq$  6.5%, or fasting blood glucose  $\geq$  7.0 mmol/L, or random blood glucose/2-h OGTT blood glucose  $\geq$  11.1 mmol/L. After excluding participants with missing data on follow-up time (n=98), education level (n=11), marital status (n=29), population weight (n=156), hyperlipidemia (n=1), and BMI (n=158), 5378 diabetic participants ( $n_{men}$ =2724,  $n_{women}$ =2654) were included (Additional file 1: Table S1).

## **Exposure assessment**

Individual food items were gathered through 24-h dietary recall interviews [20]. After initial 24-h dietary recall, second-recall conducted via telephone was conducted between 3 and 10 days later. In-person interview took place in a private room at NHANES mobile examination center, using computer-assisted dietary interview system administered by NHANES interviewer. Considering that the sample size for in the second dietary interview was relatively small, we therefore only used the data on coffee and tea intake, we utilized U.S. Department of Agriculture's Food and Nutrient Database for Dietary Studies (Agricultural Research Service, 2023) [21]. Detailed information regarding the timing of coffee and tea intake was recorded.

The timing of coffee and tea consumption was considered based on several key physiological factors. Both beverages are closely linked to cortisol production. The caffeine in coffee and tea inhibits adenosine receptors [22, 23], leading to activation of the hypothalamic-pituitaryadrenal axis and increased cortisol secretion [24, 25]. Tea also contains theanine, which has a calming effect on the central nervous system, potentially counteracting caffeine's stimulation of cortisol release [23]. Cortisol is a hormone that heightens alertness and wakefulness [26]. A population-based study that measured plasma corticosteroid levels every 30 min over a 24-h period found that cortisol levels peak within 1 to 2 h after waking, typically between 4:00 a.m. and 8:00 a.m. [27]. After this peak, cortisol gradually declines, reaching its lowest levels before bedtime [28]. The study further observed that post-8:00 a.m. cortisol concentrations are generally 75% lower than pre-8:00 a.m. levels [27], we therefore selected 8:00 a.m. as a cut-off point.

Noon was chosen as another cut-off point because it is the time of day when light exposure is strongest, melatonin levels are at their lowest, and the body is in a state of heightened alertness. Following noon, melatonin levels begin to rise gradually [29]. Six o'clock p.m. was selected as the final cut-off time for daytime consumption, as this is typically when dinner ends and the body starts preparing for rest. Given caffeine's 3–6-h half-life [30], consuming tea or coffee after 6:00 p.m. could affect sleep quality. Additionally, 5:00 a.m. was chosen as a starting cut-off, as it is a common natural wake-up time when melatonin levels decrease in response to increasing daylight.

Therefore, coffee and tea consumption was categorized into the following periods: 5:00 a.m. to 8:00 a.m., 8:00 a.m. to 12:00 p.m., and 12:00 p.m. to 6:00 p.m. Due to the lower number of consumers between 6:00 p.m. and 5:00 a.m., this period was combined into a single category.

## **Outcome assessment**

The outcomes were mortality of all-cause, cardiovascular disease (CVD), heart disease, stroke, and diabetes, which were determined by National Death Index (NDI) by 31 December 2019. NDI is a highly reliable and widely used resource for death identification. ICD-10 was used to determine disease-specific death. CVD death was defined as I00-I09, I11, I13, I20-I51, or I60-I69, heart disease death was defined as I60-I64, I69, and diabetes death was defined as E10-E14.

## **Covariate assessment**

The following covariates were included age (years), sex (men/women), race (mexican american, other hispanic, non-hispanic white, non-hispanic black or other raceincluding multi-racial), marital status (married/unmarried/divorced), education (less than high school/high school or equivalent/college/above), annual povertyincome ratio (ratio of household income to the poverty line), energy intake (kcal), night-shift work (no/yes), smoking status (current/previous/none), drinking status (current/previous/none), regular exercise habitus (yes/no), body mass index (BMI, kg/m<sup>2</sup>), frequency of coffee/tea intake across the day (no/yes), caffeine (mg), homeostasis model assessment of insulin resistance (HOMA-IR), hyperlipidemia (defined as the presence of one or more of the following serum measures: total cholesterol > 200 mg/dL, triglycerides > 200, high-density lipoprotein (HDL) < 40 mg/dL, low-density lipoproteins (LDL) > 130 mg/dL or current use of cholesterol lowering medications), hypertension (systolic blood pressure (SBP) was greater than or equal to 140 mmHg or diastolic blood pressure (DBP) was greater than or equal to 90 mmHg, or they were currently taking medication to lower high blood pressure), chronic kidney disease (CKD, defined as estimated glomerular filtration rate (eGFR) < 60 ml/

min/1.73 m<sup>2</sup> and/or urinary albumin/creatinine ratio (ACR) > 30 mg/g, medication for diabetes (yes/no), and diabetes duration (years). Moreover, to capture more variation in blood pressure, HDL, and triglycerides among the normotensive and normolipidemic participants, and to strengthen our results, we also included them as continuous variables in the Cox proportional hazards (CPH) regression models. We conducted a collinearity test for the CPH model and calculated the Generalized Variance Inflation Factor (GVIF) to assess collinearity in regression models with factor variables.

## Statistical analysis

All analyses were incorporated sample weights, stratification, and clustering to account for the complex survey design according to NHANES analytic guidelines. According to coffee and tea intake time, baseline characteristics of sociodemographic information, life behaviors, and disease status are expressed as weighted mean ± SD (standard deviation) or weighted percentage (95% confidence interval, 95% CI). General linear models and chisquare tests were used to compare differences.

To evaluate relationship of coffee and tea intake across the day with mortality outcomes, two sets of weighted CPH regression models were developed, and survival time was months between NHANES interview date and death or census date (31 December 2019). In first set, participants were categorized based on coffee and tea intake status, with those who did not drink coffee or tea as the reference groups. In the second set, participants were grouped into tertiles according to amount of coffee and tea intake, and those in the lowest tertile were considered the reference groups.

Similarly, CPH models were applied to each time period group: dawn to forenoon, forenoon to noon, noon to evening, and evening to dawn. For each period, participants who did not drink coffee or tea during that specific time frame were designated as the reference group in set 1. In set 2, reference group comprised participants in the lowest tertile of coffee or tea intake during the respective period. And a series of confounding factors were controlled, including age, sex, race, marital status, education level, smoking status, drinking status, regular exercise, BMI, poverty income ratio, energy intake, SBP, DBP, HDL, triglycerides, prevalent of CKD, hyperlipidemia and hypertension, frequency of coffee/tea intake across the day, medication for diabetes, diabetes duration, and night-shift work. The adjusted GVIF values were all below 5, indicating minimal collinearity concerns (Additional file 1: Table S2). All statistical analyses were performed using R 4.3.1, and *p*-values less than 0.05 were considered statistically significant.

## Sensitivity analysis

Seven sensitivity analyses were performed in this study. The first sensitivity analysis assessed whether our results have sex-specific differences. The second sensitivity analysis excluded participants with a follow-up period less than 2 years to evaluate whether reverse causation would influence results (n = 5155). Thirdly, because we independently assess the association of coffee and tea intake with mortalities by different time periods, some participants who drank coffee or tea multiple times a day were repeated analysis. Therefore, we excluded these participants to evaluate whether this situation would influence our results ( $n_{\text{coffee}} = 4627$ ,  $n_{\text{tea}} = 4988$ ). Fourthly, to evaluate whether our observations have diabetes-specific effects, we also repeated the main analyses among normal participants (n = 27,202). Fifth, given the significant role of caffeine in the health effects of coffee and tea, we additionally adjusted for caffeine as a variable. Sixth, we further adjusted for insulin-related data (HOMA-IR) to assess its impact on our results. Finally, in the original analysis, we defined the participants who lacked coffee or tea data as non-consumer. Therefore the last sensitivity analysis excluded participants who lacked data on coffee and tea consumption ( $n_{\text{coffee}} = 3,886, n_{\text{tea}} = 1842$ ) to evaluate whether missing information would influence the results of original analysis.

## Results

## Baseline characteristics of studying population

During 47,361 person-year follow-up, total 1639 death cases were documented, including 731 CVD deaths, 467 heart disease deaths, 99 stroke deaths, and 462 diabetes deaths. Baseline characteristics in terms of coffee intake across the day are presented in Table 1. And 39.4% of participants did not drink coffee, 19.6% drank coffee during dawn to forenoon, 26.5% drank during forenoon to noon, 7.6% drank during noon to evening, and 6.9% drank during evening to dawn. Compared to participants who did not drink coffee throughout the day, those who drank coffee from dawn to forenoon were more likely to be older, have irregular exercise habits, elevated systolic blood pressure, and higher rates of smoking and alcohol consumption (P < 0.05). Meanwhile, participants who drank coffee from noon to evening tended to be older, have higher educational levels, lower energy intake, and a higher prevalence of hypertension (P < 0.05).

Moreover, baseline characteristics in terms of tea intake across the day are presented in Table 2. And 66.1% of participants did not drink tea across the day, 2.8% drank tea during dawn to forenoon, 7.0% drank during forenoon to noon, 12.9% drank during noon to evening, and 11.3% drank during evening to

Table 1	Baseline characteristics of	participants distributed according	to coffee drinking time period

Characteristics	Total	Not drink coffee	Dawn to forenoon coffee intake	Forenoon to noon coffee intake	Noon to evening coffee intake	Evening to dawn coffee intake	P-value
	N=6352	N=2466 (39.41%)	N = 1,128 (19.56%)	N=1757 (26.53%)	N=527 (7.62%)	N=474 (6.88%)	
Age, years	60.04±0.30	56.04±0.36	62.33±0.52	62.48±0.48	65.62±0.91	60.81±0.72	< 0.001
Women, %	49.46(45.99,52.93)	51.66(49.25,54.07)	42.06(38.47,45.64)	52.46(49.22,55.70)	50.80(44.85,56.75)	44.80(38.78,50.81)	< 0.001
Race, %							< 0.001
Mexican American	9.00( 7.14,10.87)	9.02(7.05,10.99)	8.26(5.92,10.61)	9.60(7.11,12.09)	5.96(3.42, 8.49)	12.07(8.72,15.42)	
Other Hispanic	5.71( 4.46, 6.95)	5.06(3.58, 6.54)	4.14(2.99, 5.28)	6.09(4.50, 7.68)	8.66(5.59,11.74)	9.10(5.39,12.80)	
Non-Hispanic White	64.16(56.95,71.38)	56.28(52.39,60.18)	74.92(71.24,78.59)	67.26(63.18,71.35)	67.25(60.70,73.79)	63.37(56.74,70.00)	
Non-Hispanic Black	13.93(12.29,15.57)	20.64(17.66,23.63)	7.86( 6.29, 9.42)	11.47( 9.49,13.44)	8.67( 5.67,11.68)	8.02( 5.23,10.80)	
Other Race— Including Multi- Racial	7.20( 5.97, 8.43)	8.99(7.07,10.91)	4.83(3.02, 6.63)	5.58(4.14, 7.02)	9.46(5.75,13.17)	7.44(3.75,11.13)	
College graduate or above, %	18.44(16.20,20.69)	18.61(16.08,21.14)	18.49(14.68,22.29)	17.94(14.55,21.34)	19.99(14.32,25.67)	17.56(12.00,23.13)	0.820
Current smok- ing, %	34.86(31.57,38.15)	26.15(23.46,28.84)	44.12(39.92,48.33)	38.29(35.27,41.31)	43.01(36.40,49.62)	36.13(30.69,41.58)	< 0.001
Current drink- ing, %	26.50(23.60,29.39)	23.19(20.79,25.59)	28.85(25.48,32.23)	27.23(24.46,30.00)	30.67(25.12,36.22)	31.28(25.90,36.65)	< 0.001
Exercised regu- larly, %	16.67(15.17,18.18)	18.47(16.34,20.60)	14.60(12.05,17.16)	15.14(13.05,17.24)	18.06(13.18,22.94)	16.62(11.49,21.74)	0.120
BMI, kg/m <sup>2</sup>	32.54±0.16	33.46±0.22	32.23±0.35	31.81±0.22	31.40±0.44	32.22±0.43	< 0.001
Poverty income ratio	$2.72 \pm 0.04$	$2.65 \pm 0.05$	$2.89 \pm 0.06$	2.75±0.07	2.53±0.12	2.70±0.13	0.010
Energy intake(kcal), %	1958.34±20.12	1990.67±28.42	2004.43±41.47	1913.88±29.85	1795.79±40.37	2017.98±59.02	< 0.001
Hypertension, %	69.58(64.88,74.29)	67.39(64.98,69.79)	71.53(67.18,75.88)	73.50(70.77,76.24)	68.74(62.67,74.81)	62.47(55.69,69.24)	0.010
Hyperlipidemia, %	87.70(81.70,93.71)	85.69(84.02,87.35)	87.55(85.31,89.78)	90.29(88.36,92.22)	91.83(88.85,94.80)	85.17(80.75,89.59)	0.002
CKD, %	35.87(33.03,38.70)	34.50(32.46,36.55)	33.56(30.47,36.64)	38.44(35.43,41.45)	42.03(35.74,48.31)	33.52(27.66,39.38)	0.120
Systolic blood pressure, mmHg	131.06±0.48	130.14±0.60	131.35±0.97	132.18±0.77	133.81±1.23	128.14±1.10	0.003
Diastolic blood pressure, mmHg	69.34±0.37	71.12±0.52	68.44±0.62	$68.25 \pm 0.49$	66.88±1.24	68.90±0.82	< 0.001
HDL, mg/dl	$48.06 \pm 0.35$	$47.11 \pm 0.52$	$48.00 \pm 0.63$	$49.19 \pm 0.62$	$48.71 \pm 0.95$	$48.62 \pm 0.83$	0.120
Triglycerides, mg/dl	197.48±4.28	206.15±6.19	193.54±6.79	198.24±8.85	174.36±7.39	181.84±11.45	0.020
Medication for diabetes, %	52.64(48.51,56.78)	50.72(47.74,53.71)	51.93(47.65,56.21)	55.01(51.18,58.84)	49.77(42.69,56.86)	59.74(53.48,66.01)	0.020
Diabetes dura- tion, (years)	11.28±0.27	11.81±0.45	10.74±0.39	11.09±0.74	12.33±0.87	11.24±0.57	0.340
caffeine, mg	199.80±7.04	77.08±4.38	284.85±12.04	238.38±7.67	287.12±22.70	322.60±23.74	< 0.001
HOMA-IR	7.37±0.25	8.29±0.40	6.62±0.45	$7.35 \pm 0.40$	$5.96 \pm 0.40$	$5.83 \pm 0.66$	< 0.001
Shift work, %	3.37( 2.61, 4.13)	3.94(2.91,4.96)	2.31(1.13,3.49)	2.77(1.65,3.89)	3.48(0.83,6.13)	5.36(1.74,8.97)	0.012

Continuous variables are presented as mean ± Standard deviation. Categorical variables are presented as percentage (%, 95% CI)

BMI Body mass index, DM Diabetes mellitus, CKD Chronic kidney disease, HOMA-IR Homeostasis model assessment of insulin resistance

dawn. Compared to participants who did not drink tea throughout the day, those who drank tea from forenoon to noon were more likely to be older, Non-Hispanic White individuals, have lower BMI, and have a higher poverty income ratio (P < 0.05).

## Association of coffee and tea intake with all-cause and disease-specific mortality

Association of coffee and tea consumption with allcause and disease-specific mortality is presented in Fig. 1. As indicated by weighted HRs and 95% CI, after

Characteristics	Total	Not drink tea	Dawn to forenoon tea intake	Forenoon to noon tea intake	Noon to evening tea intake	Evening to dawn tea intake	P-value
	N=5915	N=4073 (66.10%)	N = 147 (2.79%)	N=394 (6.95%)	N=719 (12.87%)	N=582 (11.29%)	
Age, years	59.34±0.28	59.01±0.32	60.74±1.34	60.75±0.68	60.72±0.74	58.50±0.69	0.028
Women, %	50.86(46.90,54.81)	49.78(47.42,52.13)	57.96(47.84,68.09)	58.30(52.10,64.50)	53.05(47.32,58.78)	48.33(41.50,55.16)	0.118
Race, %							< 0.001
Mexican American	8.57( 6.78,10.37)	9.74(7.68,11.80)	3.39(0.89, 5.90)	6.27(3.61, 8.93)	6.14(3.63, 8.65)	7.19(4.33,10.04)	
Other Hispanic	5.28( 4.14, 6.42)	5.81( 4.41,7.21)	2.60(-0.38,5.57)	3.90( 1.68,6.11)	4.53( 1.77,7.28)	4.54(2.76,6.32)	
Non-Hispanic White	63.71(56.33,71.09)	61.87(57.96,65.78)	68.64(59.28,78.00)	63.82(57.75,69.89)	68.65(63.30,74.00)	67.58(62.30,72.86)	
Non-Hispanic Black	14.94(13.20,16.69)	15.81(13.56,18.06)	10.27( 4.86,15.69)	14.25(10.38,18.12)	14.12(10.94,17.31)	12.36(8.85,15.86)	
Other Race— Including Multi- Racial	7.50( 6.23, 8.77)	6.77(5.49, 8.05)	15.10(8.05,22.14)	11.77(7.42,16.12)	6.56(4.14, 8.98)	8.34(4.75,11.92)	
College graduate or above, %	18.16(16.09,20.23)	16.93(15.07,18.80)	22.25(12.63,31.87)	18.76(12.72,24.80)	20.34(15.75,24.93)	21.50(16.28,26.71)	0.065
Current smok- ing, %	32.84(29.83,35.86)	34.04(32.09,35.99)	26.92(16.83,37.01)	30.46(24.11,36.80)	33.75(28.53,38.97)	27.75(22.38,33.13)	0.023
Current drink- ing, %	25.93(23.16,28.69)	25.80(23.65,27.96)	23.13(13.70,32.56)	30.43(23.59,37.27)	24.02(19.28,28.76)	26.73(20.81,32.65)	0.125
Exercised regu- larly, %	16.83(15.26,18.40)	16.74(15.18,18.31)	22.77(13.91,31.62)	17.28(12.05,22.50)	13.44(10.11,16.78)	19.46(14.35,24.56)	0.154
BMI, kg/m <sup>2</sup>	32.84±0.17	$32.83 \pm 0.18$	$31.87 \pm 0.69$	$31.68 \pm 0.47$	$33.28 \pm 0.43$	$33.35 \pm 0.47$	0.007
Poverty income ratio	$2.76 \pm 0.04$	$2.62 \pm 0.04$	$3.20 \pm 0.17$	$2.82 \pm 0.11$	$2.99 \pm 0.09$	3.18±0.11	< 0.001
Energy intake (kcal), %	1968.03±21.27	1952.61±24.14	1925.93±86.52	1946.21±51.70	1951.35±44.10	$2093.79 \pm 54.68$	0.106
Hypertension, %	69.73(64.71,74.75)	70.25(68.33,72.17)	72.01(63.94,80.08)	66.66(60.52,72.79)	68.38(62.18,74.58)	69.58(64.51,74.65)	0.758
Hyperlipidemia, %	87.34(81.11,93.57)	87.42(86.25,88.59)	79.86(69.65,90.07)	86.98(82.55,91.40)	88.64(85.92,91.36)	87.44(82.64,92.24)	0.365
CKD, %	36.12(32.91,39.33)	35.72(33.98,37.46)	38.83(28.11,49.54)	35.66(29.71,41.61)	36.30(30.79,41.81)	37.88(31.29,44.47)	0.990
Medication for diabetes, %	52.66(48.41,56.92)	57.85(51.24,64.47)	51.46(48.58,54.35)	58.04(48.73,67.35)	52.24(46.64,57.85)	48.44(36.92,59.95)	0.405
Diabetes dura- tion, years	11.18±0.26	11.37±0.36	10.27±1.21	11.36±0.70	10.85±0.72	10.58±0.55	0.741
caffeine, mg	$187.28 \pm 6.95$	$158.07 \pm 5.24$	$155.15 \pm 16.50$	$207.94 \pm 19.43$	$259.47 \pm 19.33$	257.12±16.58	< 0.001
HOMA-IR	7.74±0.36	$7.68 \pm 0.26$	8.12±3.09	8.93±1.79	$7.25 \pm 0.65$	7.79±1.06	0.860
Shift work, %	3.14(2.51, 3.77)	3.64(2.79,4.49)	0.88(-0.50,2.25)	2.50(0.73,4.27)	2.04( 1.02,3.05)	2.43( 1.22,3.63)	0.434

 Table 2
 Baseline characteristics of participants distributed according to tea drinking time period

Continuous variables are presented as mean ± standard deviation. Categorical variables are presented as percentage (%, 95% CI) BMI Body mass index, DM Diabetes mellitus, CKD Chronic kidney disease

adjustment for potential confounders, compared with participants in the lowest tertile of tea consumption, participants in the highest tertile had lower risk of allcause mortality (HR 0.78, 95% CI 0.63–0.96) and CVD mortality (HR 0.61, 95% CI 0.45–0.84). Similarly, for the status of tea consumption, compared with participants who did not drink tea, participants drank tea had lower risk of all-cause mortality (HR 0.78, 95% CI 0.65– 0.93), CVD mortality (HR 0.66, 95% CI 0.51–0.87), and stroke mortality (HR 0.43, 95% CI 0.19–0.97). Furthermore, we did not observe any significant association of coffee intake with mortality outcomes.

# Association of coffee consumption during different time periods with all-cause and disease-specific mortality

Compared with participants in the lowest tertile of coffee intake consumed during dawn to forenoon, participants in the highest tertile were more likely to die due to all-cause (HR 1.30, 95% CI 1.03–1.64), CVD (HR 1.45, 95% CI 1.07–1.97), and heart disease (HR 1.58, 95% CI 1.04–2.40). Similarly, for the status of coffee consumption, compared with participants who did not drink coffee during dawn to forenoon, participants drank coffee during this time period had greater risk of

Characteristics		All day o	offee intake				All c	lay tea intake		
Characteristics		Proportion	HR (95% CI)		P value	5	Proportion	HR (95% CI)		P value
All-cause mortalit	ty									
	Coffee intake status	5				Tea intake status				
	no	9.05(8.05,10.05)	Reference	•		no 1	18.64(16.59,20.68)	Reference		0.007
	yes	18.83(16.58,21.07	) 0.98(0.80,1.21)	Here a	0.878	yes	8.42(7.07, 9.76)	0.78(0.65,0.93)		0.006
	Coffee intake (g/kg)	)	~ ~			Tea intake (g/kg)				0.400
	QI	9.05(8.05,10.05)	Reference	• • •	0.932	QI	18.64(16.59,20.68)	Reference		0.100
	Q2	8.36(7.12, 9.60)	0.98(0.77,1.24)			Q2	3.87( 3.26, 4.49)	0.78(0.61,0.99)		
	Q3	10.47(8.84,12.09)	0.99(0.80,1.22)			Q3	4.54( 3.48, 5.60)	0.78(0.63,0.96)		
CVD mortality						<b>.</b>				
	Coffee intake status	5				Tea intake status	0.55/5.2/ 0.5/			
	no	4.14(3.50,4.77)	Reference	• • •		no	8.55(7.36,9.74)	Reference		
	yes	8.46(7.21,9.70)	0.98(0.73, 1.32)		0.902	yes	3.74(3.00,4.48)	0.66(0.51,0.87)		0.003
	Coffee intake (g/kg)	)			0.004	Tea intake (g/kg)				
	QI	4.14(3.50,4.77)	Reference	<u>,</u>	0.801	QI	8.55(7.36,9.74)	Reference		0.003
	Q2	3.69(3.02,4.36)	0.93(0.65, 1.33)			Q2	1.86(1.39,2.33)	0.73(0.53,1.00)		
	Q3	4.77(3.81,5.72)	1.02(0.74, 1.40)			Q3	1.88(1.38,2.38)	0.61(0.45,0.84)		
Heart mortality	<b>G M 1 1 1 1 1</b>									
	Coffee intake status	5	~ ~	1		Tea intake status			1	
	no	2.62(2.15,3.10)	Reference			no	5.48(4.53,6.44)	Reference		
	yes	5.75(4.75,6.75)	0.88(0.62, 1.25)		0.472	yes	2.53(2.00,3.06)	0.76(0.54,1.07)		0.113
	Coffee intake (g/kg)			1		Tea intake (g/kg)		-	1	
	Q1	2.62(2.15,3.10)	Reference	•	0.731	Q1	5.48(4.53,6.44)	Reference	•	0.285
	Q2	2.58(2.07,3.09)	0.84(0.54, 1.30)			Q2	1.22(0.86,1.57)	0.80(0.54,1.18)		
	Q3	3.17(2.41,3.93)	0.91(0.64, 1.31)			Q3	1.31(0.95,1.67)	0.73(0.49,1.10)		
Stroke mortality										
	Coffee intake status	5				Tea intake status				
	no	0.65(0.43,0.87)	Reference	•		no	1.12(0.85,1.39)	Reference	•	
	yes	0.94(0.56,1.33)	0.63(0.29, 1.36)		0.243	yes	0.43(0.17,0.69)	0.43(0.19, 0.97)		0.042
	Coffee intake (g/kg)	)				Tea intake (g/kg)				
	Q1	0.65(0.43,0.87)	Reference	. •	0.132	Q1	1.12(0.85,1.39)	Reference		0.006
	Q2	0.45(0.24,0.66)	0.70(0.25, 1.96)		•	Q2	0.27(0.08,0.46)	0.53(0.22, 1.30)		-
	Q3	0.49(0.23,0.75)	0.58(0.29, 1.19)			Q3	0.16(0.00,0.33)	0.34(0.12, 1.01)		
Diabetes mortality	У									
	Coffee intake status	5				Tea intake status				
	no	2.53(2.08,2.98)	Reference	•		no	5.46(4.41,6.50)	Reference	. •	
	yes	5.66(4.49,6.83)	1.26(0.93, 1.70)		0.129	yes	2.94(1.91,3.96)	0.70(0.47,1.04)		0.081
	Coffee intake (g/kg)	)				Tea intake (g/kg)				
	Q1	2.53(2.08,2.98)	Reference	•	0.113	Q1	5.46(4.41,6.50)	Reference	•	0.336
	Q2	2.24(1.68,2.81)	1.14(0.79, 1.64)			Q2	1.08(0.70,1.47)	0.60(0.36,0.99)		
	Q3	3.41(2.53,4.29)	1.36(0.94, 1.95)		1	Q3	1.85(1.00,2.71)	0.79(0.52,1.19)		
Data are weigh	tod HRs and 05%	CI		0.5 1.0 1.5 2	.0				0.5 1.0	

Results were adjusted for age, sex, race, marital status, education level, smoking status, drinking status, exercise regularly, BMI, poverty income ratio, energy intake, CKD, hypertension, hyperlipidemia, diastolic blood pressure, systolic blood pressure, HLD, triglycerides, frequency of coffee/tea intake across the day, medication for diabetes, diabetes duration and night-shift work. BMI, body mass index, CKD, chronic kidney disease, HDL, high density lipoprotein. Proportion was obtained through complex sampling methods assessment. Coffee intake range: T1: 0, T2: (0.00,3.66], T3: (3.66,71.50]. Tea intake range: T1: 0, T2: (0.00,4.11], T3: (4.11, 99.50].

**Fig. 1** Data are weighted HRs and 95% CI. Results were adjusted for age, sex, race, marital status, education level, smoking status, drinking status, exercise regularly, BMI, poverty income ratio, energy intake, added sugars intake, CKD, hypertension, hyperlipidemia, diastolic blood pressure, systolic blood pressure, HLD, triglycerides, frequency of coffee/tea intake across the day, medication for diabetes, diabetes duration, and night-shift work. BMI, body mass index, CKD, chronic kidney disease, HDL, high-density lipoprotein. Proportion was obtained through complex sampling methods assessment. Coffee intake range: T1: 0, T2: (0.00,3.66], T3: (3.66,71.50]. Tea intake range: T1: 0, T2: (0.00,4.11], T3: (4.11, 99.50]

all-cause mortality (HR 1.25, 95% CI 1.05–1.50), CVD mortality (HR 1.41, 95% CI 1.07–1.86), heart disease mortality (HR 1.47, 95% CI 1.05–2.07), and diabetes mortality (HR 1.50, 95% CI 1.10–2.04). Meanwhile, compared with participants in the lowest tertile of coffee consumed during forenoon to noon, participants in the highest tertile had lower risk of all-cause mortality (HR 0.80, 95% CI 0.67–0.96) and participants in the second tertile had lower risk of heart disease mortality (HR 0.67, 95% CI 0.46–0.97). Also, for the status of coffee consumption, compared with participants who did not drink coffee during forenoon to noon, participants drank coffee during this time period had lower risk of all-cause mortality (HR 0.80, 95% CI 0.69–0.92), CVD

mortality (HR 0.79, 95% CI 0.63–0.99), and heart disease mortality (HR 0.70, 95% CI 0.52–0.94) (Fig. 2).

# Association of tea consumption during different time periods with all-cause and disease-specific mortality

Compared with participants in the lowest tertile of tea consumed during forenoon to noon, participants in the highest tertile had lower mortality risk of CVD mortality (HR 0.57, 95% CI 0.36–0.90). Similarly, for the status of tea consumption, compared with participants who did not drink tea during forenoon to noon, the participants drank tea during this time period had lower risk of CVD mortality (HR 0.62, 95% CI 0.44–0.87) (Fig. 3).

Characteristics		Dawn to for	renoon coffee intak	e		Fo	renoon to noon coffe	ee intake			Noon to evening	coffee intake			Evening	g to dawn coffee i	ntake	
Characteristics		Proportion	HR (95% CI)		P value	Propertion	HR (95% CI)	Р	value	Proportion	HR (95% CD		P value		Proportion	HR (95% CI)		P value
All-cause mortalit	ly.																	
	Coffee intake statu no yes Coffee intake (g/kg Q1 Q2 Q3	s 21.56(19.40,23.72 6.32(5.22,7.41) ) 21.56(19.40,23.72 2.70(2.12,3.29) 3.61(2.80,4.43)	<ul> <li>Reference 1.25(1.05,1.50)</li> <li>Reference 1.20(0.95,1.52)</li> <li>1.30(1.03,1.64)</li> </ul>	•••••	Coffee intal no 0.014 yes Coffee intal 0.016 Q1 Q2 Q3	se status 20.08(17.91,22.26 7.80( 6.74, 8.85) 20.08(17.91,22.26 3.41( 2.85, 3.97) 4.38( 3.58, 5.19)	<ul> <li>Reference</li> <li>0.80(0.69,0.92)</li> <li>Reference</li> <li>0.80(0.64,0.99)</li> <li>0.80(0.67,0.96)</li> </ul>		Coffee intake stat no 2,002 yes Coffee intake (g/k 0,003 Q1 Q2 Q3	us 25.18(22.74,27.62) 2.70(2.12, 3.29) 32) 25.18(22.74,27.62) 1.17(0.77, 1.58) 1.53(1.16, 1.90)	Reference 0.98(0.80,1.18) Reference 0.91(0.67,1.25) 1.04(0.77,1.40)	+	0.798 0.997	Coffee intake status no 25. yes 2. Coffee intake (g/kg) Q1 25. Q2 0. Q3 1.	.87(23.25,28.48) .01(1.61, 2.42) .87(23.25,28.48) .98(0.70, 1.25) .03(0.74, 1.33)	Reference 1.11(0.87,1.41) Reference 0.93(0.71,1.23) 1.26(0.92,1.73)	÷	0.395 0.248
CVD mortality																		
	Coffee intake statu	s			Coffee intal	ce status			Coffee intake stat	us			(	Coffee intake status				
	no yes Coffee intake (g/kg Q1 Q2 Q3	9.88(8.73,11.02) 2.72(2.13, 3.31) ) 9.88(8.73,11.02) 1.26(0.90, 1.62) 1.46(1.03, 1.88)	Reference 1.41(1.07, 1.86) Reference 1.38(0.92, 2.07) 1.45(1.07, 1.97)		0.014 yes Coffee intal 0.047 Q1 Q2 Q3	8.87(7.72,10.01) 3.73(3.04, 4.42) te (g/kg) 8.87(7.72,10.01) 1.60(1.24, 1.96) 2.13(1.58, 2.67)	Reference 0.79(0.63, 0.99) → Reference 0.75(0.55, 1.02) → 0.82(0.61, 1.09) →		no J.039 yes Coffee intake (g/k J.087 Q1 Q2 Q3	11.48(10.17,12.78) 1.12(0.82, 1.42) (g) 11.48(10.17,12.78) 0.36(0.19, 0.53) 0.76(0.51, 1.01)	Reference 0.85(0.60, 1.21) Reference 0.61(0.32, 1.14) 1.10(0.69, 1.75)	÷	0.374 0.8	no 11. yes 0. Coffee intake (g/kg) Q1 11. Q2 0. Q3 0.	.70(10.36,13.05) .89(0.63, 1.16) .70(10.36,13.05) .48(0.26, 0.69) .42(0.26, 0.57)	Reference 0.97(0.65, 1.45) Reference 0.77(0.43, 1.38) 1.16(0.66, 2.03)	+	0.891 0.852
Heart mortality																		
	Coffee intake statu no yes Coffee intake (g/kg Q1 Q2 Q3	s 6.51(5.67,7.36) 1.86(1.38,2.34) ) 6.51(5.67,7.36) 0.90(0.60,1.21) 0.96(0.64,1.28)	Reference 1.47(1.05, 2.07) Reference 1.38(0.88, 2.18) 1.58(1.04, 2.40)	•	Coffee intal no 0.025 yes Coffee intal 0.067 Q1 Q2 Q3	se status 5.95(5.11,6.79) 2.42(1.89,2.96) se (g/kg) 5.95(5.11,6.79) 1.04(0.79,1.30) 1.38(0.97,1.79)	Reference 0.70(0.52, 0.94) = Reference 0.67(0.46, 0.97) = 0.73(0.51, 1.05) =		Coffee intake stat no ).017 yes Coffee intake (g/k ).065 Q1 Q2 Q3	us 7.57(6.57,8.57) 0.80(0.53,1.07) 7.57(6.57,8.57) 0.24(0.11,0.36) 0.56(0.34,0.79)	Reference 0.81(0.49, 1.34) Reference 0.50(0.24, 1.02) 1.14(0.65, 2.00)		0.402 0.819	Coffee intake status no 7 yes 0 Coffee intake (g/kg) Q1 7 Q2 0 Q3 0	.71(6.69,8.73) 1.66(0.44,0.88) 1.71(6.69,8.73) 1.37(0.18,0.56) 1.30(0.19,0.41)	Reference 1.02(0.66, 1.58) Reference 0.74(0.32, 1.69) 1.26(0.74, 2.15)	+	0.934 0.861
Stroke mortality																		
	Coffee intake statu no yes Coffee intake (g/kg Q1 Q2 Q3	s 1.32(0.96,1.68) 0.27(0.12,0.42) ) 1.32(0.96,1.68) 0.11(0.03,0.19) 0.16(0.04,0.29)	Reference 0.77(0.45, 1.31) ← Reference 0.73(0.33, 1.64) ← 0.80(0.36, 1.76) ←	÷.	Coffee intai no 0.335 yes Coffee intai 0.461 Q1 Q2 Q3	te status 1.12(0.73,1.51) 0.47(0.27,0.67) te (g/kg) 1.12(0.73,1.51) 0.27(0.11,0.43) 0.20(0.09,0.32)	Reference 1.01(0.58, 1.75) ← Reference 1.34(0.52, 3.45) ← 0.77(0.38, 1.55) ←		0.976 yes Coffee intake (g/k Coffee intake (g/k ).792 Q1 Q2 Q3	us 1.47(1.08,1.86) 0.12(0.02,0.23) 1.47(1.08,1.86) 0.04(0.00,0.08) 0.08(-0.01,0.18)	Reference 0.80(0.44, 1.47) Reference 0.47(0.12, 1.84) 1.08(0.57, 2.08)		0.473 0.785	no 1 yes 0. Coffee intake (g/kg) Q1 1 Q2 0. Q3 0	.52(1.10,1.93) .08(-0.01,0.17) .52(1.10,1.93) .07(-0.02,0.16) 0.01(0.00,0.02)	Reference 0.82(0.46, 1.45) Reference 1.22(0.82, 1.81) 0.29(0.07, 1.25)		0.492 0.176
Diabetes mortalit	У																	
	Coffee intake statu no yes Coffee intake (g/kg Q1 Q2 Q2	s 6.40(5.35,7.45) 1.79(1.29,2.28) ) 6.40(5.35,7.45) 0.79(0.47,1.12) 0.99(0.63,135)	Reference 1.50(1.10, 2.04) Reference 1.41(0.89, 2.23)		Coffee intal no 0.011 yes Coffee intal 0.022 Q1 Q2	5.71(4.73,6.69) 2.48(1.88,3.07) te (g/kg) 5.71(4.73,6.69) 0.88(0.64,1.12) 1.69(107,2.12)	Reference 0.88(0.67, 1.16) Reference 0.74(0.51, 1.07) →		Lottee intake stat no ).368 yes Coffee intake (g/k 0.79 Q1 Q2 Q2	us 7.37(6.19,8.54) 0.82(0.48,1.16) 2) 7.37(6.19,8.54) 0.29(0.13,0.46) 0.520(0.270, 70)	Reference 1.00(0.66, 1.53) Reference 0.89(0.42, 1.90)	-	0.995 0.831	Coffee intake status no 7 yes 0 Coffee intake (g/kg) Q1 7 Q2 0 Q2 0	'.61(6.37,8.85) ).57(0.35,0.80) 7.61(6.37,8.85) 0.28(0.11,0.45) 0.28(0.11,0.45)	Reference 0.89(0.52, 1.50) Reference 0.76(0.37, 1.56)	<u> </u>	0.651
-	<b>V</b> <sup>3</sup>	000,000,000	0.	5 1.0 1.5 2.0 2	3	1.00(1.07,4.12)	0.5	1.0 1.5 2.0	Q5	0.000(0.010(0.09)	112(0:04, 1:70)	0.5 1.0 1.5 2	0	v. (	323(0110)(040)		0.5 1.0 1.5 2/	.0

Data are weighted HRs and 95% C1; 16 Jul 32 Jul 32

**Fig. 2** Data are weighted HRs and 95% Cl. Results were adjusted for age, sex, race, marital status, education level, smoking status, drinking status, exercise regularly, BMI, poverty income ratio, energy intake, added sugars intake, CKD, hypertension, hyperlipidemia, diastolic blood pressure, systolic blood pressure, HLD, triglycerides, frequency of coffee/tea intake across the day, medication for diabetes, diabetes duration, and night-shift work. BMI, body mass index, CKD, chronic kidney disease, HDL, high density lipoprotein. Proportion was obtained through complex sampling methods assessment. Dawn to forenoon coffee intake range: T1: [0, 71.50], T2: (0.00, 4.11], T3: (4.11, 69.40], forenoon to noon coffee intake range: T1: [0, 69.40], T2: (0.00, 3.70], T3: (3.70, 71.50], Noon to evening coffee intake range: T1: [0, 71.50], T2: (0.00, 3.22], T3: (3.22, 32.1], Evening to dawn coffee intake range: T1: [0, 71.50], T2: (0.00, 3.20], T3: (3.20, 36.6]

Characteristics	Dawn	to forenoon tea intake		Forenoo	on to noon tea intake		Noon to	evening tea intake	Eve	ning to dawn tea intake
Characteristics	Proportion	HR (95% CI)	P value	Proportion I	HR (95% CI)	P value	Proportion H	R (95% CI) P 1	alue Proportion	HR (95% CI) P valu
All–cause mortalit	y Tea intake status no 26.41(23.73,29.09 yes 0.64(0.43,0.86) Tea intake (g/Sg) Q1 26.41(23.73,29.09 Q2 0.24(0.11,0.37) Q3 0.40(0.20,0.60)	) Reference 0.87(0.58,1.30) • • • ) Reference 0.67(0.36,1.27) • • • • 1.05(0.64,1.74) • • • •	Tea intake status           no         25           0.497         yes         1           Tea intake (g/kg)         0.788         Q1         25           0.788         Q2         0         Q3         0	5.31(22.79,27.84) 1.74(1.27, 2.21) 0. 5.31(22.79,27.84) 0.78(0.48, 1.09) 0. 9.96(0.60, 1.32) 0.	Reference .85(0.66,1.09) Reference .90(0.61,1.33) .81(0.57,1.14)	Tea intake status no 2 0.198 yes Tea intake (g/kg) 0.179 Q1 2 Q2 Q3	3.48(21.10,25.85) F 3.58(2.83, 4.32) 0.94 3.48(21.10,25.85) F 1.95(1.48, 2.43) 1.04 1.62(1.14, 2.10) 0.85	Reference • 0. Keference • 0. H(0.81, 1.33) • • •	Tea intake status           no         24.59(22.13,27.           630         yes         2.46(1.83, 3.0)           Tea intake (g/kg)         434         Q1           434         Q1         24.59(22.13,27.           Q2         1.03(0.06, 1.3)         Q3           Q3         1.43(0.97, 1.9)	05) Reference 9) 0.85(0.67,1.09) ↔ 0.200 0.65) Reference 9) 0.83(0.61.1.14) ₩) 0.87(0.62,1.22) ↔
CVD mortality	$\begin{array}{c} \mbox{Tea intake status} \\ no & 11.98(10.55,13.40 \\ yes & 0.31(\ 0.15,\ 0.48) \\ \mbox{Tea intake (g/kg)} \\ Q1 & 11.98(10.55,13.40 \\ Q2 & 0.12(\ 0.01,\ 0.22) \\ Q3 & 0.20(\ 0.07,\ 0.33) \\ \end{array}$	) Reference 0.85(0.48,1.51) ) Reference 0.73(0.26,2.06)	Tea intake status no 11 0.580 yes () Tea intake (g/kg) 0.685 Q1 11 Q2 () Q3 ()	1.69(10.26,13.13) 0.60(0.40, 0.79) 0. 1.69(10.26,13.13) 0.29(0.14, 0.45) 0. 0.30(0.18, 0.43) 0.	Reference .62(0.44,0.87) Reference .69(0.43,1.11)	Tea intake status no 0.005 yes Tea intake (g/kg) 0.006 Q1 1 Q2 Q3	0.63(9.26,12.00) H 1.66(1.23, 2.09) 0.92 0.63(9.26,12.00) H 0.90(0.61, 1.20) 1.00 0.76(0.54, 0.98) 0.86	Reference 0. Reference 0. 10(0.70,1.42)	Tea intake status           no         11.12(9.84,12.4           590         yes         1.17(0.72, 1.6           Tea intake (g/kg)         11.12(9.84,12.4           443         Q1         11.12(9.84,12.4           Q2         0.67(0.34, 0.9)         Q3           Q3         0.50(0.24, 0.7)         Q3	(0)         Reference         •         0.480           (0)         Reference         •         0.480           (0)         Reference         •         0.221           (1)         1.18(0.78,1.78)         •         •
Heart mortality	Tea intake status no         7.80(6.75,8.85) yes         0.21(0.10,0.32)           Tea intake (g/kg)         0.1         7.80( 6.75,8.85) Q2         0.03(-0.67,8.85) yes           Q1         7.80( 6.75,8.85) Q3         0.17( 0.06,0.29)         0.17( 0.06,0.29)	Reference 0.92(0.54,1.57) Reference 0.34(0.09,1.31)	Tea intake status no 0.766 yes Tea intake (g/kg) 0.564 Q1 Q2 Q3	7.58(6.50,8.66) 0.43(0.24,0.61) 0. 7.58(6.50,8.66) 0.23(0.09,0.37) 0. 0.20(0.07,0.32) 0.	Reference .67(0.43,1.04) Reference .78(0.44,1.37) .58(0.29,1.15)	Tea intake status 0.076 yes Tea intake (g/kg) 0.076 Q1 Q2 Q3	6.75(5.75,7.75) H 1.26(0.92,1.60) 1.10 6.75(5.75,7.75) H 0.67(0.42,0.92) 1.21 0.59(0.41,0.77) 1.09	Reference 6(0.88,1.51) 0. Reference 0. 2(0.85,1.76) 0.	Tea intake status           no         7.38(6.37,8.39           293         yes         0.63(0.38,0.87)           Tea intake (g/kg)         04         7.38(6.37,8.39)           439         Q1         7.38(6.37,8.39)           Q2         0.40(0.22,0.35)         Q3         0.23(0.06,0.44)	n         Reference         ●           0         0.72(0.47,1.10)         ●         ●         0.129           9)         Reference         ●         0.057           8)         1.09(0.69,1.72)         ●         ●           0         0.45(0.20,1.04)         ●         ●
Stroke mortality	Tea intake status no         1.51(1.11,1.91) yes         0.04(-0.03,0.10)           Tea intake (g/kg)         01         1.51(1.11,1.91)           Q1         1.51(1.11,1.91)         0.04(-0.03,0.10)           Q3         0.04(-0.03,0.10)         0.04(-0.03,0.10)	Reference 0.67(0.16, 2.81)	Tea intake status no 0.582 yes Tea intake (g/kg) 0.241 Q1 Q2 0 Q3 0	1.42(1.05,1.80) 0.12(0.01,0.24) 1.: 1.42(1.05,1.80) 0.04(-0.01,0.09) 0.3 0.09(0.00,0.18) 1	Reference 14(0.43, 2.97) Reference 80(0.19, 3.30) 42(0.46, 4.40)	Tea intake status 0.796 yes Tea intake (g/kg) 0.661 Q1 Q2 Q3	1.38(1.03,1.73) F 0.17(0.04,0.29) 0.75 1.38(1.03,1.73) F 0.10(0.00,0.20) 0.83 0.07(-0.02,0.15) 0.66	Reference 0. (0.39, 1.45) 0. Reference 0. (0.21, 1.29) 0.	Tea intake status no         1.44(1.10,1.7 396           396         yes         0.10(-0.02,0.2 0.2 0.2 368         0.10(-0.01,0.0 2 0.09(-0.03,0.2 Q3         0.09(-0.03,0.2 0.09(-0.01,0.0 Q3         0.01(-0.01,0.0 0.00(-0.01,0.0)	9)         Reference         •         0.295           2)         0.55(0.18, 1.68)         •         0.295           9)         Reference         •         0.086           11)         1.01(0.32, 3.25)         •         •           3)         0.13(0.02, 0.70)         •         •
Diabetes mortalit	y Tea intake status no 8.23(6.77,9.68) yes 0.17(0.03,0.30) Tea intake (g/kg) Q1 8.23(6.77,9.68) Q2 0.02(-0.01,0.04) Q3 0.15(0.02,0.28)	Reference 0.63(0.26,1.56) Reference 0.18(0.04,0.77) 1.05(0.40,2.76) 0 2	Tea intake status no 0.318 yes Tea intake (g/g) 0.637 Q1 Q2 Q3	7.79(6.45,9.13) 0.60(0.28,0.93) 0. 7.79(6.45,9.13) 0.19(0.05,0.33) 0. 0.41(0.12,0.71) 1.	Reference 92(0.57,1.49) Reference ,72(0.34,1.56) 06(0.62,1.81)	Tea intake status 0.749 yes Tea intake (g/kg) 0.950 Q1 Q2 Q3 2	7.31(5.99,8.63)         1           1.09(0.65,1.52)         0.77           7.31(5.99,8.63)         1           0.54(0.30,0.78)         0.77           0.55(0.19,0.91)         0.77	Reference 8(0.56,1.07) . 0. Reference 0. 7(0.48,1.25)	Tea intake status         no         7.32(6.11,8.55)           127         yes         1.08(0.55,1.6)         1.08(25,1.6)           223         Q1         7.32(6.11,8.55)         Q2         0.39(0.14,8.5)           Q2         0.39(0.14,0.6)         Q3         0.68(0.31,1.0)	t)         Reference           1)         1.03(0.72,1.49)         0.860           2)         Reference         0.762           5)         0.96(0.53,1.74)

Section for dilatetes, dilatetes di artico and section level, smoking status, drinking status, exercise regularly, BMI, poverty income ratio, energy intake, CKD, hypertension, hyperlipidemia, frequency of coffee/tea intake across the day, medication for dilatetes, diration and light-shift work, BMI, hody mass index, CKD, chronic kidney disease. Proportion was obtained through complex sampling methods assessment. Dava to foreason tea intake range: T1: (9, 52, 91; 71; 63, 65, 95-50), Foremont to nom tei nintake range: T1: (9, 95, 91; 72; (20, 83, 90); T2: (20, 83, 91); T2: (20, 83, 90); T2: (20, 84, 91); T2: (20, 83, 90); T2: (20, 84, 9

**Fig. 3** Data are weighted HRs and 95% Cl. Results were adjusted for age, sex, race, marital status, education level, smoking status, drinking status, exercise regularly, BMI, poverty income ratio, energy intake, added sugars intake, CKD, hypertension, hyperlipidemia, frequency of coffee/tea intake across the day, medication for diabetes, diabetes duration, and night-shift work. BMI, body mass index, CKD, chronic kidney disease. Proportion was obtained through complex sampling methods assessment. Dawn to forenoon tea intake range: T1: [0, 75.20], T2: (0.00, 3.61], T3: (3.65, 99.50], Forenoon to noon tea intake range: T1: [0, 99.50], T2: (0.00, 3.90], T3: (3.90, 75.20], Noon to evening tea intake range: T1: [0, 99.50], T2: (0.00, 4.38], T3: (4.39, 50.10], Evening to dawn tea intake range: T1: [0, 99.50], T2: (0.00, 4.00], T3: (4.00, 19.17]

## Sensitivity analysis

The first sensitivity analysis showed that sex did not modify above association (all  $P_{\text{for interaction}} > 0.05$ ) (Additional file 1: Table S3). The second sensitivity analysis showed that after excluding the participants with less than 2 years follow-up, these association was still observed, suggested that serious illness did not influence our results (Additional file 2: Figs. S1-3). Thirdly, our results did not change after excluding the participants who drank coffee or tea at multiple time periods of the day, suggesting that people who drink coffee or tea at multiple times of the day did not influence our results (Additional file 2: Figs.

S4-6). Fourthly, among non-diabetic sample, the participants who drank coffee during dawn to forenoon had lower risk of all-cause mortality, which showed opposite association to diabetic sample. Moreover, the association of coffee or tea consumed during forenoon to noon with a decreased risk of diabetes mortality were still observed among non-diabetic patients (Additional file 2: Figs. S7-9). Fifth, after additionally adjusting for caffeine as a covariate, we were still able to observe that tea consumption in all day is associated with a reduced risk of all-cause and CVD mortality. The association between coffee consumption at different times of the day and the risk of all-cause, CVD, and heart disease mortality varied, showing both increased and decreased risks depending on the timing of intake. Additionally, tea consumption in the forenoon to noon was specifically associated with a reduced risk of CVD mortality (Additional file 2: Figs. S10-12). Sixth, after further adjusting for HOMA-IR as a covariate, all results remained consistent except for the lack of association between tea consumption throughout the day and reduced diabetes mortality. Interestingly, although no association was found between tea consumption from forenoon to noon and reduced CVD mortality, this consumption pattern was associated with a reduction in all-cause mortality (Additional file 2: Figs. S13-15). Finally, after excluding the participants who did not have coffee or tea data, the daily coffee intake was not associated with all-cause mortality and CVD-specific mortality (Additional file 2: Figs. S16). Moreover, consistent with the main results, we also observed that compared with the participants without coffee intake, the participants who consumed coffee during dawn to forenoon had greater risk for mortality of CVD (HR 1.52, 95%CI 1.13 to 2.05), heart disease (HR 1.67, 95%CI 1.17-2.40), and diabetes (HR 1.44, 95%CI 1.02-2.04), and compared with the participants consumed coffee in the lowest tertile of coffee intake, the participants in the highest tertile had greater risk for mortality of CVD (HR 1.51, 95%CI 1.00-2.29) (Additional file 2: Figs. S17). However, the association between drinking tea during forenoon to noon and lower risk of CVD mortality become non-significant, probably because of relatively small sample size after the exclusion the participants who lacked the tea intake data (Additional file 2: Figs. S18).

## Discussion

This study found that overall coffee intake throughout the day was not associated with long-term survival in diabetic patients. However, time-specific effects were observed. Diabetic patients who drank coffee from dawn to forenoon had greater risks of all-cause, CVD, heart disease, and diabetes mortality. In contrast, those who drank coffee from forenoon to noon had a reduced risk of all-cause, CVD, and heart disease mortality. Additionally, although overall tea intake throughout the day was linked to decreased risks of all-cause mortality and CVD mortality, these associations remain significant only for diabetic patients who drank tea from forenoon to noon when considering specific time periods.

Current studies on the health impacts of coffee and tea intake among diabetic patients have yielded conflicting results [12-16]. This prompted us to investigate whether the timing of coffee and tea consumption might be more critical than overall daily intake. Our study is the first to highlight that the association between coffee intake and long-term survival in diabetic patients is time-specific. Diabetic patients who drank coffee from dawn to forenoon faced higher risks of all-cause, CVD, and diabetes mortality. In contrast, among non-diabetic individuals, coffee consumption during this period showed the opposite association, reducing the risk of all-cause and CVD mortality. This suggests that the adverse effects of coffee consumed during this time may be unique to diabetic patients. Although direct research supporting these findings is limited, some biological studies offer potential mechanisms that might explain this observation. Firstly, the "dawn phenomenon" observed in diabetic patients plays a significant role. Recent research reveals that diabetic individuals experiencing the dawn phenomenon exhibited a delayed phase in the rhythmic expression of nuclear receptor subfamily 1 group D members 1 and 2 (*NR1D1*, *NR1D2*), regulated by  $\gamma$ -amino butyric acid (GABA)-ergic neurons in the suprachiasmatic nucleus (SCN) [31]. Animal experiments suggest that activation of SCN GABAergic neurons impairs glucose tolerance from dawn to forenoon, while inhibition improves it during this period [31]. Besides, caffeine enhances NMDA receptor-induced GABA release, potentially activating SCN GABAergic neurons [32]. Therefore, coffee consumption during this time may exacerbate impaired glucose tolerance in diabetic patients, intensifying the adverse effects of the dawn phenomenon and ultimately affecting longterm survival. Secondly, diabetic patients tend to have higher levels of circulating glucocorticoid from dawn to forenoon compared to non-diabetic individuals [33, 34]. Glucocorticoids stimulate hepatic glucose production, inhibit glucose clearance [35], and elevate blood pressure by promoting sodium retention, increasing in heart rate, and inducing vasoconstriction [36, 37]. Since caffeine activates the human hypothalamus pituitary adrenal axis and promotes glucocorticoid production [24, 25], coffee consumption during this period may worsen blood pressure control in diabetic patients, potentially contributing to cardiovascular complications. Third, the glutathione system is a crucial antioxidant pathway in the body [38, 39]. However, in diabetic patients, high blood glucose

levels associated with the "dawn phenomenon" often result in elevated oxidative stress [40] and increased consumption of glutathione. Although polyphenols in coffee can effectively neutralize free radicals, thereby reducing glutathione consumption and exerting antioxidant effects [41], caffeine in coffee also stimulates the sympathetic nervous system. This stimulation can lead to increased heart rate and blood pressure [42], further exacerbating oxidative stress [43, 44]. Given that oxidative stress levels are already elevated in the early morning, the stimulating effects of caffeine may intensify this state, potentially causing harm to the body. Fourth, observational studies have found that the timing of antioxidant intake is associated with long-term survival in participants [45]. As a natural antioxidant, uric acid (UA) can neutralize free radicals [46], which may be beneficial for individuals with diabetes who are often accompanied by chronic inflammation and oxidative stress. Research indicates that serum uric acid levels in diabetic patients are higher between 5 and 8 a.m. [47]. During this period, the consumption of coffee, which is rich in flavonoids and polyphenols, may compete with uric acid in scavenging free radicals, potentially leading to uric acid deposition [48]. Uric acid deposition in the vascular wall can reduce the levels of nitric oxide, resulting in endothelial dysfunction [49], thereby posing a threat to cardiovascular health.

In contrast, non-diabetic individuals, who do not experience the dawn phenomenon and generally have better cardiovascular health compared to diabetic patients, are less likely to suffer from the adverse effects of coffee consumption at this time. Additionally, in non-diabetic individuals, the absence of circadian rhythm phase shifts suggests that coffee consumption can activate *BMAL* expression through the *cAMP/Ca*<sup>2</sup> + and *AMPK* signaling pathways. Increased *BMAL* expression has been associated with lower postprandial glucose and HbA1c levels [50, 51], which positively impacts glycemic control and cardiovascular health [52].

Moreover, we observed potentially beneficial effects of coffee consumed during the forenoon to noon period on long-term survival of diabetic patients. Previous studies have documented altered expression of circadian rhythm genes in diabetic patients compared to normal subjects. Specifically, decreased brain and muscle Arnt-like protein (*BMAL*) is associated with increase in postprandial blood sugar and HbA1c levels, coupled with delayed insulin secretion [50, 51]. *BMAL* is considered a crucial circadian gene for blood glucose control among diabetic patients. *BMAL* expression initiates transcription and gradually increases during the forenoon to noon period [53]. Some studies suggest that caffeine can activate *BMAL* expression through the elevation of the *cAMP/Ca*<sup>2+</sup> and *AMPK* signaling pathway [52]. Furthermore,

as the impact of the dawn phenomenon gradually diminishes, blood glucose levels tend to stabilize and insulin sensitivity improves. At this point, the body's oxidative stress levels may be relatively low. Under these conditions, the bioactive components in coffee can activate the Nrf2-ARE pathway, promoting the synthesis of glutathione [54, 55], Moreover, a decrease in serum uric acid levels makes it less likely to deposit [47], thereby enhancing the body's ability to cope with subsequent oxidative stress. Therefore, consumption of coffee during the forenoon to noon may partially restore the disruption of BMAL rhythmic expression, aiding in glucose control in diabetic individuals, consequently improving their longterm survival.

In the context of tea consumption, beyond daily intake, consuming tea during the forenoon to noon period is associated with improved long-term survival among diabetic patients. Similar to the positive health effects of coffee consumed during this timeframe and its impact on BMAL expression, catechin in tea has been found to regulate the stability and activity of BMAL by modulating the activity of SIRT1 [56]. Furthermore, diabetic patients often exhibit a loss of the rhythm of CLOCK gene expression, which typically initiates during the forenoon to noon period [53]. Animal studies have demonstrated that the loss of CLOCK gene rhythm could lead to impaired insulin secretion in islets [57]. Notably, recent experiments on mice fed with a high-fat diet revealed that tea polyphenols can upregulate *CLOCK* gene [58]. Additionally, studies have linked an increased ratio of Firmicutes/Bacteroidetes to poor glucose control and subclinical cardiovascular diseases, such as cardiac systolic and diastolic dysfunction, among diabetic patients [59]. Interestingly, observations indicate that *Firmicutes* abundance increases in the forenoon, peaking at noon among diabetic patients [59]. Catechin could downregulate Firmicutes abundance, consequently reducing Firmicutes/Bacteroidetes ratio [60]. Therefore, consumption of tea during the forenoon to noon may contribute to the improved long-term survival of diabetic patients by mitigating disruptions in BMAL and CLOCK expression rhythms, as well as by decreasing Firmicutes/Bacteroidetes ratio.

This study has several strengths. Firstly, we emphasize that the correct timing of coffee and tea intake has the potential to enhance the long-term survival of diabetic patients in a nationally representative sample of individuals in the USA, providing valuable nutritional guidance for diabetic patients. Secondly, our findings demonstrated relative robustness, as they remained consistent even after accounting for various classical confounding factors that could potentially influence the long-term survival of diabetic patients. However, our studies still had certain limitations. Firstly, this study relied on selfreported 24-h dietary recall at one time point survey, while widely used and considered the most valid instrument for capturing dietary information in observational studies. However, it is susceptible to measurement errors due to day-to-day variations in food intake. Future study using more accurate measurement methods for dietary survey is still needed to validate our findings. Secondly, despite our efforts to control for numerous potential confounding variables, observational nature of the study means that unmeasured confounders may still exist. Thirdly, the study did not delve into the specific types of coffee and tea consumed. Future research should consider exploring this association with a focus on different types of coffee (caffeinated, decaffeinated, instant) and tea (red, green, oolong, black). Finally, the inability to distinguish types of diabetes is a limitation. Previous studies suggest that majority of diabetic patients in NHANES have type 2 diabetes [61], further investigations differentiating between type 1 and type 2 diabetes are warranted for more comprehensive evidence.

## Conclusions

Coffee consumption during dawn to forenoon is associated with increased mortality risk, whereas coffee and tea consumption during forenoon to noon is associated with reduced mortality risks of all-cause, CVD, and heart disease in diabetes patients.

#### Abbreviations

ACR	Albumin/creatinine ratio
BMI	Body mass index
CKD	Chronic kidney disease
CPH	Cox proportional hazards
CVD	Cardiovascular disease
DBP	Diastolic blood pressure
eGFR	Estimated glomerular filtration rate
GVIF	Generalized Variance Inflation Factor
HbA1c	Hemoglobin Alc
HDL	High-density lipoprotein
HOMA-IR	Homeostasis model assessment of insulin resistance
LDL	Low-density lipoproteins
NHANES	National Health and Nutrition Examination Survey
OGTT	Oral glucose tolerance test
SBP	Systolic blood pressure

## **Supplementary Information**

The online version contains supplementary material available at https://doi. org/10.1186/s12916-024-03736-x.

Additional file 1: Table S1: Baseline characteristics of participants distributed according to coffee drinking time period. Table S2: The results of collinearity analysis of covariates in regression models. Table S3: The relationship between the interaction of gender and coffee/tea consumption and the mortality rates for all causes and specific diseases through complex sampling'. Table S4: National Center for Health Statistics Ethics Review Board approval.

Additional file 2: Fig. S1: The association of coffee and tea intake across the day with all-cause and disease-specific mortality, excluding individuals

with follow-up periods less than two years. Fig. S2: The association of coffee consumption during different time periods across with all-cause and disease-specific mortality, excluding individuals with follow-up periods less than two years. Fig. S3: The association of tea consumption during different time periods across the day with all-cause and diseasespecific mortality, excluding individuals with follow-up periods less than two years. Fig S4: The association of coffee and tea intake across the day with all-cause and disease-specific mortality, excluding individuals who consumed coffee or tea multiple times a day. Fig. S5: The association of coffee consumption during different time periods across with all-cause and disease-specific mortality, excluding individuals who consumed coffee multiple times a day. Fig. S6: The association of tea consumption during different time periods across the day with all-cause and diseasespecific mortality, excluding individuals who consumed tea multiple times a day. Fig. S7: The association of coffee and tea intake across the day with all-cause and disease-specific mortality in a non-diabetic population. Fig. S8: The association of coffee consumption during different time periods across with all-cause and disease-specific mortality in a non-diabetic population. Fig. S9: The association of tea consumption during different time periods across with all-cause and disease-specific mortality in a nondiabetic population. Fig. S10: The associations between all-day coffee and tea consumption and all-cause and disease-specific mortality were further adjusted for caffeine intake. Fig. S11: The associations of coffee consumption at different time periods with all-cause and disease-specific mortality were further adjusted for caffeine intake. Fig. S12: The associations of tea consumption at different time periods with all-cause and diseasespecific mortality were further adjusted for caffeine intake. Fig. S13: The associations between all-day coffee and tea consumption and all-cause and disease-specific mortality were further adjusted for HOMA-IR. Fig. S14: The associations of coffee consumption at different time periods with all-cause and disease-specific mortality were further adjusted for HOMA-IR. Fig. S15: The associations of tea consumption at different time periods with all-cause and disease-specific mortality were further adjusted for HOMA-IR. Fig. S16: The association of coffee and tea intake across the day with all-cause and disease-specific mortality, excluding participants with missing data on coffee and tea. Fig. S17: The associations of coffee consumption at different time periods across the day with all-cause and disease-specific mortality were analyzed, excluding participants with missing data on coffee and tea. Fig. S18: The associations of tea consumption at different time periods across the day with all-cause and disease-specific mortality were analyzed, excluding participants with missing data on coffee and tea.

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#### Authors' contributions

HS, WW and JB conceived the study design. YM, LQ and LJ did the statistical analysis. SY, HJ, TW, NR and LH repeated and validated the statistical analysis. HS, WW and JB wrote the manuscript. All authors read and approved the final manuscript.

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#### Data availability

No datasets were generated or analysed during the current study.

## Declarations

## Ethics approval and consent to participate

The NHANES study protocol was approved by the NCHS Research Ethics Review Board (#98–12, #2005–06 and #2011–17), and written informed consent was provided by all participants (Additional file 1: Table S4).

#### **Consent for publication**

Not applicable.

### Competing interests

The authors declare no competing interests.

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