Article

Milk intake and risk of mortality risk in the Japan Collaborative Cohort Study - a Bayesian survival analysis

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Version June 23, 2020 submitted to Nutrients

Abstract: A single paragraph of about 200 words maximum. For research articles, abstracts should give a pertinent overview of the work. We strongly encourage authors to use the following style of structured abstracts, but without headings: 1) Background: Place the question addressed in a broad context and highlight the purpose of the study; 2) Methods: Describe briefly the main methods or treatments applied; 3) Results: Summarize the article's main findings; and 4) Conclusion: Indicate the main conclusions or interpretations. The abstract should be an objective representation of the article, it must not contain results which are not presented and substantiated in the main text and should not exaggerate the main conclusions.

Keywords: keyword 1; keyword 2; keyword 3 (list three to ten pertinent keywords specific to the article, yet reasonably common within the subject discipline.).

1. Introduction

2. Materials and Methods

2.1. The database

We used data from the Japan Collaborative Cohort (JACC) study, which was sponsored by the Ministry of Education, Sports, Science, and Technology of Japan. Sampling methods and details about the JACC study have been described extensively in the literature [1–3]. Participants of the JACC study completed self-administered questionnaires about their lifestyles, food intake (food frequency questionnaire, FFQ), and medical histories of cardiovascular disease or cancer. In the final follow-up of the JACC study, data from a total of 110585 individuals (46395 men and 64190 women) were successfully retained for the current analysis. We further excluded samples if they meet one of the following criteria: 1) with any disease history of stroke, cancer, myocardial infarction, ischemic heart disease, or other types heart disease (n = 6655, 2931 men and 3724 women); 2) did not answer the question regarding their milk consumption in the baseline FFQ survey (n = 9545, 3593 men and 5952 women). Finally, 94385 (39386 men and 54999 women) are left in the database. The study design and informed consent procedure were approved by the Ethics Review Committee of Nagoya University School of Medicine.

2.2. Exposure and the outcome of interest

Frequency of milk intake during the preceding year of the baseline was assessed by FFQ from "never", "1-2 times/month", "1-2 times/week", "3-4 times/week", and "Almost daily". The exact amount of milk consumption was difficult to assess here. However, good reproducibility and validity were confirmed previously (Spearman rank correlation coefficient between milk intake frequency and weighed dietary record for 12 days was 0.65) [4].

The causes and date of death were obtained from death certificates and were systematically reviewed. The follow-up period was defined as from the time of the baseline survey was completed, which was between 1988-1990, until the end of 2009 (administrative censor), or the date when move-out of study area, or the date of death from stroke recorded, whichever occurred first. Other causes of death were treated as censored and assumed not informative. The causes of death were coded by the 10th Revision of the International Statistical Classification of Diseases and Related Health Problems (ICD-10), therefore stroke was defined as I60-I69. We further classified these deaths into hemorrhagic stroke (I60, I61 and I62) or cerebral infarction (I63) when subtypes of stroke in their death certificates were available.

2.3. Statistical approach

We calculated sex-specific means (standard deviation, sd) and proportion of selected baseline characteristics according to the frequency of milk intake. Overall difference across the milk intake groups were tested by either analysis of variance for continuous variables or χ^2 test for categorical variables.

Full parametric proportional hazard models under Bayesian framework with Weibull distribution were fitted using Just Another Gibbs Sampler (JAGS) program [5] version 4.3.0 in R version 4.0.1 [6]. JAGS program is similar to the OpenBUGS [7] project that uses a Gibbs sampling engine for Markov Chain Monte Carlo (MCMC) simulation. In the current analysis, we specified non-informative prior distributions ($\beta_n \sim N(0, 1000)$, and $\kappa_{\text{shape}} \sim \Gamma(0.001, 0.001)$) for each of the parameters in our models. The Brooks-Gelman-Rubin diagnostic [8] was used to refine the approximate point of convergence, the point when the ratio of the chains is stable around 1 and the within and between chain variability start to reach stability was visually checked. The auto-correlation tool further identified if convergence has been achieved or if a high degree of auto-correlation exists in the sample. Then, the number of iterations discarded as 'burn-in' was chosen. All models had a posterior sample size of 100000 from three separated chains with a "burn-in" of 2500 iterations. Posterior means (sd) and 95% Credible Intervals (CrI) of the estimated HR were presented for each category of milk intake frequency taking the "never" category as the reference. Posterior probability that the estimated hazard ratio (HR) favors the milk intake for frequency that higher or equal to "1-2 times/month" is smaller compared with those who chose "never" to their milk intake frequency were calculated as $P(\text{HR} < 1)$.

3. Results

3.1. Subsection Heading Here

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Table 2. This is a table caption. Tables should be placed in the main text near to the first time they are cited.

Title 1	Title 2	Title 3
entry 1	data	data
entry 2	data	data

Table 1

	Hazard ratio (HR)					Acceleration factor (AF)			
Milk intake	Median	Mean (SD)	95% CrI	MCSE	Probability	Median	Mean (SD)	95% CrI	MCSE
Never	-	-	-	-	-	-	-	-	-
1-2 t/Mon	0.88	0.89 (0.09)	(0.73, 1.08)	0.0022	86.50%	0.93	0.93 (0.06)	(0.81, 1.06)	0.0016
1-2 t/Week	0.77	0.77 (0.07)	(0.63, 0.91)	0.0019	99.90%	0.83	0.83 (0.05)	(0.73, 0.94)	0.0014
3-4 t/Week	0.79	0.79 (0.07)	(0.66, 0.94)	0.0022	99.70%	0.85	0.85 (0.05)	(0.74, 0.96)	0.0016
Daily	0.90	0.90 (0.06)	(0.79, 1.03)	0.0018	93.47%	0.93	0.93 (0.04)	(0.85, 1.02)	0.0013
Never	-	-	-	-	-	-	-	-	-
1-2 t/Mon	0.98	0.98 (0.11)	(0.79, 1.19)	0.0027	58.70%	0.99	0.99 (0.06)	(0.87, 1.11)	0.0016
1-2 t/Week	0.84	0.84 (0.08)	(0.70, 1.00)	0.0022	97.31%	0.90	0.90 (0.05)	(0.81, 1.00)	0.0014
3-4 t/Week	0.85	0.86 (0.08)	(0.71, 1.02)	0.0021	96.05%	0.91	0.91 (0.05)	(0.82, 1.01)	0.0013
Daily	0.75	0.76 (0.05)	(0.66, 0.87)	0.0016	100.00%	0.85	0.85 (0.04)	(0.78, 0.92)	0.0011
Never	-	-	-	-	-	-	-	-	-
1-2 t/Mon	1.00	1.01 (0.12)	(0.81, 1.24)	0.0041	50.61%	1.00	1.00 (0.07)	(0.88, 1.14)	0.0029
1-2 t/Week	0.86	0.87 (0.09)	(0.72, 1.05)	0.0036	93.73%	0.92	0.92 (0.06)	(0.82, 1.03)	0.0024
3-4 t/Week	0.89	0.90 (0.09)	(0.74, 1.08)	0.0038	89.62%	0.93	0.94 (0.06)	(0.84, 1.05)	0.0026
Daily	0.80	0.80 (0.07)	(0.69, 0.93)	0.0031	99.04%	0.88	0.88 (0.05)	(0.81, 0.96)	0.0020

Note:
Abbreviations: SD, standard deviation; CrI, credible interval; MCSE, Monte Carlo Standard Error; Probability indicates that the p for HR smaller than 1.

4. Discussion

5. Conclusion

Acknowledgments: All sources of funding of the study should be disclosed. Please clearly indicate grants that you have received in support of your research work. Clearly state if you received funds for covering the costs to publish in open access.

Author Contributions: "X.X. and Y.Y. conceive and designed the experiments; X.X. performed the experiments; X.X. and Y.Y. analyzed the data; W.W. contributed reagents/materials/analysis tools; Y.Y. wrote the paper.''

Conflicts of Interest: The authors declare no conflict of interest. The founding sponsors had no role in the design of the study; in the collection, analyses, or interpretation of data; in the writing of the manuscript, an in the decision to publish the results.

Abbreviations

The following abbreviations are used in this manuscript:

JACC	Japan Collaborative Cohort
FFQ	Food Frequency Questionnaire
MCMC	Markov Chain Monte Carlo
JAGS	Just Another Gibbs Samplers

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