Supplemental material

Title: Rice consumption and incidence of bladder cancer in a United States population

Running head: Rice consumption and bladder cancer.

Authors: Antonio J. Signes-Pastor[1], M. Scot Zens[1], John Seigne[2], Alan Schned[2], Margaret R. Karagas[1,*]

Affiliations: [1]Department of Epidemiology, Geisel School of Medicine, Dartmouth College, 1 Medical Center Dr, 7927 Rubin Bldg, Lebanon NH 03756, USA. [2]Dartmouth-Hichcock Medical Center, 1 Medical Center Dr. Lebanon, NH 03756, USA.

Type of manuscript: Research letter.

Keywords: Bladder cancer, rice consumption, arsenic, case–control study, epidemiology.

Manuscript word count: 560.

Corresponding author: Margaret R. Karagas, Ph.D., Geisel School of Medicine, Dartmouth College, 1 Medical Center Dr, 7927 Rubin Bldg, Lebanon NH 03756, USA. Phone: 603-653-9010; Fax: 603-653-9093; E-mail: Margaret.R.Karagas@dartmouth.edu.

Data availability: Analytic data used in this study are included in the manuscript table and its Supplementary Information file.

eTable 1. Selected characteristics of the study population according to the bladder cancer status, rice consumption, and water arsenic.

Characteristic	Cases (*n* = 316)	Controls (*n* = 230)	Without rice consumption (*n* = 138) [b]	With any (white or brown) rice consumption (*n* = 408) [b]	<1 µg/L water arsenic concentration (*n* = 393)	≥1 µg/L water arsenic concentration (*n* = 126)
Gender						
Male	233 (73.7) [a]	133 (57.8) ***	91 (65.9)	275 (67.4)	259 (65.9)	85 (67.5)
Female	83 (26.3)	97 (42.2)	47 (34.1)	133 (32.6)	134 (34.1)	41 (32.5)
Reference age (years):						
≤40	12 (3.8)	16 (7.0) *	1 (0.7)	27 (6.6) *	22 (5.6)	5 (4.0)
41 - 50	18 (5.7)	30 (13.0)	6 (4.3)	42 (10.3)	36 (9.2)	11 (8.7)
51 - 60	86 (27.2)	52 (22.6)	36 (26.1)	102 (25.0)	104 (26.5)	28 (22.2)
61 - 67	86 (27.2)	55 (23.9)	37 (26.8)	104 (25.5)	96 (24.4)	35 (27.8)
68 - 70	55 (17.4)	35 (15.2)	29 (21.0)	61 (15.0)	69 (17.6)	19 (15.1)
≥71	59 (18.7)	42 (18.3)	29 (21.0)	72 (17.6)	66 (16.8)	28 (22.2)
Education:						
High school	165 (52.2)	83 (36.1) ***	80 (58.0)	168 (41.2) ***	177 (45.0)	58 (46.0)
College	99 (31.3)	96 (41.7)	48 (34.8)	147 (36.0)	139 (35.4)	45 (35.7)
Graduate or professional	48 (15.2)	51 (22.2)	9 (6.5)	90 (22.1)	75 (19.1)	22 (17.5)
Cigarette smoking: [c]						
Never smoked	53 (16.8)	93 (40.4) ***	33 (23.9)	113 (27.7)	106 (27.0)	37 (29.4)
Former smoker	160 (50.6)	99 (43.0)	67 (48.6)	192 (47.1)	182 (46.3)	60 (47.6)
Current smoker	102 (32.3)	38 (16.5)	38 (27.5)	102 (25.0)	105 (26.7)	29 (23.0)
Body mass index (kg/m²):						
Underweight <18.5	2 (0.6)	1 (0.4)*	1 (0.7)	2 (0.5)	3 (0.8)	0 (0.0)
Normal 18.5 - 24.9	22 (7.0)	84 (36.5)	22 (15.9)	84 (20.6)	81 (20.6)	24 (19.0)
Overweight 25.0 - 29.9	47 (14.9)	95 (41.3)	31 (22.5)	111 (27.2)	101 (25.7)	40 (31.7)
Obese >30.0	29 (9.2)	46 (20.0)	19 (13.8)	56 (13.7)	60 (15.3)	12 (9.5)
Caloric intake (kcal/day): [d]						
Quartile 1: ≤ 1440	85 (26.9)	58 (25.2)*	45 (32.6)	98 (24.0)	112 (28.5)	26 (20.6)
Quartile 2: 1440 - 1794	44 (13.9)	57 (24.8)	26 (18.8)	75 (18.4)	70 (17.8)	26 (20.6)
Quartile 3: 1794 - 2238	84 (26.6)	57 (24.8)	31 (22.5)	110 (27)	94 (23.9)	41 (32.5)
Quartile 4: >2238	103 (32.6)	58 (25.2)	36 (26.1)	125 (30.6)	117 (29.8)	33 (26.2)
Water arsenic (µg/L) (median [sd]) [e]	0.36 [10.0]	0.23 [12.7] **	0.29 [6.5]	0.31 [12.5]	0.20 [0.2]	4.98 [20.5] ***

All statistical analysis were performed with R for statistical computing version 3.5.0[1] and * *P* < 0.05, ** *P* < 0.01, *** *P* < 0.001. The *p*-values were obtained from X^2, Fisher's exact, or Wilcoxon rank sum test as appropriate. [a] *n* (%). [b] Rice consumption was derived from the food frequency questionnaire section "Breads, Cereals, Starches" items "Brown rice" and "White rice" (**eFigure 1**). [c] Cigarette smoking status at 1 year prior to the reference or diagnosis date. [d] Caloric intake quartiles determined from the control subject distribution. [e] Total arsenic was determined in household tap water samples at the Dartmouth Trace Element Analysis Core using inductively coupled plasma mass spectrometry. 27 Study participants were missing household tap water arsenic concentrations.

eTable 2. Odds ratios and 95% confidence intervals for bladder cancer according to frequency of rice consumption

Rice consumption	Overall				<1 µg/L Water Arsenic			≥1 µg/L Water Arsenic		
	Controls (n = 230)	Cases (n = 316)	OR (95% CI) [b]	p for interaction (rice g/day* water As µg/L) [e]	Controls (n = 181)	Cases (n = 212)	OR (95% CI) [c]	Controls (n = 47)	Cases (n = 79)	OR (95% CI) [c]
None	50 (22) [f]	88 (28)	1.00 (reference)		40 (22)	63 (30)	1.00 (reference)	10 (21)	15 (19)	1.00 (reference)
Any rice [a]	180 (78)	228 (72)	0.8 (0.5 - 1.3)	0.423	141 (78)	149 (70)	0.7 (0.4 - 1.1)	37 (79)	64 (81)	1.3 (0.4 - 3.5)
≤ 20 g per day	71 (31)	91 (29)	0.8 (0.5 - 1.4)	0.365	53 (29)	64 (30)	0.7 (0.4 - 1.4)	17 (36)	21 (27)	0.7 (0.2 - 2.4)
>20 g per day	109 (47)	137 (43)	0.8 (0.5 - 1.4)	0.18	88 (49)	85 (40)	0.6 (0.3 - 1.1)	20 (43)	43 (54)	1.7 (0.5 - 6.0)
White rice [a]	99 (43)	128 (40)	0.8 (0.5 - 1.4)	0.295	75 (41)	91 (43)	0.7 (0.4 - 1.3)	23 (49)	29 (37)	0.8 (0.3 - 2.6)
≤20 g per day	60 (26)	76 (24)	0.8 (0.4 - 1.3)	0.762	45 (25)	54 (25)	0.7 (0.4 - 1.3)	14 (30)	16 (20)	0.7 (0.2 - 2.5)
>20 g per day	39 (17)	52 (16)	1.0 (0.5 - 1.8)	0.192	30 (17)	37 (17)	0.8 (0.4 - 1.6)	9 (19)	13 (16)	0.5 (0.1 - 3.2)
Brown rice [a,d]	81 (35)	100 (32)	0.8 (0.5 - 1.5)	0.889	66 (37)	58 (27)	0.6 (0.3 - 1.2)	14 (30)	35 (44)	2.3 (0.6 - 9.3)
≤ 20 g per day	53 (23)	71 (22)	1.0 (0.5 - 1.9)	0.382	40 (22)	41 (19)	0.7 (0.3 - 1.5)	12 (26)	26 (33)	2.1 (0.5 - 9.3)
>20 g per day	28 (12)	29 (9)	0.7 (0.3 - 1.6)	0.003	26 (15)	17 (8)	0.4 (0.2 - 1.1)	2 (4)	9 (11)	2.3 (0.2 - 38.2)

All statistical analysis were performed in R version 3.5.0[1]. OR = odds ratio, CI = confidence interval. [a] Any frequency. To control for the possibility that rice eaters have a healthier diet associated with a reduced risk of bladder cancer we created an "alternative Health Eating Index 2010" quintiles score and it was included as a continuous covariate in our models [2,3]. [b] OR were adjusted for age group, gender, caloric intake, cigarette smoking status, education, water arsenic concentration in µg/L, as well as quintiles of the "alternative Health Eating Index 2010" determined from the control distribution. [c] OR were not adjusted for water arsenic concentration in µg/L. [d] Brown rice could include a mixture of brown and white rice. [e] The p for interaction (cross-product term in the logistic regression - water arsenic (µg/L)* rice consumption (g/day)) was calculated with a likelihood ratio test. [f] n (%). 27 Study participants were missing household tap water arsenic concentrations.

eFigure 1: Rice consumption questions from the validated food frequency questionnaire[4] used in this study.

Diet assessment: For each food listed, fill in the circle indicating how often on average you have used the amount specified during the past year.

BREADS, CEREALS, STARCHES									
	Never, or less than once per month	1-3 per month	1 per week	2-4 per week	5-6 per week	1 per day	2-3 per day	4-5 per day	6+ per day
Brown rice (1 cup [a])	○	○	○	○	○	○	○	○	○
White rice (1 cup [a])	○	○	○	○	○	○	○	○	○

[a] It was assumed that 1-cup of rice equal 250 g.

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