Supplementary Online Content

This supplementary material has been provided by the authors to give readers additional information about their work.

eTable 1. Factors Associated With All-Cause and Cardiovascular Mortality in

Rheumatoid Arthritis, NHANES III

CHARACTERISTIC	HAZARD RATIO (95% CI)[*]	
	ALL-CAUSE	**CARDIOVASCULAR**
Folate Tertile[†]		
III vs. I	0.74 (0.54-1.03)	0.44 (0.26-0.75)
II vs. I	0.63 (0.47-0.85)	0.52 (0.30-0.92)
C-reactive Protein		
>1 mg/dL vs. Undetected	1.98 (1.46-2.69)	1.23 (0.75-2.03)
0.3-1.0 vs. Undetected	1.49 (0.97-2.29)	1.36 (0.61-3.03)
Age	1.09 (1.07-1.11)	1.09 (1.06-1.13)
Female vs. Male	0.79 (0.54-1.15)	1.20 (0.55-2.66)
White vs. Other	1.11 (0.85-1.47)	1.31 (0.84-2.04)
Body Mass Index	1.00 (0.98-1.02)	0.99 (0.96-1.03)
Current smoker (Yes vs. No)	1.48 (1.18-1.86)	1.22 (0.77-1.95)
Using DMARD (Yes vs. No)	0.94 (0.51-1.73)	0.48 (0.06-3.75)
Using NSAID (Yes vs. No)	1.21 (0.71-2.06)	0.68 (0.38-1.20)
Using Steroid (Yes vs. No)	0.90 (0.69-1.18)	1.50 (0.51-4.41)
Hypertension (Yes vs. No)	1.08 (0.84-1.39)	1.23 (0.73-2.04)
Diabetes (Yes vs. No)	2.68 (1.96-3.66)	2.68 (1.38-5.19)
Existing CVD (Yes vs. No)	1.09 (0.82-1.46)	1.20 (0.74-1.93)

NHANES, National Health and Nutrition Examination Survey; CI, Confidence Interval; DMARD, disease-modifying anti-rheumatic drug; NSAID, non-steroidal anti-inflammatory drug, CVD, cardiovascular disease.
[*]Models were adjusted for NHANES survey weights.
[†]Folate Tertile cut-off values: 4.3 and 8.2 ng/mL.

eTable 2. Ten-Year Mortality Risk in Patients with Rheumatoid Arthritis by Serum Folate Tertile, NHANES III

OVERALL	FOLATE TERTILE[*]			*P* for trend
	I	II	III	
ALL CAUSE MORTALITY				
No. with events / No. at risk	61/239	65/234	75/210	
Unadjusted HR (95% CI)	Ref	0.80 (0.48-1.33	1.14 (0.73-1.77)	0.34
Adjusted HR (95% CI)[†]	Ref	0.60 (0.37-0.97)	0.66 (0.41-1.07)	0.20
CARDIOVASCULAR MORTALITY				
No. with events / No. at risk	26/239	23/234	30/210	
HR (unadjusted)	Ref	0.45 (0.22-0.94)	0.74 (0.42-1.33)	0.59
95% CI	Ref			
HR (adjusted)[†]	Ref	0.31 (0.17-0.59)	0.39 (0.22-0.69)	0.04
95% CI	Ref			

NHANES, National Health and Nutrition Examination Survey; HR, Hazard ratio; CI, Confidence Interval.
[*]Folate Tertile cut-off values: 9.7 and 18.6 nmol/L. Models were adjusted for NHANES survey weights.
[†]Hazard ratio adjusted for age, sex, race, C-reactive protein value, body mass index, smoking, disease-modifying anti-rheumatic drug use, steroid use, non-steroidal anti-inflammatory drug use, and history of hypertension, diabetes, and cardiovascular disease.

eTable 3. Characteristics of Patients With Rheumatoid Arthritis but Without

Cardiovascular Disease by Folate Tertile, NHANES III

CHARACTERISTIC	TOTAL	FOLATE TERTILE[*]		
		I	II	III
Mean Age (SE), in years	53.72 (1.08)	50.38 (1.41)	53.46 (2.07)	57.22 (1.85)
Male, n (%)	171 (29.59)	63 (35.78)	63 (31.09)	45 (22.08)
White, n (%)	383 (87.25)	119 (81.42)	133 (88.21)	131 (91.93)
Mean body mass index (SE)	27.60 (0.35)	28.27 (0.53)	27.29 (0.64)	27.29 (0.72)
Mean C-reactive protein (SE), mg/L	0.118 (0.010)	0.128 (0.019)	0.099 (0.012)	0.121 (0.018)
Current smoker, n (%)	282 (57.60)	114 (67.92)	85 (51.31)	83 (53.94)
DMARD Use, n (%)	25 (5.2)	7 (4.1)	8 (2.1)	10 (9.4)
Steroid Use, n (%)	28 (6.2)	11 (6.1)	5 (3.0)	12 (9.4)
NSAID Use, n (%)	129 (21.8)	41 (24.6)	45 (17.4)	43 (23.5)
Folic Acid Supplement Use, n (%)	146 (32.1)	24 (10.9)	28 (18.8)	94 (66.1)
Diabetes, n (%)	68 (8.01)	16 (1.92)	25 (8.20)	27 (9.88)
Hypertension, n (%)	217 (32.81)	71 (35.88)	78 (35.60)	68 (27.02)

NHANES, National Health and Nutrition Examination Survey; SE, Standard error; DMARD, Disease-modifying anti-rheumatic drug; NSAID, Non-steroidal anti-inflammatory drug.
[*]Folate Tertile cut-off values: 4.3 and 8.2 ng/mL.

eTable 4. Characteristics of Patients With Rheumatoid Arthritis but Without Diabetes by

Folate Tertile, NHANES III

CHARACTERISTIC	TOTAL	FOLATE TERTILE[*]		
		I	II	III
Mean Age (SE), in years	54.46 (1.06)	51.19 (1.30)	54.46 (2.05)	57.76 (1.92)
Male, n (%)	194 (30.81)	77 (38.77)	69 (31.06)	48 (22.49)
White, n (%)	401 (87.37)	122 (79.45)	140 (88.72)	139 (94.03)
Mean body mass index (SE)	27.35 (0.33)	28.19 (0.49)	27.05 (0.66)	26.81 (0.68)
Mean C-reactive protein (SE), mg/dL	0.121 (0.011)	0.134 (0.019)	0.111 (0.014)	0.112 (0.019)
Current smoker, n (%)	301 (57.96)	131 (69.77)	94 (52.26)	76 (51.72)
DMARD Use, n (%)	26 (5.0)	7 (3.8)	9 (2.1)	10 (9.0)
Steroid Use, n (%)	30 (5.9)	9 (5.0)	8 (3.3)	13 (9.4)
NSAID Use, n (%)	128 (19.8)	47 (26.0)	46 (15.9)	35 (17.6)
Folic Acid Supplement Use, n (%)	148 (32.5)	28 (12.0)	31 (19.6)	89 (66.3)
Cardiovascular Disease, n (%)	92 (10.42)	35 (11.12)	31 (9.06)	26 (11.07)
Hypertension, n (%)	234 (34.28)	81 (34.83)	79 (36.11)	74 (31.88)

NHANES, National Health and Nutrition Examination Survey; SE, Standard error; DMARD, Disease-modifying anti-rheumatic drug; NSAID, Non-steroidal anti-inflammatory drug.
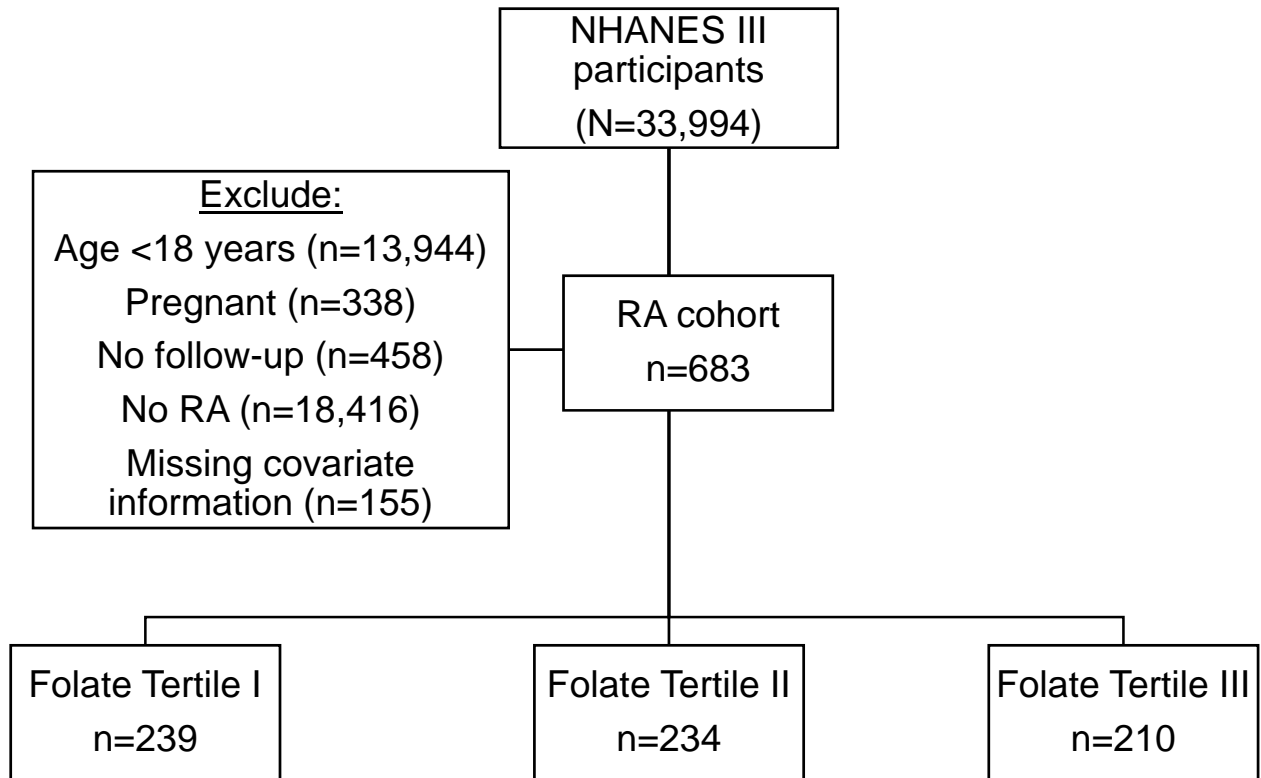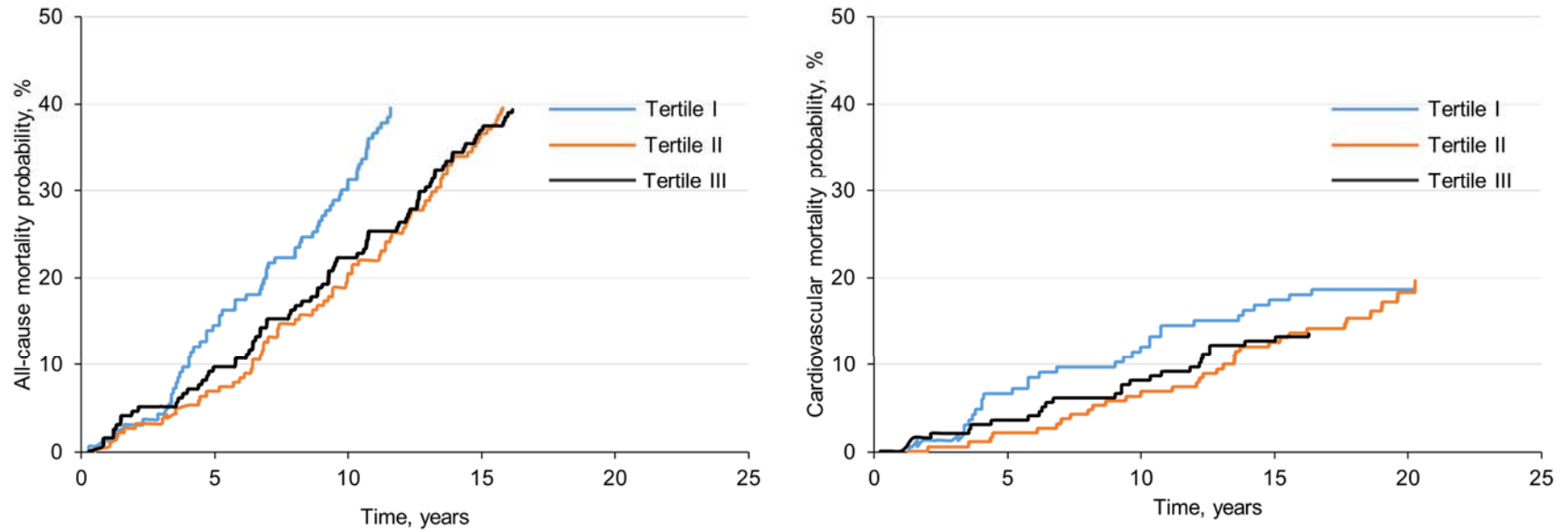[*]Folate Tertile cut-off values: 4.3 and 8.3 ng/mL.

eFigure 1. Sample Flow Diagram

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                                    ┌─────────────────────┐
                                    │   NHANES III        │
                                    │   participants      │
                                    │   (N=33,994)        │
                                    └──────────┬──────────┘
                                               │
┌────────────────────────────────┐            │
│         Exclude:               │            │
│ Age <18 years (n=13,944)       │   ┌────────┴────────┐
│   Pregnant (n=338)             ├───│   RA cohort     │
│ No follow-up (n=458)           │   │   n=683         │
│   No RA (n=18,416)             │   └────────┬────────┘
│ Missing covariate              │            │
│ information (n=155)            │            │
└────────────────────────────────┘            │
          ┌────────────────────────┬──────────┴──────────┬────────────────────────┐
┌─────────┴─────────┐    ┌─────────┴─────────┐    ┌──────┴──────────────┐
│ Folate Tertile I  │    │ Folate Tertile II │    │ Folate Tertile III  │
│   n=239           │    │   n=234           │    │   n=210             │
└───────────────────┘    └───────────────────┘    └─────────────────────┘
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eFigure 2. Cumulative Incidence Curves for All-Cause and Cardiovascular Mortality Risk in Patients With Rheumatoid Arthritis but Without Cardiovascular Disease by Serum Folate Tertile, NHANES III

eFigure 3. Cumulative Incidence Curves for All-Cause and Cardiovascular Mortality Risk in Patients With Rheumatoid Arthritis but Without Diabetes by Serum Folate Tertile, NHANES III