No association between dietary sodium intake and the risk of multiple sclerosis

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ABSTRACT

Objective: To prospectively investigate the association between dietary sodium intake and multiple sclerosis (MS) risk.

Methods: In this cohort study, we assessed dietary sodium intake by a validated food frequency questionnaire administered every 4 years to 80,920 nurses in the Nurses' Health Study (NHS) (1984–2002) and to 94,511 in the Nurses' Health Study II (NHSII) (1991–2007), and calibrated it using data from a validation study. There were 479 new MS cases during follow-up. We used Cox proportional hazards models to estimate hazard ratios (HR) and 95% confidence intervals (CI) for the effect of energy-adjusted dietary sodium on MS risk, adjusting also for age, latitude of residence at age 15, ancestry, body mass index at age 18, supplemental vitamin D intake, cigarette smoking, and total energy intake in each cohort. The results in both cohorts were pooled using fixed effects models.

Results: Total dietary intake of sodium at baseline was not associated with MS risk (highest [medians: 3.2 g/d NHS; 3.5 g/d NHSII] vs lowest [medians: 2.5 g/d NHS; 2.8 g/d NHSII] quintile: HR_{pooled} 0.98, 95% CI 0.74–1.30, *p* for trend = 0.75). Cumulative average sodium intake during follow-up was also not associated with MS risk (highest [medians: 3.3 g/d NHS; 3.4 g/d NHSII] vs lowest [medians: 2.7 g/d NHS; 2.8 g/d NHSII] quintile: HR_{pooled} 1.02, 95% CI 0.76–1.37, *p* for trend = 0.76). Comparing more extreme sodium intake in deciles yielded similar results (*p* for trend = 0.95).

Conclusions: Our findings suggest that higher dietary sodium intake does not increase the risk of developing MS. *Neurology*® 2017;89:1322–1329

GLOSSARY

ALA = α -linolenic acid; **BMI** = body mass index; **CDC** = Centers for Disease Control and Prevention; **CI** = confidence interval; **EAE** = experimental autoimmune encephalomyelitis; **FFQ** = food frequency questionnaire; **HR** = hazard ratio; **MS** = multiple sclerosis; **NHS** = Nurses' Health Study; **NHSII** = Nurses' Health Study II; **WLVS** = Women's Lifestyle Validation Study.

Environmental factors like low vitamin D levels,¹ infectious mononucleosis,² smoking,³ and adiposity during adolescence⁴ have consistently been associated with multiple sclerosis (MS) risk, but it remains important to continue searching for novel, especially modifiable, risk factors.

The results of previous studies suggest that salt intake may be involved in the pathogenesis of MS and predict disease activity.⁵ High sodium concentrations in vitro were found to induce pathogenic Th17 cells, which play an important role in MS pathology.^{6,7} Furthermore, higher sodium intake has been related to increased disease activity in adult patients with MS⁸ and in experimental autoimmune encephalomyelitis (EAE),^{6,9} an MS animal model. The worldwide changes in dietary habits towards fast and processed food rich in sodium could thus have contributed to the increase in MS prevalence and incidence over the last decades, if sodium alters MS risk.¹⁰ However, recent findings in a pediatric population do not suggest an involvement of sodium in MS pathogenesis or exacerbation.^{11,12} Further, the association between dietary sodium and the risk of adult-onset MS has not yet been determined.

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We therefore investigated prospectively whether total dietary sodium intake was associated with the risk of MS in 2 large US cohorts of women with an overall follow-up of 38 years, the Nurses' Health Study (NHS) and the Nurses' Health Study II (NHSII).

METHODS Study design. The ongoing NHS and NHSII are prospective cohort studies initiated in 1976 (NHS, 121,700 participants) and 1989 (NHSII, 116,671 participants).¹³ These are well-defined cohorts of registered nurses from different US states, 30–55 (NHS) and 25–42 (NHSII) years old at inclusion. They are followed over time with biennial self-administered postal questionnaires collecting information on different exposures, e.g., lifestyle, and health-related outcomes, with a high response rate (approximately 90%) in both cohorts in each questionnaire cycle.

Standard protocol approvals, registrations, and patient consents. These cohort studies were approved by the institutional review board of Brigham and Women's Hospital.

Assessment of dietary sodium intake. Diet was assessed in 80,920 women in NHS (in 1984, 1986, 1990, 1994, 1998, 2002) and 94,511 women in NHSII (in 1991, 1995, 1999, 2003, 2007) using a validated semiquantitative food frequency questionnaire (FFQ), described in detail elsewhere^{14–16} and sent out every 4 years as part of the main questionnaire. From 1984 in NHS and 1991 in NHSII, the FFQ remained similar, assessing the average portion size (e.g., 1 slice of bread, 2 slices of bacon, 1 8-oz glass of milk) and usual consumption (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, or 6+ per day) over the last year of about 130 food items covering the following categories: dairy products, fruits, vegetables, breads/cereals/starches, eggs/meats, beverages, sweets/baked goods/miscellaneous.

The FFQ covers the main dietary sodium sources including the top 10 food items that contribute, according to the Centers for Disease Control and Prevention (CDC), to >40% of sodium eaten daily in the United States, i.e., breads/rolls, cold cuts/cured meats, pizza, poultry, soups, sandwiches, cheese, snacks, pasta, and meat dishes.¹⁷ A question on the habitual frequency of a salt shake added at the table during meals is also included, but not salt added during cooking. The FFQ takes also into account sodium sources other than the major source, salt (sodium chloride), including sodium glutamate, bicarbonate, citrate, nitrate, and benzoate.¹⁸ According to the CDC, 77% of the sodium in the average American diet comes from restaurant and processed food, while only 5% is added during cooking, and 6% at the table.¹⁹ The remaining sodium is a natural part of foods. On average, Americans consume >3,400 mg of sodium per day,¹⁹ which corresponds to about 1.5 teaspoons of salt and exceeds the daily limit of sodium intake of 2,300 mg recommended by the 2015 US dietary guidelines.²⁰

The content of sodium in different food items was determined using the Harvard FFQ Nutrient Database, which is regularly updated and expanded for average nutrient and mineral content.²¹ Sodium intake from a specific food item was estimated by multiplying its sodium content by the reported frequency of intake, with frequency weighted such that 1 per day equaled 1. Total dietary sodium intake was calculated by summing sodium intake across the different foods. Subsequently, sodium intake was adjusted for energy intake using the residual method to isolate the mineral's contribution to risk independent of total caloric

intake or food quantity consumed.²² The measurement of sodium by FFQ has been validated in the context of the Women's Lifestyle Validation Study (WLVS) conducted among participants in the NHS and NHSII to assess measurement error possible with self-reported dietary exposures.^{23,24} Using a slightly expanded version of the FFQ used in the original cohorts with in total 152 food items to include newer foods, the energy-adjusted random-error-corrected Spearman correlation coefficients with the sodium assessment by FFQ were 0.53 for sodium from 7-day dietary records,²⁴ 0.43 for sodium from 24-hour dietary recalls,²⁴ and 0.48 for 24-hour urinary sodium (gold standard)²³ (unpublished, under review). As FFQs systematically underestimate true sodium intake,²⁵ we used sodium excretion measured in multiple 24-hour urine samples from women in WLVS to correct the sodium intake estimated by FFQ in our study for measurement error. The correction equation based on a linear regression with energy-adjusted sodium intake assessed by FFQ in WLVS as exposure and urinary sodium as outcome is (corrected sodium intake = 1,455.83 + [0.767 × uncorrected FFQ sodium intake]). Under-reporting of true sodium intake in FFQs might vary according to other characteristics such as body mass index (BMI).²⁵ However, the difference of the energy-adjusted sodium between the FFQ and biomarker measurement within WLVS was not associated with BMI ($p = 0.35$), age ($p = 0.65$), or smoking status ($p = 0.32$), suggesting that these factors are unrelated to reporting error in the study.

Case ascertainment. We requested permission from women self-reporting an MS diagnosis on the biennial questionnaires to contact their treating neurologist and review their medical record. Since 2003, our study neurologist has been reviewing all medical records for confirmation. In this study, we defined the outcome as neurologist-confirmed probable or definite diagnosis of MS according to date of diagnosis (or date of first symptom in sub-analyses). Cases of possible MS were not included. There were 130 new cases in NHS and 349 new cases in NHSII of probable or definite MS diagnosis during follow-up among women reporting dietary information.

Covariates. Ancestry, reported in 1992 (NHS) and 1989 (NHSII), was categorized into southern European, Scandinavian, other Caucasian, or other. Women reported their state of residence at age 15 in 1992 (NHS) and 1993 (NHSII). We categorized the states into northern, middle, and southern tier, as previously described.²⁶ Smoking status was updated biennially including information on number of cigarettes smoked per day, and categorized into never, <10, 10–24, and ≥25 pack-years. Women reported their height at baseline and their weight at age 18 in 1980 (NHS) and 1989 (NHSII). We calculated their BMI in kg/m² from this information and categorized women as underweight, normal, overweight, or obese (<18.5, 18.5–<25.0, 25–<30, ≥30 kg/m²) according to cutoffs defined by the WHO. Supplemental vitamin D intake was categorized into none, <400, and ≥400 IU/d. Total energy intake was calculated from the FFQ.

Statistical analyses. We estimated the association between total dietary sodium intake and MS risk during follow-up using Cox proportional hazards models. The energy-adjusted measurement error-corrected sodium was used as exposure in all analyses. Missing exposures were replaced with the last available value if the participant was not lost to follow-up. We reported (1) age- and total energy-adjusted and (2) multivariable-adjusted hazard ratios (HR) and 95% confidence interval (CI) at a significance level of 0.05. The women contributed person-years (time at risk) from return date of the baseline diet questionnaire (NHS: 1984,

NHSII: 1991) to date of MS diagnosis, date of death, loss to or end of follow-up (NHS: June 2004, NHSII: June 2009), whichever occurred first. Women with daily caloric intake of below 500 or above 3,500 kcal and those who had returned only the baseline questionnaire were excluded from the analyses.

We assessed total dietary sodium intake at baseline continuously by incremental steps of 100 mg per day and categorically in quintiles and deciles, comparing those ranking in the top to those in the bottom category. Moreover, cumulative average intake of sodium during follow-up was assessed in quintiles and deciles, using the bottom category as reference. For the categorical analyses, we also reported the *p* value for linear trend across medians in each category. The multivariable models were adjusted for ancestry, latitude of residence at age 15, BMI at age 18, pack-years of smoking, supplemental vitamin D, and total energy intake. The latter 3 were updated biennially and introduced into the model as time-varying covariates. We conducted the analyses separately for each cohort and then pooled the results using fixed-effects models with the inverse of the variance of the risk estimates as the weight, and a Q statistic to assess heterogeneity.²⁷ Mantel extension tests were performed to examine the trend across the pooled categories.

We repeated the baseline analyses in subgroups of never- and ever-smokers separately, as an association between sodium intake and another autoimmune disease has previously been reported only in smokers.²⁸

Recently, α -linolenic acid (ALA), a polyunsaturated fatty acid, was found to be inversely associated with MS risk in the same cohorts.²⁹ To assess whether this may confound the association, we adjusted the multivariable model of baseline sodium

intake in quintiles in addition for ALA in quintiles determined from the diet questionnaires as described for sodium above.

In sensitivity analyses, we followed MS cases to date of onset instead of diagnosis. There were overall 289 new patients (59 in NHS, 230 in NHSII) diagnosed with probable or definite MS during follow-up who had information on onset date and diet.

RESULTS We followed 80,920 NHS and 94,511 NHSII participants over 3,096,959 person-years (figure 1). Women with higher sodium intake had on average a higher BMI at age 18 and a lower vitamin D supplementation at baseline (table 1). Women in the NHS with high sodium intake reported more pack-years of smoking and were more likely to have lived in the Northern tier at age 15. These trends were not seen in the NHSII. There were in total 479 incident MS cases during follow-up with a median age at diagnosis of 47 years; 69.5% had relapsing-remitting MS, 15.0% progressive MS (primary or secondary), and the remaining 15.4% had an unknown/other disease course.

There was no association between sodium intake and the risk of developing MS (multivariable HR_{pooled} for 100 mg per day increases in sodium = 1.00, 95% CI 0.96–1.03). In quintile analyses, there was also no association with MS risk comparing the top to the bottom quintile at baseline or cumulatively

Figure 1 Flowchart of the study population selection and sample size

MS = multiple sclerosis; NHS = Nurses' Health Study; NHSII = Nurses' Health Study II.

Table 1 Selected characteristics of women in the Nurses' Health Study (NHS) and Nurses' Health Study II (NHSII) by quintiles of total dietary sodium intake^a at baseline^b

	Total dietary sodium intake				
	Q1	Q2	Q3	Q4	Q5
NHS					
Sodium, mg/d, median	2,513	2,691	2,817	2,953	3,175
No. of women	16,150	16,212	16,223	16,183	16,152
Age at baseline, y, mean (SD)	51.0 (7.1)	50.6 (7.2)	50.5 (7.1)	50.8 (7.2)	50.7 (7.1)
Ancestry, %					
Scandinavian	4.2	4.2	4.3	4.0	3.8
Southern European	13.6	14.6	14.8	14.7	14.9
Other Caucasian	55.4	59.0	60.3	60.7	61.0
Other ^c	26.8	22.2	20.6	20.6	20.3
Pack-years smoking, mean (SD)	12.2 (17.5)	11.2 (16.3)	11.0 (16.3)	11.4 (16.7)	13.5 (17.9)
BMI age 18, kg/m ² , mean (SD)	21.1 (2.9)	21.2 (2.8)	21.3 (2.9)	21.5 (3.0)	21.7 (3.1)
Supplemental vitamin D, IU/d, mean (SD)	132.7 (223.2)	128.0 (216.7)	122.9 (207.6)	119.8 (208.9)	120.1 (213.1)
Residence in north tier at age 15, %	33.9	36.6	37.7	38.3	38.0
NHSII					
Sodium, mg/d, median	2,767	2,968	3,101	3,237	3,455
No. of women	18,905	18,946	18,924	18,888	18,848
Age at baseline, y, mean (SD)	36.0 (4.8)	36.1 (4.7)	36.1 (4.6)	36.2 (4.6)	36.4 (4.6)
Ancestry, %					
Scandinavian	3.9	4.5	4.6	4.6	4.5
Southern European	12.9	13.5	14.2	13.9	13.9
Other Caucasian	67.9	73.7	74.5	75.4	75.7
Other ^c	15.3	8.3	6.7	6.1	5.9
Pack-years smoking, mean (SD)	4.3 (7.9)	3.8 (7.2)	3.8 (7.2)	3.9 (7.4)	4.4 (8.0)
BMI age 18, kg/m ² , mean (SD)	20.9 (3.3)	21.1 (3.2)	21.2 (3.2)	21.4 (3.3)	21.7 (3.5)
Supplemental vitamin D, IU/d, mean (SD)	135.3 (203.3)	134.3 (193.1)	130.9 (193.6)	124.3 (185.7)	118.2 (187.3)
Residence in north tier at age 15, %	30.1	30.9	31.4	30.5	29.5

Abbreviation: BMI = body mass index.

^aTotal dietary sodium intake assessed by food frequency questionnaire was adjusted for energy intake using the residual method²² and subsequently calibrated using data from the Women's Lifestyle Validation Study.^{23,24}

^bValues in each category are standardized to the age distribution in each cohort (apart from age).

^cThis group includes individuals of African, Hispanic, Asian, and other ancestry.

during follow-up, either in the age- and energy-only adjusted or in the multivariable models (table 2). Adjusting the multivariable baseline model additionally for ALA yielded similar results (top to bottom quintile of sodium intake: multivariable_{+ALA} HR_{pooled} 1.09, 95% CI 0.81–1.46, *p* for trend = 0.29); thus we did not include this covariate in the final model. More extreme comparisons led to similar results. We did not observe an association between deciles of total dietary sodium intake and MS risk, either at baseline (figure 2) (multivariable HR_{pooled} 0.79, 95% CI 0.53–1.17, *p* for trend = 0.95) or for cumulative average intake (multivariable HR_{pooled} 0.79, 95% CI 0.52–1.18, *p* for trend = 0.94), comparing women in the top to those in the bottom

category (medians in highest vs lowest decile at baseline: 3.3 g/d [NHS] and 3.6 g/d [NHSII] vs 2.4 g/d [NHS] and 2.7 g/d [NHSII], cumulatively during follow-up: 3.5 g/d [NHS] and 3.5 g/d [NHSII] vs 2.6 g/d [NHS] and 2.7 g/d [NHSII]).

In the baseline analyses stratified by smoking status, there were 82 (NHS) and 159 (NHSII) ever-smoking and 48 (NHS) and 190 (NHSII) never-smoking new patients of definite or probable MS during follow-up. We did not observe an association between baseline sodium intake and MS risk when comparing women with highest to women with lowest intake according to quintiles in the subgroups separately (ever smokers: multivariable HR_{pooled} 0.94, 95% CI 0.63–1.40, *p* for trend = 0.93; never

Table 2 Pooled hazard ratios (HRs) and 95% confidence interval (95% CI) of multiple sclerosis by quintiles of total dietary sodium intake^a at baseline and cumulatively during follow-up in Nurses' Health Study (NHS, 1984–2004) and Nurses' Health Study II (NHSII, 1991–2009)

	NHS		NHSII		Pooled HR (95% CI)	
	Sodium, mg/d, median	Cases/person-years	Sodium, mg/d, median	Cases/person-years	Age-adjusted ^b	Multivariable ^c
Baseline intake						
Quintile						
1	2,513	32/298,321	2,767	64/316,570	Ref.	Ref.
2	2,691	18/301,374	2,968	60/320,198	0.81 (0.60–1.09)	0.80 (0.59–1.08)
3	2,817	31/302,748	3,101	79/320,229	1.14 (0.87–1.50)	1.12 (0.85–1.48)
4	2,953	22/301,165	3,237	73/319,703	0.97 (0.73–1.29)	0.95 (0.71–1.27)
5	3,175	27/298,938	3,455	73/317,713	1.03 (0.78–1.37)	0.98 (0.74–1.30)
Total		130/1,502,546		349/1,594,413		
p Trend					0.51	0.75
p Het ^d					0.37	0.35
Cumulative intake						
Quintile						
1	2,695	24/295,113	2,810	64/313,754	Ref.	Ref.
2	2,853	26/302,882	2,979	63/320,954	1.00 (0.75–1.35)	1.00 (0.74–1.34)
3	2,969	22/304,725	3,092	79/321,315	1.13 (0.85–1.51)	1.11 (0.83–1.48)
4	3,095	30/304,359	3,210	73/320,706	1.15 (0.87–1.53)	1.11 (0.83–1.48)
5	3,319	28/295,468	3,397	70/317,685	1.09 (0.81–1.45)	1.02 (0.76–1.37)
Total		130/1,502,546		349/1,594,413		
p Trend					0.45	0.76
p Het ^d					0.89	0.95

^aTotal dietary sodium intake assessed by food frequency questionnaire was adjusted for energy intake using the residual method²² and subsequently calibrated using data from the Women's Lifestyle Validation Study.^{23,24}

^bAdjusted for age and total energy intake.

^cAdjusted for age, latitude of residence at age 15 (north, middle, south), ancestry (southern European, Scandinavian, other Caucasian, other), pack-years of smoking (0, <10, 10–24, ≥25), supplementary vitamin D intake (0, <400, ≥400 IU/d), body mass index at age 18 (<18.5, 18.5–<25, 25–<30, ≥30 kg/m²), and total energy intake.

^dBased on the tests for heterogeneity, we do not reject the homogeneity assumption: (1) baseline exposure: Q(1) = 0.79, *p* = 0.37 for age-adjusted model; Q(1) = 0.89, *p* = 0.35 for multivariable model; (2) cumulative exposure: Q(1) = 0.02, *p* = 0.89 for age-adjusted model; Q(1) = 0.004, *p* = 0.95 for multivariable model.

smokers: multivariable HR_{pooled} 1.06, 95% CI 0.71–1.59, *p* for trend = 0.50). This was also true for intake assessed continuously or in deciles (data not shown).

In sensitivity analyses, we used date of MS onset instead of diagnosis as outcome and the results were, similarly, null (data not shown).

DISCUSSION In this large prospective study of women, we found that total dietary sodium intake was not associated with the risk of developing MS, suggesting that a decrease in sodium intake is unlikely to reduce MS risk.

Our results do not confirm the findings from experimental studies suggesting that increased salt consumption in humans could be an environmental MS risk factor.^{6,7,30} The inconsistency between our findings and those obtained in animal models could

be explained by the sodium dose. Salt doses fed to mice displaying an accelerated onset and more severe EAE exceeded by far intakes observed in humans, even those with traditionally salt-rich diets.^{31,32} Further, although a marked in vitro Th17 cell induction was reported at salt concentrations meant to approximate interstitial sodium concentrations in humans,^{6,7} it is unclear whether these effects reproduce those observed in vivo, where sodium cations are buffered by glycosaminoglycans and interact with other molecules.³³ Rather, our findings are consistent with those in the only other study assessing disease risk in humans, a case-control study in a pediatric population,¹¹ in which no association was found between sodium intake and MS risk. It is possible that the effects on immune cells observed in experimental settings^{6,7} and in a small interventional study in healthy participants³⁴ are insufficient to induce MS, but we cannot

Figure 2 Total dietary sodium intake in deciles and multiple sclerosis risk in Nurses' Health Study (1984–2004) and Nurses' Health Study II (1991–2009)

Total dietary sodium intake assessed by food frequency questionnaire at baseline was adjusted for energy intake using the residual method²² and subsequently calibrated using data from the Women's Lifestyle Validation Study.^{23,24} Pooled hazard ratios (HR) and 95% confidence intervals (CI) adjusted for age, latitude of residence at age 15 (north, middle, south), ancestry (southern European, Scandinavian, other Caucasian, other), pack-years of smoking (0, <10, 10–24, ≥25), supplementary vitamin D intake (0, <400, ≥400 IU/d), body mass index at age 18 (<18.5, 18.5–<25, 25–<30, ≥30 kg/m²), and total energy intake.

exclude that sodium could be involved in the development of other autoimmune diseases.²⁸ As we did not investigate disease modification, we cannot evaluate whether sodium might worsen the disease course.^{5,8}

There are several possible explanations for our findings. It could be that sodium does not play a role in MS. Experimental settings do not necessarily translate to the complex human biology and epidemiologic studies play a complementary role in producing evidence, especially when randomized clinical trials cannot be performed. It is also possible that there is an effect for more extreme sodium doses, which our study, though large, was not powered to investigate. Still, we could not detect any trend, or any indication of a potential dose–response effect. This suggests that a strong involvement of sodium in the MS pathogenesis is unlikely and such a finding would have implications for few individuals. Alternatively, sodium may manifest its harmful potential only in interaction with a certain genetic predisposition, as has been suggested in one study assessing effects on EAE course,³⁵ or in interaction with other environmental factors, as has been reported for the risk of rheumatoid arthritis in smokers.²⁸ However, we could not detect an association among ever-smokers in our study. Moreover, there could be residual negative confounding present from a still unidentified factor associated with salt intake and MS risk. Our findings could also be a chance finding, although this is unlikely because they are consistent for both baseline

and cumulative exposure in 2 large cohorts and there was, as previously mentioned, no trend perceivable.

This study on the association between dietary sodium intake and risk of adult-onset MS has several strengths contributing to its validity and relevance. Information was collected prospectively, which is important for the assessment of dietary exposures, as retrospective studies on diet are especially prone to bias.²² Using a validated FFQ allows performing a study of this scale and still receiving reliable and valid information significantly correlated with the measurement from diet records. Repeated measurements allow for time-varying exposures and thus individual and secular behavioral changes over time to be considered. The regular update of the Harvard nutrient database contributed to minimizing the risk of exposure misclassification. As neurologists reviewed the medical records of every incident case, the probability of misclassification of onset and diagnosis was low in this study.

There are some limitations to this study. It includes only women and future studies need to verify whether the same observations can be made in men, who have a higher average sodium intake than women.³⁶ An association only in men, however, could not be reconciled with a more pronounced increase in MS incidence in women over the last decades, which could at least partially explain the observed higher female-to-male ratio.³⁷ Further, over 95% of women in this study are Caucasian, and we cannot conclude whether the lack of association between sodium intake and MS risk is generalizable to other ethnic groups. Moreover, we assessed sodium intake during adulthood, and it is possible that intake during childhood or adolescence may be the more relevant exposure.³⁸ Further, even though the food sources contributing most to sodium intake are included in the study questionnaires, FFQs tend to underestimate true sodium intake.²² Individuals display a high day-to-day variability of sodium consumption and salt content in similar foods might be within a range of values. However, the gold standard to assess sodium intake, excretion in multiple 24-hour urine samples, is not practical for large, prospective, epidemiologic studies. Moreover, assessments by FFQ are reasonably correlated with those achieved by the gold standard according to the WLVS.²³ By ranking individuals according to their exposure, we investigated their relative average sodium intake and compared extremes in a large population. We were thus not dependent on perfect accuracy in the estimation of absolute intake. In addition, based on data from this validation study, we could correct sodium intake reported by FFQ in our study for the systematic measurement error. Ideally, future studies should investigate the association between sodium intake and MS using the gold standard directly.³⁹

This study provides evidence that increased dietary sodium intake does not increase MS risk, as previously suggested by experimental studies. Moderating dietary sodium intake is nevertheless favorable with regard to the prevention of cardiovascular disease.⁴⁰

AUTHOR CONTRIBUTIONS

Marianna Cortese contributed to data analysis and interpretation and to drafting and revising the manuscript and figures. Changzheng Yuan contributed to data analysis and interpretation and to revising the manuscript and figures. Tanuja Chitnis contributed to data acquisition and interpretation and to revising the manuscript and figures. Alberto Ascherio contributed to obtaining funding, study concept and design, data analysis and interpretation, and revising the manuscript and figures. Kassandra L. Munger contributed to obtaining funding, study concept and design, data analysis and interpretation, and drafting and revising the manuscript and figures.

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DISCLOSURE

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This Week's *Neurology*® Podcast

ExACTly zero or once: A clinically helpful guide to assessing genetic variants in mild epilepsies (see the August 2017 issue of *Neurology*® *Genetics*)

This podcast begins and closes with Dr. Robert Gross, Editor-in-Chief, briefly discussing highlighted articles from the September 26, 2017, issue of *Neurology*. In the first segment, Dr. Jim Kiely talks with Dr. Samuel Berkovic about his *Neurology: Genetics* paper on assessing genetic variants in mild epilepsies. In the second part of the podcast, Dr. Alberto Espay focuses his interview with Dr. David Sulzer on Parkinson disease and autoimmunity.

Disclosures can be found at Neurology.org.

No CME will be offered this week: Interviews based on articles from *Neurology*® *Clinical Practice*, *Neurology: Genetics*, and *Neurology*® *Neuroimmunology & Neuroinflammation* are excluded from the CME program.

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