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The red cell distribution width and anemia in association with prevalent dementia

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Abstract

The red cell distribution width (RDW), a measure of anisocytosis, independently predicts outcomes in cardiovascular disease and chronic disease mortality. Little is known about the RDW, or the interplay between RDW and anemia, in relation to dementia risk. We evaluated the association between the RDW and prevalent dementia, overall and by anemia status, among 2556 older community-dwelling adults participating in the Chicago Health and Aging Project. RDW measurements came from complete blood counts, and participants underwent diagnosis for dementia according to standard clinical criteria. Five hundred twenty-five participants were diagnosed with dementia. Elevated RDW was associated with increased odds of having dementia: after adjusting for age, sex, race, and education, the odds of prevalent dementia increased progressively over increasing quartile of RDW ($P_{trend}=0.02$), and persons in the highest RDW quartile (14.8%) had 42% greater odds of having dementia than those in the lowest quartile (odds ratio [OR], 1.42; 95% confidence interval [CI], 1.05–1.92). Per unit (%) increment in RDW, the odds of dementia were higher by 6% (OR, 1.06; 95% CI, 1.00–1.13). Findings were similar upon further adjustment for health behaviors and diabetes. In analyses adjusted for hemoglobin

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Statistical analyses

Final analyses conducted by Mr. Todd S. Beck, MS (statistical programmer for the Rush Institute for Healthy Aging, Rush University Medical Center, Chicago, IL), under the supervision of Drs. Weuve and Evans.

Conflicts of Interest

Dr. Weuve serves as a consultant to the Alzheimer's Association and is the co-director of the AlzRisk Project. Drs. Carlos F. Mendes de Leon, David A. Bennett, Xinqi Dong, and Denis A. Evans report no disclosures.

Contributions of the Authors

Dr. Weuve: drafting and revising the manuscript for content; study concept and design; analysis or interpretation of data; study supervision/coordination; obtaining funding.

Dr. Mendes de Leon: drafting and revising the manuscript for content; study concept and design.

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concentration, the RDW-dementia association was attenuated, while the inverse association between hemoglobin and dementia remained significant. However, RDW was associated with dementia more strongly among participants without anemia (OR, 1.09; 95% CI, 1.00–1.43) than among those with anemia (OR, 0.99; 95% CI, 0.86–1.18), although this difference was not statistically significant. The RDW, a readily available and inexpensive hematologic measure, may offer novel information about dementia risk, particularly among persons without anemia. Future studies should establish the RDW's ability to predict risk prospectively.

Keywords

Alzheimer's disease; anemia; dementia; red cell distribution width; risk factors

INTRODUCTION

The red cell distribution width (RDW) is an automated measure performed as part of a complete blood cell count (CBC), and it indicates the heterogeneity of red blood cell sizes, i.e., anisocytosis. The RDW predicts outcomes in cardiovascular disease,^{1–3} as well as cardiovascular, cancer, and chronic lower respiratory disease mortality, independent of other established risk factors, anemia and nutritional deficiencies.^{4–5} These associations are present even among persons whose RDW lies within the clinical reference range. The mechanisms underlying these findings remain unclear and are likely diverse; for example, new data have raised the possibility that anisocytosis may be an integrative marker of oxidative stress and inflammation.^{3, 6}

Little is known about the RDW in relation to other chronic diseases of aging, particularly dementia. RDW's associations with cardiovascular risk factors and outcomes^{1–2, 7} suggest at least one link—that RDW may influence or reflect cerebrovascular pathology, which increases the likelihood of manifesting clinical dementia for a given level of underlying Alzheimer disease (AD) pathology.⁸ Moreover, the association between RDW and mortality appears to be stronger among individuals without anemia than those with anemia,⁹ suggesting that the RDW captures critical information about risk apart from that provided by hemoglobin. The identification of important signals of dementia is important for ongoing efforts to develop “risk scores” for dementia^{10–11} that aim to identify individuals who will most likely benefit from interventions that slow the onset or progression of the disease.^{12–13}

Therefore, we conducted an exploratory, cross-sectional epidemiologic study of the RDW in relation to dementia in a cohort of community-dwelling older adults, and further explored whether this relation depended on participants' anemia status. This investigation capitalized on available data from participants in a large established cohort study of older adults.

METHODS

Study Population

We conducted our study using data from participants in the Chicago Health and Aging Project (CHAP), a population-based, longitudinal study designed to identify risk factors for Alzheimer disease (AD) and other age-related chronic health conditions.¹⁴ The target

recruitment population was defined as all residents aged 65 years and older of three adjacent neighborhood areas on the south side of Chicago. Between 1993 and 1996, CHAP conducted a complete census of the community area. Of the 7,813 age-eligible residents, 6,158 (78.9%) were enrolled for the baseline interview. Data collection at this baseline cycle and at subsequent triennial follow-up cycles took place during in-person interviews administered by study staff at the participants' homes. As of the third cycle (in 2000), CHAP began to enroll successive age cohorts, consisting of community residents who had turned 65 since the inception of the study. As of the fourth cycle (in 2003) and continuing thereafter, CHAP also started to enroll residents aged 65 years and older from an adjacent community area. Data collection methods were identical to those employed in the original study population.

At each triennial study cycle, a stratified random sample of participants underwent an in-depth clinical evaluation, in addition to the regular evaluation in which all members of CHAP participated. We randomly selected participants for these clinical evaluations from strata defined by age, sex, race and performance on the brief cognitive assessment.¹⁴ The clinical evaluation usually took place in their homes, conducted by a team of examiners led by a neurologist. Specially trained nurse clinicians performed structured neurological examinations and medical histories. The collection of whole blood, from which RDW was measured, and the evaluation of participants for dementia took place during this evaluation. Altogether, of the 2562 participants who had valid data on RDW and dementia diagnostic status, 2556 participants had sufficient covariate data for inclusion in our analyses (no missing data on age, sex, race, education). This study was approved by the Institutional Review Board of Rush University Medical Center.

Measurement of RDW

Phlebotomists and nurses drew whole blood specimens from consenting participants. Complete blood counts (CBCs), which include estimates of the RDW, hemoglobin and mean corpuscular volume (MCV), were performed on these specimens by a Beckman Coulter MAXM Instrument (or equivalent) at the Quest Laboratory (Wood Dale, IL). Some participants had repeated CBCs, because they were randomly selected for clinical evaluation on more than one study cycle, or because they had CBCs as part of ancillary studies within the CHAP. For analyses of RDW and dementia, we used the participants' first eligible wave of data. However, we used the repeated CBCs to evaluate within-person consistency in RDW over time.

Assessment of Dementia

A senior neuropsychologist, blinded to age, sex, race, and clinical data other than the participant's educational level, occupation, and information about sensory or motor deficits, reviewed the results of 17 cognitive performance tests and summarized impairment in each of five areas (orientation, attention, memory, language, and perception). Diagnosis of dementia required the study neurologist's or geriatrician's assessment of loss of cognitive function and impairment in two or more areas on cognitive performance testing. The diagnosis of AD used the criteria of the National Institute of Neurological and

Communicative Disorders and Stroke–Alzheimer Disease and Related Disorders Association.¹⁵

Measurement of Key Covariates

Participants reported their date of birth, race, and level of attained education. Responding to structured questions¹⁶ at each regular assessment, they reported their engagement in behaviors such as cigarette smoking, alcohol consumption, and physical activity, and also provided information on their history of physician-diagnosed conditions (e.g., myocardial infarction, stroke, diabetes, cancer, high blood pressure). Blood pressure was also measured at each assessment. We classified participants as having anemia using World Health Organization hemoglobin thresholds (<12 g/dL for women; <13 g/dL for men).¹⁷

Statistical Analyses

We computed weighted frequencies of RDW to estimate the distribution of RDW in the community-based population from which the stratified random samples of participants were selected. Observation weights were the inverse of the stratified sample probabilities.¹⁴

We explored within-person consistency in RDW over time by computing Spearman correlations between pairs of repeated RDW estimates measured over a range of intervals (e.g., less than one year apart to 15 years apart). We compared the means and frequencies of several key participant characteristics across quartiles of RDW, using *F*, chi-square and Kruskal-Wallis tests.

RDW and odds of dementia—Using logistic regression models, we evaluated the relative odds of dementia by RDW level. To test the linear trend of the association between RDW quartile and dementia odds, we fit a model containing an ordinal term for RDW quartile in which participants were assigned the median of their respective quartile. Associations between the RDW and dementia odds were monotonic and approximately linear (on the logarithmic scale), thus our primary analyses concerned RDW as a continuous variable. Because the putative mechanisms linking RDW to dementia are, as of yet, unclear, we explored models that were adjusted for several different sets of covariates. The core set comprised age, sex, race (African-American, white), and education (years). To this model, we added, on an individual basis, *APOE* $\epsilon 4$ carriership (any, none) and *APOE* $\epsilon 2$ carriership (any, none). We also explored additional adjustment of the core model for, collectively, smoking status (current, former, never), alcohol intake (none, up to 1 drink/day, >1 drink/day), time spent walking (< 180, 180 minutes per week), and diabetes status. Serum vitamin B12 and kidney function, via several estimated glomerular filtration rates,^{18–20} were not associated with prevalent dementia in our data, and additional adjustment of the RDW-dementia models for these factors did not alter our findings. Thus, we did not consider these factors any further.

We also examined the RDW-dementia association within strata of *APOE* $\epsilon 4$ carriership, *APOE* $\epsilon 2$ carriership and race. In sensitivity analyses, we excluded those in the highest quartile of RDW. In separate analyses, we excluded the baseline cycle of clinical evaluation data which likely contained more prevalent cases and prevalent cases of longer duration than

cases detected in subsequent cycles. By focusing on newly developing cases, this approach more closely approximates a prospective design in which RDW level precedes diagnosis, especially if measured RDW levels remain stable over several years. Our primary analyses concerned all-cause dementia, but we also fit analogous models of dementia due to AD (excluding cases of dementias due to other causes).

RDW, anemia, hemoglobin, and dementia odds—Hemoglobin concentration in blood is strongly inversely correlated with RDW, and hemoglobin concentration²¹ and anemia status²² have been associated with dementia risk in some populations. We first explored the potential contribution of hemoglobin level and RDW to dementia risk by modeling the association of each of these hematologic parameters with dementia separately and then together. A previous study found a U-shaped association between hemoglobin and cognitive aging outcomes, with elevated risks at the lowest and highest hemoglobin levels;²¹ thus, we fitted models with and without a quadratic term for hemoglobin. To make the estimates of association more comparable, we derived the prevalence odds ratio (OR) corresponding to a standard deviation (SD) *increment in RDW* and a SD *decrement in hemoglobin* concentration. Prior research has indicated that the RDW predicts mortality more strongly among persons without anemia.⁹ Because the approach above of analyzing RDW and hemoglobin could mask a similar difference with respect to dementia, we further evaluated the relation of RDW to dementia by anemia status.

We estimated and compared each pair of stratum-specific estimates of the RDW-dementia association by including a cross-product with RDW in the model (e.g., RDW x *APOE ε4* carriership, RDW x anemia status, etc.). We performed all analyses using SAS v9.3 (Cary, NC).

RESULTS

RDW and key population characteristics

Likely owing to their older age (65+) and higher prevalence of anemia, RDW in this community-based population of older adults was higher than the RDW observed in the general non-institutionalized US population of middle-aged and older adults, with 46% of the CHAP population (Figure 1), versus about 20% of US adults aged 45 and older,⁵ having an RDW of 14% or greater. Compared with participants in the lower quartiles of RDW, those in higher quartiles were significantly more likely to be older, African American (versus white), and to have attained fewer years of formal education (Table 1). Those with higher RDW were also significantly more likely to have greater levels of disability and less likely to regularly engage in walking. RDW was not associated with blood pressure, but higher RDW corresponded to lower total cholesterol and triglyceride levels. As expected, higher RDW corresponded to greater likelihood of anemia. However, while the RDW followed an inverse, monotonic association with red cell hemoglobin concentration, its association with red cell volume (i.e., mean corpuscular volume [MCV]) was slightly U-shaped, with higher RDW with both low and high MCV (Figure 2) indicating that RDW may reflect both microcytotic and macrocytotic phenomena in these older adults. Finally, in

these unadjusted analyses, higher RDW was associated with significantly worse global cognitive score.

In the entire CHAP population, 285 participants had RDW measurements from more than one study cycle. RDWs generally preserved their ranks over intervals of several years: the Spearman correlations were 0.71, 0.59, and 0.72 among participants with RDWs assessed 1 year (N=44), 2–3 years (N=123), and 4–5 years (N=34) apart (all $P < 0.0001$). Correlations were less consistent and generally weaker over longer intervals, although sample sizes for these comparisons were smaller.

RDW and odds of dementia

In this study population, 525 persons were diagnosed with dementia. In analyses adjusted for age, sex, race, and education, RDW was associated with increased odds of having dementia (Table 2). The odds of dementia were greater with progressively increasing quartile of RDW ($P_{trend} = 0.02$), and the odds of dementia among those in the highest quartile of RDW were 42% higher than the odds among those in the lowest RDW quartile (95% confidence interval [CI] of the odds ratio [OR], 1.05–1.92). Modeling RDW as a continuous variable, a single-unit (%) increment in RDW corresponded to a 6% increase in prevalence odds, although this finding was of borderline statistical significance. This result remained unchanged with adjustment for smoking status, alcohol intake, time spent walking, and diabetes status. Likewise, it remained similar with adjustment for *APOE ε4* and *APOE ε2* carriership (results not shown). The association between RDW and prevalent dementia did not vary notably or significantly by race or by *APOE ε4* carriership (Table 2). Among persons not carrying an *APOE ε2* allele, the association (OR, 1.09; 95% CI, 1.01–1.17) was somewhat stronger than among persons carrying an *ε2* allele (OR, 0.94; 95%, 0.78–1.14), but the difference in these associations was not statistically significant. Exclusion of persons in the highest quartile of RDW did not meaningfully change the findings (Table 2). However, the association between RDW and prevalent dementia became statistically significant when we excluded observations from the baseline evaluation cycle (Table 2) which likely contained a larger fraction of prevalent cases of longer duration. Finally, the association of RDW with dementia due to AD (OR, 1.07; 95% CI, 1.00–1.14; based on 492 cases) was similar to that with all-cause dementia.

RDW, anemia, hemoglobin, and dementia odds

Adjusting for age, sex, race, and education, one SD decrement in hemoglobin concentration corresponded to a dementia prevalence OR of 1.17, a statistically significant association that was noticeably larger than the OR corresponding to a SD increment in RDW (OR, 1.10; $P=0.07$) (Table 3). In analyses mutually adjusted for RDW and hemoglobin, both OR were attenuated—the OR for RDW considerably, while the OR for hemoglobin remained statistically significant. Modeling hemoglobin as a quadratic term did not change these findings.

The association of RDW with dementia was more pronounced among participants without anemia (OR, 1.09; 95% CI, 0.99–1.20) than among participants with anemia (OR, 0.99; 95%

CI, 0.90–1.09), although this difference did not reach statistical significance ($P_{interaction}=0.1$)(Table 2).

DISCUSSION

In this study of 2556 community-dwelling older adults, higher RDW was associated with modestly increased odds of prevalent dementia, independent of age, sex, race, and education. This finding was unchanged with further adjustment for other factors such as *APOE ε4* carriership, diabetes, and smoking history. Elevated RDW was also associated with increased odds of prevalent AD. The association was especially pronounced among persons not carrying an *APOE ε2* allele. Adjustment for hemoglobin level attenuated the RDW-dementia association in the overall study population, whereas the association of hemoglobin with dementia was significant, even after adjusting for RDW. However, the RDW-dementia association appeared to vary by anemia status: RDW was associated with increased dementia odds among persons without anemia but not among those with anemia.

To our knowledge, our study is the first to directly evaluate in detail the association between RDW and a measure of neurocognitive aging. Previous studies reported associations that were not adjusted for other factors, and their findings were inconsistent. A study of older women found a higher prevalence of impaired cognitive function among those with higher RDW.⁶ By contrast, in a small case-control study, RDW was not associated with AD or AD duration in unadjusted analyses.²³ Likewise, a larger investigation of hemoglobin in relation to cognitive decline and AD computed unadjusted associations between incident dementia and several hematologic parameters, and found no association with RDW.²¹

The mechanisms linking RDW to dementia are not clear yet likely to be numerous. While anisocytosis could reduce oxygen delivery to the brain—representing a direct relation of RDW to dementia risk—it is more conceivable that RDW is an integrative marker for underlying processes that both cause anisocytosis and influence dementia risk. Among the processes that promote anisocytosis are alterations in DNA synthesis (e.g., via folate or vitamin B12 deficiency), rapid red cell restoration (due to oxygen-related disruption of erythropoietin or other perturbations of erythropoiesis), and impaired heme synthesis.^{3, 24} The most common cause of elevated RDW in older adults may be the “anemia of inflammation and chronic disease,” which, in addition to encompassing folate or vitamin B12 deficiency, can arise from chronic kidney disease.²⁵ Elevated RDW also has been associated with: systemic inflammation;^{4, 6} indices of oxidative stress;⁶ increased blood viscosity as indicated by elevated fibrinogen;⁵ diabetes;^{5, 26} history of coronary heart disease;⁴ and history of stroke.⁵ Each of these factors appears also to be associated with poor cognition, cognitive decline, dementia, or dementia pathology.^{8, 27–34}

Higher RDW is strongly correlated with lower hemoglobin concentration, and many of the hypothesized mechanisms listed above may pertain to hemoglobin as well. Several studies have found worse cognitive decline and increased dementia risk among persons with lower hemoglobin.^{21–22} Interestingly, in new brain autopsy data, lower hemoglobin three years prior to death corresponded to chronic macroscopic infarction but not chronic microscopic infarction or other dementia-related neuropathologies,³⁵ meaning that elevated RDW could

offer information about dementia risk in addition to what hemoglobin provides, if RDW is related to pathways other than macroscopic vascular damage. A variant on this scenario appears to be present in data on *mortality*, in which RDW remained a significant predictor of mortality risk even after adjusting for hemoglobin and other covariates.⁴⁻⁵ By contrast, in our study, adjustment for hemoglobin substantially attenuated the association of RDW with *dementia* risk. Lower hemoglobin level was significantly associated with dementia, consistent with previous studies. Moreover, this association persisted even after adjustment for RDW, which is a new finding. However, similar to the pattern of findings on RDW and mortality,⁹ the association between RDW and dementia was noticeably (although not statistically) stronger among non-anemic persons than anemic ones, providing evidence that the RDW may provide novel information about risk, at least in non-anemic persons.

Several limitations of our study warrant mention. Most important, because of our study's cross-sectional design, it is not possible to distinguish elevated RDW that precedes dementia from elevated RDW caused by dementia. Notably, while elevated RDW is associated with increased cardiovascular disease and stroke mortality,^{4, 9, 26} a recent study found no association between RDW and incident disease.²⁶ However, when we excluded dementia cases identified in the baseline cycle, RDW remained significantly associated with increased odds of dementia. This sensitivity analysis may approximate a prospective design, given our preliminary findings suggesting that RDW levels preserve their ranks over several years. Nonetheless, a study of incident disease will be able to address this temporal question more directly. The exclusion of baseline cases also may have addressed another potential source of bias: the cases remaining in this analysis were likely to have developed more recently than those included and less likely to include a disproportionate number of persons with traits associated with surviving dementia (traits including a normal RDW). Uncertainty about the mechanisms linking RDW to dementia make it difficult to construct analytical models that address sources of confounding while not inappropriately adjusting for causal intermediates between RDW and dementia. While it is unlikely that any of the variables included in our primary analyses mediate an association between RDW and dementia, it is possible that other sources of confounding remain, such as vitamin deficiency. Finally, as the CHAP study population comprises older adults who are African American or white and who reside in a specific urban region, our findings may not generalize to other older adult populations.

Because the RDW is inexpensively and routinely measured and could be informative about dementia risk, particularly in individuals without anemia, future studies should examine its ability to predict *incident* dementia and whether interventions on this measure are effective in reducing dementia risk.

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Figure 1.
Estimated^a distribution of red cell distribution width (RDW) in CHAP, a community-based population of African American and white older adults.

Figure 2.
Mean corpuscular volume (MCV) and red cell distribution width (RDW).

Table 1

Characteristics of study participants, by quartile of RDW.

	Quartile of RDW				P value ^d
	Lowest N=611	2nd 13.1–13.8% N=690	3rd 13.9–14.7% N=613	Highest 14.8% N=642	
Age, mean (sd), years	78.9 (6.4)	80.1 (6.3)	79.6 (6.7)	79.5 (6.4)	0.01
Male, %	42	41	39	36	0.1
African American (vs white), %	37	46	62	72	<0.0001
Education, % ^b					<0.0001
0–8 years	11	10	14	17	
9–12 years	40	44	42	46	
13–16 years	37	34	35	29	
17–30 years	13	12	9	8	
APOE ε4 (any), %	33	31	34	34	0.7
APOE ε2 (any), %	14	19	18	18	0.07
Anemic, %	16	25	29	47	<0.0001
Smoking status, %					0.5
Never	51	49	50	47	
Former	41	42	40	43	
Current	8	9	10	10	
Alcoholic drinks consumed per day, %					<0.0001
None	59	63	66	76	
>0 to 1	33	31	30	19	
2 or more	8	6	4	5	
Walks 3 hours/week, %	29	17	19	15	<0.0001
Disability, median Nagi score (higher=worse)	0	1	1	1	<0.0001
Self-rated health, 75 th percentile (higher=worse)	2	3	3	3	<0.0001
Total cholesterol, mean (sd), mg/dL	208 (39)	201 (41)	196 (43)	191 (45)	<0.0001
Triglycerides, mean (sd), mg/dL	162 (88)	144 (77)	138 (79)	130 (72)	<0.0001
Systolic blood pressure, mean (sd), mm Hg	136 (18)	138 (20)	136 (20)	136 (22)	0.2
Diastolic blood pressure, mean (sd), mm Hg	76 (11)	77 (11)	75 (12)	77 (13)	0.1

Self-reported history of:

	Quartile of RDW					<i>P</i> value ^a
	Lowest N=611 13.0%	2nd 13.1–13.8% N=690	3rd 13.9–14.7% N=613	Highest N=642 14.8%		
Hypertension, %	49	56	63	70		<0.0001
Cardiovascular disease, %	13	15	17	18		0.03
Stroke, %	9	11	11	16		0.003
Diabetes, %	5.4	8.1	9.1	12.0		0.0005
Cancer, %	26	25	22	24		0.5
Global cognitive score, ^c mean (sd), standard units	0.15 (0.72)	0.05 (0.74)	−0.06 (0.76)	−0.19 (0.71)		<0.0001

^a*P* value corresponding to *F* test (comparing means), likelihood chi-square test (comparing percentages), or Kruskal-Wallis test (comparing medians).

^bThe percentages in the lowest RDW quartile column do not add to one hundred due to rounding.

^cThe average *z* score from 17 tests of cognitive function administered as part of the clinical evaluation.

Table 2Multivariable-adjusted^a association of the RDW with prevalent dementia.

Model	# cases/total # of participants	Prevalence odds ratio (95% confidence interval)	P value
All participants, by quartile of RDW			
Lowest quartile (13.0%)	94/611	<i>Referent</i>	
2 nd quartile (13.1–13.8%)	134/690	1.17 (0.86–1.58)	0.3
3 rd quartile (13.9–14.7%)	134/613	1.24 (0.91–1.68)	0.2
Highest quartile (14.8%)	163/642	1.42 (1.05–1.92)	0.02
<i>P_{trend} = 0.02</i>			
<i>Per % increment in RDW</i>			
All participants	525/2556	1.06 (1.00–1.13)	0.07
+ adjusted for smoking status, alcohol intake, and walking	525/2555	1.06 (0.99–1.13)	0.1
+ adjusted for smoking status, alcohol intake, walking, and diabetes	525/2555	1.06 (0.99–1.13)	0.1
Excluding participants in the highest quartile of RDW	362/1552	1.12 (0.94–1.33)	0.2
Excluding participants in the baseline evaluation cycle	294/1782	1.12 (1.04–1.21)	0.003
Participants with anemia	219/752	0.99 (0.90–1.09)	0.8
Participants without anemia	306/1804	1.09 (0.99–1.20)	0.07
<i>P_{interaction} = 0.1</i>			
African American participants	346/1388	1.06 (0.98–1.14)	0.2
White participants	179/1168	1.07 (0.95–1.19)	0.3
<i>P_{interaction} = 0.9</i>			
Participants with an <i>APOE ε4</i> allele	190/761	1.05 (0.93–1.18)	0.5
Participants without an <i>APOE ε4</i> allele	275/1563	1.08 (0.99–1.17)	0.08
<i>P_{interaction} = 0.4</i>			
Participants with an <i>APOE ε2</i> allele	73/397	0.94 (0.78–1.14)	0.5
Participants without an <i>APOE ε2</i> allele	392/1927	1.09 (1.01–1.17)	0.03
<i>P_{interaction} = 0.2</i>			
RDW and dementia due to Alzheimer disease	492/2523	1.07 (1.00–1.14)	0.06

^a Unless otherwise specified, all results were adjusted for age, sex, race, and education.

Table 3Comparison of RDW and hemoglobin associations^a with prevalent dementia.

Model	RDW		Hemoglobin concentration	
	Prevalence odds ratio per SD ^b increment (95% confidence interval)	P value	Prevalence odds ratio per SD ^b decrement (95% confidence interval)	P value
RDW	1.10 (0.99–1.21)	0.07	-	-
Hemoglobin concentration	-	-	1.17 (1.05–1.30)	0.005
RDW + hemoglobin concentration	1.06 (0.95–1.17)	0.3	1.15 (1.03–1.29)	0.02

^a All results were adjusted for age, sex, race, and education.^b SD, standard deviation. The SD of RDW was 1.52%, and the SD of hemoglobin was 1.55 g/dL.