Letters

RESEARCH LETTER

Variation in Rates of Autoimmune Thyroid Disease by Race/Ethnicity in US Military Personnel

The relationship between Graves disease and race/ethnicity is undefined. Based on thyroid antibody prevalence, the rates of Hashimoto thyroiditis may be highest in whites and lowest in blacks.[1,2]

Using a large and comprehensive data set of medical diagnoses for all US active duty service personnel, we calculated age-standardized incidence rates for Graves disease and Hashimoto thyroiditis by race/ethnicity.

Methods | The institutional review boards of Walter Reed National Military Medical Center, Johns Hopkins Bloomberg School of Public Health, and University of Queensland School of Population Health approved this study. All data were deidentified and aggregated. No individual consent was required.

The Defense Medical Surveillance System (DMSS) maintains comprehensive records of inpatient and outpatient medical diagnoses among all active-duty military personnel, recorded using *International Classification of Diseases, Ninth Revision, Clinical Modification* (*ICD-9-CM*) codes. The study population was all US active duty military aged 20 to 54 years from January 1, 1997, to December 31, 2011.

Race/ethnicity was self-reported at enrollment. The DMSS groups race/ethnicity as non-Hispanic white (white); Hispanic; non-Hispanic black (black); Asian/Pacific Islander, American Indian/Alaskan Native; other; or unknown. Because the latter 3 groups had few cases and were unable to be standardized, we performed an analysis using the first 4 categories. The 2010 US resident population aged 20 to 54 years by race/ethnicity, sex, and age was obtained from the US Census Bureau for use as a standard population.[3]

Cases were identified with a specific diagnosis of either Graves disease (*ICD-9-CM* code 242.0) or Hashimoto thyroiditis (*ICD-9-CM* code 245.2). Cases were defined as individuals with an inpatient *ICD-9-CM* diagnosis code in any diagnosis position or 2 or more first diagnosis-position outpatient codes separated by at least 7 days.

Because persons with Graves disease and active thyroiditis are not eligible to enlist in the US military, the first diagnosis code was considered the incidence date. We calculated directly standardized incidence of Graves disease and Hashimoto thyroiditis among race/ethnicities, standardized to

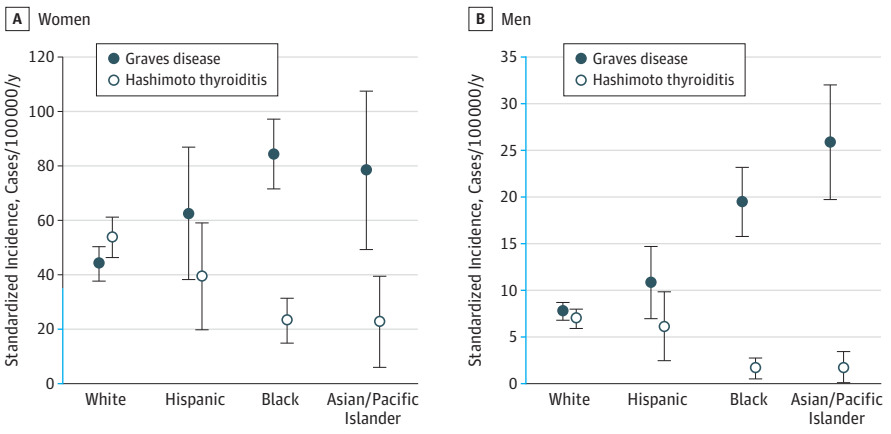
Table. Demographics and Total Case Numbers

	Non-Hispanic White	Hispanic	Non-Hispanic Black	Asian/ Pacific Islander	American Indian/Alaskan Native	Other[a]	Unknown	Total
Women, person-years of follow-up (in 1000s)	1445	286	829	120	38	66	93	2877
Age group, %								
20-24 y	38.1	47.1	32.8	34.8	47.4	48.5	35.1	
25-29 y	25.4	26.5	24.8	28.7	25.7	27.0	29.1	
30-34 y	14.3	13.2	17.1	16.8	12.7	12.4	16.3	
35-44 y	18.2	11.5	22.1	16.3	11.9	10.5	16.5	
45-54 y	3.9	1.6	3.1	3.3	2.2	1.7	2.9	
No. of cases								
Graves disease	497	121	563	94	6	41	56	1378
Hashimoto thyroiditis	517	76	86	22	4	19	34	758
Men, person-years of follow-up (in 1000s)	11 351	1646	2769	655	193	297	483	17 394
Age group, %								
20-24 y	33.8	40.5	29.1	28.5	42.3	44.5	29.5	
25-29 y	23.3	25.4	22.7	24.1	25.5	25.2	25.1	
30-34 y	15.9	15.4	18.2	17.5	14.6	13.3	17.9	
35-44 y	22.8	16.5	26.6	24.6	15.5	14.6	23.7	
45-54 y	4.1	2.2	3.3	5.2	2.2	2.3	3.8	
No. of cases								
Graves disease	671	138	339	142	6	42	50	1388
Hashimoto thyroiditis	442	44	20	7	5	9	21	548

[a] Self-reported as other.

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Figure. Graves Disease and Hashimoto Thyroiditis by Race/Ethnicity



Incidence rates for each race/ethnicity were age-standardized to the 2010 US resident population. Error bars indicate 95% confidence intervals. The y axis segments shown in blue indicate range from 0 to 35 in both graphs.

the 2010 US population, and generated incidence rate ratios (IRRs) using Stata version 12.1 (StataCorp).

Results | The DMSS recorded 20 270 688 person-years of eligible active-duty service during the study period (85.8% male). There were 1378 cases of Graves disease in women and 1388 cases in men and 758 cases of Hashimoto thyroiditis in women and 548 cases in men (**Table**).

Compared with whites, the IRR for Graves disease was significantly elevated in black women (IRR, 1.92; 95% CI, 1.56-2.37) and men (IRR, 2.53; 95% CI, 2.01-3.18) and Asian/Pacific Islander women (IRR, 1.78; 95% CI, 1.20-2.66) and men (IRR, 3.36; 95% CI, 2.57-4.40) (**Figure**). In contrast, Hashimoto thyroiditis incidence was highest in whites and lowest in black women (IRR, 0.33; 95% CI, 0.21-0.51) and men (IRR, 0.22; 95% CI, 0.11-0.47) and Asian/Pacific Islander women (IRR, 0.31; 95% CI, 0.17-0.56) and men (IRR, 0.23; 95% CI, 0.07-0.72) (Figure).

Discussion | To our knowledge, this is the first report to identify that Graves disease is more common in blacks and Asian/Pacific Islanders compared with whites. In contrast, the relationship between Hashimoto thyroiditis and race is well known,[1,2] and is confirmed by our results.

The differences in incidence by race/ethnicity may be due to different environmental exposures, genetics, or a combination of both. Our results are not easily attributable to the strongest known environmental risk factor, cigarette smoking.

Smoking is associated with an increased risk for Graves disease and a decreased risk of Hashimoto thyroiditis.[4,5] Whites have the highest smoking rates in the US military.[6] However, whites had higher rates of Hashimoto thyroiditis and lower rates of Graves disease.

Our data set presumes accurate coding; it is possible that some cases of Hashimoto thyroiditis causing hypothyroidism were coded as unspecified-acquired hypothyroidism and not Hashimoto thyroiditis. The military population may also tend to have lower Hashimoto thyroiditis estimates because it is younger than the general population and has higher smoking prevalence.

Another potential limitation is the misclassification of prevalent cases as incident cases, although this is unlikely to be important because diagnosis during the teenage years is rare. We also cannot rule out military-specific exposures affecting the pattern of autoimmune thyroid disease, which could limit the generalizability of our findings.

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Drafting of the manuscript: McLeod, Matos, Hutfless.
Critical revision of the manuscript for important intellectual content: McLeod, Caturegli, Cooper, Hutfless.
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Study supervision: Cooper, Hutfless.

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COMMENT & RESPONSE

Dopamine vs Nesiritide for Acute Heart Failure With Renal Dysfunction

To the Editor Dr Chen and colleagues[1] evaluated the role of low-dose dopamine and nesiritide as individual strategies in treating patients with acute decongested heart failure while attempting to preserve or improve renal function. The trial found no benefit from low-dose dopamine or nesiritide with standard diuretic therapy. Despite significant advances in understanding the pathophysiology of acute heart failure, contemporary therapies have failed to have an effect.[2]

The Renal Optimization Strategies Evaluation (ROSE) trial raises more questions than it answers. The trial included a fair proportion of patients with heart failure and preserved ejection fraction. In subgroup analyses, only patients with heart failure with reduced ejection fraction showed a suggestion of a response to low-dose nesiritide and dopamine. Heart failure with preserved and reduced ejection fraction are often treated as one entity in clinical practice and research.

Similar drugs are used for heart failure with reduced and preserved ejection fraction, with little to no success. Mechanistic, observational, and randomized studies have revealed important differences in these heart failure subgroups.[3,4] Is it time to start designing trials targeting these groups separately?

Chen et al[1] used cystatin C as a clinical end point for response to therapy. Cystatin C appears to be promising as a biomarker for acute heart failure because it is less reliant on muscle mass. This is an important issue in the heart failure population, which tends to be predominantly elderly. However, more experience needs to be gained regarding its potential for evaluation as a therapeutic end point.

The trial included patients with advanced renal disease and lower glomerular filtration rates than in other contemporary trials. This population might more closely reflect a real-world practice. However, it is unclear whether the advanced renal disease in itself makes such patients nonresponders to any therapeutic measure. It is important that investigators dissect these issues when designing future trials.

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Conflict of Interest Disclosures: The author has completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest and none were reported.

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In Reply Dr Kumar brings up 3 relevant queries regarding the ROSE trial: (1) whether future clinical trials in acute heart failure should target heart failure with preserved ejection fraction and heart failure with reduced ejection fraction separately; (2) the relevance of cystatin C as a surrogate end point; and (3) whether the advanced renal disease in the study population makes them nonresponders to any therapeutic measure.

In the ROSE trial, there was a suggestion of differential treatment effects according to the ejection fraction in both the low-dose dopamine and low-dose nesiritide strategies. Compared with patients with reduced ejection fraction, those with heart failure and preserved ejection fraction may have experienced greater decreases in blood pressure and lesser increases in stroke volume in response to the decrease in systemic vascular resistance with low-dose dopamine or nesiritide,[1] likely due to differential ventricular vascular properties. We agree with Kumar that these findings suggest that further investigation of other acute heart failure therapies may need to assess the potential for differential responses in heart failure with preserved vs reduced ejection.

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