

Editorial

Racial Disparities in the Modern Gout Epidemic

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Gout is a common hyperuricemic metabolic condition, leading to recurrent inflammatory arthritis and some of the most severe pain experienced by humans. As detailed in a recent Global Burden of Disease analysis of 195 countries and territories between 1990 and 2017,¹ the incidence, prevalence, and disability burden of gout have risen worldwide for decades, and the condition now affects > 10 million US adults (4%).² The disease burden of gout is also complicated by a higher prevalence of the metabolic syndrome and risk of cardiometabolic comorbidities.³ Further, this “modern gout epidemic” and suboptimal gout care⁴ have contributed to high rates of recurrent gout flares worldwide, rising ambulatory⁵ and emergency room visits,⁶ and hospitalizations due to gout over the past several decades.^{7,8} For example, from 1993 to 2011, US hospitalization rates due to gout doubled, whereas hospitalization rates for rheumatoid arthritis declined, narrowing the gap and soon reversing the rates between the 2 diseases.⁷ These data indicate the clear unmet need for improved gout prevention and care.

Gout has historically been considered a disease of White men who overindulged in red meats and other rich foods, and epidemiologic studies have focused on White individuals. A few epidemiologic studies have reported higher risks of gout or hyperuricemia among Black individuals (Table 1),^{2,9,10,11} particularly among women⁹; however, no studies have evaluated

the risks among other races or ethnicities in the US. Similarly, evaluation of gout risk factors (including genetics) has heavily focused on White individuals, including the deleterious factors of meat, seafood, and alcohol consumption, excess adiposity, and diuretic use,¹² and protective factors of low-fat dairy and coffee consumption, vitamin C, and healthy dietary patterns.^{12,13} This stems from a paucity of suitable multiethnic exposure data together with sufficient numbers of gout cases ascertained over time. Nevertheless, race-specific data about differential disease risk and underlying etiologic drivers are essential to address the racial disparity and health equity for prevention and care of this excruciatingly painful condition. The study by Thompson et al in this issue of *The Journal of Rheumatology*¹⁴ is the first to address these important knowledge gaps in a large-scale prospective cohort. By linking prospective data for older-aged participants from 5 self-reported racial/ethnic groups (White, Black, Native Hawaiian, Latino, and Japanese American) in the Multiethnic Cohort Study (N = 92,264 participants recruited from California and Hawaii, mean age 68 yrs) to Medicare gout claims between 1999 and 2016, the authors compared gout incidence among different race/ethnic groups within 1 cohort (ie, internal comparison), and evaluated the potential race-specific effects of several behavioral factors (diet, alcohol, vitamin C, and smoking).

The authors found Native Hawaiian, Black, and Japanese participants had a 220%, 34%, and 14% higher risk of incident gout compared to White participants, respectively, during the follow up (mean 9.6 years), whereas Latino participants had a 22% lower risk. The excess risk among Black participants agreed with previous Atherosclerosis Risk in Communities (ARIC) study findings, although its magnitude was somewhat smaller (hazard ratio 1.69 among women and 1.92 among men in the ARIC),⁹ whereas the excess risk among Native Hawaiian and Japanese participants is the first reported in the field. Various risk factors could explain these racial differences, including genetics, environmental factors, and interactions between the 2 factors. As suggested by analyses of Māori and Pacific Peoples, the excess risk among Native Hawaiians is likely influenced by genetics, their interactions with environmental factors, as well as

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Table 1. Studies reporting on racial disparities in gout burden and care in the US.

Racial Disparity	Comparison for Black vs White Race (95% CI)	Comments
Prevalence		
Chen-Xu et al, 2019 ²	4.8% (3.8–6.0) vs 4.0% (3.1–5.3)	Nationally representative sample > 99% male (VHA)
Helget et al, 2021 ¹¹	7.0% (7.0–7.1) vs 6.0% (5.9–6.0)	
Incidence		
Hochberg et al, 1995 ¹⁰	RR 1.69 (1.02–2.80)	All male physicians
Maynard et al, 2014 ⁹	Men: HR 1.92 (1.44–2.56); women: HR 1.69 (1.29–2.22)	ARIC study cohort, age 45–64 yrs at enrollment
Helget et al, 2021 ¹¹	IR 7.3 (7.1–7.5) vs 5.9 (5.8–6.0) per 1000 PY	> 99% male (VHA)
Ambulatory visits for gout		
Castro et al, 2018 ⁵	OR 1.33 (1.03–1.72)	Nationally representative sample
ULT use		
Krishnan et al, 2008 ²⁷	OR 0.18 (0.04–0.78)	Nationally representative sample
Chen-Xu et al, 2019 ²	OR 0.84 (0.53–1.34)	Nationally representative sample

ARIC: Atherosclerosis Risk in Communities; HR: hazard ratio; IR: incidence rate; OR: odds ratio; PY: person-years; RR: relative risk; ULT: urate-lowering therapy; VHA: Veterans Health Administration.

excess adiposity and lower dietary quality as evident in the study baseline. The higher risk among Japanese American participants was surprising, given the low prevalence in Japan (1.1%¹⁵) and the lower levels of BMI at baseline compared to White participants, and may be explained by their high frequency of gout risk genes¹⁶ and potentially strong interactions with Western lifestyles. Indeed, increasing serum urate levels with emergence of metabolic syndrome features were observed among Japanese immigrants who moved to the US, unlike those who continued to live in Japan.¹⁷ Widespread use of urate-lowering therapy for asymptomatic hyperuricemia in Japan (unlike in the US) may also contribute to the low prevalence of gout in Japan. Although the relative risk among Japanese participants tended to be higher than among White participants, their overall alcohol consumption was lower than that of White participants, making it unlikely as a reason for the elevated risk of gout. Higher risk among Black individuals is likely due to BMI, poor diet quality, and higher prevalence of advanced-stage chronic kidney disease, rather than genetics.¹⁸ These speculations call for mediation analyses that account for plausible causal pathways and that consider how additional social and economic factors influence the lifestyle factors studied by Thompson et al.¹⁴

Further, the authors found that the roles of alcohol, the Dietary Approaches to Stop Hypertension (DASH) diet, and vitamin C intake on gout risk, previously reported in cohorts predominantly comprising White individuals,^{13,19} largely persist among other races, despite relatively minor variations of statistical significance. Japanese tended to have a higher relative risk associated with alcohol consumption than White participants, who tended to have more clear protective effects from the DASH diet (Figure 1), whereas vitamin C supplementation (of any dose) was associated with a decreased risk of gout only among Japanese participants. Measurement errors stemming from single dietary exposure assessment (with a 21-year span, on average, between exposure and incident outcome),¹⁴ accuracy of gout endpoint ascertainment (ie, 1 International Classification of Diseases code), and older study population

(with survival effects)¹⁴ are potential reasons that could bias the findings toward null. To that end, the findings reported are likely conservative. Future studies with time-updated exposures and accurate outcome measurements would be valuable for precise quantification of risks, particularly among a wider age group that includes younger individuals. Further, given the distinctive differences between gout in male and female individuals in terms of their absolute risk as well as risk factors (eg, higher frequency of obesity and diuretic use among White females with gout, as compared to White males, and lower frequency of alcohol use),¹⁹ sex-specific studies are also warranted.

By documenting these racial disparities in the future risk of gout and investigating the effect of modifiable lifestyle factors across multiple racial/ethnic groups in the US, Thompson et al¹⁴ have made an important contribution to the field. Their race-specific findings warrant external replication, along with evaluation of modifiable risk factors in other racial/ethnic groups disproportionately affected by cardiometabolic and inflammatory rheumatic diseases, including Native American populations and descendants of other Asian countries. At the same time, advancing the field also requires a better understanding of how these and other risk factors contribute to the racial differences in gout risk, and the suitable approaches for addressing them, including mediation analyses.

From a population health standpoint, determining the attributable risk fraction of gout within each racial/ethnic group would inform both the theoretical fraction of incident gout cases avoided by eliminating each factor from the source population, and the relative importance among these factors. For example, we have shown recently that 22% of incident gout cases among a cohort of White men could be theoretically prevented by adherence to a DASH-style eating pattern alone.²⁰ For the racial groups in the Thompson et al study where DASH adherence was particularly low (eg, only 11% of Native Hawaiians and 13% of Japanese in the top quintile of DASH scores, thus with more room to improve), the attributable risk fractions of gout for diet quality could be substantially larger.

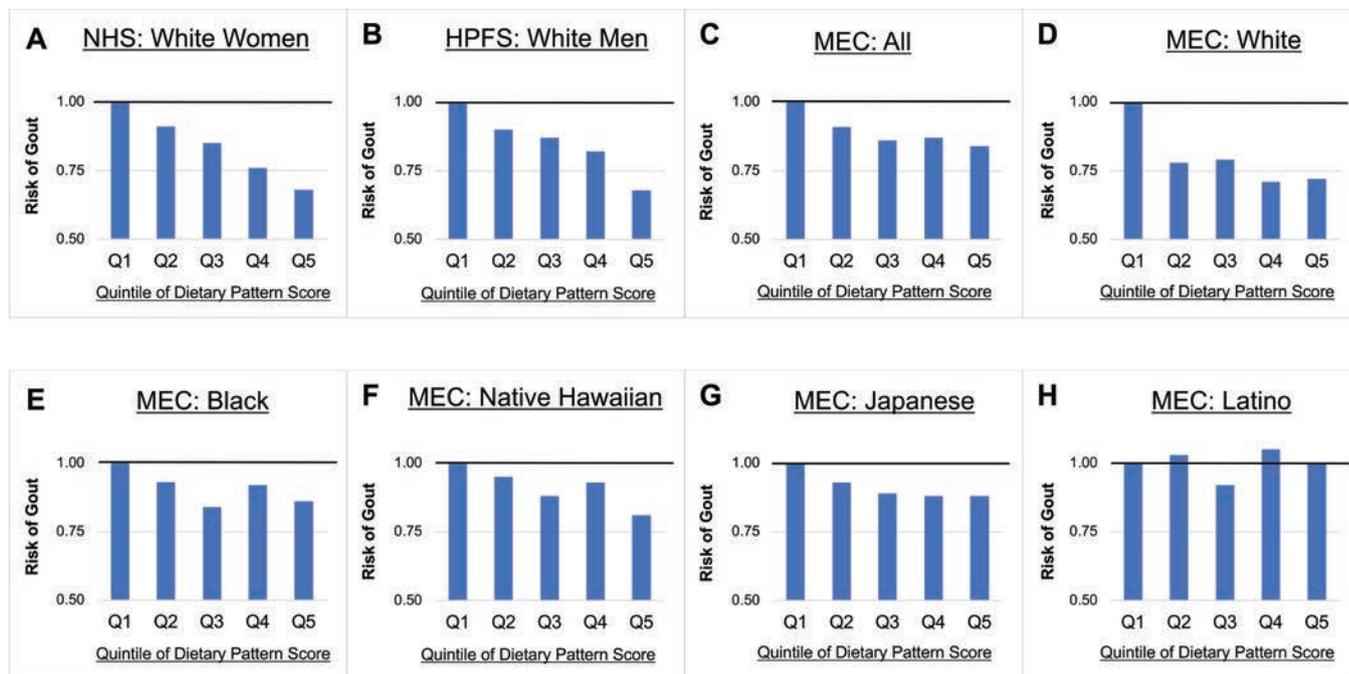


Figure 1. Multivariable hazard ratios for incident gout according to quintiles of the Dietary Approaches to Stop Hypertension (DASH) score in (A) the Nurses Health Study (NHS) cohort (predominantly White)^a; (B) Health Professionals Follow-Up Study (HPFS) cohort (predominantly White); and (C) the Multiethnic Cohort (MEC) overall^b and according to self-reported race/ethnicity: (D) White, (E) Black, (F) Native Hawaiian, (G) Japanese, and (H) Latino. ^a Adapted from Yokose et al¹⁹, JAMA Intern Med 2022 Jan 31 (Epub ahead of print). ^b Adapted from Rai et al, BMJ 2017;357:j1794 with permission from BMJ Publishing Group Ltd.

Finally, alongside these environmental factors, there is also a strong genetic component in gout, with serum urate heritability estimates of 25–60%²¹ and 183 urate-associated variants identified in the latest transethnic, multicohort genome-wide association study (GWAS).²¹ In that study and in a prior GWAS,²² some individual variants were identified that suggested ancestry-specific effects for Japanese and other populations, although no systemic ancestry-related heterogeneity was detected. Further elucidation of the genetic architecture of gout among different minority groups and of ancestry-specific gene–environmental interactions could inform on the relative contribution of genetics and modifiable factors toward the development of gout, facilitating a more personalized approach to gout prevention. For example, racial differences were observed in a recent analysis of the interactions between dietary patterns, genetic risk scores, and risk of metabolic syndrome, a condition closely related to gout.²³ Such work would build upon the gene–environmental interactions demonstrated for adiposity²⁴ and alcohol,²⁵ and suggested for sugar-sweetened beverage consumption,²⁶ for gout and hyperuricemia in European ancestry populations.

The racial disparities in gout incidence described by Thompson et al¹⁴ almost certainly reflect a complex interplay of clinical and lifestyle factors and, in many circumstances, social inequities. Lifestyle modification has the potential to reduce the risk and burden of the modern gout epidemic in all races, and of related cardiometabolic conditions, but interventions must be culturally informed and tailored to the community of interest.

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