Preventing a Large Majority of Incident Gout Cases By Modifying Key Risk Factors: Findings from a Prospective Cohort of 44,629 Men over 26 Years

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Background/Purpose: Many modifiable risk factors have been found to be independently associated with the risk of developing gout, including dietary factors (e.g., intakes of red meat and fructose), adiposity, alcohol intake, and diuretic use. Conversely, healthy dietary patterns (e.g., the Dietary Approaches to Stop Hypertension [DASH]) and a high intake of vitamin C have been shown to be independently associated with lower gout risk. However, the potential combined impact of these factors on the risk of developing gout is unknown. We aimed to estimate the proportion of incident gout cases that could theoretically be avoided through the simultaneous adoption of multiple low-risk behaviors, including low body mass index (BMI), consumption of a DASH-style eating pattern, no alcohol intake, vitamin C supplementation, and no diuretic use.

Methods: From 1986 to 2012, we prospectively followed 44,629 men free from gout at baseline in the Health Professionals Follow-up Study. Lifestyle, anthropometric, and medical information was collected at baseline and updated biennially. Dietary data were obtained using validated food frequency questionnaires at baseline and approximately every 4 years during follow-up. We ascertained incident cases of gout using the American College of Rheumatology survey criteria for gout. We defined low-risk groups according to combinations of the following five factors: a low BMI (<25kg/m²), adherence to a DASH-style diet, no alcohol intake, vitamin C supplementation (≥1500mg), and no diuretic use. Cox proportional hazard regression models were used to estimate the association of each risk factor with the development of gout and calculate the population attributable risk percent (PAR%).

Results: During 950,086 person-years of follow-up, incident gout developed in 1,687 participants. All five modifiable risk factors were independently associated with incident gout. Obesity was the single most important predictor of gout; all other risk factors were also associated with a statistically significant increased risk of gout, even after adjustment for BMI. As compared with the rest of the cohort, men in the low-risk group (comprised of all five low-risk factors; 4.4% of men) had a relative risk of gout of 0.30 (95% confidence interval [CI], 0.12 to 0.72) (Table). Accordingly, the PAR% for all
five risk factors combined was 70% (Table). The PAR% for four and three risk factors was 64% and 50%, respectively (Table).

**Conclusion:** Five modifiable risk factors accounted for 70% of incident gout cases in this large prospective cohort of male health professionals. Assuming a causal relation, our findings support the hypothesis that the vast majority of cases of gout could be prevented by modifying key risk factors.

| Table. Relative and Population Attributable Risks of Gout for Groups Defined by Combinations of Modifiable Risk Factors |
|--------------------------------------------------|-----------------|-----------------|-----------------|-----------------|
| Percentage of Men (%) | Number of Gout Cases | Relative Risk (95% CI) | PAR% |
| 3 factors in low-risk category a | 11.0 | 24 | 0.49 (0.33, 0.74) | 50 |
| 4 factors in low-risk category b | 10.3 | 15 | 0.35 (0.21, 0.59) | 64 |
| 5 factors in low-risk category c | 4.4 | 5 | 0.30 (0.12, 0.72) | 70 |

Abbreviations: BMI, body mass index. CI, confidence interval. DASH, Dietary Approaches to Stop Hypertension. PAR%, Population attributable risk percent.

Relative risks were adjusted for total energy intake, coffee intake, and histories of renal failure and hypertension.

- a Low BMI, highest quintile of DASH diet score, and no alcohol intake.
- b Low BMI, highest quintile of DASH diet score, no alcohol intake, and no diuretic use.
- c Low BMI, highest quintile of DASH diet score, no alcohol intake, no diuretic use, and vitamin C supplementation.

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