Published in final edited form as:

Arthritis Care Res (Hoboken). 2011 August ; 63(8): 1108–1114. doi:10.1002/acr.20479.

Younger age at gout onset is related to obesity in a community-based cohort

Mara A. McAdams DeMarco¹, Janet W. Maynard², Mary Margret Huizinga³, Alan N. Baer², Anna Köttgen^{1,4}, Allan C. Gelber^{1,2}, and Josef Coresh¹

¹ Department of Epidemiology, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, USA

² Division of Rheumatology, Johns Hopkins University School of Medicine, Baltimore, MD, USA

³ Division of General Internal Medicine, Johns Hopkins University School of Medicine, Baltimore, MD, USA

⁴ Renal Division, University Hospital Freiburg, Freiburg, Germany

Abstract

Objective—Obesity is associated with gout risk. It is unclear whether obesity is associated with a younger age of gout onset. We examined whether obesity is related to age at gout onset and quantified the risk of incident gout by obesity status in the Campaign Against Cancer and Heart Disease (CLUE II) study, a longitudinal community-based cohort.

Methods—CLUE II began in 1989 as a cohort study of residents living within or surrounding Washington County, Maryland. Follow-up questionnaires queried whether each participant had been diagnosed with gout by a healthcare professional. Among participants with gout, we assessed whether obesity was related to age at disease onset. We also ascertained the eighteen-year risk of incident gout according to obesity status (BMI ≥ 30 kg/m²) at baseline with cumulative incidence ratios (RR) and 95% confidence intervals (CI) from Poisson regression.

Results—Among the study population (n=15,533), 517 developed incident gout. The prevalence of obesity at baseline was 16.2%. The overall mean age at gout onset was 59.3 years. The onset of gout was 3.1 years (95% CI: 0.3, 5.8) earlier in those who were obese at baseline and 11.0 years earlier (95% CI: 5.8, 16.1) in participants who were obese at age 21, compared to their non-obese participants. The 18-year adjusted RR of gout in obese participants compared to non-obese participants was 1.92 (95% CI: 1.55, 2.37).

Conclusion—Obesity is not only a risk factor for incident gout but was associated with an earlier age at gout onset.

Keywords

Gout; Obesity; Epidemiology; Age

In the US, the incidence and prevalence of both obesity and gout is rising (1–3). Obesity has been associated with an increased risk of gout (4–7). However, two of the studies that identified this gout risk factor were conducted among male healthcare professionals (4, 5) and another included only a few women with gout (7). These findings may not be

Corresponding Author and Request for Reprints: Mara McAdams DeMarco, MS, 2024 E. Monument St, Suite 2-600, Baltimore, MD 21287, mmcadams@jhsph.edu, Phone: (410) 614-3822, Fax: (410) 550-2072.

Disclosure: None of the authors have a conflict of interest to declare.

generalized to women or to persons at risk of gout in the community setting. Community-based cohort studies are few in number yet necessary to characterize the risk of gout associated with obesity in both sexes and across a range of ages.

Although there is an established association between body weight, obesity and gout, the influence of obesity on the age of gout onset is not defined. Obesity has been shown to be associated with an earlier onset of other chronic diseases, including diabetes (8). Hospital and clinic-based studies have found that the age of gout onset was younger in men than in women (9, 10), differed across populations (11, 12), and was younger in people with a family history of gout (12, 13). However, the age of gout onset has not to date been studied in a US community-based population.

An improved understanding of the impact of obesity in relation to the age of gout onset will translate into better estimation of the risk of gout among patients who present with acute arthritis. As the prevalence of obesity continues to rise in the United States, it is important to quantify the risk of gout across the range of BMI values in both women and men, and to understand the impact of obesity on the age of gout onset in the community setting. Therefore, we estimated the risk of incident gout by baseline and early adult obesity status over 18 years of follow-up, as well as the impact of obesity on the age of gout onset. We conducted this study among 15,533 men and women in the Campaign Against Cancer and Heart Disease (CLUE II) study, a longitudinal community-based cohort with valuable information on body weight, and prospective ascertainment of gout diagnoses.

Materials and Methods

Ascertainment of Exposures and Outcome

CLUE II is a community-based cohort undertaken to identify risk factors for cancer and cardiovascular disease. At its inception in 1989, the cohort enrolled individuals, aged 13 to 87 years, who resided within or surrounding Washington County, Maryland. A baseline health assessment including a questionnaire and exam with blood pressure and phlebotomy was performed at cohort entry. Follow-up health history questionnaires were administered to participants in 1996, 1998, 2000, 2003 and 2007.

For the present study, the population was restricted to 16,103 of the original CLUE II participants who answered the gout query on the 2000, 2003 or 2007 questionnaire, as these were the only questionnaires to query the participants about gout. The dataset was further restricted to participants who self-reported white race due to the limited number of non-white participants (n=165, 1%). Additionally, participants with prevalent gout were similarly excluded from the study population. Prevalent gout was defined as self-reported age of gout diagnosis younger than the age at cohort entry, or self-reported year of gout diagnosis prior to 1989 (n=405, 3%). We defined the age of gout onset as the participant's reported age of physician diagnosis at the first affirmative report of gout. All participants provided written consent at cohort entry in 1989. The study was approved by the Institutional Review Board at the Johns Hopkins Bloomberg School of Public Health.

At baseline, participants were sent a questionnaire to self-report demographic data, including health status, gender, race, age, height, weight, weight at age 21, and treatments received for high cholesterol and hypertension. Additionally, blood pressure and cholesterol were measured at the baseline assessment. Alcohol consumption was ascertained by a self-reported food frequency questionnaire. The questionnaire collected information regarding the frequency of beer consumption (12 ounce can or bottle), wine or wine coolers (1 medium glass), and liquor (1 shot). The three alcohol intake variables were categorized as

never or less than once per month, 1 time per month to once a week, or 1 time per week or more.

Body mass index (BMI) at baseline was calculated as weight (kg) divided by height (m) squared, using the 1989 self-report of weight and height. Additionally, we calculated BMI at age 21, based on the baseline-reported values for height and weight at age 21 years.

Follow-up questionnaires were sent to the CLUE II participants in 2000, 2003 and 2007 (response rates: 63.5%, 62.2% and 55.6%, respectively). Each of these three follow-up questionnaires queried the participants as to whether they had ever received a diagnosis of gout by a healthcare professional. Additionally, participants were asked the year of diagnosis (1989 or before, 1990–1994, or 1995 or after) on the 2000 questionnaire and the age of diagnosis on the 2003 and 2007 questionnaires. We defined an incident case of gout for any participant who self-reported gout on at least one of the 2000, 2003 or 2007 follow-up questionnaires and who self-reported the onset of gout after 1989, or at an age greater than the age at cohort entry. Notably, age at gout onset was found to be reliable (correlation coefficient=0.85), self-reported gout status has been found to be reliable (3-year reliability kappa=0.73) and sensitive in this population (sensitivity=84%) (14).

Analysis of age of gout onset in relation to obesity status

We assessed the association between the various anthropometric measures and age of gout onset among the participants who reported the age of gout onset on at least one of the questionnaires. Specifically, we compared the age of gout onset by obesity status, both at baseline and at age 21 years, for all participants who responded to the 2003 or 2007 questionnaires and self-reported the age of onset. If there were any discrepancies in the reported age of onset, the first reported age was used. The 2000 questionnaire was not used because participants self-reported the categorical year of onset rather than the age of onset. T-tests were used to compare the mean age of gout onset. Additionally, we examined whether the age of gout onset differed with BMI modeled as a continuous variable, both at cohort entry and at age 21 years, using linear regression analysis. Both models were adjusted for sex, baseline blood pressure and beer, wine and liquor intake, as these factors were associated with the age of gout onset.

Analysis of the association between BMI, obesity and gout

Using all participants who responded to the gout query, we examined the association of known risk factors for gout, including age, sex, high blood pressure, elevated serum cholesterol level, and beer, wine and liquor intake with baseline obesity in this population. We then assessed the eighteen-year risk of incident gout associated with baseline obesity with cumulative incidence ratios (RR), referred to as the risk of gout; 95% confidence intervals (CI) were derived from Poisson regression analyses. We modeled the RR rather than the odds ratio using Poisson regression as gout is not a rare disease in a community cohort of adults and we reported robust standard errors. However, results were similar when ran as a logistic regression. To allow analysis of all reported cases of gout across the three follow-up surveys (2000, 2003, and 2007), the primary analysis focused on the cumulative incidence of gout (ever vs. never). We considered baseline body mass index (BMI) as a continuous variable, and present these results in 5 kg/m² increments as the exposure of interest. Next, obesity in 1989 was modeled as a categorical variable, defined as those participants having a BMI value ≥ 30 kg/m². BMI at baseline was grouped into four categories: normal weight (BMI less than 25 kg/m²), overweight (BMI 25 to 29.9 kg/m²), class I obesity (BMI 30 to 34.9 kg/m²), and class II or III obesity (BMI ≥ 35 kg/m²) (15). There were too few participants with a BMI < 18.5 kg/m² to categorize BMI as

underweight. Obesity status at age 21 was also examined, using the standard cutoff for obesity of a BMI $\geq 30 \text{ kg/m}^2$.

In multivariable analyses, we adjusted the above models for known risk factors of gout that may confound the obesity and gout association. These risk factors included sex, age, baseline alcohol intake, baseline measures of blood pressure and cholesterol, treatment for high blood pressure and hypercholesterolemia. All analyses were performed in SAS, version 9.1 (SAS Institute, Cary, North Carolina).

Results

The study population consisted of 15,533 participants, 39.3% of whom were male. The mean BMI at cohort entry, in 1989, was 25.8 kg/m^2 (SD=4.8). At baseline, 47.8% of participants were of normal weight whereas 36.0% of the participants were overweight. 2,508 participants were obese at the initial examination, in 1989, corresponding to a 16.2% baseline prevalence of obesity. Other population demographics are displayed in Table 1.

The mean BMI at age 21 was 22.1 kg/m^2 (SD=3.5). There were 449 participants who were obese at age 21 (3.1%). In addition, 882 participants did not self-report their weight at age 21. Overall, the participants reported lower BMI levels at age 21, corresponding to few participants described as being overweight and obese in young adult life.

Baseline obesity status was statistically associated with all the measured gout risk factors, suggesting that these factors may confound the association of obesity and gout (Table 1). Female and older aged participants were more likely to be obese at baseline. Additionally, obese participants had higher mean cholesterol and blood pressure values and were more likely to be treated for these conditions. Finally, beer and wine intake were associated with a decreased prevalence of obesity at baseline.

Risk of incident gout

Between 1989 and 2007, 517 CLUE II participants developed gout; there were 185 women and 332 men with incident gout. Therefore, the overall 18-year cumulative incidence of gout in this community-based population was 3.3%, corresponding to a cumulative gout incidence of 5.4% among the men and 2.0% among the women in the CLUE cohort. Additionally, gout patients were more likely to be male (RR: 2.78, 95% CI: 2.33, 3.31). There were 392 participants with gout (76% of the total gout cases) who reported both their age at the onset of gout and having gout on the 2003 or 2007 follow-up questionnaires. The overall mean age of gout onset in the population was 59.3 years (Median=59, SD=12.9, Range 25–90). For men, the mean age of gout onset was 57.8 years (SD=12.4) and for women it was 62.2 years (SD=13.3) (Figure). For men, the distribution of ages appears to have a non-Gaussian distribution, suggesting that there may be different risk factors for gout in earlier adulthood and later adulthood. As such, men developed gout at a younger age – on average, approximately four years earlier – than did the women in the study.

Age of gout onset

The age of gout onset was younger in participants who were obese compared to those who were not obese at baseline (57.1 vs. 60.2 years, t-test p-value=0.03). However, obesity at baseline was marginally associated with a difference in the age at onset of gout for women and was associated with a significantly younger age of disease onset for men (Table 2). At age 21, obesity was similarly associated with a younger age of gout onset; a difference of eleven years in those who were obese compared those who were normal weight or overweight (49.2 vs. 60.1 years, p-value<0.001). Moreover, this association persisted when examined separately for both men and women.

Though the sample size was small for the comparison of age of onset by obesity status, we additionally observed a younger age of onset for participants who were overweight or obese at age 21 in a post-hoc sensitivity analysis (data not shown).

The linear model to assess the association between BMI modeled as a continuous variable with the age of gout onset suggested that increasing values of BMI translate into an earlier age at disease onset. After adjustment for sex, blood pressure and alcohol intake a five kg/m² change in BMI was associated with a 1.11 year decrease in the age of gout onset (p-value=0.13). For every five kg/m² increase in BMI at age 21 years, there was a 4.5-year, adjusted, decrease in the age of gout onset (p-value<0.001).

Association of obesity with incident gout

The 18-year unadjusted risk of developing gout was more than two times higher (RR 2.26; 95% CI=1.89, 2.72) in obese compared to the non-obese participants. The risk of incident gout increased for every five-unit increase in BMI (RR=1.51, 95% CI=1.42, 1.59). In the categorical BMI analysis with normal baseline BMI as the comparator, the risk of incident gout was 2.62 (95% CI=2.11, 3.25) in participants who were overweight, 4.01 (95% CI=3.13, 5.14) for those who were class I obese and 3.35 (95% CI=2.33, 4.82) in those who were class II or III obese.

In the three adjusted models, baseline obesity, categorical BMI and continuous BMI were each associated with incident gout (Table 3). In the age and sex-adjusted Model 1, obesity remained associated with incident gout. Further adjustment, as portrayed in Model 2, to control for potential confounding by beer, wine and liquor intake, did not significantly change the results. In the final, fully adjusted Model 3, the risk of gout was nearly two times higher (RR 1.92; 95% CI: 1.55, 2.37) for participants who were obese, compared to those who were not obese at baseline. In addition, there was an increased risk of gout for every five-unit increase in BMI at baseline. The risk of developing gout for class I obese participants was similar to that of those who were class II or III obese, arguing for a dose-response for categorical BMI that plateaus at BMI's greater than 30. Additionally, an increased risk of gout was also observed for those participants who were obese at age 21 years. In the adjusted models, the risk of incident gout was nearly twice as high for participants who were obese at age 21 (RR=1.82, 95% CI=1.21, 2.73) compared to those who were not obese.

In sex-stratified, adjusted analyses, no differences were observed in the association of obesity and gout between the sexes (Male: RR=1.98, 95% CI= 1.52, 2.58; Female: RR=1.78, 95% CI=1.25, 2.54). Nor were the sex-stratified analyses different for obesity at age 21 and gout: (Male: RR=1.55, 95% CI= 0.91, 2.64; Female: RR=2.29, 95% CI=1.22, 4.30). There was no sex by obesity interaction for obesity at baseline and early adult obesity. Therefore, there is not a difference in the associations observed between obesity incident gout by sex.

To evaluate for survival bias we analyzed whether prevalent gout was related to mortality. These sensitivity analyses suggest that prevalent gout was not related to reporting on the 2003 and 2007 questionnaires or 3- and 7-year mortality. Additional sensitivity analyses suggested that the results were similar when the odds ratios (OR) were calculated using logistic regression (OR=2.01, 95% CI: 1.61, 2.52; for obese vs. non-obese) and when incident rate ratios (IR) were calculated using Poisson regression and imputation for categorical onset (IR=1.99, 95% CI: 1.59, 2.48; for obese vs. non-obese) suggesting that the results are robust to the analytic method. However, the Poisson regression for the RR is the most comprehensive analysis because it does depend on the reported onset and is not inflated due to the prevalence of gout in this population.

Discussion

In a community-based cohort of both men and women, we quantified the 18-year risk of incident gout associated with obesity and found that being obese at study entry, as well as at age 21 years, were both associated with an earlier age of gout onset. Our study confirms that obesity is a strong risk factor for gout even after accounting for known risk factors and co-morbid conditions. Additionally, this is the first study to show that those who were obese at age 21 developed gout 11 years earlier than their non-obese counterparts.

Our study confirms the previously noted association of obesity and gout (4–7). Our study extends the research that has been previously limited to males (7) and male health professionals (4, 5). One prospective study of male physicians noted a greater than two-fold increase in risk of gout in those whose BMI increased more than 1.88 kg/m² prior to 35 years of age (4). The Johns Hopkins Precursors study of male medical students found the relative risk of gout to be 1.12 per one unit increase in BMI at age 35, yet this relationship was not seen when evaluating weight at age 22 years (4). In contrast to the Precursors cohort, our study did find that early life obesity was associated with incident gout in men (4). These differences may be secondary to power as there were only sixty cases of gout in this cohort; there may not have been adequate power to detect such a difference. Additionally, the association between obesity on the development of gout was also examined in the Health Professionals Follow-up Study (5). Results similar to our own were reported according to the three categories of BMI common to both studies: 25–29.9, 30–34.9 and ≥35 kg/m². Though we did not adjust for dietary factors, we found that the risk of gout was similar to Choi (5), who reported a relative risk of 1.95, 2.33 and 2.97, respectively. Additionally, this study found the risk of gout for those who were obese at age 21 was 1.66 times greater compared to those with normal BMI, which was similar to our results about early adult obesity. Unlike this study of male health professionals, we were unable to test short-term vs. long-term effects of obesity because this was not the focus of our study. Similar to our results, a long-term follow-up study of gout in the Framingham cohort, obesity was associated with greater than two-fold risk in both men and women (6).

Within the hospital-based setting, the age of gout onset has been demonstrated to be younger in men than in women (9, 10). It is also clinically important to determine whether the age of onset varies by obesity status over adulthood. One study reported the association of BMI and the age of first rheumatology clinic visit in Taiwan (13). For study participants aged 19–44, 45–64 and 65 years or older, the odds ratios of gout for overweight compared to normal weight gout patients were 1.70, 1.17 and 1.36, respectively. Additionally, this study found that a higher percentage of gout patients who were aged 14–44 years at their first visit were overweight than those patients with gout who first presented for medical care in mid-adult and late-adult life. However, this study did not assess the association between obesity prior to the development of gout in relation to the age of disease onset. Notably, our study quantified the association between two measures of adult BMI prior to gout onset and suggests that an earlier onset of gout is in fact associated with obesity. However, we were unable to assess all the components of metabolic syndrome and future studies should address this hypothesis in a community-based cohort.

Studies over the past decades have provided evidence that obesity causes insulin resistance and this in turn may lead to hyperuricemia and gout. The degree of insulin resistance correlates directly with the serum urate level and inversely with the renal urate clearance (16, 17). In one trial of patients with gout, weight loss following a prescribed change in macronutrient intake was associated with a decrease in serum urate levels and in the frequency of gout attacks (18). The components of insulin resistance, hyperinsulinemia, hypertension, dyslipidemia and obesity were all related to hyperuricemia in one

epidemiology study, though obesity was the strongest risk factor (19). Leptin has been found to be a pathogenic factor for hyperuricemia in patients with obesity and has been hypothesized to be the link between the two (20, 21). These findings have supported the argument that hyperuricemia is an integral component of the insulin resistance syndrome (19, 22).

The main strength of this study is our large sample size, with over 15,533 participants in CLUE II. This large population-based study and the prospective nature of the study design allowed us to estimate the risk of incident gout rather than focus on prevalent gout alone. Therefore, we can be more confident that our measures of adiposity precede the development of gout. Additionally, this study is well suited to test the hypothesis that BMI at age 21 years is related the age of gout onset because CLUE II collected health data from adult participants of all ages. Recall of early adult weight has been shown to be valid in a previous epidemiology study (23). Therefore, we were able to assess the role of early adult obesity on the age of onset without introducing bias that would occur in cohorts with an age inclusion criteria. Our sensitivity analyses suggest a limited role of survival bias.

We acknowledge that the present study defined incident gout by self-report of a physician diagnosis of gout instead of either confirmation of monosodium urate crystals from a gouty effusion or fulfillment of the ACR Criteria (24). Additionally, the survey did not collect information on how the physician diagnosed gout for each participant. Self-report of a physician diagnosed gout may under- or over-represent cases. However, our results will only be affected if there is differential misclassification of gout. There is no evidence that the presence of obesity leads to an under- or over-diagnosis of gout. We have found a self-report of gout and the self-report of the age of onset to be both reliable and valid (14). Additionally, community-based cohorts that collect the outcomes data through questionnaires do not routinely allow for assessment of measured clinical risk factors such as serum urate, hormone levels or renal insufficiency. However, this community-based cohort study did measure cholesterol and blood pressure at baseline.

We were unable to adjust for the number of grams of alcohol intake but rather categorical beer, wine and liquor intake. However, the results did not differ when we used different parameterizations of these measures of alcohol intake. Additionally, the study did not obtain the baseline menopause status of the female participants. This study did not measure weight or height and therefore, relies on self-report of height, weight and weight at age 21. Previous studies have suggested that self-report of height and weight in addition to early adult weights are valid for population-based studies (23, 25). Nor did the study routinely collect multiple measures of weight to allow for analysis of time-varying BMI and obesity. Finally, our study like all observational studies is limited by missing data. However, this missing data is unlikely to bias our results because we only adjusted for baseline factors, which are unlikely to be missing based on obesity status. Additionally, using cumulative incidence ratios assumes that all participants were followed until the development of gout or end of the study and that loss to follow-up does not differ by obesity status. Finally, we used age at diagnosis as a proxy for the age of first attack and the age of onset analyses were limited to small sample sizes for those who were obese at age 21. However, we performed sensitivity analyses to test the association between increased BMI in the overweight category and observed comparable results. Our results do not rule out the possibility that obese participants frequent their physician's office more often than non-obese participants and are thus more likely to be diagnosed with gout at a younger age.

Our study confirms an increase in risk of developing gout in obese men and extends these findings to women. We further found that early adulthood obesity impacts upon the age of gout onset, with gout occurring at substantially younger ages, in those who are obese at

cohort entry or at body weight levels reported at age 21 years. The results of this community-based cohort contribute important clinical findings to the gout literature pertaining to the risk and age of gout onset in relation to body mass index, an association particularly important in the context of the growing epidemic of obesity in the US and other countries. In the clinical setting our study suggests that gout should be considered in the differential diagnosis of acute arthritis in both obese men and women at all ages.

Acknowledgments

We would like to thank the CLUE II participants for their ongoing participation. Additionally, we would like to thank Judith Bolton Hoffman for her help with obtaining the data.

Funding: CLUE II was supported by the National Institute of Aging (Grant number U01 AG18033) and National Cancer Institute (Grant number R01 CA105069). A T32 training grant from the National Heart, Lung, and Blood Institute grant (5T32HL007024) to MMD. A KL2 Research Grant from the National Center for Research Resources (1KL2RR025006-01) to JWM, and the Donald B. and Dorothy Stabler Foundation to ACG.

References

1. Ogden CL, Carroll MD, Curtin LR, McDowell MA, Tabak CJ, Flegal KM. Prevalence of overweight and obesity in the United States, 1999–2004. *JAMA*. 2006; 295(13):1549–55. [PubMed: 16595758]
2. Arromdee E, Michet CJ, Crowson CS, O’Fallon WM, Gabriel SE. Epidemiology of gout: is the incidence rising? *J Rheumatol*. 2002; 29(11):2403–6. [PubMed: 12415600]
3. Lawrence RC, Felson DT, Helmick CG, Arnold LM, Choi H, Deyo RA, et al. Estimates of the prevalence of arthritis and other rheumatic conditions in the United States. Part II. *Arthritis Rheum*. 2008; 58(1):26–35. [PubMed: 18163497]
4. Roubenoff R, Klag MJ, Mead LA, Liang KY, Seidler AJ, Hochberg MC. Incidence and risk factors for gout in white men. *JAMA*. 1991; 266(21):3004–7. [PubMed: 1820473]
5. Choi HK, Atkinson K, Karlson EW, Curhan G. Obesity, weight change, hypertension, diuretic use, and risk of gout in men: the health professionals follow-up study. *Arch Intern Med*. 2005; 165(7):742–8. [PubMed: 15824292]
6. Bhole V, de Vera M, Rahman MM, Krishnan E, Choi H. Epidemiology of female gout: 52-Year follow-up of a prospective cohort. *Arthritis Rheum*.
7. Hall AP, Barry PE, Dawber TR, McNamara PM. Epidemiology of gout and hyperuricemia. A long-term population study. *Am J Med*. 1967; 42(1):27–37. [PubMed: 6016478]
8. Hillier TA, Pedula KL. Characteristics of an adult population with newly diagnosed type 2 diabetes: the relation of obesity and age of onset. *Diabetes Care*. 2001; 24(9):1522–7. [PubMed: 11522693]
9. Lally EV, Ho G Jr, Kaplan SR. The clinical spectrum of gouty arthritis in women. *Arch Intern Med*. 1986; 146(11):2221–5. [PubMed: 3778053]
10. Puig JG, Michan AD, Jimenez ML, Perez de Ayala C, Mateos FA, Capitan CF, et al. Female gout. Clinical spectrum and uric acid metabolism. *Arch Intern Med*. 1991; 151(4):726–32. [PubMed: 2012455]
11. Annemans L, Spaepen E, Gaskin M, Bonnemaire M, Malier V, Gilbert T, et al. Gout in the UK and Germany: prevalence, comorbidities and management in general practice 2000–2005. *Ann Rheum Dis*. 2008; 67(7):960–6. [PubMed: 17981913]
12. Yu KH, Luo SF. Younger age of onset of gout in Taiwan. *Rheumatology (Oxford)*. 2003; 42(1):166–70. [PubMed: 12509631]
13. Chen SY, Chen CL, Shen ML. Manifestations of metabolic syndrome associated with male gout in different age strata. *Clin Rheumatol*. 2007; 26(9):1453–7. [PubMed: 17256101]
14. McAdams MA, Maynard JW, Baer AN, Köttgen A, Clipp S, Coresh J, et al. Reliability and validity of the self-report of physician-diagnosed gout in the Campaign Against Cancer and Heart Disease (CLUE II) and Atherosclerosis Risk in the Community (ARIC) Cohorts. 2010. ePublished ahead of print in the *Journal of Rheumatology*

15. World Health Organization. Obesity : Preventing and managing the global epidemic: Report of a WHO consultation. Geneva: World Health Organization; 2000.
16. Vuorinen-Markkola H, Yki-Jarvinen H. Hyperuricemia and insulin resistance. *J Clin Endocrinol Metab.* 1994; 78(1):25–9. [PubMed: 8288709]
17. Facchini F, Chen YD, Hollenbeck CB, Reaven GM. Relationship between resistance to insulin-mediated glucose uptake, urinary uric acid clearance, and plasma uric acid concentration. *JAMA.* 1991; 266(21):3008–11. [PubMed: 1820474]
18. Dessein PH, Shipton EA, Stanwix AE, Joffe BI, Ramokgadi J. Beneficial effects of weight loss associated with moderate calorie/carbohydrate restriction, and increased proportional intake of protein and unsaturated fat on serum urate and lipoprotein levels in gout: a pilot study. *Ann Rheum Dis.* 2000; 59(7):539–43. [PubMed: 10873964]
19. Rathmann W, Funkhouser E, Dyer AR, Roseman JM. Relations of hyperuricemia with the various components of the insulin resistance syndrome in young black and white adults: the CARDIA study. *Coronary Artery Risk Development in Young Adults. Ann Epidemiol.* 1998; 8(4):250–61. [PubMed: 9590604]
20. Fruehwald-Schultes B, Peters A, Kern W, Beyer J, Pfutzner A. Serum leptin is associated with serum uric acid concentrations in humans. *Metabolism.* 1999; 48(6):677–80. [PubMed: 10381138]
21. Bedir A, Topbas M, Tanyeri F, Alvur M, Arik N. Leptin might be a regulator of serum uric acid concentrations in humans. *Jpn Heart J.* 2003; 44(4):527–36. [PubMed: 12906034]
22. Emmerson B. Hyperlipidaemia in hyperuricaemia and gout. *Ann Rheum Dis.* 1998; 57(9):509–10. [PubMed: 9849306]
23. Troy LM, Hunter DJ, Manson JE, Colditz GA, Stampfer MJ, Willett WC. The validity of recalled weight among younger women. *Int J Obes Relat Metab Disord.* 1995; 19(8):570–2. [PubMed: 7489028]
24. Wallace SL, Robinson H, Masi AT, Decker JL, McCarty DJ, Yu TF. Preliminary criteria for the classification of the acute arthritis of primary gout. *Arthritis Rheum.* 1977; 20(3):895–900. [PubMed: 856219]
25. McAdams MA, Van Dam RM, Hu FB. Comparison of self-reported and measured BMI as correlates of disease markers in US adults. *Obesity (Silver Spring).* 2007; 15(1):188–96. [PubMed: 17228047]

Figure.
The density plot of the age distribution of gout onset for men and women. The density represents the percentage of CLUE II participants that developed gout at a given age.

Table 1

Risk factors for gout among 15,533 CLUE II participants by baseline (1989) obesity status

Baseline risk factors	Full cohort	Non-obese population	Obese population
Male sex	6,100 (39.3%)	5,190 (39.9%)	907 (36.2%) **
Age (years)	47.0 (15.3)	46.7 (15.7)	48.9 (12.9) **
Cholesterol (mg/dL)	204.8 (39.2)	203.0 (38.9)	214.6 (39.5) **
Blood pressure (mmHg)			
Systolic blood pressure	124.8 (16.3)	123.3 (16.1)	132.5 (15.4) **
Diastolic blood pressure	78.7 (9.5)	77.8 (9.3)	83.7 (9.1) **
Treated hypertension	2,393 (15.4%)	1,660 (12.7%)	731 (29.1%) **
Treated hypercholesterolemia	581 (3.7%)	477 (3.1%)	104 (4.2%) **
Beer			
Never or < 1 per month	9,208 (70.5%)	7,630 (69.3%)	1,572 (77.1%) **
1 time per month-1 per week	1,918 (14.7%)	1,677 (15.2%)	241 (11.8%)
1 per week or more	1,932 (14.8%)	1,707 (15.5%)	225 (11.0%)
Wine			
Never or < 1 per month	10,191 (77.9%)	8,441 (76.4%)	1,744 (85.9%) **
1 time per month-1 per week	2,281 (17.4%)	2,037 (18.5%)	244 (12.0%)
1 per week or more	607 (4.6%)	565 (5.1%)	42 (2.1%)
Liquor			
Never or < 1 per month	10,530 (80.7%)	8,797 (79.9%)	1,727 (84.7%) **
1 time per month-1 per week	1,635 (12.5%)	1,414 (12.8%)	221 (10.8%)
5 times a week or more	890 (6.8%)	798 (7.3%)	92 (4.5%)

Mean and standard deviations were reported for continuous variables. Obesity is defined as a body mass index greater than or equal to 30 kg/m².

* p-value < 0.05 comparing obese to non-obese

** p-value < 0.001 comparing obese to non-obese

Table 2

Age at gout onset according to body mass index (BMI), and obesity status, at baseline and age 21, in CLUE II cohort

	Total		Women		Men	
	N	Mean age in years (SD)	N	Mean age in years (SD)	N	Mean age in years (SD)
Baseline BMI						
Not obese	271	60.2 (12.4)	83	62.5 (13.2)	188	59.2 (11.9)
Obese	121	57.1 (13.6)	45	61.6 (13.6)	76	54.5 (13.0)
<i>Difference (95% CI)</i>		3.1 (0.3, 5.8)*		0.9 (-4.0, 5.9)		4.7 (1.40, 8.0)*
BMI at age 21						
Not obese	365	60.1 (12.5)	119	63.3 (12.8)	246	58.6 (12.1)
Obese	24	49.2 (10.5)	8	49.6 (12.2)	16	48.9 (8.7)
<i>Difference (95% CI)</i>		11.0 (5.8, 16.1)**		13.6 (4.4, 22.9)*		9.7 (3.6, 15.8)*

** t-test P-value <0.001

* t-test P-value < 0.01

SD is standard deviation. Obesity is defined as a body mass index greater than or equal to 30 kg/m². CI is 95% confidence interval.

Table 3

Adjusted cumulative incidence ratios (RR) of incident gout by body mass index (BMI), and obesity status, at baseline and age 21 in the CLUE II cohort

	Model 1	Model 2	Model 3
	RR (95% CI)	RR (95% CI)	RR (95% CI)
Obesity at baseline	2.25 (1.84, 2.75)	2.23 (1.82, 2.73)	1.92 (1.55, 2.37)
Categorical baseline BMI			
Normal weight	1	1	1
Overweight	2.03 (1.61, 2.58)*	2.01 (1.59, 2.56)*	1.88 (1.47, 2.39)*
Class I obesity	3.34 (2.54, 4.39)	3.31 (2.52, 4.36)	2.86 (2.15, 3.80)
Class II and III obesity	3.51 (2.36, 5.20)	3.49 (2.35, 5.19)	2.72 (1.80, 4.12)
5 unit (kg/m²) change in baseline BMI	1.53 (1.43, 1.65)	1.53 (1.42, 1.65)	1.44 (1.33, 1.56)
Obesity at age 21	2.06 (1.38, 3.07)	2.06 (1.38, 3.08)	1.82 (1.21, 2.73)

*
p-value for trend <0.001

Model 1: Age and sex adjusted

Model 2: Model 1 + beer, wine and liquor intake

Model 3: Model 2 + measures blood pressure and cholesterol and treatment for high blood pressure and high cholesterol

BMI is body mass index (kg/m²). Obesity is defined as a body mass index greater than or equal to 30 kg/m². CI is 95% confidence interval.