

# Calorie Control Council Response to Choi & Curhan “Soft drinks, fructose consumption, and the risk of gout in men: prospective cohort study”

Choi HK, Curhan G. *Brit Med J*. 2008 Feb 9;336:309-12.

## Background

Author Choi is an associate professor of medicine at the Arthritis Research Centre of Canada, Department of Medicine, Vancouver General Hospital, University of British Columbia, Vancouver, BC. Author Curhan is associate professor of medicine in the Channing Laboratory, Department of Medicine, Brigham and Women’s Hospital, Harvard Medical School, Boston, MA. The authors have written widely on the subject of gout<sup>i,ii,iii,iv</sup>, occasionally with influential Harvard nutritionist Walter Willett<sup>v,vi</sup>, a sometimes critic of HFCS. Willett is thanked at the end of the paper for his critical review of the manuscript. Since this paper was not internally peer reviewed by the *British Medical Journal*, but rather was externally reviewed, it may be reasonably concluded that Walter Willett performed the external review.

## Hypothesis

The authors seem to have adopted the hypothesis of Bray *et al*<sup>vii</sup> that fructose/HFCS are uniquely responsible for the obesity/metabolic syndrome epidemic. They have extended the Bray hypothesis to contend in this paper that fructose/HFCS are also unique contributors to gout.

## Justifications

- Dietary recommendations to gout patients focus on restrictions of purine and alcohol intake, with no restriction on sugar sweetened soft drinks; although
- Sugar sweetened soft drinks contain “large amounts of” fructose; and
- Fructose is the only carbohydrate known to increase uric acid levels.

## Experimental Design

Choi & Curhan followed a population of 51,529 male health professionals in a prospective cohort study over a 12-year period. The data were gathered via annual validated food frequency questionnaires covering the entire previous year. Cox proportional hazards modeling was used to estimate the relative risk for incident gout in all multivariate analyses.

## Author Conclusions

1. This study provides prospective evidence that consumption of sugar sweetened soft drinks and fructose is strongly associated with an increased risk of gout.
2. Fructose rich fruits and fruit juices may also increase the risk.
3. Diet soft drinks are not associated with the risk of gout.
4. The[se] various benefits and risks associated with individual fructose rich food items should be carefully considered in the potential public health applications of our findings.

## Critique

- Cited evidence of a fructose role in increased uric acid production includes a

recent study by Nakagawa & Johnson<sup>viii</sup>, and questionable 30-year old studies by Emmerson<sup>ix</sup> and others<sup>x,xi,xii</sup>.

- The Nakagawa & Johnson citation is one of the first in which a link was hypothesized between increasing prevalence of the metabolic syndrome in the US and fructose-induced hyperuricemia.
  - Emmerson reported in 1974 that fructose but not glucose (both at 50% of total calories) elevated serum and urine uric acid levels in human subjects.
  - The authors also cite a study by Beck-Nielsen<sup>xiii</sup> from 1980, in which 1000 extra kcal as fructose for 7-days reduced insulin binding and insulin activity in healthy subjects.
  - Emmerson and Beck-Nielsen's results are typical of other reported fructose-induced metabolic upsets at excessive concentrations and in the absence of glucose. Their applicability to the human diet is of questionable significance, since they represent two monosaccharide intake extremes (pure fructose or pure glucose) that are rarely encountered outside the laboratory.
  - Significantly, Lowndes & Rippe<sup>xiv</sup> recently reported no effect of HFCS vs. sucrose on uric acid production in normal human subjects.
- 755 cases of gout were reported over the 12 years in a cohort subset of 46,393 men — an incidence of 1.6%. This is consistent with the incidence of gout in the general population reported by Lawrence et al<sup>xv</sup> (1.3%), but is somewhat lower than that reported by Kramer & Curhan<sup>xvi</sup> (2.7%).
  - The authors reported that increasing intake of “sugar sweetened soft drinks” was associated with increased risk of gout (Table 2). However, the effect was significant only at soft drink serving frequencies of 5-6/week and greater, which accounted for 143 of the 755 reported gout cases (19%). But it must be noted that the 0.3% incidence of gout represented by this serving frequency (143 cases ÷ 46,393 subjects) represents a very small fraction of the 2.7% incidence reported earlier by author Curhan for the general population.

Furthermore, the significant fructose effect for “sweetened cola” and “other sweetened soft drinks” appeared only at serving frequencies of 1/day and greater (Table 2). These serving frequencies presented even fewer (7%) of the 755 reported gout cases. And it must be further noted that the 0.1% incidence of gout represented by this serving frequency represents an even smaller fraction of Curhan's estimate for the general population (2.7%).

Thus, incident gout attributed to elevated sugar sweetened soft drink consumption of all types in this study is very low, indeed.

- It is worth noting, as well, that the authors found no correlation between BMI, hypertension or chronic renal failure and fructose (free and total) intake (Table 1). Thus, these data do *not* support the hypothesis of Bray et al<sup>7</sup> that HFCS/fructose is uniquely responsible for the increased incidence of obesity. Nor do they, incidentally, support the hypothesis of Gersch et al<sup>xvii</sup> that fructose accelerates the progression of chronic kidney disease.

- The authors noted that intake of caffeine, fructose, meats and high fat dairy foods tended to increase with increasing consumption of sugar sweetened soft drinks (Table 1). However, the authors made no attempt to explain the contradictory observation that BMI and intake of alcohol, caffeine, meats and high fat dairy foods decrease with increasing consumption of free fructose. This contradiction necessarily casts doubt on the quality of the data and/or the method of analysis, since the nutritive sweetener in U.S. sugar sweetened soft drinks is predominantly HFCS — about half free fructose and half free glucose. It is simply not possible for sugar sweetened soft drinks and a principal caloric constituent (free fructose) to have divergent associations with intakes of caffeine, meats and high fat dairy foods.
- It was noted above that the authors have published extensively on the role of purines, alcohol, dairy foods, proteins, obesity, hypertension and lifestyle choices in the development of gout. Given their vast experience in the field, it is most unfortunate that they missed the opportunity to put into perspective the hypothesized risk of gout due to fructose versus these well-established and proven causative factors.

### **Industry Reaction**

British Soft Drinks Association<sup>xviii</sup>

"The leading research in this field does not support the notion that gout is caused by either soft drinks or fruit juice consumption. The strongest risk factor for developing gout is family history yet this was not taken into account in the research. Neither the National Institute of Health nor the National Institute for Arthritis and Musculoskeletal and Skin Diseases in the USA, where this study was conducted, implicate fructose as a causal risk factor for gout. Research conducted on gout over the last century shows that it is foods and beverages that are high in purines, (such as alcohol, and certain meats) that are more strongly linked to uric acid metabolism, which causes gout. Soft drinks do not contain purines and scientific studies have shown that neither sucrose nor high fructose corn syrup affect uric acid excretion."

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