Review

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Hyperuricemia as risk factor for coronary heart disease incidence and mortality in the general population: a systematic review and meta-analysis

DOI 10.1515/cclm-2015-0523
Received June 5, 2015; accepted June 16, 2015; previously published online July 21, 2015

Abstract: Previous meta-analyses reported no significant or weak association between hyperuricemia (HU) and coronary heart disease (CHD). We updated the literature search, systematically reviewing retrieved papers. The peer-reviewed literature published from 1965 to December 2014 was searched using Medline and Embase. We included prospective cohort studies involving adults (sample size ≥100) with no cardiovascular disease (CVD) and a follow-up of at least 1 year. Studies were excluded if they considered as outcome the CVD incidence/mortality without separately reporting data on CHD, did not adjusted for major confounders and if the 95% confidence interval (CI) for risk ratio (RR) was not available. Relative risk or hazard ratio estimates, with the corresponding CIs, were obtained. For CHD incidence 12 populations were included (457,915 subjects [53.7% males]). For CHD mortality seven populations were included (237,433 subjects [66.3% males]). The overall combined RR were 1.206 (CI 1.066–1.364, p=0.003) for CHD incidence and 1.209 (CI 1.003–1.457, p=0.047) for CHD mortality, respectively. Subgroup analysis showed a marginal (incidence) and not significant (mortality) association between HU and CHD in men, but an increased risk for CHD incidence and mortality in hyperuricemic women (RR 1.446, CI 1.323–1.581, p<0.0001, and RR 1.830, CI 1.066–3.139, p=0.028, respectively). The risk markedly increases for urate concentrations >7.0 mg/dL. HU appears to increase the risk of CHD events in the general population, mainly in adult women. This finding requires, however, further investigation.

Keywords: coronary heart disease; meta-analysis; uric acid.

Introduction

In humans, uric acid represents the end-product of the catabolism of the purine nucleosides arising from dietary and endogenous nucleic acid. The total body pool of exchangeable urate greatly differs among genders, from ~600 mg in adult women up to 1200 mg in men. It increases at values ranging from 18,000 to 30,000 mg in patients with gout. Most of excreted urate (~75%) is lost in the urine and the remainder into the gastrointestinal tract [1]. The existence of an association between uric acid and cardiovascular disease (CVD) was hypothesized more than 50 years ago and since then a number of epidemiologic studies have reported a relation between hyperuricemia (HU) and a variety of cardiovascular conditions, including hypertension, stroke, coronary heart disease (CHD), kidney disease, peripheral vascular disease, heart failure, metabolic syndrome, obesity, and diabetes [2].

The specific relationship between HU and CVD risk (incidence of major cardiovascular events and/or cardiovascular mortality) has been studied in three meta-analyses, with a scarce agreement in obtained results [3–5]. Wheeler et al. [3] did not find a significant association between HU and CHD in the combined analysis of eight studies with adjustment for possible confounders. In a meta-analysis of 26 eligible studies, Kim et al. [4] showed that HU may marginally increase the CHD incidence...
(pooled risk ratio [RR] 1.09; 95% confidence interval [CI] 1.03–1.16) and mortality (RR 1.16; CI 1.01–1.30), independently of traditional risk factors. More recently, in an analysis of 11 studies, Zhao et al. [5] have shown a significant, albeit modest, association between HU and future CVD mortality (RR 1.37; CI 1.19–1.57). By these results the evidence that serum uric acid acts as an independent risk factor for CHD is weak and the importance of this association remains controversial. However, a reliable evaluation of the strength of association with respect to all of the other major CHD risk factors is needed to elucidate the potential implications for primary prevention and for the development of possible treatment options [6]. Some authors have proposed to treat asymptomatic HU with urate-lowering drugs, but there is no agreement on the cost-benefit of this strategy and on the effects of preventing CHD events [7, 8].

A relevant practical aspect to be considered in evaluating a biomarker as a risk factor is the definition of the threshold that identifies the level at which the risk of disease escalates on follow-up. This threshold is useful in selecting those subjects that may benefit from a therapeutic intervention. Previously published meta-analyses do not provide a risk threshold for serum uric acid, as there were different definitions of HU across the studies. Some of the included primary studies defined HU as serum urate concentrations above a widely variable baseline level, ranging from 5.3 to 7.7 mg/dL. Other studies defined the uric acid increase by partitioning the population according to quantiles of the marker distribution and by comparing the risk among the highest and the lowest quantiles.

Given the inconsistency of previously published results, the aim of the present study was to update the literature search and systematically evaluate the available observational prospective cohort studies on the association between HU and future CHD incidence and mortality in the CHD-free adult population by using well defined selection criteria, also trying to identify the uric acid threshold above which the risk, if present, becomes clinically important.

Materials and methods

Data sources and searches

The peer-reviewed literature published up to December 2014 was searched (since 1965) using Medline (PubMed) and Embase databases, with MeSH terms [Uric Acid OR Hyperuricemia OR Urate] AND [Coronary Disease OR Myocardial Infarction OR Angina OR Cardiovascular Diseases OR Coronary Heart Disease], and with limits “Title/Abstract, Human Subjects, English”. In addition, the reference lists of retrieved articles were screened to identify further studies. The final aim of the search was to identify those original articles with a prospective enrolment for investigating the risk of CHD occurrence and/or related mortality in HU CHD-free adult subjects in order to provide a synthesis of the scientific evidence by the meta-analysis process.

Study selection

Two investigators (SP and FB) independently assessed the eligibility of all preliminary identified records on the basis of the title first and then of the abstract. After this preliminary selection, the complete manuscript of the relevant studies was carefully read to confirm the eligibility and extract the useful information. Any disagreement regarding eligibility of an article was settled by consensus with a third reviewer (SF).

Studies were selected if they: 1) evaluated prospective cohorts of adult individuals, with a sample size ≥100 subjects and at least 1 year of follow-up, 2) enrolled subjects from approximately general populations, with no history of CVD or gout, 3) reported results after adjusting for the major CHD risk confounders. No geographic restrictions were applied. Papers were excluded if they: 1) related to interventional and secondary prevention trials; 2) reported duplicative results from the same authors’ group; 3) considered CVD incidence and/or mortality as outcome without separately reporting data on CHD; 4) did not report defined uric acid thresholds or range limits for quantiles; 5) enrolled group of subjects all carrying specific cardiovascular risk factors (e.g. essential hypertension, left ventricular hypertrophy, etc.); 6) did not report relative risk/hazard ratio and related CI or these data were not retrieved by contacting the study investigators.

Data extraction and quality assessment

Two authors (FB and SP) examined the main features of each retrieved article, reporting the following data: year of publication, country where the study was performed and population source, total number of individuals, gender and age, analytical method used for serum urate determination, outcome, duration of follow-up, statistical analysis, HU definition and employed threshold, and investigated confounding factors included in the statistical model to adjust the relative risk or the hazard ratio. In
addition, relative risk and hazard ratio estimates, with the corresponding CIs, were obtained. Out of these estimates, for each enrolled study we selected the first value resulting statistically significant after adjustment for confounders. When relative risk/hazard ratio was not statistically significant, the estimate corresponding to the highest urate concentration was selected.

We did not explicitly score the quality of the selected studies, as the use of quality scoring in meta-analyses of observational studies is controversial and results may not be associated with quality [9]. Conversely, we performed the sensitivity analysis as previously recommended by Stroup et al. [10].

Data synthesis and analysis

Meta-analyses of studies were conducted in accordance with Meta-analysis Of Observational Studies in Epidemiology (MOOSE) guidelines [10]. All quantitative data of selected studies were uniformed as RR as effect size (ES), with corresponding CI, by Comprehensive Meta-Analysis (CMA) software version 2.2 (Biostat Inc, Englewood, NJ, USA). Using CMA, a test for outliers was first performed. Q and I² statistics were used to test the heterogeneity among ES results. Low, moderate, and high degree of heterogeneity correspond to I² values of 25%, 50% and 75%, respectively. As the assumption of heterogeneity was confirmed (see below), the random effect model was used in the meta-analyses to calculate overall combined ES. Resulting RRs were presented as forest plots with the corresponding CI. The Q statistic was also used to test the significance of moderators. The Egger linear regression method (available in CMA) was used to estimate potential publication bias.

Role of the founding source

The study was partially supported by an unconditional grant by Momento Medico, Medical – Pharmaceutical Publishing, Salerno, Italy. It had no role in the study design, conduct, and result reporting.

Results

Features of retrieved studies

The search strategy retrieved a total of 7394 potentially eligible papers, restricted to 4394 after removing duplicate records. After evaluation of titles and abstracts, a further 4335 records were excluded and a total of 59 original articles were preliminary considered eligible for the full text examination. Among 59 eligible full text articles, 44 papers were excluded because of:

- duplicate results from the same group of authors were reported (n=2);
- an outcome different from the one of interest was considered (n=14);
- definition of urate cut-offs or range limits were lacking (n=6);
- subjects carrying specific cardiovascular risk factors or with history or current CVD were enrolled (n=20); and
- a retrospective study was carried out (n=2).

Finally, a total of 15 articles met the inclusion criteria.

HU and CHD incidence

Nine articles evaluated HU as a risk factor for CHD incidence and data from 12 populations were extracted (7 cohorts of men, 3 of women and 2 mixed, respectively) to be included in the meta-analysis (Table 1) [11–19]. The overall sample size was of 457,915 subjects (53.7% males; overall age range, 30–85 years). The length of the follow-up varied from 8 to 23 years. Two studies were carried out on US communities [13, 15], four on European cohorts [14, 16, 18, 19], two on Japanese-American men [11, 12] and one on Nagasaki atomic bomb survivors [17]. The three oldest studies used the method based on phosphotungstic acid as reagent for urate determination [11, 12, 13], while the remaining used an enzymatic assay. With regard to the evaluated outcome, six studies considered the CHD incidence [11–13, 15–17], while the remaining three only incident myocardial infarctions (MI) [14, 18, 19]. The statistical model used in all studies was the Cox proportional hazards multivariate regression. Four [11, 12, 15, 17] expressed the ES as relative risk, the others as hazard ratio. The HU definition criteria used by the evaluated studies were based on quantile estimates, except for one study using an a priori established threshold [17].

HU and CHD mortality

Six studies evaluated the relation of HU to CHD mortality and data of seven populations (4 cohorts of men and 3 of women, respectively) were extracted and included in the following meta-analysis (Table 2) [20–25]. The overall
Table 1: Main characteristics of selected studies on hyperuricemia as a risk factor for coronary heart disease (CHD) incidence in the general population.

<table>
<thead>
<tr>
<th>Author, year [references]</th>
<th>Population</th>
<th>Age, years</th>
<th>Gender</th>
<th>Sample size</th>
<th>Urate assay principle</th>
<th>Follow-up, years</th>
<th>Outcome</th>
<th>Statistical model</th>
<th>Investigated factors (adjustment for confounders)</th>
<th>Hyperuricemia definition criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Culleton, 1999 [13]</td>
<td>American</td>
<td>47±15a</td>
<td>Men</td>
<td>3075</td>
<td>Phosphotungstic acid procedure</td>
<td>23</td>
<td>CHD</td>
<td>Cox proportional hazards regression model (HR)</td>
<td>Age, BMI, SBP, use of antihypertensive agents or diuretics, CHOL, DM, smoking, alcohol, left ventricular hypertrophy</td>
<td>Quartiles</td>
</tr>
<tr>
<td>Culleton, 1999 [13]</td>
<td>American</td>
<td>47±15a</td>
<td>Females</td>
<td>3688</td>
<td>Phosphotungstic acid procedure</td>
<td>23</td>
<td>CHD</td>
<td>Cox proportional hazards regression model (HR)</td>
<td>Age, BMI, SBP, use of antihypertensive agents or diuretics, CHOL, DM, smoking, alcohol, left ventricular hypertrophy, menopausal status</td>
<td>Quartiles</td>
</tr>
<tr>
<td>Liese, 1999 [14]</td>
<td>European</td>
<td>45–64</td>
<td>Men</td>
<td>960</td>
<td>Enzymatic</td>
<td>8</td>
<td>MI</td>
<td>Cox proportional hazards model (HR)</td>
<td>Age, alcohol, TC/HDL ratio, hypertension, diuretics use, smoking, BMI, education</td>
<td>Quartiles</td>
</tr>
<tr>
<td>Bos, 2006 [16]</td>
<td>European</td>
<td>62.5–76.2</td>
<td>Mixed</td>
<td>4385 (1551 men)</td>
<td>Enzymatic</td>
<td>8.4</td>
<td>CHD</td>
<td>Cox proportional hazards model (HR)</td>
<td>Age, gender, SBP, CHOL, HDL, DM, smoking, diuretics use, waist/hip</td>
<td>Quartiles</td>
</tr>
<tr>
<td>Meisinger, 2008 [18]</td>
<td>European</td>
<td>45–74</td>
<td>Men</td>
<td>3424</td>
<td>Enzymatic</td>
<td>18</td>
<td>MI</td>
<td>Cox proportional hazards model (HR)</td>
<td>Age, survey, smoking, alcohol, leisure time physical activity, hypertension, BMI, DM, dyslipidemia, serum creatinine, diuretics use</td>
<td>Quartiles</td>
</tr>
<tr>
<td>Holme, 2009 [19]</td>
<td>European</td>
<td>30–85</td>
<td>Men</td>
<td>221,178</td>
<td>Enzymatic</td>
<td>12</td>
<td>MI</td>
<td>Cox regression analysis (HR)</td>
<td>Age, CHOL, TRYG, hypertension, DM</td>
<td>Quartiles</td>
</tr>
<tr>
<td>Holme, 2009 [19]</td>
<td>European</td>
<td>30–85</td>
<td>Females</td>
<td>196,556</td>
<td>Enzymatic</td>
<td>12</td>
<td>MI</td>
<td>Cox regression analysis (HR)</td>
<td>Age, CHOL, TRYG, hypertension, DM</td>
<td>Quartiles</td>
</tr>
</tbody>
</table>

*Mean±SD. ARIC, Atherosclerosis Risk in Communities Study; BMI, body mass index; CHOL, serum cholesterol; DBP, diastolic blood pressure; DM, diabetes mellitus; FEV, forced expiratory volume; GLU, plasma glucose; HDL, high density lipoproteins; HR, hazard ratio; LDL, low density lipoproteins; MI, myocardial infarction; PAI, physical activity index; RR, relative risk; SBP, systolic blood pressure; TRYG, serum triglycerides; VR, ventricular rate.
<table>
<thead>
<tr>
<th>Author, year [references]</th>
<th>Population</th>
<th>Age, years</th>
<th>Gender</th>
<th>Sample size</th>
<th>Urate assay principle</th>
<th>Follow-up, years</th>
<th>Outcome</th>
<th>Statistical model</th>
<th>Investigated factors (adjustment for confounders)</th>
<th>Hyperuricemia definition criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Freedman, 1995 [20]</td>
<td>American</td>
<td>≥25</td>
<td>Females</td>
<td>2909</td>
<td>Phosphotungstic acid procedure</td>
<td>13.5</td>
<td>IHD</td>
<td>Cox proportional hazards regression model (HR)</td>
<td>Age, race, BMI, CHOL, DBP, smoking, alcohol, education, antihypertensive and diuretics use</td>
<td>Cut-off ≥7.0 mg/dL</td>
</tr>
<tr>
<td>Gerber, 2006 [22]</td>
<td>Israeli</td>
<td>49±7&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Men</td>
<td>9125</td>
<td>Phosphotungstic acid procedure</td>
<td>23</td>
<td>CHD</td>
<td>Cox proportional hazards regression model (HR)</td>
<td>Age, BMI, SBP, DM, CHOL, smoking, left ventricular hypertrophy</td>
<td>Quintiles</td>
</tr>
<tr>
<td>Strasak, 2008 [23]</td>
<td>European</td>
<td>18–96</td>
<td>Men</td>
<td>83,683</td>
<td>Enzymatic</td>
<td>20</td>
<td>CHD</td>
<td>Cox proportional hazards ratio (HR)</td>
<td>Age, BMI, SBP, DBP, CHOL, TRYG, GGT, GLU, smoking, year of examination</td>
<td>Quintiles</td>
</tr>
<tr>
<td>Strasak, 2008 [24]</td>
<td>European</td>
<td>50–95</td>
<td>Females</td>
<td>28,613</td>
<td>Enzymatic</td>
<td>21</td>
<td>CHD</td>
<td>Cox proportional hazards ratio (HR)</td>
<td>Age, BMI, SBP, DBP, CHOL, TRYG, GGT, GLU, smoking, occupational status, year of examination</td>
<td>Quartiles</td>
</tr>
<tr>
<td>Chen, 2009 [25]</td>
<td>Asian</td>
<td>51.7±12&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Men</td>
<td>41,879</td>
<td>Enzymatic</td>
<td>9</td>
<td>CHD</td>
<td>Cox proportional hazards model (HR)</td>
<td>Age, gender, BMI, CHOL, TRYG, DM, hypertension, heavy cigarette smoking, alcohol</td>
<td>&gt;7.0 mg/dL</td>
</tr>
<tr>
<td>Chen, 2009 [25]</td>
<td>Asian</td>
<td>51.4±11&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Females</td>
<td>48,514</td>
<td>Enzymatic</td>
<td>9</td>
<td>CHD</td>
<td>Cox proportional hazards model (HR)</td>
<td>Age, gender, BMI, CHOL, TRYG, DM, hypertension, heavy cigarette smoking, alcohol</td>
<td>&gt;7.0 mg/dL</td>
</tr>
</tbody>
</table>

<sup>a</sup>Mean±SD. BMI, body mass index; CHOL, serum cholesterol; DBP, diastolic blood pressure; DM, diabetes mellitus; GGT, γ-glutamyl transferase; GLU, plasma glucose; HR, hazard ratio; IHD, ischemic heart disease; RR, relative risk; SBP, systolic blood pressure; TRYG, serum tryglycerides.
sample size was of 237,421 subjects (66.3% males; overall age range, 18–96 years). The lengths of follow-up varied from 9 to 23 years. Two studies were carried out on Asian populations [21, 25], two on European cohorts [23, 24], one study on American women [20] and one on Israeli male population aged ≥40 years on inclusion [22]. Two studies considered the mortality from ischemic heart disease [20, 21], while others evaluated the CHD mortality as outcome. The statistical model used in all studies was the Cox proportional hazards multivariate regression. One of them [21] expressed the ES as relative risk, the remaining as hazard ratio. The HU definition used by the evaluated studies was based on a fixed cut-off in two studies [20, 25] and on the partitioning of value distribution in quartiles [24] or quintiles [21–23] in the remaining.

**Meta-analysis results**

**HU and CHD incidence**

Among the nine studies included in the meta-analysis, none was identified as outlier. Figure 1A shows the random overall combined ES shown as a forest plot of the RR and corresponding CI. The overall combined RR (1.206; CI 1.066–1.364) was statistically significant (p = 0.003) in a set of studies with relatively high degree of heterogeneity (Q = 33.6, p < 0.0001, I² = 67.3%). Urate assay principle and gender were analyzed as moderators. Gender significantly (p < 0.0001) influenced total ES and a subgroup analysis was performed, showing a marginal association between HU and CHD incidence in men (7 studies: RR 1.109; CI 0.985–1.249; p = 0.087), but a markedly increased risk for CHD events in hyperuricemic women (3 studies: RR 1.446; CI 1.323–1.581; p < 0.0001). The Egger linear regression showed no publication bias (p = 0.83). However, it should be noted that the study by Holme et al. [19] enrolled an extremely large number of individuals, so results from other trials could be dwarfed by the AMORIS (Apolipoprotein MOrtality RISk study) results in the meta-analysis.

For men, the threshold used to define HU was very homogeneous, being between 6.6 and 6.8 mg/dL in 70% of studies. However, trials involving women used lower, but highly heterogeneous thresholds to define HU (from 5.2 to 6.3 mg/dL).

**HU and CHD mortality**

No studies were identified as outlier. Figure 1B displays the random overall combined ES shown as a forest plot of the RR and corresponding CI. The overall combined RR for
CHD mortality (1.209; CI 1.003–1.457) was slightly statistically significant (p=0.047), once again in a set of studies with relatively high degree of heterogeneity (Q=16.8, p=0.01, I²=64.3%). Although marginally (p=0.052), gender appeared to influence total ES: subgroup analyses revealed no association between HU and CHD mortality in men (4 studies, RR 1.058; CI 0.944–1.185; p=0.332), but an increased risk of CHD mortality in HU women (3 studies, RR 1.830; CI 1.066–3.139; p=0.028). No publication bias was observed (p=0.35).

In four out of six trials evaluating concentrations of uric acid in serum as a risk factor for CHD mortality a threshold of 7.0 mg/dL was used to define HU.

Discussion

The association between HU and CVD incidence and/or mortality in the general population has already been investigated by some meta-analyses with controversial conclusions [3–5]. However, the interventional studies reporting on the effectiveness of urate-lowering drugs in reducing cardiovascular adverse events have provided contrasting data [7, 8]. In addition, it is still unclear which urate threshold is associated to an increased CHD risk, if any, and if this should be gender-specific or not. Thus, we have considered relevant to update the information on the relation between HU and CHD by performing a new meta-analysis study and systematically reviewing retrieved papers by applying more stringent selection criteria. For instance, some studies considered by Kim et al. in their meta-analysis [4] were not included in our study as they did not fulfill the established inclusion criteria [3, 26–36]. Accordingly, we are confident that our results can be more accurate in defining or not if raised serum uric acid is a cause of CHD events in ostensibly healthy people. To support the robustness of our data, we should also note that in our meta-analyses the Egger linear regression method was unable to show publication bias, whereas in the meta-analysis by Kim et al. there was evidence of publication bias for both outcomes [4].

With regard to the association between HU and increased risk of CHD incidence, the subgroup analysis performed in our study provided different results in comparison with those by Kim et al. [4]. For this outcome, those authors were unable to find any association in both genders (RR 1.04, CI 0.90–1.17, for men and RR 1.07, CI 0.82–1.32, for women, respectively). Conversely, we estimated a marginal risk for HU men and a substantially increased risk for CHD incidence in HU women (RR 1.45, CI 1.32–1.58).

The gender dependence of the CHD risk was confirmed even when only CHD mortality was considered. The most important information derived from our study is therefore the confirmation that there is a more pronounced CHD risk in hyperuricemic adult women than in men. It is well known that the epidemiology and mortality for CHD are quite different in the two genders. For instance, women have higher rates of recurrent MI and age-adjusted mortality after their first MI [37]. 38% of women suffering for a MI die within 1 year compared with 25% of men. In addition, 35% of women have a recurrent MI within 6 years from the first event, sudden cardiac death will claim the lives of 6%, and 46% will be disabled with heart failure [38].

With regard to the serum urate threshold for defining the CHD risk in women, selected primary studies show that the risk, above all for mortality, markedly increase for uric acid concentrations >7.0 mg/dL (420 μmol/L), even if concentrations <6.0 mg/dL (360 μmol/L) can be considered desirable.

The strengths and potential limitations of this review and meta-analyses deserve mention. Even if the MOOSE approach used in this study did not recommend the use of scoring systems for quality assessment [10], all studies included in our meta-analyses resulted of good quality. The studies had recruited participants from approximately healthy populations, therefore reducing any effects of clinically evident pre-existing disease on urate concentrations. Only prospective cohort studies with at least a year follow-up duration were eligible, limiting the possibility of selection or recall bias. Finally, using the CHD endpoint and excluding studies with cardiovascular endpoints having different etiologies (such as stroke) maximized comparability [39].

The main limitation may be ascribed to the varying degree of confounder adjustment in individual studies: in evaluating the applicability of our data, one should consider that the number and type of potential confounders included in the statistical model of each study to adjust relative risk or hazard ratio were different. For instance, among major confounders reported by primary papers, the renal function, estimated by serum creatinine concentrations, was considered only in one study reporting on the risk of CHD occurrence [18]. We could, however, speculate that by considering only studies recruiting healthy populations free of CVD, the presence of renal impairment is an unexpected event. An additional limitation is the significant heterogeneity (I²=65%) of the two sets of recruited studies that can partially confound meaningful interpretation of the meta-analyses. In our study, we first tested studies to exclude outliers and then performed specific statistics for evaluating homogeneity (or the lack of
it) among ES results: because we studied a heterogeneous set of studies, we used the random effect model, which allowed inclusion of the studies in the meta-analysis, while acknowledging their flaws. Displayed forest plots also revealed information about heterogeneity. Finally, the number of papers included in our meta-analyses is rather few, especially when we partitioned the studies by gender. The results should therefore be interpreted in context of the limitations available.

In conclusion, HU appears to slightly increase the risk of CHD events in the general population, but this relation gains much more statistical significance when only adult HU women are considered. The risk markedly increases when serum uric acid concentrations are >70 mg/dL (420 μmol/L). However, due to the low number of available studies, this association needs to be confirmed in further specifically designed trials. As a general consideration, a therapeutic option lowering serum uric acid in apparently healthy women with concentrations higher than the above mentioned threshold would need higher relative risk/hazard ratio estimates, as the CHD prevalence in the general population is low (~7% in our country) and, thus, the cost-benefit ratio of a treatment might not be relevant [40].

Author contributions: All the authors have accepted responsibility for the entire content of this submitted manuscript and approved submission.

Research funding: The study was partially supported by an unconditional grant by Momento Medico, Medical – Pharmaceutical Publishing, Salerno, Italy.

Employment or leadership: None declared.

Honorarium: None declared.

Competing interests: The funding organization(s) played no role in the study design; in the collection, analysis, and interpretation of data; in the writing of the report; or in the decision to submit the report for publication.

References


