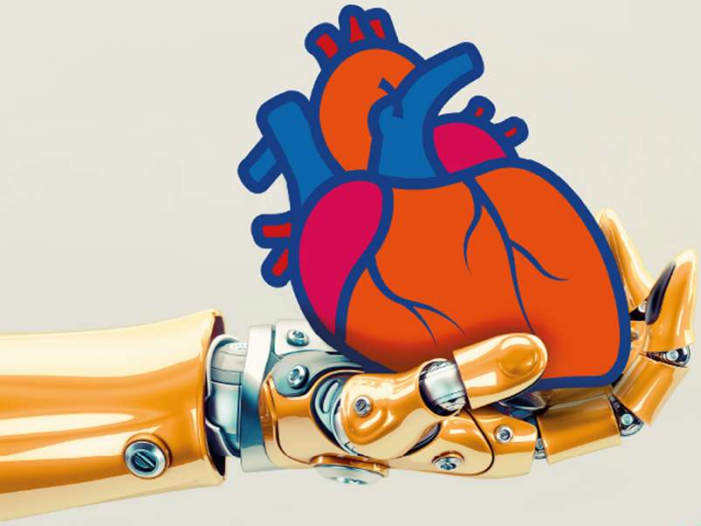


17° Meeting

CardioLucca

Heart Brings Heart 2023

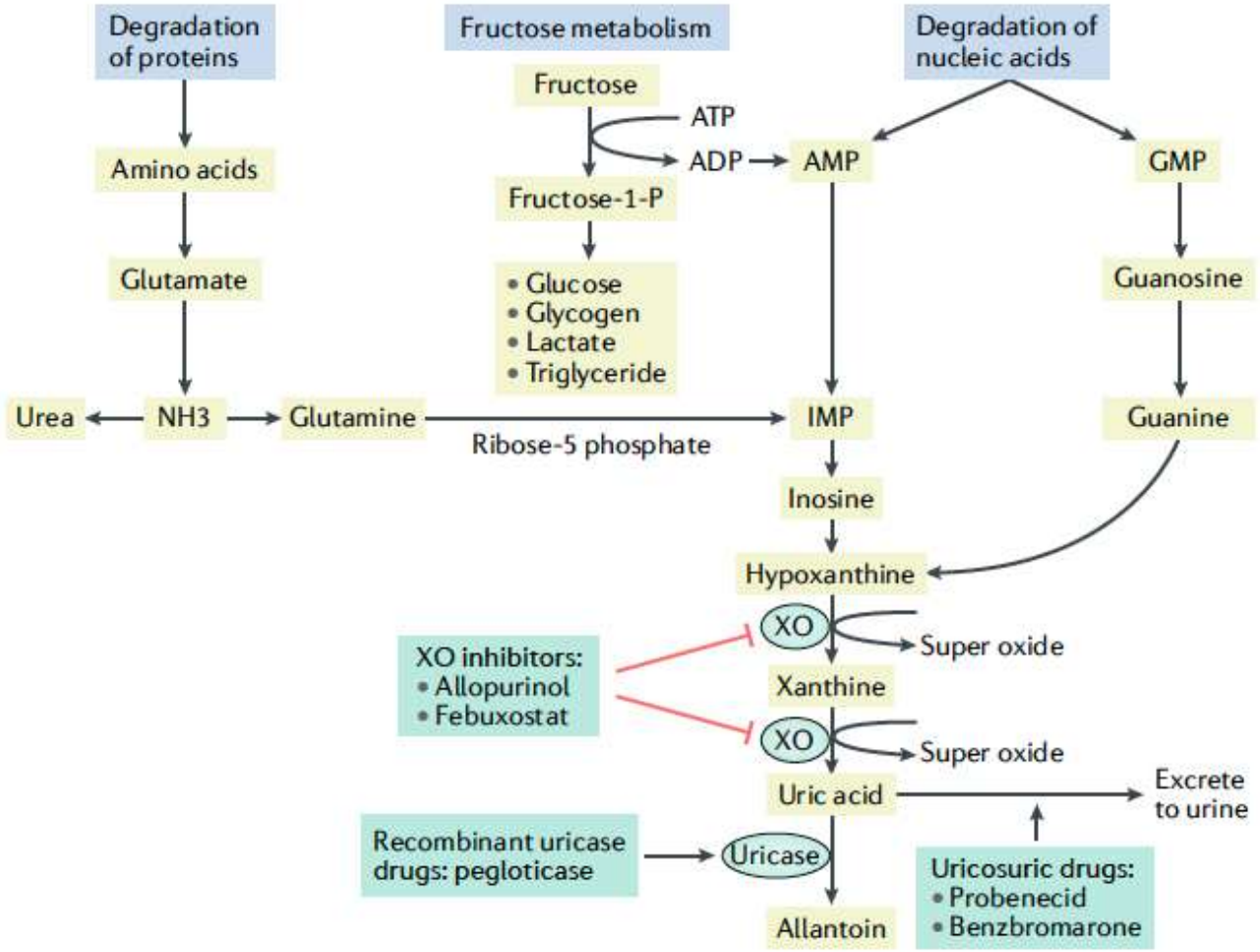
Lucca, 22-24 Giugno 2023

Centro Congressi Auditorium San Francesco

Claudio Borghi

L'iperuricemia da Cenerentola dei fattori di rischio CV a protagonista di un opportuno trattamento precoce ed intensivo

Mechanisms of production of Uric Acid

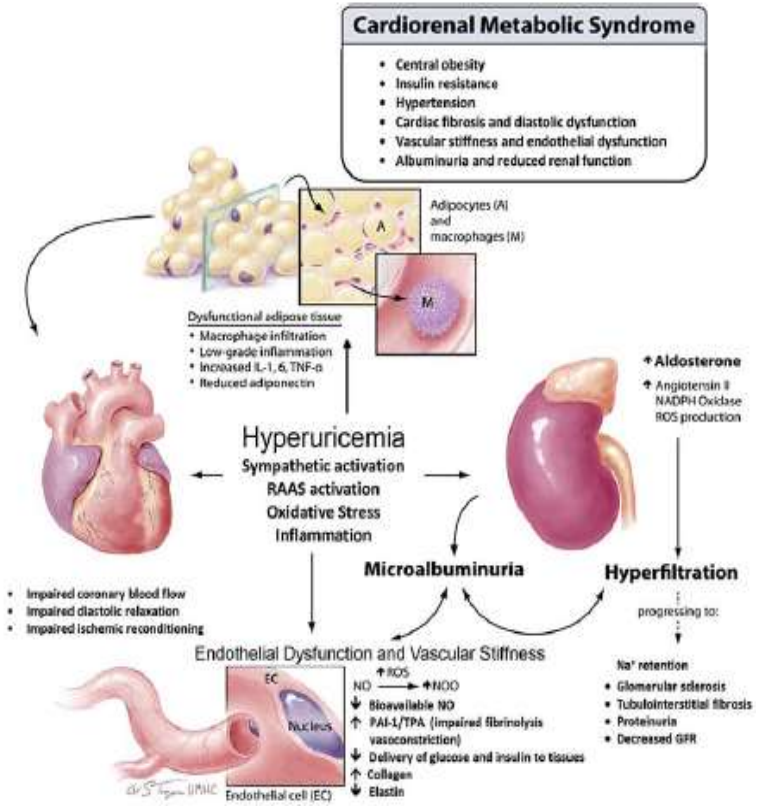


OPINION

The case for uric acid-lowering treatment in patients with hyperuricaemia and CKD

Yuka Sato, Daniel I. Feig, Austin G. Stack, Duk-Hee Kang, Miguel A. Lanaspa, A. Ahsan Ejaz, L. Gabriela Sánchez-Lozada, Masanari Kuwabara, Claudio Borghi and Richard J. Johnson

Mechanisms by which elevated uric acid promotes components of the cardio-renal and metabolic syndrome



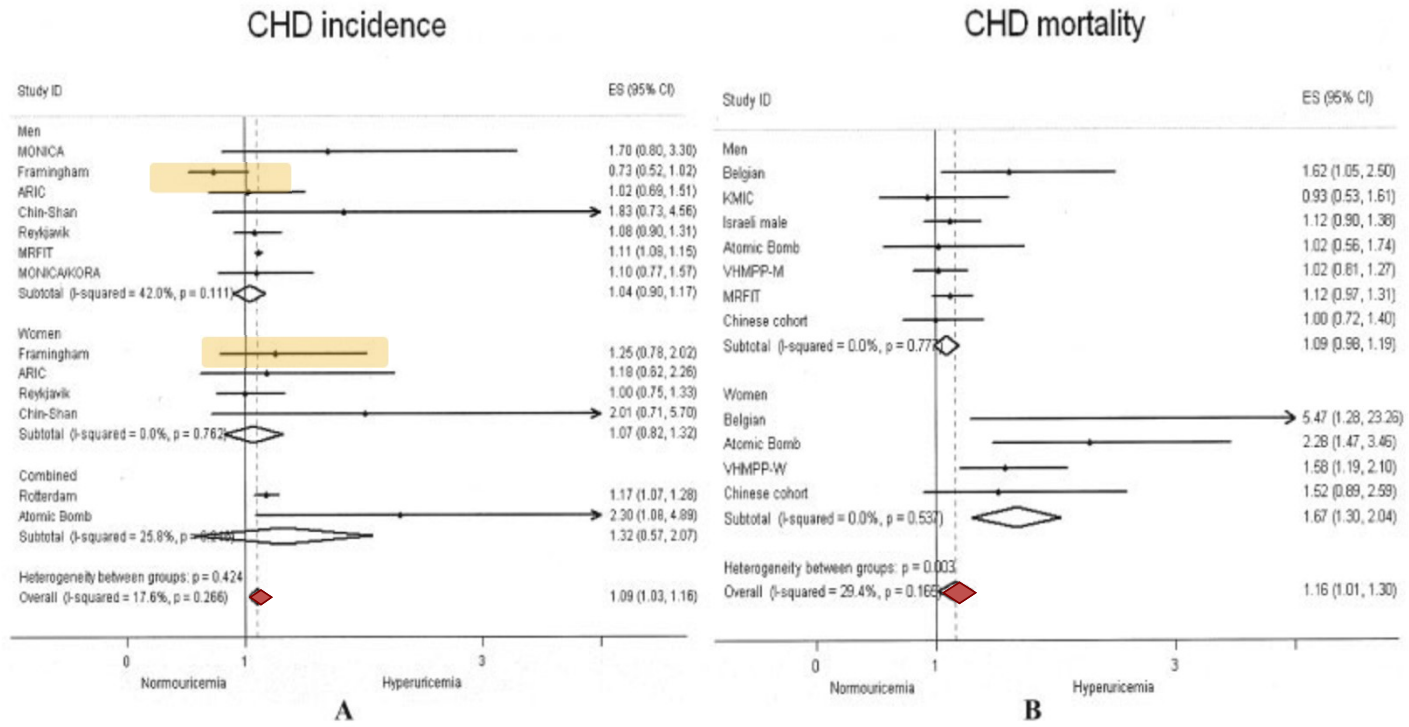
Chaudhary K et Al., Cardiorenal Med 2013;3:208–220

Arthritis Care & Research
Vol. 62, No. 2, February 2010, pp 170–180
DOI 10.1002/acr.20065

ORIGINAL ARTICLE

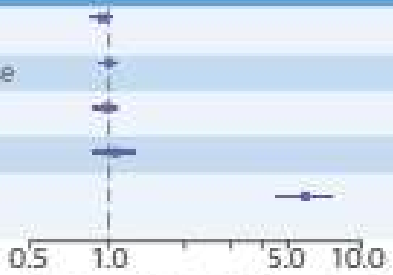
Hyperuricemia and Coronary Heart Disease: A Systematic Review and Meta-Analysis

SEO YOUNG KIM,[1] JAMES P. GUEVARA,[2] KYOUNG MI KIM,[3] HYON K. CHOI,[4] DANIEL F. HEITJAN,[5] AND DANIEL A. ALBERT[6]



Urate genetic score: association of genetically raised urate with cardiometabolic outcomes

Outcome	OR	95% CI	p value
Type 2 Diabetes	0.95	(0.86, 1.05)	0.28
Coronary Heart Disease	1.02	(0.92, 1.12)	0.73
Ischemic Stroke	0.99	(0.88, 1.12)	0.93
Heart Failure	1.07	(0.88, 1.30)	0.51
Gout	5.84	(4.56, 7.49)	4.2E-44



OR per SD increase in Serum Urate Conferred by Genetic Score

Keenan, T. et al. J Am Coll Cardiol. 2016; 67(4):407-16.

A genetic score was created using single nucleotide polymorphisms exclusively associated with serum urate levels. For a 1 SD increase in serum uric acid levels, the odds ratio (OR) of gout conferred by the urate-specific genetic score was 5.84 (95% confidence interval [CI]: 4.56 to 7.49), which was directionally consistent with the observed OR of 2.12 (95% CI: 1.90 to 2.33) for gout in epidemiological studies. However, a 1 SD increase in serum urate due to the genetic score had no relationship with type 2 diabetes, coronary heart disease, ischemic stroke, or heart failure. SD = 1.427 mg/dl urate.

Keenan T et al, JACC 2016

European Journal of Internal Medicine xxx (xxxx) xxx

Contents lists available at ScienceDirect

European Journal of Internal Medicine

journal homepage: www.elsevier.com/locate/ejim

Clinical Insights

Xanthine oxidase inhibition and cardiovascular protection: Don't shoot in the dark

Giovambattista Desideri [a,*], Claudio Borghi [b]

[a] Department of Life, Health and Environmental Sciences, University of L'Aquila, Via Spennati, Delta 6 Medicina, Coppito, 67100 L'Aquila, Italy
[b] Department of Medical and Surgical Sciences, University of Bologna, Italy

ARTICLE INFO

Keywords:
Uric acid
Gout
Cardiovascular disease
Xanthine oxidase

Substantial evidence suggests that chronic hyperuricemia is an independent risk factor for hypertension, metabolic syndrome, chronic kidney disease and cardiovascular disease [1,2]. However, whether lowering serum UA can improve cardiovascular and renal outcomes, and what therapeutic mechanism of action could provide more clinical benefits to patients, is still a matter of discussion. Evidence from observational studies suggests possible cardiovascular benefits associated with ULT, in particular for the XO-inhibitors, while the evidence from randomized controlled trials is scarce and somewhat conflicting [2]. These discrepancies could be explained by the existence of different phenotypes across hyperuricemic patients with a non-homogeneous distribution of clinical benefits from ULT.

1. In the beginning there were monosodium urate crystals

The relationship between gout and cardiovascular disease has been supported by epidemiological observations demonstrating a significant increase of the risk of death from cardiovascular disease and coronary artery disease in patients with gout [2,3]. From a pathophysiological point of view this association could be explained by the precipitation of MSU crystals within the vessel wall leading to a chronic vascular [4] and systemic inflammation that characterizes both acute and chronic gout [5]. The observed increase in coronary calcium score described in patients with hyperuricaemia and the asymptomatic joint urate deposition could explain the increased cardiovascular risk in patients with "symptomless gout" [2].

Thus, a first phenotype of interest might include patients with increased cardiovascular risk related to either overt or subclinical MSU crystal deposition (Fig. 1). In patients with this phenotype, a guideline-based ULT aimed at promoting the dissolution of MSU deposits and at preventing the formation of new accumulations has also the biological possibility to exert a cardiovascular protection by reducing both vascular and systemic inflammation.

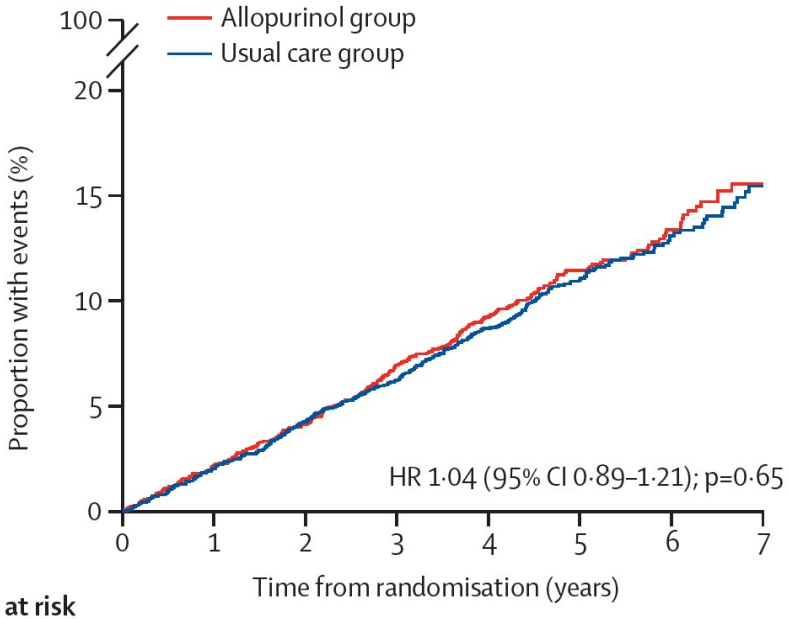
2. Then, was the time for uric acid

The inflammation promoted by the deposition of MSU crystals cannot entirely explain the relationship between UA and cardiovascular disease which is already evident when UA levels are in the normal to high range (5.0–5.5 mg/dL), largely below the precipitation threshold of MSU that occurs at 6.4 mg/dL (aqueous solution, 37 °C, pH 7.4) [6]. From a pathophysiological point of view, UA can modify its biological properties based on the concentrations reached in the biological fluids and the presence of concomitant environmental conditions. In particular, the antioxidant properties described for low serum UA levels can turn into pro-oxidant properties for high-normal serum UA levels [1,2]. Some evidence describes a direct vascular damage caused by UA because of oxidative stress leading to endothelial activation and dysfunction [1, 2].

Thus, at this point we should consider a second phenotype of patients

Allopurinol versus usual care in UK patients with ischaemic heart disease (ALL-HEART): a multicentre, prospective, randomised, open-label, blinded-endpoint trial

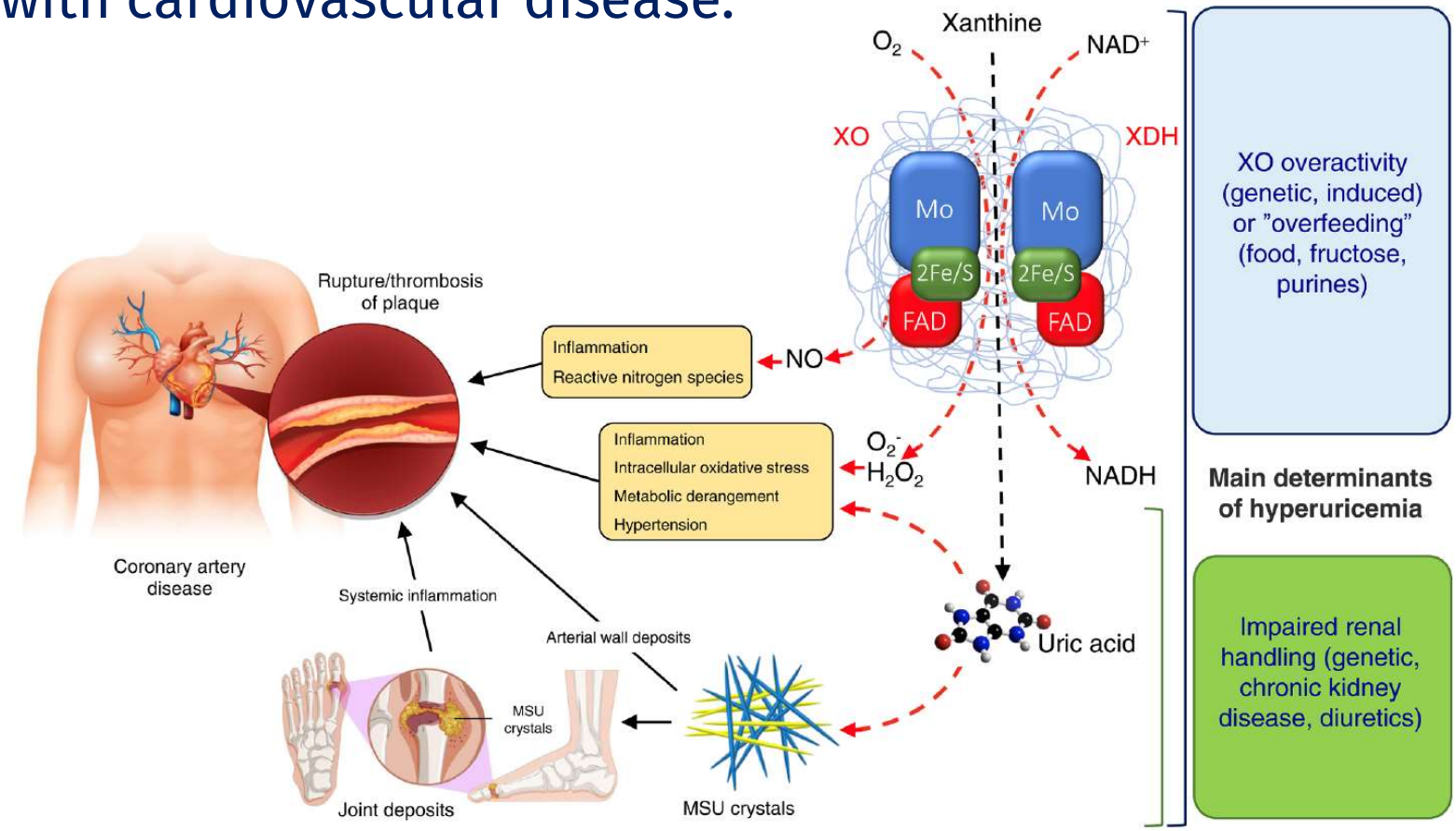
Isla S Mackenzie, Christopher J Hawkey, Ian Ford, Nicola Greenlaw, Filippo Pigazzani, Amy Rogers, Allan D Struthers, Alan G Begg, Li Wei, Anthony J Avery, Jaspal S Taggar, Andrew Walker, Suzanne L Duce, Rebecca J Barr, Jennifer S Dumbleton, Evelien D Rooke, Jonathan N Townend, Lewis D Ritchie, Thomas M MacDonald, on behalf of the ALL-HEART Study Group*



Number at risk

Allopurinol group	2853	2681	2556	2419	2148	1140	502	151
Usual care group	2868	2790	2676	2579	2367	1280	655	210

Pathophysiological mechanisms linking uric acid metabolism with cardiovascular disease.



Desideri G & Borghi C, Eur J Int Med 2023

Hypertension

REVIEW

Uric Acid and Hypertension: a Review of Evidence and Future Perspectives for the Management of Cardiovascular Risk

Claudio Borghi, Davide Agnoletti, Arrigo Francesco Giuseppe Cicero, Empar Lurbe, Agostino Virdis

ABSTRACT: Uric acid is the final product of purine metabolism, and its increased serum levels have been directly involved in the pathogenesis and natural history of hypertension. The relationship between elevated uric acid and hypertension has been proven in both animals and humans, and its relevance is already evident in childhood and adolescent population. The mechanism responsible for blood pressure increase in hyperuricemic subjects is implicating both oxidative stress and intracellular urate activity with a primary involvement of XOR (xanthine-oxidoreductase activity). An increase in the relative risk of hypertension has been confirmed by genetic data and by large meta-analyses of epidemiological data. The effects of urate-lowering treatment on blood pressure control in patients with elevated serum uric acid has been investigated in a small number of reliable studies with a large heterogeneity of patient populations and study designs. However, 2 large meta-analyses suggest a significant effect of urate-lowering treatment on blood pressure, thus confirming the significant relationship between high serum urate and blood pressure. The future research should be focused on a more appropriate identification of patients with cardiovascular hyperuricemia by considering the correct cardiovascular threshold of serum urate, the time-course of uricemia fluctuations, and the identification of reliable markers of urate overproduction that could significantly clarify the clinical and therapeutic implications of the interaction between serum uric acid and hypertension.

Key Words: adolescent ■ cardiovascular disease ■ hypertension ■ uric acid ■ xanthine-oxidoreductase

Cardiovascular disease is the most common cause of death across the world.[1] A remarkable proportion of this clinical burden of disease can be prevented by an effective control of cardiovascular risk factors.[2] Among cardiovascular risk factors, hypertension plays a primary role because of its large prevalence (about 40% of the adult population), its association with other risk factors, and its impact in terms of major cardiovascular events.[3]

In the last century, a large body of evidence has been published supporting the direct involvement of elevated serum uric acid (SUA) in the pathogenesis and natural history of HTN.

The effect of SUA on blood pressure (BP) control was hypothesized in the 19th century by Frederick Akbar Mahomed who postulated a causal role for elevated SUA.[4] Since this historical observation, an increasing number of articles have been published reporting a growing consensus of a close interaction between uric acid and HTN.[5] Here, we review the current state of the evidence relating SUA and hypertension with the primary goal to discuss both the facts and some of the major controversies that have complicated the interpretation of this challenging topic.

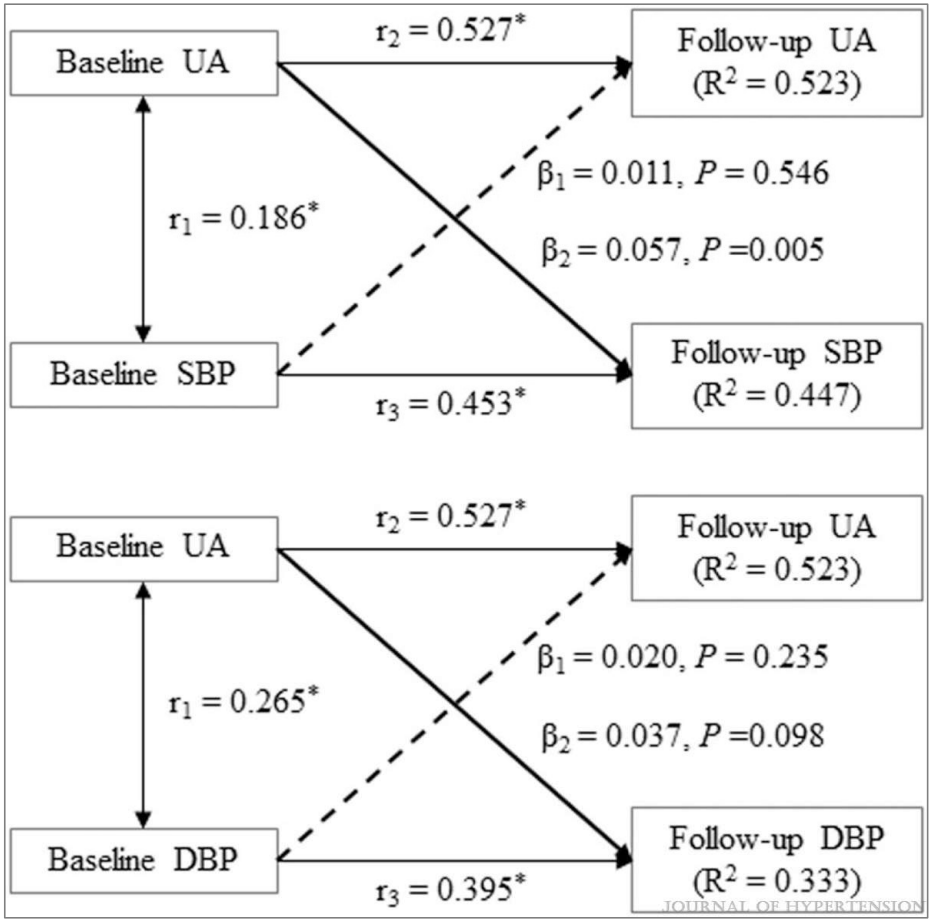
BIOLOGY OF URIC ACID PRODUCTION AND EXCRETION

Uric acid is the final product of the metabolism of purines mainly generated from degradation of amino acids, diet (alcohol or fructose consumption) or DNA and RNA breakdown (tumor lysis syndrome).[6] SUA increases with age and is usually lower in premenopausal women than in age-matched men. Other factors contribute to increase the levels of SUA as high salt and glucose-rich

Correspondence to: Claudio Borghi, Unità Operativa Complessa di Medicina Cardiovascolare, Ospedale S.Orsola-Malpighi, Via Alberoni 15, 40138 Bologna, Italy. Email claudio.Borghi@unibo.it
For Sources of Funding and Disclosures, see page XXX.

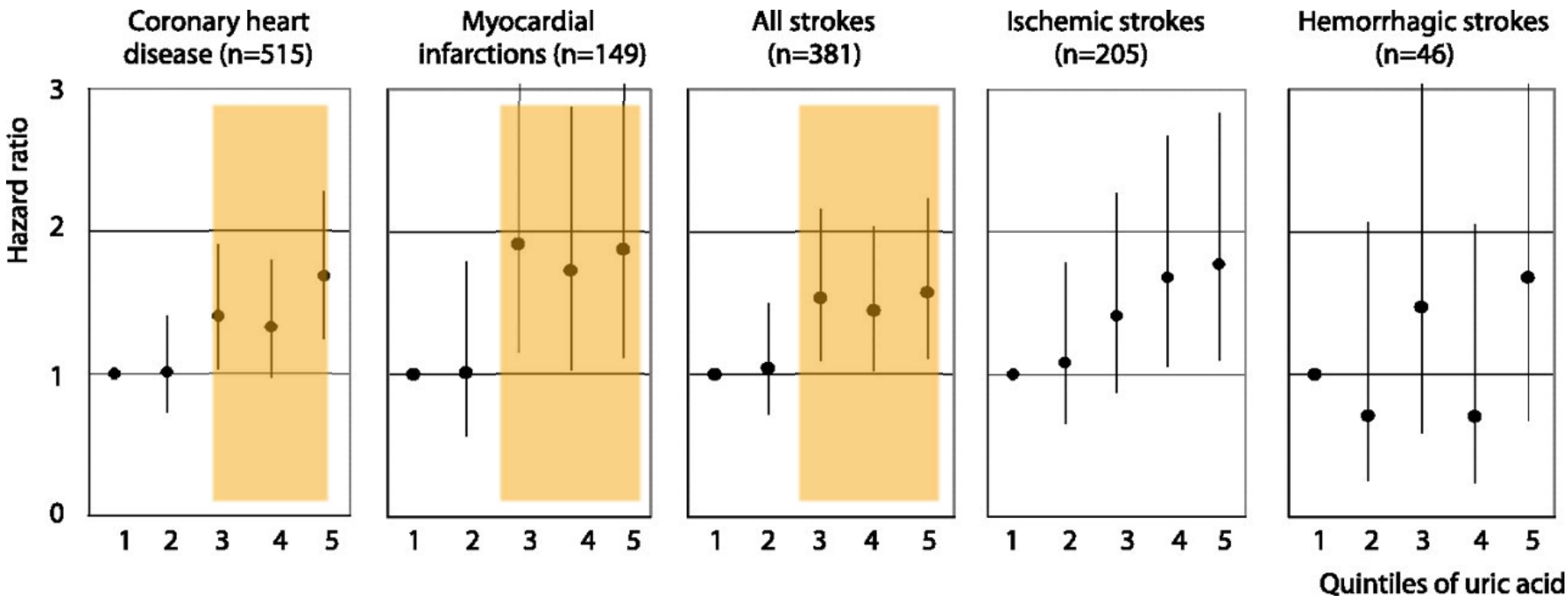
Hypertension is available at www.ahajournals.org/journal/hyp

Cross-lagged panel analysis models of serum uric acid, Blood Pressure and urinary albumin/creatinine ratio



Jiang Y et al, J Hypertension38(4):625-632, 2020.

Age and BP-adjusted HR for the associations between serum uric acid and cardiovascular disease: The Rotterdam Study

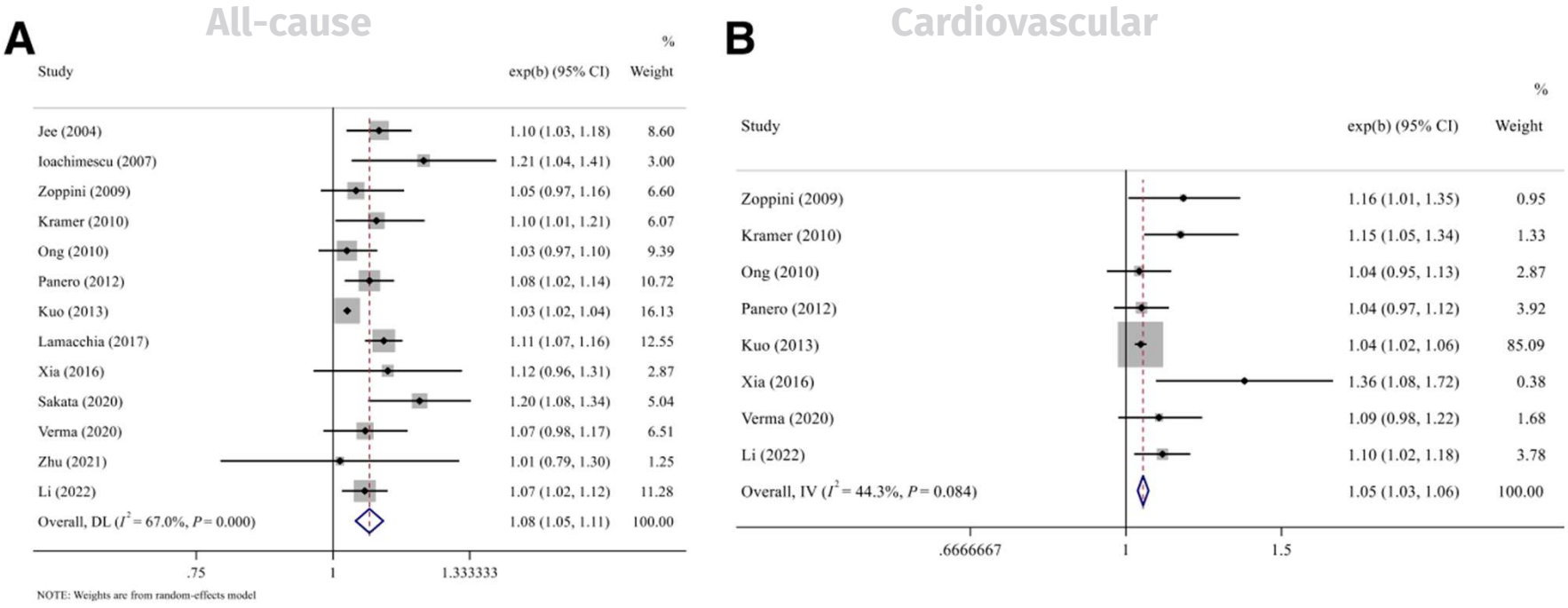


American Heart Association

Bos M J et al. Stroke. 2006;37:1503-1507

From: Association of Serum Uric Acid With All-Cause and Cardiovascular Mortality in Diabetes

Forest-plot and metanalysis of SUA and All-cause and CVD mortality in patients with DM (HR per 1 mg/dL)



Diabetes Care. 2022;46(2):425-433. doi:10.2337/dc22-1339

Wang et al. Genome Medicine (2022) 14:63
https://doi.org/10.1186/s13073-022-01067-1

Genome Medicine

RESEARCH Open Access

Mendelian randomization analysis of 37 clinical factors and coronary artery disease in East Asian and European populations

Kai Wang[1], Xian Shi[1], Ziwei Zhu[1], Xingjie Hao[1], Liangkai Chen[2], Shanshan Cheng[1], Roger S. Y. Foo[3,4] and Chaolong Wang[1*]

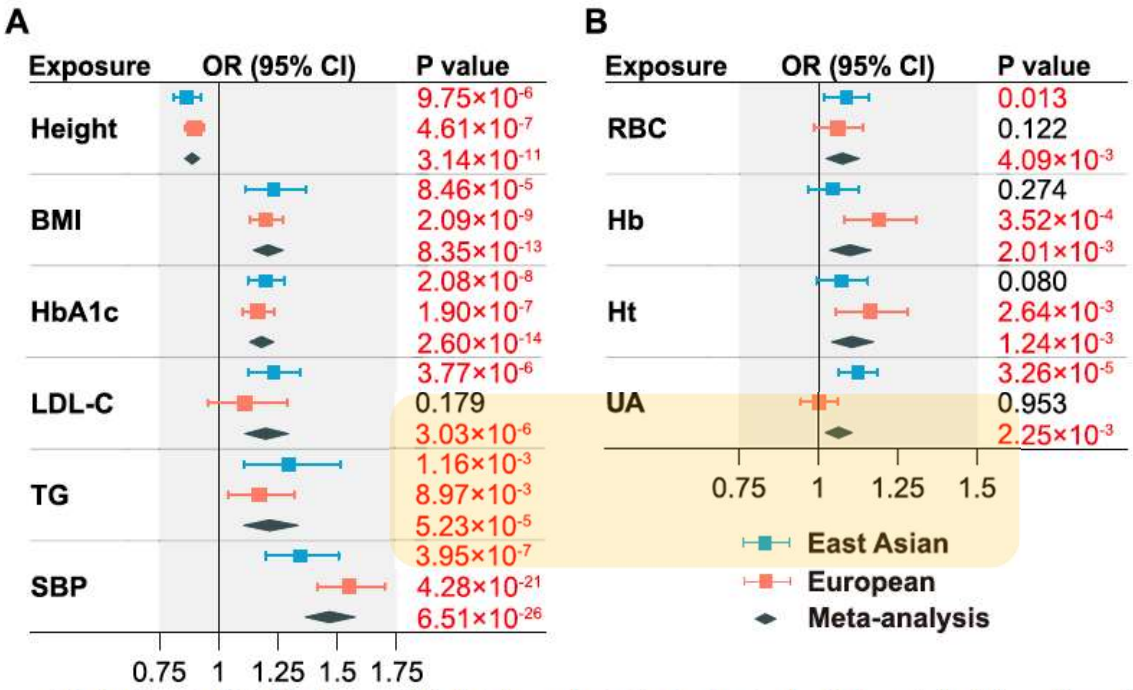


Fig. 5 MVMR analyses of 10 significant clinical factors on CAD. **A** Independent effect estimates by joint analysis of six cardiometabolic factors. **B** Independent effect estimates for each of RBC, Hb, Ht, and UA after adjusting for six cardiometabolic factors in panel **A**. Effect sizes are represented by OR per SD increment in the exposure. The horizontal bars represent 95% CIs. $P < 0.05$ are highlighted in red

Journal of the American Heart Association

ORIGINAL RESEARCH

Association of Normal Serum Uric Acid Level and Cardiovascular Disease in People Without Risk Factors for Cardiac Diseases in China

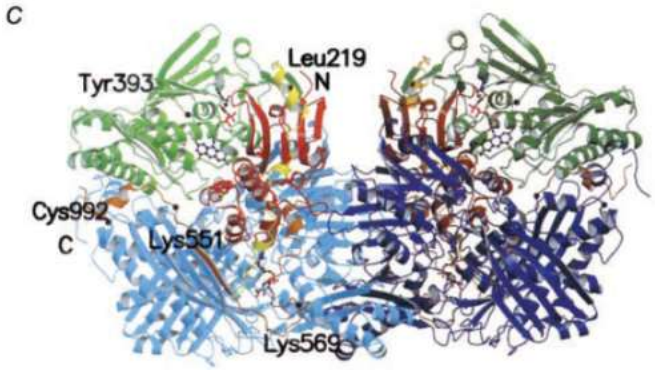
Xue Tian, PhD*; Penglian Wang, MD*; Shuohua Chen, MD*; Yijun Zhang, PhD; Xiaoli Zhang, BS; Qin Xu, PhD; Yanxia Luo, PhD; Shouling Wu, MD; Anxin Wang, PhD

Reclassification and Discrimination Statistics for Cardiovascular Disease by SUA

	C-statistic		IDI		NRI	
	Estimate (95% CI), %	*P* Value	Estimate (95% CI), %	*P* Value	Estimate (95% CI), %	*P* Value
Cardiovascular disease						
Framingham score	0.71 (0.69–0.72)		Reference		Reference	
Framingham score + SUA	0.72 (0.71–0.74)	0.0003	0.07 (0.01,0.13)	0.0198	11.78 (5.30–18.25)	0.0004
Stroke						
Framingham score	0.71 (0.69–0.72)		Reference		Reference	
Framingham score + SUA	0.72 (0.70–0.73)	0.0040	0.04 (–0.01–0.09)	0.1408	11.10 (4.00–18.21)	0.0022
Myocardial infarction						
Framingham score	0.70 (0.67–0.74)		Reference		Reference	
Framingham score + SUA	0.74 (0.70–0.77)	0.0056	0.04 (–0.01–0.09)	0.1428	18.91 (4.24–33.57)	0.0117

IDI, indicates integrated discrimination improvement; NRI, net reclassification index; and SUA, serum uric acid.

J Am Heart Assoc. 2023



Heart Failure
CKD
Diabetes
Low grade inflammation

International Journal of
Environmental Research and Public Health

MDPI

Article

Plasma Xanthine Oxidoreductase Activity Is Associated with a High Risk of Cardiovascular Disease in a General Japanese Population

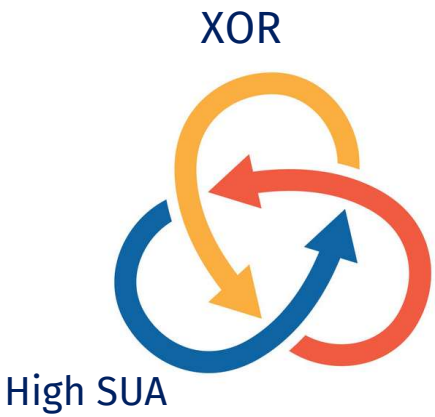
Yuka Kotozaki [1], Mamoru Satoh [1,2,*], Kozo Tanno [1,3], Hideki Ohmomo [1], Ryo Otomo [1], Fumitaka Tanaka [1,4], Takahito Nasu [1,2,5], Satoru Taguchi [5], Hiroto Kikuchi [5], Takamasa Kobayashi [5], Atsushi Shimizu [1,2], Kiyomi Sakata [1,3], Jiro Hitomi [1,6], Kenji Sobue [7] and Makoto Sasaki [1,8]

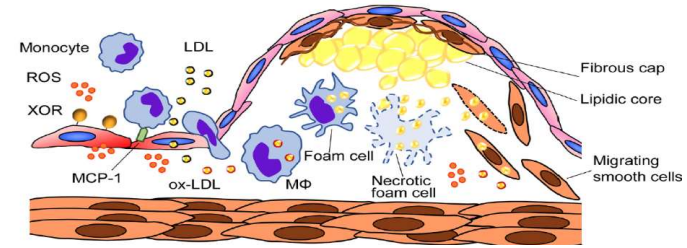
Table 6. Multivariate adjusted ORs for the high risk for CVD (FRS $\geq$ 15) by XOR quartiles.

XOR Quartiles	OR	95% CI	*p* Value
Q1	Reference		
Q2	1.56	0.56–4.35	0.396
Q3	1.68	0.63–4.50	0.298
Q4	2.93	1.16–7.40	0.023

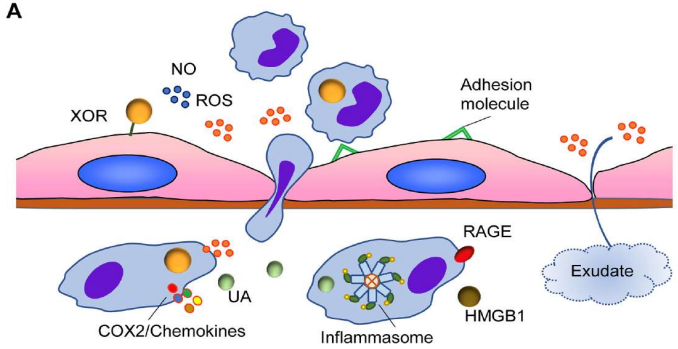
Statistical significant ($p < 0.05$). OR, Odd ratios; 95% CI, 95% confidence intervals. Covariates: BMI, Log10UA.

XOR,UA and mechanisms of atherosclerosis

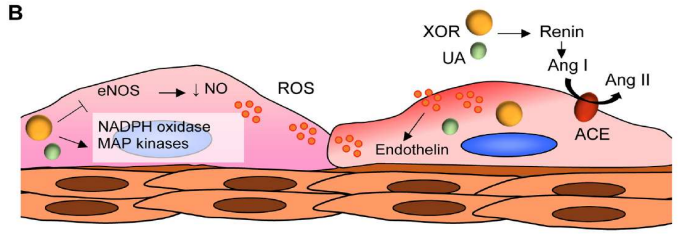




Plaque formation



Inflammation



Tissue RAAS Activation

Polito L et al, Redox Biology 2021

Editorial Commentary

Urate-Lowering Drugs and Prevention of Cardiovascular Disease

The Emerging Role of Xanthine Oxidase Inhibition

Claudio Borghi, Giovambattista Desideri

See related article, p xxx

(*Hypertension*. 2016;67:00-00.
DOI: 10.1161/HYPERTENSIONAHA.115.06531.)

Hypertension is available at http://hyper.ahajournals.org
DOI: 10.1161/HYPERTENSIONAHA.115.06531

Forest plot of randomized controlled trial estimates for change in mean systolic BP in patients receiving urate-lowering therapy or placebo/no treatment.

Hypertension

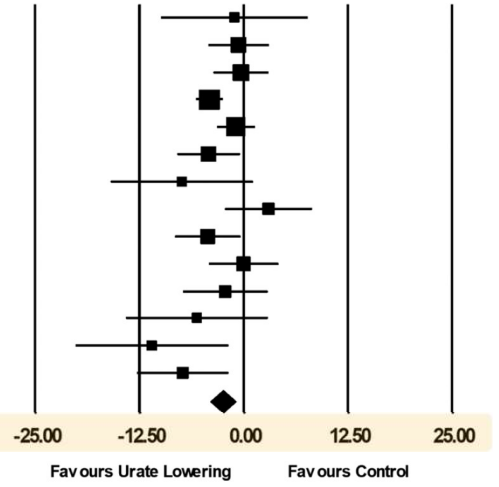
MENDELIAN RANDOMIZATION

Urate, Blood Pressure, and Cardiovascular Disease

Evidence From Mendelian Randomization and Meta-Analysis of Clinical Trials

Dipender Gill; Alan C. Cameron; Stephen Burgess, Xue Li, Daniel J. Doherty, Ville Karhunen, Azmil H. Abdul-Rahim, Martin Taylor-Rowan, Verena Zuber, Philip S. Tsao, Derek Klarin, VA Million Veteran Program, Evangelos Evangelou, Paul Elliott, Scott M. Damrauer, Terence J. Quinn, Abbas Dehghan, Evropi Theodoratou,† Jesse Dawson,† Ioanna Tzoulaki†

Study name	Statistics for each study						
	Difference in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Alshahawey, 2017	-1.100	4.521	20.441	-9.961	7.761	-0.243	0.808
Gingles, 2019	-0.590	1.886	3.556	-4.286	3.106	-0.313	0.754
Gunawhardana, 2017	-0.300	1.712	2.933	-3.656	3.056	-0.175	0.861
Kimura, 2018	-4.100	0.863	0.744	-5.791	-2.409	-4.753	0.000
McMullan, 2017	-0.900	1.199	1.437	-3.249	1.449	-0.751	0.453
Segal, 2015	-4.200	1.945	3.781	-8.011	-0.389	-2.160	0.031
Higgins, 2014	-7.400	4.380	19.181	-15.984	1.184	-1.690	0.091
Dogan, 2011	3.000	2.688	7.226	-2.269	8.269	1.116	0.264
Kanbay, 2011	-4.300	2.027	4.110	-8.273	-0.327	-2.121	0.034
Goicoechea, 2010	0.000	2.153	4.635	-4.220	4.220	0.000	1.000
Momeni, 2010	-2.200	2.619	6.859	-7.333	2.933	-0.840	0.401
Khan, 2008	-5.600	4.368	19.076	-14.160	2.960	-1.282	0.200
Siu, 2006	-11.000	4.706	22.148	-20.224	-1.776	-2.337	0.019
Morgan, 2018	-7.300	2.828	7.998	-12.843	-1.757	-2.581	0.010
	-2.552	0.767	0.589	-4.056	-1.048	-3.326	0.001



Hypertension. 2021;77:383–392. DOI: 10.1161/HYPERTENSIONAHA.120.16547

Hypertension

MENDELIAN RANDOMIZATION

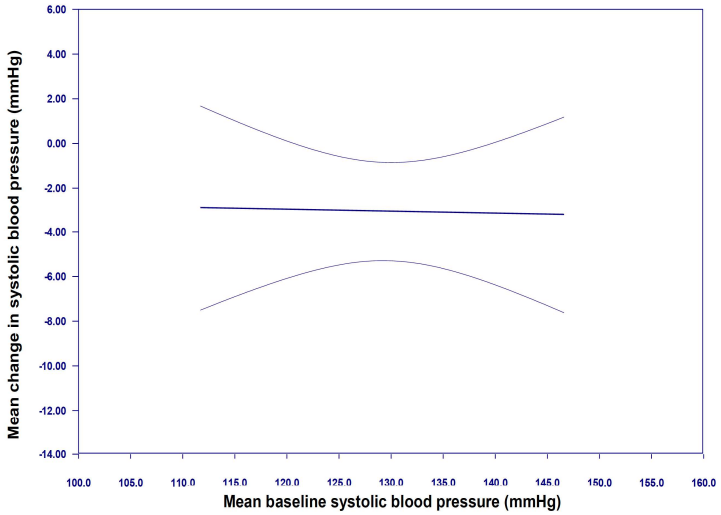
Urate, Blood Pressure, and Cardiovascular Disease

Evidence From Mendelian Randomization and Meta-Analysis of Clinical Trials

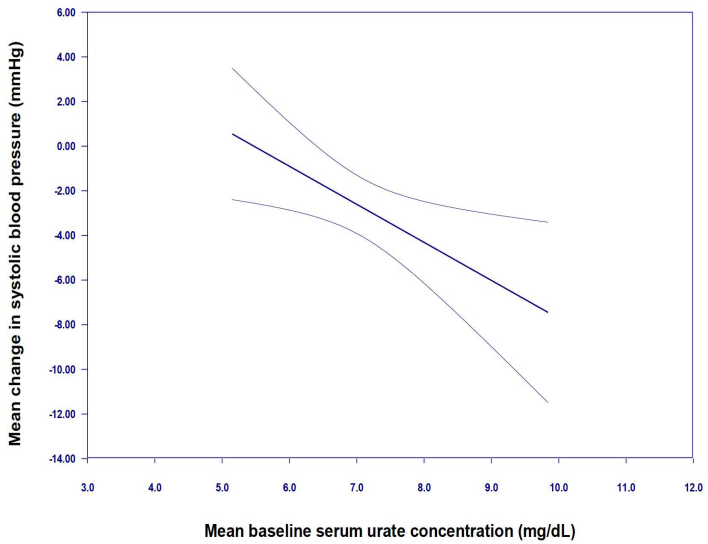
Dipender Gill; Alan C. Cameron; Stephen Burgess, Xue Li, Daniel J. Doherty, Ville Karhunen, Azmil H. Abdul-Rahim, Martin Taylor-Rowan, Verena Zuber, Philip S. Tsao, Derek Klarin, VA Million Veteran Program, Evangelos Evangelou, Paul Elliott, Scott M. Damrauer, Terence J. Quinn, Abbas Dehghan, Evropi Theodoratou,† Jesse Dawson,† Ioanna Tzoulaki†

Meta-regression analysis of the association between changes in systolic BP and baseline BP and Uric acid

Baseline SBP



Baseline SUA



Hypertension. 2021;77:383–392. DOI: 10.1161/HYPERTENSIONAHA.120.16547

Forest plot of RCT estimates for risk of major adverse cardiovascular events in all patients receiving urate-lowering therapy or placebo/no treatment.

Hypertension

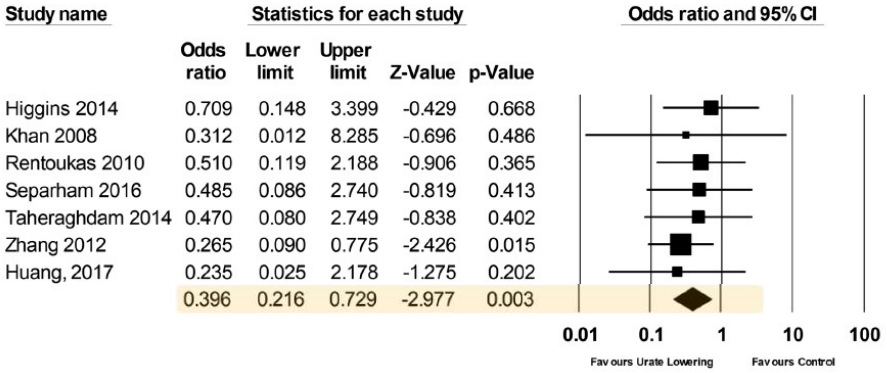
MENDELIAN RANDOMIZATION

Urate, Blood Pressure, and Cardiovascular Disease

Evidence From Mendelian Randomization and Meta-Analysis of Clinical Trials

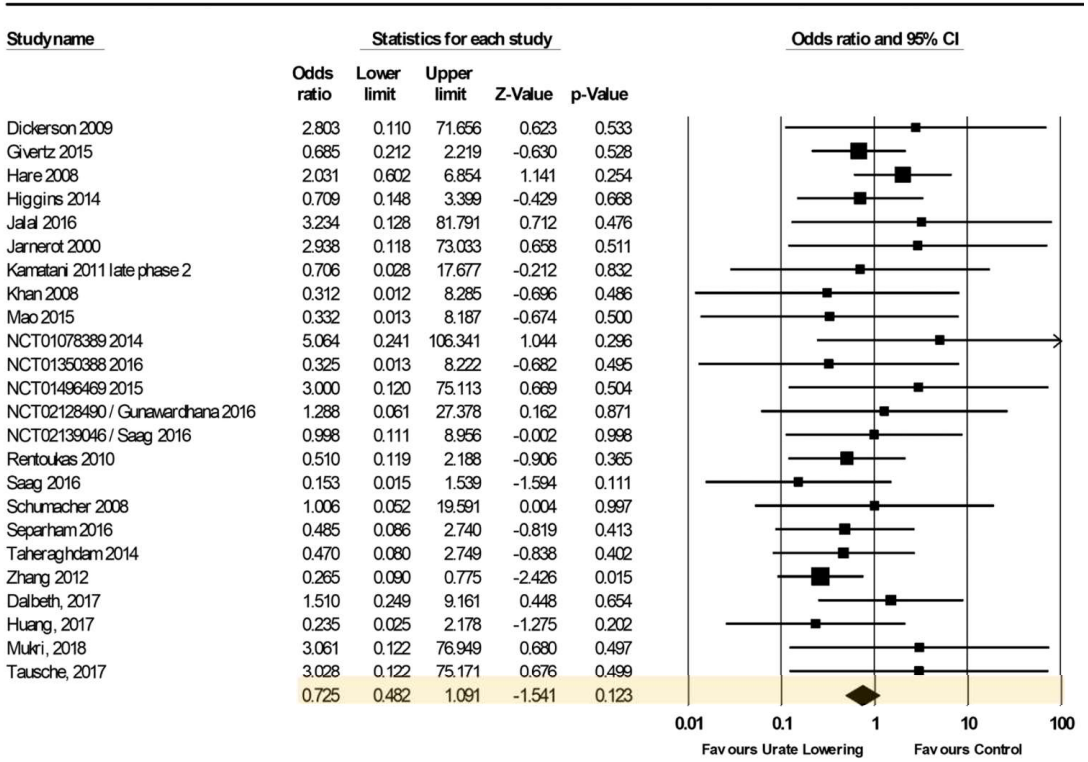
Dipender Gill; Alan C. Cameron; Stephen Burgess, Xue Li, Daniel J. Doherty, Ville Karhunen, Azmil H. Abdul-Rahim, Martin Taylor-Rowan, Verena Zuber, Philip S. Tsao, Derek Klarin, VA Million Veteran Program, Evangelos Evangelou, Paul Elliott, Scott M. Damrauer, Terence J. Quinn, Abbas Dehghan, Evropi Theodoratou,† Jesse Dawson,† Ioanna Tzoulaki†

Previous CVD



Study name	Odds ratio	Lower limit	Upper limit	Z-Value	p-Value
Higgins 2014	0.709	0.148	3.399	-0.429	0.668
Khan 2008	0.312	0.012	8.285	-0.696	0.486
Rentoukas 2010	0.510	0.119	2.188	-0.906	0.365
Separham 2016	0.485	0.086	2.740	-0.819	0.413
Taheraghdam 2014	0.470	0.080	2.749	-0.838	0.402
Zhang 2012	0.265	0.090	0.775	-2.426	0.015
Huang, 2017	0.235	0.025	2.178	-1.275	0.202
	0.396	0.216	0.729	-2.977	0.003

All studies



Study name	Odds ratio	Lower limit	Upper limit	Z-Value	p-Value
Dickerson 2009	2.803	0.110	71.656	0.623	0.533
Givertz 2015	0.685	0.212	2.219	-0.630	0.528
Hare 2008	2.031	0.602	6.854	1.141	0.254
Higgins 2014	0.709	0.148	3.399	-0.429	0.668
Jalal 2016	3.234	0.128	81.791	0.712	0.476
Jarnerot 2000	2.938	0.118	73.033	0.658	0.511
Kamatani 2011 late phase 2	0.706	0.028	17.677	-0.212	0.832
Khan 2008	0.312	0.012	8.285	-0.696	0.486
Mao 2015	0.332	0.013	8.187	-0.674	0.500
NCT01078389 2014	5.064	0.241	106.341	1.044	0.296
NCT01350388 2016	0.325	0.013	8.222	-0.682	0.495
NCT01496469 2015	3.000	0.120	75.113	0.669	0.504
NCT02128490 / Gunawardhana 2016	1.288	0.061	27.378	0.162	0.871
NCT02139046 / Saag 2016	0.998	0.111	8.956	-0.002	0.998
Rentoukas 2010	0.510	0.119	2.188	-0.906	0.365
Saag 2016	0.153	0.015	1.539	-1.594	0.111
Schumacher 2008	1.006	0.052	19.591	0.004	0.997
Separham 2016	0.485	0.086	2.740	-0.819	0.413
Taheraghdam 2014	0.470	0.080	2.749	-0.838	0.402
Zhang 2012	0.265	0.090	0.775	-2.426	0.015
Dalbeth, 2017	1.510	0.249	9.161	0.448	0.654
Huang, 2017	0.235	0.025	2.178	-1.275	0.202
Mukri, 2018	3.061	0.122	76.949	0.680	0.497
Tausche, 2017	3.028	0.122	75.171	0.676	0.499
	0.725	0.482	1.091	-1.541	0.123

Hypertension. 2021;77:383–392. DOI: 10.1161/HYPERTENSIONAHA.120.16547

The Impact of Urate-Lowering Therapy in Post-Myocardial Infarction Patients: Insights from a Population-Based, Propensity Score-Matched Analysis

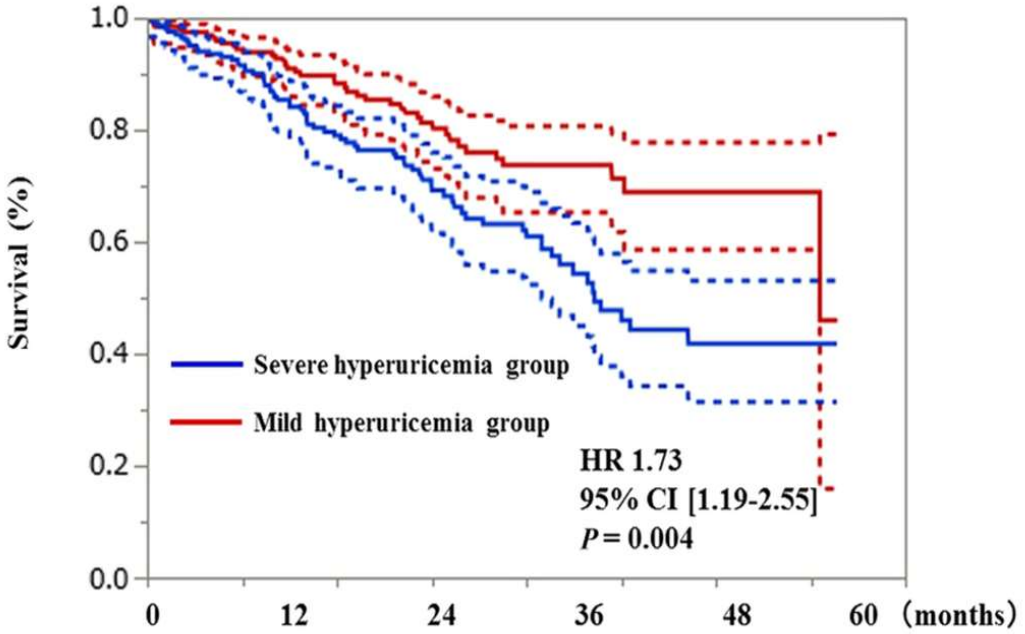
Chi-Jung Tai[1,2,3], Chin-Chung Wu[2], Kun-Tai Lee[4], Tzyy-Guey Tseng[1], Hui-Chun Wang[2,5,6,7], Fang-Rong Chang[2,5,6,7,*] and Yi-Hsin Yang[8,9,*]

Table 2 Comparison of all-cause mortality and cardiovascular outcomes between patients with and without ULT

	ULT (+) (*n* = 963)	ULT (−) (*n* = 963)	Adjusted HR[a] (95% CI)	*P* value[a]	Bootstrap adjusted HR (bootstrap 95% CI)[b]
Primary end points					
All-cause mortality	86 (8.9%)	245 (25.4%)	0.67 (0.51–0.87)	0.003*	0.66 (0.48–0.90)
Secondary end points					
Composite CV outcomes[c]	315 (32.7%)	376 (39.0%)	0.90 (0.76–1.08)	0.26	0.90 (0.75–1.10)
Recurrent MI with revascularization by PCI or CABG	138 (14.3%)	188 (19.5%)	0.67 (0.53–0.86)	0.001*	0.69 (0.53–0.90)
Recurrent MI with revascularization by heparinization	190 (19.7%)	245 (25.4%)	0.79 (0.64–0.97)	0.02*	0.81 (0.64–1.01)
Heart failure hospitalization	160 (16.6%)	157 (16.3%)	1.25 (0.97–1.60)	0.09	1.40 (1.08–1.83)
Stroke hospitalization	35 (3.6%)	69 (7.1%)	0.60 (0.38–0.96)	0.03*	0.58 (0.35–0.95)
Cardiac arrhythmias hospitalization[d]	47 (4.9%)	68 (7.1%)	0.86 (0.55–1.34)	0.51	0.91 (0.57–1.51)

Lowering Uric Acid May Improve Prognosis in Patients With Hyperuricemia and Heart Failure With Preserved Ejection Fraction

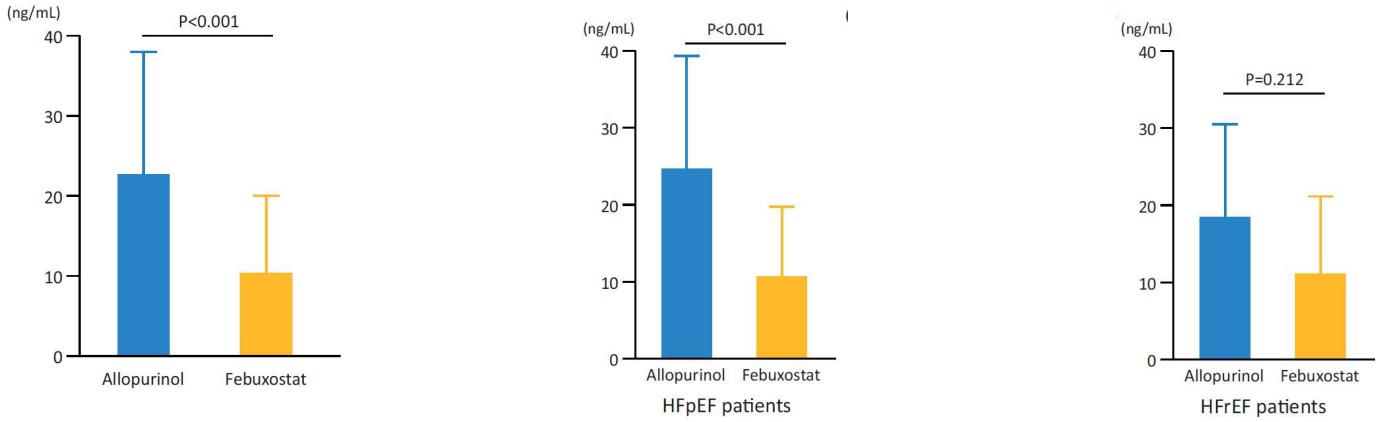
A



Number at risk								
Severe hyperuricemia group	238	181	121	74	58	28	6	4
Mild hyperuricemia group	226	182	124	82	63	30	5	3

Sakata Y et al, . Journal of the American Heart Association, 2022 ,

Comparison of urine 8-hydroxy-20-deoxyguanosine (8-OHdG) levels at 3 years between allopurinol and febuxostat



Prospective Clinical Research Report

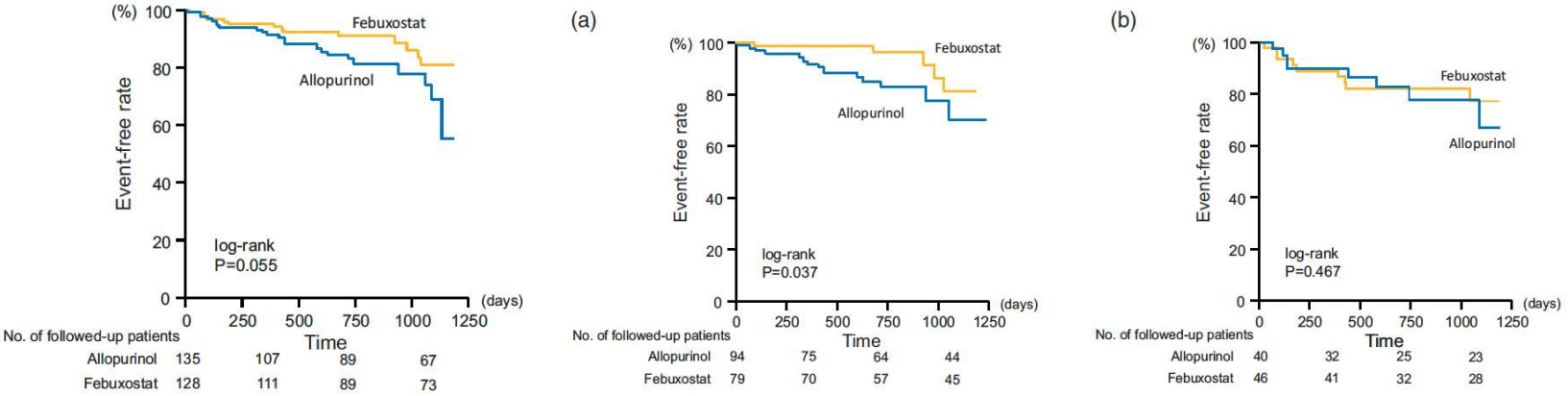
Journal of INTERNATIONAL MEDICAL RESEARCH

Journal of International Medical Research
49(12) 1–15
© The Author(s) 2021
Article reuse guidelines:
sagepub.com/journals-permissions
DOI: 10.1177/03000605211062770
journals.sagepub.com/home/imr
SAGE

Comparison between febuxostat and allopurinol uric acid-lowering therapy in patients with chronic heart failure and hyperuricemia: a multicenter randomized controlled trial

Suzuki S. Journal of International Medical Research 2021

Kaplan–Meier analyses for patients free from hospitalization due to worsening heart failure in the febuxostat and allopurinol groups



SUA and drug treatment

Effects of non urate-lowering drugs on SUA in randomized controlled trials in cardiovascular disease

Drug	Study	Patients	Uric acid (all significant)	Clinical outcome (% mediation)
Empagliflozin	EMPAREG-OUTCOME	DM2	-1.04 mg/dL vs Placebo	Reduced MACE **(24.6%)**
Empagliflozin	EMPEROR-RED	HFrEF	-1.11 mg/dL vs Placebo	Reduced-MACE
Empagliflozin	EMPEROR-PRES	HFpEF	-0,8 mg/dL vs Placebo	Reduced MACE
Dapagliflozin	DAPA-HF	HfrEF	-0.84 mg/dL vs Placebo	Reduced MACE
Dapagliflozin	DELIVER	HFpEF	?	Reduced MACE
Sacubitril-Valsartan	PARADIGM-HF	HFrEF	-0.24 mg/dL vs.ACEi	Reduced-MACE
Sacubitril-Valsartan	PARAGON-HF	HfpEF	-0.32 mg/dL vs valsartan	Partially improved-MACE
Vericiguat	SOCRATES-HF	HFrEF	-6.5 to -10.3% vs Placebo	Reduced-MACE
Losartan	LIFE	HTN	-3.6 to -6.6% vs Atenolo	Reduced MACE **(29%)**
Losartan	RENAAL	HTN	-3.2 to-6.8 % vs Placebo	Less decline GFR Reduced MACE

Serum Uric Acid and CVD:
Facts, Evidence and Future targets of research

- Hyperuricemia (H-SUA) is highly prevalent in the population and contributes to the new-onset HBP and cardiovascular morbidity and mortality.
- The risk of persists after adjustment for all confounding RF's and can be prevented by controlling SUA
- The negative impact of H-SUA on BP and CV risk is dependent on some integrated mechanism primarily involving the activity of XO and leading to oxidative stress, and functional vascular damage.
- The negative prognostic effect of H-SUA in patients with HTN and CVD can be improved by ULT particularly in patients with high XO activity (genetic, CAD, HF, CKD, etc)