

RHNe

**Réseau
Hospitalier
Neuchâtelois**

« La goutte : ce que le médecin de premier recours doit savoir »

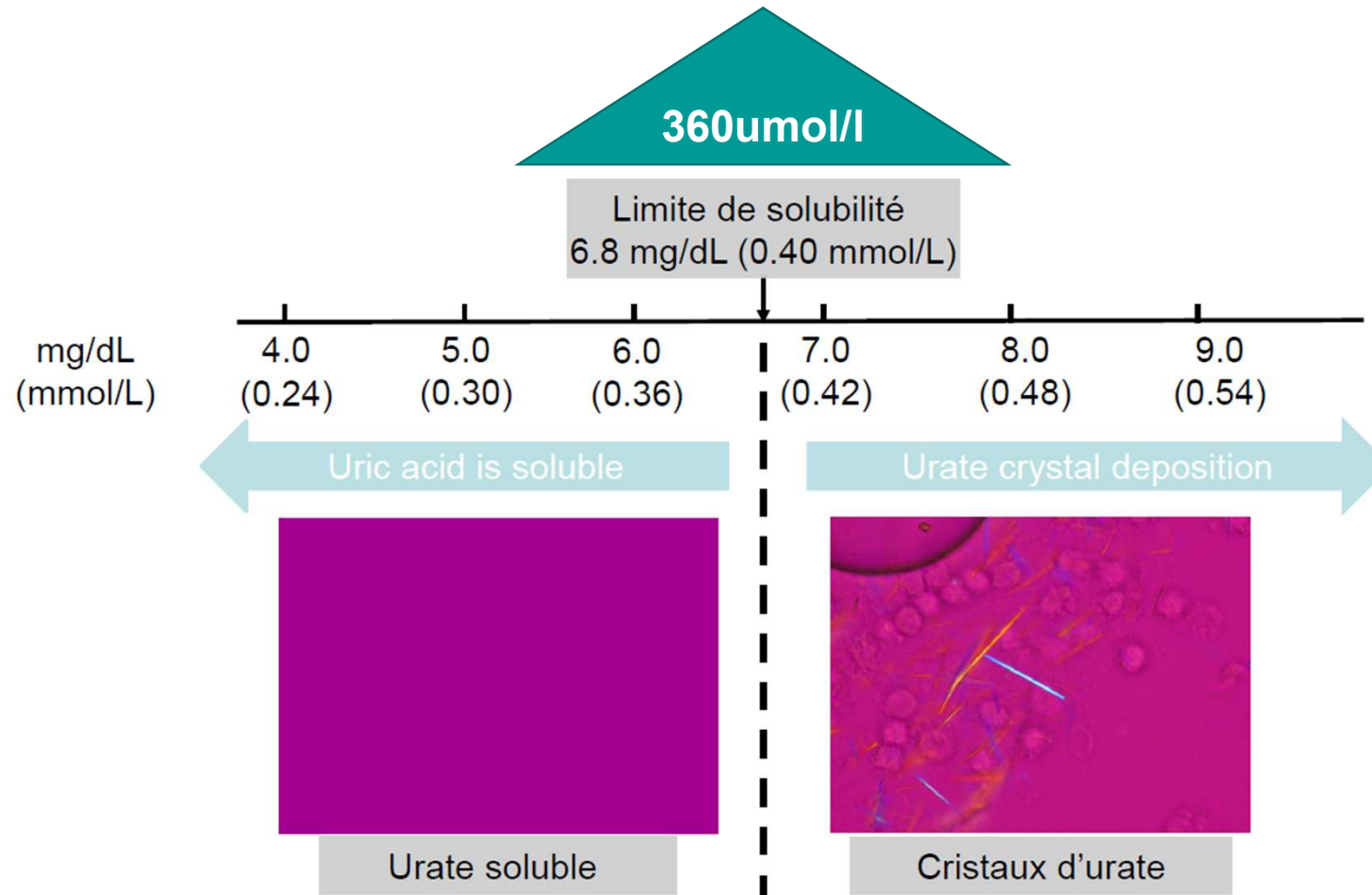
Dre Laure Brulhart

21.02.2024



Conséquence des dépôts de cristaux d'urate de sodium

Consécutives à une hyperuricémie prolongée dans le sang



CONCISE REPORT

Relationship between serum urate concentration and clinically evident incident gout: an individual participant data analysis

Nicola Dalbeth,¹ Amanda Phipps-Green,² Christopher Frampton,³ Tuhina Neogi,⁴
William J Taylor,⁵ Tony R Merriman²

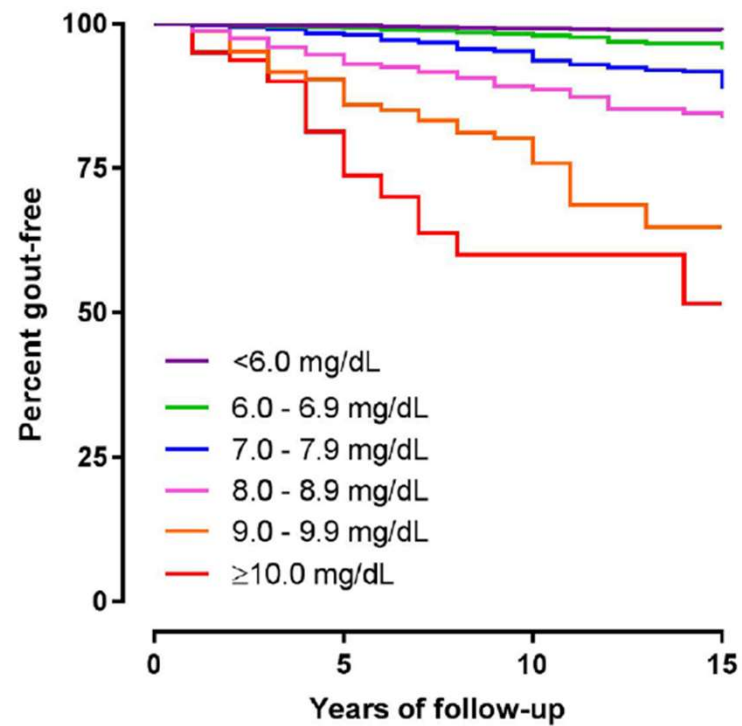
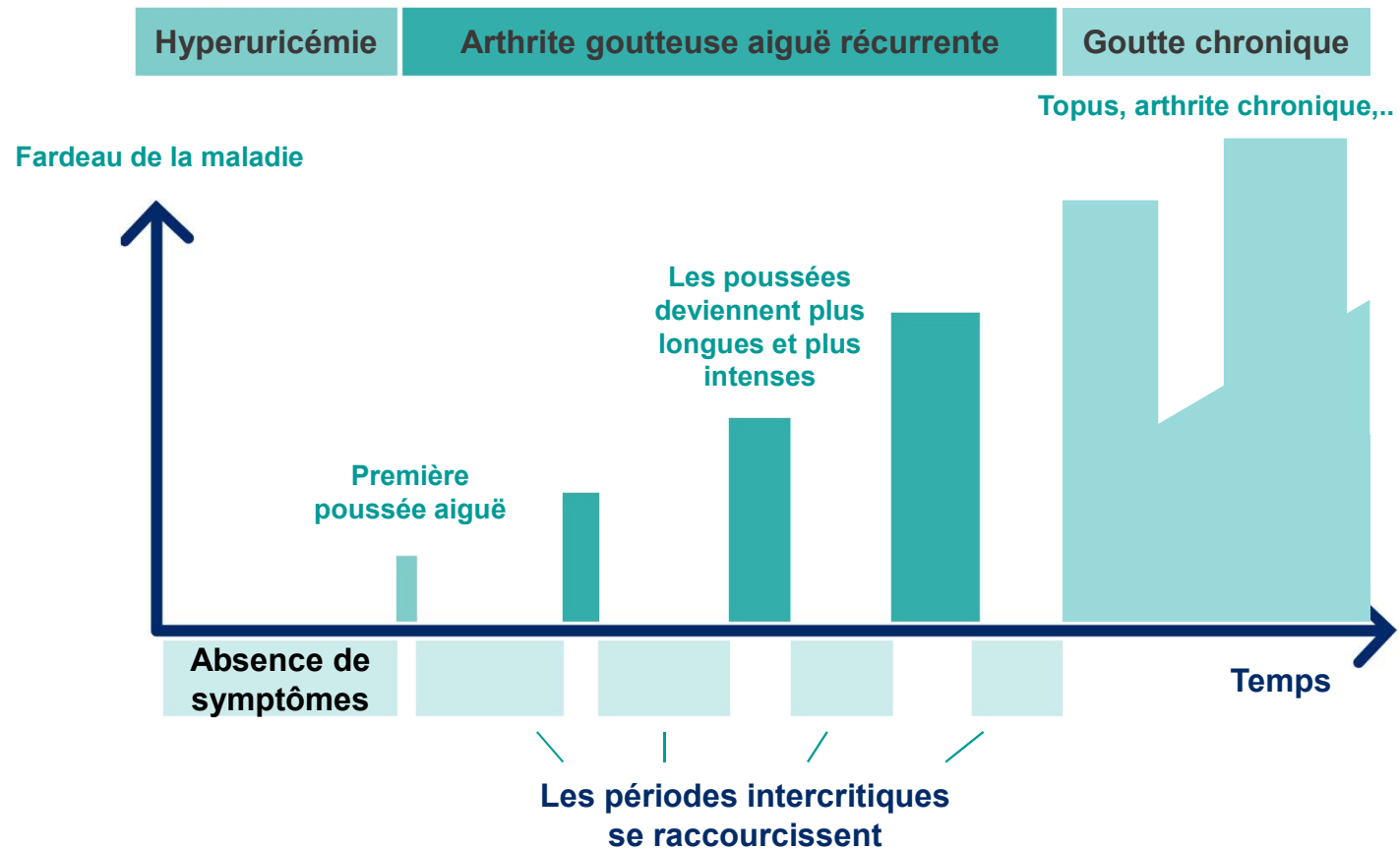


Figure 1 Kaplan-Meier plot showing the percentage of participants who were gout-free over the follow-up period, based on baseline serum urate categories in mg/dL.

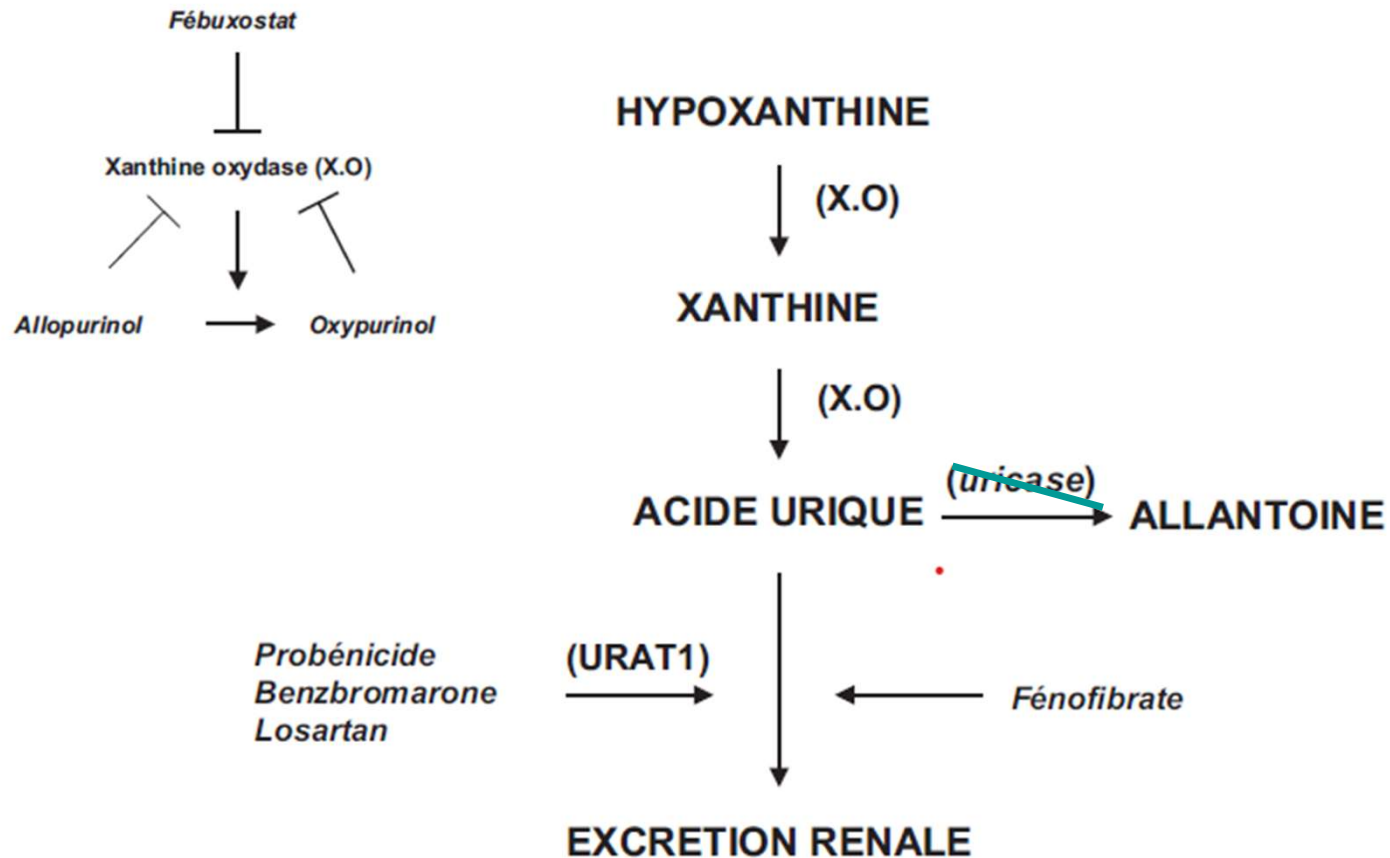
Évolution de la goutte

4

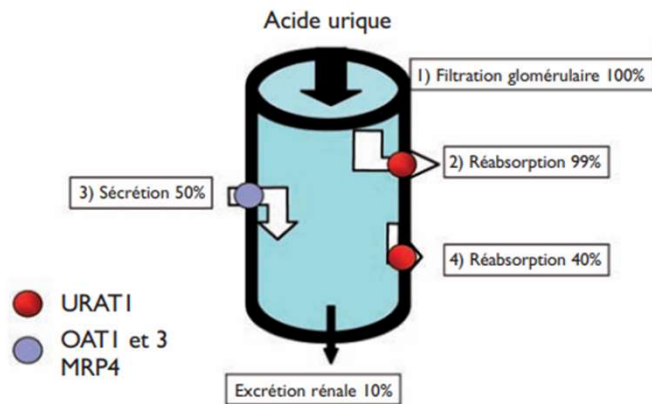


Production d'acide urique

Produit de dégradation des purines



La goutte: une maladie rénale



Nom	Fonction	Localisation	Commentaire
URAT1	Réabsorption d'acide urique	Tubule proximal Segment S1	Mutation dans le syndrome de l'hypouricémie rénale
OAT1	Sécrétion d'anion organique et médicament	Tubule proximal Segment S2	
OAT3	Sécrétion d'anion organique et médicament	Tubule proximal Segment S2	
MRP4	Sécrétion d'anion	Tubule proximal	Dépend de l'adénosine organique triphosphate (ATP)

Figure 2. Transporteurs principaux d'acide urique dans le rein

Fonction rénale et incidence de la goutte

582 Clinical Journal of the American Society of Nephrology

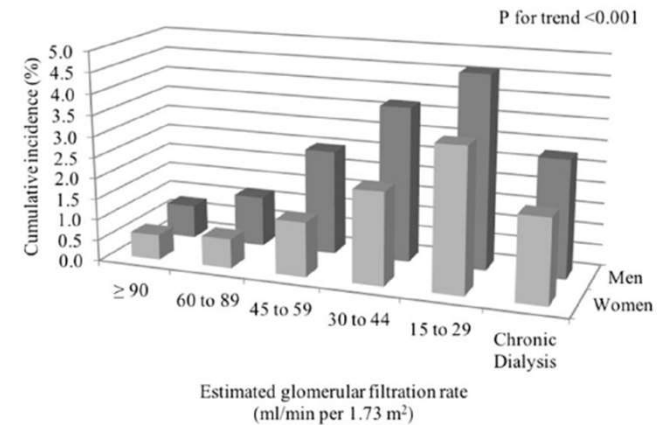
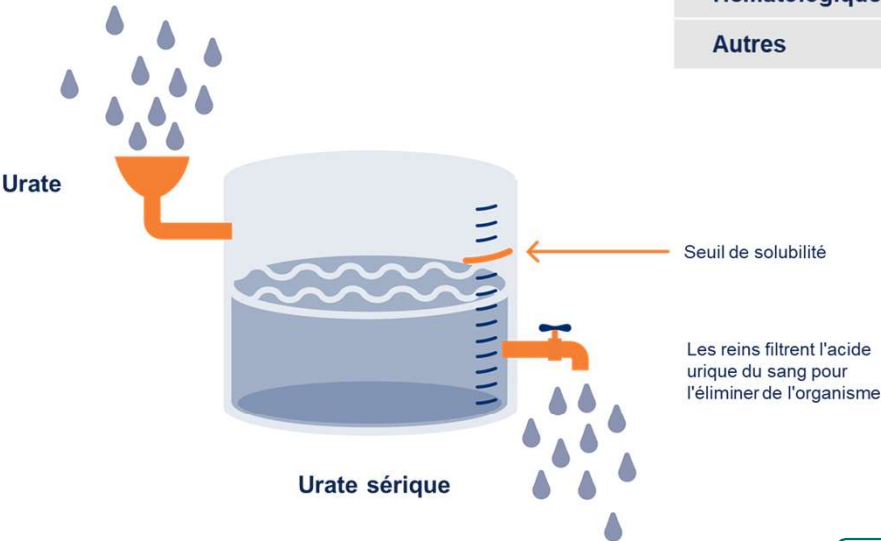


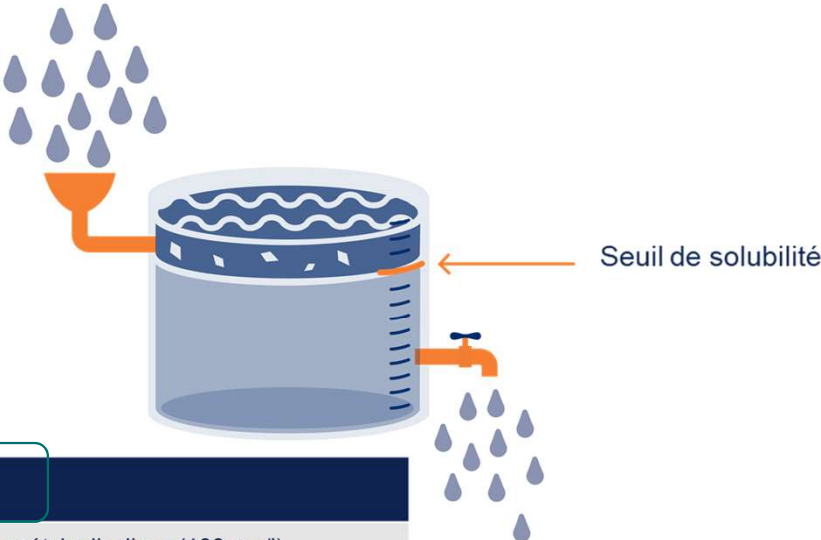
Figure 1. | Three-year cumulative incidence of a gout diagnosis presented by level of kidney function and sex. The 3-year cumulative incidence of diagnosed gout was higher across the five groups of older adults defined by progressively lower levels of eGFR for both men and women (P for trend <0.001); however, persons on chronic dialysis had a lower incidence of gout than those with a moderate reduction in kidney function.

Alimentation riche en purine et turnover cellulaire



Excès de production: 10%

Alimentaires	Aliments riches en purines et en fructose, soda, perte de poids (jeûne)
Hématologiques	Maladies myéloprolifératives et lymphoprolifératives
Autres	Psoriasis, syndrome de lyse tumorale (SLT), maladie de Paget



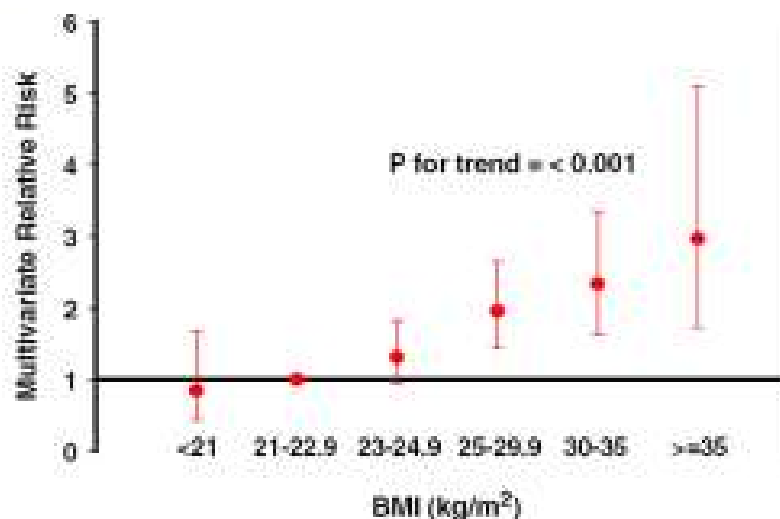
Causes de la diminution de l'excrétion de l'urate 90%

Médicaments	Cyclosporine, thiazides, diurétiques de l'anse, acide acétylsalicylique (100 mg/j)
Rénales	Hypertension, maladie polykystique des reins, insuffisance rénale chronique d'étiologies diverses, prédisposition génétique (hypoexcrétion)
Métaboliques/ endocrinologiques	Déshydratation (souvent associée à une chirurgie), acidose lactique, cétose, hypothyroïdie
Autres	Obésité

Facteurs associés

FACTEURS DE RISQUE

- Age
- Homme
- Race
- HTA (74%)
- Obésité
- Diabète (26%)
- IRC (47-71%)
- Intoxication au plomb
- Aliment et médication



H. Zhu Am J of med 2012
H. Choi Rheum Clin Dis N Am 2006

L'alimentation

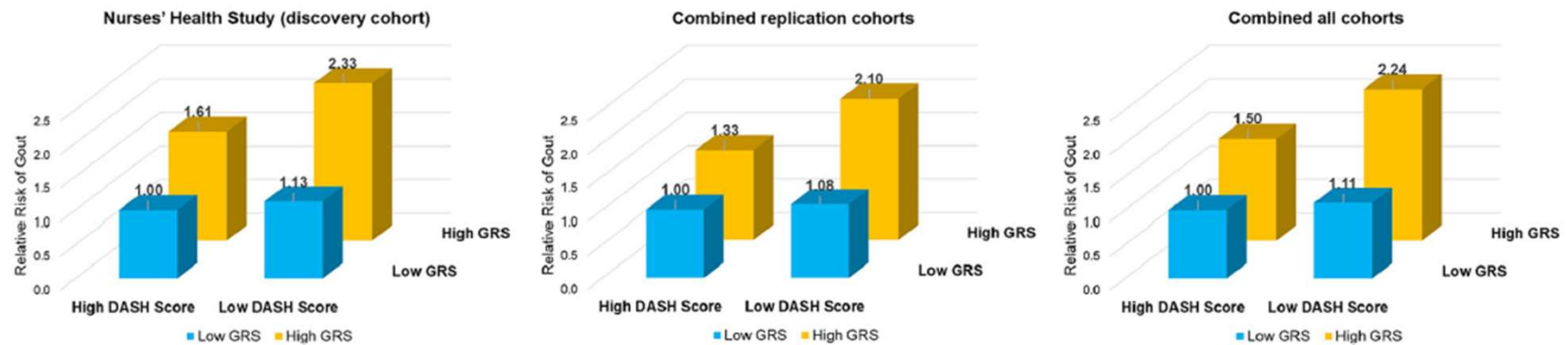
Table 1 | Diet wide significant associations with serum urate levels (μmol/L) in full, male, and female study cohorts

Food items	Full cohort					Male cohort				Female cohort			
	No	β (95% CI)†	P _β	R ² (%)‡	β§	No	β (95% CI)	P _β	R ² (%)	No	β (95% CI)	P _β	R ² (%)
Associated with higher urate levels													
Beer	16 724	1.38 (1.02 to 1.74)¶	<0.001	0.99	3.91	8392	1.33 (0.93 to 1.74)¶	<0.001	1.31	8332	1.78 (1.22 to 2.34)	<0.001	0.49
Liquor	16 743	1.38 (0.79 to 1.98)¶	<0.001	0.40	2.46	8403	1.16 (0.46 to 1.86)¶	0.001	0.41	8340	1.84 (1.21 to 2.48)	<0.001	0.44
Wine	16 743	1.07 (0.34 to 1.80)¶	0.004	0.17	NA	8402	1.30 (0.64 to 1.96)	<0.001	0.16	8341	0.89 (−0.17 to 1.94)¶	0.10	0.20
Potato	16 754	0.87 (0.42 to 1.32)¶	<0.001	0.17	NA	8392	0.87 (0.42 to 1.32)¶	<0.001	0.17	8343	0.77 (0.15 to 1.40)	0.02	0.09
Poultry	16 740	0.70 (0.29 to 1.11)¶	<0.001	0.17	NA	8392	0.70 (0.29 to 1.11)¶	<0.001	0.17	8337	0.50 (−0.02 to 1.02)	0.06	0.05
Soft drink	16 745	0.68 (0.34 to 1.02)¶	<0.001	0.17	NA	8392	0.68 (0.34 to 1.02)¶	<0.001	0.17	8341	0.55 (0.09 to 1.01)¶	0.02	0.16
Beef, pork, or lamb	16 757	0.63 (0.32 to 0.94)¶	<0.001	0.17	NA	8392	0.63 (0.32 to 0.94)¶	<0.001	0.17	8345	0.47 (0.02 to 0.92)	0.04	0.04
Associated with lower urate levels													
Eggs	16 736	−1.10 (−1.54 to −0.66)¶	<0.001	0.14	NA	8409	−0.73 (−1.07 to −0.38)	<0.001	0.19	8333	−0.45 (−1.74 to 0.84)¶	0.49	0.01
Peanuts*	12 504	−0.88 (−1.25 to −0.51)¶	<0.001	0.14	NA	8409	−0.73 (−1.07 to −0.38)	<0.001	0.19	8333	−0.45 (−1.74 to 0.84)¶	0.49	0.01
Cold cereal	16 751	−0.72 (−0.97 to −0.47)	<0.001	0.14	NA	8409	−0.73 (−1.07 to −0.38)	<0.001	0.19	8342	−0.67 (−1.04 to −0.30)	<0.001	0.08
Skim milk	16 714	−0.63 (−0.78 to −0.48)	<0.001	0.40	−0.63	8390	−0.78 (−1.00 to −0.56)	<0.001	0.55	8324	−0.48 (−0.68 to −0.28)	<0.001	0.24
Cheese	16 755	−0.62 (−0.89 to −0.35)	<0.001	0.09	NA	8410	−0.64 (−1.05 to −0.23)	0.002	0.10	8345	−0.64 (−0.99 to −0.29)	<0.001	0.09
Brown bread	16 710	−0.60 (−0.77 to −0.42)	<0.001	0.22	NA	8382	−0.68 (−0.93 to −0.44)¶	<0.001	0.34	8328	−0.45 (−0.71 to −0.20)	<0.001	0.11
Margarine	16 716	−0.29 (−0.44 to −0.15)	<0.001	0.10	NA	8383	−0.25 (−0.69 to 0.18)¶	0.26	0.10	8333	−0.34 (−0.53 to −0.14)	<0.001	0.11
Non-citrus fruit	16 760	−0.28 (−0.43 to −0.13)	<0.001	0.06	NA	8414	−0.43 (−0.66 to −0.19)	<0.001	0.14	8346	−0.14 (−0.33 to 0.04)	0.13	0.01

but each explained ≤0.3% of variance in serum urate levels and 23.9% was explained by common, genome wide single nucleotide variation

Interactions Between Genetic Risk and Diet Influencing Risk of Incident Female Gout: Discovery and Replication Analysis of Four Prospective Cohorts

Kehuan Lin,¹  Natalie McCormick,²  Chio Yokose,³  Amit D. Joshi,⁴ Na Lu,⁵ Gary C. Curhan,⁶ Tony R. Merriman,⁷  Kenneth G. Saag,⁸ Paul M. Ridker,⁹ Julie E. Buring,¹⁰ Daniel I. Chasman,⁹ Frank B. Hu,¹¹ and Hyon K. Choi¹²



A propos d'un patient

Homme de 84 ans

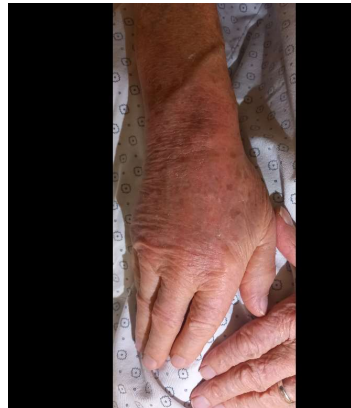
- 15 février : érythème et d'une tuméfaction de la face dorsale de la main droite.
 - Suspicion d'érysipèle: Co-amoxicilline
 - 19.02: évolution défavorable, urgences pour suspicion de crise de goutte
- Complément de traitement : Colchicine, Allopurinol, s/p PTH bilatérale
- Antécédents : diabète, hypertension artérielle, crise de goutte

→ Crise de goutte (2^{ème} épisode en 40 ans)
Quel traitement?
Introduction d'un hypouricémiant?



...que :
érythème et tuméfaction
algique de mobilité
co 8.8, GFR 76ml/mn

- Ponction articulaire:
 - Liquide « purulent »
 - Pyrophosphates et acide urique
 - Pas de germe au gram – culture en cours



Présentation clinique

Crise de goutte typique

- Crises récurrentes d'inflammation monoarticulaire aiguë très douloureuse
- La podagre est le symptôme classique (goutte touchant le gros orteil)
- Les autres foyers courants sont le pied, la cheville, le genou, le doigt, le poignet et le coude
- Apparition rapide caractéristique d'une douleur intense, d'une tuméfaction et d'une hypersensibilité
- Les crises apparaissent souvent la nuit ou au petit matin – pic d'intensité en ≤ 24 h
- Résolution généralement en 7-10 jours sans traitement spécifique
- 10% oligoarticulaire – rarement polyarticulaire
- Bursite et tendinopathie



Tophus

Importance de l'examen clinique

- Nodules facilement visibles et palpables
- Péri-articulaires, sous-cutané
- Hélix: caractéristique



Photo : Avec l'autorisation du professeur Jean Dudler



Bilan sanguin

Syndrome inflammatoire et uricémie

- Hyperuricémie

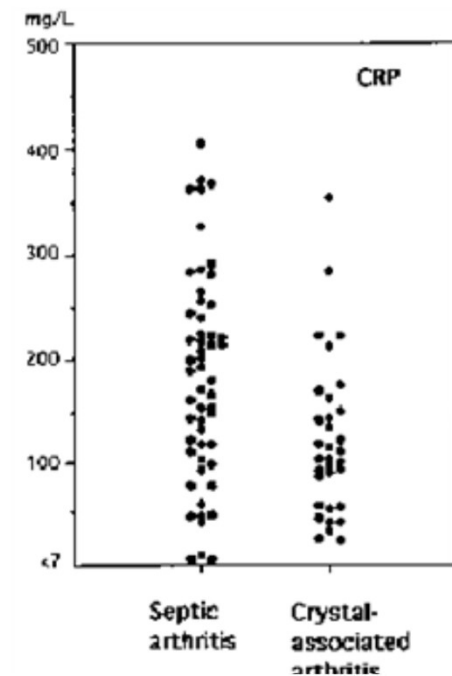
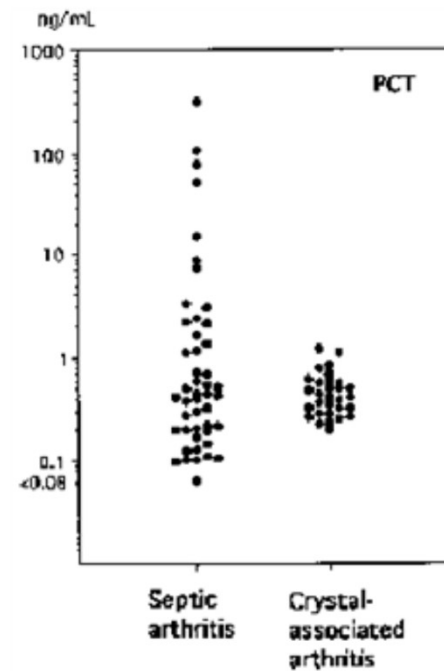
Peux être normale en cas de crise -> à répéter après 2 semaines

Bonne valeur prédictive négative

-> uricémie normale à plusieurs reprises: considérer un autre diagnostic

Bacterial or Crystal-associated Arthritis? Discriminating Ability of Serum Inflammatory Markers

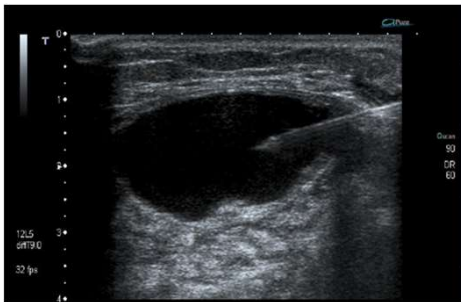
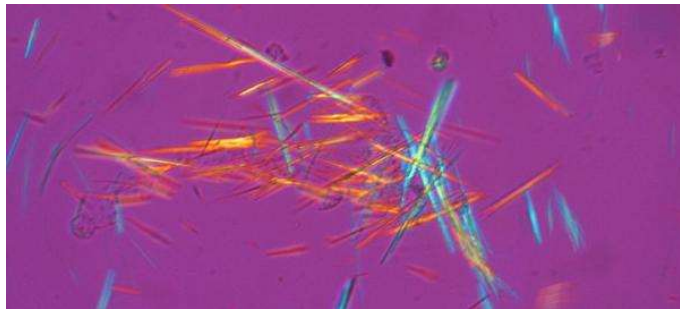
BO SÖDERQUIST¹, IAN JONES², HANS FREDLUND³ and TOMAS VIKERFORS¹



overlap between the groups was present, resulting in low sensitivity, specificity

Diagnostic

Ponction articulaire



La démonstration de cristaux d'urate monosodique à l'examen microscopique du liquide synovial ou d'un aspirat de tophus permet un diagnostic définitif de goutte

Les cristaux d'urate sont intracellulaires ou extracellulaires

Les cristaux examinés à travers un filtre polarisant

Ponction articulaire

➤ Aucune contre-indication absolue à la ponction en cas de suspicion d'arthrite septique

➤ Lésions cutanées

➤ Bactériémie

➤ Prothèse -> orthopédiste

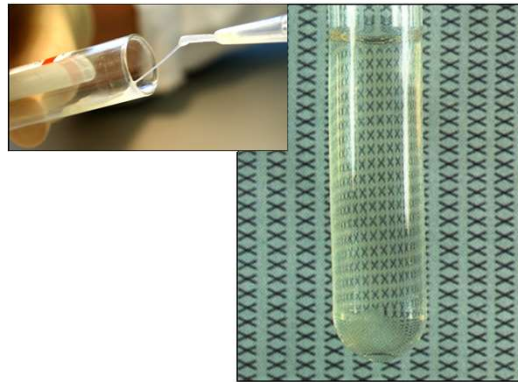
➤ Trouble de l'hémostase:

➤ *INR supra-thérapeutique*

➤ *Thrombopénie <50 G/l*

Observez le liquide articulaire

Normal: transparent



Inflammatoire: opaque

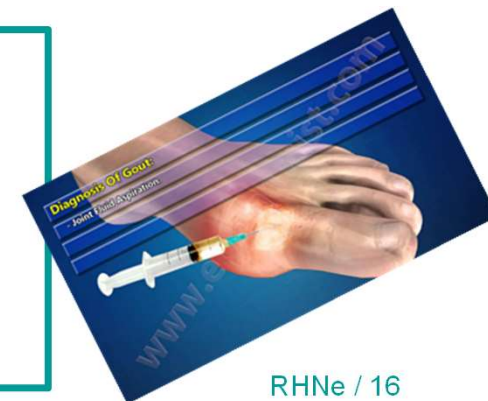


Analyse du liquide synovial:

➤ Comptage leucocytaire (>2000/mm³: inflammatoire)

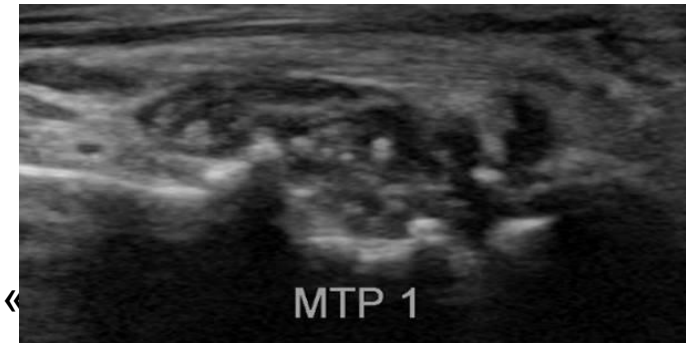
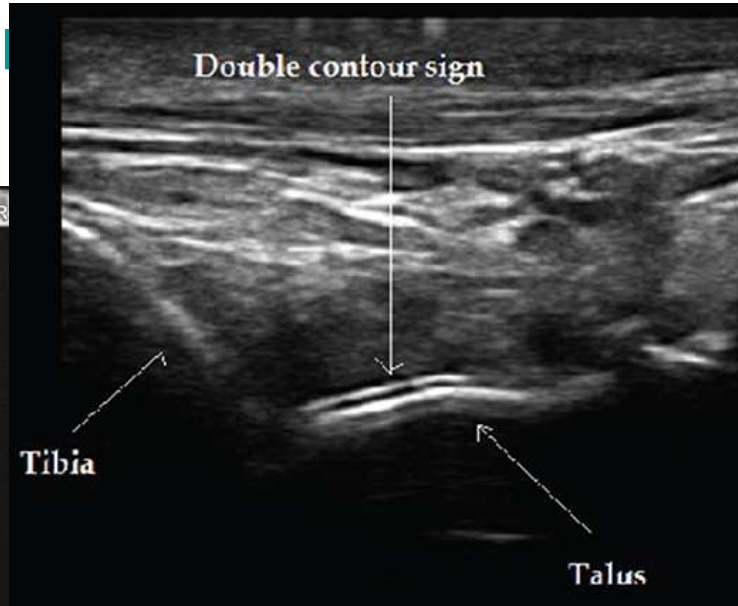
➤ Examen bactériologique

➤ Recherche de cristaux



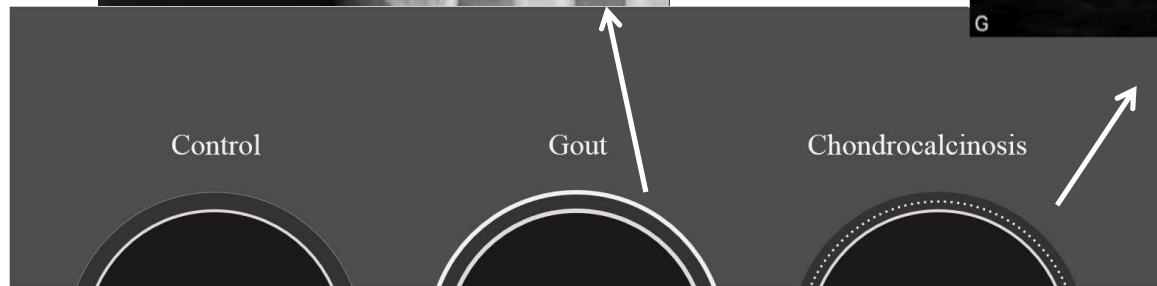
Radiographie

Echographie



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Diagnostic

EULAR recommendations

Table 1 Final set of eight recommendations for the diagnosis of gout				
	Recommendations			
1	Search for crystals in synovial fluid or tophaceous deposits; demonstration of MSU crystals is confirmatory	Gout should be considered in the diagnosis of any acute arthritis in an adult. When synovial fluid analysis is not feasible, a clinical diagnosis of gout is supported by the following suggestive features: monoarticular involvement of a foot (especially the first MTP) or ankle joint; previous similar acute arthritis episodes; rapid onset of severe pain and swelling (at its worst in <24 hours); erythema; male gender and associated cardiovascular diseases and hyperuricaemia. These features are highly suggestive but not specific for gout.		
2	Gout should be considered in the diagnosis of any acute arthritis in an adult. When synovial fluid analysis is not feasible, a clinical diagnosis of gout is supported by the following suggestive features: monoarticular involvement of a foot (especially the first MTP) or ankle joint; previous similar acute arthritis episodes; rapid onset of severe pain and swelling (at its worst in <24 hours); erythema; male gender and associated cardiovascular diseases and hyperuricaemia. These features are highly suggestive but not specific for gout.			
3	It is strongly recommended that synovial fluid aspiration and examination for crystals is undertaken in any patient with undiagnosed inflammatory arthritis	3	C	8.8±0.3
4	The diagnosis of gout should be supported by the following suggestive features: monoarticular involvement of a foot (especially the first MTP) or ankle joint; previous similar acute arthritis episodes; rapid onset of severe pain and swelling (at its worst in <24 hours); erythema; male gender and associated cardiovascular diseases and hyperuricaemia. These features are highly suggestive but not specific for gout.			
5	When a clinical diagnosis of gout is uncertain and crystal identification is not possible, patients should be investigated by imaging to search for MSU crystal deposition and features of any alternative diagnosis.			
6	Plain radiographs are indicated to search for imaging evidence of MSU crystal deposition but have limited value for the diagnosis of gout flare. Ultrasound scanning can be more helpful in establishing a diagnosis in patients with suspected gout flare or chronic gouty arthritis by detection of tophi not evident on clinical examination, or a double contour sign at cartilage surfaces, which is highly specific for urate deposits in joints.	1b	A	8.2±0.9
7	Risk factors for chronic hyperuricaemia should be searched for in every person with gout, specifically: chronic kidney disease; overweight, medications (including diuretics, low-dose aspirin, cyclosporine, tacrolimus); consumption of excess alcohol (particularly beer and spirits), non-diet sodas, meat and shellfish.	1a	A	8.2±1.3
8	Systematic assessment for the presence of associated comorbidities in people with gout is recommended, including obesity, renal impairment, hypertension, ischaemic heart disease, heart failure, diabetes and dyslipidaemia.	1a	A	8.7±0.6

Diagnostic différentiel

Table 2. Distinguishing Clinical Features of Common Gout Mimics.*

Differential Diagnosis	Clinical Findings Suggestive of Other Diagnosis†
Gout flare	
Pseudogout from CPPD	Symptoms associated with hyperparathyroidism, hypothyroidism, hemochromatosis, and hypomagnesemia
	CPPD crystals in synovial fluid (rhomboidal morphology and weak or positive birefringence)
	Articular chondrocalcinosis shown on radiograph
Septic arthritis	Prosthetic joint involvement
	Prominent systemic symptoms (e.g., temperature >38.5°C, rigors, and chills)
	Evidence of distant infection (e.g., bacteremia and endocarditis)
	Marked synovial leukocytosis (e.g., white-cell count >50,000 cells per ml)
	Positive synovial Gram's stain or culture
Trauma	Preceding trauma or injury
	Imaging reveals trauma (e.g., stress fracture)
Cellulitis	Cutaneous erythema distant from joint
Osteoarthritis	Insidious onset, chronic course
	Absent or minimal inflammation on exam
	Noninflammatory synovial fluid
	Characteristic imaging findings (e.g., asymmetric joint space loss, subchondral sclerosis, or osteophytes)
Palindromic rheumatism	Rheumatoid factor, anti-CCP antibody positivity

Tophaceous gout

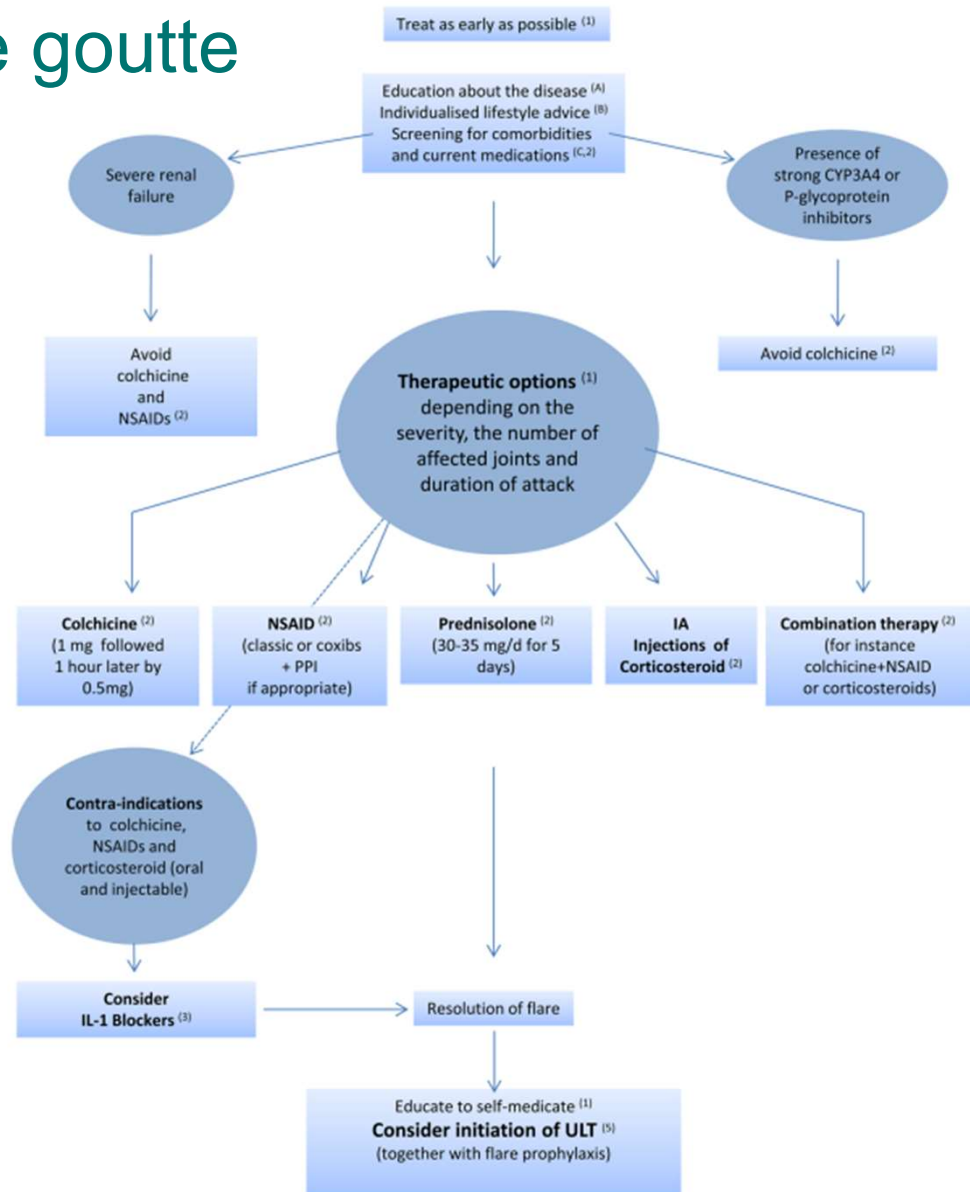
Osteomyelitis	Persistent, marked elevations in ESR or CRP
	Positive bacterial tissue or bone cultures
Rheumatoid arthritis	Insidious onset, chronic course
	Subcutaneous nodules associated with chronic, symmetric arthritis of small joints
	Rheumatoid factor, anti-CCP antibody positivity
	Presence of other extraarticular features (e.g., interstitial lung disease and Felty's syndrome)
Dactylitis	
From reactive arthritis	Preceding dysentery or sexually transmitted disease; presence of sacroiliitis, conjunctivitis, urethritis, keratoderma blennorrhagicum, or circinate balanitis
From psoriatic arthritis	Presence of skin psoriasis, nail pitting or onycholysis, or sacroiliitis

n engl j med 387;20 nejm.org November 17, 2022

Traitement de la crise de goutte

Recommandations EULAR

- Importance de l'éducation du patient
- Traiter aussi tôt que possible
- Colchicine:
 - High = Low dose
 - Interaction!! Cyclosporine, diltiazem



Diagnostic

EULAR recommendations

Table 1 Final set of eight recommendations for the diagnosis of gout

	Recommendations	Level of evidence	Grade of recommendation	Level of agreement
1	Search for crystals in synovial fluid or tophus aspirates is recommended in every person with suspected gout, because demonstration of MSU crystals allows a definitive diagnosis of gout.	2b	B	8.6±1.0
2	Gout should be considered in the diagnosis of any acute arthritis in an adult. When synovial fluid analysis is not feasible, a clinical diagnosis of gout is supported by the following suggestive features: monoarticular involvement of a foot (especially the first MTP) or ankle joint; previous similar acute arthritis episodes; rapid onset of severe pain and swelling (at its worst in <24 hours); erythema; male gender and associated cardiovascular diseases and hyperuricaemia. These features are highly suggestive but not specific for gout.	2b	B	8.6±0.8
3	It is strongly recommended that synovial fluid aspiration and examination for crystals is undertaken in any patient with undiagnosed inflammatory arthritis.			
4	The diagnosis of gout should not be made on the presence of hyperuricaemia alone.			
5	When a clinical diagnosis of gout is uncertain and crystal identification is not possible, patients should be investigated with imaging to search for MSU crystal deposition and features of any alternative diagnosis.			
6	Plain radiographs are indicated to search for imaging evidence of MSU crystal deposition but have limited value for the diagnosis of gout flare. Ultrasound scanning can be more helpful in establishing a diagnosis in patients with suspected gout flare or chronic gouty arthritis by detection of tophi not evident on clinical examination, or a double contour sign at cartilage surfaces, which is highly specific for urate deposits in joints.			
7	Risk factors for chronic hyperuricaemia should be searched for in every person with gout, specifically: chronic kidney disease; overweight, medications (including diuretics, low-dose aspirin, cyclosporine, tacrolimus); consumption of excess alcohol (particularly beer and spirits), non-diet sodas, meat and shellfish.	1a	A	8.2±1.3
8	Systematic assessment for the presence of associated comorbidities in people with gout is recommended, including obesity, renal impairment, hypertension, ischaemic heart disease, heart failure, diabetes and dyslipidaemia.	1a	A	8.7±0.6

MSU, monosodium urate; MTP, metatarsophalangeal.

Évaluation systématique des facteurs associés et de facteurs de risque modifiables

Risque cardiovasculaire

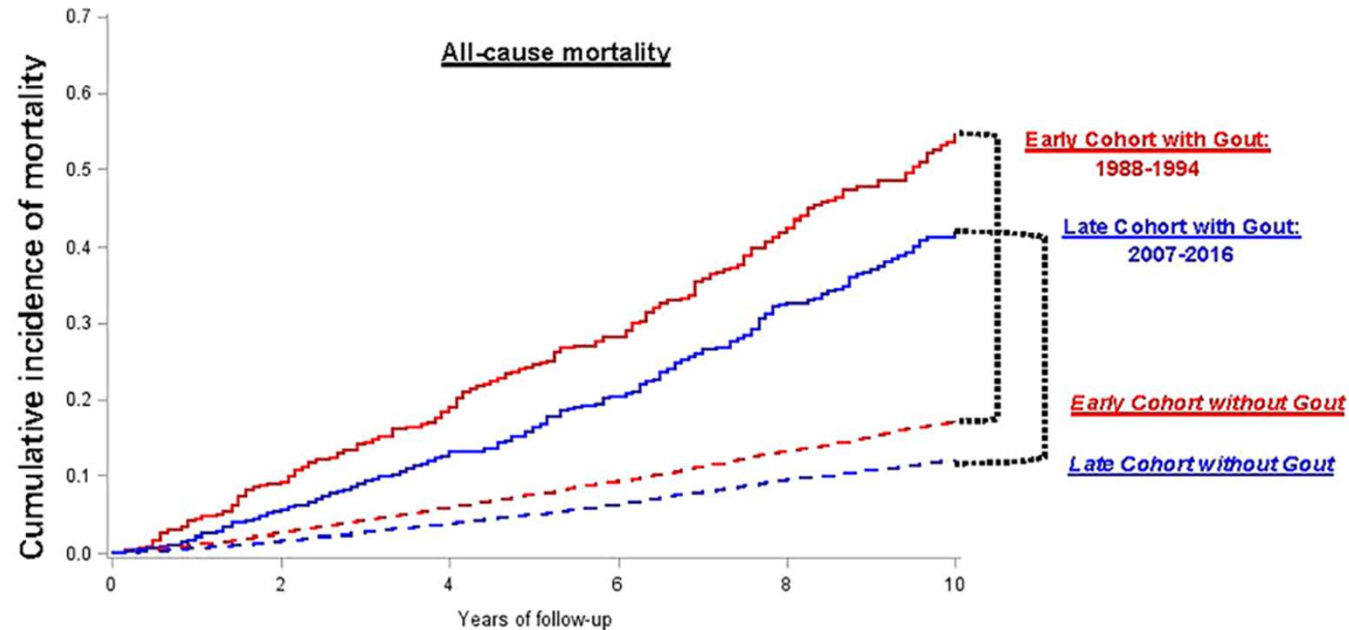


Figure 1. Cumulative incidence of all-cause mortality by time period and gout status in the nationwide US cohort.

- Indépendant des autres facteurs de risque cardiovasculaire et de l'uricémie

Risque cardiovasculaire

A retrospective case-control study using electronic health records from the Clinical Practice Research Datalink in England

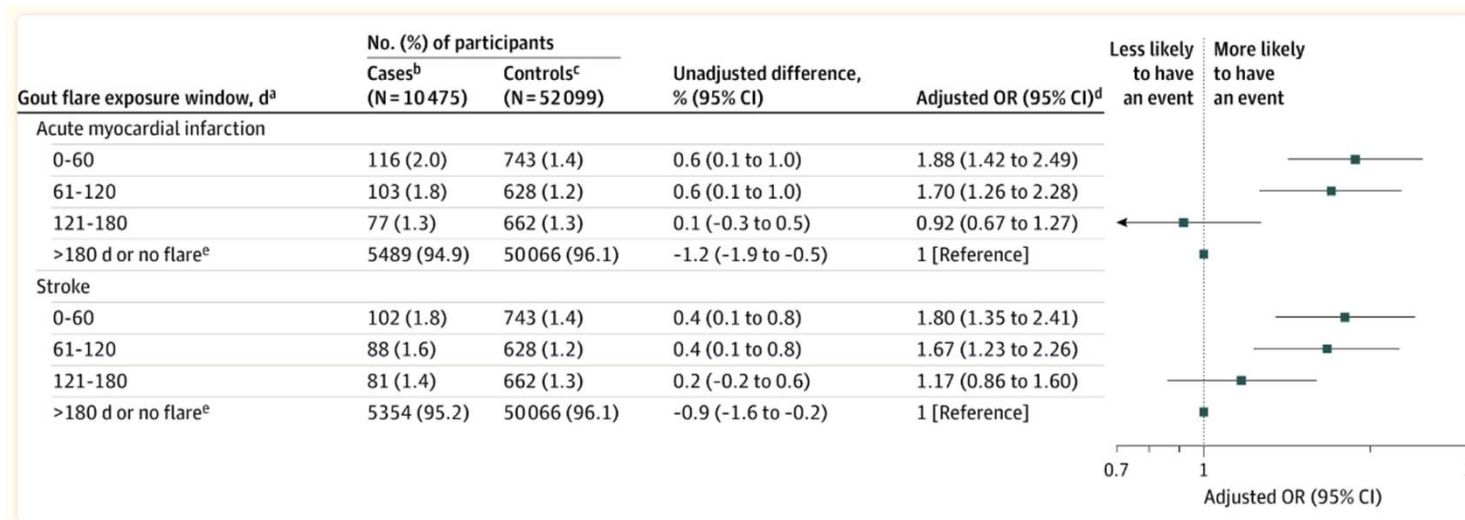


Figure 3.

Association Between Acute Myocardial Infarction, Stroke, and Recent Prior Gout Flares in a Nested Case-Control Study

Conclusions and Relevance

Among individuals with gout, those who experienced a cardiovascular event, compared with those who did not experience such an event, had significantly higher odds of a recent gout flare in the preceding days. These findings suggest gout flares are associated with a transient increase in cardiovascular events following the flare.

Traitement hypouricémiant

Pour quels patients?

- Crises récurrentes ≥ 2 /an
- Tophus ou érosions
- Néphropathie à acide urique – calculs rénaux

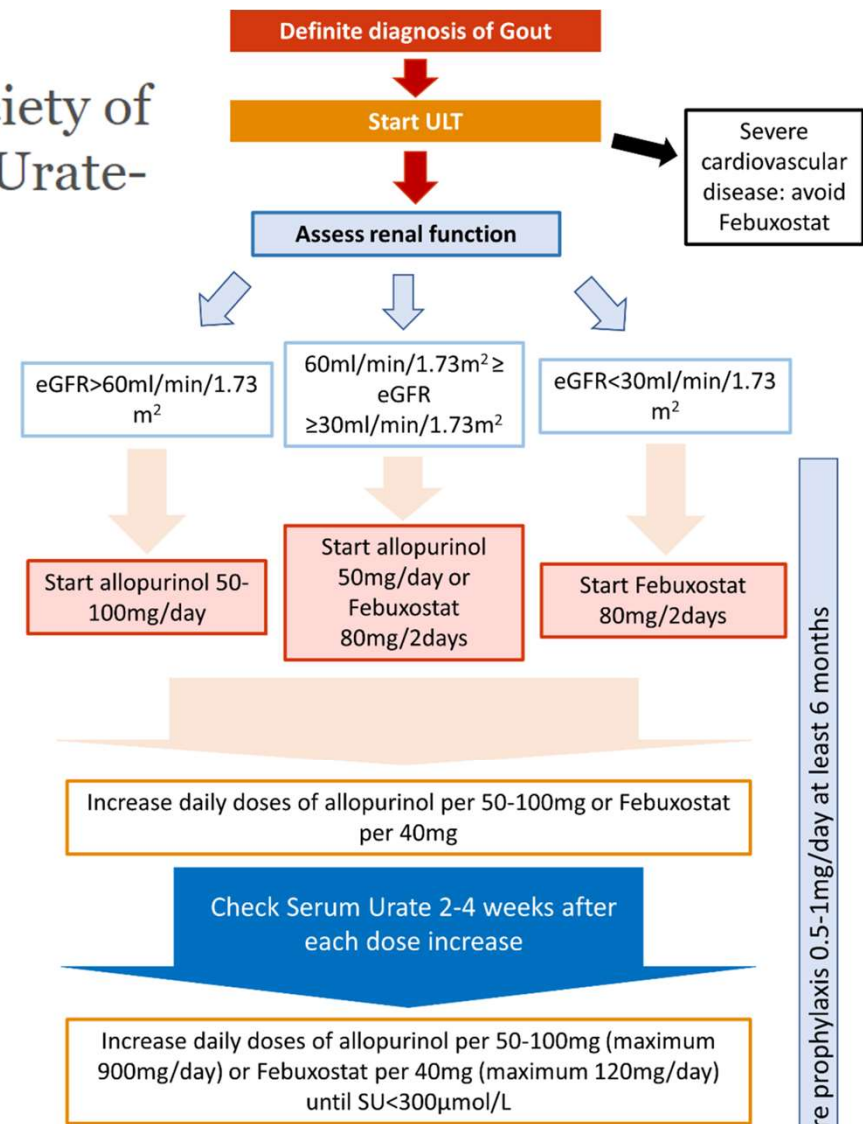
Dès la première crise si

- Jeune âge: <40 ans
- Insuffisance rénale chronique ($\geq$ stade 3), HTA, cardiopathie
- Uricémie >480umol/l

hypouricémiant

2020 recommendations from the French Society of Rheumatology for the management of gout: Urate-lowering therapy  

- Allopurinol: 1^{er} choix thérapeutique
 - Asie de l'Est: risque de DRESS associé au HLA-B*58:01 (test de dépistage)
 - Interaction avec l'azathioprine
- Prophylaxie: colchicine 0,5-1mg/j pour 6 mois
- Febuxostat: élimination hépatique et rénale
- Traitements uricosurique: probénécide et benzbromarone
- Autre: Uricase



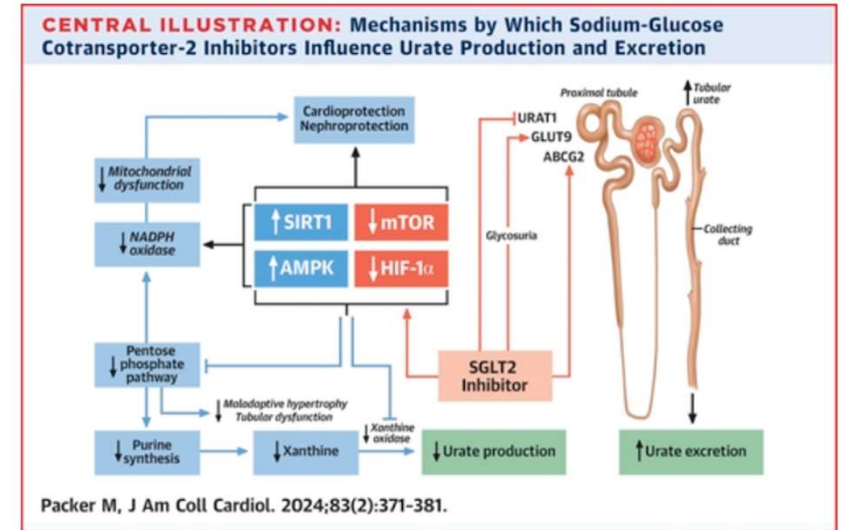
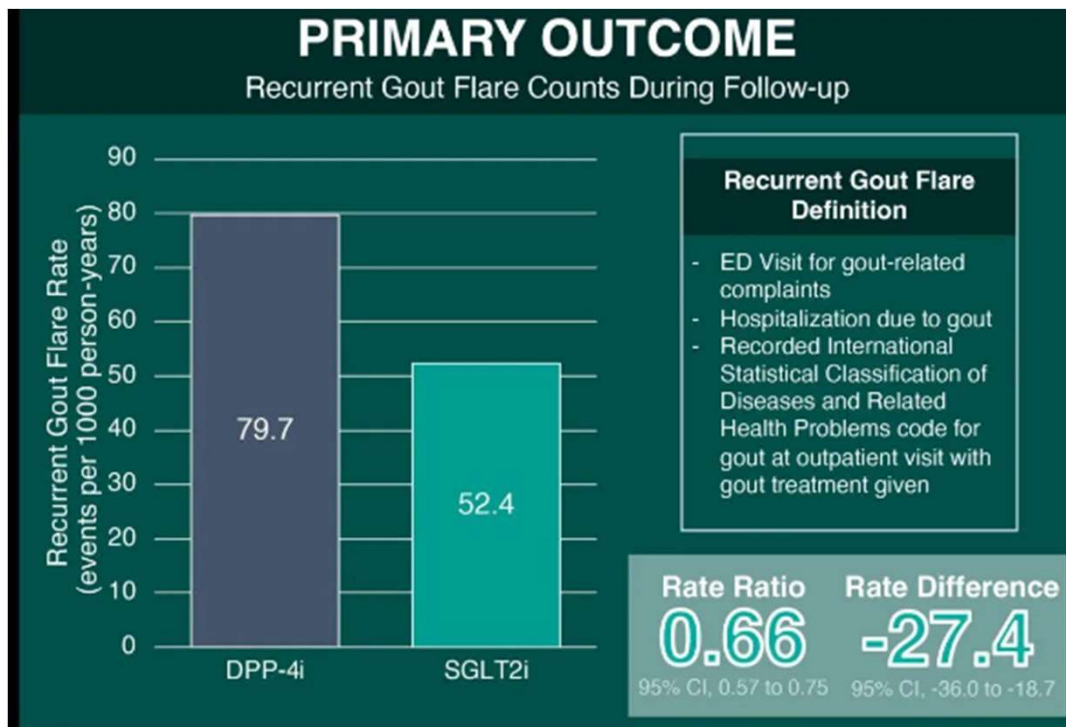
Sodium-glucose cotransporter-2 inhibiteur (SGLT2)

Original Research | August 2023

Comparative Effectiveness of Sodium–Glucose Cotransporter-2 Inhibitors for Recurrent Gout Flares and Gout-Primary Emergency Department Visits and Hospitalizations

A General Population Cohort Study

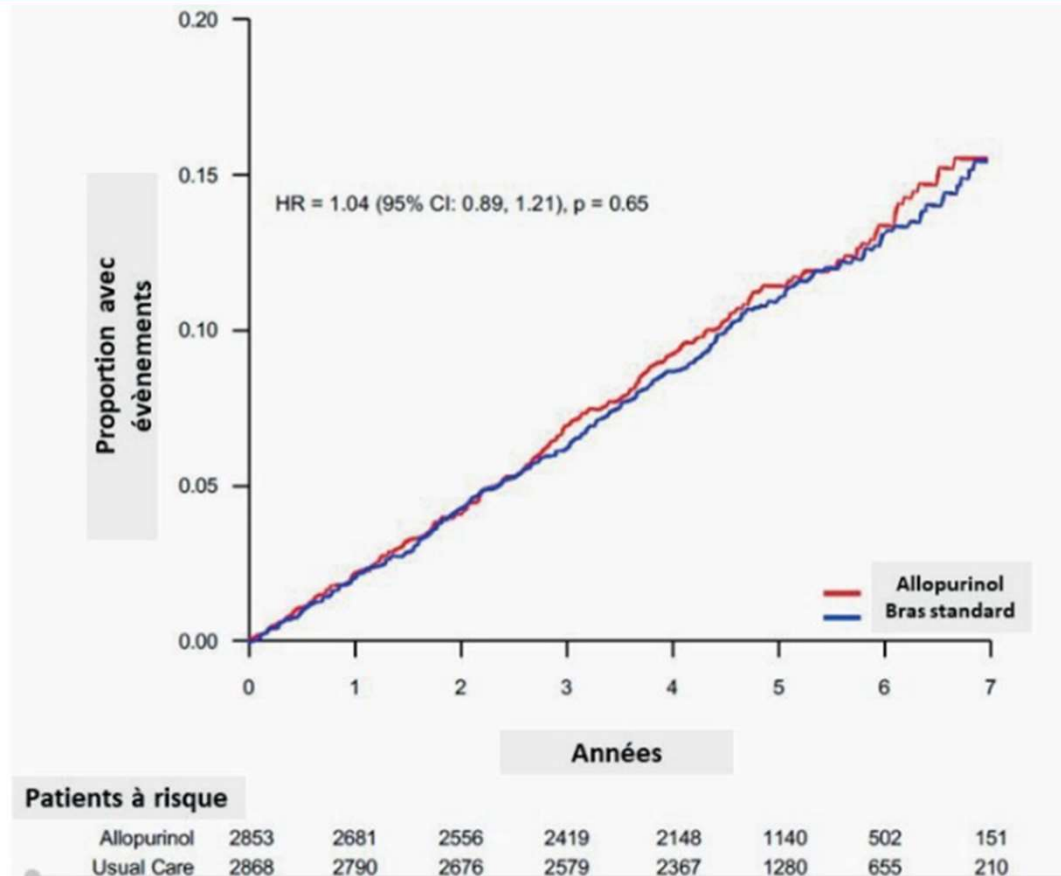
Natalie McCormick, PhD^{*}, Chio Yokose, MD, MSc^{*}, Jie Wei, PhD^{*}, Na Lu, MPH, ... [See More](#)



Hyperuricémie asymptomatique

All- Heart – ESC 2022

FIGURE 1 :
Critère de jugement principal :
IDM, AVC ou décès
cardiovasculaire



Take Home Message

Treat to Target

- Traiter dès la première crise
- Eduquer nos patients
- Cible thérapeutique: uricémie < 360
- Traitement de la crise:
 - Colchicine – AINS – Stéroïdes p.o ou i.a
 - Anti-IL1
 - Prophylaxie : pendant six mois
- Hyperuricémie asymptomatique: pas de traitement
- Traitement des comorbidités: Obésité, diabète, hypertension, dyslipidémie..

