

Update on the Management of Gout

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Webinar

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Case History

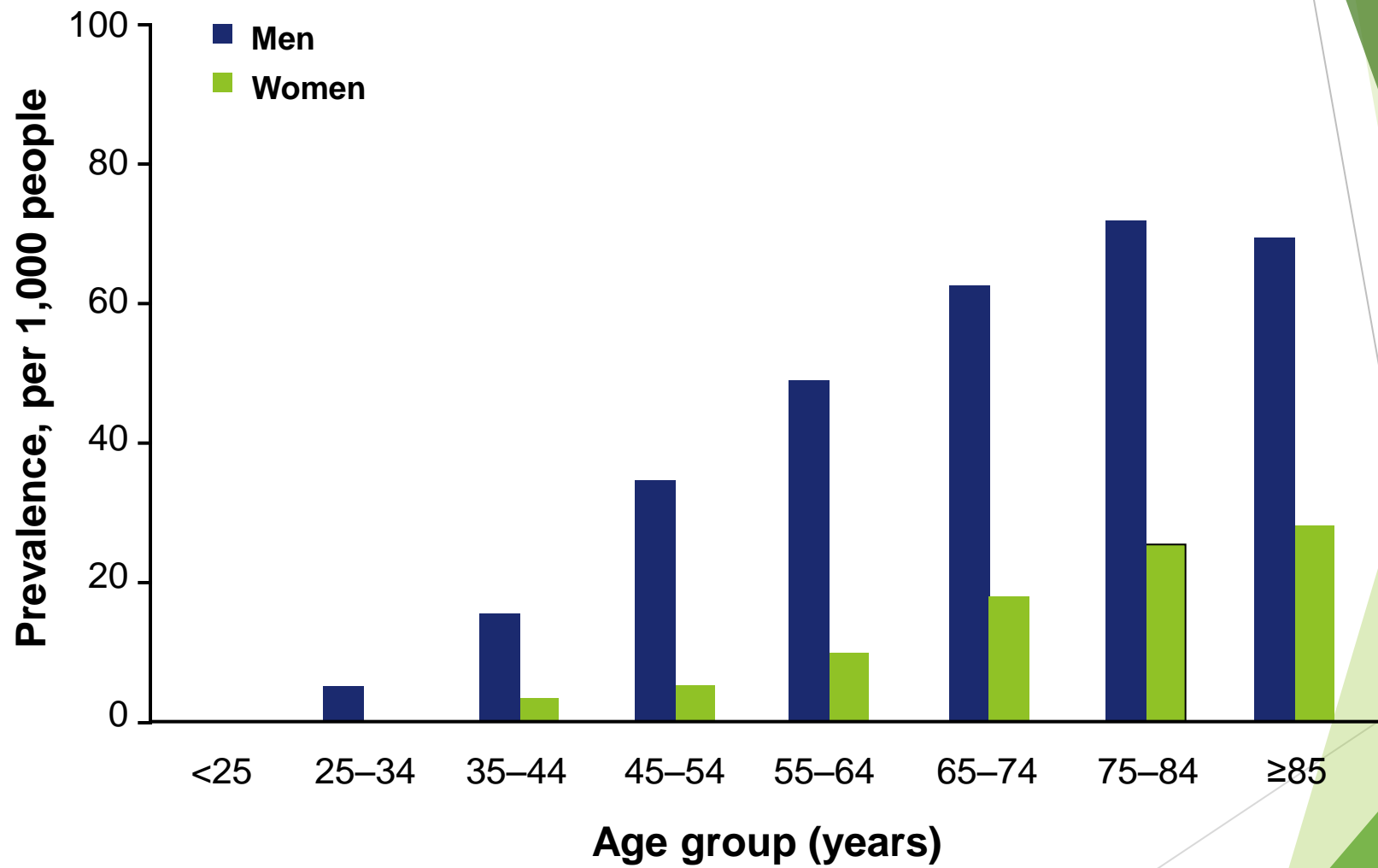
- ▶ 46 year Taxi driver, male, obese
- ▶ 2 -3 years of intermittent joints flares: toes, ankles, knees, fingers, olecranon
- ▶ Developed tophi over 18 months, Xrays feet - 1st MTPJ 'punched out' erosions, urate 650 $\mu\text{mol/L}$
- ▶ Symptoms now every day, debilitating, unable to work
- ▶ GP tried NSAID & Colchicine - not effective, Allopurinol - flares. Referred on Pred 40mg daily (flares at doses below) taken for 4 months



Background Overview

- ▶ Most common inflammatory arthritis
- ▶ UK Incidence steadily increased from 1.5% in 1997 to 2.5% in 2012
- ▶ More common in men - male:female ratio 4:1
- ▶ Most important risk factor is sustained hyperuricaemia
 - ▶ Caused by overproduction or under-excretion of urate
 - ▶ Deposition of monosodium urate crystals in joints and tissues
- ▶ Studies have repeatedly identified increased cardiovascular mortality with gout

Epidemiology - prevalence increases with age



Risk factors for gout

Non-modifiable

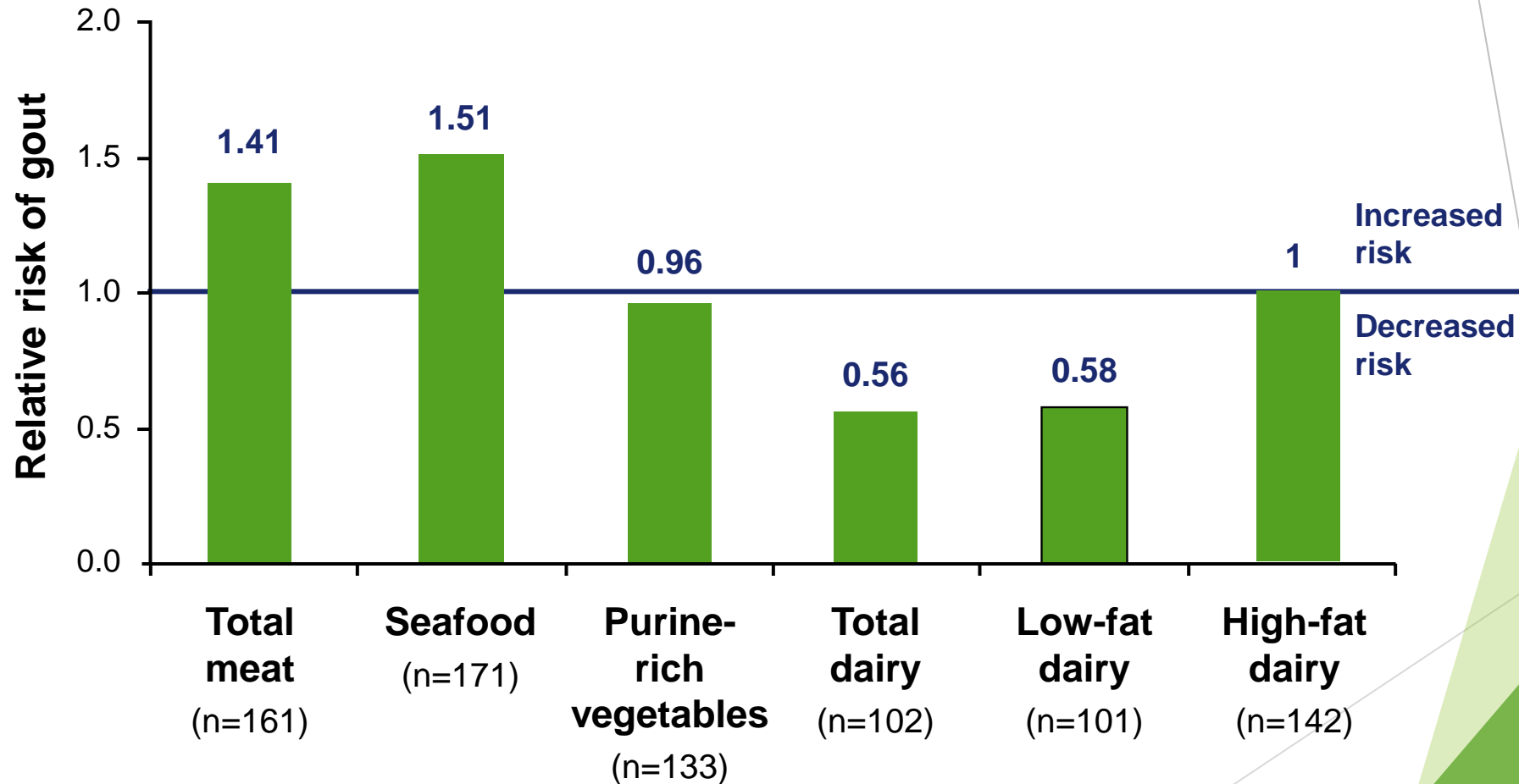
- Age
- Male gender
- Race
- Genetic factors
- Impaired renal function

Modifiable

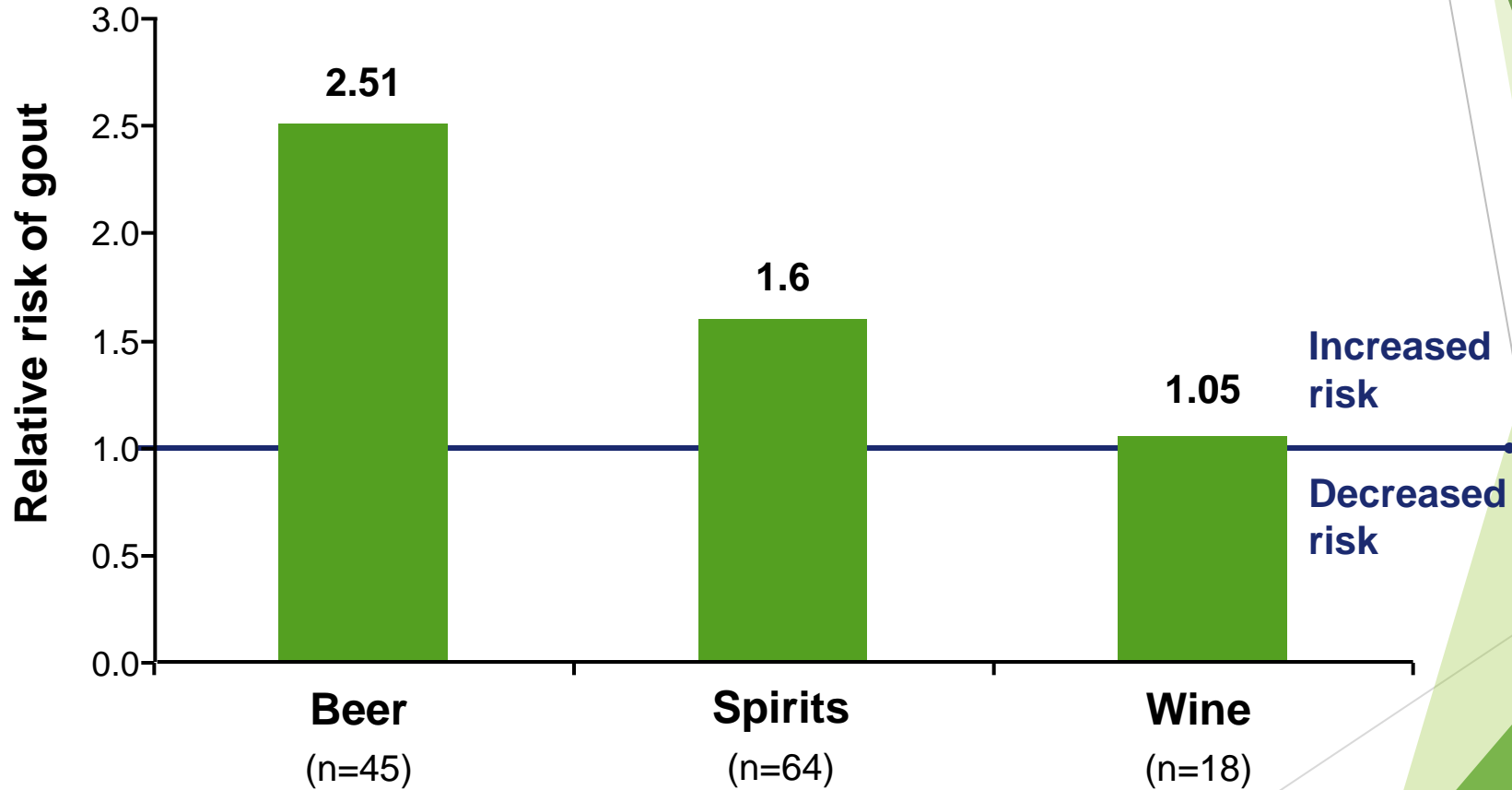
- ▶ High-purine diet
- ▶ Alcohol consumption
- ▶ Obesity
- ▶ Certain medications
 - ▶ Diuretics
- ▶ **Hyperuricaemia**

Modifiable risk factors for gout: purine-rich foods

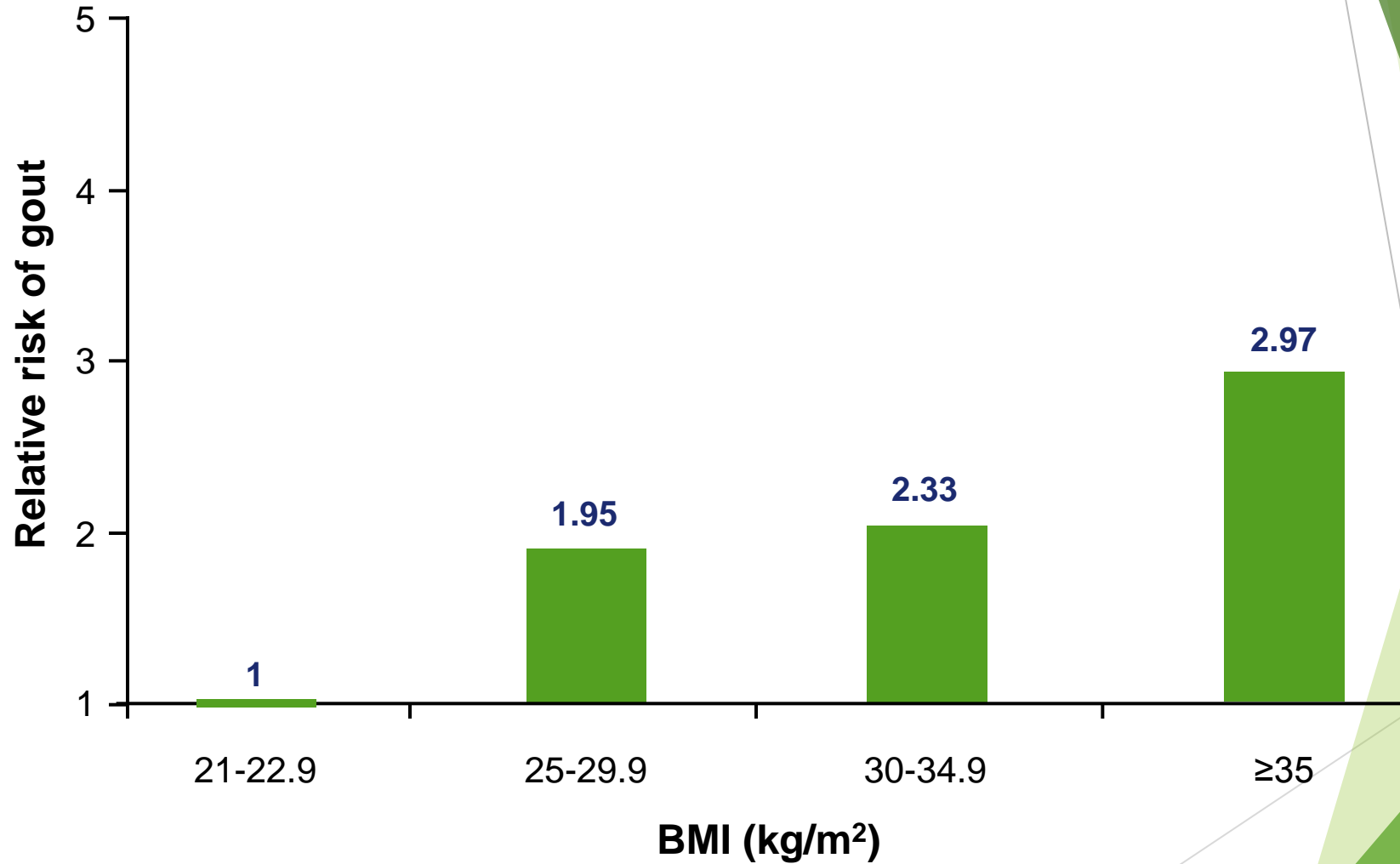
Relative risk of gout in the highest quintile of purine-rich foods and dairy intake compared to the lowest quintile of intake



Modifiable risk factors for gout: alcohol intake



Modifiable risk factors for gout: obesity

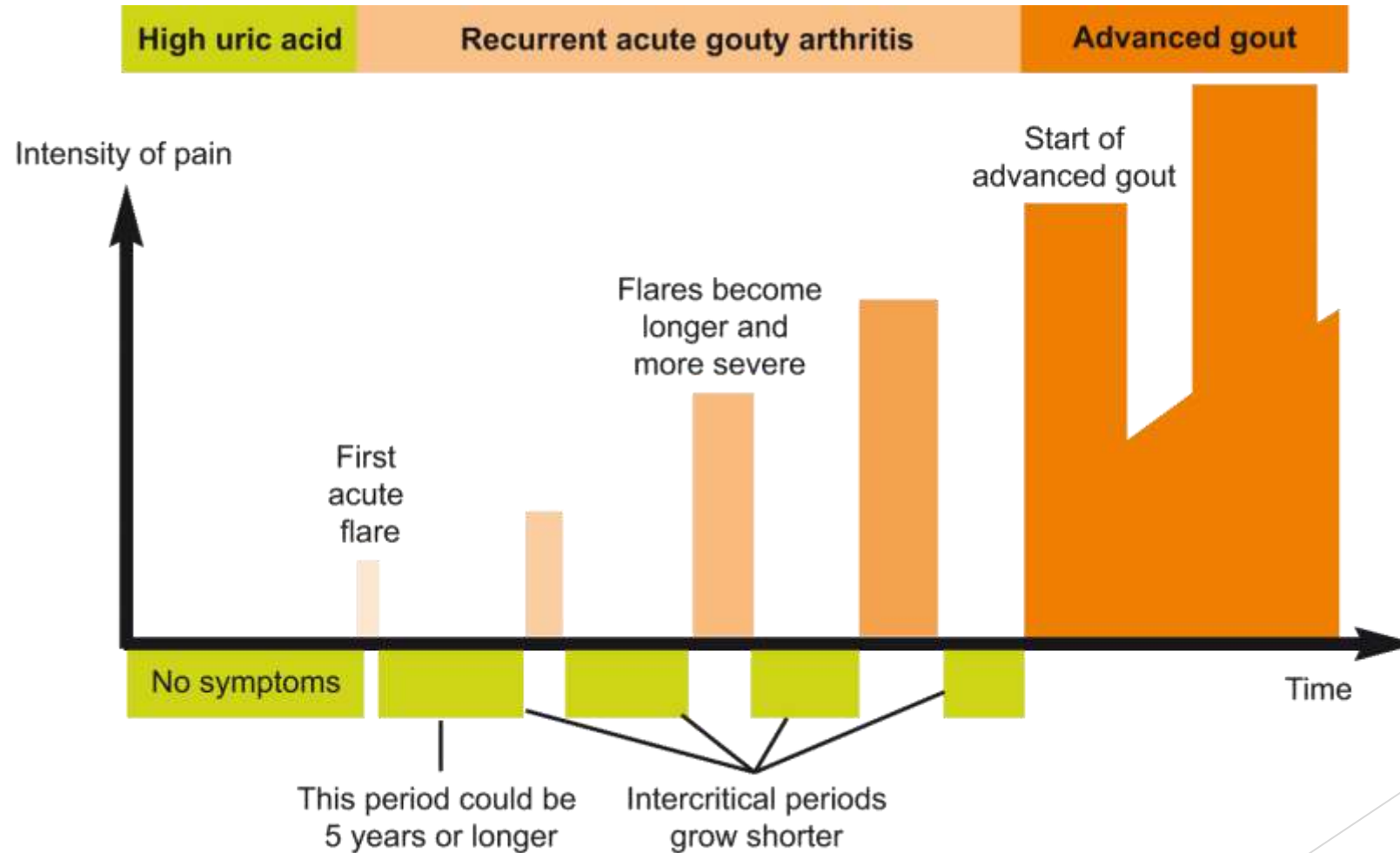


Diagnosis

Four Stages of Gouty Arthritis

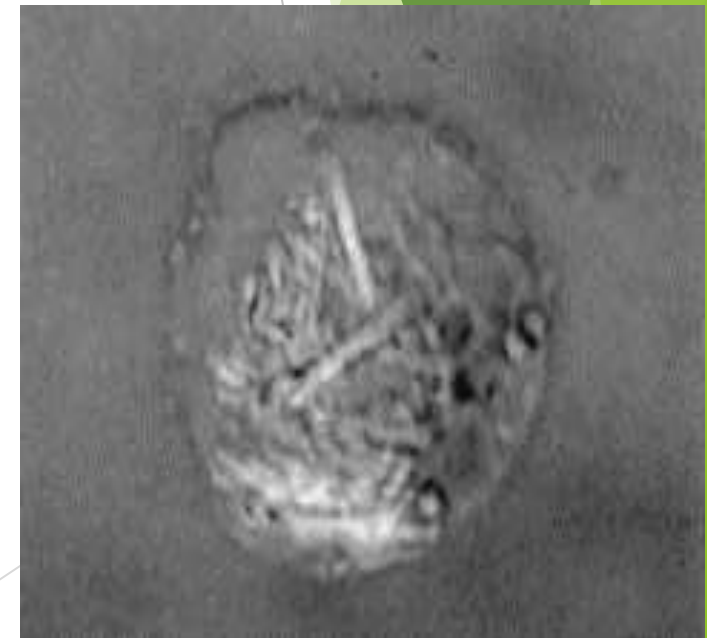
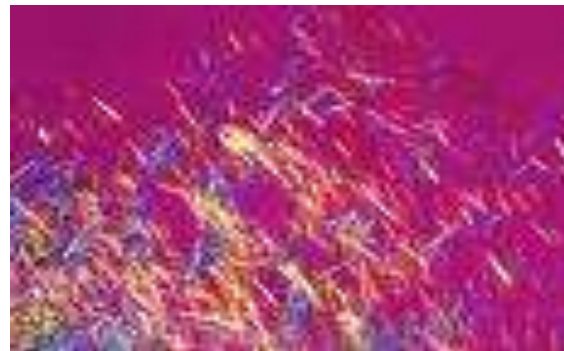
- ▶ Asymptomatic hyperuricaemia
- ▶ Acute gouty arthritis
- ▶ Intercritical gout
- ▶ Chronic tophaceous gout

Gout is recurrent and progressive



Gold standard Gout diagnosis

- ▶ Demonstration of monosodium urate crystals by microscopic examination for negatively birefringent crystals in synovial fluid or tophus aspirates permits a definitive diagnosis of gout
- ▶ Urate crystals are intra- or extracellular
 - ▶ Long needles, typically 10-20 μm
- ▶ Crystals examined under a polarizing filter will be:
 - ▶ Yellow when aligned parallel to the axis of the red compensator
 - ▶ Blue when aligned perpendicular to the direction of polarization



Diagnostics in gouty patients

Clinical examination for tophi	Extensor surface of forearm, olecranon, Achilles tendon, pinna
Imaging	No juxta-articular osteopaenia of other inflammatory arthritides Punched out lateral erosions with sclerotic margins and over-hanging edges (so-called “rat-bite erosions”)
sUA measurement	May decrease during an acute attack
Full blood count	To exclude myeloproliferative disorders; raised WBC may suggest septic arthritis
Renal function	Association of renal failure with hyperuricaemia Lower allopurinol dose in renal impairment
Urinary urate excretion	Risk of renal stones? Uricosurics contraindicated in patients with high urate excretion
Fasting lipids and glucose	Association of gout with metabolic syndrome
Thyroid function	Association with hypothyroidism and possibly hyperthyroidism

Men with gout are at risk of other complications

- Joint Damage / Deformity
- Cardiovascular risk
- Kidney Stones
- Kidney Damage

BMJ review 2018

- ▶ Acute attack - likely to require treatment with a NSAID + PPI or colchicine
- ▶ ULT is targeted to patients with recurrent attacks, tophi, urate arthropathy, or renal damage and to symptomatic patients with very high serum uric acid levels
 - ▶ Allopurinol is the first line option
- ▶ Shared decision making about ULT
- ▶ All patients taking ULT require regular monitoring of renal function and serum uric acid level to ensure that the dose is appropriate
 - ▶ For most, allopurinol 300 mg daily will be insufficient to achieve target serum uric acid reductions
- ▶ Despite limited evidence, patients should be encouraged to manage their weight & increase exercise

EULAR recommendations 2016

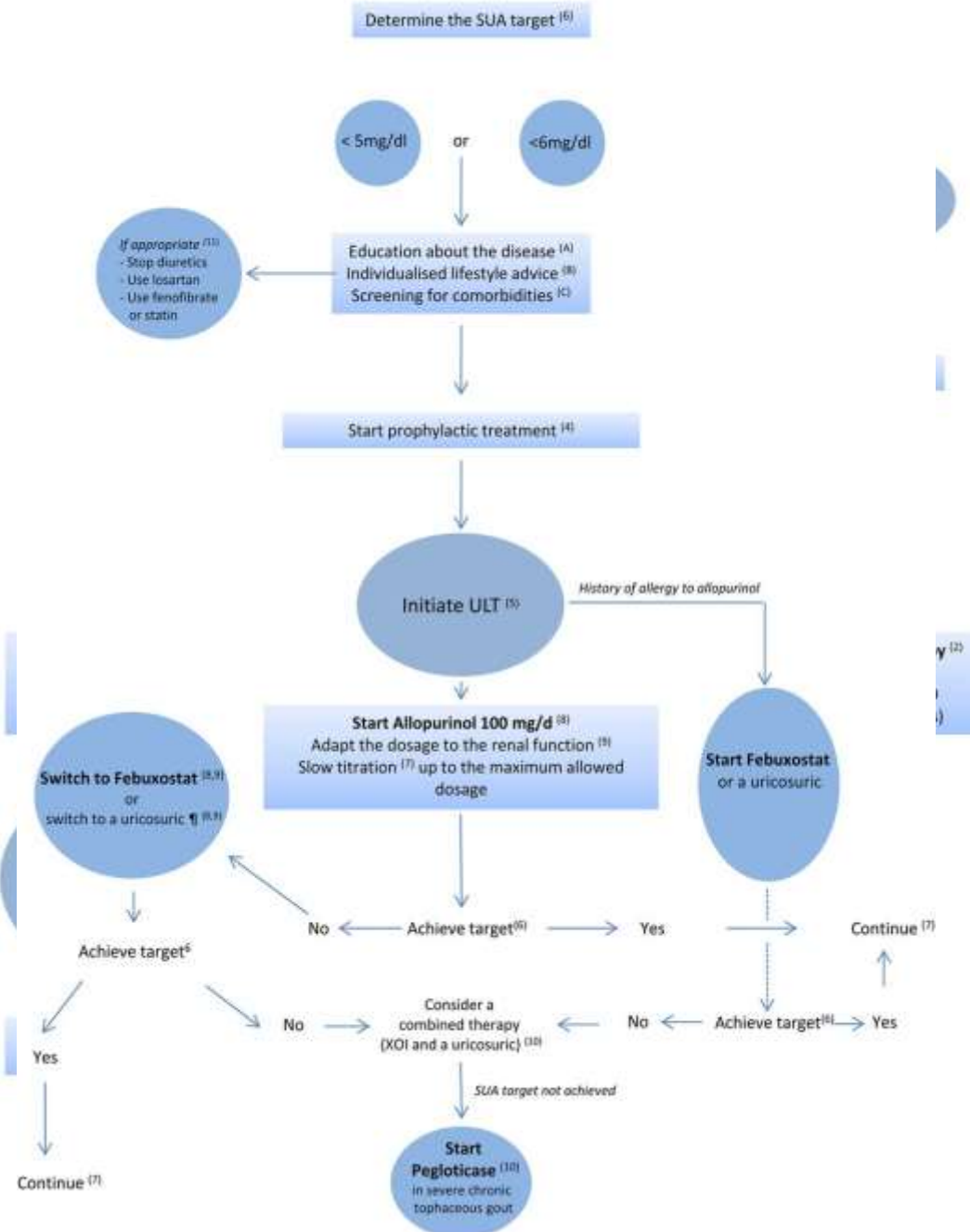
▶ General principles:

- ▶ (a) Provide education
- ▶ (b) Implement lifestyle interventions
- ▶ (c) Screen for co-morbidities (esp CVD)

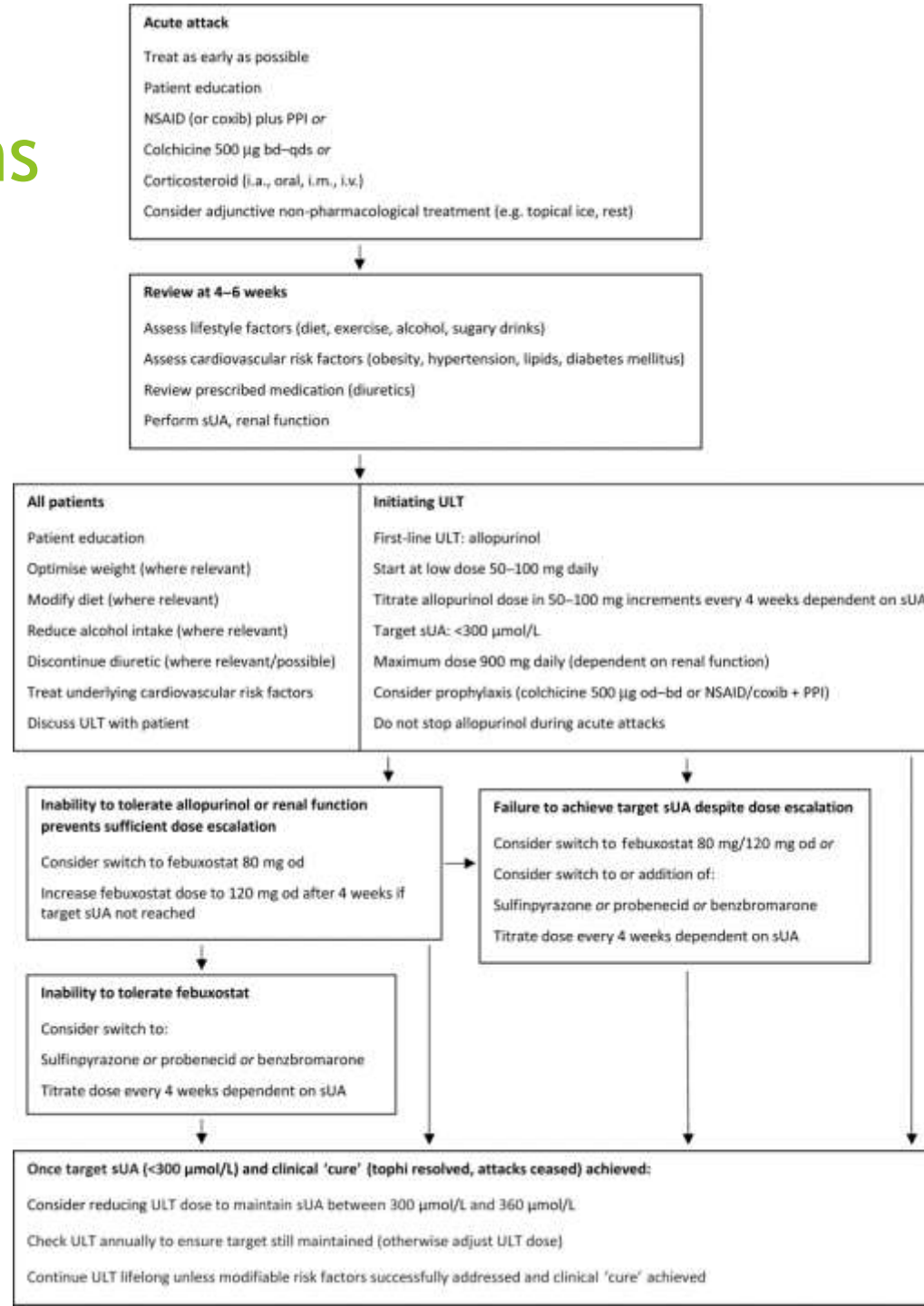
▶ 11 Recommendations:

1. Treat acute flare asap
2. 1st line acute flare Rx Colchicine, others: NSAIDs, Steroids (PO/IA)
3. If frequent / recurrent flares: consider IL1 inhibitor
4. Prophylaxis against flares for 6 months (Colchicine / NSAIDs)
5. ULT should be considered in all patients with definite Dx esp those with recurrent flares, tophi, urate arthropathy and/or renal stones, CVD risk
6. With ULT, aim to reduce sUA to $<360 \mu\text{mol/L}$ ($<300 \mu\text{mol/L}$ in higher risk cases)
7. ULT should be started at lower dose and titrated
8. In normal renal function, 1st line is Allopurinol 100mg / day, increase by 100mg every 2 -4 weeks until sUA target reached. Febuxostat and other medications
9. In renal disease, consider lower Allopurinol dose, switch to other agents
10. In patients with crystal-proven, severe debilitating chronic tophaceous gout and poor quality of life, Pegloticase is indicated
11. If diuretic used, consider losartan or calcium channel blockers; for hyperlipidaemia, consider a statin or fenofibrate

**2016 EULAR RECOMMENDATION FOR THE MANAGEMENT OF HYPERURICEMIA
IN PATIENTS WITH GOUT**



BSR Recommendations 2017



BSR Recommendation Changes

- ▶ Emphasis on education
- ▶ NSAID & Colchicine for acute attacks, can consider combination
- ▶ Screen for CVD risk & treat accordingly
- ▶ After maintaining sUA of $<300\mu\text{mol/l}$, consider reducing strictness of target to $360\mu\text{mol/l}$
- ▶ For patients with severe symptomatic tophaceous gout in whom hyperuricaemia cannot be controlled, Pegloticase can be considered

- ▶ Special Cases:
 - ▶ Renal impairment: colchicine safer than NSAID, adjust Allopurinol, consider alt ULT
 - ▶ Severe refractory Gout: can use Pegloticase (not approved by NICE - cost)
 - ▶ Pregnancy: NSAIDs can be used in mid-trimester, Steroids are generally safe, Probenacid for ULT

Lifestyle modifications

▶ Diet

- ▶ Reduce purine intake (reduce red meat, avoid liver, kidneys, shellfish and pulses)
- ▶ Reduce fructose-containing drinks
- ▶ Include skimmed milk, low fat yoghurt, vegetable protein and cherries
- ▶ Vitamin C is uricosuric

▶ Decrease alcohol consumption (especially beer)

▶ Weight loss

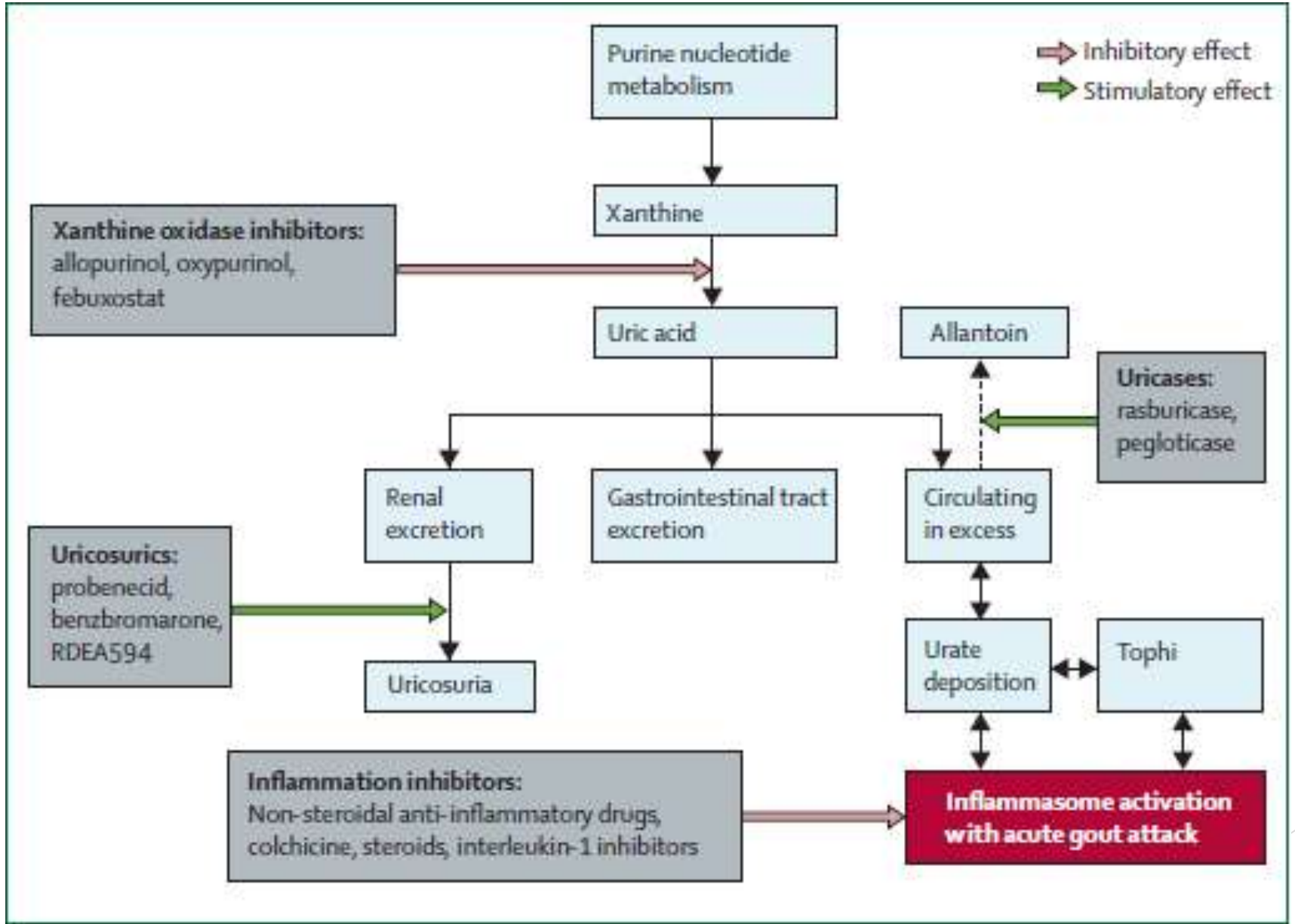
- ▶ 1 kg/month (avoid crash diets)
- ▶ Avoid high protein diets

▶ Patients with urolithiasis should be encouraged to drink >2 litres of water/day

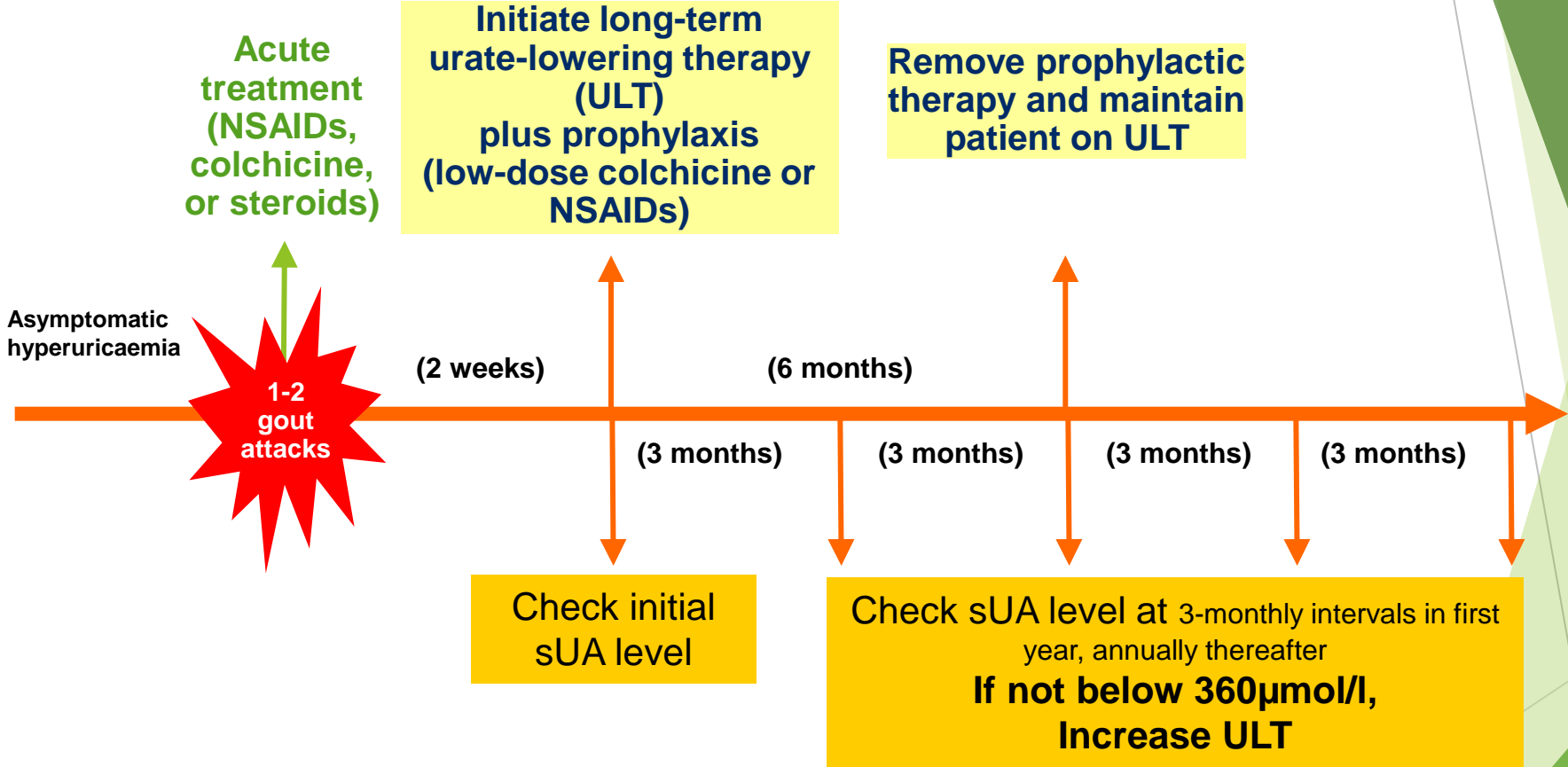
▶ Moderate exercise

Goals of treatment

- ▶ **Acute attacks:**
 - ▶ Relieve pain rapidly and reduce inflammation
 - ▶ Non-pharmacological (coldpacks)
 - ▶ NSAIDs or Coxibs (Etoricoxib)
 - ▶ Colchicine
 - ▶ Corticosteroids
 - ▶ There is no need to discontinue allopurinol during an acute attack
 - ▶ Never commence allopurinol during an acute attack
- ▶ **Long-term treatment (gout is curable by dissolving all crystals and preventing further crystal formation):**
 - ▶ Prevent further acute attacks
 - ▶ Prevent joint damage
 - ▶ Eliminate tophi



Effective gout management



Allopurinol and renal failure

Estimated GFR ml/min/1.73 m ²	Allopurinol starting dose
<5	50 mg/week
5–15	50 mg twice weekly
16–30	50 mg every 2 days
31–45	50 mg/day
46–60	50 mg and 100 mg on alternate days
61–90	100 mg/day
91–130	150 mg/day
>130	200 mg/day

Case History - management

- ▶ Lifestyle review: high sweetened drinks intake (fructose)
- ▶ No alcohol (previously high), no red meat / shellfish, no renal disease / psoriasis, no iatrogenic causes, no FH
- ▶ Acute attack(s): IV Steroids?
- ▶ Rasburicase (uricase) - lowered sUA to unrecordable levels. Allopurinol started but then flared badly within 1 week
- ▶ Re-tried Rasburicase and then followed with Febuxostat - same issue, mild reaction to uricase
- ▶ **MDT held:** Anakinra daily SC - after 2 weeks then Rasburicase, followed immediately by Febuxostat 120mg daily. Consider Benzbromarone.

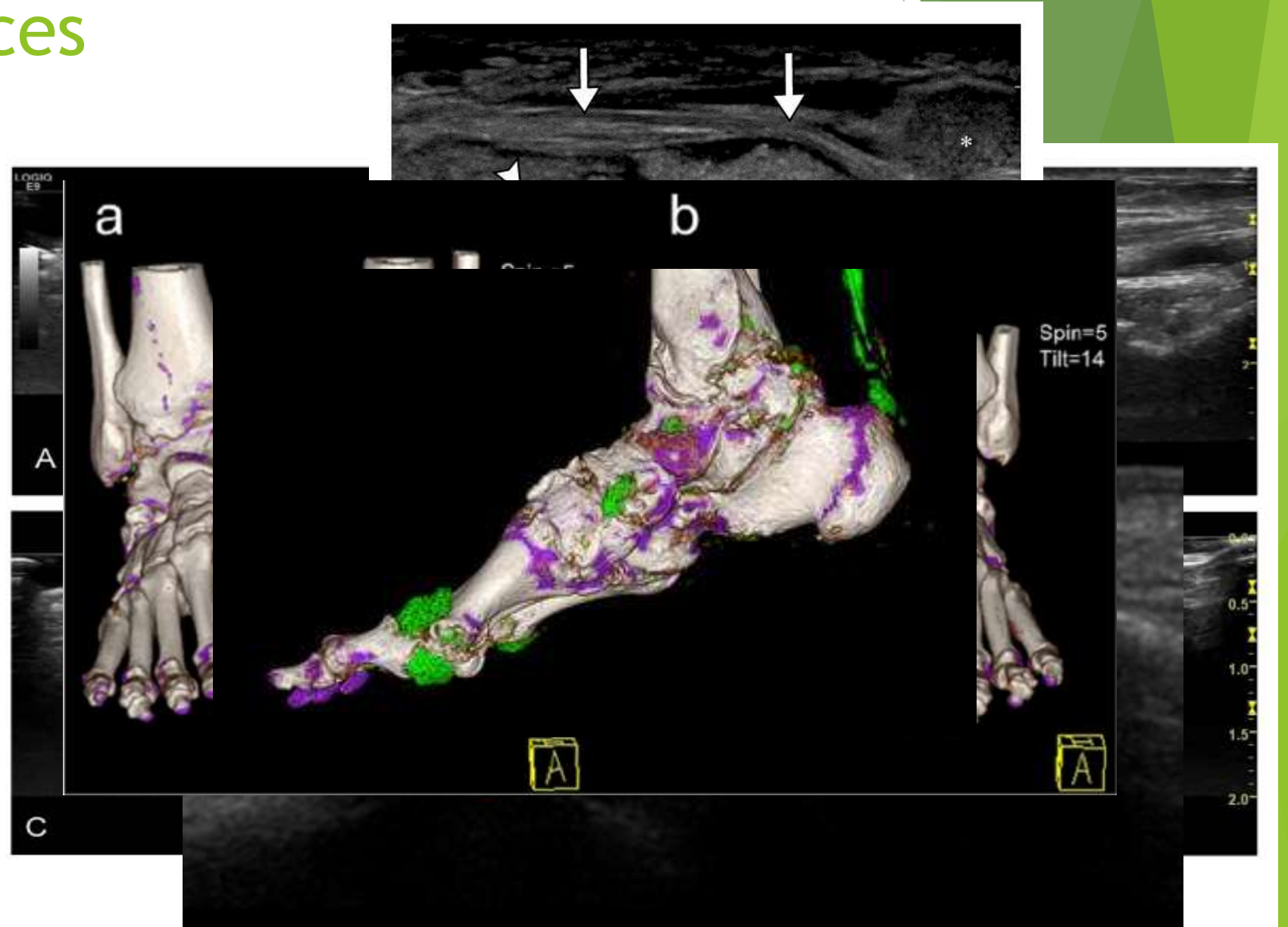
Advances in Gout

- ▶ **New drug targets**
 - ▶ IL1 inhibitors - Canakinumab, Anakinra
- ▶ **New approaches to serum urate lowering**
 - ▶ Uricases - Pegloticase, Raburicase
 - ▶ Lesinurad - selective, highly potent uric acid reabsorption inhibitor - CLEAR 1, CLEAR 2, CRYSTAL, LIGHT studies showed that Lesinurad + either Allopurinol or Febuxostat was more effective by as much as 2.5-fold
 - ▶ Arhalofenate - pipeline drug with a dual mechanism of action (ULT and anti-inflammatory effects)
- ▶ **New Guidance** - ACR, BSR, EULAR
- ▶ **New genetics for screening**
 - ▶ HLA-B*58:01 - predicts risk of reaction to Allopurinol (recommended in ACR guidelines for at risk populations)

Imaging Advances

► Ultrasound

► Dual-Energy CT (DECT)





Thank You

Now let's go enjoy a drink!