Gout

Professor Lisa Stamp

Canterbury District Health Board
Te Poari Hauora ō Waitaha

University of Otago
Te Whare Wānanga o Otāgo
NEW ZEALAND

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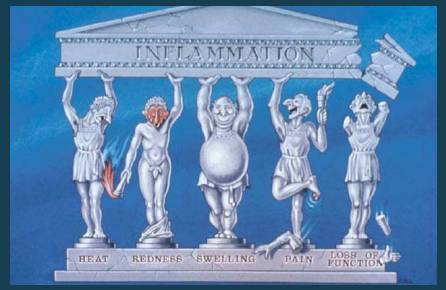
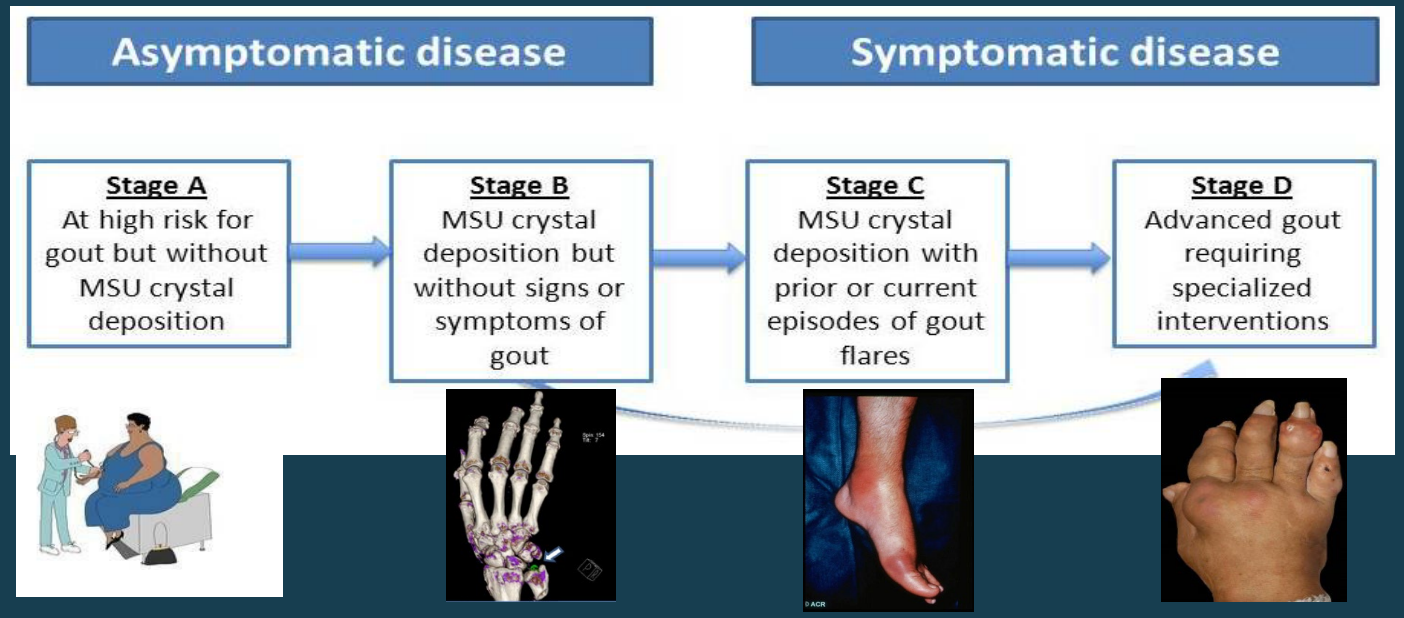
Gout the disease



- Arthritis = joint inflammation
- Gout is form of arthritis caused by the immune response to monosodium urate crystals deposited in and around joints – could be called uric acid arthritis



Dalbeth & Stamp *Nat Rev Rheum* 2015

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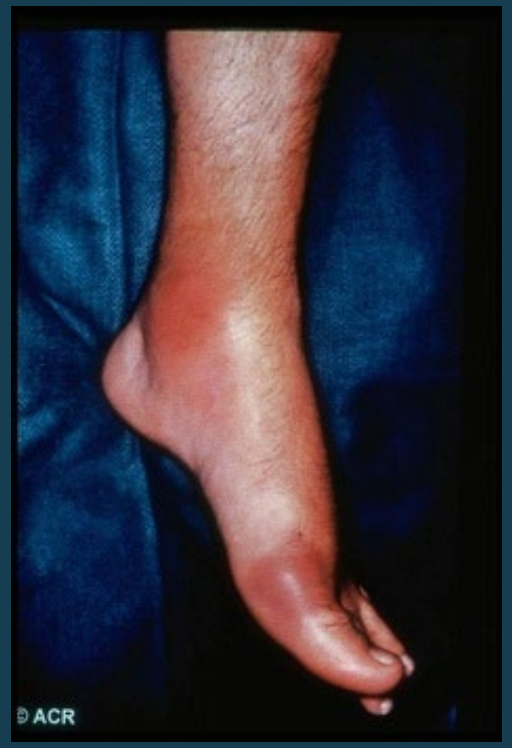
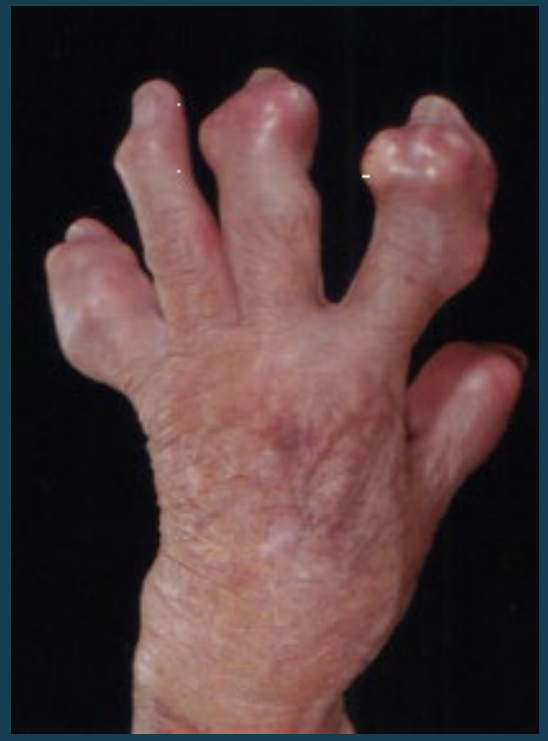
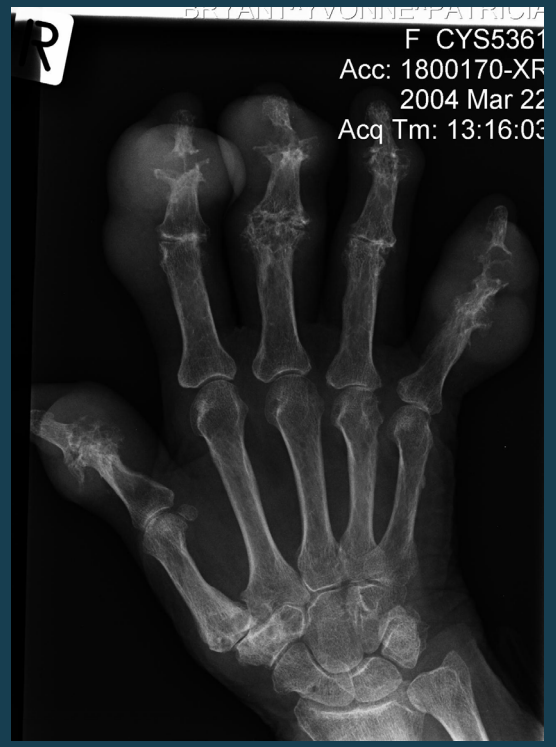
Gout is a chronic disease not just a flare



Gout flare



Tophaceous gout



Erosive gout

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Disparities in gout

Disease burden disparities

- Prevalence of gout
- Gout more severe
- Co-morbidities: CVD, diabetes
- Worse health-related quality of life

Treatment disparities

- Less regular dispensing of urate lowering therapy
- Inequities in access – prescribing bias, structural barriers, cost and access to medicines and healthcare, background determinants of health
- Under representation in industry clinical trials of gout therapies of Māori and Pacific peoples

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Prevalence of gout in Aotearoa New Zealand

- Gout is estimated to affect around 6% of adult New Zealanders aged 20 years and over.
- Males have approximately three times the prevalence of gout compared with females.
- Māori are approximately two times more likely to live with gout compared to non-Māori, non-Pacific peoples.
- Pacific peoples are approximately three times more likely to live with gout compared to non-Māori, non-Pacific peoples.
- Māori and Pacific peoples have a younger population disproportionately affected by gout.

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Gout is a more severe disease

- Māori and Pacific peoples experience disproportionately severe disease, with more frequent gout flares, higher rates of hospitalisation for gout, and more tophaceous disease.

- Gout is associated with cardiovascular and kidney disease, which also disproportionately affect Māori and Pacific peoples, and this may be particularly so for those living in rural areas.

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Gout clinical presentation and co-morbidities from participants in the 'Genetics of Gout in Aotearoa study'

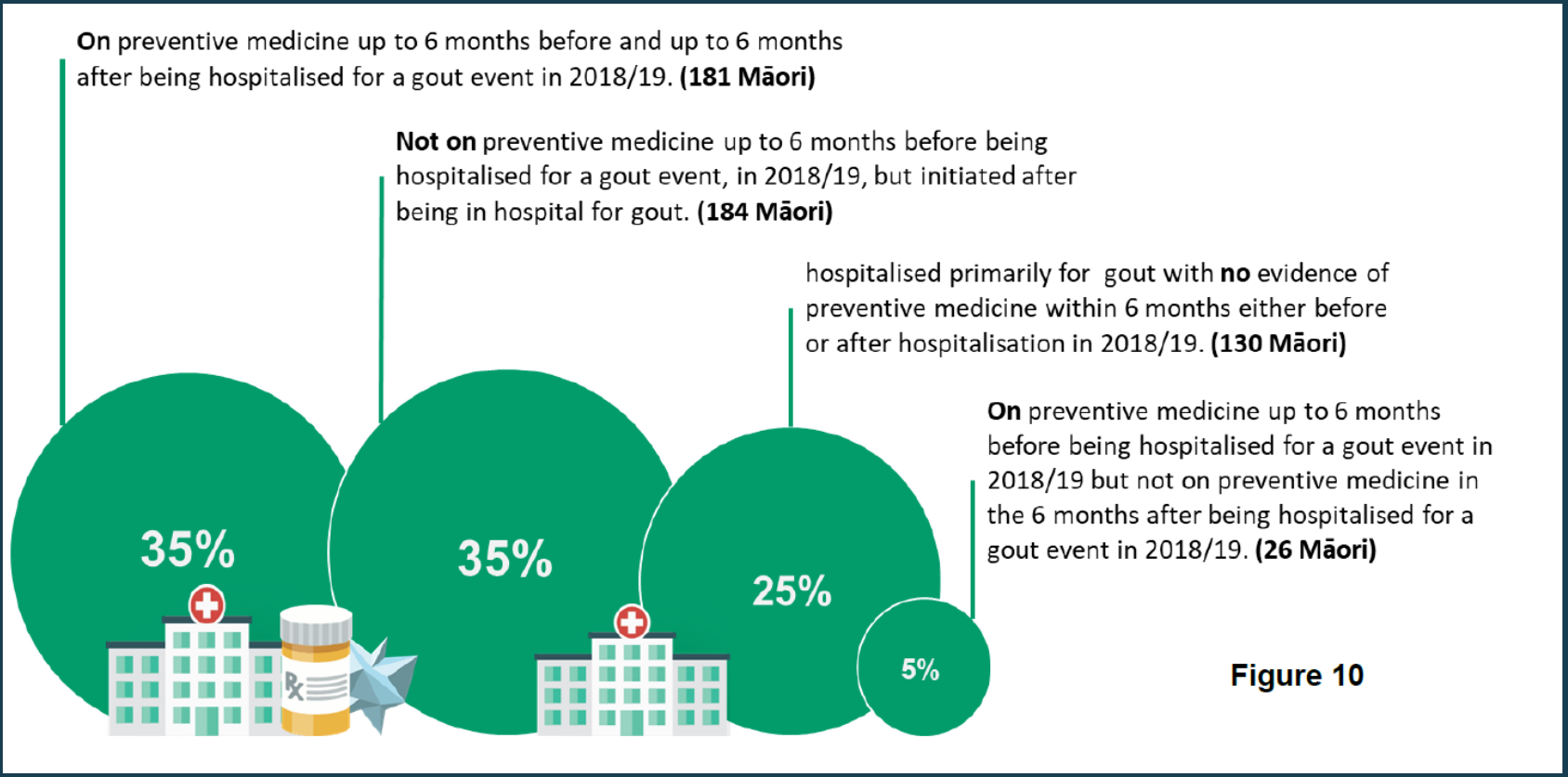
	Māori (n = 185)	Pacific peoples (n = 173)	NZ European (n = 214)
Mean age of onset (years)	39.0	33.5	46.2
Mean (range) no. of gout flares in past year	13.1 (0 to >1/week)	18.6 (0 to >1/week)	8.5 (0 to >1/week)
% with first-degree relative with gout	71.8	62.8	51.2
Co-morbidities (%)			
Type 2 diabetes	28.6	21.4	15.7
Hypertension	65.5	53.6	51.6
Cardiovascular disease	47.9	24.2	42.1
Kidney disease	35.0	29.7	30.0

Phipps-Green A, et al. A strong role for the ABCG2 gene in susceptibility to gout in New Zealand Pacific Island and Caucasian, but not Māori, case and control sample sets. *Hum Mol Genet*. 2010;19(24):4813-9.

Hospitalisation for gout

Māori are 6.9 times more likely to be hospitalised with a primary diagnosis of gout compared with non-Māori, non-Pacific peoples.

Pacific peoples are 13.2 times more likely to be hospitalised with a primary diagnosis of gout than non-Māori, non-Pacific peoples.



Health related quality of life

- HR-QoL in people with gout tends to be worse in Indigenous populations.
- Māori and Pacific peoples with gout have greater activity limitation assessed by HAQ-II and lower physical role function on the SF-36 compared to non-Māori non-Pacific peoples (Dalbeth 2018).
- Qualitative studies involving Māori men have demonstrated immense suffering, isolation and negative effects on employment and relationships (Te Karu 2013).
- These effects impact not only the individual but also their whānau and community.

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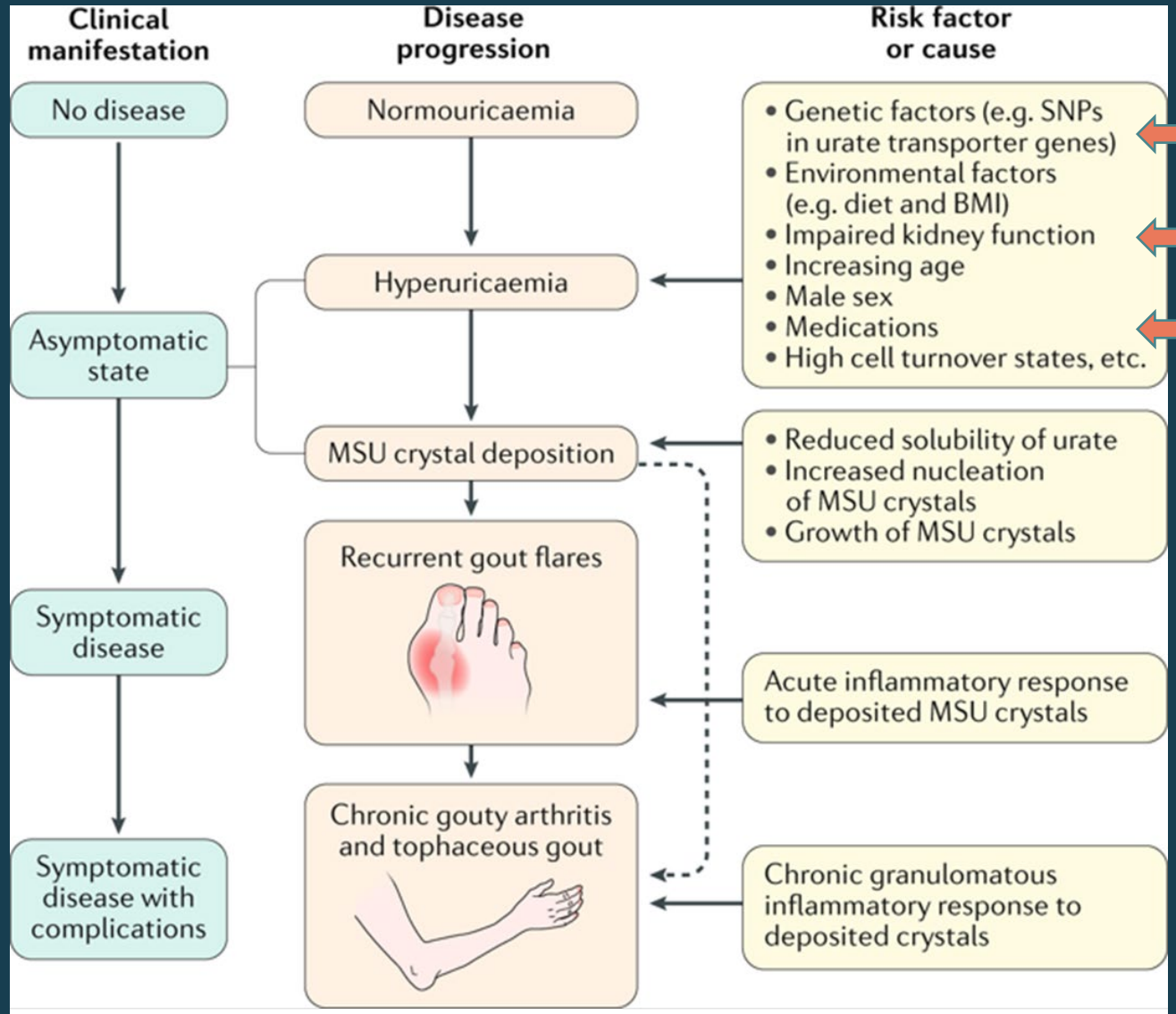
Factors contributing to gout



Dalbeth, Stamp et al. (2019) Gout
Nat. Rev. Dis. Primers doi.org/10.1038/s41572-019-0115-y

Nature Reviews | Disease Primers

These genetic variants also contribute to gout risk in Māori and Pacific peoples in Aotearoa New Zealand, and population-specific variations in urate transporters influence the development of gout and complications of treatment in Māori and Pacific peoples.

Diet - stigmatising

To reduce gout harm, healthcare providers can:

Scout: Aged 20 to 40, joint pain? Think gout.

Enquire: Question and/or review recurrent NSAID-only treatment for gout.

Shape: Explore beliefs about causes and treatments. Talk genetics.

Identify, act: Prescribers – preventive medicine early and regularly is essential. Pharmacists – look for patterns of irregular dispensing.

Reflect: How is your communication helping people see a better future?

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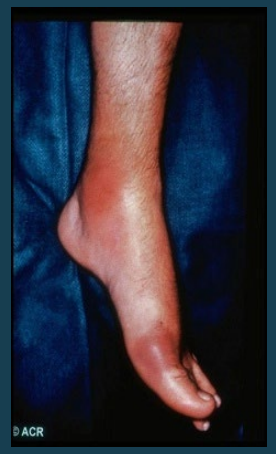
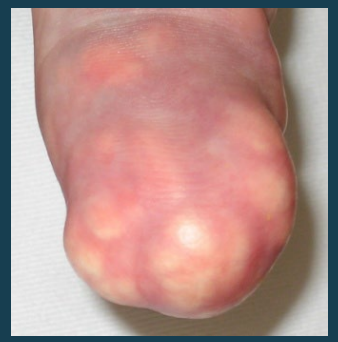
Diagnosis

- Red hot swollen joint
  - Acute onset (<24 hrs to maximum pain)
  - Foot, especially 1st MTP
- Serum urate can be low during acute attack
- Joint aspiration
  - Important to exclude infection
  - Gold standard





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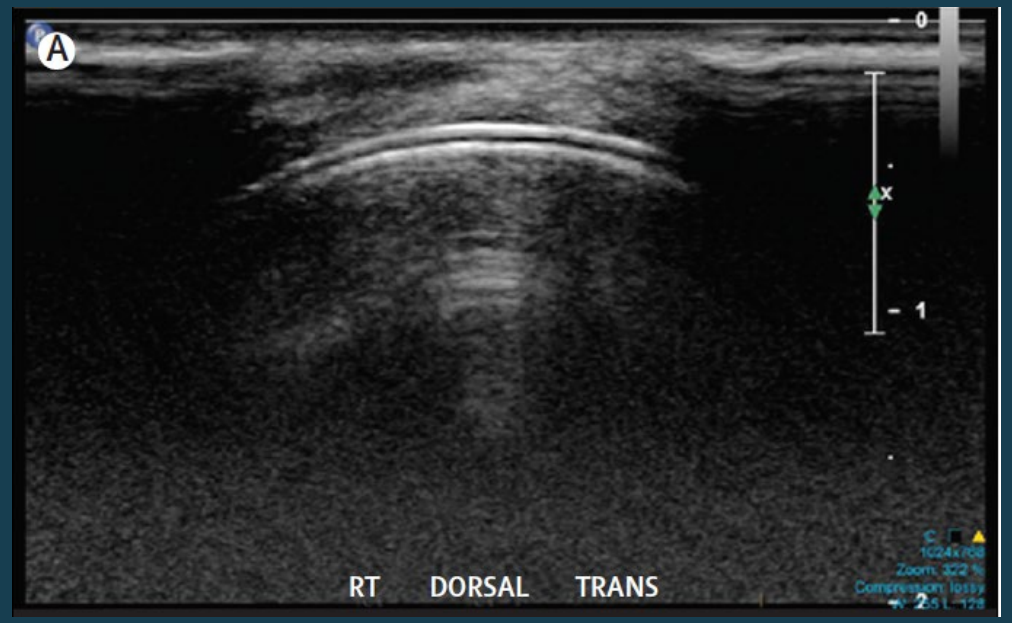
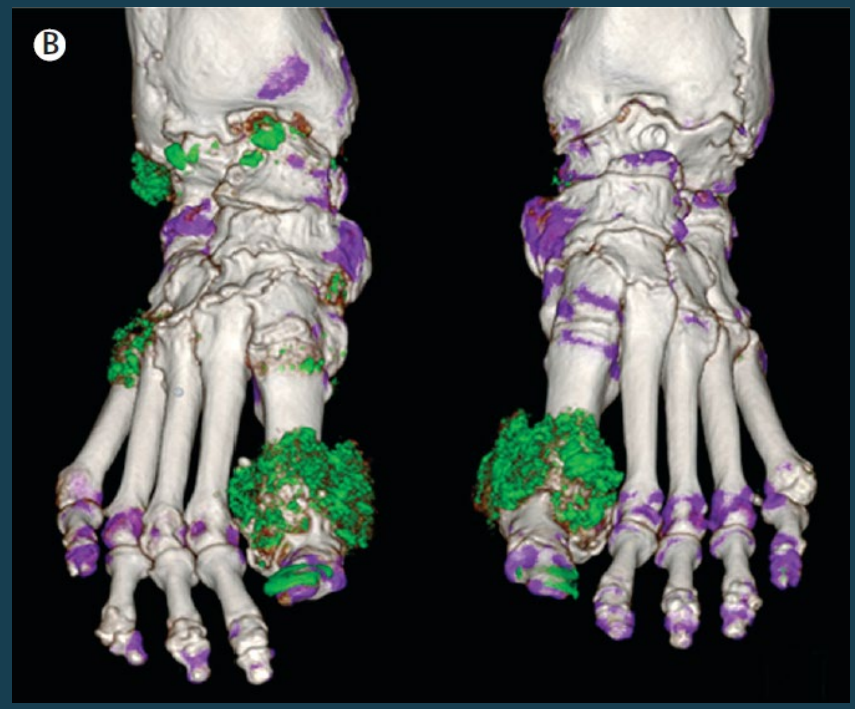
Diagnosis





Dalbeth, Merriman and Stamp. *Lancet* 2016

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Three central strategies in gout treatment

1. Long-term urate-lowering therapy to treat the central cause of gout (hyperuricaemia)

2. Prevention of gout flares with low dose anti-inflammatory medications at the time of initiating urate-lowering therapy

3. Rapid and effective treatment of the gout flare (NSAIDs, colchicine, steroids)

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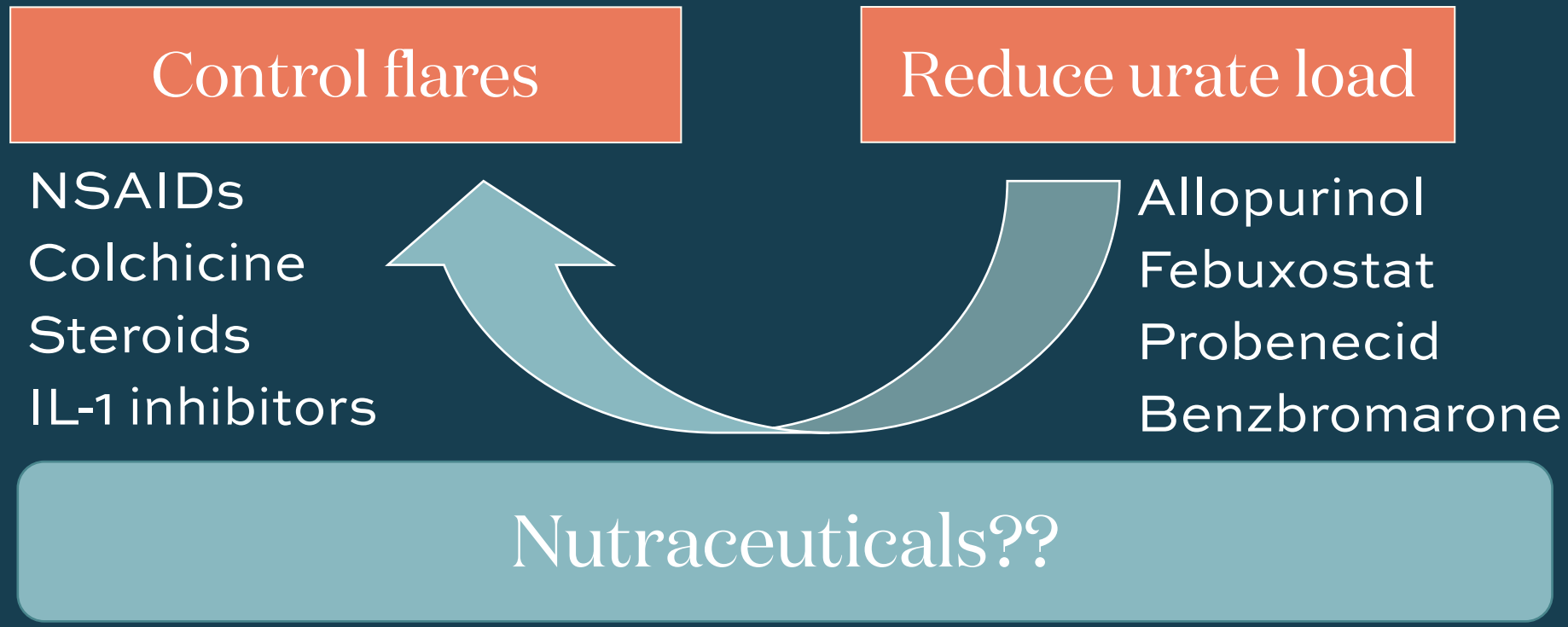
Control flares
Reduce urate load
NSAIDs
Colchicine
Steroids
IL-1 inhibitors
Allopurinol
Febuxostat
Probenecid
Benzbromarone
Nutraceuticals??
Omega-3
Tart cherry
Curcumin/turmeric
Tart cherry
Vitamin C
Curcumin/turmeric

Management of gout flares

NSAIDs

Best avoided in CKD

In patients with pre-existing renal impairment NSAIDs may lead to worsening renal function.

Multiple drug interactions, ACE + diuretic + NSAID particularly renal toxic.

Colchicine

High doses best avoided in CKD

AGREE low dose – limited evidence of high risk in CKD - no dose reduction in mild-moderate renal impairment.

GI intolerance - may be poorly tolerated in those with pre-existing renal impairment.

Contraindicated in patients with renal impairment receiving CYP3A4 or P-glycoprotein inhibitors.

Corticosteroids

Mainstay of gout flares treatment in CKD.

May be the lesser of the “three evils” in patients with renal impairment.

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NSAID dispensing

- The prescribing and dispensing of non-steroidal anti-inflammatory drugs (NSAIDs) for people with gout is high, especially for Māori and Pacific peoples.

- People with gout, dispensed an NSAID in 2019:
  - 45.5% (n=13,648) Pacific peoples
  - 40.6% (n=16,639) Māori
  - 35.1% (n=48,284) non-Māori/non-Pacific

[HQSC, 2021]

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NSAID dispensing

- The long-term use of NSAIDs for gout also causes harm, such as by increasing risk of upper GI bleeding, kidney damage and heart failure.

- Pacific peoples have higher incidence of hospitalisation for NSAID-related harms compared to the NZ European population (Tomlin et al 2020).

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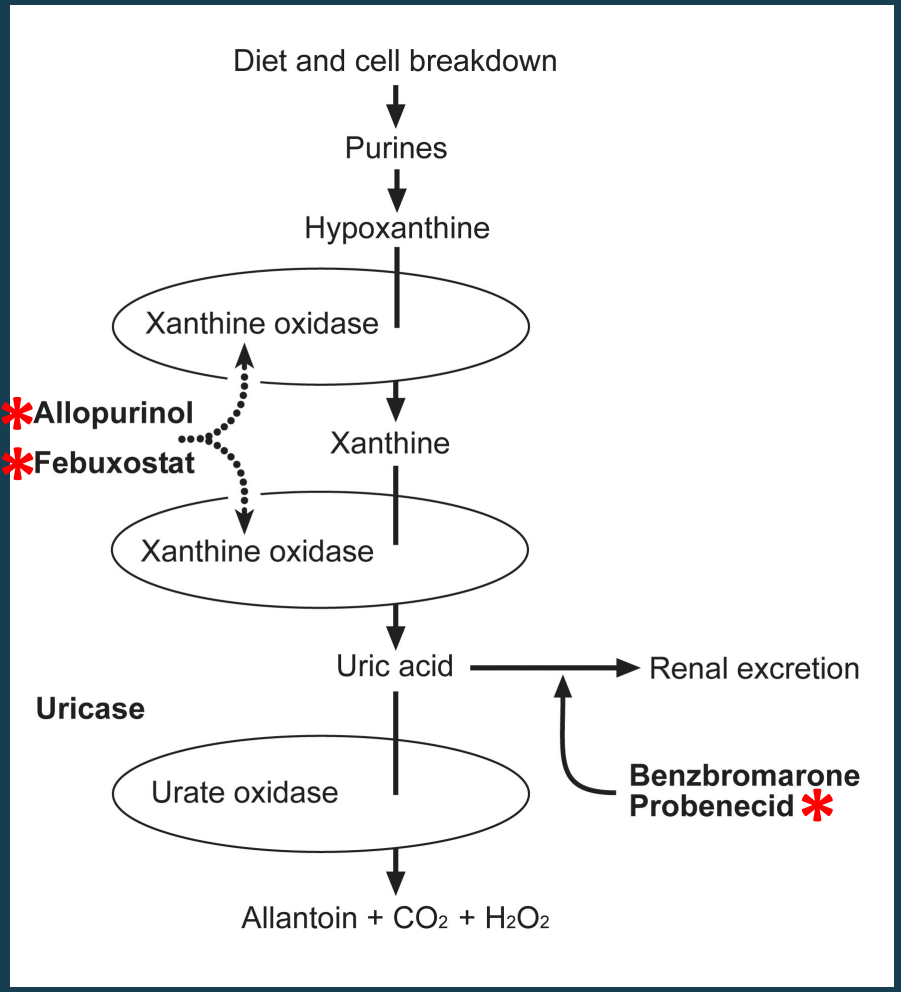
Sustained urate lowering <0.36mmol/L is critical in the long-term management of gout

- Sustained urate <0.36mmol/L leads to:
  - monosodium urate crystal dissolution
  - suppression of gout flares
  - tophus regression.

Outcome:	SU Responder	SU Non-responder	Difference Between Groups (95% CI)	P-value
	Adjusted - Baseline flare, SU, tophi, (and randomized group in Nottingham data)			
Combined	N= 343	N=245		
Gout flare, n (%)	91 (26.5%)	156 (63.7%)	0.29 (0.17 to 0.51)	<0.001
Number of gout flares (mean, SE)	0.69 (0.06)	2.09 (0.17)	-0.41 (-1.77 to -1.04)	<0.001

Urate lowering therapies



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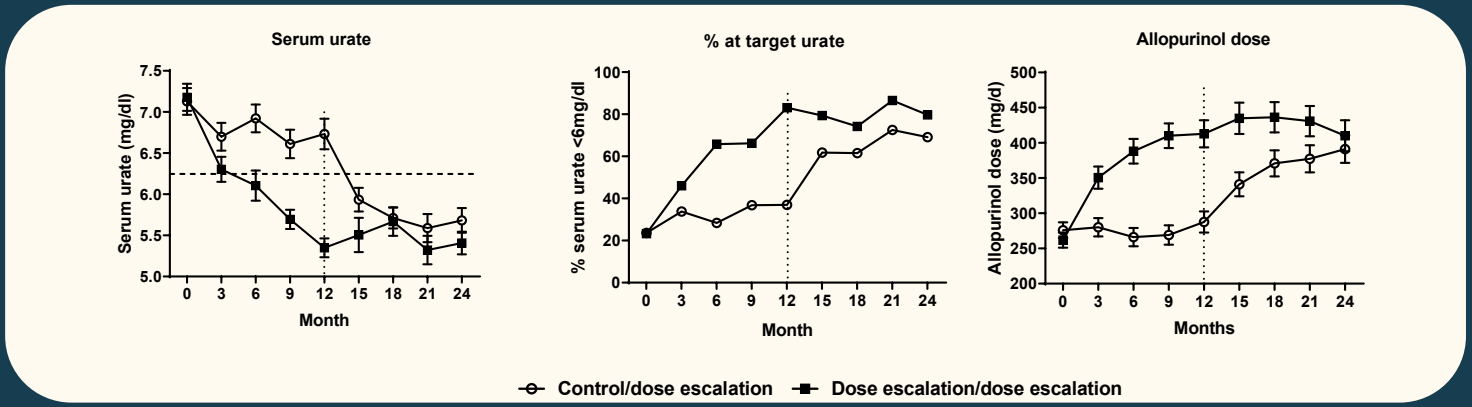
Allopurinol is first line urate lowering treatment worldwide

- Allopurinol is safe and effective even in those with renal impairment.



- In clinical practice less than half of patients on allopurinol achieve target SU <0.36mmol/L (Singh 2015).

- Dose escalation to achieve target urate remains challenging, frequently due to healthcare provider inertia.

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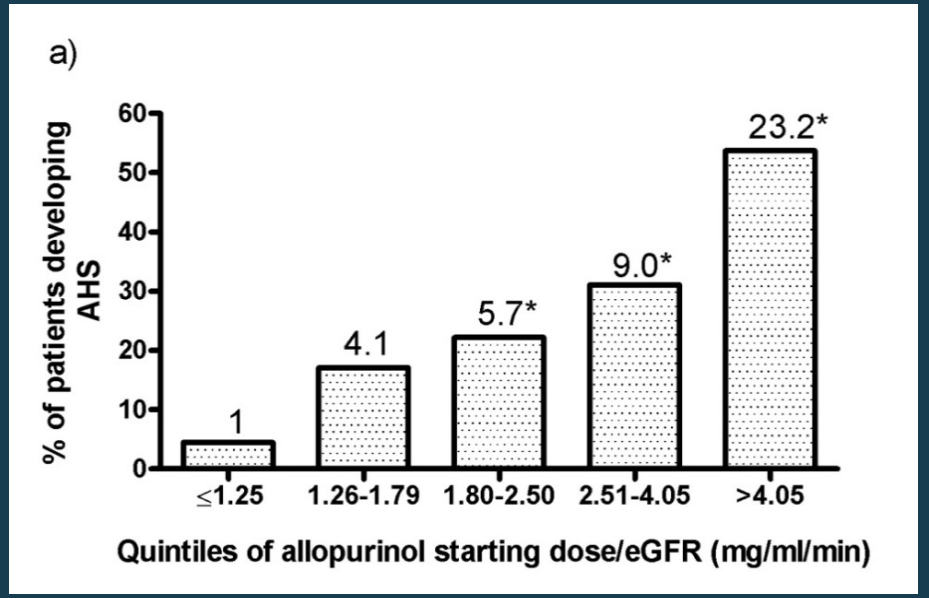
Starting ULT

- Current ACR recommendations: ≥1 subcutaneous tophi; evidence of radiographic damage attributable to gout; OR frequent gout flares defined as ≥2 annually (Fitzgerald 2020).

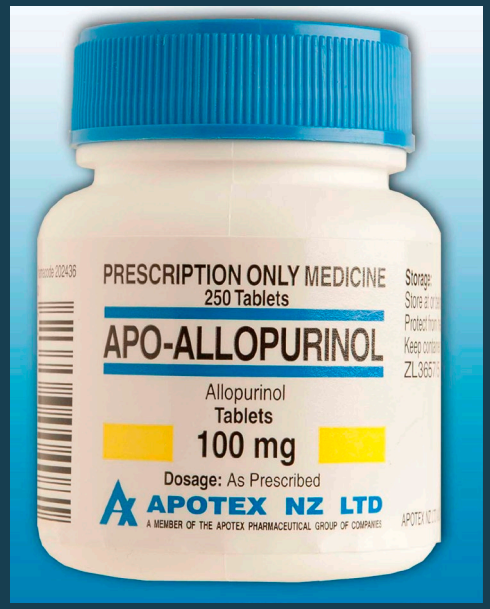
- Allopurinol starting dose is a risk factor for AHS
  - eGFR >60mL/min/1.73m^2 100mg daily
  - eGFR 30-60mL/min/1.73m^2 50mg daily
  - eGFR <30mL/min/1.73m^2 25mg daily



Starting ULT in Aotearoa

- There is no current evidence that the available treatments for gout are less effective in Māori or in Pacific peoples.

- Māori and Pacific peoples with gout have comparable rates of any dispensing of urate-lowering therapy to other New Zealanders with gout; while this may appear at first reassuring, equitable care would see substantially higher rates of urate-lowering therapy prescribed to those groups with higher burden of disease.



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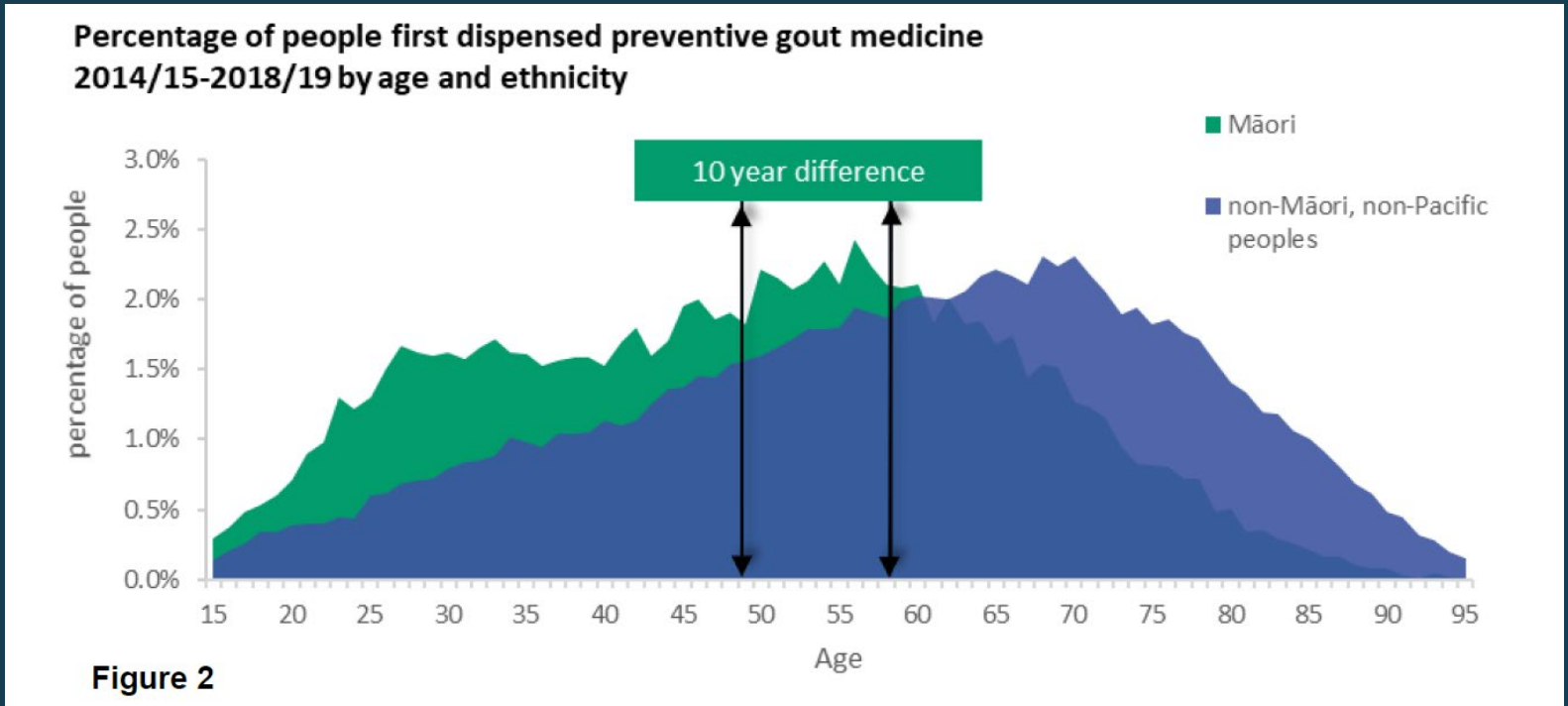
Starting ULT in Aotearoa

- Māori and Pacific peoples start ULT treatment earlier but given the higher disease burden and younger age of onset may need to start even earlier.



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ULT is critical to control gout

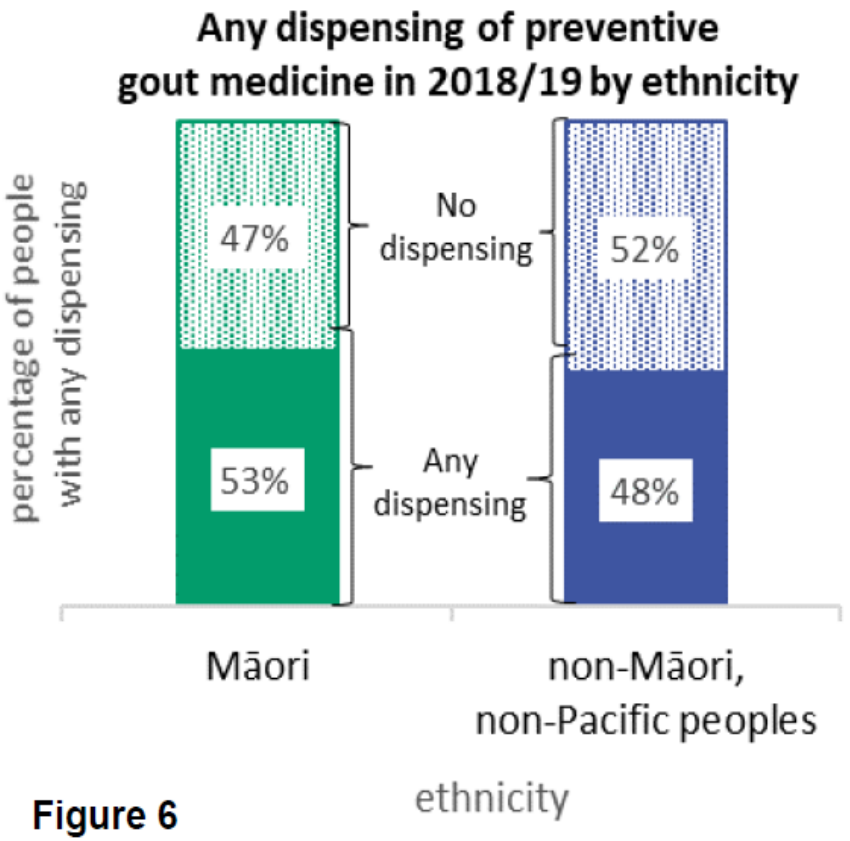


Figure 6

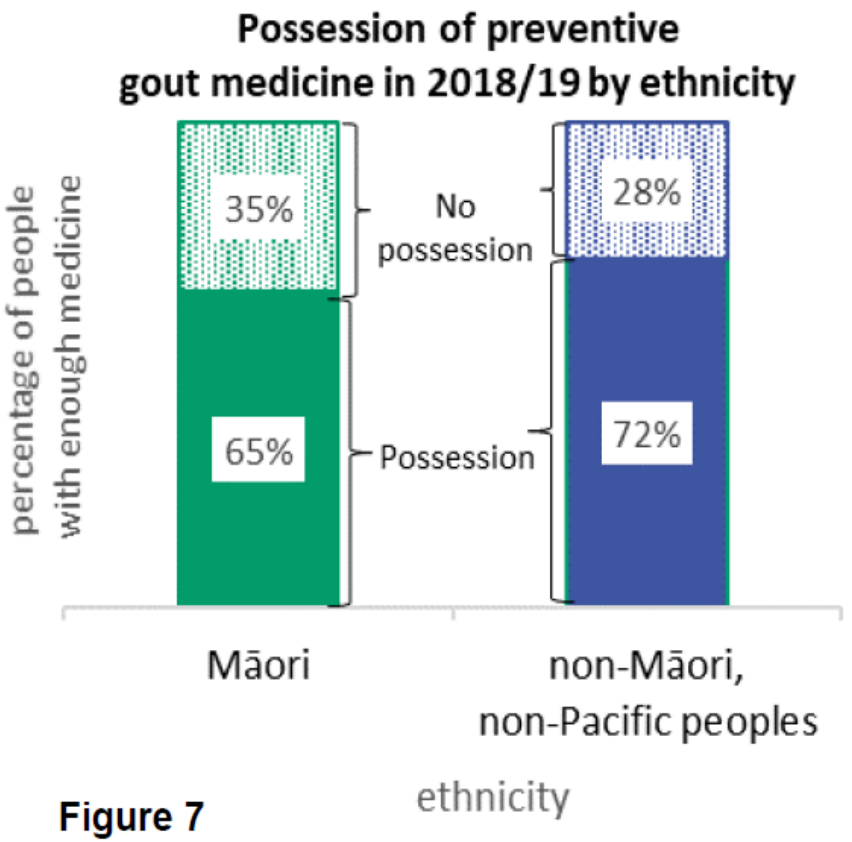
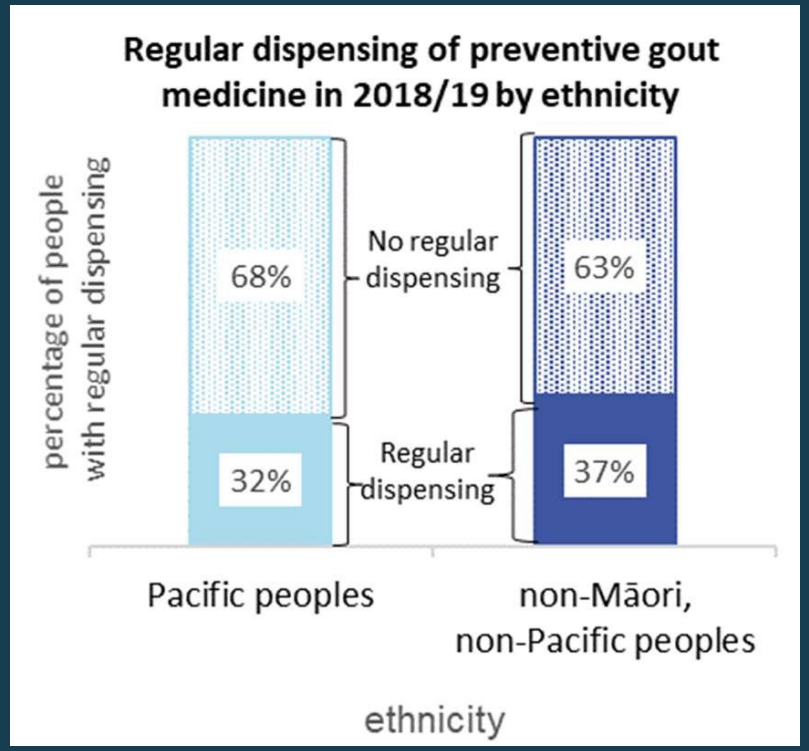


Figure 7

ULT is a long-term treatment

- In Aotearoa we have low rates of continuing ULT once started



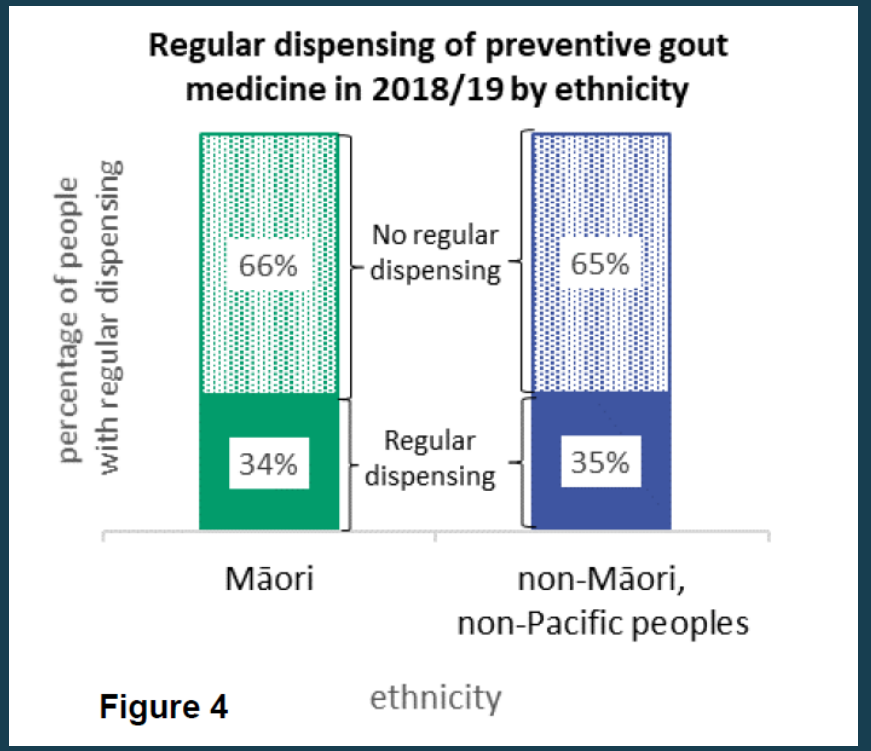


Figure 4

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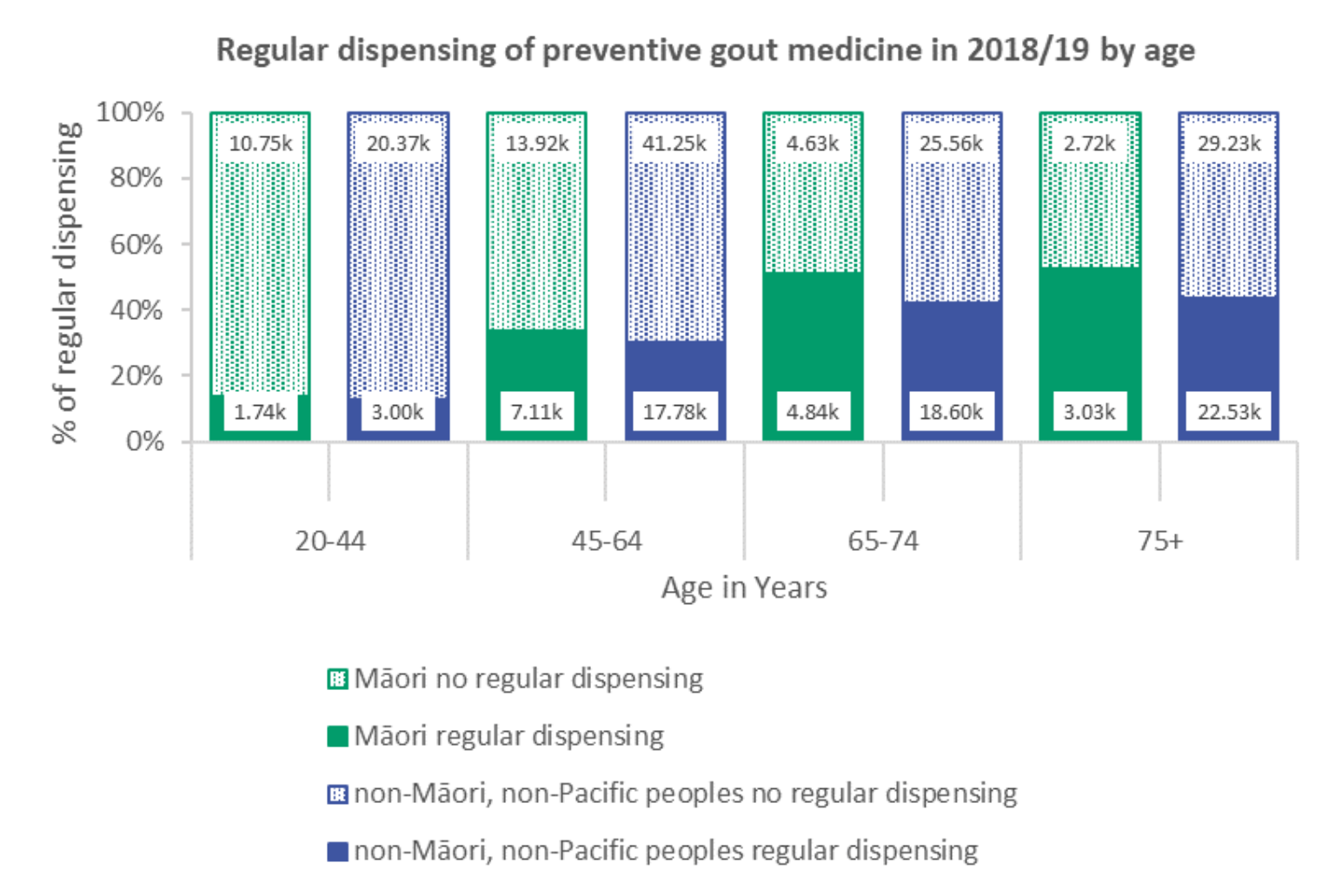
For both Māori and Pacific peoples, the younger the person, the less likely they are to be regularly dispensed preventive gout medicine



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Reasons for non persistence with ULT

- Barriers to access
  - Prescribing bias
  - Racism
  - Structural barriers
  - Cost and access to medicines and healthcare
  - Background social determinants of health
  - The system is hard to negotiate, full of jargon and lacking in cultural literacy, with health practitioners' practice variable
- Knowledge barriers
  - ULT is a long-term treatment
  - Need to achieve target urate and sustain this – can take 12 months for flares to settle
  - Starting ULT can precipitate flares – need adequate prophylaxis against flares

SYSTEMS CHANGES

EDUCATION OF HEALTHCARE PROVIDERS AND PEOPLE WITH GOUT

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Strategies to improve equity

Equitable approaches to management would include building systems that **reduce barriers** to receiving regular urate-lowering therapy for younger people with gout such as:

- no associated costs of dispensing urate lowering therapy
- comprehensive adherence support programmes potentially delivered by community pharmacists, nurses and community health workers
- workplace partnerships with general practice to support people with gout
- out of hours phone access to holistic care for gout sufferers.

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People with gout are more likely to have other long-term conditions

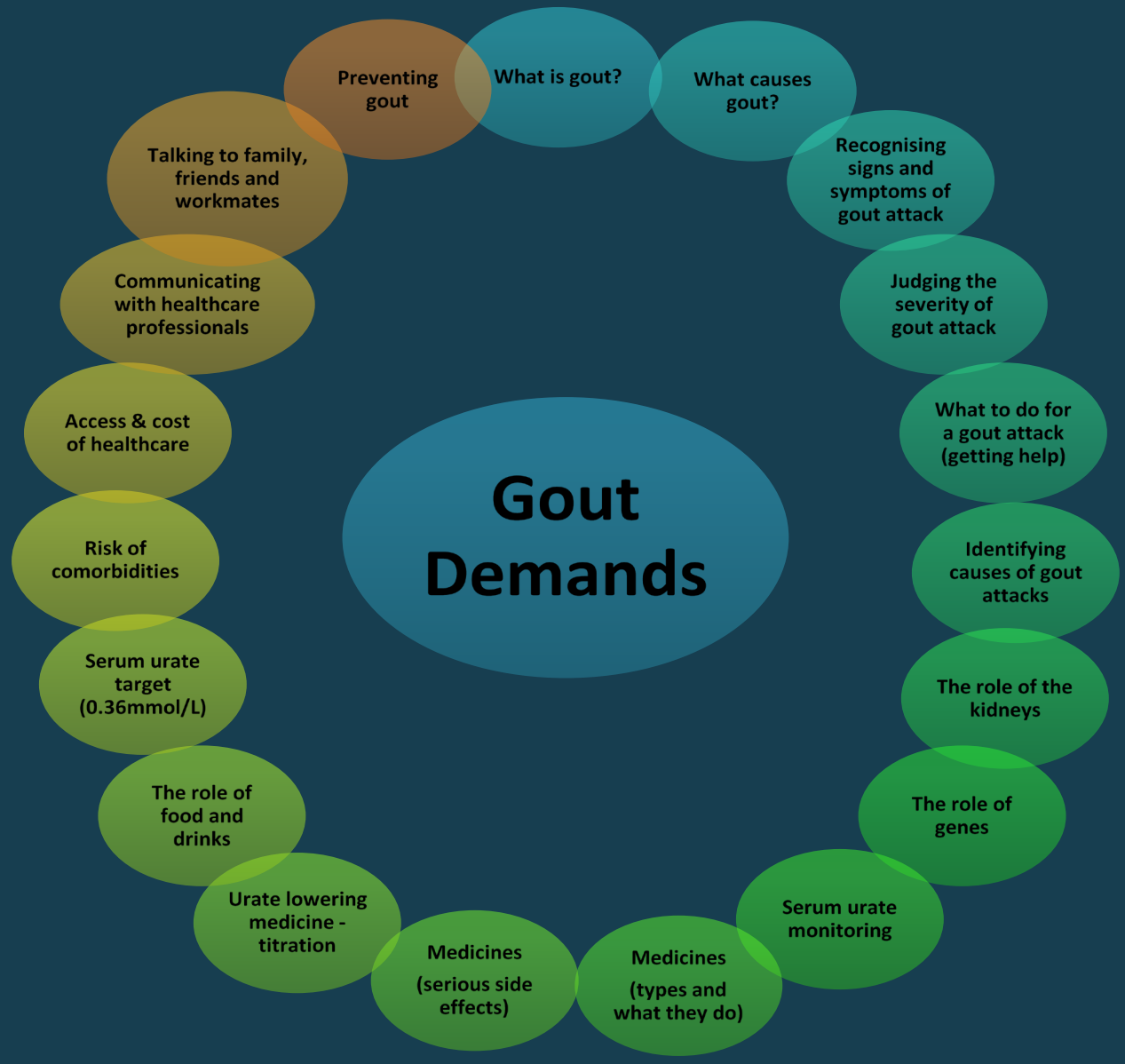
	Māori (n = 185)	Pacific peoples (n = 173)	NZ European (n = 214)
Type 2 diabetes	28.6	21.4	15.7
Hypertension	65.5	53.6	51.6
Cardiovascular disease	47.9	24.2	42.1
Kidney disease	35.0	29.7	30.0

- Screening for co-morbidities
- Opportunistic gout management

Models of care

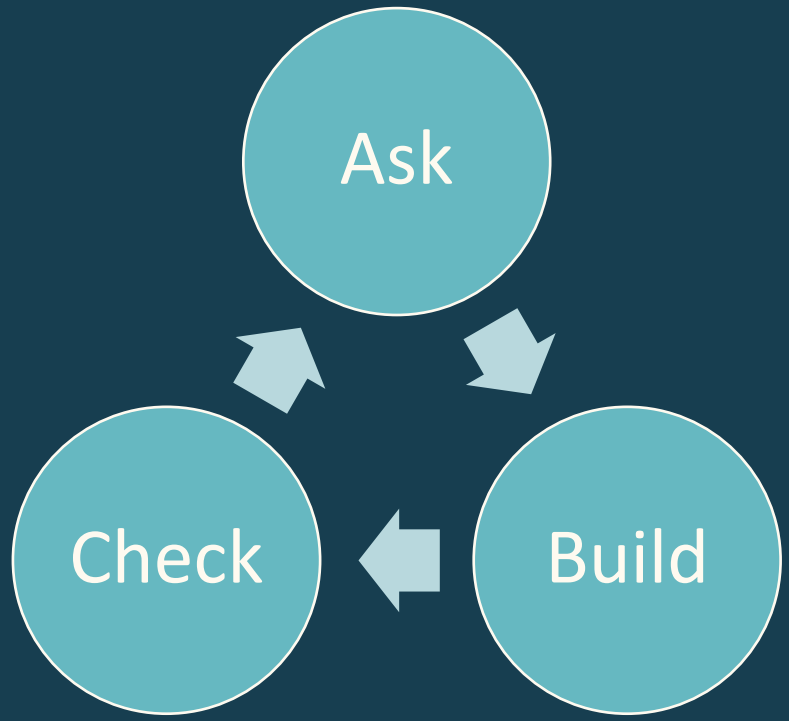
- Novel interventions to improve gout care
  - Nurse led clinics
  - Pharmacy led care - in person or by automated telephone.

- Buy-in and engagement of all practitioners in the healthcare team, to ensure patients receive consistent messages about the core aspects of gout management is essential.



Education - ABC health literacy model

- Key element of gout management
- Iterative process
- Key talking points
  - Gout is not your fault
  - Caused by too much uric acid
  - Stop gout by reducing urate
  - Get your uric acid checked regularly



Resources

- Health Literacy New Zealand was funded by Pharmac to develop a new gout booklet for individuals and whānau.
- The booklet will be available in English, Samoan and Tongan.
- The booklet is available for viewing here: www.healthnavigator.org.nz/media/15434/change-your-life-gout-booklet-english-2022.pdf
- To order booklets please click on this link: https://forms.gle/5sf653PGzqhjXgVq7

Team Gout

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