

Update in Internal Medicine 2026

Saturday, May 2 • 8 a.m. – 4 p.m.

UT Southwestern Medical Center, T. Boone Pickens Medical Education & Conference Center



Updates on Nephrolithiasis

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UT Southwestern
Medical Center

Outline

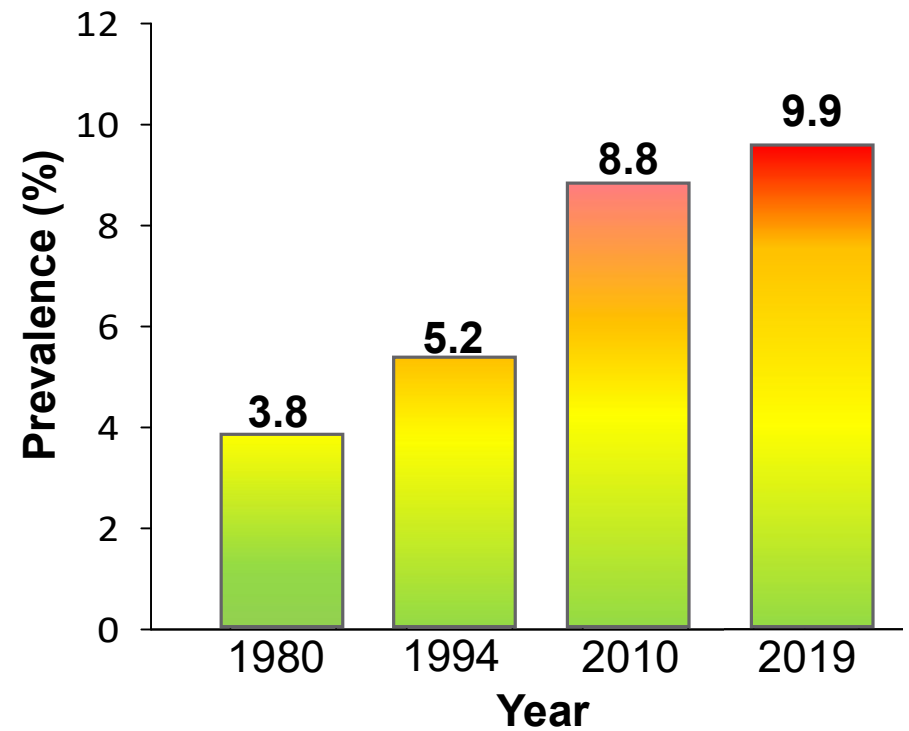
Epidemiology of kidney stone disease

Evaluation of kidney stone formers

Prevention of recurrent stones

Prevalence of Nephrolithiasis in the U.S.

NHANES cross-sectional surveys:
“Have you ever had kidney stones?”

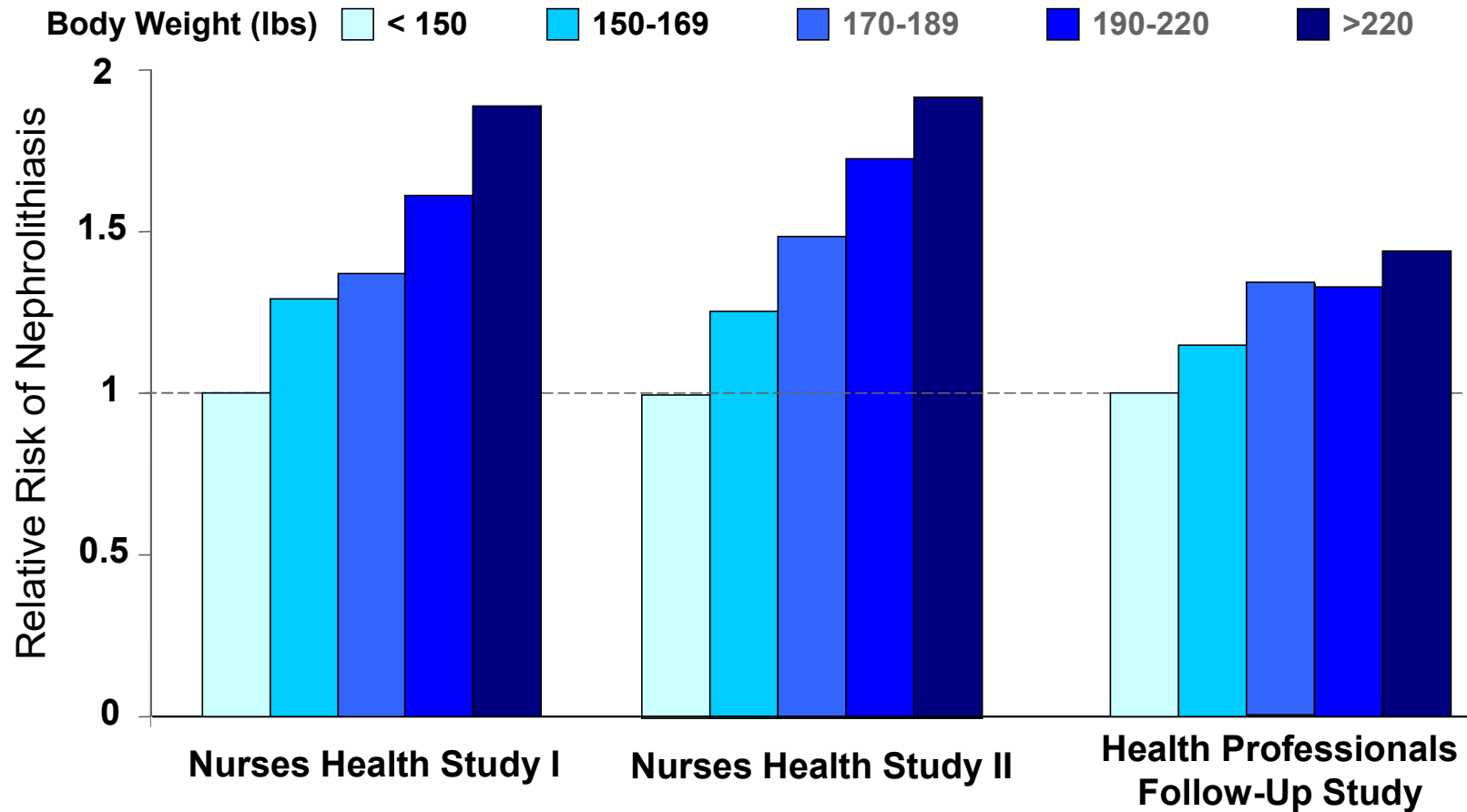


Stamatelou KK, Kidney Int, 1994
Chew BU, JU Open Plus, 2024

What Explains the Rising Prevalence of Stones?

- Growing use of abdominal imaging → Detection of asymptomatic stones
- Increasing antibiotic exposure → Change in gut microbiota / urine chemistry
- Stone-provoking medications → Vitamins C/D, Carbonic anhydrase inhibitors
- Changing dietary patterns → ↑ intake of protein, salt, sweetened beverages
- Obesity / Metabolic syndrome

Obesity and Incident Nephrolithiasis

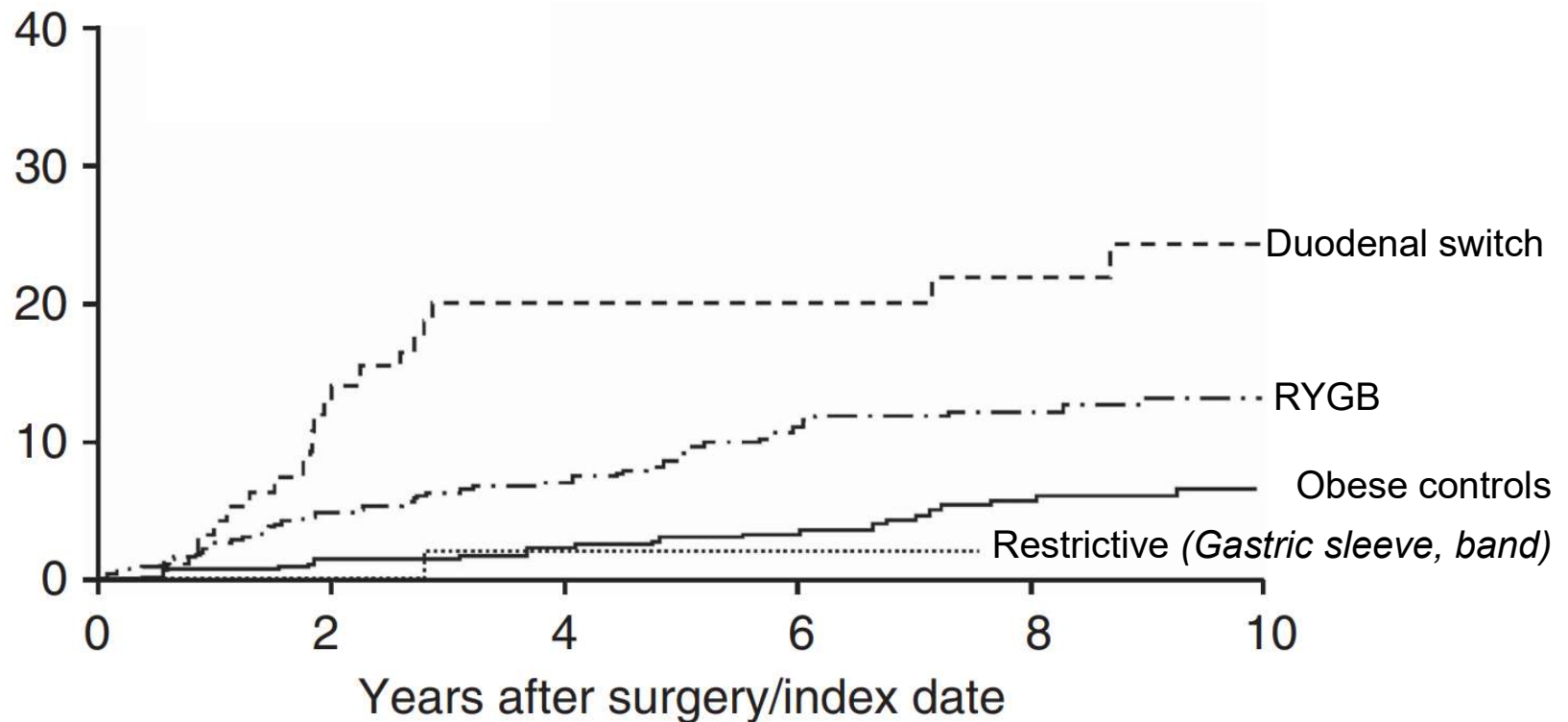


Weight gain independently associated with incident nephrolithiasis

Taylor EN, JAMA, 2005

Bariatric Surgery and Kidney Stones

New onset nephrolithiasis (%)

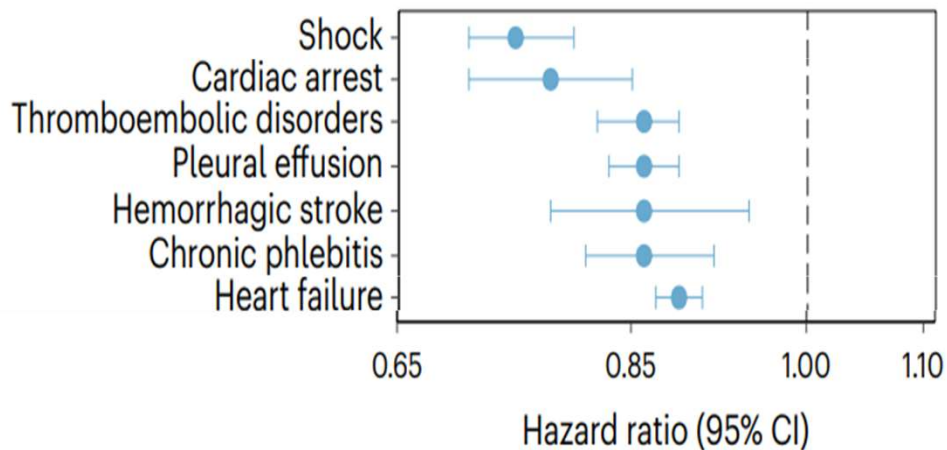


Mechanisms: Enteric hyperoxaluria (fat malabsorption), low urine volume, other

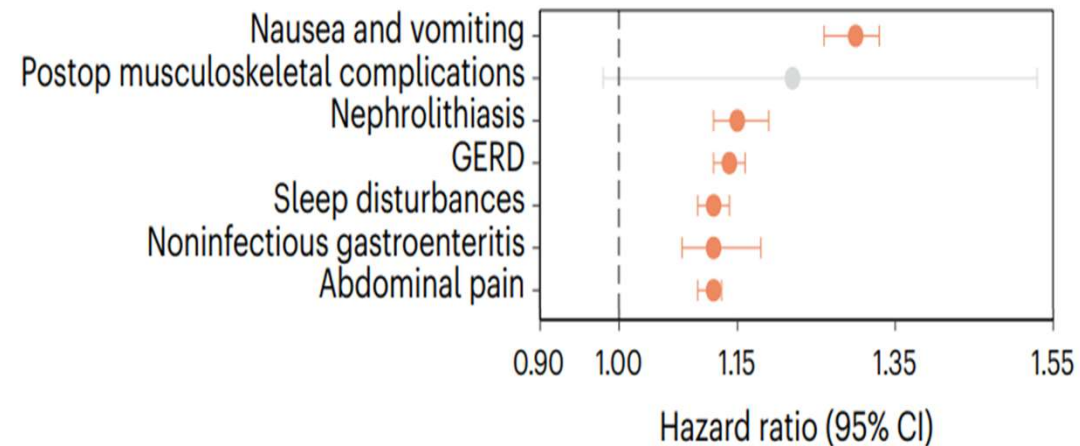
Glucagon-like Peptide-1-based Therapy and Stones

- 1 out of 8 U.S. adults have used a GLP-1 receptor agonist at some point
- Diabetics starting GLP1-RA (N=215,970) vs. other diabetes meds (N=1.2 M)

Most Common Benefits



Most Common Side-effects



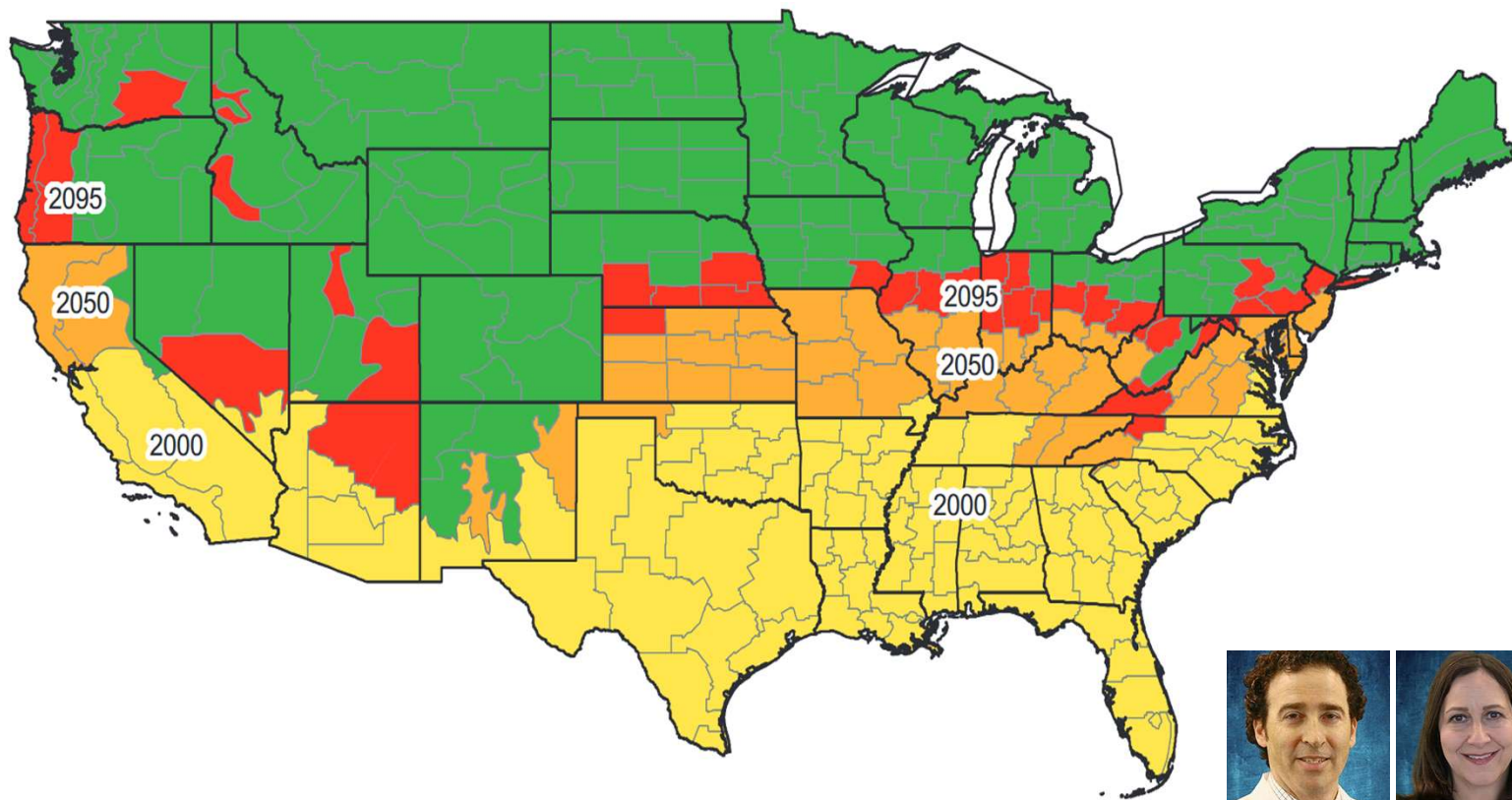
- Mechanisms: Change in diet / fluid intake vs. GLP1 renal receptors vs. other?
- Higher incidence of stones NOT described in RCTs of GLP1-RA for obesity

What Explains the Rising Prevalence of Stones?

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- Changing dietary patterns → ↑ intake of protein, salt, sweetened beverages
- Obesity / Metabolic syndrome → Insulin resistance, diet, obesity Rx
- Climate change → Greater dehydration, urban heat islands

Predicted Growth of the U.S. Stone Belt

- “Stone belt”: Southeastern portion of the U.S. with highest stone prevalence



Brikowski TH, Lotan Y, Pearle MS, PNAS, 2008

Outline

Epidemiology of kidney stone disease

Evaluation of kidney stone formers

Prevention of recurrent stones

Evaluation of Kidney Stone Formers

History

- **Medical History**
GI disease/surgery, diabetes, gout, RTA
- **Medications**
Stone-provoking (next slide)
- **Dietary History**
Inatke of protein, calcium, salt, oxalate, fluids
- **Social History**
Occupation, Exercise, Sweating
- **Family History**

Laboratory Tests

- **Blood Chemistry**
CMP, Phos, Mg, Uric Acid
- **Urinalysis and Culture**
specific gravity, pH, crystalluria
- **Stone Analysis**

Medications Associated with Kidney Stones

Drugs That Crystallize

Triamterene

Antibiotics (Sulfonamides, ceftriaxone, ciprofloxacin)

Protease Inhibitors (Indinavir, nelfinavir, atazanavir)

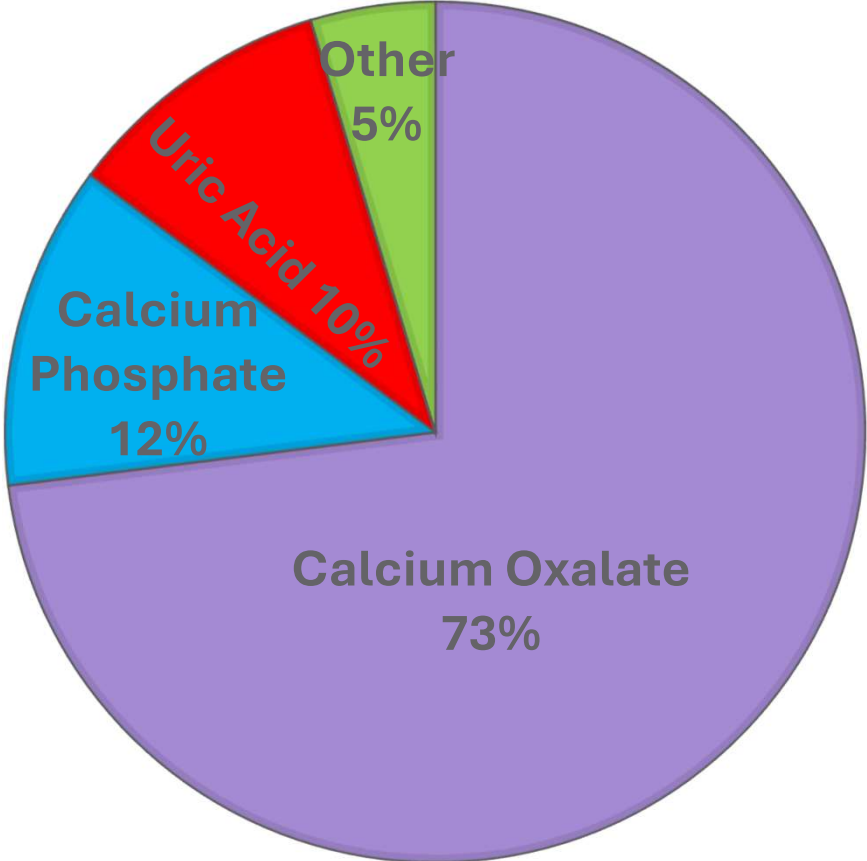
Guaifenesin, ephedrine, others...

Drugs That Cause “Metabolic Stones”

Class (example)	Stone Type	Mechanism
Carbonic Anhydrase Inhibitors (Topiramate)	CaP, CaOx	↑Urine pH and Calcium, Hypocitraturia
Calcium /Vitamin D supplements	CaOx, CaP	Hypercalciuria
Uricosuric agents (Probenecid, losartan,...)	CaOx, UA	Hyperuricosuria
Vitamin C (doses \geq 1 gram/day)	CaOx	Hyperoxaluria
PTH analogs (Teriparatide, Abaloparatide)	CaOx, CaP	Hypercalciuria

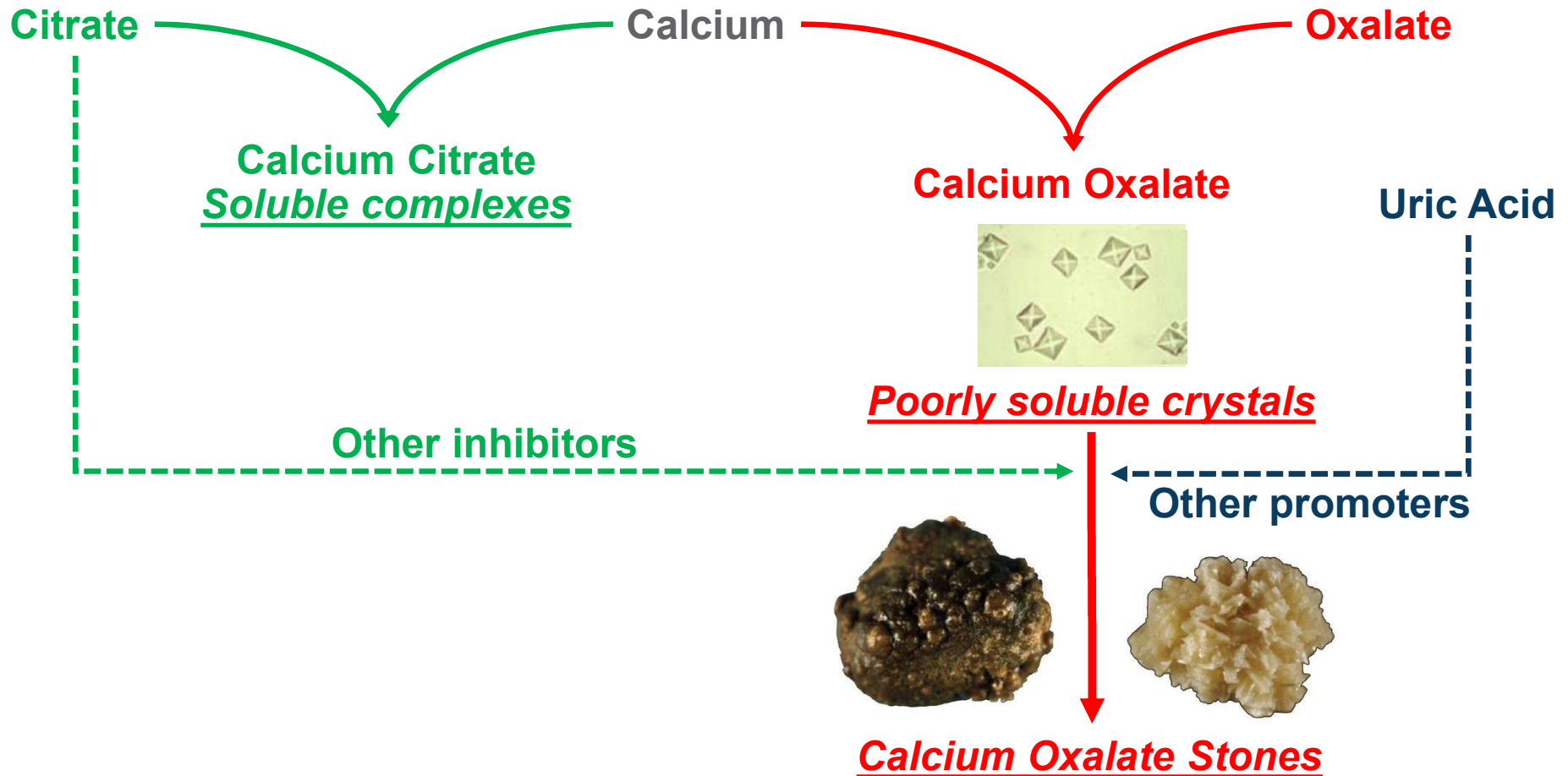
Stone Composition at UTSW Mineral & Urology Clinics

2009-2018



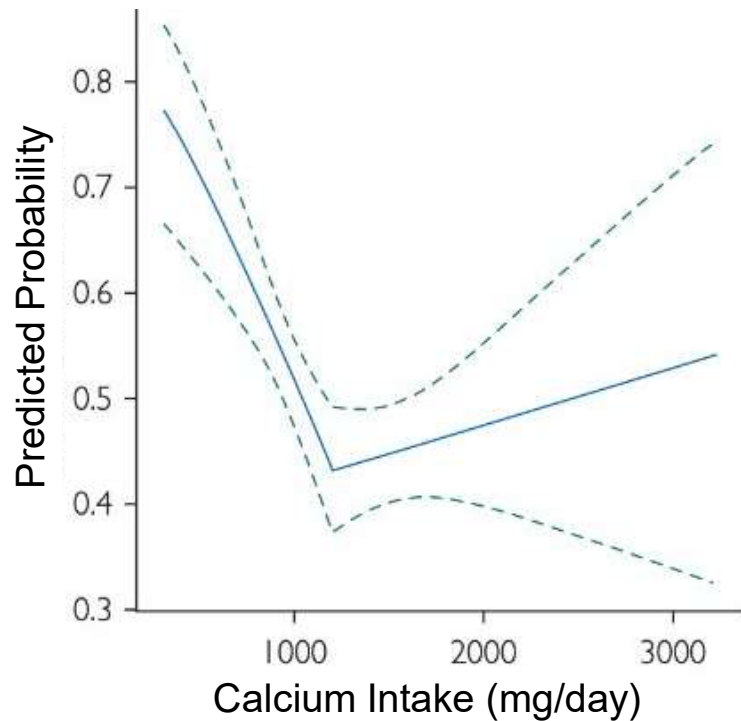
N=3,190

Pathogenesis of Calcium Oxalate Stones



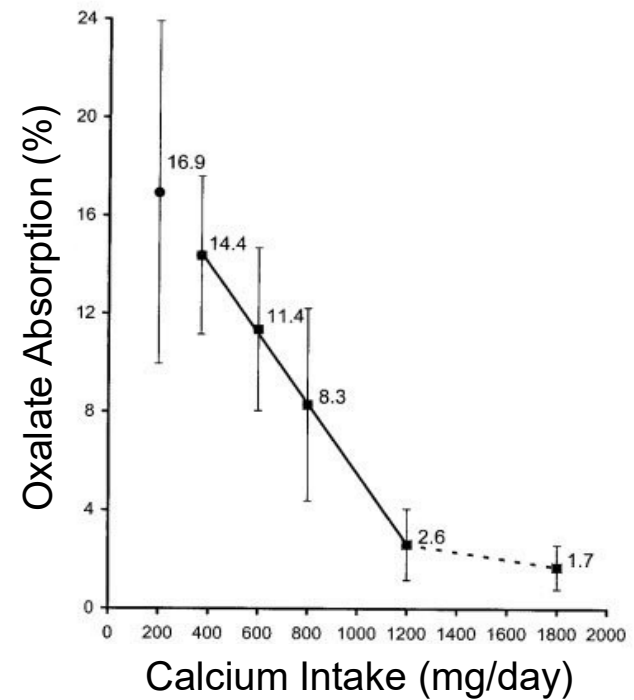
Dietary Calcium Intake and Nephrolithiasis

Probability of being a stone former across dietary Ca intake



Chewcharat A, Mayo Clin Proc, 2022

Lower dietary calcium intake enhances intestinal oxalate absorption



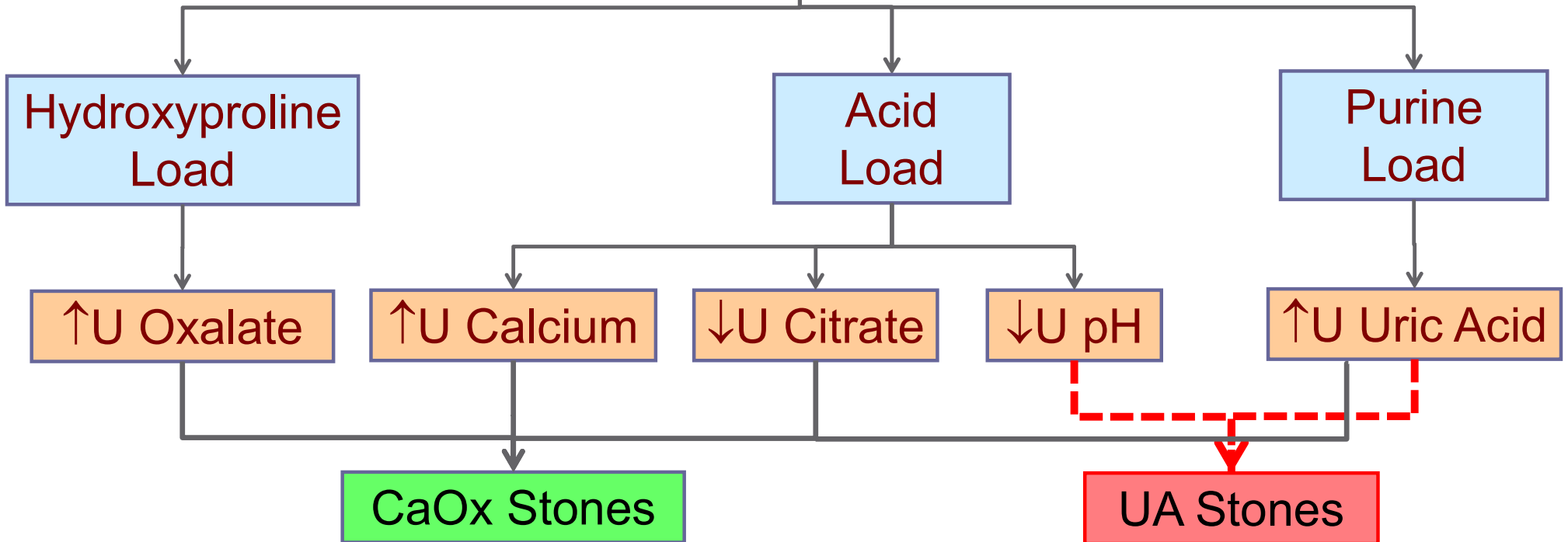
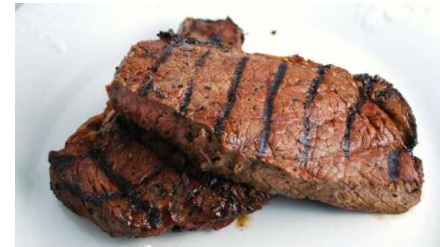
von Unruh GE, JASN, 2004

Dietary Protein Intake and Kidney Stone Risk



**EASY
EVERYDAY
KETO**

Animal proteins

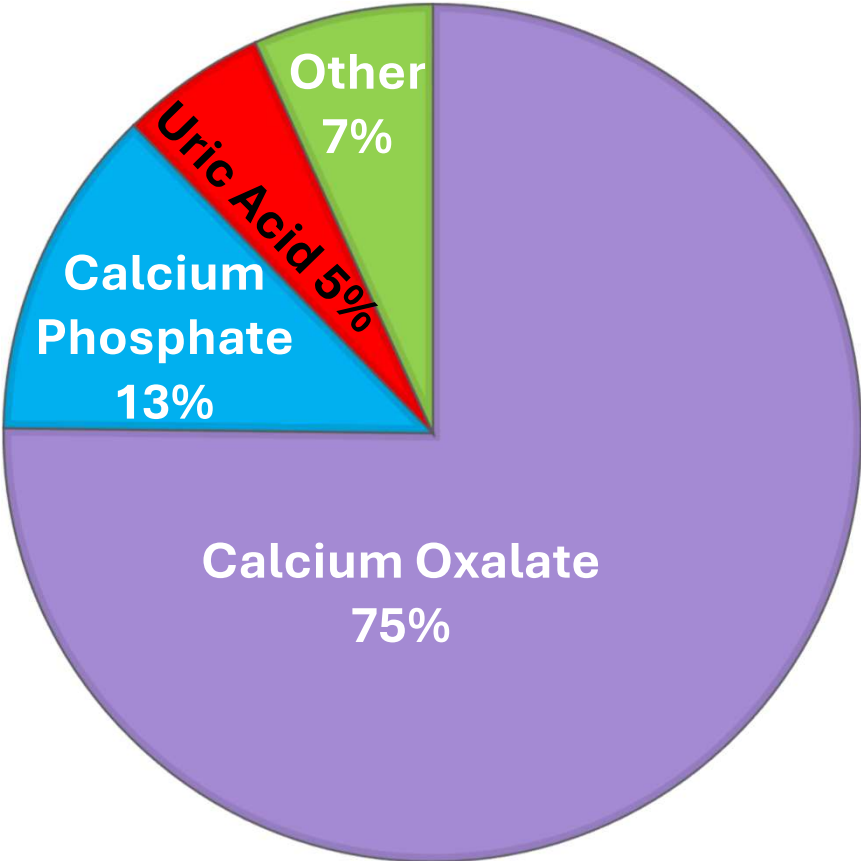


Pathogenesis of CaOx Nephrolithiasis

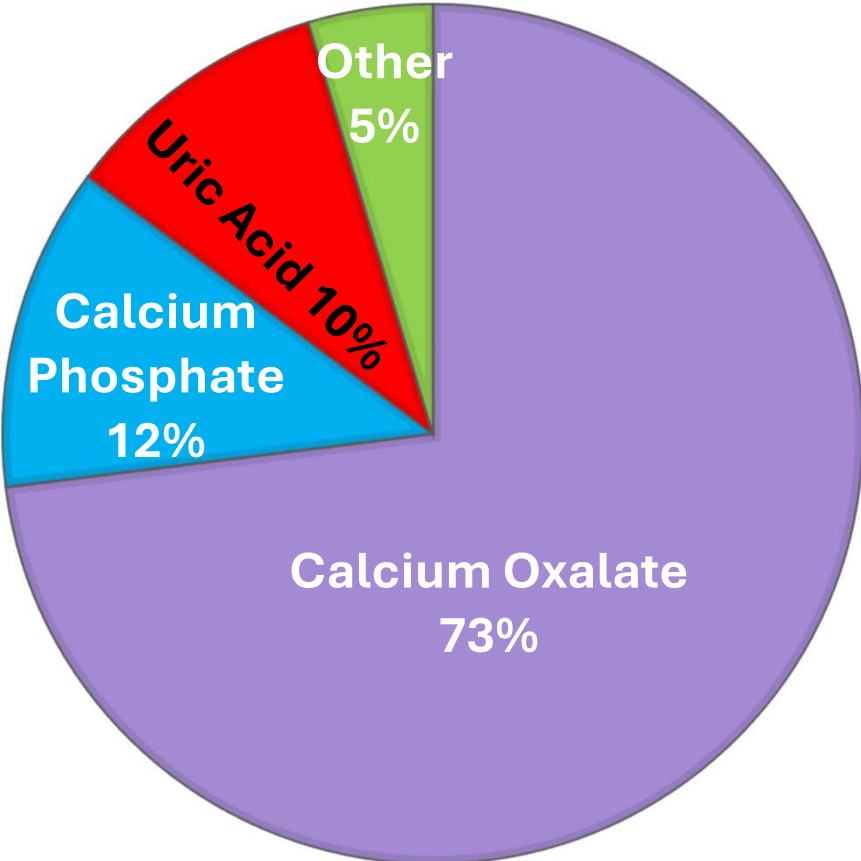
Abnormality	Major etiologies
↑ Urine Calcium	1ry hyperparathyroidism, distal RTA, medications, ↑ dietary protein/sodium intake, idiopathic

Stone Composition at UT Southwestern Clinics

1980

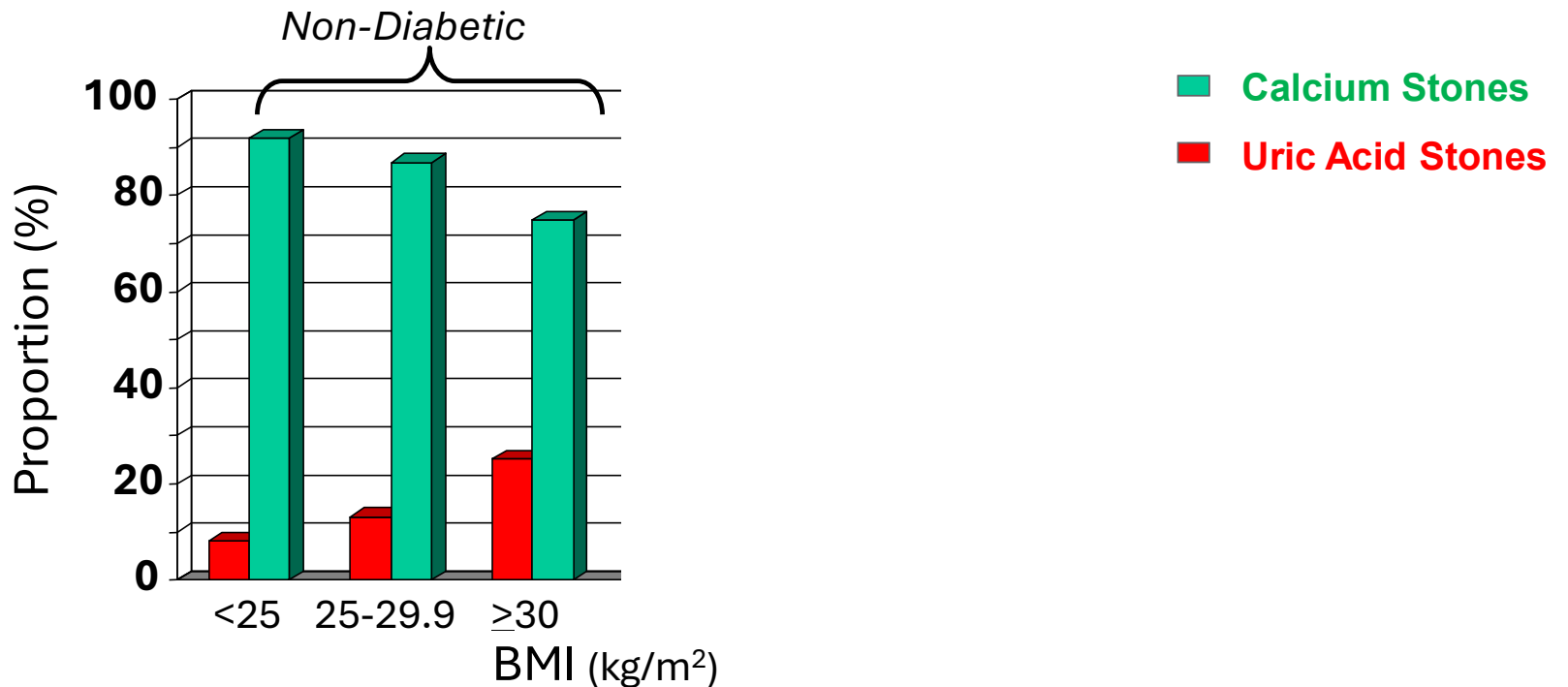


2014



Obesity, Diabetes, and Stone Composition

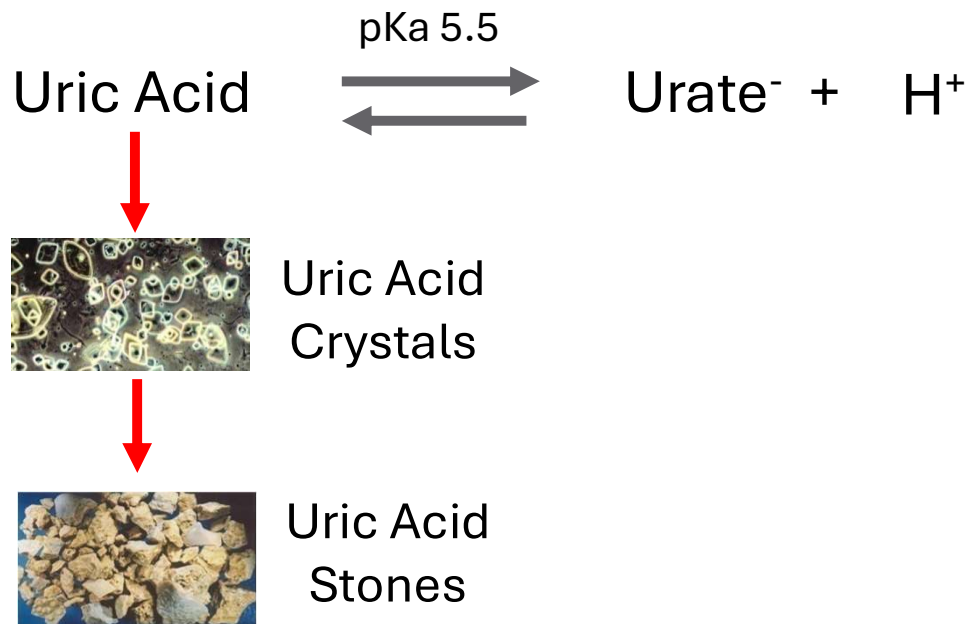
- 2,464 calculi: 272 (11%) patients with T2DM, and 2,192 without diabetes



Daudon, JASN, 2006

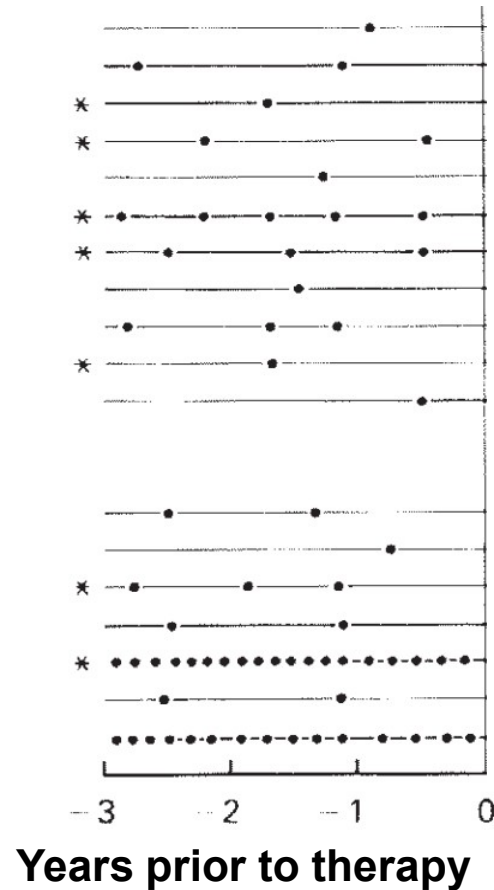
Uric Acid Stones: A Disease of Low Urine pH

- Low urine pH is the most important risk factor for uric acid stone formation:



Alkali Therapy Prevents UA stone recurrence

- 18 UA stone formers
- KCitrate 30-80 mEq/day
- Titrated for 24-hr urine pH between 6.0-6.5
- Follow-up: 1-5.5 years



Evaluation of Patient with Recurrent Kidney Stones

History

- **Medical History**
GI disease/surgery, diabetes, gout, RTA
- **Medications**
Stone-provoking (next slide)
- **Dietary History**
Inatke of protein, calcium, salt, oxalate, fluids
- **Social History**
Occupation, Exercise, Sweating
- **Family History**

Laboratory Tests

- **Blood Chemistry**
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- **Urinalysis and Culture**
specific gravity, pH, crystalluria
- **Stone Analysis**
- **24-hour Urine Chemistry**
- **Genetic Testing**

24-hour Urine in Patients with Kidney Stones

Identifying Causes: Detects metabolic abnormalities and dietary aberrations

Guiding Treatment: Specific, personalized diet/fluid advice and selection of appropriate medication to prevent recurrence

Monitoring Effectiveness: Follow-up monitoring, response to treatment

Stone Risk Factors

DATE	SAMPLE ID	Vol 24	SS CaOx	Ca 24	Ox 24	Cit 24	SS CaP	pH	SS UA	UA 24
07/02/01	S33501	2.13	3.93	157	35	549	1.27	6.485	0.23	0.644
03/19/01	S29214	0.68	13.42	239	22	222	5.47	6.134	1.17	0.526
03/18/01	S29215	1.01	11.04	258	30	281	1.49	5.640	2.21	0.611
NORMAL RANGE		0.5 - 4L	6 - 10	male <250 female <200	20 - 40	male >450 female >550	0.5 - 2	5.8 - 6.2	0 - 1	male <0.800 female <0.750

Outline

Epidemiology of kidney stone disease

Evaluation of kidney stone formers

Prevention of recurrent stones

Something Old

Something New

Something Borrowed

Something Blue

Kidney Stone Prevention: Something Old

2014 AUA guidelines

LIFESTYLE

Increase fluid intake

Goal 24-hr urine volume > 2.5 L/day

↓ protein, ↓ sodium, ↔ Ca diet

Recommended over ↓ Ca diet in CaSFs

Low oxalate diet

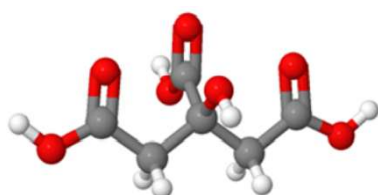
Insufficient data for most stone formers

Generic vs tailored diet

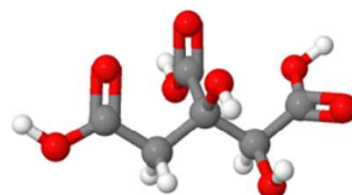
Insufficient data

Kidney Stone Prevention: Something New

-Hydroxycitrate: Structural analog of citrate



Citrate (CA)



Hydroxycitrate (HCA)

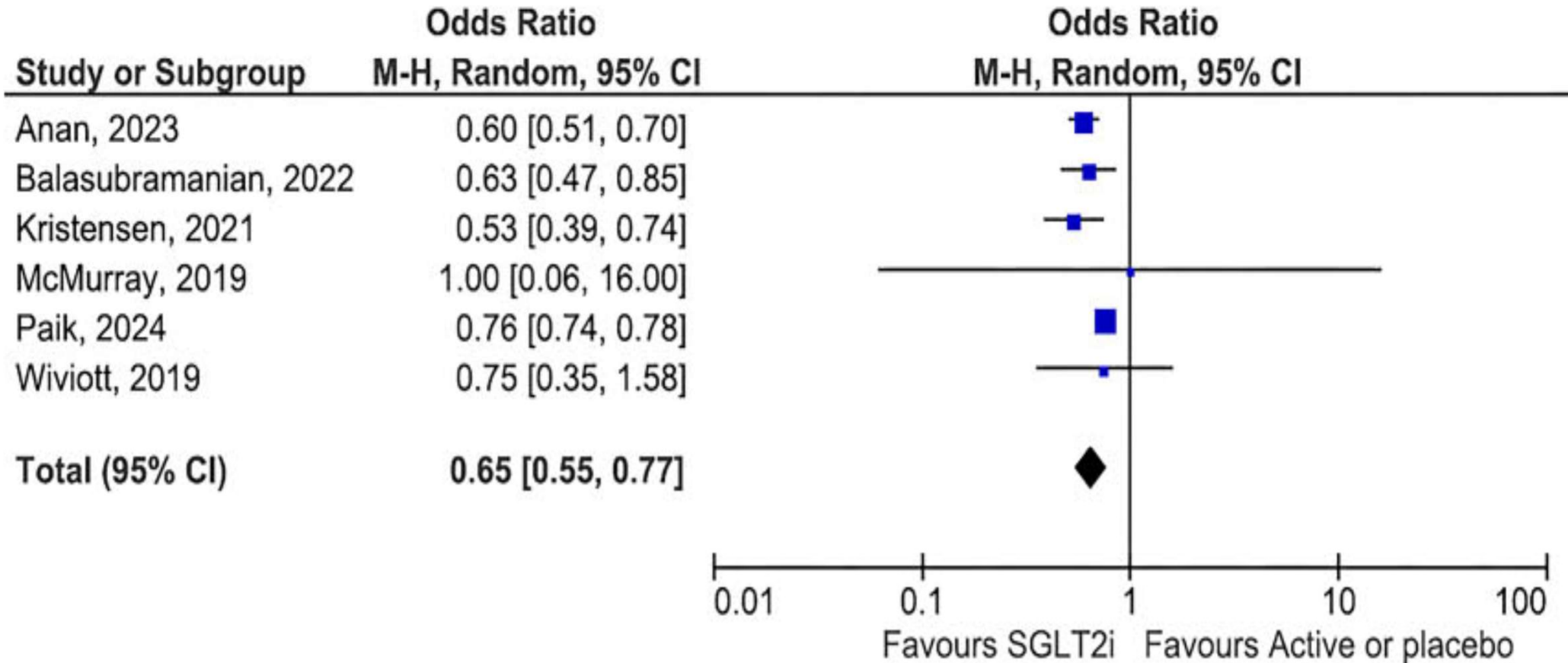
- In vitro:
 1. Capacity to complex calcium equivalent to citrate
 2. Effective inhibitor of CaOx and CaPhos crystallization
 3. Dissolves CaOx crystals in supersaturated solution
- In vivo: Orally-ingested hydroxycitrate appears in urine
- Ongoing studies in kidney stone formers to test efficacy

Something Borrowed: SGLT2-i and Nephrolithiasis

- SGLT2 inhibitors: Inhibit proximal tubule Na-glucose co-transporter 2
- Approved indications:
 - Glycemic control in type 2 diabetes
 - CV disease in type 2 diabetes
 - HFrEF and HFpEF
 - CKD (irrespective of diabetes)
- Incident stones in empagliflozin registration data in T2D (20 phase I-IV RCTs):
1.01 events/100 pt-yrs in placebo vs 0.63 events/100 pt-yrs on empagliflozin

Something Borrowed: SGLT2-i and Nephrolithiasis

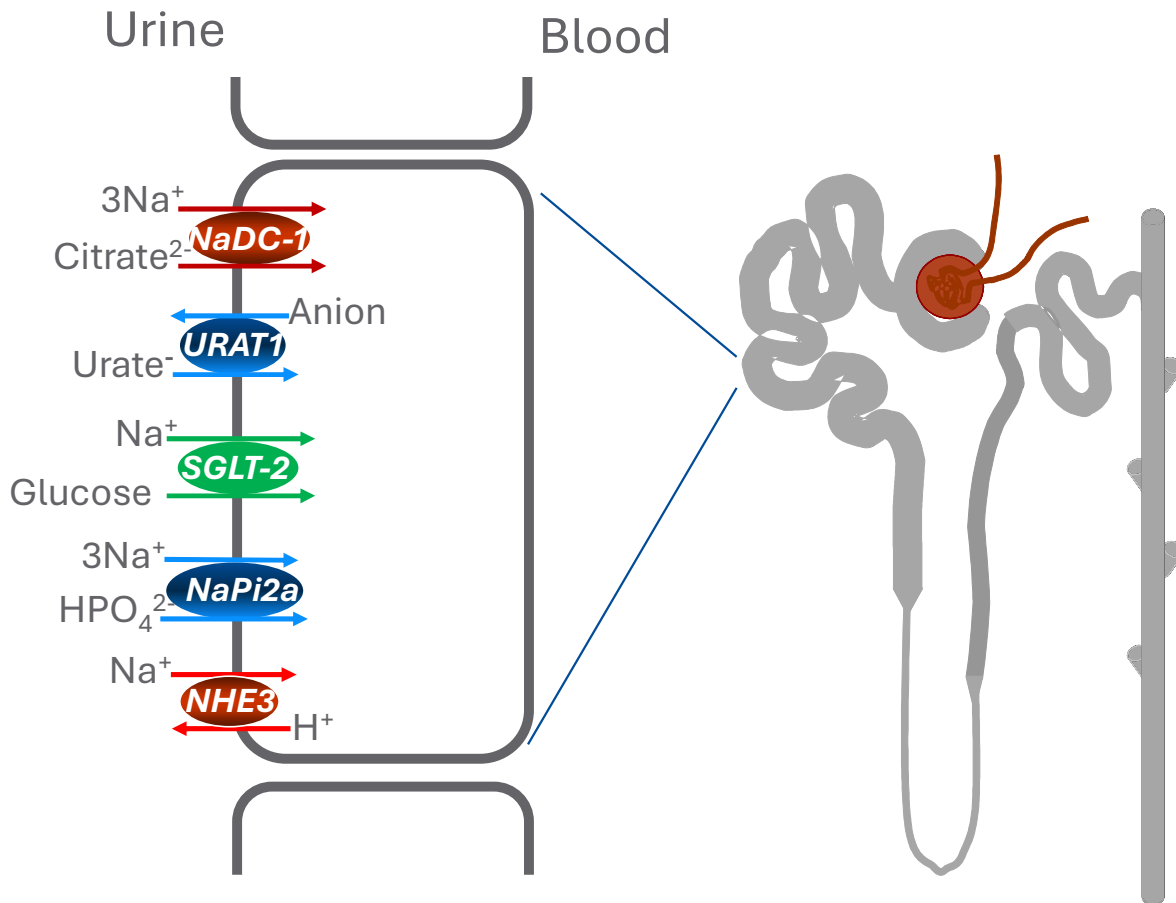
- Meta-analysis: Stone events in 11 635 698 participants in 6 clinical trials



Kanbay M, Nephrol Dialysis Transplant, 2025

How Do SGLT2-inhibitors Alter Urine Stone Risk?

- Proximal Tubule: Reabsorption of molecules relevant to nephrolithiasis



Empagliflozin 25 mg x 2 wks
in stone formers w/o diabetes:

↑↑↑ urine Glucose

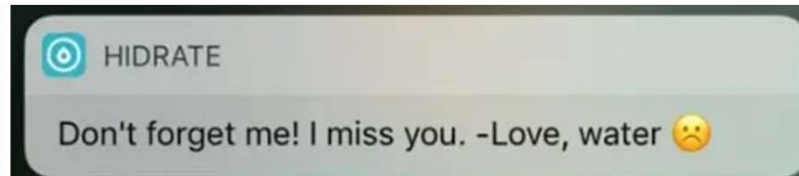
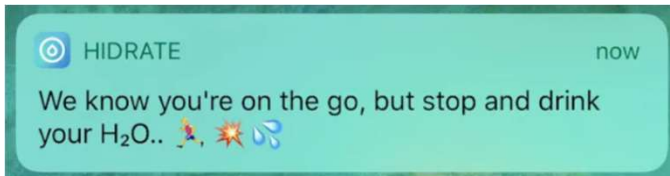
↑↑ urine Citrate

↑ urine Volume

Variable changes in urine pH

Something Blue...tooth: Smart Water Bottle

- Accurately tracks fluid intake
- Transmits data via Bluetooth to phone or smartwatch
- Reminds user to drink (glows, sends messages)



- 12-week study in stone formers with low urine volume:
Greater increase in 24-hour urine volume compared with usual care

Stout TE, J Renal Nutr, 2022

Something Bluetooth: Smart Water Bottle

- Prevention of Urinary Stones with Hydration (PUSH): Multi-center RCT of behavioral interventions in 1,658 stone formers age ≥ 12 years
- Hypothesis: A program of behavioral interventions to raise fluid intake will reduce stone recurrence in stone formers with low urine volume
- Interventions: Fluid prescription (monitored by smart bottle), tapering financial incentives, coaching, reminders
- Results: Behavioral intervention raised fluid intake / urine volume early on (at 6 months), but did not reduce new symptomatic stone events at 2 yrs

Summary

Evolving epidemiology of kidney stone disease

↑↑ Stone prevalence- ↑protein/salt intake, obesity, antibiotic use, climate

Evaluation of kidney stone formers

Detailed history (diet, meds), stone analysis, 24-hr urine collection

Prevention of recurrent stones

- Something old Fluids, low-protein, low-salt diet, thiazides, KCitrate
- Something new Hydroxycitrate
- Something borrowed SGLT2-inhibitors
- Something Bluetooth Smart water bottle