Diagnosis & Therapeutic Approach in Nephrolithiasis:

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Isfahan University of Medical Sciences

Outline

1. Introduction
2. Epidemiology
   - ROKS
3. Diagnosis
4. Management
5. Two articles from Iran
6. Case presentation
7. Take-Home Message

Introduction

- ✓ Nephrolithiasis describes a **syndrome** characterized by the development of solid crystalline masses within the urinary space of the kidney.
- ✓ Predisposing factors can be genetic, metabolic, & environmental.
- ✓ Nephrolithiasis is now recognized as a marker for **systemic disease** & a predictor of metabolic & CV complications.

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The Medical Community's Perspective on Nephrolithiasis

Primarily urologic illness

→ Chronic medical condition requiring long-term surveillance & management

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Epidemiology

- ✓Nephrolithiasis is common, affecting approximately 1 in 11 people in the US.
- ✓By age 70, 19.1% of men & 9.4% of women report ever having a kidney stone.

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Epidemiology

- ✓The M/F ratio has decreased from 3:1 to about 2:1 in the past 2 decades, attributed to an increasing prevalence of obesity.
- ✓Obesity & DM are strongly associated with a history of kidney stones in multivariate models, particularly for women.

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Epidemiology

- ✓Nephrolithiasis has been associated with significant morbidity beyond the urologic system including:
  - CKD
  - Cardiovascular disease
    - HTN
    - Possibly increased carotid wall thickness
    - MI
  - Reduced BMD & fractures

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Epidemiology

✓The risk of stone recurrence: 50% in 5-10 ys & 75% in 20 ys.

✓Risk factors for recurrent stones:

- Multiple prior stone episodes
- Younger age of onset
- Male gender
- FH of kidney stones
- Higher BMI
- Presence of ≥ 2 stones across both kidneys, the presence of stones in the renal pelvis or lower kidney pole
- A stone composition consisting of uric acid, struvite, or brushite

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Epidemiology

- ✓The online Recurrence of Kidney Stone (ROKS) nomogram estimates the risk of recurrence at varying time points in symptomatic stone-formers using baseline characteristics.

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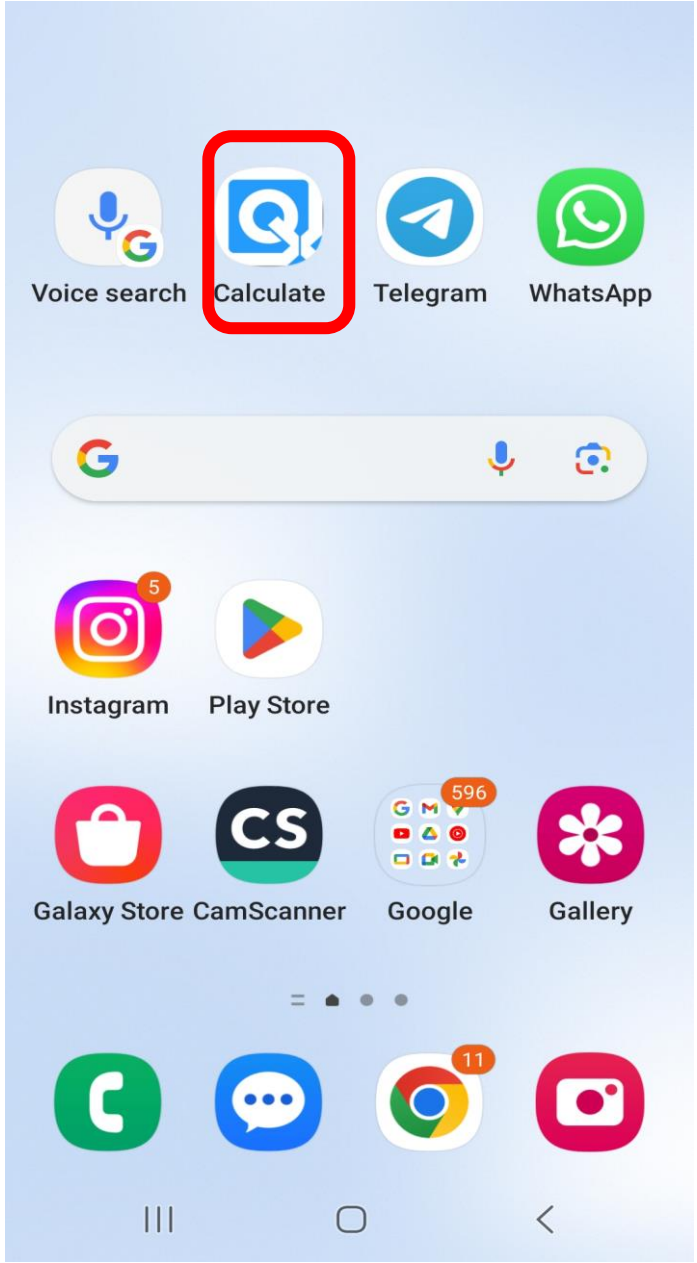
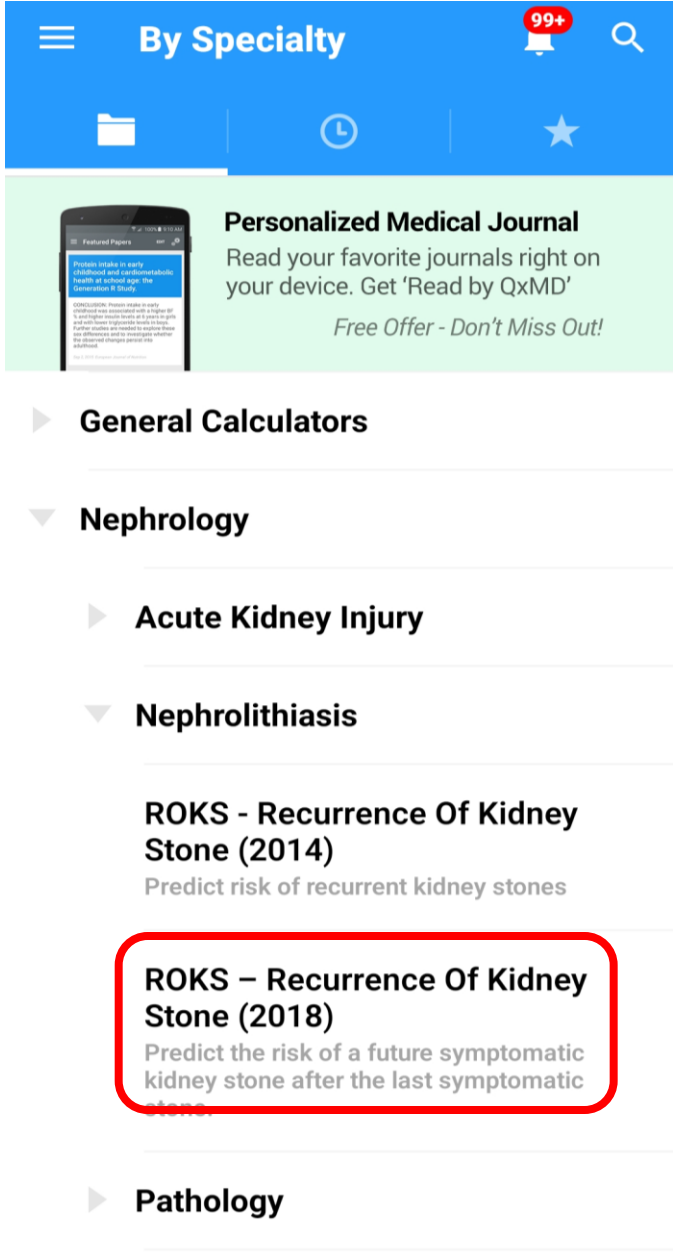
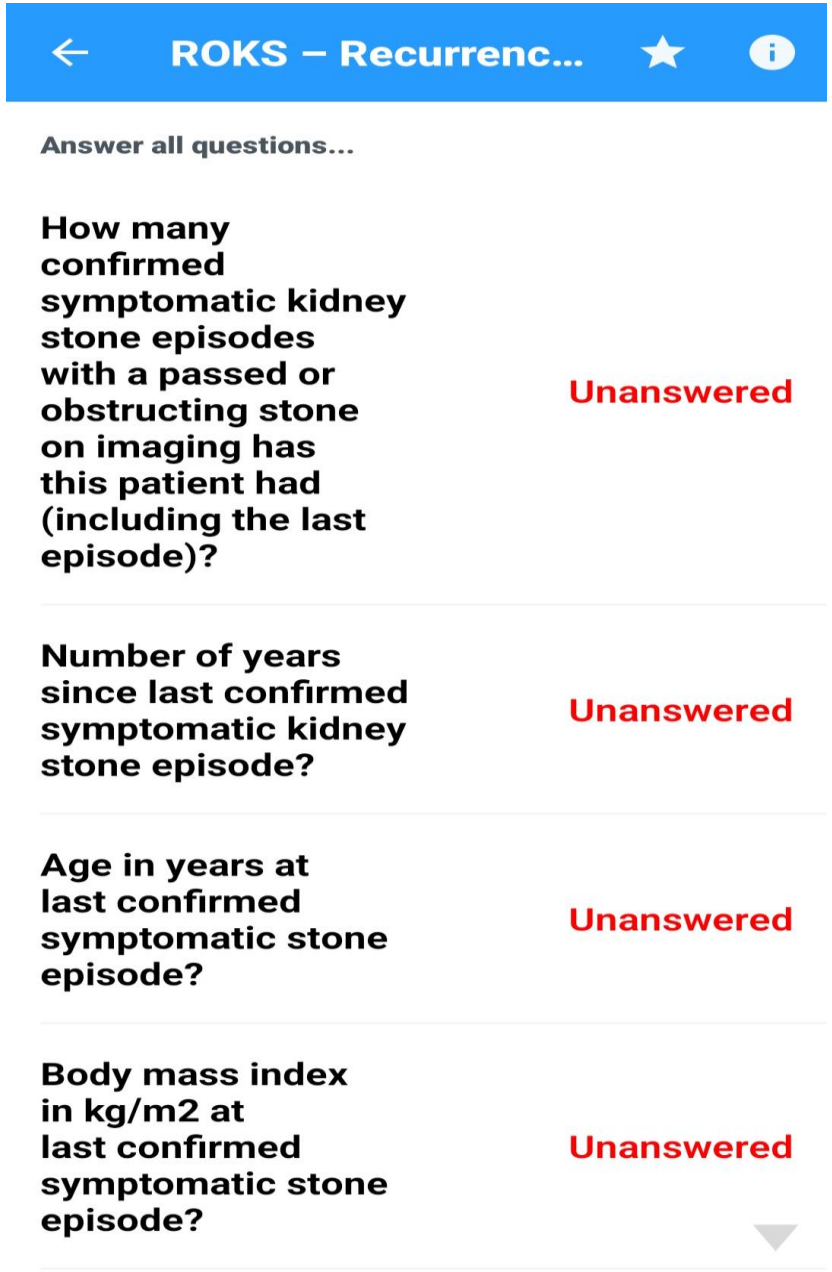
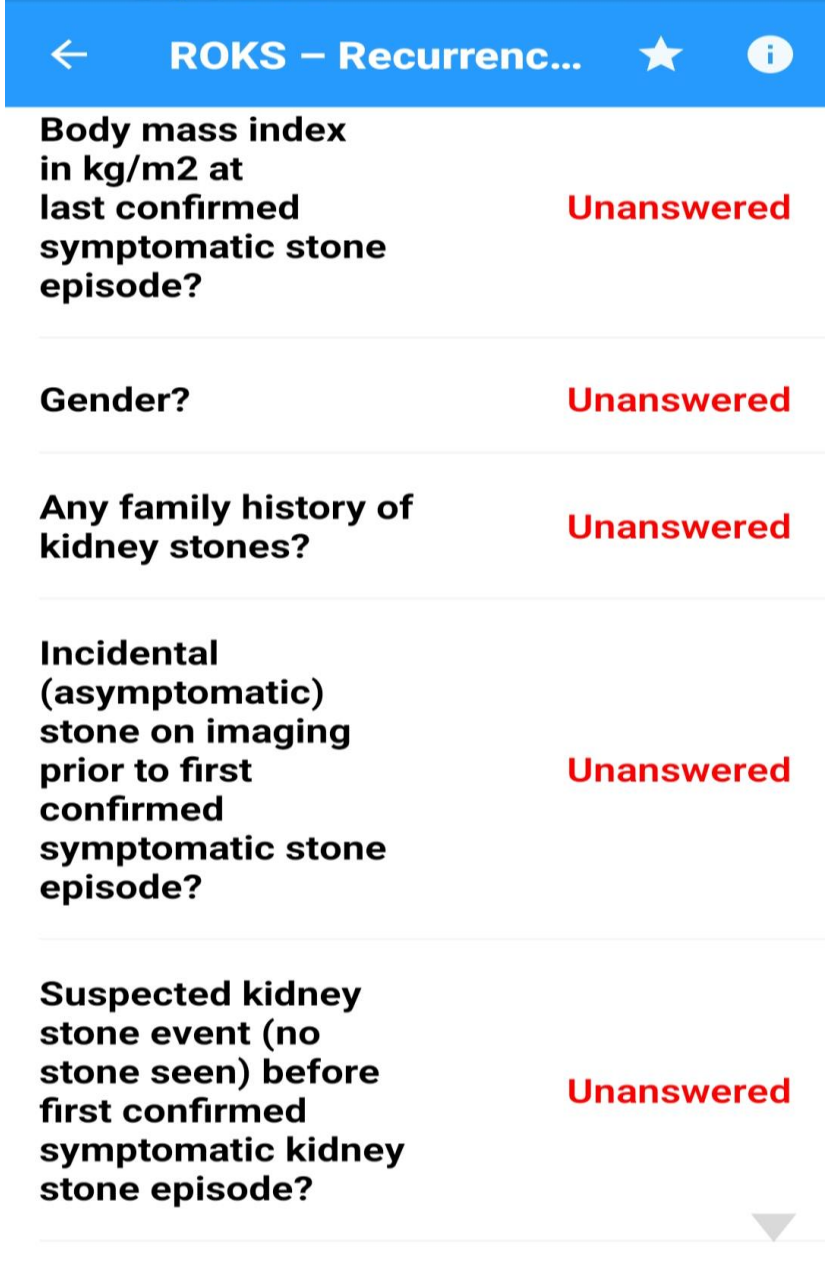
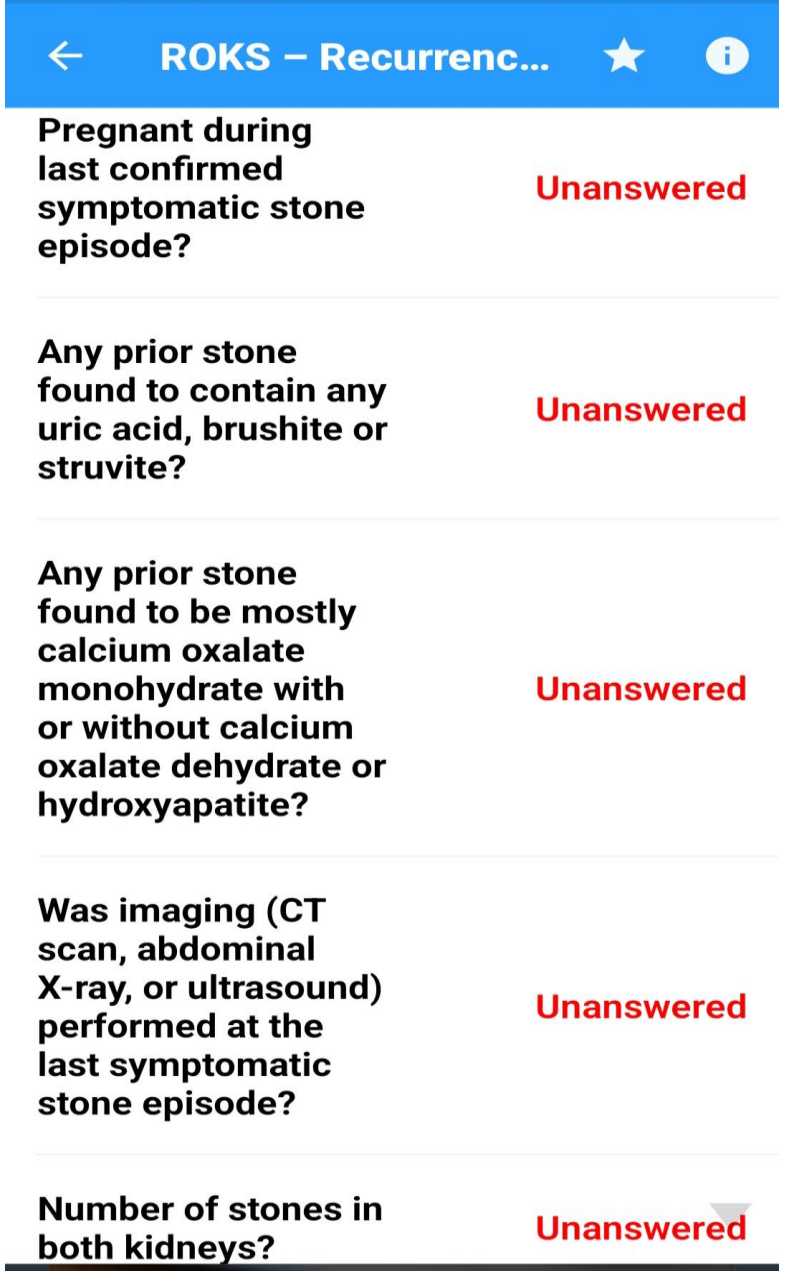
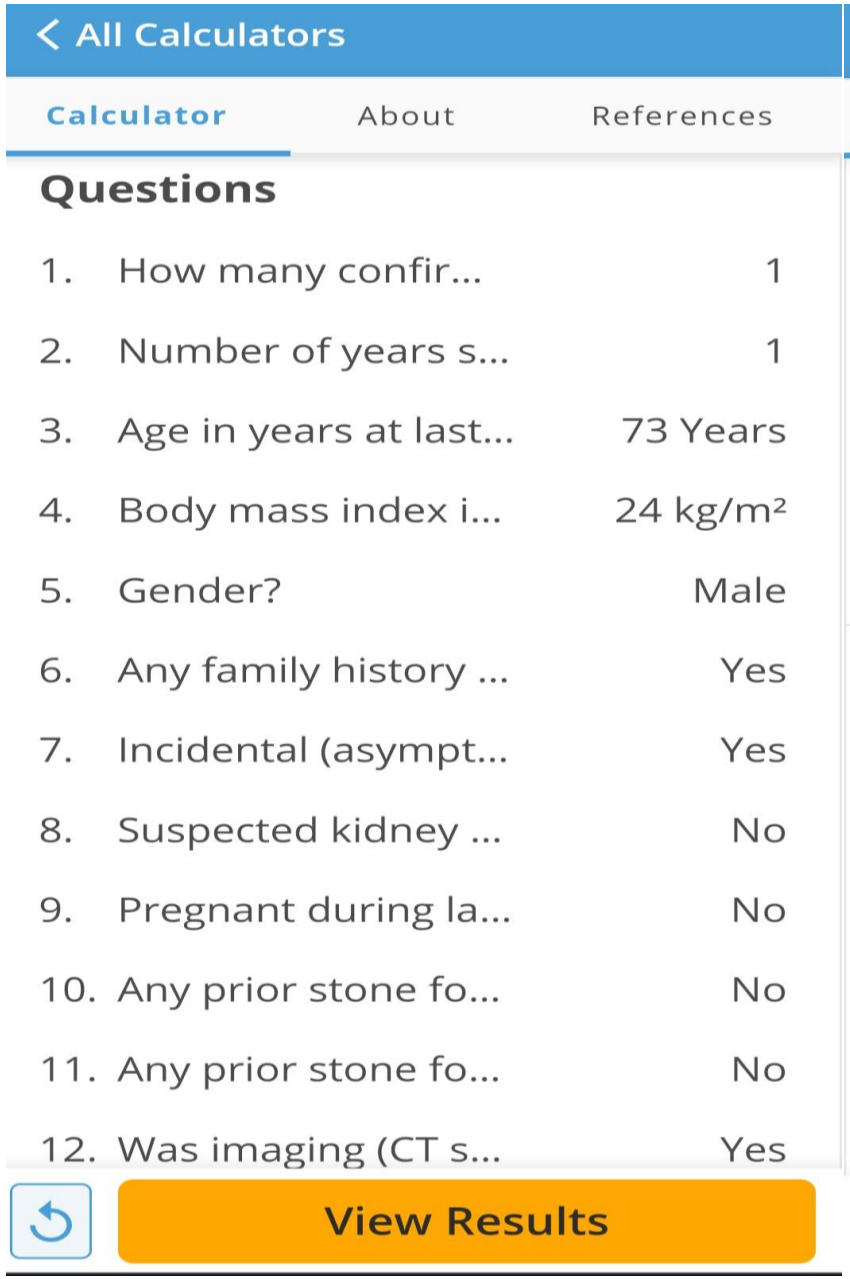

Voice search
Calculate
Telegram
WhatsApp
Instagram
Play Store
Galaxy Store
CamScanner
Google
Gallery

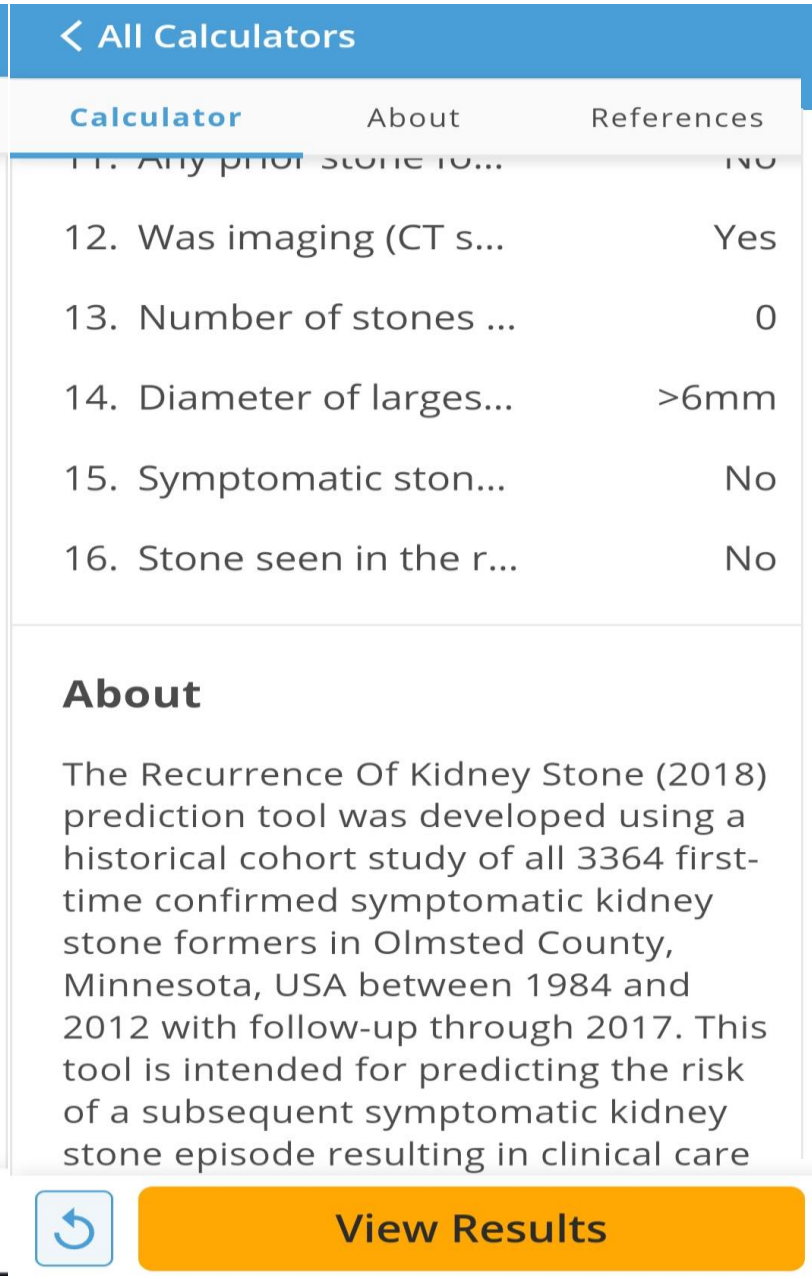

By Specialty
99+
Personalized Medical Journal
Read your favorite journals right on your device. Get 'Read by QxMD'
Free Offer - Don't Miss Out!
General Calculators
Nephrology
Acute Kidney Injury
Nephrolithiasis
ROKS - Recurrence Of Kidney Stone (2014)
Predict risk of recurrent kidney stones
ROKS – Recurrence Of Kidney Stone (2018)
Predict the risk of a future symptomatic kidney stone after the last symptomatic
Pathology

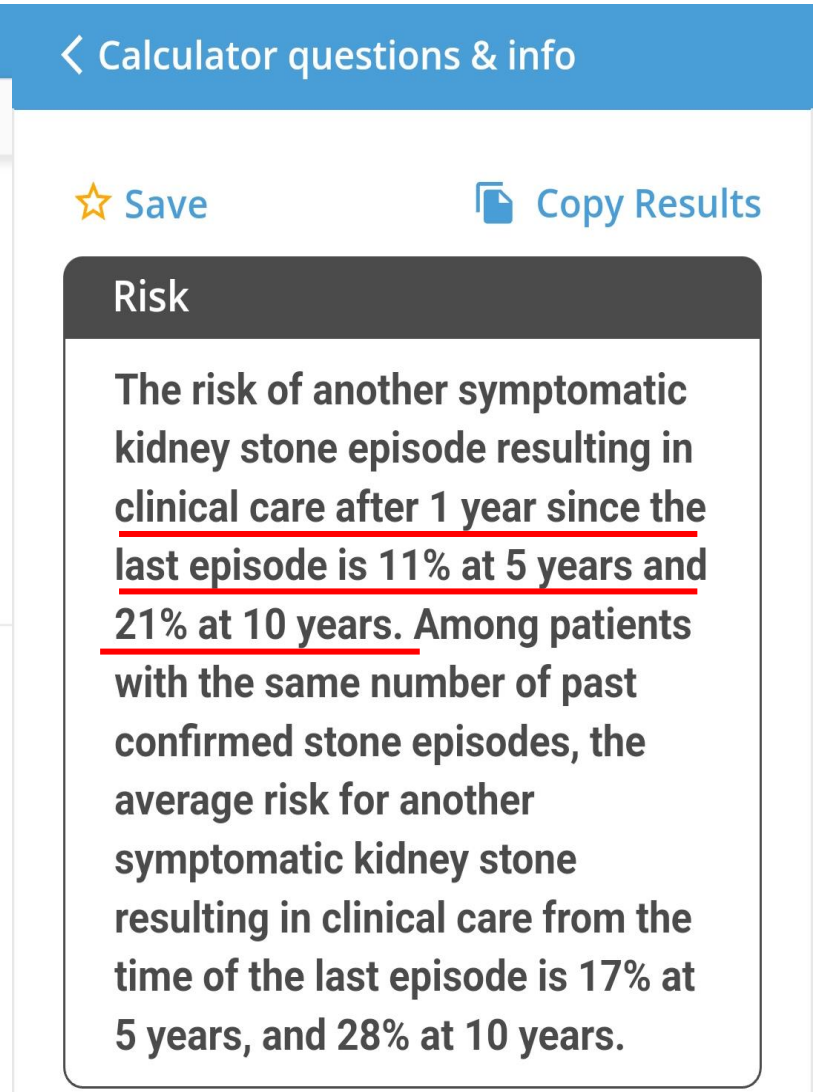

ROKS – Recurrenc...
Answer all questions...
How many confirmed symptomatic kidney stone episodes with a passed or obstructing stone on imaging has this patient had (including the last episode)?
Unanswered
Number of years since last confirmed symptomatic kidney stone episode?
Unanswered
Age in years at last confirmed symptomatic stone episode?
Unanswered
Body mass index in kg/m2 at last confirmed symptomatic stone episode?
Unanswered


ROKS – Recurrenc...
Body mass index in kg/m2 at last confirmed symptomatic stone episode?
Unanswered
Gender?
Unanswered
Any family history of kidney stones?
Unanswered
Incidental (asymptomatic) stone on imaging prior to first confirmed symptomatic stone episode?
Unanswered
Suspected kidney stone event (no stone seen) before first confirmed symptomatic kidney stone episode?
Unanswered


ROKS – Recurrenc...
Pregnant during last confirmed symptomatic stone episode?
Unanswered
Any prior stone found to contain any uric acid, brushite or struvite?
Unanswered
Any prior stone found to be mostly calcium oxalate monohydrate with or without calcium oxalate dehydrate or hydroxyapatite?
Unanswered
Was imaging (CT scan, abdominal X-ray, or ultrasound) performed at the last symptomatic stone episode?
Unanswered
Number of stones in both kidneys?
Unanswered


All Calculators
Calculator
About
References
Questions
1. How many confir... 1
2. Number of years s... 1
3. Age in years at last... 73 Years
4. Body mass index i... 24 kg/m²
5. Gender? Male
6. Any family history ... Yes
7. Incidental (asympt... Yes
8. Suspected kidney ... No
9. Pregnant during la... No
10. Any prior stone fo... No
11. Any prior stone fo... No
12. Was imaging (CT s... Yes
View Results


All Calculators
Calculator
About
References
12. Was imaging (CT s... Yes
13. Number of stones ... 0
14. Diameter of larges... >6mm
15. Symptomatic ston... No
16. Stone seen in the r... No
About
The Recurrence Of Kidney Stone (2018) prediction tool was developed using a historical cohort study of all 3364 first-time confirmed symptomatic kidney stone formers in Olmsted County, Minnesota, USA between 1984 and 2012 with follow-up through 2017. This tool is intended for predicting the risk of a subsequent symptomatic kidney stone episode resulting in clinical care
View Results


Calculator questions & info
Save
Copy Results
Risk
The risk of another symptomatic kidney stone episode resulting in clinical care after 1 year since the last episode is 11% at 5 years and 21% at 10 years. Among patients with the same number of past confirmed stone episodes, the average risk for another symptomatic kidney stone resulting in clinical care from the time of the last episode is 17% at 5 years, and 28% at 10 years.

Diagnosis

Diagnosis: Detailed history

- Age at the first episode
- Number of stones
- Bilateral or unilateral stones
- Frequency of stone formation
- Type of stone
- Type & number of surgical interventions
- Family Hx of stone disease
- Any associated infections
- Detailed dietary habits
- Certain medications

Medications associated with stone formation

Medication	Mechanism
Acetazolamide	Hypocitraturia
Vitamin C	Hyperoxaluria
Vitamin D	Hypercalciuria
Antacids	Hypercalciuria
Theophylline	Hypercalciuria
Nifedipine	Hypercalciuria
Probenecid, aspirin	Hyperuricosuria
Topamax	Hypocitraturia
Indinavir	Precipitation within the tubule
Acyclovir	Precipitation within the tubule

Diagnosis: PE

- Except during an acute episode of stone passing, most patients will have a normal PE.
- PE may sometimes reveal findings of systemic condition such as presence of tophi in patients with hyperuricosuria & uric acid stones.

Conditions that can mimic renal colic (DD)

- ✓Ectopic pregnancy in women
- ✓Bleeding within the kidney leading to formation of clots
- ✓Hemorrhagic cysts
- ✓Loin pain hematuria syndrome
- ✓Malingering

Metabolic Evaluation

✓**Blood tests**

- **FBS**
- **Lipid profile**
- **Na / K**
- **Ca (× 2-3) / P**
- **BUN / Cr**
- **PTH**
- **Uric acid**
- **VBG**

✓**Urinalysis**

✓**Stone analysis**

✓**24 – hours urine collections (× 2-3)**

- **Volume /pH**
- **Cr**
- **Na / K**
- **Ca / P**
- **Uric acid**
- **Oxalate**
- **Citrate**
- **Sulfate / Ammonium**
- **Mg**
- **Cystine**
- **Cl**

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- **~~Mg~~**
- **Cystine**
- **~~Cl~~**

Interpreting 24-Hour Urine Studies to Address Risk for Recurrent Stones

Creatinine
- Allows an assessment of the completeness of 24-hour collection.
- Expect 15-20 mg/kg/d for females and 20-25 mg/kg/d for males.

Total Volume
- A goal of 2.5 L/d, sometimes more, is typical for reducing recurrence risk.

Calcium
- Though > 4 mg/kg is clearly excessive, a graded increase in stone risk is noted with levels > 150 mg/d.
- Correlate with urine sodium to determine of hypercalciuria is driven by excessive sodium intake.

Sodium
- A goal of <100 mg/d is sought if hypercalciuria is present.

Oxalate
- Values > 40 mg/d are excessive, though lower excretion rates may also increase risk.
- For values > 80 mg/d, consider primary hyperoxaluria.

Citrate
- Values > 400 mg/d may limit risk for calcareous stones, with even higher levels sometimes needed.

pH
- Values < 6.0 may increase the risk of uric acid stones.
- Values > 6.0 with metabolic acidosis suggests renal tubular acidosis and a risk for calcium phosphate stones.
- Values > 7.0 may indicate urine infection by bacteria with urease and a risk for struvite stones.

Uric Acid
- Consider xanthine oxidase inhibitor or reduced purine intake if >750-800 mg/d and other measures for calcium oxalate stones or uric acid stones fail.

Ammonium
- Values of >45 mmol/d suggest excess acid production from diet, chronic diarrhea, or other cause.

Sulfate
- Values of >30 mmol/d suggest excessive dietary animal protein.

Cystine
- Normal individuals typically excrete < 30 mg/d.
- Patients with cystinuria generally excrete > 400 mg/d.
- For cystinuria patients, target a concentration < 250 mg/L to limit stone risk.

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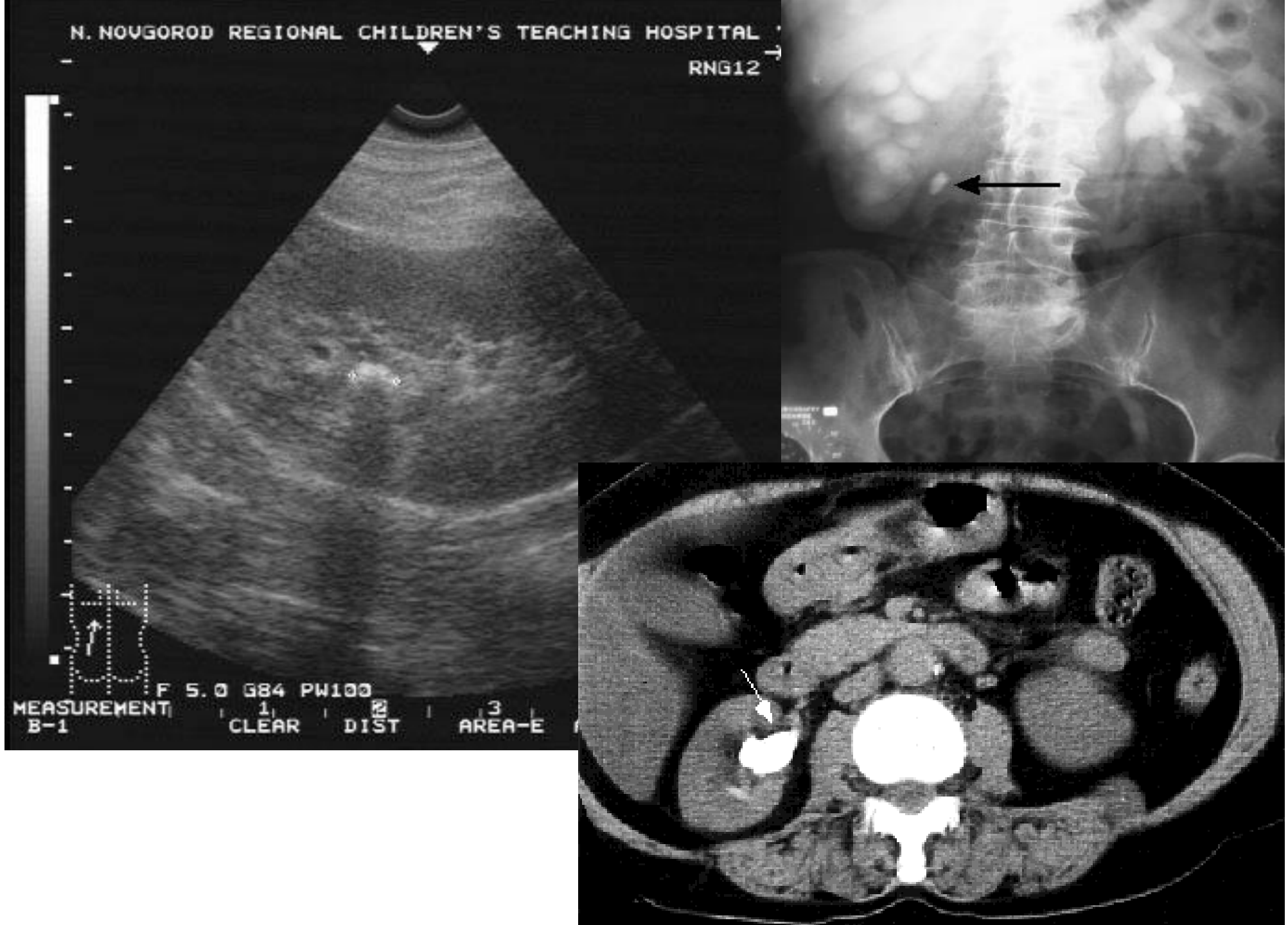
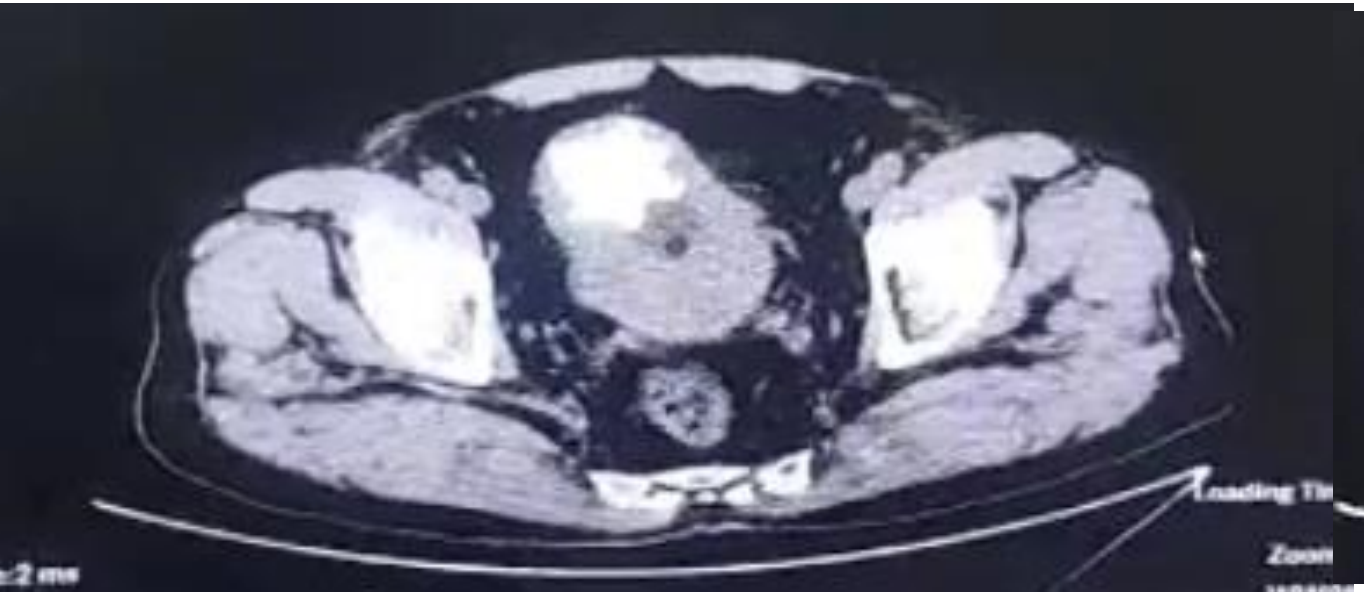
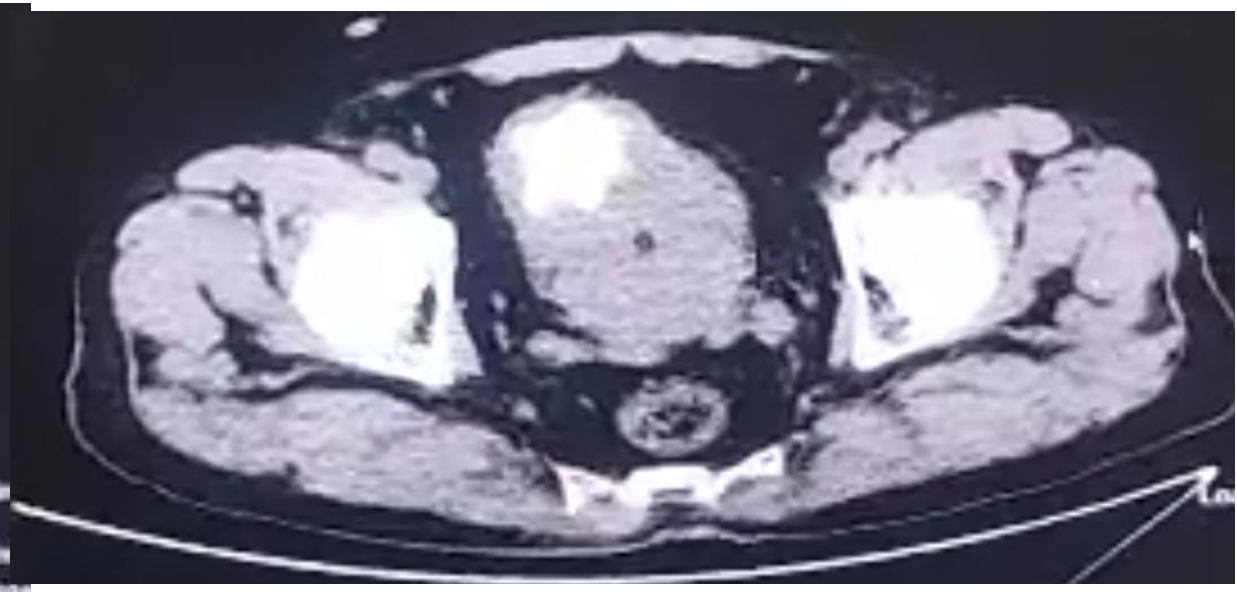
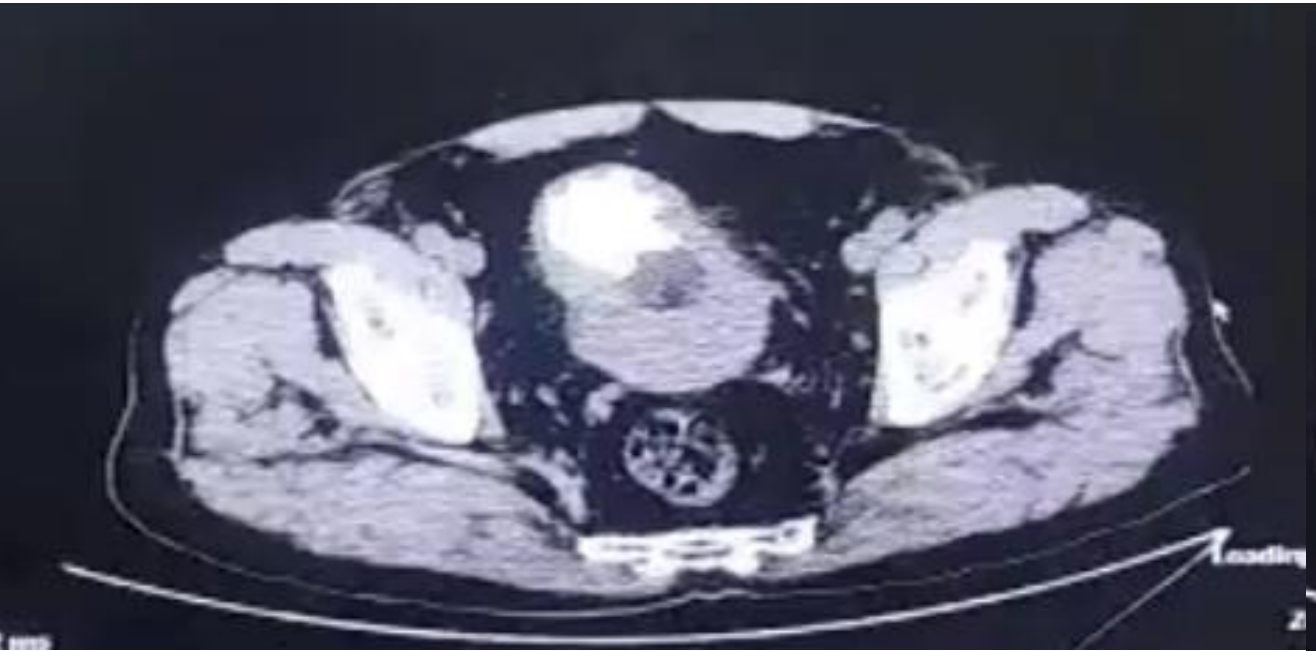
Timing of collections

- While the patient is on their usual diet
- Should not be measured immediately after the acute stone episode
- To wait at least **1 - 2 months** after a stone event to obtain the collections


N. NOVGOROD REGIONAL CHILDREN'S TEACHING HOSPITAL
RNG12
F 5.0 G84 PW100
MEASUREMENT
B-1
1
CLEAR
2
DIST
3
AREA-E







Monitoring

Ultrasonography or KUB at 1 year, if negative, every 2 – 4 years thereafter depending upon the likelihood of recurrence

سوال

فواصل آزمایشات در بیماران سنگ کلیه چقدر است؟

سوال

فواصل آزمایشات در بیماران سنگ کلیه چقدر است؟

هر ۳-۶ ماه تا رسیدن به goal درمانی و سپس سالانه

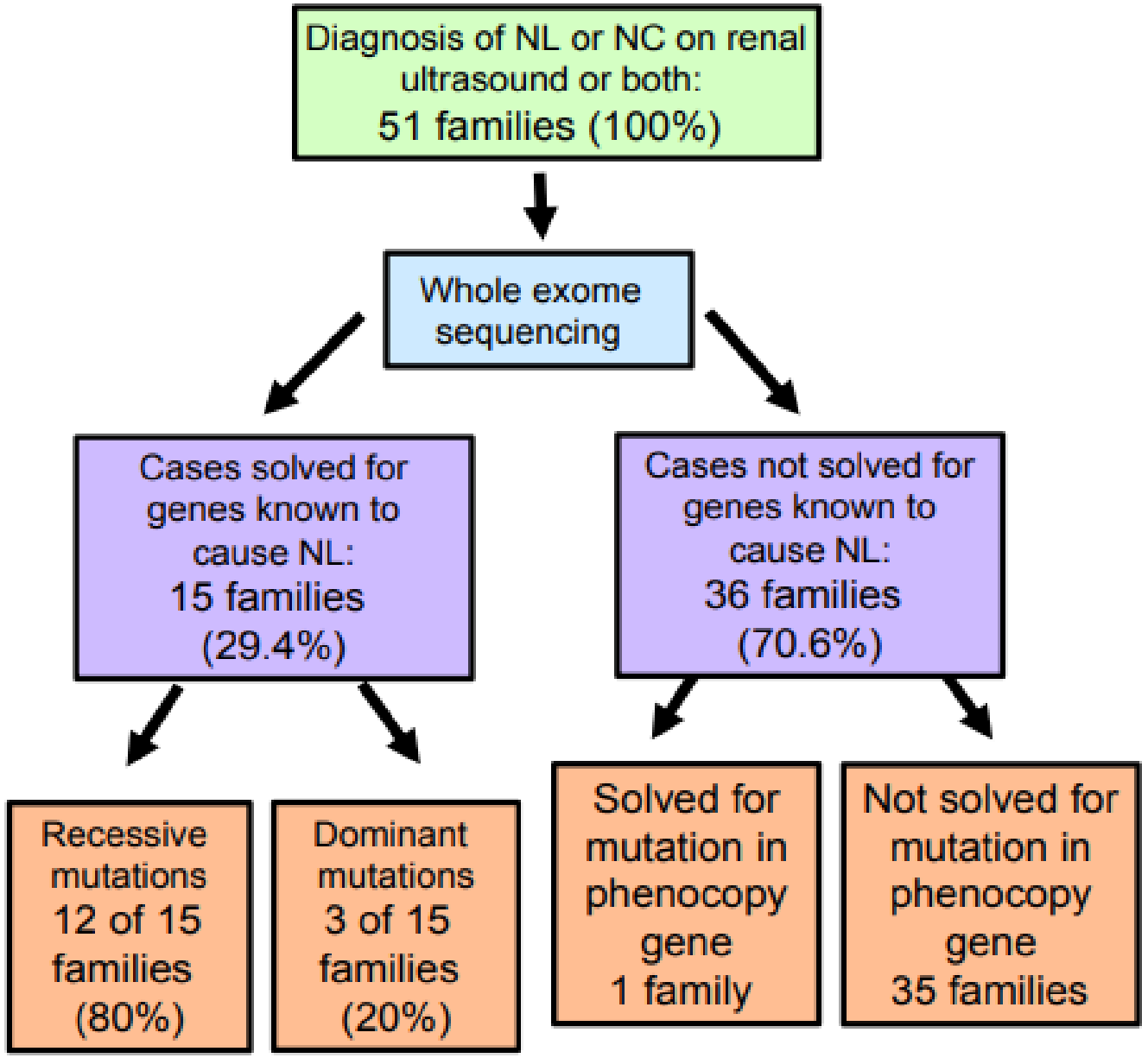
clinical investigation www.kidney-international.org

2018

Whole exome sequencing frequently detects a monogenic cause in early onset nephrolithiasis and nephrocalcinosis

see commentary on page 15

Ankana Daga[1,20], Amar J. Majmundar[1,20], Daniela A. Braun[1], Heon Yung Gee[2], Jennifer A. Lawson[1], Shirlee Shril[1], Tilman Jobst-Schwan[1], Asaf Vivante[1], David Schapiro[1], Weizhen Tan[1], Jillian K. Warejko[1], Eugen Widmeier[1], Caleb P. Nelson[3], Hanan M. Fathy[4], Zoran Gucev[5], Neveen A. Soliman[6,7], Seema Hashmi[8], Jan Halbritter[9], Margarita Halty[10], Jameela A. Kari[11], Sherif El-Desoky[11], Michael A. Ferguson[1], Michael J.G. Somers[1], Avram Z. Traum[1], Deborah R. Stein[1], Ghaleb H. Daouk[1], Nancy M. Rodig[1], Avi Katz[12], Christian Hanna[12], Andrew L. Schwaderer[13], John A. Sayer[14], Ari J. Wassner[15], Shrikant Mane[16,17,18], Richard P. Lifton[16,17,18], Danko Milosevic[19], Velibor Tasic[5], Michelle A. Baum[1] and Friedhelm Hildebrandt[1]



Flow diagram on detection by whole exome sequencing of causative monogenic mutations in 30% nephrolithiasis or nephrocalcinosis or both (NL/NC) genes in 51 families with NL/NC

Daga A. KI.2018

Conclusion

We established WES as an efficient approach toward a molecular genetic diagnosis in individuals with nephrolithiasis/nephrocalcinosis who manifest before age **25** years.

Daga A. KI.2018

Management

Urologic consultation

1. AKI
2. Anuria
3. Sepsis with an obstructive stone
4. Stones > 10 mm
5. Failure of conservative management
6. Presence of anatomic abnormalities that would prevent passage of the stone

Lifestyle Modificaion

- ✓The most important lifestyle modification is to **increase fluid intake** to guarantee diuresis of 2 to 2.5 L/d & a urine SG < 1.010.
- ✓Fluids should be consumed throughout the day & should consist of beverages with a neutral pH.
- ✓The diet should be with normal Ca content (1.0 to 1.2 g/d) & limited Nacl (4 to 5 g/d) & animal pr (0.8 to 1.0 g/kg/d).
- ✓Normal body weight through dietary modification & increased physical activity.

Fontenelle LF. Am Family Phys. 2019

Tips to Reduce Your Sodium Intake

- ✓ Adults should aim to consume **< 2.3 gr/d**
- ✓ One teaspoon of table salt has 2.3 g of sodium
- ✓ Check the %DV for Na on the Nutrition Facts label found on many foods.
- ✓ Low in Na is ≤ 5%, & high in Na is ≥ 20%.

NIH National Institute of Diabetes and Digestive and Kidney Diseases

National Institute of Diabetes and Digestive and Kidney Diseases

Nutrition Facts

8 servings per container

Serving size **2/3 cup (55g)**

Amount per serving

Calories **230**

	% Daily Value*
Total Fat 8g	**10%**
Saturated Fat 1g	**5%**
Trans Fat 0g	
Cholesterol 0mg	**0%**
Sodium 160mg	**7%**
Total Carbohydrate 37g	**13%**
Dietary Fiber 4g	**14%**
Total Sugars 12g	
Includes 10g Added Sugars	**20%**
Protein 3g	
Vitamin D 2mcg	10%
Calcium 260mg	20%
Iron 8mg	45%
Potassium 235mg	6%

Medications

1. K citrate
2. Hydrochlorothiazide
3. Allopurinol
4. Vitamin B_6
5. **…..**

Potassium citrate

- ✓Dose:**10 - 20 mEq bid – tid**
- ✓Titrate dose to achieve urinary citrate 320-640 mg/day & urinary pH 6.0-7.0 (maximum dose 100 mEq/day)
- ✓Administer dose with meals or within 30 minutes after meals or bedtime snack
- ✓Contraindications:
  - Hypersensitivity, hyperkalemia, Addison's disease, anuria, uncontrolled DM, acute dehydration, adrenal insufficiency, renal insufficiency (**GFR <0.7ml/kg/min**),…

Overview of K.Citrate Administration in Different Types of Calculi

Type of calculus	Indication	Urinary pH goal	Dose
Calcium	• Low urinary pH or hypocitraturia • Added to thiazide despite normal urine calcium level on thiazide • Recurrent calculus formers whose metabolic profile is normal or has been normalized (alone or combined with thiazide)	5.5 to 6.5	10 mEq to 20 mEq, 2 to 3 times per day
Uric acid	All	6.0 to 7.0	10 mEq to 20 mEq, 3 times per day
Cystine	All	7.0 to 7.5	15 mEq to 30 mEq, 3 times per day

Shadman A. IJKD. 2017


60 ER Tablets
Alkaneph® 10 mEq
Potassium Citrate ER
Each Tablet Contains:
Potassium Citrate Monohydrate 10 mEq
equivalent to 1.080 g
Raha Pharma. Co. Isfahan-Iran
RAHA Pharma Co.
Isfahan - IRAN


۹۰ قرص
اوروسیترا ۵ میلی اکی والان
پتاسیم سیترات
هر قرص حاوی:
پتاسیم سیترات ۵ میلی اکی والان
سیحان دارو
2020/04/13
2022/04/01
99001

Lit control pH up

بهشاد دارو

کپسول لیت کنترل پی اچ آپ

Lit Control PH Up Capsule

دریافت اپلیکیشن دارویاب | در کدام داروخانه موجود است؟

اجزا فراورده/نام ژنریک : ترکیب گیاهی برای کلیه (جهت مشاهده اطلاعات بیشتر اینجا کلیک کنید)

تولید کننده :بهشاد دارو [ایران]

مارتیندل : داروهای گیاهی

طبقه بندی درمانی : فاقد طبقه بندی فارماکولوژی-درمانی AHFS > گیاهی

Lit control pH balance

Nutrition declaration	Per 2 capsules**	Per 100 g
Energy (kJ/kcal)	9.13 kJ/ 2.19 kcal	660 kJ/ 158 kcal
Fat	0.01 g	0.72 g
Saturated fat	0.01 g	0.70 g
Carbohydrate	0.35 g	25.12 g
Sugars	0.00 g	<0.05 g
Fibre	0,28 g	20.00 g
Protein	0,04 g	2.7 g
Salt	0.00 g	0.20 g
Vitamin A	1000 IU %37.50 NRV***	
Zinc* (as Zinc Gluconate)	2.60 mg %26.00 NRV***	
Magnesium (as Magnesium Oxide)	110 mg %29.60 NRV***	
Phytin	510 mg	
Polyphenols	237.5 mg	

* Contributes to normal acid-base metabolism

Solvestone®

Herbal stone breaker (Complementary treatment)

سولوستون® سنگ شکن گیاهی (کمک درمان)

بسته بندی و شکل دارویی: هر جعبه حاوی ۱۰ ساشه ۱۰ گرمی پودر می‌باشد.

موارد مصرف:

- کمک به انحلال سنگ های کلیه و جلوگیری از تشکیل کریستال های کلسیم اگزالات و اسید اوریکی در کلیه.
- بهبود عفونت مجاری ادراری و کمک به عملکرد بهتر آن.

اجزا و مواد مؤثره:

عصاره گیاه سنگ شکن (استاندارد شده بر مبنای ۵٪ فیلانتوس نیروری)	mg 200	Phyllanthus niruri
عصاره گیاه انگور خرس	mg 200	Arctostaphylos uva-ursi
پودر منیزیم سیترات	mg 2181	Magnesium citrate
پودر پتاسیم سیترات	mg 4561	Potassium citrate

سایر اجزا: فروکتوز، سیتریک اسید، فلیور میوه‌ای، کبوسیل، سوکرالوز.

- ✓**هر بسته پودر** عصاره گیاه سنگ شکن یا فیلانتوس نیروری: 300 mg استاندارد شده بر مبنای ۵ میلی‌گرم پلی‌فنل در هر ساشه
- ✓عصاره گیاه انگور خرس: 300 mg
- ✓ 2181 mg پودر منیزیم سیترات
- ✓ 4561 mg پودر پتاسیم سیترات

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 MARCH 2, 2023 VOL. 388 NO. 9

Hydrochlorothiazide and Prevention of Kidney-Stone Recurrence

Nasser A. Dhayat, M.D., Olivier Bonny, M.D., Ph.D., Beat Roth, M.D., Andreas Christe, M.D., Alexander Ritter, M.D., Nilufar Mohebbi, M.D., Nicolas Faller, M.D., Ph.D., Lisa Pellegrini, M.D., Giulia Bedino, M.D., Reto M. Venzin, M.D., Philipp Grosse, M.D., Carina Hüsler, M.D., Irene Koneth, M.D., Christian Bucher, M.D., Rosaria Del Giorno, M.D., Luca Gabutti, M.D., Michael Mayr, M.D., Urs Odermatt, M.D., Florian Buchkremer, M.D., Thomas Ernandez, M.D., Catherine Stoermann-Chopard, M.D., Daniel Teta, M.D., Bruno Vogt, M.D., Marie Roumet, Ph.D., Luca Tamò, Ph.D., Grazia M. Cereghetti, Ph.D., Sven Trelle, M.D., and Daniel G. Fuster, M.D.

ABSTRACT

Methods

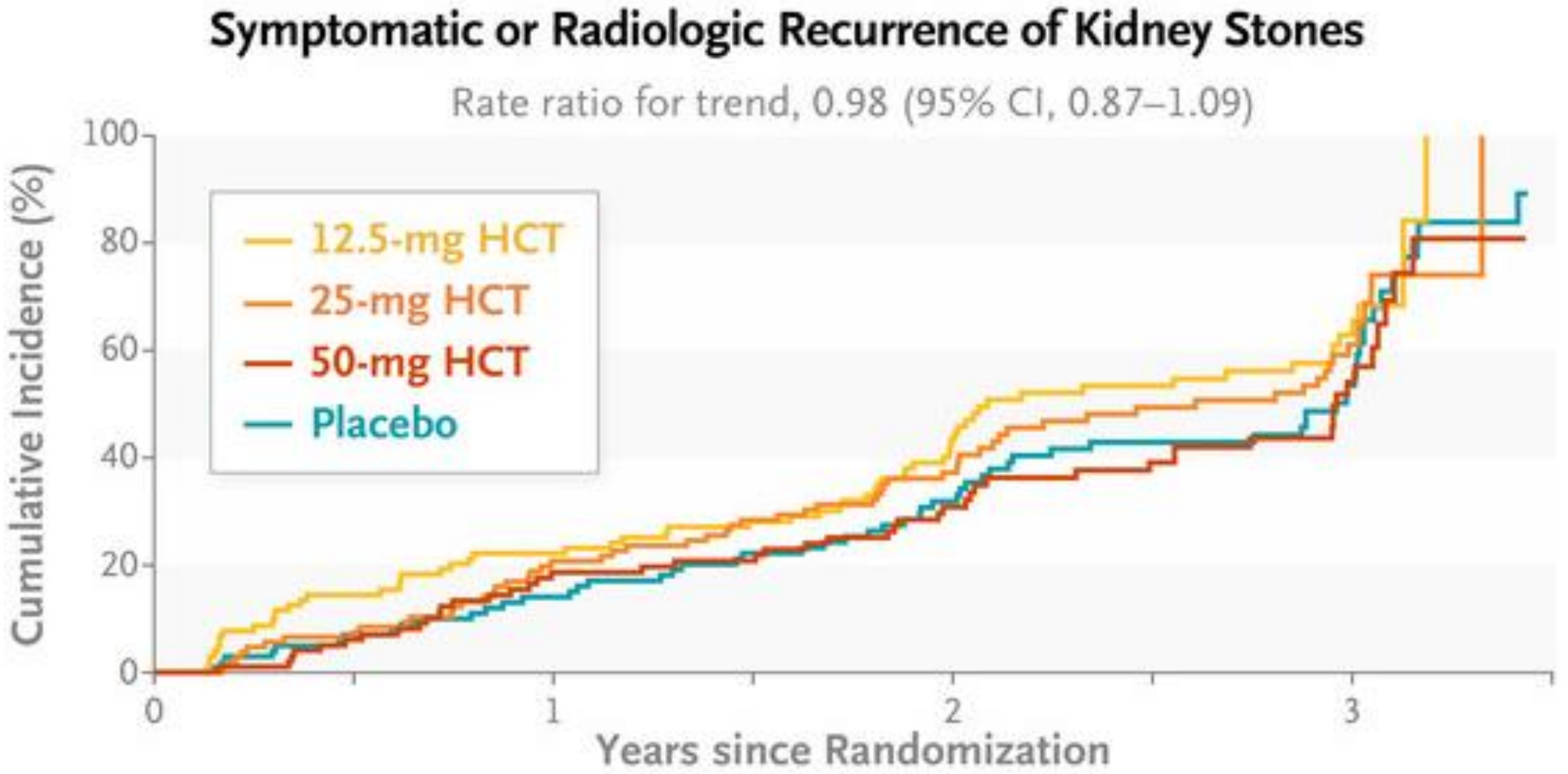
- ✓In this double-blind trial, we randomly assigned patients with recurrent ca containing kidney stones to receive hydrochlorothiazide at a dose of 12.5 mg, 25 mg, or 50 mg once daily or placebo once daily.
- ✓The main objective was to investigate the dose–response effect for the primary end point, a composite of symptomatic or radiologic recurrence of kidney stones.
- ✓Safety was also assessed.

Dhayat NA. NEJM. 2023

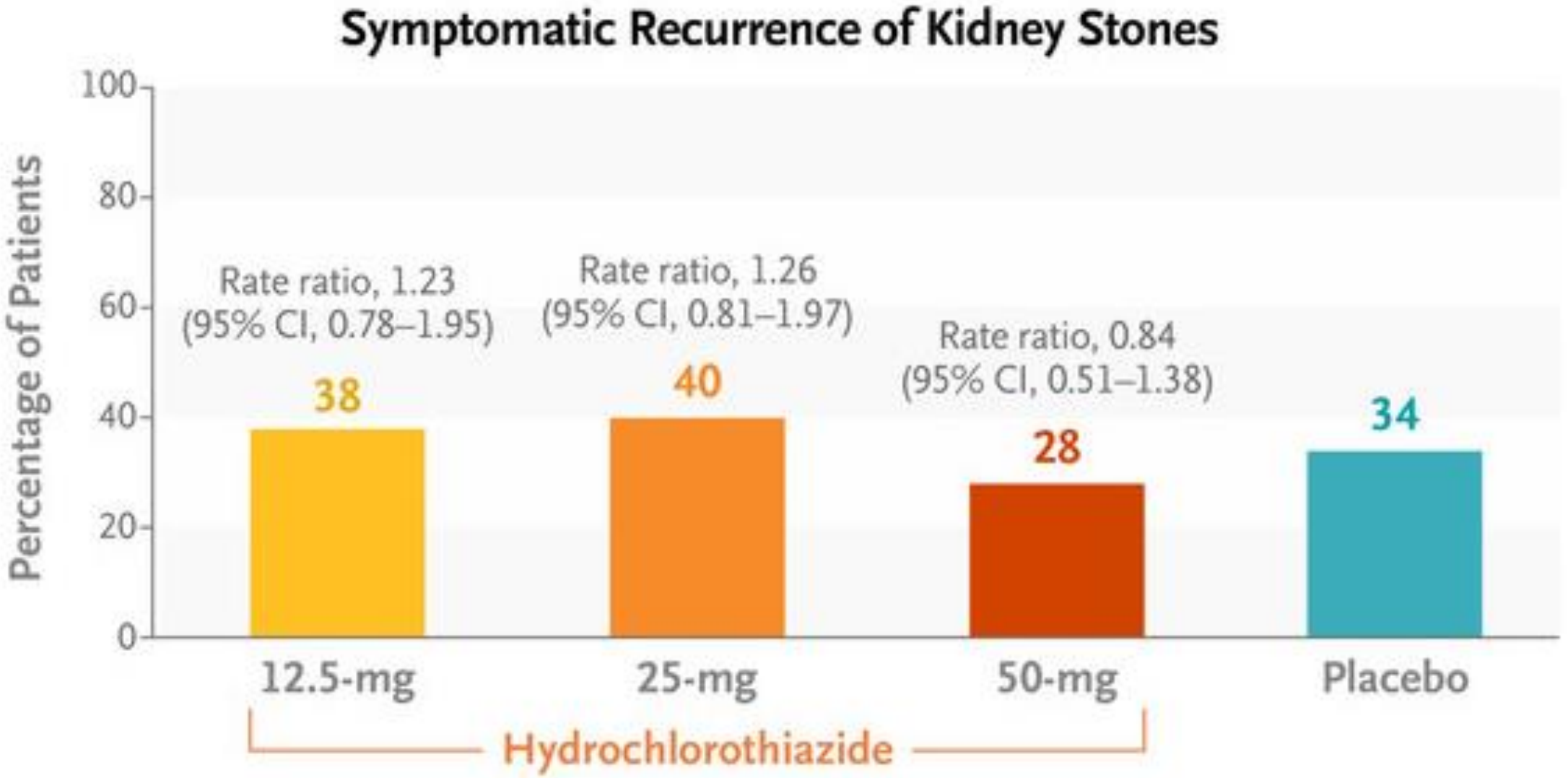
Results

- ✓In all, **416** patients underwent randomization and were followed for a median of **2.9** ys.
- ✓A primary end-point event occurred in:
  - 60 of 102 patients (59%) in the placebo group
  - 62 of 105 patients (59%) in the 12.5-mg hydrochlorothiazide group
  - 61 of 108 patients (56%) in the 25-mg hyd. group
  - 49 of 101 patients (49%) in the 50-mg hyd. group.
- ✓There was no relation between the hydrochlorothiazide dose & the occurrence of a primary end-point event (P=0.66).

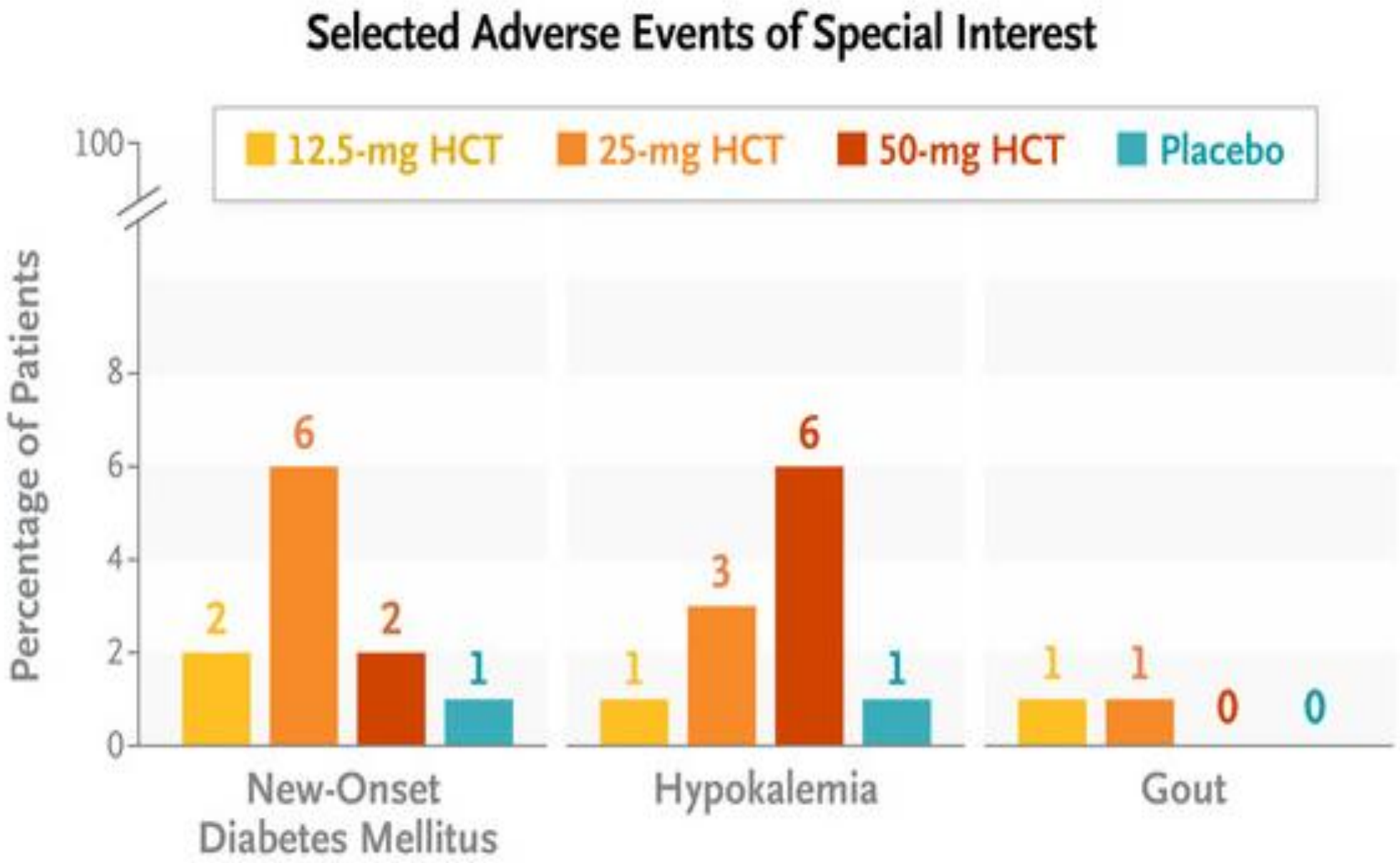
Dhayat NA. NEJM. 2023



Dhayat NA. NEJM. 2023



Dhayat NA. NEJM. 2023



Dhayat NA. NEJM. 2023

Conclusion

- ✓ Among patients with recurrent kidney stones, the incidence of recurrence **did not appear** to differ substantially among patients receiving hydrochlorothiazide once daily at a dose of 12.5 mg, 25 mg, or 50 mg or placebo once daily.

Dhayat NA. NEJM. 2023

Leave NOSTONE unturned: are thiazides useless in preventing kidney stone recurrence?

François Brazier[1,2], Nicolas Cornière[1,2] and Dominique Eladari[1,2]

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Kidney International (2023) **104,** 640–643; https://doi.org/10.1016/j.kint.2023.06.030

KEYWORDS: diuretics; kidney stones; nephrolithiasis; urolithiasis

Nephrolithiasis, or kidney stone disease, is the second most frequent kidney disease after hypertension, affecting up to approximately 20% of men and approximately 10% of women in industrialized countries. The prevalence of nephrolithiasis has consistently increased over the last 50 years.[1] Nephrolithiasis represents a considerable burden for health care systems, with the total health care expenditure for kidney stones exceeding US $10 billion in 2006 in the United States alone.[2]

Kidney stones are commonly recurrent, with up to 15%, 30%, and 50% of individuals experiencing a second episode within 3, 5, or 10 years of their initial presentation,

Brazier F. KI. 2023

Are thiazides useless in preventing kidney stone recurrence?

1. At randomization, half of the participants in NOSTONE exhibited a urine Na output 168 mmol/24 hs (equivalent to daily NaCl intake of approximately 9 g/24 hs), indicating very poor dietary control.
2. Poor dietary control persisted throughout F/U with mean urine output remaining < 2.15 liters/24 hs & mean urine Na excretion >181 mmol/24 hs.
3. Urine oxalate excretion was also relatively high during the F/U period.

Brazier F. KI. 2023

Are thiazides useless in preventing kidney stone recurrence?

✓Indeed, thiazide diuretics are generally recommended as second-line therapy after dietary control which includes:

- Increased water intake of > 2.5 liters/d
- The reduction of salt

Brazier F. KI. 2023

Conclusion

✓The NOSTONE trial provides:

- Hydrochlorothiazide is ineffective at reducing the recurrence of symptomatic kidney stones at 3 ys in the absence of dietary control including abundant water intake & reduced dietary Na.
- However, additional studies are required to conclude that hydrochlorothiazide is a useless therapy for kidney stone recurrence

Brazier F. KI. 2023

Clinical Follow-up

- ✓ **Annual** clinical visit

1. Medical history
2. PE
3. Laboratory examination for full serum chemistries & urine profiles
4. Ultrasonography

Sakhaee K. J Clin Endoc Metab. 2012

Acta Medica Iranica

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ORIGINAL ARTICLE

An Epidemiological Survey on Kidney Stones and Related Risk Factors in the Iranian Community

Shahrzad Shahidi , Shahaboddin Dolatkhah ✉ , Mojgan Mortazavi , Abdolamir Atapour , Farshad Aghaaliakbari , Rokhsareh Meamar , Mohammadali Badri , Diana Taheri

Abstract- Increasing number of patients with kidney stones is a major worldwide concern that needs more attention for recognizing the disease in order to set up suitable prevention systems. In this study, we aimed to assess the prevalence and related risk factors of kidney stones in our local area (Isfahan, Iran). In 2011, we celebrated World Kidney Day (WKD) with several training programs for informing people about kidney diseases. A questionnaire containing demographic data, past medical history, and familial and self-history of kidney disease was fulfilled by each individual who participated in WKD. Blood pressure and body mass index (BMI) were also measured using standard methods. Statistical analysis with SPSS-20 software was done. 556 participants with a mean age of 44.69±15.32 were included in the study, of which 107 cases (19.2%) with a mean age of 50.24±12.33 had a kidney stone, and 449 cases (80.8%) with a mean age of 44.69±15.32 had no

Variables		History of kidney stone		Total	*P*
		Yes	No		
Daily work	High activity	16(21%)	60(13.4%)	76(13.7%)	0.91
	Low activity	91(85%)	389(86.6%)	480(86.3%)	
Place of living	Isfahan (Urban area)	64(59.8%)	271(60.3%)	335(60.3%)	0.92
	Rural area near Isfahan	37(34.6%)	157(35%)	194(34.9%)	
	Other cities	6(5.6%)	21(4.7%)	27(4.8%)	
Diabetes Mellitus	Present	23(21.5%)	64(14.2%)	87(15.6%)	0.64
	Absent	84(78.5%)	385(85.8%)	469(84.4%)	
Cardiovascular diseases	Present	13(12.1%)	26(5.8%)	39(7%)	0.02
	absent	94(87.9%)	423(94.2%)	517(93%)	
Hypertension	Present	36(33.6%)	86(19.1%)	122(21.9%)	0.001
	Absent	71(66.4%)	363(80.9%)	434(78.1%)	
Vitamin C consumption	Yes	2 (1.9%)	9(2.1%)	11(1.9%)	0.21
	No	105 (98.1%)	440(97.9%)	545(98.1%)	
Vitamin D consumption	Yes	2(1.9%)	11(2.5%)	13(2.3%)	0.13
	no	105(98.1%)	438(97.5%)	543(97.7%)	
Familial history of kidney stone	No	57(53.3%)	343(76.4%)	400(71.9%)	<0.001
	First degree	46(43%)	93(20.7%)	139(25%)	
	Second degree	4(3.7%)	13(2.9%)	17(3.1%)	
Total		107(19.2%)	449(80.8%)	556(100%)	-

Probable risk factors of kidney stone

KIDNEY DISEASES IJKD

Metabolic Disorders in Patients with Nephrolithiasis in Iran

Shahrzad Shahidi,[1] Golsa Ghasemi[2]

[1]Isfahan Kidney Diseases Research Center, Internal Medicine Department, Khorshid Hospital, Isfahan University of Medical Sciences, Isfahan, Iran
[2]Isfahan Kidney Diseases Research Center, Isfahan University of Medical Sciences, Isfahan, Iran

Keywords. Nephrolithiasis, Urolithiasis, Kidney Stone, Renal Calculi, Metabolic Disease, Etiology, Iran

Nephrolithiasis is a common disease entity around the world, with an increasing prevalence and incidence. There is no consolidated information available on the cause of kidney stones in Iranian patients. As a result, we decided to review the etiology of kidney stones in Iran. PubMed, Scopus, Web of Science, Google scholar, and Scientific Information Database (SID) were searched with the following keywords "Nephrolithiasis", "Renal stone", "Kidney stone", "Urolithiasis", "Etiology", "Metabolic abnormalities", and "Iran". There was no time period limit for selection of the papers. The inclusion criteria included any paper on evaluation of urine biochemistry regarding stone formation in Iranian adult patients (with or without children) with nephrolithiasis. We found 217 articles, of which 9 were eventually included. In conclusion, 1896 patients with nephrolithiasis from 6 provinces and 7 cities of Iran with different climates from 2000 to 2019 were evaluated collectively. The results showed that in contrast to western countries, hypercalciuria was not the most common biochemical disorder of patients with nephrolithiasis (18.2% vs. 30 to 60%). Low urine volume (49.6%) and hypocitraturia (27%) were the most frequent urine abnormalities in our country.

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DOI: 10.52547/ijkd.7055

Review

Author	Year	Design	Population	Place	Laboratory Tests	First Author Specialty	Most Common Abnormality
Mahmoudi H.[8]	2000-2001	Cross-sectional	79	Kashan	Blood: [5]Cr, [9]Na, [7]K, Ca, uric acid 24-hour urine: Cr, Ca, uric acid	Urologist	1. Low urine volume 2. Hypercalciuria 3. Hyperuricosuria
Hosseini MM, et al.[9]	2010	Cross-sectional	376	Shiraz	Blood: [3]CBC, Bun, Cr, Na, K, [2]Ca, [10]Ph, uric acid U/A, U/C 24-hour urine: volume, Ca, Ph, [8]Mg, oxalate, citrate, uric acid	Urologist	1. Low urine volume 2. Hypercalciuria 3. Hyperuricosuria
Nouri-Majalan N, et al.[10]	2010	Cross-sectional	150	Yazd	Blood: Cr, K, Ca, Ph, Uric acid 24-hour urine: volume, pH, Cr, Na, K, Ca, uric acid	Nephrologist	1. Hypercalciuria 2. Hyperuricemia
Goodarzi MT, et al.[11]	2012	Case-control	28	Hamadan	U/A 24-hour urine: Cr, citrate, uric acid	-	Hypocitraturia
Emami-Naini A, et al.[12]	2012	Cross-sectional	437	Isfahan	Blood: [1]BUN, Cr, Na, K, Ca, Ph, albumin, uric acid 24-hour urine: volume, Cr, Na, Ca, citrate, oxalate, uric acid, cystine	Nephrologist	1. Hypocitraturia 2. Hyperoxaluria
Ghorbani A, et al.[13]	2012	Case-control	140	Ahwaz	Blood: [6]FBS, Cr, uric acid, [4]Chol, bicarbonate, Ph, [11]PTH [13]U/A: [12]SG, pH [14]U/C 24-hour urine: Na, Ca, Ph, Mg, citrate, oxalate, uric acid, cystine	Nephrologist	1. Hypocitraturia 2. Hyperuricosuria 3. Hyperuricemia
Hadian B, et al.[14]	2018	Cross-sectional	232	Lorestan	Blood: Ca, Ph, uric acid 24-hour urine: Ca, citrate, oxalate, uric acid	Nephrologist	Hyperoxaluria
Pakfetrat M, et al.[15]	2019	Cross-sectional	376	Shiraz	Blood: BUN, Cr, Ca, albumin, uric acid, PTH 24-hour urine: volume, Cr, Na, Ca, Ph, citrate, oxalate, uric acid	Nephrologist	1. Low urine volume 2. Hypercalciuria 3. Hyperoxaluria
Mohammadi Sichani M, et al.[16]	2019	Cross-sectional	78	Isfahan	Blood: BUN, Cr, Ca, Ph, Mg, uric acid, PTH 24-hour urine: volume, Cr, Na, Ca, Ph, citrate, oxalate, uric acid, cystine	Urologist	1. Cystinuria 2. Hyperoxaluria 3. Hypernatriuria

Characteristics of the Included Studies

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Summary of Biochemical Disorders in the Included Studies

	Low Urine Volume	Hypercalcuria	Hyperuricosuria	Hypocitraturia	Hyperoxaluria	Hypernatriuria	Hyperphosphaturia	Cystinuria
Mahmoudi H. et al (n = 79)	62	22	9	Not available	Not available	Not available	Not available	Not available
Hosseini MM, et al. (n = 376)	219	67	57	7	9	Not available	Not available	Not available
Nouri-Majalan N, et al. (n = 150)	Not available	36	21	Not available	Not available	Not available	Not available	Not available
Goodarzi MT, et al. (n = 28)	Not available	Not available	Not available	12	Not available	Not available	Not available	Not available
Emami-Naini A, et al. (n = 437)	71	40	58	177	126	139	Not available	8
Ghorbani A, et al. (n = 140)	Not available	Not available	30	83	Not available	Not available	Not available	Not available
Hadian B, et al. (n = 232)	Not available	55	33	58	93	Not available	Not available	Not available
Pakfetrat M, et al. (n = 376)	277	90	17	69	73	57	12	Not available
Mohammadi Sichani M, et al. (n = 78)	Not available	5	10	10	13	13	0	15
Total (%)	629 (49.6)	315 (18.2)	235 (12.6)	416 (27)	314 (20.9)	209 (23.4)	12 (3.2)	23 (4.5)

Shahidi Sh. IJKD. 2022

AKDH

Nephrolithiasis

Megan L. Prochaska and Anna L. Zisman

Kidney stone prevalence is rapidly increasing worldwide, and decreasing stone growth and recurrence is critical to reducing morbidity. Preventative approaches vary with kidney stone type, so knowledge of stone composition and a thorough history and metabolic evaluation are necessary to individualize therapy. The cases presented herein highlight treatment strategies for the most common stone types seen in clinical practice with practical pearls for the nephrologist.

Kidney stones are common and increasing in prevalence.[1] Lifestyle, diet, medical history, and family history all contribute to an individual's kidney stone risk. Patients who form kidney stones not only experience acute pain and hematuria but are also at higher risk for conditions such as bone fracture,[2] chronic kidney disease,[3] cardiovascular disease,[4] and diabetes.[5] However, kidney stones are largely preventable, and all patients with recurrent stones should have a full evaluation including medical and dietary history with serum and urine testing.[6] The cornerstone of prevention of all stone types is decreasing urine supersaturation (SS)—the ratio of the solute concentration to its solubility.[7]

sodium diet.[8] A low-sodium diet reduces calcium kidney stone risk by increasing calcium reabsorption in the proximal tubule and thus lowering urine calcium[9,10] (Fig 1). This patient's high sodium intake is likely contributing to her elevated urine calcium levels. Recommending a low-sodium diet is the first step to reduce urine calcium and subsequent kidney stone risk. After the patient has made this change, a follow-up 24-hour urine collection will help assess the patient's ability to achieve a low-sodium diet. Dietitian support is often helpful in guiding patients to follow a low-sodium diet.

No therapy would not be the recommended strategy for this patient. Her risk of future stone growth and new stone

Case 1

- ✓A 55-year-old female with no prior medical history except recurrent kidney stones, 5 over the lifetime. Last stone composition was 90% CaOx & 10% CaP.
- ✓Her BP is 110/75. Prior to meeting you, she completed 2 24-hour urine collections.

Day	Volume (L)	Calcium (mg)	Oxalate (mg)	Citrate (mg)	Urine pH	Sodium (mmol)	Creatinine (mg)	CaOx SS	CaP SS
1	2.50	341	39	550	5.8	270	1505	7.9	1.3
2	2.75	355	36	470	5.9	255	1495	7.7	1.4

Megan L. Adv in Kidney Disease and Health 2024

Case 1

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2	2.75	355	36	470	5.9	255	1495	7.7	1.4

What is the best next step in the management of this patient?

A. No therapy or changes in diet

B. Recommend low calcium diet

C. Recommend low sodium diet

D. Recommend starting hydrochlorothiazide 12.5 mg daily

E. Increase fluid intake

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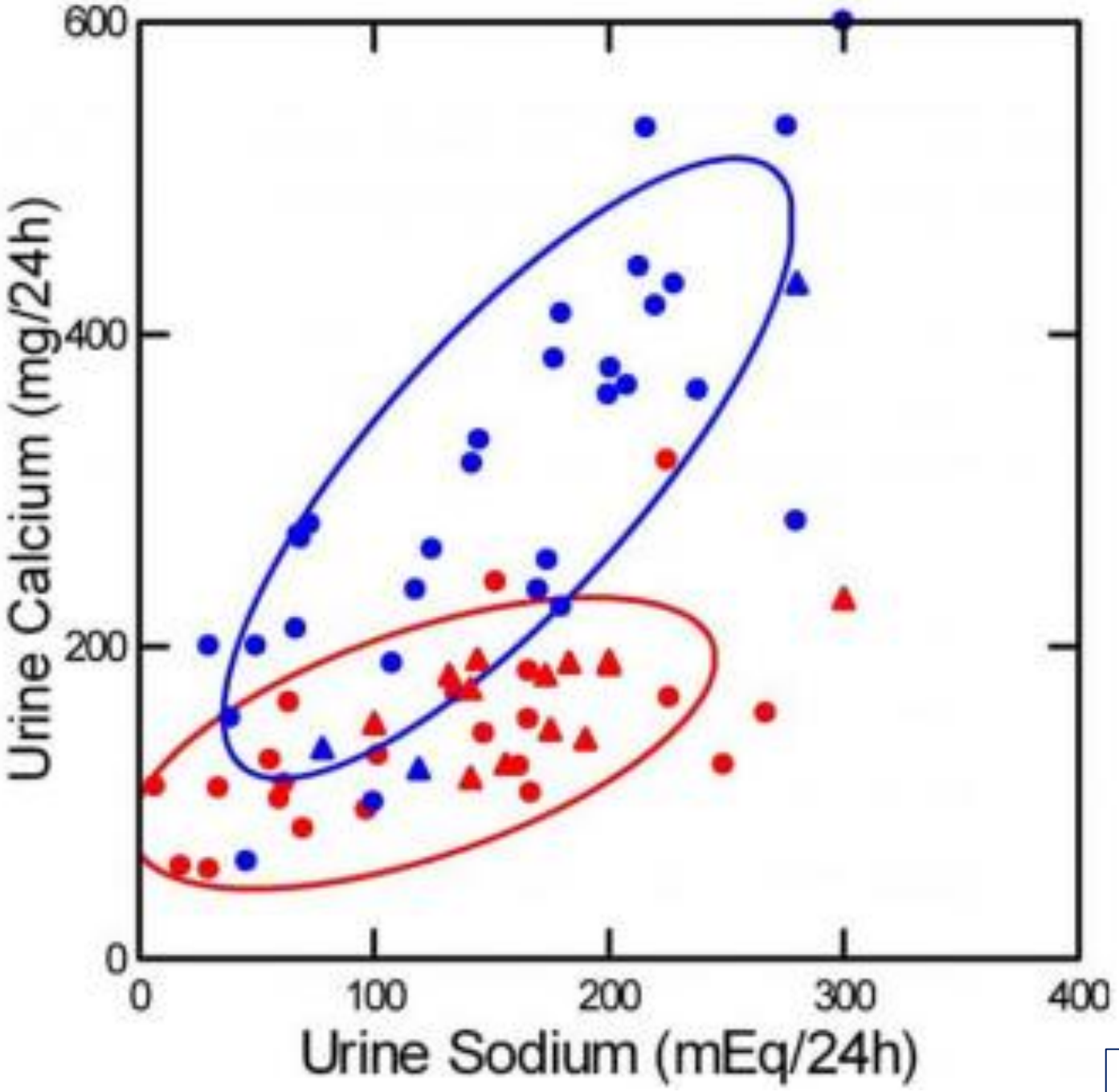

Relationship of urine Ca & urine Na by stone former status.

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Case 2

- ✓A 48-year-old female with a past medical history notable for HTN & migraine headaches, both of which have been well controlled.
- ✓Her medications: include hydrochlorothiazide 12.5 mg daily & topiramate 50 mg twice daily. Over the last 5 years, she has had 3 episodes of renal colic, one requiring surgical intervention. Her stone composition was 100% CaP.

Day	Volume (L)	Calcium (mg)	Oxalate (mg)	Citrate (mg)	Urine pH	Sodium (mmol)	Creatinine (mg)	CaOx SS	CaP SS
1	2.60	311	22	220	6.7	250	1407	5.5	1.8
2	2.36	298	29	223	6.9	255	1389	4.9	2.1

Case 2

Day	Volume (L)	Calcium (mg)	Oxalate (mg)	Citrate (mg)	Urine pH	Sodium (mmol)	Creatinine (mg)	CaOx SS	CaP SS
1	2.60	311	22	220	6.7	250	1407	5.5	1.8
2	2.36	298	29	223	6.9	255	1389	4.9	2.1

What is the next best step in management?

A. Start potassium citrate 20 meq 3 times daily.

B. Increase fluid intake to facilitate urine volume of at least 3L/day.

C. Increase hydrochlorothiazide to 25 mg/d.

D. Decrease dietary sodium intake to ,2300 mg/d.

E. Confer with neurology regarding alternate therapeutic options so topiramate can be discontinued.

CAIs

- ✓CAIs such as acetazolamide, topiramate, & zonisamide are commonly used in the management of obesity, migraines, intracranial hypertension, altitude sickness, & epilepsy & are associated with increased risk of CaP stones, with up to **10%** of long-term users affected.
- ✓**Ophthalmic** use of CAIs for management of glaucoma has also been implicated in CaP stone formation.

Take-Home Message

1. Nephrolithiasis is a common problem that is increasing in prevalence & is associated with significant morbidity.
2. Although urinary supersaturation is a necessary substrate for stone formation, it is not sufficient.
3. Local & systemic factors interact with supersaturated solutes to cause stones.
4. These systemic factors can have important consequences beyond the urologic system, including adverse effects on bone & cardiovascular health.

Take-Home Message

5. Kidney stones are preventable.

6. A complete workup is crucial to identifying an individual patient's stone risk & developing a tailored prevention strategy, which can include lifestyle & dietary changes as well as medications.

7. Prevention of nephrolithiasis is fundamental to reducing the acute & chronic morbidity associated with kidney stones.

Megan L. Adv in Kidney Disease and Health 2024

05 PREVENTION