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Stone composition among first-time symptomatic kidney stone formers in the community

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Abstract

Objective—To determine the variation in kidney stone composition and its relationship to risk factors and recurrence among first-time stone formers in the general population.

Patients and Methods—Medical records were manually reviewed and validated for symptomatic kidney stone episodes among Olmsted County, Minnesota residents from January 1, 1984 to December 31, 2012. Clinical and laboratory characteristics and the risk of symptomatic recurrence were compared between stone compositions.

Results—There were 2961 validated first-time symptomatic kidney stone formers. Stone composition analysis was obtained in 1508 (51%) at the first episode. Stone formers were divided into the following mutually exclusive groups: any brushite (0.9%), any struvite (0.9%), any uric acid (4.8%), majority calcium oxalate (76%) or majority hydroxyapatite (18%). Stone composition varied with clinical characteristics. A multivariable model had a 69% probability of correctly estimating stone composition, but assuming calcium oxalate monohydrate stone was correct 65% of the time. Symptomatic recurrence at 10 years was approximately 50% for brushite, struvite, and uric acid, but approximately 30% for calcium oxalate and hydroxyapatite stones ($P<.001$). Recurrence was similar across different proportions of calcium oxalate and hydroxyapatite (*P-trend*=.10). However, among calcium oxalate stones, 10-year recurrence rate ranged from 38% for 100% calcium oxalate dihydrate to 26% for 100% calcium oxalate monohydrate (*P-trend*=.007).

Conclusion—Calcium stones are more common (94% of stone formers) than has been previously reported. While clinical and laboratory factors associate with the stone composition,

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they are of limited utility for estimating stone composition. Rarer stone compositions are more likely to recur.

Keywords

kidney calculi; chemical composition; recurrence; epidemiology

Introduction

Symptomatic kidney stones are prevalent in 7.2 to 7.7% of the US adult population[1,2] and are often classified by stone composition.[3–6] Clinical practice guidelines disagree with urological associations recommending,[7,8] but the American College of Physicians not recommending stone compositional analysis in all stone formers.[9] Prior studies have classified stone composition in the following overlapping groups: any calcium oxalate monohydrate (COM) 40–60%, any calcium oxalate dihydrate (COD) 40–60%, any hydroxyapatite 20–60%, any brushite 2–4%, any uric acid 5–10%, any struvite 5–15%, and any cystine 1–2.5%.[10–12] The common calcium stone (calcium oxalate and/or hydroxyapatite) is thought to occur in 75–85% of stone formers. However, most prior studies assessed stone composition in referral centers of prevalent stone formers that may be enriched for stone compositions that are more likely to recur or require surgery. Stone composition characteristics of first-time (incident) stone formers in the general population are unknown.

In practice, stone composition is often not available as the stone is not collected. Clinical and laboratory characteristics of the patient are often used to estimate composition.[3] However, the accuracy of estimating stone composition is largely unknown. The stability of stone composition between episodes and the extent to which stone composition predicts recurrence in the community is also unclear. To address these important questions, we carefully analyzed a large population-based cohort of first-time symptomatic stone formers. Our goals were to 1) characterize stone composition of first-time stone formers in detail, including composition stability with recurrence; 2) determine whether stone composition can be estimated when not available; and 3) determine whether risk of recurrence differs by stone composition.

Methods

Study Sample

After institutional review board approval, first-time (incident) symptomatic kidney stone formers in Olmsted County, MN from January 1, 1984 to December 31, 2012 were identified by diagnostic codes and then validated and detailed by chart review using the Rochester Epidemiology Project[13] as described in the Supplemental Methods.

Stone composition

All stone composition reports in these stone formers were identified and reviewed. Stone composition analysis was not routine for each episode, especially after first obtained. Thus, stone composition was assessed at the first episode and compared between the first, second,

and third available composition reports (regardless of episode number). Stone compositions were determined by infrared spectroscopy (Supplemental Methods). Stone formers were divided into the following mutually exclusive groups: cystine (if any), brushite (if any), struvite (if any), uric acid (if any), and calcium oxalate (if majority) or hydroxyapatite (if majority) (Figure 1). Majority calcium oxalate stones were further subclassified as COM (if majority) or COD (if majority). Other compositions (e.g. urate and drugs) were too rare for meaningful analysis and excluded.

Statistical Analysis

A trend in the ratio of stone compositions (common calcium versus other less common compositions) between the first, second, and third available composition report was assessed using a logistic generalized estimating equation model. Clinical and laboratory characteristics were compared across stone composition at the first episode using Kruskal-Wallis and Wilcoxon tests for continuous variables and Chi-square tests for nominal variables. A model to estimate stone composition from clinical and laboratory characteristics was developed using multinomial logistic regression. The highest probability stone composition as determined by the model was treated as the estimated composition for comparison with the actual composition.

The risk of symptomatic recurrence by stone composition at the first episode was estimated using survival methods (log-rank test, Cox model) with censoring at symptomatic recurrence or date of last known residency in the county. The proportionality assumption was tested and confirmed in all models. For calcium oxalate and hydroxyapatite subtypes, linear trend in risk of recurrence was assessed by a Cox model with coding as follows: (1=100% hydroxyapatite, 2=mixed but ≥50% hydroxyapatite, 3=mixed but >50% calcium oxalate, 4=100% calcium oxalate). For struvite and brushite compositions, observed incidence of recurrence was compared to estimated incidence based upon the recurrence of kidney stone (ROKS) nomogram.[14] For calcium oxalate subtypes, linear trend in risk of recurrence was assessed by a Cox model with coding as follows: (1=100% COM, 2=mixed but >50% COM, 3=mixed but ≥50% COD, 4=100% COD). Statistical analyses were performed using the SAS software, version 9.3 (SAS Institute, Cary, NC; www.sas.com).

Results

There were 6380 coded stone formers between January 1984 and December 2012, of which, 2961 were validated as first-time symptomatic kidney stone formers. Of these, only 22 (0.7%) were attributed to another disease or disorder (10 primary hyperparathyroidism; 3 intestinal disease causing enteric hyperoxaluria; 4 ileostomy, colostomy, or gastric bypass; 4 renal tubular acidosis; and 1 medullary sponge kidney). A total of 1807/2961 (61%) had at least one stone composition with 1508/2961 (51%) occurring within 3 months of the first stone episode. We further excluded those with no stone material identified on composition analysis (n=13), leaving 1495 for further analysis. Due to small sample size, ammonium urate (n=1), sodium urate (n=1), drug stones (n=3), and cystine stones (n=2) were also excluded from most analyses (n=1488).

The stone composition distribution at the first episode is presented in Figure 1. At the first episode, 94% (1391/1488) of stones were common calcium stones (76% (1127/1488) calcium oxalate and 18% (264/1488) hydroxyapatite), 4.8% (71/1488) were uric acid, 0.9% (13/1488) were brushite, and 0.9% (13/1488) were struvite. Pure (100%) stone compositions were present in 71% (796/1127) of calcium oxalate, 31% (82/264) of hydroxyapatite, 39% of brushite (5/13), 0% of Struvite (0/13), and 68% (48/71) of uric acid stones. Among calcium oxalate stone formers, 85% (954/1127) were majority COM and 15% (173/1127) were majority COD. The comparison of stone composition distribution at the first episode, the first available composition, the second available composition, and the third available composition is presented in Figure 2 (cystine stones included). Calcium oxalate decreased, whereas cystine, brushite, struvite, and uric acid increased with subsequent compositions. The likelihood of uncommon stone compositions (uric, acid, brushite, and struvite) to common calcium stone compositions (calcium oxalate and/or hydroxyapatite) increased with each subsequent composition analysis (OR=1.39, *P-trend*=.02)

Among the 842 recurrent stone formers (at least 2 episodes), 672/842 (80%) had at least one stone composition analysis. Among the 343/842 (41%) recurrent stone formers with both a 1st and 2nd stone composition, stone composition was most stable for calcium oxalate (87% (208/240) no change), followed by uric acid (72% (18/25) no change), and hydroxyapatite (60% (41/68) no change); overall 79% (271/343) had no change in composition and 21% (72/343) had a change in composition (Table 1). Among the common calcium stones, the proportion of hydroxyapatite (versus calcium oxalate) in a stone decreased between the first and second composition (25% vs 20% hydroxyapatite, $P<.001$), particularly in stones with a high proportion of hydroxyapatite (Supplemental Figure 1).

Table 2 compares stone composition with clinical characteristics, while Table 3 compares stone composition with blood and urine laboratory characteristics. Uric acid stones were associated with older age, male gender, white race, higher body mass index (BMI), hypertension, diabetes, gout, gross hematuria, higher serum uric acid, lower serum bicarbonate, lower urine pH, and higher urine uric acid and were less likely to associate with a family history of stones or require surgery. Struvite stones were associated with older age, female gender, hypertension, gross hematuria, urinary tract infection, fever, and lower serum phosphorus. Struvite stone formers were also more likely to have multiple stones on imaging, staghorn stones, and require surgery; but were unlikely to have stones located in the ureterovesical junction. Brushite stones were more likely to be located at the ureterovesical junction and less likely to present with gross hematuria. Hydroxyapatite stones were associated with younger age, female gender, family history of stones, more stones on imaging, higher urine pH, lower urine oxalate, and were less likely to associate with diabetes or hypertension.

Calcium oxalate stones were associated with male gender, absence of urinary tract infection or fever, family history of stones, and higher urine oxalate. Characteristics of the subset with majority COD rather than majority COM stones were younger age, lower BMI, family history of stones, gross hematuria, lower urinary tract symptoms, higher serum calcium, higher urine pH, higher urine calcium, and they were less likely to have diabetes and hypertension. Patients with unknown stone compositions had smaller stones, were more

likely to have a stone on imaging that was located in the ureterovesical junction, and were less likely to have a family history of stones or require surgery. Overall, only 1.6% (24/1488) received stone prevention medications at the first stone episode. There was documented recommendations for increased water intake in 87% (1287/1488) and diet alterations in 29% (431/1488), but these treatments did not vary by stone composition (p=.10 for both).

A multivariable multinomial regression model was developed to estimate the four most common stone compositions: uric acid, hydroxyapatite, COM, or COD at the first episode. Struvite and brushite were too rare to include in the model. Included predictors were age, gender, family history of stones, loose stools, body mass index, diabetes, hypertension, gout, obstructing stone in renal pelvis, serum calcium, serum phosphorus, serum uric acid, urine calcium, urine oxalate, urine pH, and microhematuria. Only the 24% (353/1462) with complete data were included in the model. Age, gender, body mass index, diabetes, obstructing stone in renal pelvis, serum phosphorus, and urine calcium were statistically significant in the multivariable model ($p<0.05$ for all). However, the ability of the model to improve discrimination of composition was limited. Assuming a stone was COM was correct 65% of the time, whereas using the model to estimate composition was correct 69% of the time.

The risk of stone recurrence varied by the major composition groups (Figure 3A, $P<.001$). At 10 years, the risk of symptomatic recurrence was higher for uric acid (53%), struvite (49%), and brushite (47%) compared to hydroxyapatite (31%) and calcium oxalate (29%) stones ($P<.001$). Using the ROKS nomogram to account for other clinical and radiographic characteristics predictive recurrence besides composition,[14] the actual risk of recurrence in brushite and struvite stone formers was more consistent with the estimated risk of recurrence assuming a stone composition of uric acid rather than common calcium (not uric acid) (Supplemental Figure 2). For common calcium stones, the ratio of hydroxyapatite to calcium oxalate category was not significantly associated with recurrence (Figure 3B, *P-trend* = .10), even with modeling the ratio as continuous (p=0.53). Graphically there was an increased risk of early recurrence for pure hydroxyapatite stones. Among calcium oxalate stones, a higher fraction of COD than COM associated with higher risk of recurrence (Figure 3C, *P-trend*=.007). Symptomatic recurrence was not significantly higher for those with unknown vs known first stone composition (Figure 3D, $P=.06$), though graphically, the risk appeared to be higher in those with unknown compositions after 15 years.

Discussion

Referral-based studies of prevalent stone formers have commonly reported 75–85% of all stones are common calcium stones.[10–12,15] However, we found that first-time stone formers in the community were even more likely to have a common calcium stone (94% overall). Uric acid accounted for 4.8% of first-time stone formers, while brushite and struvite compositions were rare (0.9%) and cystine was very rare (0.1%). Among common calcium stones, calcium oxalate (76% overall) was a very common composition. Consistent with this finding, one prior report of first-time stone formers in the community identified 78% of

women and 86% of men as having calcium oxalate stone compositions, but other compositions were not reported.[16]

We found that stone compositions were less likely to change between episodes for the common compositions, particularly calcium oxalate. Overall, 21% had a different composition between the first and second episode, findings that are similar to another study.[17] A transition from rare to common composition was more likely than a transition from a common to rare composition consistent with regression to the mean. In other words, regardless of the first stone composition there is propensity toward more common compositions with the next stone.

Common calcium stones were more likely to associate with a family history of stones, suggesting a stronger genetic component to formation of these stones. Consistent with prior studies, calcium oxalate stones are more common in men.[15,18,19] We also found that higher urine oxalate and family history of stones associated with calcium oxalate stones. Prior investigations have shown that COD stones are relatively more common among younger patients with higher urine pH and urine calcium levels compared to COM.[20] While confirming these findings, we have further found that COD is associated with higher serum calcium than COM. The COD subgroup also experienced more gross hematuria and lower urinary tract symptoms. This is consistent with urothelium injury from the sharp edges of bipyramidal crystals in COD stones compared to the smooth or mulberry shaped surfaces of COM stones.[21,22] First-time uric acid stone formers associated with many of the same characteristics reported in referral-based prevalent stone former studies including lower urine pH,[3,23] higher serum uric acid,[24] higher BMI,[25] older age,[15,26] diabetes,[3,27] gout,[28] and hypertension.[29] We also confirm that in first-time stone formers, hydroxyapatite stones associated with female gender, younger age, and higher urine pH.[15,19,30,31]

While clinical and laboratory characteristics varied with stone composition, there was also considerable overlap. Estimating stone composition (COM, COD, hydroxyapatite, or uric acid) from these characteristics had a 69% probability of being accurate compared to assuming a COM stone, which had 65% probability of being accurate. This model did not include struvite, brushite, or cystine stones because they were too rare among first-time stone formers. Notably, most of the first-time stone formers lack key laboratory tests (particularly urine chemistries) needed to even attempt to estimate stone composition. Since 94% of first-time stone formers have common calcium stones, prevention strategies can assume a common calcium stone when composition is not available.

When available, stone composition helps with estimating risk of recurrence after the first stone. The natural history of recurrence was feasible in this study because few received stone prevention medications. Uric acid, struvite, and brushite stone formers were more likely to have symptomatic recurrence (approximately 50% at 10 years) than common calcium stone formers (approximately 30% at 10 years). Thus, the ROKS nomogram[14] can include brushite and struvite as being equivalent to uric acid as high-risk compositions for predicting symptomatic recurrence. Uric acid stones primarily occur from low urine pH and high urate excretion, and until these metabolic abnormalities are treated, a high rate of recurrence is expected.[32] Brushite stone formers often have hypercalcuria and other

metabolic abnormalities (e.g., distal renal tubular acidosis) that contribute to a high rate of recurrence.[31] Recurrent urinary tract infections likely contribute to the higher risk of recurrence with struvite stone. Cystine stones have a high rate of recurrence due to genetic cystinuria.[33,34] Consistent with their high recurrence rates, uric acid, struvite, brushite, and cystine stones became progressively more common among stone formers with each subsequent stone composition analysis.

Among common calcium stone formers, the proportion of hydroxyapatite to calcium oxalate was not predictive of recurrence. Prior work found a higher proportion of phosphate than oxalate in stones among recurrent calcium stone formers, but this may have been due to the brushite (not hydroxyapatite) form of calcium phosphate stones (4% of stone formers in this referral population had brushite).[35] Among calcium oxalate stone formers, a higher proportion of COD than COM predicts a higher risk of recurrence, as previously hypothesized.[20]

The current study has potential limitations. Stone composition was unknown in half of the stone formers at their first event consistent with another study of first-time stone formers.[16] Most first-time stone formers have spontaneous passage of their stone without requiring surgery affording less opportunity for stone collection and analysis. However, clinical and laboratory characteristics between stone formers with known and unknown stone composition were similar. The few differences suggesting unknown composition associates with a stone being discarded or lost without composition analysis (symptomatic stone detected by imaging rather than passage, smaller stone located in ureterovesical junction, and no surgery). In a separate ongoing prospective study, we have found very few stone formers save stones that were not initially analyzed for composition at the first stone event. Novel computed tomography techniques have the potential to determine stone composition,[36,37] but are currently not widely implemented in clinical practice. Blood and urine chemistry data was also unavailable in many first-time stone formers, reflecting the reality of limited metabolic evaluations in first-time stone formers. The studied population of Olmsted County, Minnesota was predominantly white (88%) and findings may be less generalizable to other ethnic groups or geographic locations.

Conclusion

If the stone is not available for analysis in a first-time symptomatic stone former, prevention interventions can be based on the assumption that the patient has a common calcium stone (94% probability). However, the 5% with uric acid stones and the 1% with even rarer compositions are more likely to recur and stone composition analysis to identify these high-risk patients is of benefit. In particular, knowing stone composition informs stone prevention diets and medications (for example, potassium citrate would be more effective than a thiazide diuretic for uric acid stones)

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgements

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Abbreviations

COM	Calcium Oxalate Monohydrate
COD	Calcium Oxalate Dihydrate
BMI	Body Mass Index
ROKS	Recurrence Of Kidney Stone

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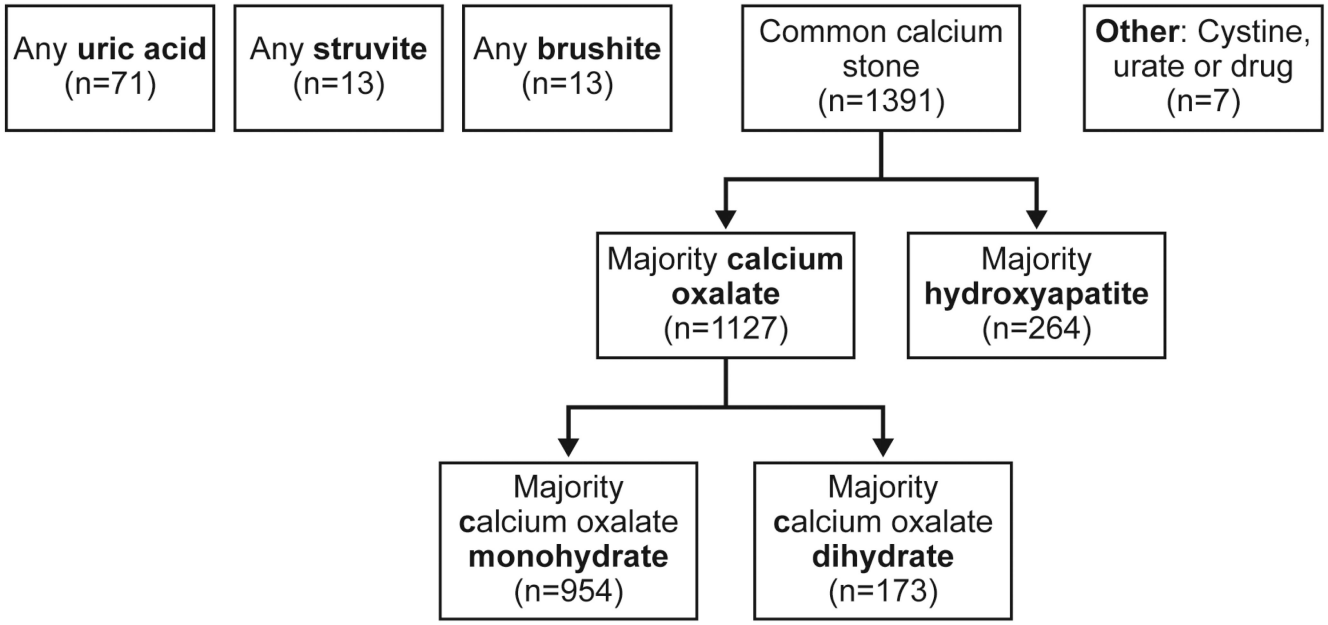
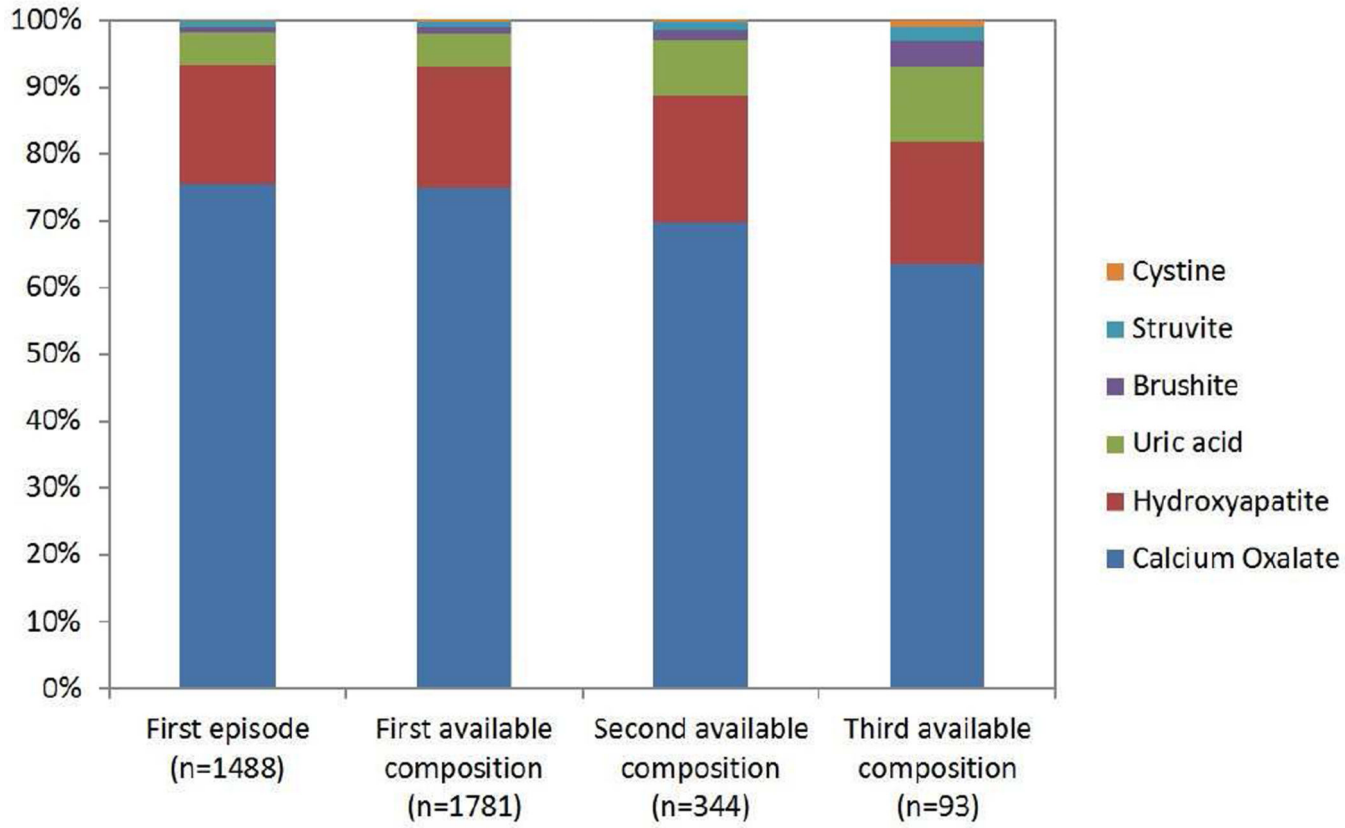


Figure 1.
Stone composition classification of first-time stone formers in Olmsted County.



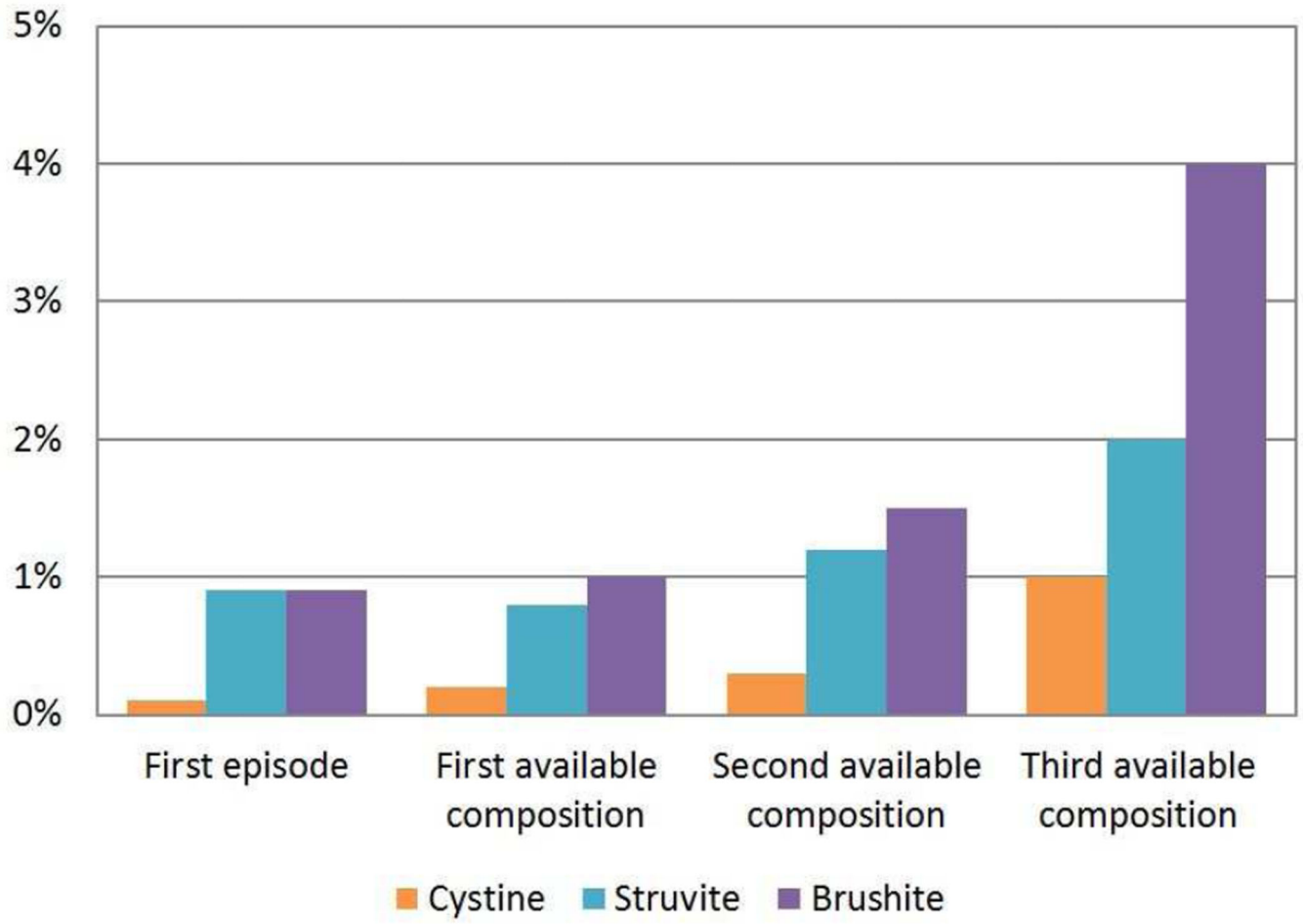
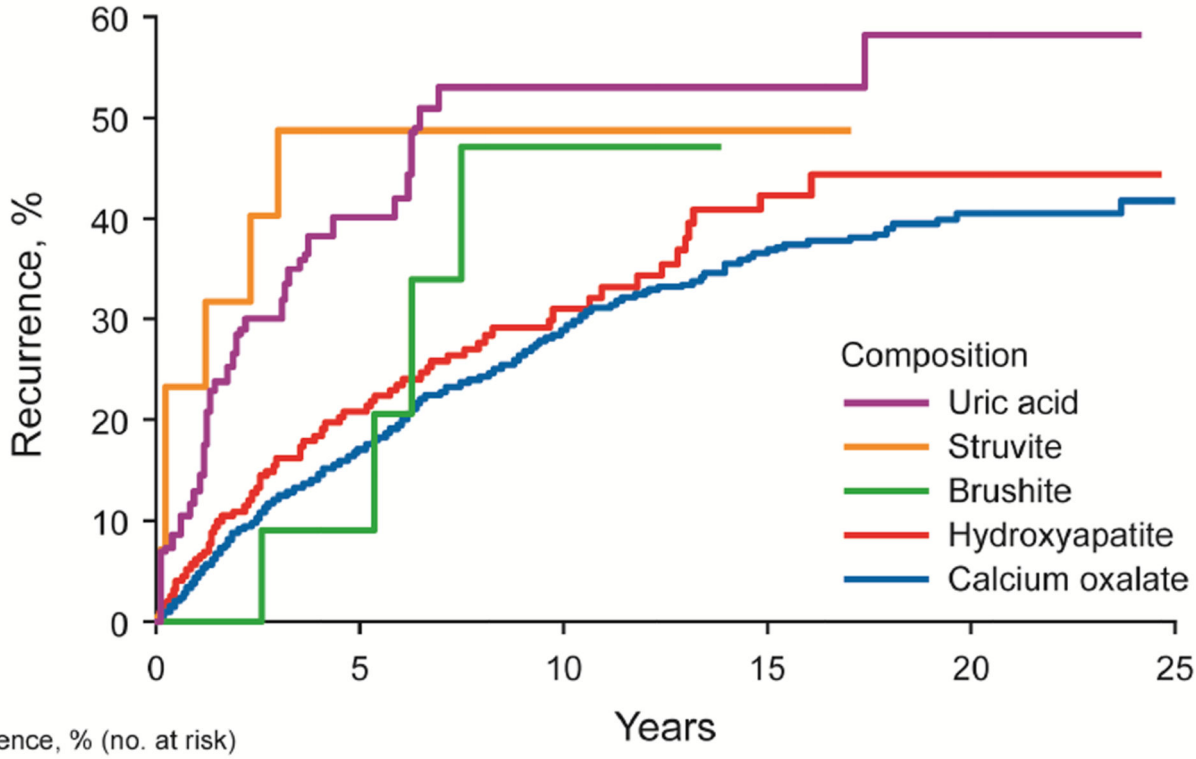
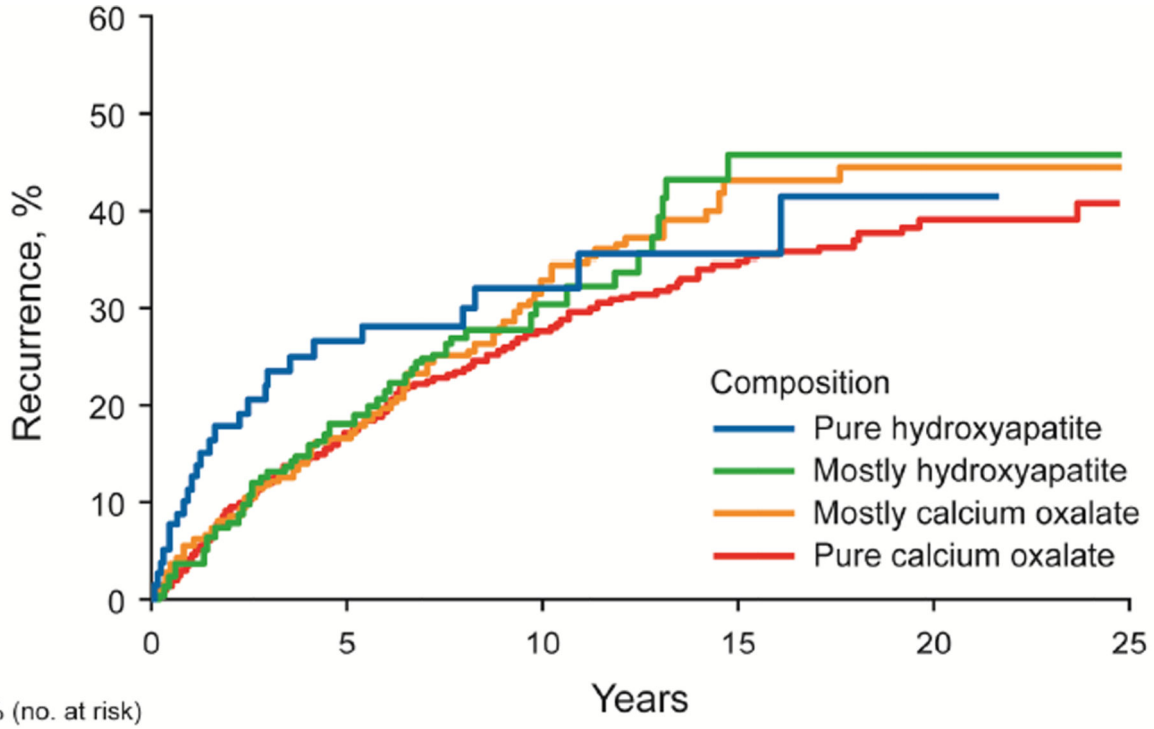


Figure 2.

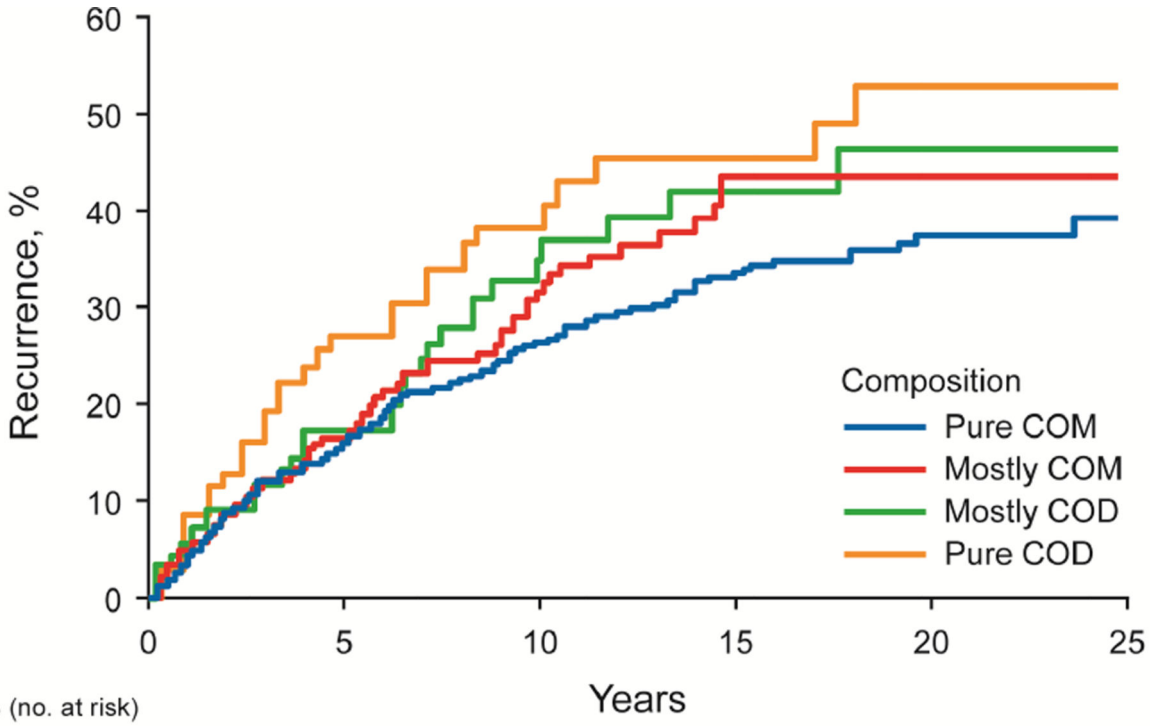
Proportion of each stone composition at first episode and at first, second, and third available composition (first available composition could be at a subsequent episode if not obtained at the first episode). The second available composition was a median 3.2 years after the first available composition and the third available composition was a median 7.8 years after the first available composition. A) All compositions. B) Magnified view of the rarer compositions.



Recurrence, % (no. at risk)						
Uric acid	0 (71)	40 (33)	53 (18)	53 (13)	58 (4)	58 (1)
Struvite	0 (13)	49 (6)	49 (3)	49 (1)		
Brushite	0 (13)	9.1 (8)	47 (3)			
Hydroxyapatite	0 (264)	21 (152)	31 (74)	42 (38)	44 (14)	44 (3)
Calcium oxalate	0 (1127)	17 (694)	29 (418)	37 (236)	40 (115)	42 (24)



Recurrence, % (no. at risk)						
Pure hydroxyapatite	0 (82)	26 (45)	32 (25)	35 (15)	41 (5)	41 (2)
Mostly hydroxyapatite	0 (182)	18 (107)	30 (49)	46 (23)	46 (9)	46 (1)
Mostly calcium oxalate	0 (331)	17 (197)	32 (114)	43 (55)	44 (32)	44 (3)
Pure calcium oxalate	0 (796)	17 (497)	27 (304)	35 (181)	39 (83)	41 (21)



Recurrence, % (no. at risk)						
Pure COM	0 (720)	16 (453)	26 (278)	33 (163)	37 (78)	39 (20)
Mostly COM	0 (234)	16 (140)	32 (82)	43 (37)	43 (22)	43 (2)
Mostly COD	0 (97)	17 (57)	35 (32)	42 (18)	46 (10)	46 (1)
Pure COD	0 (76)	27 (44)	38 (26)	45 (18)	53 (5)	53 (1)

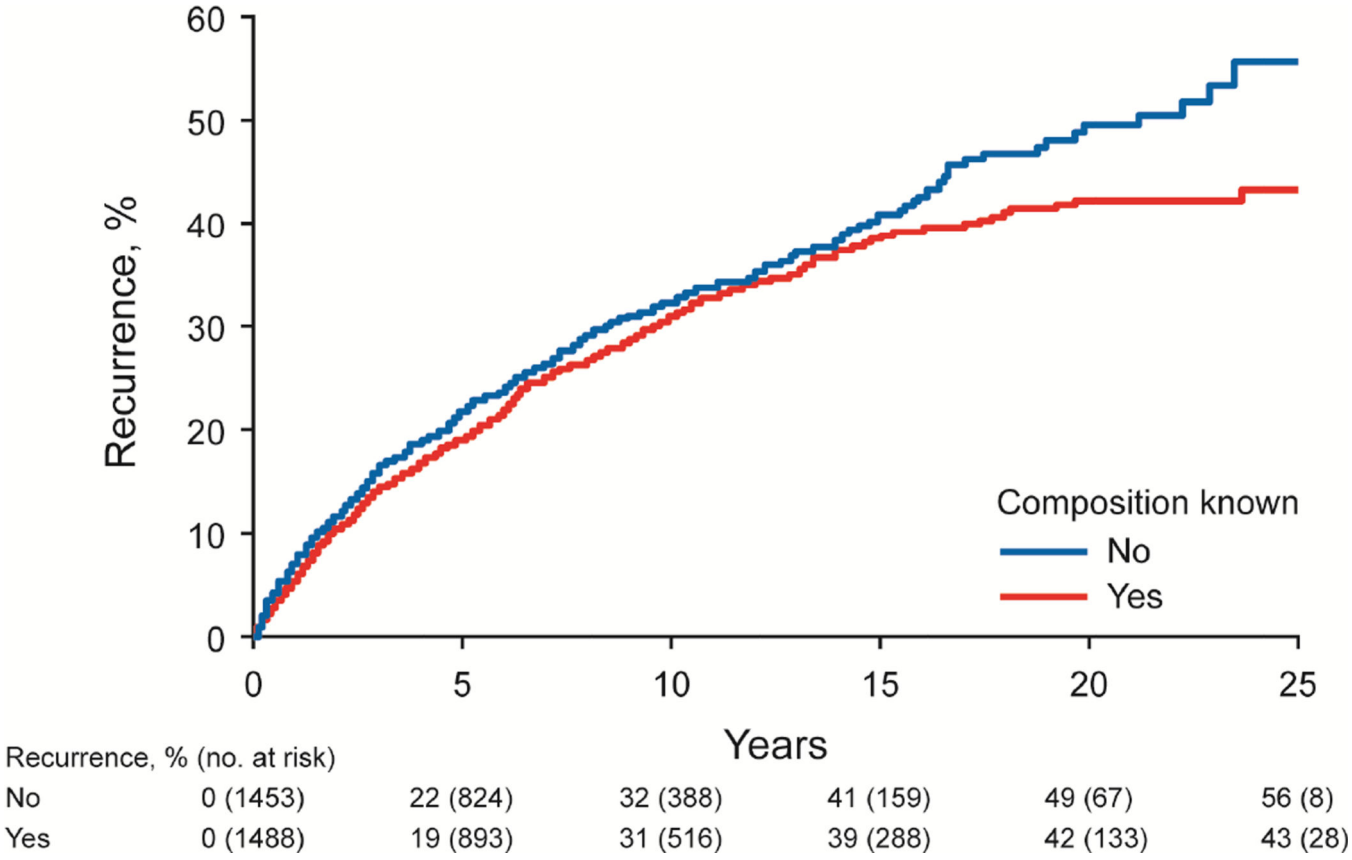


Figure 3.
Cumulative rate of a second symptomatic stone by

A. major stone composition groups (n=1488, $P < .001$)

B. common calcium stone subgroups (n=1391, *P-trend* = .10)

C. calcium oxalate stone subgroups (n=1127, *P-trend* = .007)

D. known vs unknown composition (n=2961, $P = .06$)

among first-time stone formers in Olmsted County, MN (mostly defined as ≥50%).

Table 1

Second stone composition stratified by first stone composition among 343 first-time stone formers with two stone compositions a median of 3.2 years apart.

First stone	Second stone				
	Majority calcium oxalate n=240	**Majority hydroxyapatite n=65**	**Any brushite n=5**	**Any struvite n=4**	**Any uric acid n=29**
Majority calcium oxalate n=240	208(87%) [a]	19	2	1	10
Majority hydroxyapatite n=68	25	41 (60%) [a]	1	1	0
Any brushite n=6	2	2	2(33%) [a]	0	0
Any struvite n=4	0	1	0	2(50%) [a]	1
Any uric acid n=25	5	2	0	0	18(72%) [a]

[a]The proportion with no change in stone composition between first and second available compositions. Overall, 79% had no change in stone composition.

Table 2

Clinical Characteristics at the first stone episode by different stone compositions

Clinical Characteristic		Known Composition			Composition						Calcium Oxalate		
		No (n=1453)	Yes (n=1488)	P-value [b]	Calcium Oxalate (n=1127)	Hydroxy-apatite (n=264)	Brushite (n=13)	Struvite (n=13)	Uric Acid (n=71)	P-value [b]	Di-hydrate (n=173)	Mono-hydrate (n=954)	P-value [b]
Mean (SD) Age, years		42 (16)	43 (15)	**.009**	44 (15)	35 (14)	47 (19)	51 (22)	54 (15)	**<.001**	38 (15)	46 (14)	**<.001**
Male, %		59	62	.08	69	31	54	23	73	**<.001**	69	69	.94
White, %		88	89	.20	90	87		69	96	**.02**	86	90	.10
Family history of stones, %		22	26	**.01**	27	28	15	15	14	.10	34	26	**.04**
Mean (SD) body mass index, kg/m^2		29 (6.7)	29 (6.3)	.40	29 (6.1)	27 (6.6)	29 (6.9)	27 (6.3)	31 (6.9)	**<.001**	28 (5.1)	29 (6.3)	**.03**
Diabetes, %		4.6	5.9	.11	5.6	1.9	23	15	21	**<.001**	2.3	6.2	**.04**
Hypertension, %		24	26	.09	27	16	23	54	56	**<.001**	20	28	**.04**
Gout, %		3.4	3.8	.57	3.6	1.5	7.7	15	11	**<.001**	1.7	4.0	.15
Loose stools, %		9.1	9.9	.46	9.0	13	7.7	0.0	14	.12	8.7	9.0	.88
Abdominal pain/renal colic, %		90	91	.16	92	91	88	69	89	**.001**	91	92	.64
Gross hematuria, %		23	21	.49	20	22	15	39	37	**.01**	28	19	**.008**
Urinary tract infection, %		5.1	5.4	.67	3.8	9.1	15	62	5.6	**<.001**	3.5	3.9	.80
Fever, %		6.0	6.7	.46	5.1	11	15	23	9.9	**<.001**	3.5	5.3	.30
Lower urinary tract symptoms, %		34	35	.40	35	39	31	62	30	.16	45	33	**.002**
[a] Number of stones on imaging	0 (%)	9.2	17	**<.001**	17	12	17	15	22	**.006**	19	17	.72
	1 (%)	56	48		50	42	42	31	49		52	50	
	2+ (%)	35	35		33	46	42	54	29		30	33	
[a] Mean (SD) largest diameter, mm		4.3 (2.7)	5.4 (3.4)	**<.001**	5.2 (3.3)	5.5 (2.8)	8.0 (8.7)	14 (10)	5.9 (4.4)	.09	5.3 (3.7)	5.2 (3.2)	.62
[a] Staghorn stone, %		0.9	1.2	.40	0.7	1.2	8.3	31	1.5	**<.001**	0.6	0.8	.81
[a] Renal pelvic stone,%		14	15	.67	14	18	8.3	31	18	.25	13	14	.55
[a] Ureteropelvic junction stone, %		6.5	6.1	.64	6.1	6.9	0.0	7.7	4.4	.83	4.2	6.4	.27
[a] Ureter stone, %		35	38	.12	37	42	25	23	44	.31	39	37	.53
[a] Ureterovesical junction stone, %		35	28	**<.001**	28	29	50	0.0	16	**.01**	27	28	.84

Clinical Characteristic	Known Composition			Composition						Calcium Oxalate		
	No (n=1453)	Yes (n=1488)	P-value *b*	Calcium Oxalate (n=1127)	Hydroxy-apatite (n=264)	Brushite (n=13)	Struvite (n=13)	Uric Acid (n=71)	P-value *b*	Di-hydrate (n=173)	Mono-hydrate (n=954)	P-value *b*
a Underwent stone surgery, %	22	44	**<.001**	43	49	39	85	35	**.008**	44	43	.74

a Abdominal imaging studies at the time of the first stone episode were obtained in 2789 (94%); of these, 1372 (49%) were computed tomography scans.

b Unadjusted associations; Kruskal-wallis, Wilcoxon and T-tests were used to calculate p-values for continuous variables; chi-squared tests were used to calculate p-values for categorical variables.

Table 3

First available serum and urine laboratory characteristics after the first stone episode by different stone compositions.

	Known Composition			Composition						Calcium Oxalate		
Laboratory characteristic [a] mean (SD) or %	**No (n=1453)**	**Yes (n=1488)**	**P-value [b]**	**Calcium Oxalate (n=1127)**	**Hydroxy apatite (n=264)**	**Brushite (n=13)**	**Struvite (n=13)**	**Uric Acid (n=71)**	**P-value[b]**	**Dihydrate (n=173)**	**Mono hydrate (n=954)**	**P-value [b]**
Serum calcium, mg/dl	9.4 (0.55)	9.4 (0.63)	.24	9.5 (0.63)	9.4 (0.63)	9.6 (0.42)	9.2 (0.87)	9.4 (0.58)	.14	9.6 (0.56)	9.4 (0.63)	**.007**
Serum phosphorus, mg/dl	3.3 (0.73)	3.3 (0.68)	.83	3.3 (0.67)	3.4 (0.71)	3.1 (0.82)	2.9 (0.98)	3.6 (0.69)	**.008**	3.2 (0.84)	3.3 (0.63)	.64
Serum uric acid, mg/dl	5.7 (1.6)	5.5 (1.6)	**.005**	5.6 (1.5)	4.8 (1.4)	4.8 (1.6)	4.9 (1.8)	6.8 (2.0)	**<.001**	5.3 (1.3)	5.6 (1.5)	.29
Serum bicarbonate, mmol/l	26 (2.8)	26 (2.7)	.12	26 (2.7)	25 (2.9)	25 (2.1)	26 (1.6)	25 (2.7)	**.008**	26 (2.7)	26 (2.7)	.41
Urine calcium, mg/24 hr	225 (126)	219 (131)	.29	220 (129)	224 (131)	N/A‡	N/A	152 (91)	**.02**	253 (148)	214 (124)	**.03**
Urine citrate, mg/24 hr	621 (286)	631 (289)	.71	640 (277)	570 (245)	N/A	N/A	661 (364)	.09	611 (199)	645 (289)	.60
Urine oxalate, mmol/24 hr	0.32 (0.15)	0.34 (0.18)	**.04**	0.36 (0.20)	0.28 (0.11)	N/A	N/A	0.32 (0.14)	**<.001**	0.34 (0.16)	0.37 (0.20)	.24
Urine phosphorus, mg/24hr	938 (360)	932 (362)	.73	938 (368)	883 (338)	N/A	N/A	955 (314)	.35	886 (407)	948 (359)	.12
Urine uric acid, mg/24 hr	602 (232)	599 (220)	.82	616 (224)	523 (168)	N/A	N/A	635 (271)	**.01**	595 (173)	619 (232)	.75
Urine sodium, mmol/24 hr	140 (2.5)	147 (41)	.18	148 (44)	144 (29)	N/A	N/A	145 (40)	.91	151 (51)	148 (43)	.94
Urine volume, ml/24 hr	1671 (849)	1730 (832)	.18	1752 (805)	1644 (899)	N/A	N/A	1763 (1032)	.25	1659 (725)	1769 (819)	.39
Urine pH	6.0 (0.78)	6.0 (0.77)	.32	6.0 (0.75)	6.3 (0.79)	N/A	N/A	5.5 (0.70)	**<.001**	6.1 (0.66)	5.9 (0.76)	**.01**
Microhematuria, %	90	89	.23	88	89	100	100	93	.41	90	88	.46

[a] Laboratories were available in a subset for serum calcium (75%), phosphorus (65%), uric acid (61%), and bicarbonate (41%); for urine calcium (37%), citrate (34%), oxalate (44%), phosphorus (30%), uric acid (29%), sodium (49%), volume (39%), and pH (83%); and microhematuria (85%).

[b] Unadjusted associations; Kruskal-wallis, Wilcoxon and T-tests were used to calculate p-values for continuous variables; chi-squared tests were used to calculate p-values for categorical variables.

N/A: Not available as number of subjects too few for analysis