

# Trends in urinary calculi composition from 2005-2015: a tertiary center study



Vidit Talati, BS; Ricardo O. Soares, MD FEBU; Robert B. Nadler, MD; Kent T. Perry, MD  
Department of Urology, Northwestern Medicine, Northwestern University - Feinberg School of Medicine



## Background

Urolithiasis is a common and burdensome urinary disease affecting approximately 1 in 11 people in the United States<sup>1</sup> with as many as 13% of men and 7% of women having a kidney stone in their lifetime<sup>2</sup>. This has resulted in dramatic increases in direct and indirect costs of over \$5 billion to the United States' national healthcare system<sup>2</sup>. The reasons for these trends are not entirely clear, but studies show correlations between age<sup>4, 5</sup>, gender<sup>4, 5</sup>, diet<sup>4</sup>, climate<sup>4</sup>, and race<sup>6</sup> and the risk of suffering from certain urinary calculi. Yet, to date, little research has been done comparing the trends in the concurrent presence of certain minerals in mixed stones.

Here, we performed a retrospective study of urinary calculi-affected patients to both confirm established trends in stone composition and elucidate novel changes in the composition of mixed stones containing COM and UA over a ten-year period.

## Methods

### Data acquisition

This is a retrospective study of stones from patients at NMH who underwent PCNL or ureteroscopy for the management of urolithiasis and had their calculi analyzed between the years 2005-2015. Birthdate, sex, race, ethnicity, and stone analysis results were retrieved via the NMEDW.

### Stone Composition Analysis

Stones were classified based on the mineral that comprised the largest percentage of the stone: calcium oxalate monohydrate/dihydrate (COM/COD), carbonate apatite (CA), uric acid (UA), struvite, calcium phosphate (CP), and/or cystine. Stones classified as "dual-majority" (DM) had an equal majority percentage of two minerals. The frequency of each stone type was compared over the ten-year period and between each age group and sex. UA stones containing solely UAA and UAD were deemed mixed, but were not further sub-classified. Mixed stones containing any amount of COM or UA were further analyzed to compare the concurrent prevalence of other minerals within these stones over the ten-year period.

### Statistical Analysis

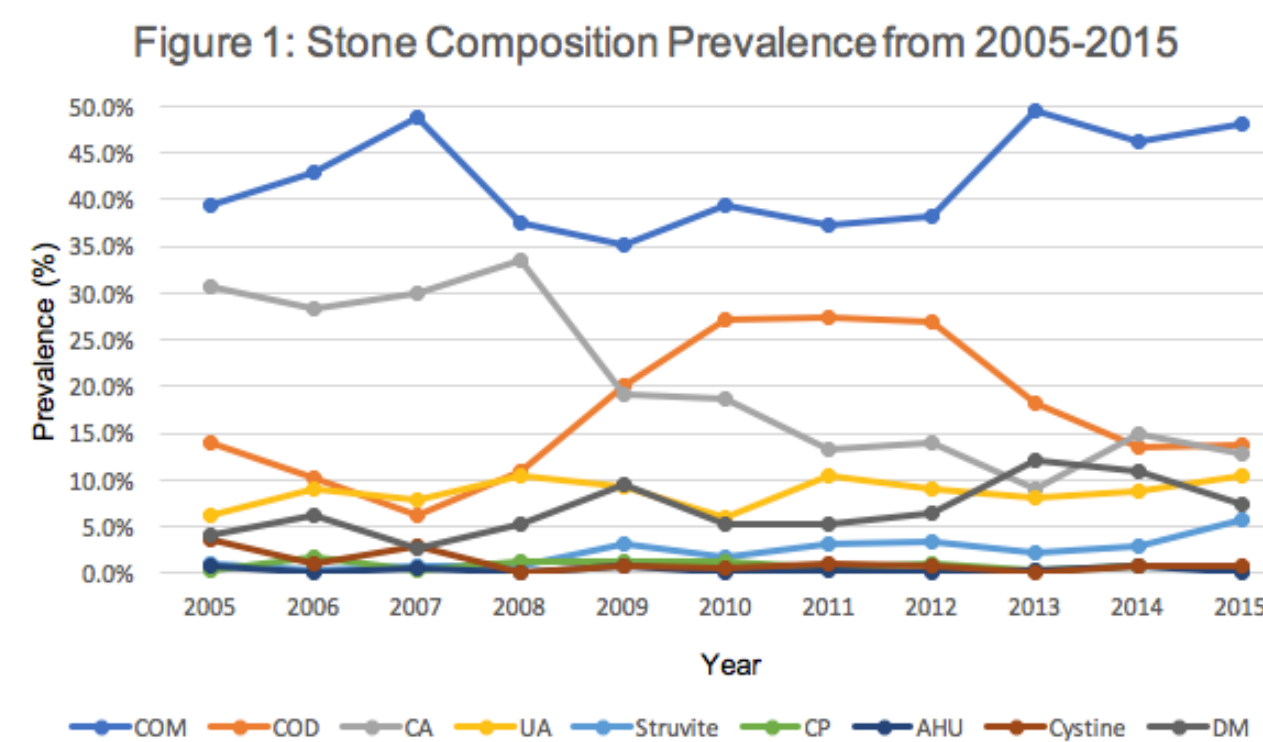
Binary logistic regression was used to assess trends for each stone type with year, sex, and age groups treated as covariates and each stone type treated as a separate dependent variable. Chi-squared tests were used to calculate notable differences in stone prevalence across sex and age group in 2005 versus 2015. SPSS version 23 was used for all statistical analyses. Statistical significance was set at  $P < 0.05$ .

## Results

|                 | Count         | %    | Stone Type | Pure Stones (Count) | Pure Stones (%) | Mixed Stones (Count) | Mixed Stones (%) | Overall (%) |
|-----------------|---------------|------|------------|---------------------|-----------------|----------------------|------------------|-------------|
| Total Stones    | 5268          | --   | COM        | 69                  | 10.8            | 2171                 | 46.8             | 42.2        |
| Total Mixed     | 4635          | 88.0 | COD        | 0                   | 0.0             | 956                  | 20.6             | 18          |
| Total Pure      | 633           | 12.0 | CA         | 476                 | 74.6            | 492                  | 10.6             | 18.2        |
| Male            | 3036          | 57.6 | UA         | 14                  | 2.2             | 449                  | 9.7              | 8.7         |
| Female          | 2232          | 42.4 | Struvite   | 2                   | 0.3             | 128                  | 2.8              | 2.5         |
| White           | 3625          | 68.8 | CP         | 27                  | 4.2             | 17                   | 0.4              | 0.8         |
| Black/AA        | 552           | 10.5 | AHU        | 1                   | 0.2             | 15                   | 0.3              | 0.3         |
| Hispanic/Latino | 445           | 8.4  | Cystine    | 35                  | 5.5             | 16                   | 0.3              | 1.0         |
| Asian           | 113           | 2.1  | MSUM       | 9                   | 1.4             | 0.0                  | 0.0              | 0.0         |
| Age Range       | 17-90         | --   | DM         | --                  | --              | 391                  | 8.4              | 7.4         |
| Mean Age        | 53.46 ± 15.86 | --   |            |                     |                 |                      |                  |             |
| Median Age      | 55            | --   |            |                     |                 |                      |                  |             |

Table 1: Demographic data and counts relating to the whole stone population

### Trends in Stone Composition from 2005-2015



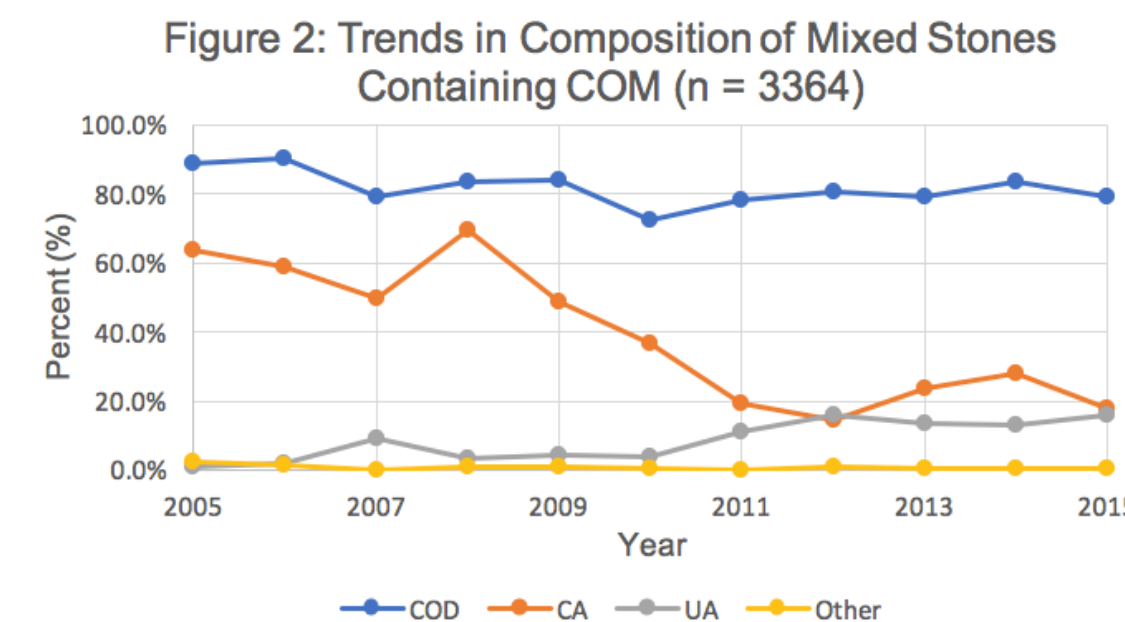
The proportions of mixed stones and sex did not change remarkably in 2015 versus 2005. Changes in stone type prevalence within both sexes reflected gender effects on stone composition and trends in overall stone composition (Figure 1). In males, COM and UA increased by 12.5% ( $p < 0.01$ ) and 8.3% ( $p = 0.01$ ), respectively, whereas COD and CA decreased by 7.2% ( $p < 0.05$ ) and 11.9% ( $p < 0.001$ ), respectively. In females, CA was the predominant calculus in 2005, but decreased by 26.2% ( $p < 0.001$ ) such that COM was predominant in 2015. COD and struvite increased significantly by 10.6% ( $p < 0.01$ ) and 10.1% ( $p = 0.01$ ), respectively, as well. Relative to 2005, stone formers were older on average in 2015, with significant increases in the prevalence of 60-74 and 75+ year olds by 9.9% and 10.0%, respectively, and decreases in the younger age groups.

### Stone Type Stratification Across Gender

| Sex    | COM            | COD           | CA           | UA             | Struvite     | CP             | AHU           | Cystine       | DM           |
|--------|----------------|---------------|--------------|----------------|--------------|----------------|---------------|---------------|--------------|
| Male   | 49.2           | 16.8          | 12.5         | 11.3           | 1.8          | 1.0            | 0.4           | 0.9           | 6.0          |
| Female | 33.4           | 20.0          | 26.4         | 5.4            | 3.3          | 0.6            | 0.2           | 1.1           | 9.4          |
| p      | 0.00           | .171          | .000         | 0.000          | 0.018        | 0.007          | .400          | .806          | .000         |
| OR     | 1.755          | .904          | .417         | 1.741          | .646         | 2.529          | 1.588         | .931          | .675         |
| 95% CI | [1.562, 1.971] | [.781, 1.045] | [.359, .485] | [1.397, 2.171] | [.450, .928] | [1.296, 4.935] | [.541, 4.665] | [.525, 1.650] | [.546, .835] |

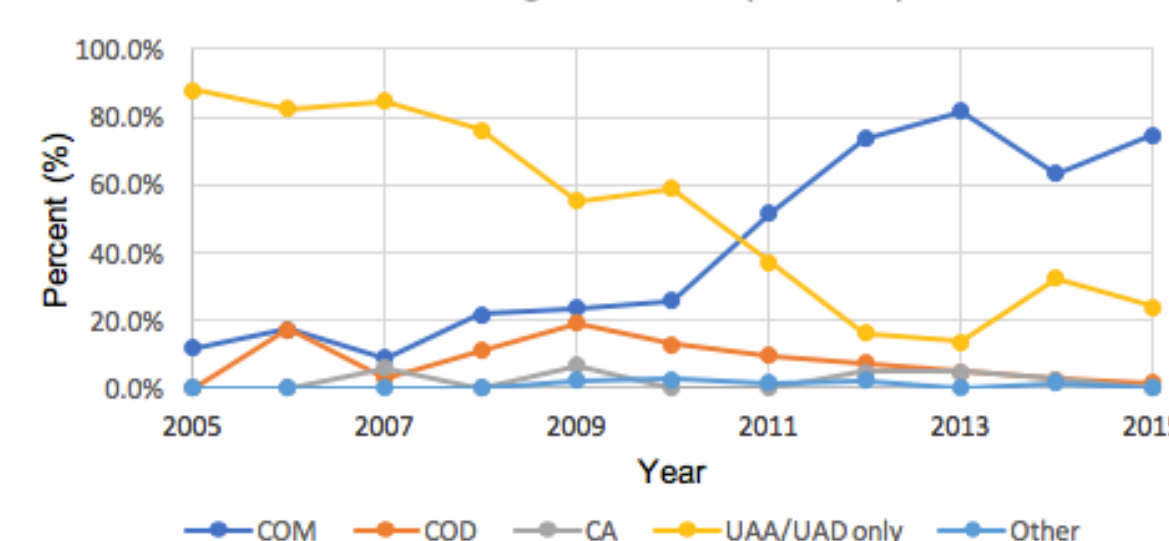
COM was the most prevalent in both sexes, and was more common in men (49.2% vs. 33.4%,  $p < 0.001$ ). Women formed CA stones more than twice as often as men ( $p < 0.000$ ). Struvite was about twice as common in women as well at 3.3% vs. 1.8% ( $p < 0.05$ ). As in other studies, men formed UA stones twice as often as women ( $p < 0.001$ ).

### Composition of Mixed Stones



A majority of stones in Figure 2 contained COD and/or CA. Mixed stones with COM contained CA less often as time progressed, peaking at 69.5% in 2008 and decreasing to 17.8% by 2015 ( $p < 0.001$ ; OR: 0.786). There was also a steady increase in UA from 1.0% in 2005 to 15.9% in 2015 ( $p < 0.001$ ; OR: 1.282). COD also fell, albeit less deeply, and the presence of other minerals did not change significantly.

### Figure 3: Trends in Composition of Mixed Stones Containing UA/UAD (n = 587)



In Figure 3, the prevalence of COM increased substantially from 11.8% in 2005 to 74.6% in 2015 ( $p < 0.001$ ; OR: 1.515) with a complementary fall in stones containing exclusively UAA or UAD ( $p < 0.001$ ; OR: 0.657). COD was relatively less prevalent with a noted decrease from 19.2% in 2009 to 1.5% in 2015 ( $p < 0.05$ ; OR: 0.884).

## Conclusion

The small amount of pure stones in this study is surprising. This could be from epidemic obesity/metabolic syndrome in our population, which induces urine acidification and increases excretion of UA, sodium, and phosphate<sup>4</sup>. Our sub-analysis also confirms a decrease in CO stones after age 60<sup>5</sup>, which we found to be mostly due to COD.

Men form more stones due to excreting more oxalate and less citrate and possibly due to a higher animal protein intake that promotes calcium oxalate stone formation<sup>7</sup>. In our study, however, the M/F ratio evolved from 1.8 in 2007 to 1.08 in 2014, with 57.6% of stones being from males. The rise in female stones was mainly due to the increase in COD (from 8 to 18.6%) and struvite (from 1.8 to 11.9%). Therefore, we postulate that increased female obesity in Cook County (while male obesity has been stable) leveled the M/F ratio.

The geriatric population is known to have an increased incidence of isolated hypocitraturia and uric acid calculi. The UA increase amongst mixed stones with COM and UA prevalence rise coincide with a higher proportion of population being 75+ in 2015.

Limitations of this study include its retrospective design, the fact that it is a single center analysis and therefore is not representative of the whole USA, and the inclusion being limited to surgically removed stones.

## References

1. Scales, Charles D., et al. "Prevalence of kidney stones in the United States." *European urology* 62.1 (2012): 160-165.
2. Turney, Benjamin W., et al. "Trends in urological stone disease." *BJU international* 109.7 (2012): 1082-1087.
3. Knoll, Thomas, et al. "Urolithiasis through the ages: data on more than 200,000 urinary stone analyses." *The Journal of urology* 185.4 (2011): 1304-1311.
4. Lee, Ming-Chak, and Simon Virgil Bariol. "Changes in upper urinary tract stone composition in Australia over the past 30 years." *BJU international* 112.S2 (2013): 65-68.
5. Lieske, John C., et al. "Stone composition as a function of age and sex." *Clinical Journal of the American Society of Nephrology* 9.12 (2014): 2141-2146.
6. Yang, Xiong, et al. "Multivariate Analyses of Urinary Calculi Composition: A 13-Year Single-Center Study." *Journal of clinical laboratory analysis* 30.6 (2016): 873-879.
7. Borghi, Loris, et al. "Comparison of two diets for the prevention of recurrent stones in idiopathic hypercalciuria." *New England Journal of Medicine* 346.2 (2002): 77-84.