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Supplemental Methods

Study Sample

All data was obtained through the Rochester Epidemiology Project (REP), a resource that provides access to medical records of nearly all providers for all residents of Olmsted County, MN. Diagnostic codes dating back to 1935 are indexed and linked to a comprehensive medical record. Over 95% of the population has at least one clinic visit with a local health care provider every 2–3 years, allowing essentially complete enumeration of the local population.(1, 2) Residents of Olmsted County, MN are more white, educated, and wealthier than the general US population but have similar mortality rates.(3) Residents with their first urological stone episode between 1984 and 2012 were identified using all International Classification of Diseases (ICD)-9 codes available for urinary tract stones: 592, 594, and 274.11. County residents who did not have Minnesota Research Authorization (5% of population) and those with coded stone disease prior to 1984 were excluded. Newly coded stone formers from January 1984 to December 2012 were validated and detailed in a random order. The comprehensive medical records were carefully reviewed by dedicated abstractors under the supervision of two nephrologists (ADR, JCL) and a urologist (AEK) to validate the first and any recurrent episodes (through 2014).

Stone episode validation criteria

Validation criteria to be considered an incident symptomatic kidney stone included receiving clinical care between 1984 and 2012 for a stone in a location that caused partial, complete, or intermittent obstruction in the ureter, uteropelvic junction, uterovesical junction,

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kidney pelvis, or "unattached" in the lower kidney pole as documented by imaging, or documentation of a passed stone. Imaging modalities were abdominal radiography, excretory urography, ultrasonography, and computed tomography. A stone was considered symptomatic if the patient presented for clinical care of gross hematuria or pain. Pain could be typical renal colic or atypical, defined as vague or nonlocalized abdominal, pelvic, or back pain. Patients with a documented stone in the presence of a symptomatic urinary tract infection caused by a urease splitting organism (urine culture with $>10^5$ colony forming units and urine pH >7.0) or known composition of struvite were also considered symptomatic. Patients who first presented with incidental asymptomatic kidney stones (even if associated with microhematuria), bladder stones, or suspected stones that lacked confirmatory imaging or documented passage were not considered valid. Any recurrent episode was similarly validated and had to be a different stone at least 1 month later.

This approach to identify symptomatic stone formers in the general population has been validated. The prevalence of symptomatic kidney stone formers is 7.2% among the residents in Olmsted County, Minnesota based on this approach.(4) Similarly, a survey of adults in the US population found the self-reported prevalence of symptomatic kidney stones to be 7.7%.(5)

Clinical and laboratory characteristics of stone formers

Medical charts were systematically abstracted for clinical and laboratory characteristics within 90 days of the first stone episode and prior to any 2nd stone episode. Race was analyzed as white versus nonwhite. Any family history of kidney stones was identified. Comorbidities present at the time of the incident kidney stone included: body mass index, diabetes mellitus

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(consecutive fasting glucoses >126 mg/dl or use of anti-diabetic medications), hypertension (consecutive blood pressures >140/90 mmHg or use of anti-hypertensive medications for high blood pressure), gout, loose stools (or diarrhea), and urinary tract infections (>100,000 colony forming units per ml). Symptoms at the incident stone episode included pain (renal colic or atypical), gross hematuria, fever, and lower urinary tract symptoms (e.g. urgency, frequency, nocturia). Imaging studies (computed tomography, excretory urography, abdominal radiography, or ultrasonography) at the initial stone event were abstracted for number of stones on imaging, largest stone diameter, presence of a staghorn, and any symptomatic renal pelvic (or lower pole) stone. Stones in the ureter were mutually exclusively classified as located at the ureteropelvic junction, ureterovesical junction or just ureter (if in-between). Available laboratory studies at the first stone episode included spot urine pH, and microscopic hematuria (>3 cells per high powered field). Since serum chemistries and 24-h urine studies (serum calcium, phosphate, uric acid, and urine volume, pH, calcium, citrate, oxalate, and phosphate) were often missing, the first laboratory available after the initial stone episode was used for analysis. Any disease or disorder attributed to causing kidney stones was identified.

Stone composition analysis

More than 99.9% of all stone composition analyses were performed at a Mayo Clinic laboratory using the following protocol in place since 1980 and throughout the study period. A representative specimen (~1 mg) was taken from all identifiable layers of the stone and crushed with a mortar and pestle into a fine powder. The infrared spectrum was recorded using a Frontier FTIR spectrometer with Universal ATR Sampling Accessory and a diamond/ZnSe crystal

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(PerkinElmer, Waltham, MA). The resulting spectrum was compared against reference spectrum of all known kidney stone compositions. For stones with multiple compositions, the percentage of each composition was determined by comparing the ratio of peak heights of the compositions within a given sample to the ratio of peak heights in a library of known quantities of mixed compositions. Stones with multiple compositions were also rounded to the nearest 10 percentile interval (or the nearest 5 percentile interval if 5% or 95%) for each composition.

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References

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