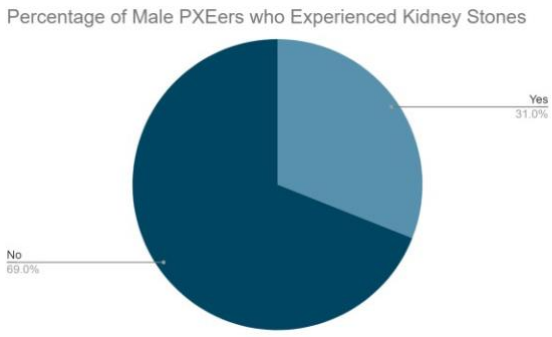
PXE Guide

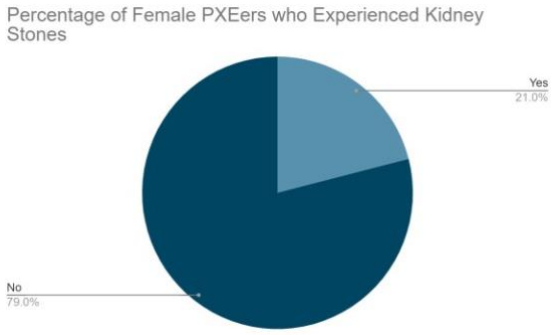
Kidney Stones

How did we discover that kidney stones were a potential result of PXE?
PXE International enlisted Douglas Ralph, Rina Allawh, Jouni Uitto, and Qiaoli Li from Thomas Jefferson University. We recruited 563 individuals to participate in the study. Participants were asked to complete a survey. The PXE International survey asked, "Have you ever had a kidney stone? How old were you when you first experienced a kidney stone? How many times have you passed a kidney stone?" The researchers examined questionnaires and analyzed the data.

What are the results?
We found that 23.4% of people with PXE had kidney stones. About 31% of the men who responded to the question stated they experienced kidney stones, while 21% of women experienced kidney stones.

How does this compare to the general population?

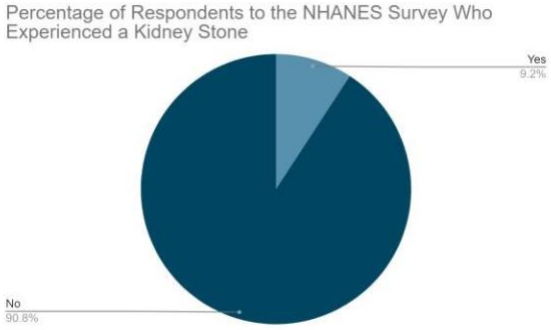


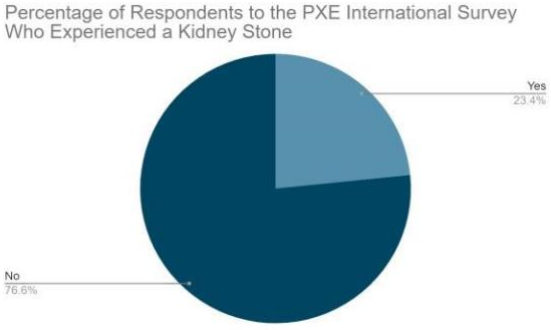


I It is important to determine whether these kidney stones are caused by pseudoxanthoma elasticum (PXE) or by other factors. For example, if we say that 80% of people with PXE have brown hair and 20% have blond hair, this does not necessarily mean PXE causes hair color. To clarify, we would compare the hair colors of PXE patients with those of the general population from the same region. If no difference is found, then hair color is not influenced by PXE. This illustrates that some traits are unrelated to PXE. A better question to ask is: are kidney stones more common in PXE patients than in the general population? To answer this, researchers compared the prevalence of kidney stones in the PXE group with that in the overall US population.

A good reference for the average US population is the National Health and Nutrition Examination Survey (NHANES). It is a well-known study that has been running in the US for many years. These surveys are conducted by the Centers for Disease Control and Prevention (CDC) and cover a wide range of health topics. NHANES had 28,629 participants aged 20 years or older in the dataset the researchers analyzed. The researchers used kidney stone data from 2007 to 2016. The responses to the question "Have you ever had a kidney stone?" were particularly interesting in this study. Individuals aged 20 years or older at the time of the PXE International survey were compared with the NHANES population.

9.2% of respondents in the NHANES survey had experienced kidney stones. In contrast, 23.4% of the PXE group reported experiencing kidney stones. PXEers are 2.5 times more likely to develop kidney stones. In the PXE population, 17.8% of PXE respondents experienced their first kidney stone before age 18. It is difficult to determine how common kidney stones are for individuals 18 and younger in the general population.





However, it appears that PXEers get kidney stones earlier and more often than people without PXE. Males are more likely to develop kidney stones in the general population, and this is also true in the PXE population.

This study showed that people with PXE experience kidney stones more often than the general population. This does not mean that all people with PXE will develop kidney stones. About 1 in four PXEers will develop kidney stones. We do not know why people with PXE get more kidney stones, but we suspect that low inorganic pyrophosphate levels allow more stones to build up.

What else do we need to study? Overall, individuals with PXE have an increased risk of developing kidney stones. The current Phenodex Score, which PXE International created to assess your skin, eye, vascular, cardiac, and gastrointestinal signs/symptoms, does not include kidney function. We think it might be important to include this in the Phenodex, our index for mapping the changes and progression of PXE.

In summary, this study published as “Kidney Stones are Prevalent in Individuals with Pseudoxanthoma Elasticum, a Genetic Ectopic Mineralization Disorder” documented an elevated lifetime prevalence of kidney stones in a large PXE cohort relative to U.S.

population survey data, reinforcing the idea that nephrolithiasis may be part of the PXE spectrum linked to *ABCC6*-related mineralization dysregulation. In contrast, the 2024 paper by Harmsen et al. (https://pmc.ncbi.nlm.nih.gov/articles/PMC10766656/) assessed incidental stones on blinded CT imaging in PXE patients versus hospital controls and found no significant difference in prevalence when corrected for age and sex, challenging the generalizability of questionnaire-based prevalence estimates. Together, these studies highlight persistent uncertainty: descriptive evidence of an association varies by method, and neither study provides definitive mechanistic insight into stone composition, mineral metabolism, or a direct link to pyrophosphate pathways—key gaps ripe for targeted investigation.

What can you do?

- Make sure you hydrate enough, particularly when you exercise. This is probably the number-one preventive.
- Calcium is Not the Enemy. In fact, too little calcium causes kidney stones! So make sure you have enough calcium in your diet.
- Eat less sodium. Too much salt in the urine prevents calcium from being reabsorbed from the urine to the blood. This causes high urine calcium, which may lead to kidney stones.
- Eat fewer oxalate-rich foods. Some kidney stones are made of oxalate, a natural compound found in food, which binds with calcium in the urine to form them. Limiting oxalate-rich foods may help prevent stones from forming. Foods high in oxalate include spinach, chocolate, sweet potatoes, coffee, beets, peanuts, rhubarb, soy products, and wheat bran.
- Eat less animal protein. Foods high in animal protein are acidic and may increase urine acid. High urine acid may cause both uric acid and calcium oxalate kidney stones.

What we know:

- People with PXE have reported kidney stones.
- One large PXE International survey found a higher reported lifetime prevalence than NHANES.
- Some stones occurred before age 18.
- General kidney stone prevention still applies.

What we do not know:

- Whether PXE directly causes kidney stones.
- Whether stone composition differs in PXE.
- Whether low PPi explains the risk.
- Whether all people with PXE need kidney-specific screening.
- How best to include kidney stones in Phenodex or clinical monitoring.

This is a summary of a paper by:

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Link to the original paper:

https://pmc.ncbi.nlm.nih.gov/articles/PMC8680818/