

Urologic Diseases in America Podcast Series
Episode 4: Urinary Stone Disease
Presented by: Brian Matlaga, MD, MPH, *Johns Hopkins University*
Guests: Ryan Hsi, MD, *Vanderbilt University*

Brian Matlaga, MD: Hello. My name is Brian Matlaga. I'm a professor of urology at Johns Hopkins University. And I also serve as one of the principle investigators for the Urologic Diseases in America Project. And I'm very excited to be speaking with you today through this platform that this partnership with the American Urological Association has provided us. And today, what we'll be reviewing is another condition that we've studied in the Urologic Diseases in America Project, this one being kidney stones and joining us on this podcast, I'm very excited to introduce Dr. Ryan Hsi, who is an assistant professor at Vanderbilt University Medical Center, who has also devoted his both academic as well as clinical career to the treatment of patients with urinary stone disease. So Ryan, thank you for joining on this podcast.

Ryan Hsi, MD: Thank you for inviting me, Brian. It's a pleasure to be here and thank the AUA and the Urologic Diseases in America Project for inviting me.

Brian Matlaga, MD: Thanks. Yeah, I'm excited to be joining you. And what we'll do is probably over the next 15 to 20 minutes, we'll go through what we consider to be, if you want to call them highlights or important aspects of what we found when we looked through the kidney stones data sets. And we looked at a number of data sets in this project. We looked at NHANS, which is the National Health And Nutrition Survey. We looked at Optum Clinical Data Mart, which is essentially a data set of privately insured individuals, so this represents a working age population. We also looked at a pediatric cohort and via the Optum data. And then finally, we looked at the CMS data to understand this condition in the over 65 years of age population and essentially the Medicare population.

Brian Matlaga, MD: And Ryan and I have organized our time together, in what we think is somewhat of a logical fashion. So we'll go through a sharing of what we found looking at prevalence data. We'll explore a little bit of what we learned with regards to diagnostics, surgical therapeutics. One of the great things that we have now with both Medicare part D data, as well as using a data set such as the Optum private payer data set is we have pharmacologic data or pharmaceutical utilization. And so also talk a little bit about pharmacotherapy in the context of stone disease. Again, the nature of these data sets is they're very powerful because they also provide us some longitudinal information.

Brian Matlaga, MD: So we can begin to track how patients move through the healthcare system, which is important because as we all know, there's increasing emphasis on trying to understand what quality is in healthcare. And that's obviously a very complex discussion, but one of the ways we can begin to understand some aspects of quality and care is using longitudinal data via these large administrative data sets. And so we'll share some of our findings in that with regards to outcomes, and then we'll try to wrap it all together in terms of what we think the message from the NIDDK's Urological Diseases in America Project is, going forward. So I'll pause there. And Ryan, what I'll ask you to do, if you can share with us some of the findings with regards to prevalence rates that we've seen among the stone forming patients.

Ryan Hsi, MD: Yeah, certainly. So using these three different data sets, we get a unique view from the NHANS dataset on the prevalence ... As you know, that NHANS data set is a self-reported kidney stone. And we looked at between years 2007 and 2012. And in the prior studies before this in the 1990s and early 2000s, we found that the prevalence of stone disease risen dramatically over that time period. But during 2007, 2012, it seems to have plateaued. And that plateau seems to be very interesting.

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- Ryan Hsi, MD: When we look further into prevalence rates among men and women, we see a very stark difference than prior years. And here we see that in among women, the prevalent dramatically increased from about 6.5%, from 2007 to 2008, to about 8.9%, from 2011 to 2012. Whereas in men, the prevalence declined from about 11.5% to 8% in the same period. And so these dramatic changes in prevalence, we're not quite sure what is the driving forces that explain this, but we suspect there may be in part related to the changes in lifestyle, diet, increase in obesity, especially among women during the same period.
- Brian Matlaga, MD: Yeah. And one other, I think, powerful aspect of the Urologic Diseases Project is by having access to the private payer data. We can start to look at unique populations within that, that we have not had an ability to do previously. And one of those is the pediatric population. And I know because prior to my work with urologic diseases, I've personally tried to get a better understanding of what is the burden of stone disease among the pediatric population, just because clinically, we were seeing more and more children with stones. And so we had a perception that there may be an increase in incidents and prevalence. And what we found when I tried to look at this is that there's not great, or at the time, there were not great data sets.
- Brian Matlaga, MD: So you had things like the kid's inpatient data set, but again, as the name implies, that's inpatient setting data. And as we all know, most stone patients are treated, not in an inpatient setting, but in an outpatient setting. And what the literature shows is there are well done studies, but they tend to be either a single institution series or from fairly specialized centers, such as freestanding children's hospitals. And there wasn't a good set of data to try and understand what the burden of stone disease is among children. And so what we're able to do with Urological Diseases Project is leverage the Optum Data Mart cases and use that data set to try to better understand what the burden of stone diseases among children.
- Brian Matlaga, MD: And what we found through these data is that ... we looked at the years, 2006 up to about 2016 ... and what we found was that if we first looked at rates, we saw that there was an increasing number of children with a diagnostic code or a medical code for some disease that rose up around the year 2011 and then plateaued and started to decline to some extent, but there was a fairly market increased from 2005, 2006 up to through 2011. The other thing that was very interesting is that when we broke the cohorts down both by age and gender, females consistently had a higher rate of stone disease than did males. And this tended to be clustered in the teen years, and then also white enrollees had a higher rate than other ethnic groups.
- Brian Matlaga, MD: And so I think these data are important because they do show us that there was an increase in the rates of stone disease among children, which seems to have plateaued and stabilized and it starts to decline as we moved into more recent years. And it also gave us, I think, more information on which populations may be at risk so that we can begin to focus some effort to better understanding why, for example, in the teen years, or for example, in the female gender, how come we're seeing increased rates among that population.
- Brian Matlaga, MD: One other aspect that we can do if we move from prevalence into essentially diagnostics, and before I do that, I just wanted to ask, Ryan, do you have any other thoughts on in the adult population? What particularly struck you at this prevalence?
- Ryan Hsi, MD: Yeah. We also able to look at coexisting medical conditions, and we also saw that rates of hypertension and diabetes also increased over the same period. And so we understand that

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many of these chronic conditions have shared risk factors and maybe the combination of these diet and lifestyle changes across time maybe contributed to both risk in adults and children.

- Brian Matlaga, MD: Yeah. And towards the end of this podcast, we'll come up with our take home messages, but as you're listening in, I think one thing that by looking at large data sets such as what urologic diseases can do, it can identify new questions to ask. And that's something that both Ryan and I will be sharing as we read these data.
- Brian Matlaga, MD: As we all know, kidney stones, there is almost always going to be a diagnostic test that's going to confirm the presence of a kidney stone, and it's going to be some form of a radiographic imaging study. And so with claims data, which is essentially what we're using with Medicare and with Optum, we can look at how imaging testing is utilized among patients with kidney stones. And that's exactly what we did. We wanted to understand ... We broke the imaging tests into different categories. So we broke them into CT imaging, plain x-ray imaging, such as a KUB exam, ultrasound, and then test that we knew would be less commonly utilized, but still would be interesting to look at, and that would be things like intravenous pyelography and magnetic resonance imaging.
- Brian Matlaga, MD: And we wanted to understand over time how or have practice patterns changed. And as we looked at the imaging data, both in Medicare and in Optum there are several striking findings. And initially, we'll restrict our discussion just to the adult population, and what we found was that CT imaging for both the working age population, as well as the over 65 population, the Medicare cohort CT imaging was by far the most commonly utilized imaging study for patients with stone disease. About much greater than ultrasound, for example, utilized almost twice as often, actually, as ultrasound was. In the United States, CT imaging is the cornerstone or foundation imaging test for stone formers.
- Brian Matlaga, MD: After CT imaging, the second most commonly utilized is actually plain radiography. It's not ultrasound. Ultrasound is the third most commonly utilized test. And all of the data we're sharing today, they reside in a compendium, and that's available on the NIDDK's website. It's very easy to find. You can just put in a browser search bar, "NIDDK urologic diseases in America". It'll take you to the site. And there's an expanded compendium that presents all of these data and other data. But as you look at the charts and figures associated with imaging, you'll see the lines are very flat. CT imaging is the most commonly utilized, all that plain radiography, followed by ultrasound.
- Brian Matlaga, MD: And it's not changing over time. And that's probably disappointing to many of us because we know that less exposure to ionizing radiation is better, just as a principle. And we know that at this point there's likely overutilization of CT imaging for the diagnosis of stones. And there is efforts spent on the part of American Urological Association with multiple educational initiatives, as well as other groups trying to grow provider's comfort with ultrasound as an imaging modality. And we just haven't yet seen traction of it in the adult population. And again, we're using CT imaging twofold greater than we are using ultrasound imaging. And now again, our data stopped in the mid 2000 and teens. And so as we hope to, with your urologic diseases in America, look at more recent data, one hope is that we may start to see an inflection point with increased utilization of ultrasound.

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- Brian Matlaga, MD: Now, as we talked about in the prevalence discussion that we looked at the pediatric population, we also looked at the pediatric population when it came to diagnostics. And this was I think, a little bit of a more happier story if you will, or more satisfying story, meaning that we did actually see that although at the initial years we studied, so in the mid 2000s, CT was utilized quite commonly. Ultrasound had a very positive slope, meaning that ultrasound was increased in utilization and eventually became more commonly utilized in CT. So in the pediatric cohorts, we are seeing a movement away from CT as the dominant imaging modality. And so our hope is that as further educational initiatives, training efforts are brought out to the urologic community, that we will see in the adult population, perhaps some movements away from CT towards ultrasound as more of a mainstay or staple diagnostic modality.
- Brian Matlaga, MD: And then moving from diagnostic to actual the therapeutics, Ryan, I'll ask you to share your thoughts on the therapies for patients with stone disease.
- Ryan Hsi, MD: Thanks, Brian. I think one of the things that we get from these types of claims-based data is we get a pretty confident estimate of the surgeries that are produced for kidney stone disease. As you know, primarily these are going to be shockwave lithotripsy, ureteroscopy and percutaneous stone procedures. And overall, what we saw was that surgical procedures for kidney stone disease increased overall during this time period. But the percentage of kidney stone patients undergoing surgery has declined. And we'll get to this later, and that some patients will get second procedures or second stage procedures. And this may reflect also, improved surgical outcomes, or it may reflect that perhaps we are observing more stones than we used to.
- Ryan Hsi, MD: And we also found that there was a trend towards more ambulatory surgery and ambulatory care. And among the ambulatory surgeries performed, there was an overall rise in ureteroscopy utilization and less reliance in shockwave lithotripsy. In fact, ureteroscopy has now become the dominant stone procedure overall. And there may be different reasons for this. As we know, the AUA guidelines include all three techniques, but ureteroscopy seems to be very versatile for most stone sizes and locations. And during the same time period, we know that there's been many improvements in technique, newer generation reader scopes, newer lasers, advances in baskets and other disposable tools and sheets.
- Ryan Hsi, MD: We also found that percutaneous nephrolithotomy was relatively stable and utilization across these [inaudible 00:18:19], very uncommonly used, approximately 1% of all stone patients. And as expected, the percutaneous nephrolithotomy procedures were performed in the inpatient setting. We did start to see some more and more ambulatory procedures performed. Although again, the vast majority were shocked with lithotripsy and ureteroscopy procedures.
- Brian Matlaga, MD: And that's what struck me as well, is that just how in the United States, especially as we compare it to other healthcare systems across the globe, percutaneous nephrolithotomy is a very seldomly performed procedure. And it gets back into, I know the group from Michigan has looked at this years ago of the idea of is there some even centralization or regionalization of care when it comes to the procedures such as percutaneous nephrolithotomy. And what we found when we looked in the pediatric population was also analogous to the adult population, that ureteroscopy was also the dominant form of surgical therapy. And I certainly was surprised by that. It's classic, almost dogma, that we learn as we go through training that children tend to do very well, even perhaps better than adults when treated with shockwave lithotripsy.

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- Brian Matlaga, MD: And certainly the AUA's surgical managements of stones guidelines document, when you look at the source data for it, that was reinforced by the source data also. But when you actually look at what is the clinical practice, ureteroscopy is utilized more commonly in that pediatric population. And it could be, as you said, Ryan, that as the technology has increased, [inaudible 00:20:16]scopes are more miniaturized. And plus, that we know from prevalence that it tends to be a condition that manifests more commonly in the teenage years, that it may be the smaller scopes, plus larger children may align better for ureteroscopy, but that was something in the pediatric population that certainly struck me.
- Brian Matlaga, MD: The other therapy besides surgical therapy, is obviously medical therapy. And as I said at the beginning of the podcast, the great thing of this iteration of the Urologic Diseases Project is that we have access to pharmacy benefits information, or essentially pharmaceutical utilization in the Medicare population and in the Optum population. And so as we look at what pharmacotherapies are used for stone disease, I'll be clear there are some challenges in that data set. For example, we know that certain agents like biocide diuretics may be used for medical therapy, for example, for patients with hypercalcemia. But those agents are also used as a blood pressure control agent. So we weren't able to get data about some types of medical therapies associated with stone disease, because there is some contamination of the data, but there are other agents that we are able to get, especially when they're prescribed around the time of a stone event.
- Brian Matlaga, MD: And those agents that I thought were particularly interesting as we looked at were alpha blockers and then opioid agents. And we'll talk about the alpha blockers first. And so our data went from 2006 up to 2013. And what we found over that period is that corresponds to the time when there is emerging evidence that utilization of alpha blockers may promote the passage of certain ureteral stones. Now we know now at present, based on two well performed randomized controlled trials, one from the United States, one from United Kingdom, fairly convincingly have shown us that alpha blockers are not effective in medical expulsive therapy. But if we look at these data, this was in a time before those randomized controlled trials existed, we saw that there was progressive increase in utilization of alpha blocker agents prescribed in the setting of a stone event. And so these were obviously agents that were utilized, or likely agents that were used for medical expulsive therapy.
- Brian Matlaga, MD: Presumably if we were to now carry the data into 2020, we would see hopefully a declining utilization, which again, reflects what the clinical evidence tells us. But I think that's a very interesting question for the next data review for the Urologic Diseases in America, as we look at stone disease again. But I think the more striking medication agents that is prescribed in the setting of a stone event is opioids. Obviously, no news to any of us who live in the United States, that there is an opioid epidemic, if you want to term it that, but there's a great utilization of opioid agents in a problematic way in this country. And it's made us turn our attention to just how we're using these agents in the treatment of patients with conditions, such as stone disease, where we know there is pain associated with it.
- Brian Matlaga, MD: And what we've found is that opioids are by far the most commonly utilized agents for adult stone formers, both in the Medicare population, as well as in the Optum population, the privately insured cohort. And it's a positive slope, unfortunately in both groups that each year, there's greater utilization of opioid agents than there was in the year previous to it. And so this is obviously a very concerning trend to all of us in the urologic community. And it points out an

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area, and again, we'll talk about this in the take home message, but this is an area where probably we can take away some point from this that there's a way to improve the care we're delivering to move away from this tremendous utilization of opioid agents that we've found among stone formers.

Brian Matlaga, MD: When we look at the pediatric population again, the pediatric population hopefully is a bit of a bellwether in all of this, because we do see that, although there is high utilization of opioids in the pediatric population that has somewhat stabilized and maybe beginning to decline. So similar to how the pediatric population seems to have taken up the mantle of ultrasound as a diagnostic earlier than in the adult population, our hope is that with this opioid, that we start to see trends away from utilization of these agents among the stone formers. I think now this brings us to a good point. We've talked about diagnostics, we've talked about therapeutics, and then the next discussion is what about outcomes of treatment? And so Ryan, I'll let you share with what you found about treatment outcomes.

Ryan Hsi, MD: Great. Brian, as you mentioned before, I think the value of these data sets is that we can assess the effectiveness of kidney stone management over time. And so a couple points that I found interesting was that not only do people get diagnostics and treatment, but they get multiple episodes of treatment and care over time. So for example, between 2009 and 2013, 70% of kidney stone patients had at least one imaging study, but up to 5% had 10 to 19 of these imaging studies. Another example is that about a third, or 30%, of patients between 2009 and 2013 had a least one ER visit, but many had more, 7% had two and 3% had three or more ER visits. And so we get to see these trends and potentially who is at risk.

Ryan Hsi, MD: We also get data on retreatment rates. And we talked about surgeries and procedures earlier, but what we found that retreatment for kidney stone procedures was most commonly observed after PCNL. This, I think, was expected. Oftentimes we do second look procedures, and this is often planned after PCNL. And I think many people would get CT scans while patients are hospitalized overnight to look for residual fragments. But I think what was striking about this data was that there were very high retreatment rates after shockwave lithotripsy ureteroscopy. And so for ureteroscopy, this was about 26% retreatment rate within 120 days. And this was about 32% for ureteroscopy within 120 days.

Ryan Hsi, MD: I'm not quite sure what's driving these high retreatment rates. We know that both procedures have residual fragments, there's a risk for that. And that the literature suggests that the outcomes for ureteroscopy are superior than shockwave lithotripsy, so we would have expected less real treatment for ureteroscopy. And so this may be because that perhaps urologists are increasingly treating more complex stones. Ureteroscopy for the reasons I mentioned before, as it's a versatile procedure, or maybe there's a publication by some prior studies and this is the true what we're seeing in practice.

Brian Matlaga, MD: Yeah. That captures the essence of it when we talk about the outcomes. And the great thing with these administrative data sets is we can begin to identify patterns, such as what you just described. And then as we start to peel back the layers to try to then understand what do the patterns reflect and we lose some granularity and that then brings us to the next set of questions, if you will, that can be answered. And I think that's a very natural segue into what our thoughts at least are some of the take home messages. And I'm sure anyone who's listening will have other thoughts too. And I would encourage anyone to go to the NIDDK website, actually

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download the compendium, it's just a large PDF, but it's incredibly comprehensive and has way more data than what we're able to share in a 20 minute podcast episode.

Brian Matlaga, MD: And that's something I think that again, as I see the value of Urologic Diseases, one of its roles is to help identify what are the questions that we want to ask. And I think, Ryan, you and I can just go through a couple of points. One thing that struck me, I'll just throw this out there to begin with is that we're using ionizing radiation to a great extent among stone formers. And that probably is an opportunity for, whether it's process improvement or care pathway improvement, but I would say that in an ideal world, something should shift and we should start to see increasing utilization of modalities, such as ultrasound and perhaps decreasing utilization of something like CT. Ryan, what would your thoughts be on another area of interest?

Ryan Hsi, MD: I thought the UDA datasets and this effort helps shine the light on the burden of disease. And I think also, in this data set that we didn't have a chance to mention as some of the costs. So not only the burden and the prevalence of disease, but also the cost burdens. I also think that we saw not only in the adult and pediatric population, that there was a rise in the dominance of ureteroscopy over time, over shockwave lithotripsy and percutaneous nephrolithotomy.

Brian Matlaga, MD: Yeah. And that's something that's remarkable. And then when you start to break it down into the other populations, especially in the pediatric population where ureteroscopy has replaced shockwave as the treatment of choice, it seems, but yet that hasn't yet been reflected in the literature. And it's just, as you said, Ryan, there may be a publication bias towards that, or perhaps something else driving it.

Brian Matlaga, MD: One other factor that struck me was the utilization of opioids, and this is likely a phenomenon of the United States. I think if there's international listeners, this probably won't resonate as much, but certainly to all urologists who are practicing United States that there's a tremendous utilization, probably overutilization to be honest, of opioids for stone formers. And that's, again, an opportunity for care improvements going forward.

Ryan Hsi, MD: I also thought that it was interesting that retreatment rates were much higher than I had expected. And I think what we're seeing is practice patterns and outcomes across the United States, not just at what we see in publications. And this is what's happening in the real world. That up to a third of patients after ureteroscopy, shockwave lithotripsy have a retreatment within 120 days. I thought that was remarkable.

Brian Matlaga, MD: Yeah, I agree. And we've been discussing the Urologic Diseases Project is a tremendous project. It's very visionary by the NIDDK to support it. And what are the goals of the project? And I think it's to create, one, an awareness of what is, as you termed it, the burden of disease. And then also, what are opportunities where care can be improved, where questions can be asked? It helps with some of the genesis of discovery in the field, which ultimately leads to improved outcomes for our patients. And I think that we've highlighted just a couple of areas and it's very much scratching the surface of areas that could inform future projects, grant proposals that are going to have meaningful changes to actually how care is being delivered, not at expert centers of excellence, which tends to be what we see in publications, but rather at what's going on, on a day to day basis in the urologic community with regards to treatment.

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- Brian Matlaga, MD: And one of my goals with Urologic Diseases in America is to have this serve as essentially the reference point for that scope of the problem question that always comes up in a grant application. And so I think that as the listeners, hopefully you go to the compendium and peel back a few more layers of the project. You can see what those data are and what opportunities for questions exist. I'd like to, before I close it out, Ryan, do you have any other closing thoughts?
- Ryan Hsi, MD: No. Brian, thank you for including me. I think this really motivates me to think of other projects and to address some of these treatment gaps. So thank you for including me.
- Brian Matlaga, MD: Yeah. And Ryan, thank you very much for being a part of this project. It's a great opportunity to work with you. And of course, I'd like to thank Dr. Kevin Abbott, Dr. Ziya Kirkali, Dr. Tamara Bavendam from the NIDDK, who have supported with their leadership and vision, this project, and Lydia Feinstein, Julia Ward from Social Scientific Systems who provided all the analytics support for this project. It's obviously a large, heavy lift and there's lots of people that worked on it.
- Brian Matlaga, MD: And then of course, I think one of the great successes in the past year with Urologic Diseases in America Project is our partnership with the American Urological Association in supporting our efforts to disseminate these findings, to broadcast them to the urologic community, through podcasts and forums at various meetings. And that's something that the American Urological Association has been a tremendous partner with us for. And so I just want to thank the AUA for that.
- Brian Matlaga, MD: And I hope this was an informative 20 or so minutes that you spent with us. And again, if there's questions or interest from this, I would encourage you to go to the NIDDK website, look at the compendium for this, for stone disease, as well as BPH urinary incontinence, the other conditions we discussed through prior podcasts, and then there'll be other urologic conditions coming to that website as well. So again, it's easy to find just on any search bar, if you type in "NIDDK Urologic Diseases in America," it'll be the first link that pops up. So thank you again for joining us. And I hope this was informative.