Exhibit 430

Consultation to The Department of Justice

Re: Jacqueline J. Tukes
DOB: [redacted]1965

Dear Attorneys and Staff of the United States Department of Justice,

I have reviewed primary and summary documents for Mrs. Jacqueline J. Tukes regarding her chronic kidney disease. She is the wife of Marine Corp veteran Willie Lee Tukes, and as his spouse, she lived at Camp Lejune for over 1 year, from 12/17/1985 – 1/8/1987; she may have also resided or spent time on-base at Camp Lejeune for intermittent periods from 6/1985 to 12/1985. She developed chronic kidney disease over the course of thirteen years. I have been asked to provide my opinions on her condition, including her kidney function, life expectancy, and need for future care. She is seeking judgement against the US Government for her kidney disease.

This opinion includes 5 sections:

1) My qualifications, on which this opinion is based.
2) An explanation of kidney function, chronic kidney disease, dialysis, and kidney transplantation.
3) A description of Mrs. Tukes's clinical history.
4) My overall conclusions on kidney function for Mrs. Tukes, following her kidney transplant, including her life expectancy and need for future care.
5) Responses to the report of Dr. Matthew Cooper.

1. My qualifications to serve as an expert witness.

I have been a practicing nephrologist for nearly 20 years. I am currently the Clinical Director of Nephrology and Associate Professor in the Department of Medicine at the University of Kansas. In this position, I am responsible for the care of patients with kidney disease at the University of Kansas Hospital, including oversight of hospitalized patients, evaluation of outpatients with kidney disease, with a goal of delaying or preventing progression, or patients with rare electrolyte disorders, care of patients on dialysis, quality

improvement initiatives regarding these patients, and involvement with the teaching of nephrology to students and resident physicians.

My professional affiliations include the American Society of Nephrology, the National Kidney Foundation, the American College of Physicians, and the Renal Physicians Association. I have authored over 25 journal articles, a book chapter, edited the Nephrology syllabus for the University of Pittsburgh Medical School, and served as a peer reviewer for professional journals and for annual meetings of the American Society of Nephrology and the American College of Physicians. My education included Harvard College with a degree in History and Science, a combined MD and PhD degree from the University of Washington, Medicine Residency at Northwestern University, Nephrology Fellowship training at the University of Michigan, and then faculty appointments at the University of Michigan, the University of Pennsylvania, Temple University, the University of Pittsburgh, and the University of Buffalo.

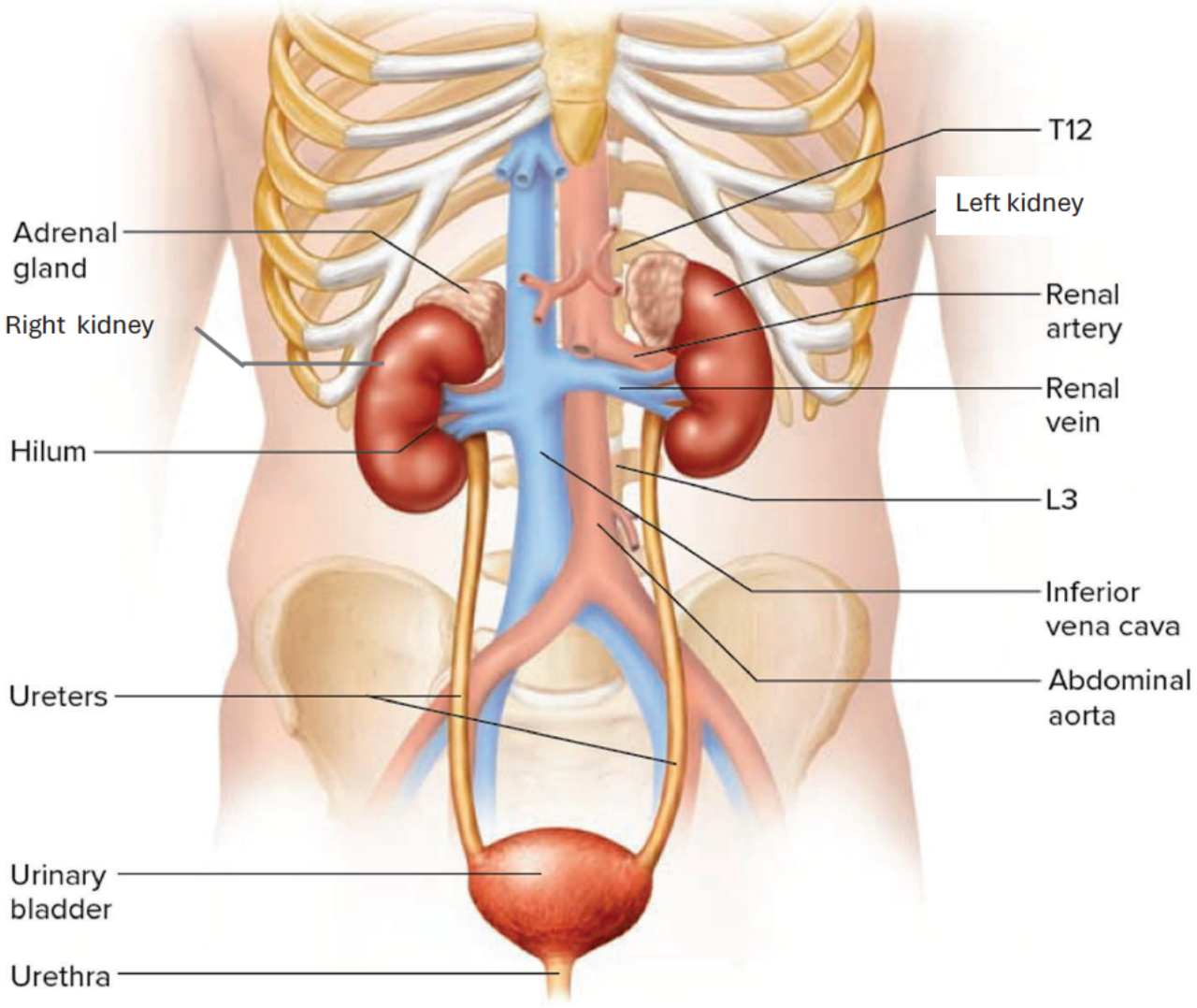
I have received awards for Teaching and Clinical Service from the University of Pennsylvania, four from Temple University, and two from the University of Pittsburgh. My clinical area of expertise is glomerular disease, but I have never placed limits on who I will see in clinic. I have cared for patients with kidney stones, electrolyte disorders, chronic kidney disease caused by common or rare disorders, patients receiving hemodialysis in clinic, dialysis patients receiving home therapy, and recipients of kidney transplants. In summary, based on my training and professional experience, I feel qualified to discuss kidney disease across a wide spectrum.

I am being charging $850/hour for my work on this matter. I have not testified at trial or by deposition in the previous four years. I reserve the right to supplement my opinions in light of new information.

2. General Introduction of kidney function, chronic kidney disease, dialysis, and kidney transplantation.

2a. What do kidneys really do?

We have two kidneys, each about the size of a clenched fist. Our kidneys are shaped- not surprisingly- like kidney beans. Both kidneys are located in the upper retroperitoneum, which roughly means- as shown in the picture below, in your mid-back, behind the stomach and intestines, on either side of the aorta and inferior vena cava, which are the largest blood vessels in the body.



Each kidney filters your blood, every minute of every day, to accomplish two basic tasks: to keep your blood and all the cells of your body in a stable balance of salts and water, and to remove toxins and waste products from your body (in cooperation with the liver). To maintain chemical balance, your kidneys sense what is happening in your body and respond accordingly, to keep the concentration of multiple salts and acid-base level within your blood stable. For example, if you are walking on a hot day and losing water and sodium, your brain and kidneys sense these losses, and the kidneys respond by holding onto as much

water and sodium as possible. If your blood is too high or too low in potassium, calcium, magnesium, phosphorous, or alkali, your kidneys will sense these changes and respond accordingly to bring you abnormal level back into balance. If you drink a half-gallon of water that you do not really "need," your brain and kidneys sense that your blood is becoming dilute, and your kidneys will dump all the excess water quickly as dilute urine. If you eat salted jerky, your kidneys will dump the excess sodium, sulfates, and phosphates in urine. In the end, no matter what is coming into your body through eating and drinking, or being removed from your body through sweating, diarrhea, vomiting, bleeding, and more, the kidneys sense and respond to changes in blood chemistry to keep our bodies in balance.

To understand the second task of toxin removal, it may come as a surprise that most of the toxins and waste products removed by your kidneys every day come from your own metabolism. When cells make energy, build proteins, synthesize new DNA, and carry out all cellular metabolic functions, the biological chemistry involved in these processes creates waste products that must be removed. A single-cell organism excretes these waste products into the environment around them, whereas people excrete metabolic waste products from cells into the blood. Once in the blood, most metabolic waste products and other toxins are removed from our bodies by the kidney, liver or by the cooperative action of both organs. Once the waste products are small-sized and electrically charged, they are easily filtered by kidneys and excreted in urine.

Separate from their work maintaining balance of water and electrolytes, and removing waste products from your body, your kidneys also regulate other organs in your body. First, if you become anemic and your body needs to make more red blood cells, this is sensed by special cells in the kidney that release the hormone erythropoietin, which in turn tells your bone marrow to make new red blood cells. When your anemia resolves, the kidneys turn down release of erythropoietin to avoid making your blood too thick. Second, your kidneys regulate your skeleton, including the main components of bones, which are calcium and phosphate. To accomplish this, the kidney makes the enzyme that converts the storage form of vitamin D into the biologically active form (1,25 dihydroxy vitamin D), which increases reabsorption of calcium from urine, increases absorption of dietary calcium and phosphorous from intestines, and increases the activity of osteoclasts, which "chew holes" in bone to release more calcium and phosphorous. The kidneys also sense and regulate the amount of calcium and phosphorous we reabsorb from urinary filtrate directly, without vitamin D. Third, your kidneys are considered part of your immune system because they synthesize molecules that are part of our response to infection, inflammation, and trauma, including colony stimulating factor, interleukin1, and tumor necrosis factor. Lastly, the kidneys convert certain amino acids into glucose, which is critical because our brain cells only use glucose for energy. Many people think the liver is the only organ that creates glucose for our brains, but the kidney can produce up to 50% of glucose production.

In summary, when kidneys are healthy, they work 24-hours per day, 7 days a week to regulate and stabilize the water and electrolyte concentrations in our blood, to remove metabolic waste products and toxins from our blood, to instruct other organs what to do, including our bone marrow, skeleton, intestines, and inflammatory system, and to produce glucose for our brain cells.

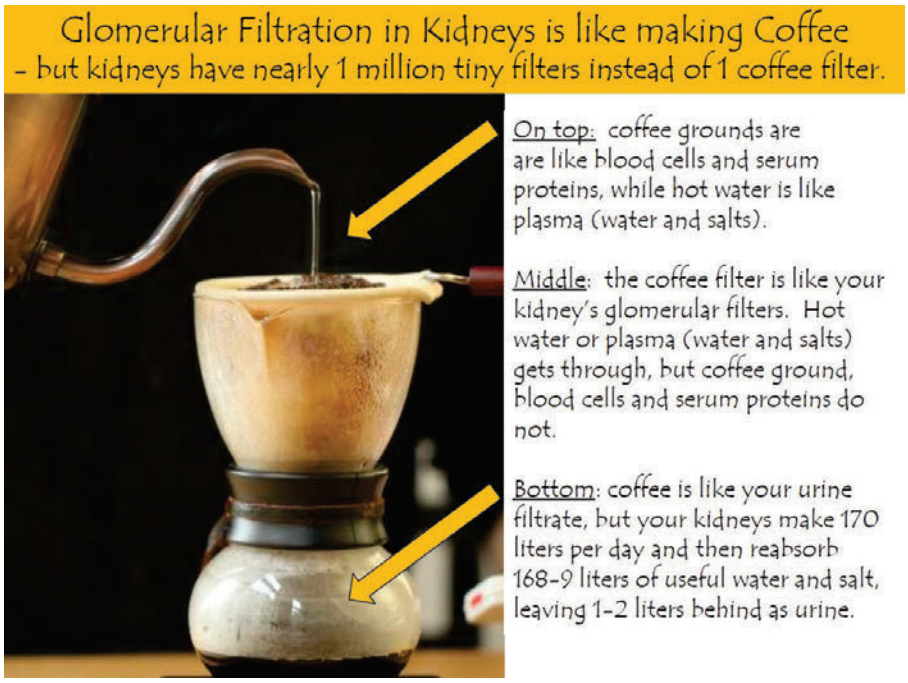
2b. What is Chronic Kidney Disease?

Chronic kidney disease (CKD) arises when kidneys lose function due to disease, aging, or other circumstances. Patients who are referred by their primary doctors for chronic kidney disease often protest that they are still making plenty of urine, but we can make a normal amount of urine with only 1-2 % of

normal kidney function, as is true for some patients on dialysis. Understanding what we mean by kidney function helps appreciate the stages of chronic kidney disease.

Kidneys make urine in two basic steps. In the first step, the heart pumps a large amount of blood to kidneys through the renal arteries, which branch out into many thousands of smaller blood vessels, eventually branching into nearly 1 million capillaries called glomeruli, which filter the blood. The amount of blood that is filtered by our kidneys is huge, about 172 liters, or 45 gallons of urinary filtrate each day. This raw urine filtrate is then processed through renal tubules, which reabsorb everything from the filtrate that is useful, and excrete a few more toxins through secretion. The vast majority of salt water in the filtrate is useful and is reabsorbed by tubules. At the end of these long tubules, everything that has not been reabsorbed becomes our urine, which includes excess water and salts, unwanted metabolic waste products, and other toxins.

This first step, when the kidneys filter blood in glomeruli to create a large volume of filtrate is what we mean by "kidney function," and it is also called the glomerular filtration rate, or GFR. To understand glomerular filtration, imagine a drip-coffee maker as shown in the figure below, with coffee grounds and hot water on top, a coffee filter in the middle, and a filtrate of coffee on the bottom. Our kidneys filter blood within glomeruli similar to a coffee maker. Our blood has plasma, akin to hot water, that will be pushed across the filter under pressure, and our blood has serum proteins and blood cells, akin to coffee grounds, that should not cross the filter.



The glomerular filter is composed of special proteins in a matrix and lets water and small molecules through but keeps large proteins and large cells within the blood. Kidney function refers to the rate at which all glomeruli in both kidneys filter blood, and collectively, if our glomeruli make about 172 liters of filtrate per day, then our normal glomerular filtration rate (GFR), or normal kidney function, is 120 milliliters per minute.

2c. Kidney Function and the Stages of Chronic Kidney Disease:

Chronic kidney disease (CKD) is divided into stages of severity based, primarily, on kidney function, and secondarily on the amount of albumin in urine. To appreciate how kidney function is related to the stages of

CKD, consider the drip coffee maker for comparison. If a coffee machine normally makes 1 cup per minute, but a damaged coffee machine makes only ½ cup per minute, then the machine is working at only 50% function and is moderately "diseased." A coffee machine that makes only ¼ cup per minute is working at only 25% function and is severely "diseased."

We divide chronic kidney disease into stages of severity according to kidney function as follows (remembering that a normal glomerular filtration rate, or GFR, is 120 mL per minute):

- Stage 1 CKD (or stage G1): GFR 90-120 mL/min (75-100% of normal kidney function).
- Stage 2 CKD (or G2): GFR of 60-89 mL/min (50%- 75% kidney function).
- Stage 3 CKD (or G3): GFR of 30-59 mL/min (25%-50% kidney function).
- Stage 3 is subdivided into Stage 3a (G3a): GFR 45-59 mL/min.
  And Stage 3b (G3b): GFR 30-44 mL/min.
- Stage 4 CKD (or G4): GFR 15-29 mL/min (12.5% to 25% kidney function).
- Stage 5 CKD (or G5): GFR less than 15 mL/min (less than 12.5% kidney function).
- End Stage Kidney Disease (ESRD): patients who start dialysis or receive a kidney transplant.

GFR can be measured directly, but this is difficult, invasive, and rarely done in clinical practice. More often, we "estimate" GFR based on the level of creatinine in blood (eGFR). Creatinine is produced by active, healthy muscle cells release creatine into blood, where it is converted to creatinine and then removed from blood by the kidneys, primarily by glomerular filtration. If the level of creatinine in blood is rising, then kidney function is falling (with rare exceptions). There are additional considerations, because muscle mass can increase with exercise or decrease with malnutrition or illness, and the kidneys also remove creatinine from blood by tubular secretion, which can contribute 10-30% of total creatinine clearance, and this tubular secretion is separate from kidney function based on glomerular filtration. Nevertheless, as long as the level of creatinine in your blood is stable (an important requirement that we call "the steady state") then by measuring your blood creatinine level, we can estimate your kidney function / glomerular filtration rate (GFR) fairly accurately. These estimates of kidney function are not valid if we know only a single value of creatinine, as discussed below.

The second component to determining CKD stage is the amount of protein in the urine, or specifically the amount of albumin in urine. Albumin is the most common protein in blood. Even with a normal, healthy glomerular filter, a small albumin of albumin leaks across the glomerular filter from blood into the urine filtrate, and our kidneys reabsorb the majority of albumin that gets through, but a tiny amount of albumin is always left behind in normal urine (about 15-30 milligrams per day). If we see higher amounts of albumin in urine, the primary reason is excessive leakage across a diseased glomerular filter. Using drip coffee as an analogy again, if we poke holes in a coffee filter with a pencil, then coffee grounds will leak into our cup of coffee, and the more coffee grounds we find in our coffee, the worse the damage must have been to the coffee filter. Similarly, if we see excessive albumin in urine, then kidney disease must be creating microscopic "holes" in the glomerular filter. To account for the process of urine concentration, which occurs in the kidney after blood is filtered, we measure the ratio of albumin to creatinine in urine (ACR). A normal ACR is less than 15 to 30 mg of albumin per gram creatinine in the urine and is classified as "A1." A moderately elevated urine ACR of 30 to 300 mg/gram is classified as "A2," and a high urine ACR of more than 300mg/gram is "A3." Extremely high urine ACR of 3000mg/gram and more is termed "nephrotic range," and is a subset of severe kidney disease. Combining kidney function/GFR with urine albumin leakage, there are 15 stages of chronic kidney disease: CKD stage G1-G5 based on the GFR, each of which

is divided by urine ACR into A1-A3. This combined CKD stage is important because it predicts, at a population level, three important outcomes:

1. The likelihood a patient with CKD will progress to end-stage kidney disease.
2. The likelihood a patient with CKD will have a major adverse cardiac event, such as heart attack or new heart failure, which are closely associated with kidney disease severity.
3. The likelihood a patient with CKD will die from any cause, which increases with kidney disease severity.

The figure below, for example, is a "heat map" showing the Relative Risk of progression to End Stage Kidney Disease.[1] Green boxes indicate no statistical difference in risk compared to people with normal kidney function, yellow boxes indicate moderate risk, orange indicates high risk, and red alerts to a very high risk. The precise relative risk varies a bit from study to study. To provide one example, in the 2013 publication of the CKD consortium, patients with CKD stage G3aA1 with low urine protein (yellow box) had a relative risk of ESKD of 5.2, meaning that ESKD is expected 5.2 times as frequently as people with similar medical problems who have normal kidney function. Patients in the same study with equivalent kidney function but high urine protein (CKD stage G3aA3, red box on the same row), had a relative risk of 147, meaning that ESKD is expected 147 times more frequently as people with similar medical problems and normal kidney function.[2]

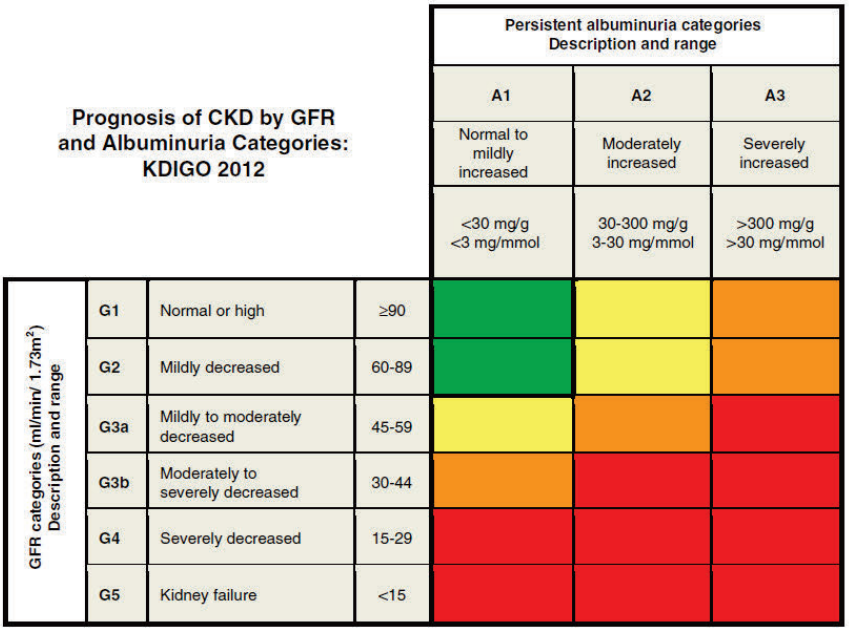


Figure 9 | Prognosis of CKD by GFR and albuminuria category. Green, low risk (if no other markers of kidney disease, no CKD); Yellow, moderately increased risk; Orange, high risk; Red, very high risk. CKD, chronic kidney disease; GFR, glomerular filtration rate; KDIGO, Kidney Disease: Improving Global Outcomes. Modified with permission from Macmillan Publishers Ltd: *Kidney International*. Levey AS, de Jong PE, Coresh J, et al.[30] The definition, classification, and prognosis of chronic kidney disease: a KDIGO controversies conference report. Kidney Int 2011; 80: 17-28; accessed http://www.nature.com/ki/journal/v80/n1/full/ki2010483a.html

Recent research has helped to create a clinical tool, the Kidney Failure Risk Equation (KFRE) that can estimate the absolute risk for that a patient with CKD will progress to End Stage Kidney Disease, based on

[1] KDIGO Guideline for Chronic Kidney Disease. Kidney International Supplements (2013) 3, 1; doi:10.1038/kisup.2012.73

[2] Matsushita K, et. al., "Cohort Profile: The Chronic Kidney Disease Prognosis Consortium," International Journal of Epidemiology 2013;42:1660–1668. doi:10.1093/ije/dys173.

stable measurements of serum creatinine and urine ACR.[3] The KFRE is most accurate for a population of people, and most accurate for common causes of kidney disease, but with the understanding that the tool is only an estimate, it has helped with clinical decision making. For example, a 65-year-old man with CKD stage 3a, eGFR 50 cc/min and a normal urine ACR of 20 mg/g has only a 0.25% chance of progressing to End Stage in 2 years, and only 0.79% of progressing to End Stage in 5 years. In comparison, a 50-year-old woman with diabetes and eGFR 29 cc/min and urine ACR 350 mg/g has a 28.02% chance of being on dialysis in 5 years.

2d. Important details on how we correctly determine the Stage of Chronic Kidney Disease.

The diagnosis of CKD requires a person to have a persistently elevated creatinine, or excessive albumin in the urine, or both, for at least 3 months. A single, elevated level of creatinine is never sufficient to diagnose chronic kidney disease, because a person may have acute kidney injury, which most often heals (just like a cut with a kitchen knife can heal). Acute kidney injury is different than chronic kidney disease with respect to causes, the chance for full recovery of kidney function, and the associated risks of illness and death. In fact, serum creatinine must be stable for at least several days in order to use the creatinine-based equations that estimate kidney function.

To illustrate this, pretend that I have normal kidney function, with serum creatinine of 1 mg/dL, and I am on an operating table. If someone clamps off both of my kidneys, my kidney function at that point becomes zero. Five minutes later, a blood test will show my serum creatinine is barely above 1mg/dL, and IF this level were stable, the estimating equations would say that I have normal kidney function. However, at the time of this blood test, my actual kidney function is zero, so the equation is grossly overestimating my kidney function. Twelve hours later, my creatinine would be 1.5 and the equation might estimate a kidney function of 60%. Twenty-four hours later, my creatinine would be 2.0 and the equation might estimate kidney function of 40%, but still these are incorrect overestimates of actual kidney function (which is 0%), and the estimating equations should not be used, because the serum creatinine is still rising from one day to the next. To reverse this thought process, if the creatinine rose to 10 and then clamps were removed, my kidney function would start to heal and recover. If the creatinine fell from 10 to 8 mg/dL in one day, we might estimate that I have a GFR of 7 cc/min or about 6% normal kidney function, but this would be true only if my creatinine stays at 8. If the creatinine keeps improving each day, then my actual kidney function is much better than 6% (and we cannot use the estimating equations until the healing is complete and my creatinine is stable again).

Even if serum creatinine is stable, it is not a perfect test of kidney function. First, some medications including trimethoprim, cimetidine, and cyclin-dependent kinase inhibitors such as palbociclib can raise serum creatinine by blocking tubular secretion without changing actual kidney function/glomerular filtration, leading to a falsely low estimate of GFR and a false impression of kidney disease. Second, people with high or low extremes of muscle mass or muscle metabolism will generate atypically high amounts of creatinine in the blood, leading to an erroneous impression that they have kidney disease. Conversely, a patient who has lost muscle mass from Lou Gehrig's disease or a similar condition might have moderately severe kidney disease, but their serum creatinine could be normal, resulting in false reassurance about their kidney function. Kidney function can be measured without using creatinine by measuring the rate of clearance from blood of inulin, iothalamate, or iohexol, but these tests are difficult, may require

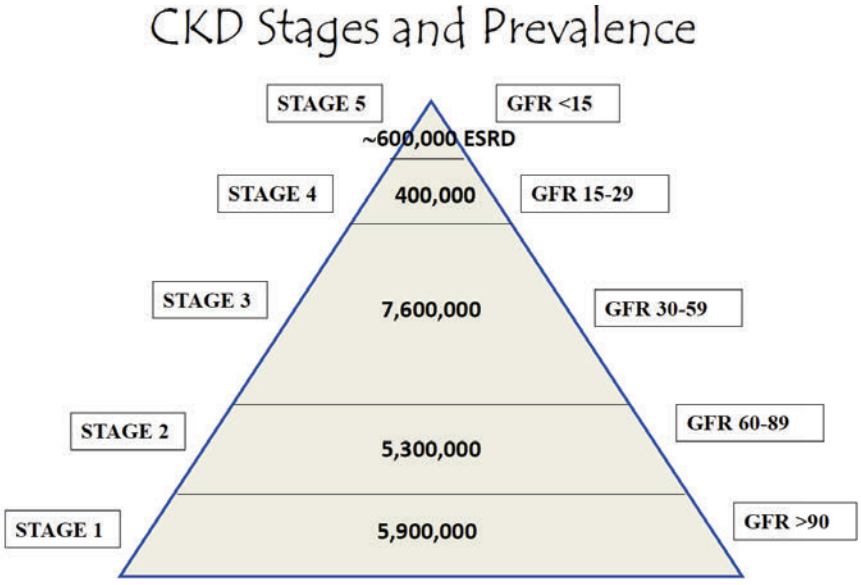
[3] Tangri N, et al, "A Predictive Model for Progression of Chronic Kidney Disease to Kidney Failure." *JAMA. 2011;305(15):1553-1559*. doi:10.1001/jama.2011.451.

radionuclides, and are usually reserved for clinical research only. In recent years, blood testing of cystatin-C has become a favored alternative to creatinine for estimating kidney function. The level of cystatin-C in blood is much less dependent on muscle mass and has fewer interactions with medications. Cystatin-C can be falsely high in patients with inflammation, so it is not a perfect test, but it is a convenient and increasingly available alternative to serum creatinine for estimating the presence and severity of CKD.

2e: The Prevalence of Chronic Kidney Disease.

It is quite common to have a modest elevation in creatinine with age over 40-45, as will be discussed in additional later, and the result is that mild-moderate CKD is quite common in the general population. From recent statistics, 14% of adults in the USA (1 in 7) have CKD, mostly at mild-moderate stages.[4] Because mild-moderate CKD has no symptoms, up to 90% of adults with CKD are not aware they have kidney disease, and even with severe CKD (stages 4-5), 30% of adults are not aware they have kidney disease due to lack of symptoms.

The prevalence of each stage of CKD in the USA can be illustrated with a Pyramid diagram, as shown below. The base of the pyramid is widest for CKD stage 1 to illustrate the largest number of affected patients, and at each stage of increasing severity, the pyramid narrows, to illustrate that fewer people are affected (the prevalence is lower). Severe CKD (stages 4-5) is less prevalent/common than milder stages for two reasons: first, some forms of kidney disease tend to progress very slowly and do not reach higher stage before someone reaches the end of life; second, patients with CKD stages 4 & 5 have high cardiovascular risks and may pass away from stroke or heart attack before reaching End Stage Kidney Disease.

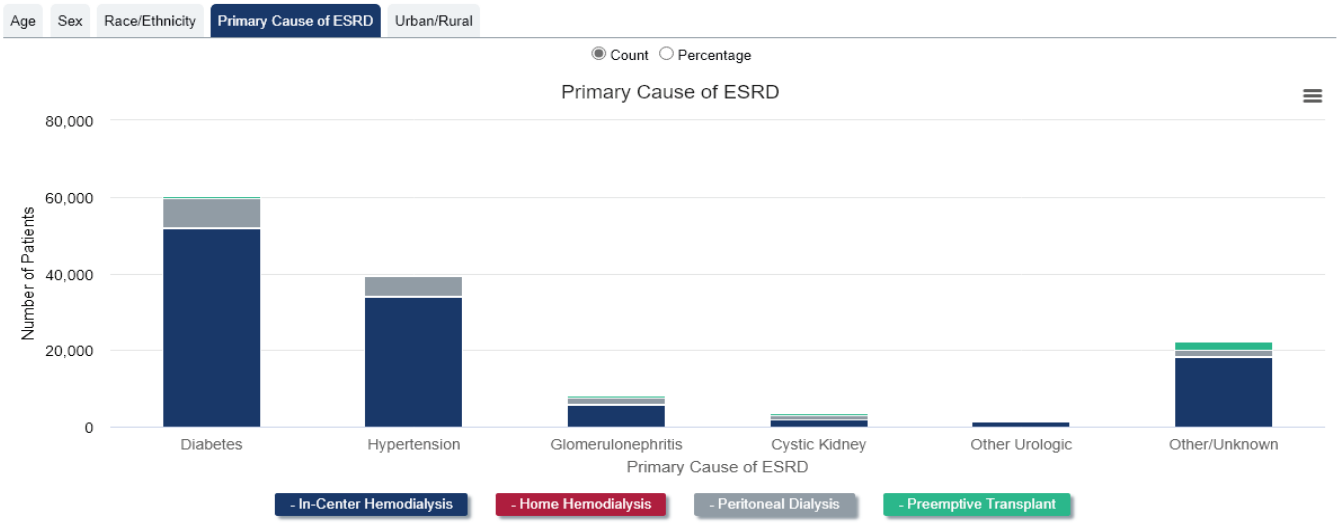


2f. What are the Causes of Chronic Kidney Disease?

[4] "Chronic Kidney Disease in the United States, 2023" https://www.cdc.gov/kidney-disease/media/pdfs/CKD-Factsheet-H.pdf

In this section, we will distinguish causes of kidney disease from risk factors that are associated with developing kidney disease but may not be the direct cause. The most common cause of chronic kidney disease (CKD) is diabetes. Among patients with diabetes, up to 40% have at least moderate kidney disease, CKD stage G3 or higher. To look at this from the other end, for 50% of people in the USA every year who reach End Stage Kidney Disease (ESKD, or ESRD) the cause was diabetes. Other common causes of CKD include genetic disease such as polycystic kidney disease, vascular disease, congestive heart failure, glomerular diseases (many of which are rare), various urologic conditions, certain types of cancer, severe kidney injury from critical illness without recovery, and the deleterious effects of prescription or non-prescription medications. For some patients the cause of kidney disease is certain, with proof obtained by kidney biopsy or genetic testing. For other patients, the cause of CKD is not proven and is based on an educated guess. Among patients who start dialysis every year, the 5 most common causes of ESKD according to the United States Renal Data Systems annual report are listed in the figure below: diabetes, hypertension, glomerulonephritis, cystic kidney diseases, other Urologic disorders, and "other/unknown."[5]

Figure 1.9 Modality at incidence of ESRD by patient characteristics, 2021



Data Source: USRDS ESRD Database. U.S. and U.S. territories ESRD patients. Persons with "Uncertain Dialysis" type were excluded.

We should recognize that "cause" of kidney disease in this chart comes from checking a box on a form 2728 submitted to the government in the first month someone begins dialysis, and this cause is often not "proven" by high quality testing. For example, the USRDS report lists "hypertension" as the #2 cause of ESKD but this is controversial. Rather than hypertension causing CKD, increasing evidence suggests it is the other way around, with unidentified causes of CKD resulting in hypertension.[6,7] Similarly, risk factors for CKD such as age, obesity, and our diet (whether we eat fresh food versus food with preservatives) do not have an established cause-and-effect with kidney disease, but any activity good for overall health is likely good, on average, for long term kidney function. The figure below combines diseases that we know cause

[5] USRDS 2023 annual report. Annual Data Report | USRDS (nih.gov). Among 113,309 incident dialysis patients in 2021, diabetes was believed to be "the cause" in 60,101 patients.
[6] Shantha M et al, "Renal function during antihypertensive treatment," The Lancet Vol 345: 749-51. 1995. DOI:10.1016/S0140-6736(95)90638-X.
[7] Freedman BI and Sedor JR, "Hypertension-associated kidney disease: perhaps no more," J Am Soc Nephrol Vol 19:2047-41. 2008. doi: 10.1681/ASN.2008060621.

CKD (such as polycystic kidney disease and diabetes) with conditions that are not the cause *per se* but which are correlated with kidney disease.[8]

Box 2 | **Risk factors for chronic kidney disease onset**

- Monogenic kidney disease (for example, autosomal dominant polycystic kidney disease, podocytopathies causing steroid-resistant nephrotic syndrome, Fabry disease, Alport syndrome and complementopathies such as atypical haemolytic-uraemic syndrome)
- Congenital abnormalities (for example, congenital anomalies of the kidney and the urinary tract and vesico-ureteric reflux)
- Type 1 or type 2* diabetes mellitus
- Poorly controlled arterial hypertension
- Obesity*
- Prolonged exposure to nephrotoxins* (for example, chemotherapy for cancer treatment, proton pump inhibitors, NSAIDs, antimicrobial agents, contaminated herbs and plant-based food, agricultural chemicals, heavy metals and irradiation)
- Climate (excessive heat exposure and dehydration)
- Infections and chronic inflammation* (for example, HIV, hepatitis virus, malaria, bacterial infections and autoimmune diseases)
- Malignancy* (for example, multiple myeloma)
- Episodes of acute kidney injury*
- Low nephron endowment at birth (due to low birthweight or fetal dysmaturity)
- Obstructive uropathy

*Denotes risk factors that also influence chronic kidney disease progression, which also include arterial hypertension, proteinuria, obstructive uropathy, smoking, hyperhomocysteinaemia and hyperuricaemia.

Most people loose kidney function with age, which can either contribute to CKD severity or provide reassurance, depending on the circumstances. Aging can contribute to CKD severity if someone already has CKD by middle age (for example, from diabetes, heavy cigarette smoking or other causes). At that point, even if they become health conscious, CKD can continue to worsen over time due to aging. On the other hand, aging can provide reassurance for adults over 70 who are labeled as having CKD but are otherwise very healthy. In one study of active adults without diabetes, heart disease, or hypertension, serum creatinine was high enough for a diagnosis of CKD stage 3 in about 50% of adults >70 years, and at the rate these people were losing kidney function with aging, the worst 5-10% might need dialysis by age 105-110 years old.[9] In other words, to a large degree, "CKD of aging" is a natural process of life, and if no other causes of CKD are found on evaluation, then the risk of reaching End Stage Kidney Disease during one's lifetime is not increased, leading to suggestions by leading kidney doctors that these patients do not really have a kidney "disease," and should be dismissed from requiring kidney clinic visits.[10],[11]

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[8] Romagnani P, et al; "Chronic Kidney Disease," *Nat Rev Dis Primers* **3**, 17088 (2017). doi.org/10.1038/nrdp.2017.88.

[9] Wetzels JFM et al, "Age- and gender-specific reference values of estimated GFR in Caucasians: the Nijmegen Biomedical Study," Kidney Int, 2007. 72(5):632-7. doi: 10.1038/sj.ki.5002374.

[10] Liu P, et al "Accounting for Age in the Definition of Chronic Kidney Disease," JAMA Intern Med. 2021. Vol 181(10):1359–1366. doi: 10.1001/jamainternmed.2021.4813.

[11] Oliva-Damaso N et al, "Risk-based versus GFR threshold criteria for nephrology referral in chronic kidney disease," Clin Kidney J. 2022. Vol 15(11):1996-2005. doi: 10.1093/ckj/sfac104.

2g. What are the treatments for Chronic Kidney Disease?

The best treatment for CKD depends on the cause. Some forms of progressive kidney disease can be reversed or at least markedly improved if accurately diagnosed, especially if these reversible causes are identified early, before fibrosis occurs. Examples of the benefits of early diagnosis and treatment include tolvaptan for Polycystic Kidney disease, enzyme therapy for Fabry's disease, immunosuppression for ANCA vasculitis, chemotherapy for Myeloma kidney, or discontinuation of medications that cause allergic interstitial nephritis.

Additional treatments are applicable to most kidney diseases. These treatments do not directly block the cause of a kidney disease, but they slow progression of most kidney diseases. First, inhibition of the renin-angiotensin-aldosterone axis with either angiotensin converting enzyme inhibitors or aldosterone receptor blockers (Ace-I or ARB) slows the rate of progression to ESRD in patients with CKD and proteinuria, whether the cause is diabetes or other glomerular diseases.[12] Related medications that block aldosterone activity at the mineralocorticoid receptor are also helpful for reducing proteinuria in CKD, as well as controlling resistant hypertension in patients with kidney disease.[13]

Two recent classes of medications intended to treat diabetes have additional benefit for slowing progression of chronic kidney disease. Sodium/glucose co-transporter inhibitors, collectively referred to as "flozins," inhibit reabsorption of glucose in the proximal tubule and mildly improve glucose control. When added to Ace-I or ARB therapy, these SGLT-2 inhibitors decrease the rate of kidney disease progression, especially in patients with proteinuria due to diabetic or non-diabetic CKD.[14] Similarly, GLP-1 agonists such as semaglutide and liraglutide, which improve glucose control by reducing appetite, stimulating insulin release and reducing glucagon release, have the added benefits of reducing the rate of progression of chronic kidney disease, and of reducing the risk of heart diseases in patients with CKD.[15]

Lastly, there are treatments that are widely beneficial for most causes of CKD. First, for most causes of CKD, treatment of hypertension is recommended, with a goal blood pressure 130/80 or less, and possibly under 120 in high-risk patients. Whether hypertension is the cause or the effect of kidney disease is controversial, as described above in section 2f, but regardless of cause or effect, good control of hypertension significantly reduces a patient's risk of stroke, and probably reduces the risk of heart attack. In CKD patients with high urine protein (>300 mg/gm spot ratio), good control of hypertension also slows the rate of progression towards End Stage Kidney Disease.[16] A second treatment for most causes of CKD is

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[12] Heerspink H.J.L. et al, "Drug-Induced Reduction in Albuminuria Is Associated with Subsequent Renoprotection: A Meta-Analysis," 2015. J Am Soc Nephrol, 26(8): 2055-64. doi: 10.1681/ASN.2014070688.

[13] Bomback A.S. et al, "Change in proteinuria after adding aldosterone blockers to ACE inhibitors or angiotensin receptor blockers in CKD: a systematic review," 2008, Am J Kidney Dis. 51(2):199-211. doi: 10.1053/j.ajkd.2007.10.040.

[14] Reyes-Farias, C.I. et al, "The effect of sodium-glucose cotransporter 2 inhibitors in patients with chronic kidney disease with or without type 2 diabetes mellitus on cardiovascular and renal outcomes: A systematic review and meta-analysis" 2023, PLoS One, Vol 18(11):e0295059. doi: 10.1371/journal.pone.0295059.

[15] Chen, J-Y. et al, "Kidney and Cardiovascular Outcomes Among Patients With CKD Receiving GLP-1 Receptor Agonists: A Systematic Review and Meta-Analysis of Randomized Trials," Am J Kidney Dis, 2025. doi:10.1053/j.ajkd.2024.11.013.

[16] Lewis, C.E. et al, "Final Report of a Trial of Intensive versus Standard Blood-Pressure Control," N Engl J Med 2021;384:1921-30. DOI: 10.1056/NEJMoa1901281.

the use of HMG-CoA reductase inhibitors, or "statins," which block cholesterol biosynthesis to slow atherosclerosis and reduce the rate of heart attack. CKD patients have particularly high rates of cardiovascular disease, for several reasons, and "statins" are effective in reducing these risks. "Statins" are particularly important for patients with CKD caused by atherosclerosis of the renal arteries, which is also called chronic ischemic nephropathy.[17]

2h. What are the long-term complications of Chronic Kidney Disease?

The two long-term complications of kidney disease are an increased risk of major adverse cardiovascular events (including stroke, heart attack, and sudden cardiac death) and progression to ESRD (including dialysis, kidney transplantation, and conservative care).

Major adverse cardiovascular events increase with higher stages of kidney disease. As illustrated in the heat map of cardiovascular mortality below,[18] the red box with the number "4.3" indicates that a patient with CKD stage G3a, A3, has a relative risk 4.3 times greater than someone without kidney disease but with similar age, smoking, diabetes, and family history. In contrast, for CKD stage 2 with minimal proteinuria, the relative risk of death due to heart disease is not significantly increased, as illustrated by the green numbers "1.0" and "1.1."

Cardiovascular Mortality

	ACR <10	ACR 10-29	ACR 30-299	ACR ≥300
eGFR > 105	0.9	1.3	2.3	2.1
eGFR 90-105	Ref	1.5	1.7	3.7
eGFR 75-90	1.0	1.3	1.6	3.7
eGFR 60-75	1.1	1.4	2.0	4.1
eGFR 45-60	1.5	2.2	2.8	4.3
eGFR 30-45	2.2	2.7	3.4	5.2
eGFR 15-30	14	7.9	4.8	8.1

In patients with advanced age and multiple cardiovascular risk factors, the most likely complication of CKD stage 4/5 is death by heart attack, but the complication that concerns patients the most is the question of dialysis. Patients who progress to ESRD actually have 3 options: dialysis, kidney transplantation, and conservative care, and the "best" choice depends on the patient's risks and goals.

If patients chose dialysis, the main benefit is to sustain life, especially as a bridge to kidney transplantation. The best time to start dialysis, once a patient reaches stage 5, remains an active area of research. The most straightforward reasons for starting dialysis are:

- Recurrent hyperkalemia that is resistant to diuretics and dietary counselling and is severe enough to risk cardiac arrythmia.

[17] Hicks, C.W. et al, "Atherosclerotic Renovascular Disease: A KDIGO (Kidney Disease: Improving Global Outcomes) Controversies Conference," Am J Kid Dis, 2022, Vol 79(2): 289-301. DOI: 10.1053/j.ajkd.2021.06.025.

[18] Matsushita K, et. al., "Cohort Profile: The Chronic Kidney Disease Prognosis Consortium," International Journal of Epidemiology 2013;42:1660–1668. doi:10.1093/ije/dys173.

- Volume overload that is resistant to diuretics and dietary counselling and is severe enough to cause shortness of breath or hospitalization for hypertension.
- "Uremia," which is the term for the symptoms caused by CKD, which are improved by dialysis.

As mentioned above in section 2e, up to 30% of patients with CKD stage 4/5 were never aware they had kidney disease and had no symptoms. Uremic symptoms sometimes start when GFR falls below 15 cc/min, but more often, there are no symptoms until the GFR is lower than 10 cc/min, and rare patients continue to feel fine even when GFR is 5 cc/min or less (about 4% of total kidney function). Uremic symptoms are caused by several molecules that we do not routinely measure, which rise in tandem with BUN and creatinine. These unmeasured molecules, such as indoxyl sulfate & p-cresyl sulfate, interfere with nerve conduction and irritate brain areas related to eating, smelling, and taste, resulting in symptoms of decreased appetite, a foul or metallic taste in the mouth, intolerance of meat/umami flavors, and nausea. Uremia also interferes with circadian sleep cycles, and eventually leads to decreased activity of our entire brain, resulting in symptoms of progressive sleepiness. Uremia can also predispose to seizures, and can result in inflammation of the pericardium, which is the fibrous sac that surrounds the heart. In patients with CKD 5 who have no symptoms, stable potassium and stable volume, there is no evidence that starting dialysis is helpful, and as GFR continues to fall, the KDIGO (Kidney Disease Improving Global Outcomes) expert suggestion is to "consider" starting dialysis when eGFR reaches 6-8 cc/min/1.73m2.

If a patient choses dialysis, there are three basic modalities available: in-center hemodialysis, home hemodialysis, and home peritoneal dialysis. Each of these three options can substitute as an artificial kidney to clean the blood and remove fluid, and the final choice of modality depends on patient preference. In some countries, such as Hong Kong and Australia, home peritoneal dialysis and home hemodialysis are quite popular. For historical reasons, in-center hemodialysis is the most common dialysis modality in the USA. Patients receiving in-center hemodialysis receive 3 dialysis sessions per week, each about 3.5-4 hours long, and this short amount of time replaces what their kidneys used to do 24 hours per day, 7 days per week. As such, the 3.5-4 hour dialysis treatments require rapid removal of fluid and toxins. Patients may gain 4-10 pounds of fluid between dialysis sessions and need to have all this fluid removed during a single treatment, along with all excess salts, by-products of metabolism, and toxins. Removing 10 pounds of fluid during dialysis means that, as fluid is removed from the vascular space, the fluid must be refilled from other parts of the body, or else a patient's blood pressure will drop precipitously. Shifts of fluid and salt during dialysis can lead to muscle cramping (which can be painful), headaches, changes in heart rhythm, or changes in blood pressure that result in fainting or rarely, in cardiac arrest. Afterwards, most dialysis patients in surveys report severe fatigue lasting from 2-10 hours.[19] Many patients on chronic dialysis continue to work, support their families, and have fulfilling lives, but dialysis treatments are not easy.

Hemodialysis requires ultrapure water. Contamination problems of dialysis water include bacteria, which can result in infection, chloramines, which can result in hemolytic anemia, aluminum, which can result in arthritis or dementia, and more. Ultrapure water and concentrated dialysate are mixed and then adjusted for each patient, to account for varied needs of sodium, potassium, and acid removal. Overall, the risk of infection is lowest among patients who use a native arteriovenous fistula, increases in patients with a synthetic graft, and is highest among patients using a tunneled dialysis catheter, because the artificial

[19] Rayner HC et al, "Recovery time, quality of life, and mortality in hemodialysis patients: the Dialysis Outcomes and Practice Patterns Study (DOPPS)." Am J Kidney Dis. 2014. 64(1):86-94. doi: 10.1053/j.ajkd.2014.01.014.

material provides a haven for bacteria to hide from the immune system. Infections sometimes result in sepsis, and may spread to other parts of the body, causing endocarditis, septic thrombophlebitis, septic arthritis, or an abscess. Next to cardiovascular disease, infectious complications are the major risk of morbidity and mortality among dialysis patients. In combination, if we combine the increased risks of infection with the increased risk of cardiovascular disease among dialysis patients, the risk of death is significantly higher than the general population and is similar to patients with Duke's Stage C colon cancer. A recent study from Ontario, Canada found that the risk of death among dialysis patients is a bit worse than patients with breast or colon cancer (including all stages of cancer).[20]

With the pros and cons of dialysis in mind, it will be easy to appreciate why kidney transplantation is the preferred treatment for patients with End Stage Kidney Disease. Transplantation offers improved 5 and 10-year rates of survival to dialysis, and better quality of life compared to dialysis. The figure below is based on risk of mortality, over 8 years, of patients with ESRD who received a kidney transplant, compared with matched patients with ESRD who were still on dialysis, awaiting transplant.[21] It shows an increased risk of death from the transplant surgery itself, at day 0, and by 106 days following transplant surgery, the risks and benefits for mortality are even. Thereafter, we see a clear mortality benefit for transplantation (about 1/3rd the risk of death for patients after kidney transplantation compared to matched patients on hemodialysis). Transplant also dramatically improves quality of life, including energy level, dietary options, strength, sleep, and even the ability to become pregnant.

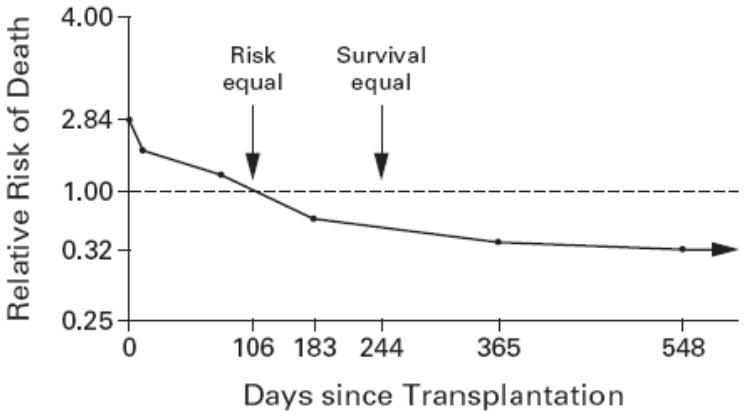


Figure 2. Adjusted Relative Risk of Death among 23,275 Recipients of a First Cadaveric Transplant.

Transplantation, in addition to its many benefits, caries certain risks and requires careful clinical monitoring of potential complications. The major risk following kidney transplantation is organ rejection. Careful matching of patients with recipient organs has helped to reduce incompatibility and rejection rates, as have advances in immunosuppression medications that promote "tolerance" of transplanted organs. Nevertheless, acute and chronic rejection remain a major concern, especially within the 1st year after

[20] Naylor, K.L. et al, "Mortality in Incident Maintenance Dialysis Patients Versus Incident Solid Organ Cancer Patients: A Population-Based Cohort," Am J Kidney Dis. 2019. 73(6):765-776. doi: 10.1053/j.ajkd.2018.12.011.

[21] Wolfe, R.A. et al, "Comparison of mortality in all patients on dialysis, patients on dialysis awaiting transplantation, and recipients of a first cadaveric transplant." N Engl J Med. 1999. 341(23):1725-30. doi: 10.1056/NEJM199912023412303.

transplant, and can lead to loss of transplant (necessitating immediate return to dialysis), or severe illness (necessitating hospital care).

The chance that a kidney transplant successfully works, which is known as "graft survival," is shown below, along with the range expressed as a 95% confidence interval. A transplant from a living donor (family or friend) has the highest chance of long-term success, with 97.5% working at 1 year, and 85.6% working at 5 years. Cadaveric donors, from patients who die of other causes and wish to donate their organs, have a lower but still appreciable success of 93.2% at 1 year, and 74.4% at 5 years.

Organ Procurement and Transplantation Network

Kidney Kaplan-Meier Graft Survival Rates For Transplants Performed : 2008 - 2015

Information! Based on OPTN data as of January 26, 2025.

Change Report (Optional):

Create a New Report

Kidney | Graft | Go

export print portrait landscape

Region	Donor Type	Years Post Transplant	Number Functioning / Alive	Survival Rate	95% Confidence Interval
U.S.	Cadaveric	1 Year	42400	93.2	(93.0, 93.4)
U.S.	Living	1 Year	21739	97.5	(97.3, 97.7)
U.S.	Cadaveric	3 Year	35582	85.1	(84.7, 85.4)
U.S.	Living	3 Year	20743	92.5	(92.2, 92.9)
U.S.	Cadaveric	5 Year	28854	74.4	(74.0, 74.8)
U.S.	Living	5 Year	18925	85.6	(85.2, 86.1)

Data subject to change based on future data submission or correction.This report shows OPTN data for Kidney Kaplan-Meier Graft Survival Rates For Transplants Performed : 2008 - 2015 through January 26, 2025. OPTN Data

Due to advances in organ matching, surgical techniques, and medical therapies, recently transplanted kidneys are expected to last longer than in the past, and transplanted patients are expected to survive longer. As shown in the figure below, when all transplant patients since 1996 are grouped into 4-year intervals according to date of their surgery, the progressive improvement in kidney transplant function and patient survival is evident.[22] The most recent data are from 2012-2015, because it is too soon to have long-term data on 2016-2019, much less for 2020-2023.

[22] Hariharan S, et al, "Long term survival after Kidney Transplantation," New Eng J Med. 2021. 385(8):729-743. doi: 10.1056/NEJMra2014530.

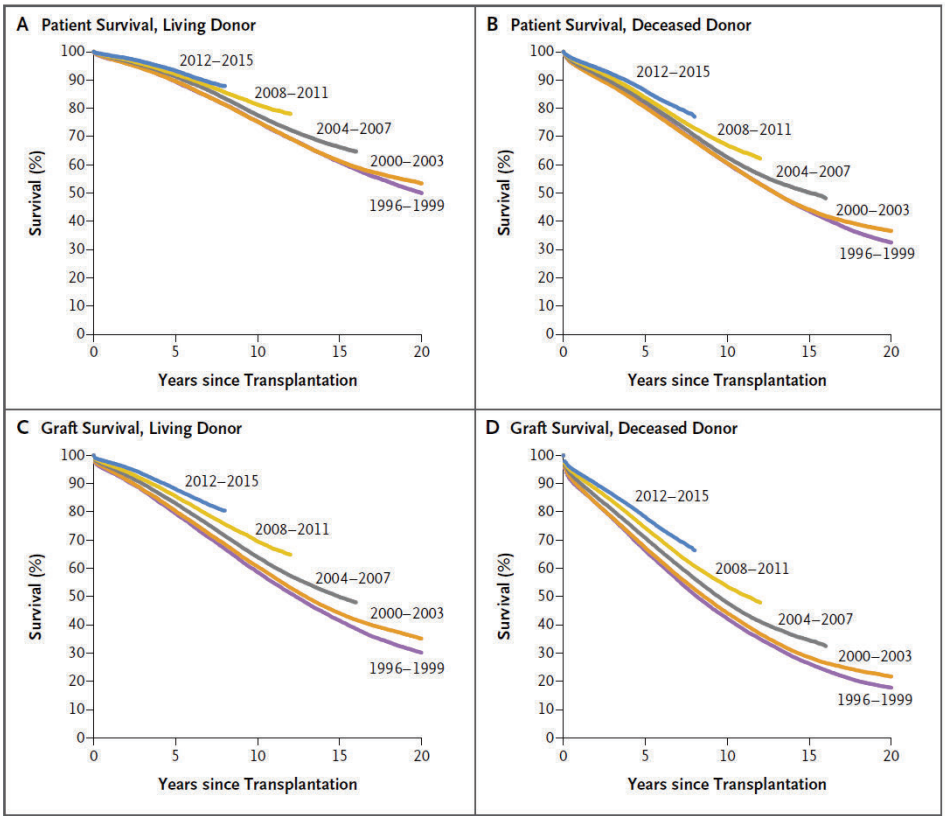
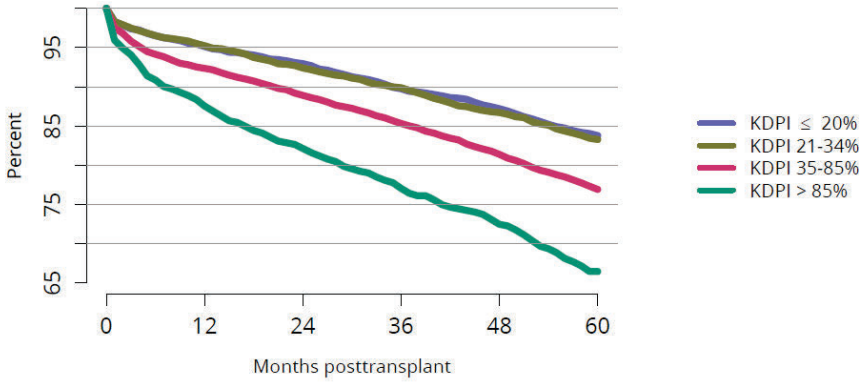


Figure 2. Graft and Patient Survival after Kidney Transplantation in the United States.
Shown are Kaplan–Meier estimates of patient survival (Panels A and B) and graft survival (Panels C and D) after transplantation of grafts from living donors (Panels A and C) and deceased donors (Panels B and D), with the data grouped in 4-year cohorts from 1996 to 2015. There were gradual improvements in patient and graft survival from the 1996–1999 period to the 2012–2015 period.

A large majority of kidney transplants are from cadaveric donors, and the quality of the donor kidney makes a significant difference on long term transplant outcomes. The Kidney Donor Prediction Index provides a scoring system for the quality of a cadaveric kidney. The lower the KDPI, the better the quality of the organ, and lower KDPI score correlates with longer transplant function for patients, as shown below. However, the benefit of having the highest quality kidney is counterbalanced by how long it might take on the transplant waitlist to receive such a kidney. For patients on dialysis, a lower quality kidney (higher KDPI) that comes quickly is often preferable to remaining on the waitlist, hoping for a high-quality kidney. Prolonged time on the waitlist caries a lower quality of life while on dialysis, and a higher risk of adverse cardiovascular and infectious outcomes, including death.

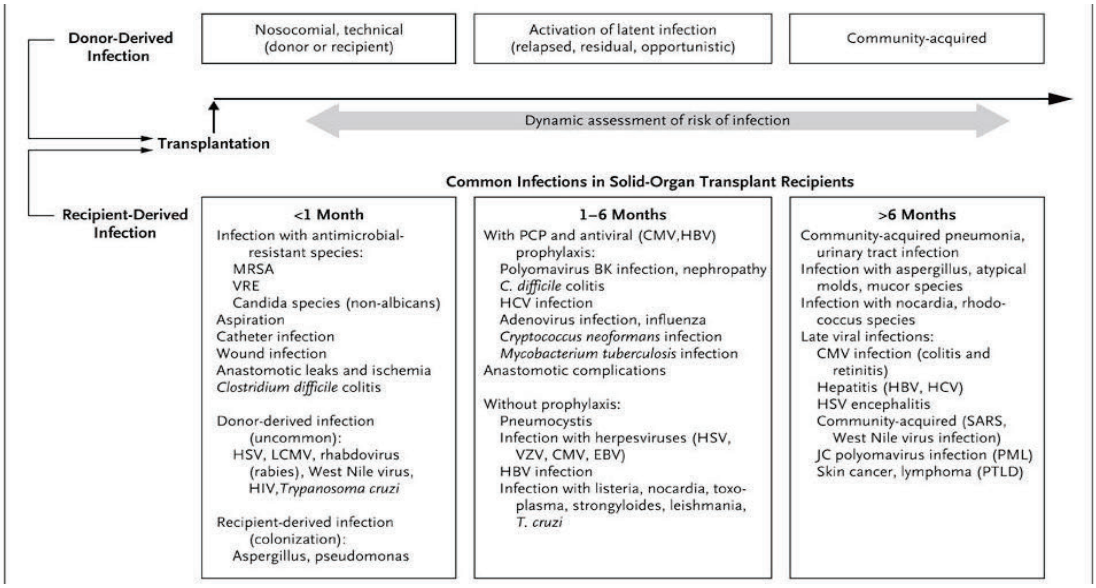


After a successful surgery, a kidney transplant patient requires clinical monitoring. There is no universal standard for management of patients after kidney transplantation, and each medical center has small differences in medication management and required testing. A comprehensive general reference is the 2009 KDIGO Clinical Practice Guideline for the Care of Kidney Transplant Patients.[23] The general aims of post-transplantation clinical monitoring are as follows:

1. Blood tests to monitor transplant kidney function for purposes of detecting and treating any episodes of rejection as soon as possible
2. Blood tests to ensure transplant immune suppressing medications remain at the goal level (high enough to minimize the risk of rejection, but not so high as to cause side effects or toxicity. For example, high levels of the calcineurin inhibitors cyclosporine or tacrolimus can cause acute kidney injury, chronic kidney disease, predispose to new onset diabetes, tremor, and hypertension.
3. Clinical monitoring and blood tests for signs of infection. Transplant medications, by virtue of suppressing the immune system enough to prevent rejection, also predispose to infections. This includes infections that arise only in the immunosuppressed, such as Pneumocystis or BK virus, and increased chance of infections seen in the general population. Because the levels of immune suppression are highest shortly after transplant can are gradually tapered over 1 year, the most likely infectious in transplant patients change if within 1 month of transplantation, if within 6-12 months, or if 1 year after transplantation, as shown in the figure below.[24]

[23] Kidney Disease: Improving Global Outcomes. Transplant Work Group. KDIGO clinical practice guideline for the care of kidney transplant recipients. *Am J Transplant*. 2009;9(Suppl 3):S1–S157.

[24] Fishman, J.A. "Infection in Solid-Organ Transplant Recipients." N Engl J Med. 2007 357:2601-2614. DOI: 10.1056/NEJMra064928



4. Clinical monitoring and treatment for cardiovascular disease after kidney transplantation, which includes appropriate treatment for hypertension, dyslipidemia, and any new onset diabetes.
5. Clinical monitoring for cancer after kidney transplantation, particularly skin cancer. Many recent advances in cancer treatment help augment the body's immune system to attack anything foreign, with the aim of attacking cancer cells. The converse of this is that transplant patients, by virtue of immune suppressing medications, have a decreased ability to fight off cancer. The risk of cancer after kidney transplantation in the USA, expressed as a Standardized Incidence Ratio, is more than twice that of the general population, and is especially high for skin cancer in sun-affected areas, and for non-Hodgkin's lymphoma.[25] In some cases, the treatment for cancer includes reducing immune suppressing medications, especially for post-transplant lymphoproliferative disorder, but reducing medications also increases the risk of transplant rejection.

A succinct table that summarizes most of the scheduled monitoring for the care of a patient following kidney transplantation is shown below, from a summary of the 2009 KDOQI guidelines for transplant care.[26] A more comprehensive table is shown below that, which includes suggestions for the frequency of clinical visits, blood testing, monitoring for cardiovascular disease, and monitoring for cancer.[27]

[25] Chapman, J.R. et al, "Cancer in the transplant recipient," Cold Spring Harb Perspect Med. 2013 3(7):a015677. doi: 10.1101/cshperspect.a015677.

[26] KDOQI US commentary on the 2009 KDIGO clinical practice guideline for the care of kidney transplant recipients. *Am J Kidney Dis*. 2010;56:189-218.

[27] Hariharan, S. "Recommendations for Outpatient Monitoring of Kidney Transplant Recipients." 2006. AJKD 47(4) S22-S36.

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SCREENING and GRAFT MONITORING

- Detecting kidney allograft dysfunction as soon as possible will allow timely diagnosis and treatment that may improve outcomes.
- Suggest including a kidney allograft ultrasound examination as part of the assessment of kidney allograft dysfunction. [R 8.4 (2C)]

ROUTINE SCREENING AFTER KIDNEY TRANSPLANTATION

Screening Test	Screening Intervals by Time After Transplantation					
	1 week	1 month	2-3 months	4-6 months	7-12 months	>12 months
Creatinine[a]	Daily	2-3 per week	Weekly	Every 2 weeks	Monthly	Every 2-3 months
Urine protein[b]	Once		Every 3 months			Annually
Complete blood count[c]	Daily	2-3 per week	Weekly	Monthly		Annually
Diabetes[d]	Weekly		Every 3 months			Annually
Lipid profile[e]	–	–	Once	–	–	Annually
Tobacco use[f]	Prior to discharge		–	–	–	Annually
BKV NAT[g]	Monthly			Every 3 months		–
EBV NAT (seronegative)[h]	Once	Monthly		Every 3 months		–
Blood pressure, pulse, height, body weight	Each clinical visit					

BKV, BK polyoma virus; EBV, Epstein-Barr virus; NAT, nucleic acid testing.

[a]Serum creatinine. Suggest estimating GFR whenever serum creatinine is measured [R 8.3.1 (2D)] using one of several formulas validated for adults (2C), or the Schwartz formula for children and adolescents (2C).

[b]Urine total protein and/or urine albumin.

[c]Complete blood count, including white blood count, hemoglobin and platelet counts.

[d]Screen for diabetes with fasting blood glucose, glucose tolerance test, or HbA_{1c} level.

[e]Lipid profile includes fasting cholesterol, LDL-C, HDL-C, and triglycerides.

[f]Screen for tobacco use.

[g]Screen for BKV using plasma NAT.

[h]Screen for EBV using plasma NAT in patients with no antibody to EBV at transplant.

Table 1. Recommended Schedule for Posttransplantation Monitoring of Adult Kidney Transplant Recipients[1]

	0-1 Month	1-3 Months	4-6 Months	7-12 Months	13-24 Months	>25 Months
Physical examination/history	3 times/wk	1 time/wk	1 time/2 wk	1 time/mo	1 time/6 mo	1 time/6 mo
Blood pressure	3 times/wk	1 time/wk	1 time/2 wk	1 time/mo	1 time/6 mo	1 time/6 mo
Weight and body mass index	3 times/wk	1 time/wk	1 time/2 wk	1 time/mo	1 time/6 mo	1 time/6 mo
Drug-related side effects	3 times/wk	1 time/wk	1 time/2 wk	1 time/mo	1 time/6 mo	1 time/6 mo
Adherence	3 times/wk	1 time/wk	1 time/2 wk	1 time/mo	1 time/6 mo	1 time/6 mo
Graft function						
Renal function (SCr, blood urea nitrogen)	3 times/wk	1 time/wk	Every other wk	1 time/mo	1 time/1-3 mo	1 time/1-3 mo
Urinalysis	Within first 2 wk, then every 3-6 mo for 1 y, then every 6-12 mo					
Urine spot (protein-creatinine ratio)	Within first 2 wk, then every 3-6 mo for 1 y, then every 6-12 mo					
CrCl/GFR	3 times/wk	1 time/wk	Every other wk	1 time/mo	1 time/1-3 mo	1 time/1-3 mo
Renal histology*	At 1 mo	At 3 mo	At 6 mo	At 12 mo		
Hematologic						
Complete blood count	3 times/wk	1 time/wk	1 time/2 wk	1 time/mo	1 time/1-3 mo	1 time/1-3 mo
Platelets	3 times/wk	1 time/wk	1 time/2 wk	1 time/mo	1 time/1-3 mo	1 time/1-3 mo
Hemoglobin/hematocrit	3 times/wk	1 time/wk	1 time/2 wk	1 time/mo	1 time/1-3 mo	1 time/1-3 mo
Anti-HLA antibodies*	At 1 mo	At 3 mo	At 6 mo	At 12 mo	At 24 mo	Annually
Metabolic/other						
Lipids	Every 6 mo for 1 y, then at least annually					
Blood glucose (fasting)	1 time/wk	1 time/wk	1 time/2 wk	1 time/mo	1 time/1-3 mo	1 time/1-3 mo
Hemoglobin A_{1c}	Annually after the first transplantation y					
Uric acid	Every 6 mo for 2 y, then 1 time/y					
Calcium and phosphorous	1 time/wk	1 time/mo	1 time/3 mo	1 time/3 mo	Annually	Annually
Parathyroid hormone†	At 1 mo		At 6 mo	At 12 mo	Annually	Annually
Liver function	1 time/mo 1, followed by 1 time/3 mo during the first y and then every 6 mo					
Therapeutic drug levels‡	3 times/wk	1 time/wk	1 time/2 wk	1 time/mo	1 time/1-3 mo	1 time/1-3 mo
Virology						
CMV§ (blood, by PCR)		Every 3 mo for the first y				
EBV§ (blood, by PCR)		Every 3 mo for the first y				
BK virus‖ (blood and urine, by PCR)	At 1 mo	At 3 mo	At 6 mo	At 12 mo	At 24 mo	
Hepatitis B and C	No specific recommendation; however, patients with hepatitis B and C infection may need periodic liver function evaluation and selected individuals may need viral load monitoring					
Bone densitometry	At the time of transplantation, 6 mo, and then annually, if previous results abnormal				Every other y	

(Continued)

Table 1 (Cont'd). Recommended Schedule for Posttransplantation Monitoring of Adult Kidney Transplant Recipients[1]

	0-1 Month	1-3 Months	4-6 Months	7-12 Months	13-24 Months	>25 Months
Malignancy						
Skin examination				Annually		
Papanicolaou smear				Annually		
Mammography				Annually		
Prostate-specific antigen				Annually		

NOTE. In addition to the published article cited,[1] some recommendations in this table are based on the clinical experience of Sundararm Hariharan, MD (written communication, November 2005).

Abbreviations: CrCl, creatinine clearance; SCr, serum creatinine; GFR, glomerular filtration rate; CMV, cytomegalovirus; EBV, Epstein-Barr virus; PCR, polymerase chain reaction.

*Not routinely recommended; may be performed, depending on immunologic risk and potential for intervention.

†Additional tests to be performed when patients experience hypercalcemia.

‡Primarily cyclosporine, tacrolimus, and sirolimus. The utility of obtaining mycophenolic acid levels is under investigation.

§For seronegative recipients of a seropositive donor kidney only.

‖BKV screening is recommended if transplant center has a high rate of BK virus infection.

Adapted from Kasiske BL, Vasquez MA, Harmon WE, et al. Recommendations for the outpatient surveillance of renal transplant recipients. J Am Soc Nephrol 2000;11:S1-S86.

The last option for patients who progress to End Stage Kidney Disease is conservative care. Dialysis and transplantation are sometimes not attractive options for patients who are too frail for surgery, or too frail for outpatient dialysis, or for personal reasons would prefer to let nature takes its course. These

patients are treated with medications to preserve the quality of life, and the quantity of good life, as they see fit.[28]

In summary, ESRD is a life-changing event. Early diagnosis and treatment of chronic kidney disease is always the preference, to prolong kidney function and delay the onset of ESRD. As a kidney doctor, delaying the need for dialysis as long as possible is always a primary aim. Unfortunately, because kidney disease often lacks symptoms, some people have already progressed to advanced stage CKD at the time of diagnosis. Regardless of cause, when ESRD becomes inevitable, physicians and patients work together to plan for dialysis at home or in-center, line up for kidney transplantation, or opt for conservative care.

[28] Bansal A.D. et al, "Ten Tips Nephrologists Wish the Palliative Care Team Knew About Caring for Patients with Kidney Disease," J Palliat Med. 2018 A21(4):546-551. doi: 10.1089/jpm.2018.0087.

3. Relevant Clinical History for Mrs. Jacquline Tukes.

Chronologically, Mrs. Tukes's medical documentation begins with malignant hypertension, which preceded her other kidney issues, leading to a CT kidney arteriogram at Naval Hospital in June 2010. We do not have clinic notes that describe why this arteriogram was ordered, but in medical practice a common reason is for suspected secondary hypertension due to renal artery atherosclerosis or fibromuscular dysplasia, such as in patients under 30, or in patients with uncontrolled hypertension despite taking 3 or more medications. The arteriogram was officially negative with no blockage of either renal artery, but she had atypical early bifurcation of her renal arteries, 2.1 cm from the origins. The significance of this rare vascular variant is uncertain. Whether hypertension causes chronic kidney disease, or whether the causation is the other way around, remains a topic of controversy and research, as discussed in the separate "General Introduction" document.

Incidentally, this CT angiogram also identified a small, 1.6 cm enhancing mass on the right kidney. Mrs. Tukes followed up with Urology at University of North Carolina in July 2010 for this small kidney mass. CT scan on July 29, 2010, replicated the finding from Naval Hospital the prior month, showing a 1.5 cm enhancing mass in the right kidney interpolar region consistent with cancer. On 8/20/2010 she underwent partial nephrectomy on the right, and the pathology confirmed clear cell renal cell carcinoma. Follow up Urology visits at UNC found no cancer for several years, including an MRI in June 2016 with a complex left renal cyst but no overt cancer recurrence, and a March 2017 renal ultrasound without recurrence.

In March 2018, Mrs. Tukes switched Urology providers to Dr. McCarthy in Wilmington, NC. A small, 0.2 cm solid mass was noted on the left kidney. She opted for surgical resection. On 4/26/2018 she had her 2nd surgery, a left partial nephrectomy, and 3 small, separate masses were removed. The pathology of all 3 masses was clear cell papillary kidney cancer. In April, a note from UNC Pathology for a 2nd opinion concurred with the diagnosis.

Out of concern that Mrs. Tukes may have a hereditary papillary renal cancer syndrome, she met with Dr. Berg in the University of North Carolina Genetics Division in August 2018. She reviewed prior negative testing for the vHL gene and underwent additional testing through Invitae with a panel of 30 common kidney cancer genes, but no causal mutation was found. The initial Invitae report included mention of two "variants of unknown significance" from these 30 genes in PSM2 (Arg799Trp) and SMARCA4 (Val1404Gly), but in 2022, based on additional information in the field of human genetics, these 2 variants were clarified to be "likely benign," indicating the amino acid changes should not alter protein folding or function. She also met with a genetic counsellor on 11/26/2018, after the initial Invitae results, whose recommendations included a discussion that the 30 gene test is not perfect in ruling out hereditary renal papillary cancer. UNC offered her full genome sequencing, based on her personal history, and on the prevalence of cancers of the kidney, breast, stomach, and lung in her family, as shown in the family history at the 8/18/2018 appointment, and she declined enrolling in this clinical study (NCGENES).

The prior month, Mrs. Tukes saw UNC Urology on 10/24/2018 with Mary Dunn, NP. From recent imaging, they discussed the complex cyst on the right kidney and the "small" left lower pole mass. An MRI on Oct 24 showed a stable, 4.1cm complex cyst in the right upper pole, a stable 0.9 cm enhancing mass in the left lower pole, and a stable 1.7 cm non-enhancing mass in the left mid-pole consistent with a hemorrhagic cyst. NP Dunn recommended continued surveillance and stated simply, "each surgery makes the subsequent one more difficult and places the kidney at risk. We also discussed the potential for dialysis and that this can outweigh the risk from the cancer. Specifically, we reviewed the natural history of

kidney cancer, the low risk of mortality, and the very good prognosis of her clear cell papillary disease."[29,30,31]

Mrs. Tukes opted for surgical resection of these papillary carcinomas, and over the next few years, she would undergo more surgeries with Dr. McCarthy at Atlantic Urology. Each surgery resected a small cancer. The 3rd surgery for Mrs. Tukes, a laparoscopic partial left nephrectomy, took place 3/14/2019 and found another clear cell papillary renal cancer, either 1.5cm or 0.9cm in size. In November 2019, she met Dr. Donner of Southeastern Nephrology, I believe for the first time, and he noted a creatinine-based eGFR of 50 ml/min, and a "normal" urinalysis. In April of 2022, a CT scan from Advanced Imaging found three abnormalities, one of which was a 1.5x1.3 cm enhancing mass on the lower pole of the right kidney. On 5/23/2022, with a note indicating the options for surveillance, cryotherapy or surgery were discussed, Mrs. Tukes underwent her 4th surgery. Intended as a partial nephrectomy, she was converted to a right total nephrectomy intra-operatively. The records I reviewed did not include a detailed operative note, so I am uncertain if the total nephrectomy was required due to prior surgical scarring, or an elective decision, but this did mean loss of 8-10 cm of well-functioning kidney tissue along with the small cancers. Pathology report revealed two renal cell carcinomas of 1-1.5cm and 1cm, respectively.

Two months later, at nephrology follow up on 7/14/2022 with South-Eastern Nephrology, her BUN and creatinine were 20 and 1.65. This creatinine is about what I would expect after a left partial nephrectomy and a right total nephrectomy, and indicates that Mrs. Tukes now had Stage 3 Chronic Kidney disease. This degree of kidney disease, as discussed in section 2 (General Introduction to Kidney Disease), would not result in symptoms, and by itself, progression to End Stage would be very unlikely in 10-20 years, provided she did not experience new diabetes, uncontrolled hypertension, or have exposure to nephrotoxins.

Prior to her 5th surgery, her nephrologist Dr. Donner on 11/19/2022 wrote that he suspected she "will be anephric in future," (anephric means without any nephrons, which is the same as saying without any functioning kidneys), and she would immediately require dialysis. Dr. Donner arranged for surgical evaluation for a hemodialysis fistula and plans for eventual in-center hemodialysis.
Mrs. Tukes had also been following with a medical oncologist, Dr. Jayaram at SMOC, from October 2019-April 2023. Dr. Jayaram's notes from the 6/16/2022 visit included discussion of recurrent kidney cancer with Dr. Rose of UNC Urologic Oncology and documents, "with low grade papillary clear cell, unlikely to metastasize, no adjuvant therapy, only surveillance."

Mrs. Tukes proceeded with plans from her medical providers. I do not find discussions in provider notes at this time regarding efforts to preserve kidney tissue and kidney function along the lines discussed in the paragraph above. On 1/5/2023 she had vascular surgery by Dr. Eskew to create a dialysis fistula on the left arm. On 2/7/2023 with her Urologist Dr. McCarthy, he reviewed images from a CT with contrast the prior month that described a new 1.3cm left kidney Bosniak 3 lesion (which means likely to be kidney cancer). On 3/15/23, her nephrology follow-up with Dr. Donner noted "fistula ready for use per surgery in 2 weeks." On 5/2/23 a repeat CT with contrast described a 1.5 cm enhancing mass.

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[29] Hering, J.C. et al, "PARENCHYMAL SPARING SURGERY IN PATIENTS WITH HEREDITARY RENAL CELL CARCINOMA: 10-YEAR EXPERIENCE," J. Urology, 2001, Vol. 165: 777–781.
[30] Marszalek, M et al, "ELECTIVE OPEN NEPHRON-SPARING SURGERY FOR RENAL MASSES: SINGLE-CENTER EXPERIENCE WITH 129 CONSECUTIVE PATIENTS" UROLOGY 64: 38–42, 2004.
[31] Yanus, G.A. et al, "Hereditary Renal Cancer Syndromes," Med Sci (Basel), 2024. 12(1):12, 1-24. doi: 10.3390/medsci12010012.

On 6/2/2023 she had her 5th Urologic surgery with Dr. McCarthy, a total left nephrectomy. The 1.5 cm mass, on subsequent Pathology examination, was actually two distinct, small, renal cell carcinomas of 6 mm and 3.5 mm (0.6cm and 0.35 cm), for a low tumor staging of pT1a. Quite a bit of functioning left kidney was removed to resect these two small cancers.

Mrs. Tukes had no kidneys from this point onwards and she promptly started hemodialysis. On 6/13/23, Dr. Greco noted that her dialysis AV fistula was not ready for use, as previously assumed, and he placed a tunneled dialysis catheter. From 6/20/2023 onwards, Mrs. Tukes appears to have transferred her kidney disease care on dialysis from Dr. Donner to Dr. Thomas. From July 2023 through March 2024, she remained on dialysis at DaVita, while undergoing evaluation for kidney transplant at University of North Carolina, then Duke, then East Carolina University. Her time on dialysis at DaVita includes weekly notes from Dr. Thomas and treatment data from the dialysis center. Her blood pressure was both high and labile on dialysis, including the following details:

- 6/29/23, Dr. Thomas, increase losartan, plan eventual change to peritoneal dialysis, transplant wait likely to be 2 years due to cancer.
- 7/723, Dr. Thomas, stop losartan, start telmisartan for hypertension.
- 7/26/23, Dr. Thomas, add amlodipine for hypertension.
- 8/7/23, Dr. Thomas, add doxazosin for hypertension.
- 9/1/23, Dr. Thomas, restart spironolactone for hypertension.
- 10/2/23, Dr. Thomas, cardiology adding medications (clonidine) for hypertension. Labile BP. Mrs. Tukes delayed PD catheter surgery.
- 12/5/23, Dr. Harris of Surgical Associates notes Mrs. Tukes has an AVF “does not want to use,” and they discussed peritoneal dialysis catheter placement “possible that prior abdominal surgeries may cause some difficulties.”
- 1/2/24, Dr. Harris, Operative report for successful peritoneal dialysis catheter placement, with lysis of adhesions in the right upper quadrant due to her prior cholecystectomy.
- 2/5/24 Dr. Thomas, notes Mrs. Tukes has uncontrolled blood pressure. “Was asked to have EDW challenged but refused.” Plan: challenge EDW, increase doxazosin to 4mg twice daily.
- 2/18/24, Emergency Department visit for shortness of breath, orthopnea, cough, Chest X-Ray showing pulmonary interstitial edema, diagnosed with hypertensive emergency due to fluid overload.
- 2/19/2024 Hospital echocardiogram showing normal LV function, grade 2 diastolic dysfunction, moderate mitral regurgitation, dilated left atrium.
- DaVita Dialysis monthly lab values are acceptable, except for increasing parathyroid hormone necessitating adjustment to Hectoral dose, hyperphosphatemia between 9 and 10 in April 2024 (goal of 5.4 or less), and a hemoglobin that was above goal, leading to a hold on Mircera on March 7, 2024.

Mrs. Tukes underwent kidney transplantation on 4/23/24 at East Carolina University. The donor kidney she received had an elevated KDPI of 62, with a prolonged cold ischemia time of 17hrs 31 minutes, and was a 4-allele mismatch (2A, 2B, 2DR, 2DQ), with her surgeon’s caution that there was visible lower pole ischemia at the time of transplant. Despite these several cautionary predictive factors, her transplanted kidney has functioned extremely well. She received induction immunosuppression with thymoglobulin and has been maintained on Envarsus (tacrolimus), Myfortic (mycophenolic acid), and low-dose prednisone. Three days after transplantation, she was discharged from the hospital with a creatinine of 7.43, which improved to 4.12 by end of the first week, improved to 1.32 by May 6, and reached best creatinine values of 0.96-0.97 in July and August of 2024. These results meet all “best” expectations.

As of November 18, 2024, her kidney transplant clinic notes from Dr. McLawhorn report a creatinine that week of 1.15 with a baseline creatinine of 0.9-1.1. In a kidney transplant patient, creatinine values cannot be translated accurately into an eGFR to calculate the stage of chronic kidney disease as is done for native kidneys (the relationship between creatinine, eGFR, and stages of CKD is described above in the General Introduction) but a creatinine of 1.15 at 6 months post-transplant is considered superb. The transplant clinic note on November 18 summarizes her success. She had not experienced any episodes of rejection at that point, and the risks of rejection are highest within the first year. Her immune suppressing medications included Envarsus (a once-daily preparation of tacrolimus), Myfortic at reduced dose due to a history of leukopenia and viremia, and prednisone 5mg. She had finished all medications for prophylaxis against infections, including 6 months Bactrim, 3 months of valganciclovir (Valcyte), and nystatin in the weeks immediately after surgery to prevent thrush. Some of her transplant notes vary in detail, but her overall CMV risk was judged to be "Intermediate", and she did experience both CMV viremia and BK viremia per transplant notes, but as of the November 18 clinic visit, due to gentle reduction of Myfortic, both viruses had become undetectable on blood tests. (To clarify, CMV or BK viremia indicates detectable virus in blood without any known deleterious organ involvement.) Viremia is milder and clinically distinct from CMV "disease." Viremia is often treated by gently reducing the dose of immune suppressing medications, and for Mrs. Tukes, this approach worked well. One last success is that the malignant hypertension Mrs. Tukes had struggled with while on dialysis fully resolved after kidney transplantation, and she was off all blood pressure medications at her November 2024 transplant clinic visit.

Section 4) Conclusions on the clinical course of Mrs. Tukes, including future expectations following her kidney transplant, and the need for future care.

Plaintiff is seeking judgement against the USA on the basis that contaminated water from Camp Lejune caused kidney cancer, which resulted in bilateral nephrectomy, resulting in the need for dialysis, and eventually led to kidney transplantation.

a) From Mrs. Tukes's clinical records, I have reviewed the clinic notes from her visits with UNC geneticists, who wrote that she may have had hereditary renal papillary cancer syndrome, despite the negative genetic testing, based on her clinical phenotype. I have also read the expert opinion of Dr. Gail Vance, who elaborates on the reasons to suspect a hereditary renal papillary cancer syndrome, despite the negative testing on a 30 gene panel. I have also read the expert opinion of Dr. Walt Stadler, who opines that Mrs. Tukes's kidney cancer is most likely genetic in origin.
b) Following kidney transplantation, as of her November 2024 transplant clinic follow up, Mrs. Tukes was faring much better than she was while on dialysis, and her transplant kidney function was excellent.
c) Regarding her future care, we can make cost estimates for Mrs. Tukes, using expansive estimates for clinical monitoring. A list of these visits and tests is described at the end of this section. She will need these services for as long as her transplant remains functional, or mostly similar services following any future transplant.
d) Regarding predictions on how long her kidney transplant will last (and when she might have to resume dialysis, if ever), or how many years she is expected to survive, and with what quality of life, we can only speculate. As described below, there is information from nationwide transplant outcomes for how long a kidney transplant lasts, and how often kidney transplant recipients die,

but these general predictions are based on the US population overall. I expect Mrs. Tukes will fare better than the average kidney transplant patient, as described below.

A deceased donor kidney transplant is expected to last about 10-12 years, with wide variation. Some transplants last only months, and the risk of transplant rejection or transplant failure for other reasons is highest within the first 6 to 12 months. Fortunately, at 6 months post-transplant, Mrs. Tukes has not experienced adverse surgical complications, a severe infection, or an episode of transplant rejection, so she is already "beating the curve," and is expected to better than the median. From the "General Introduction" section above, deceased donor kidney transplant grafts have about 70% chance of working after 10 years. Another way to think about the chance Mrs. Tukes will have a functioning kidney transplant in the future is shown below in Figure 3D "Rate of Graft Loss, Deceased Donor."[32] At the time of this writing, Mrs. Tukes is about 1 year post kidney transplant, so the chance her transplant graft will stop working per year is about 5%. Mrs. Tukes was at increased risk for delayed graft function based on use of an ECD kidney with high KDPI and visible ischemia of the inferior pole. Delayed graft function, defined as the need for hemodialysis in first week after transplant surgery, is a major risk factor for early transplant graft loss. Fortunately, Mrs. Tukes did not experience delayed graft function, which means her long-term prognosis will be better than the average patient. The 2nd major predictor for early graft loss is acute rejection, which is most common within the 1st year after kidney transplant. Mrs. Tukes was at increased risk for acute rejection based on using an ECD, high KDPI donor kidney, and based on her 4 HLA-allele mismatch, but as of November 2024 she had not experienced any episodes of acute rejection. Thus, the two major predictors of transplant graft loss—delayed graft function and acute rejection within the first year—are both quite favorable for Ms. Tukes and make it more likely than not that her kidney transplant will last longer than the average.

The same figure below also shows predictions for overall survival (see Fig 3B, "Rate of Death, Deceased Donor.")[33] Since Mrs. Tukes is about 1 year post transplant as of this writing, the average rate of death is around 2%. Compared to other recipients of kidney transplant her same age, who likely needed transplants due to kidney disease from diabetes mellitus or cardiovascular disease, Mrs. Tukes should have a lower burden of cardiovascular risks. To elaborate, diabetes takes 15-40 years to progress from diagnosis to End Stage Kidney Disease, and during this time, diabetes is also causing systemic disease to the vascular system, leading to increased risks of stroke and heart attack. Compared to patients with diabetes, Mrs. Tukes did not have decades of a systemic disease like diabetes adversely and chronically affecting her cardiovascular system. As such, it is more likely than not that Mrs. Tukes will have a longer lifetime survival than the average kidney transplant patient (or with regard to Fig 3B below, her yearly "Rate of Death, Deceased donor," should be lower than the average kidney transplant patient).

[32] Hariharan S, et al, "Long term survival after Kidney Transplantation," New Eng J Med. 2021. 385(8):729-743. doi: 10.1056/NEJMra2014530. [33] Hariharan S, et al, "Long term survival after Kidney Transplantation," New Eng J Med. 2021. 385(8):729-743. doi: 10.1056/NEJMra2014530.

[33] Hariharan S, et al, "Long term survival after Kidney Transplantation," New Eng J Med. 2021. 385(8):729-743. doi: 10.1056/NEJMra2014530.

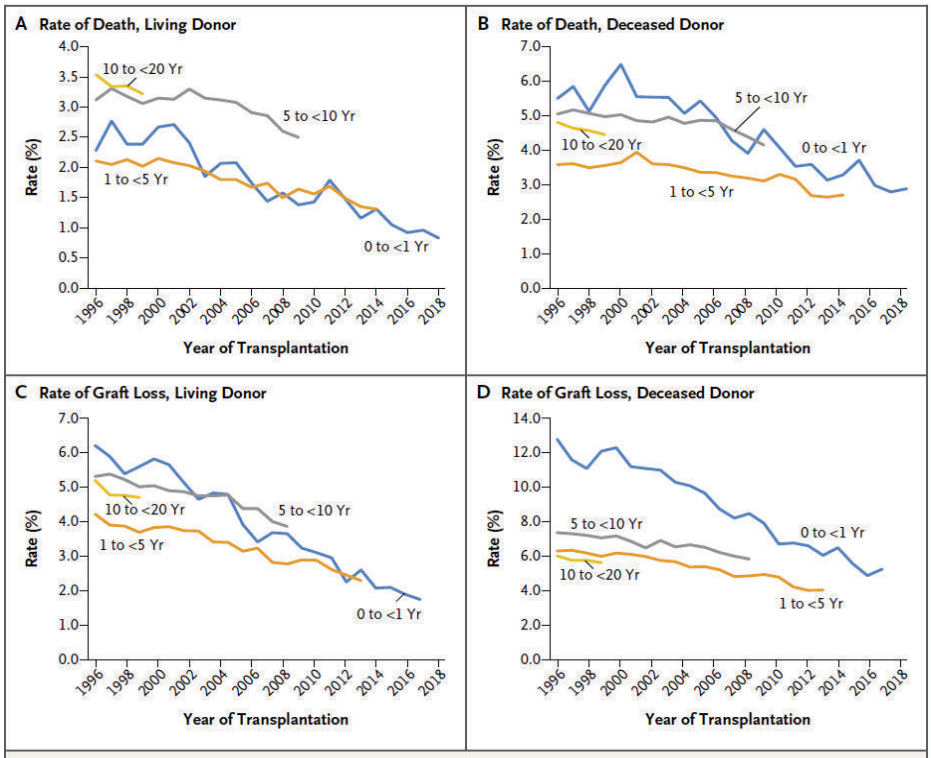

Figure 3. Rates of Death and Graft Loss after Kidney Transplantation in the United States, 1996–2018, According to Years after Transplantation.

Panels A and B show rates of death among recipients of grafts from living donors and deceased donors, respectively, and Panels C and D show rates of graft loss among recipients of grafts from living donors and deceased donors, respectively. The rates are shown for four periods: less than 1 year after transplantation, 1 to less than 5 years after transplantation, 5 to less than 10 years after transplantation, and 10 to less than 20 years after transplantation. There were reductions in short- and long-term death rates and graft loss rates from 1996 to 2018.

a) If her transplant kidney function remains stable, with no episodes of acute rejection by 1 year post-transplant, then the main barriers to long term transplant kidney function are chronic transplant rejection, often mediated by alloantibodies, and chronic tacrolimus toxicity, often due to intermittently high tacrolimus blood levels. To minimize the risks of chronic rejection and medication toxicity from 1 year onwards, Mrs. Tukes will require monitoring as is summarized in section 2h of the General Introduction, with some detail as follows:
    a. regular clinical visits (every 6 months) with a nephrologist or transplant specialist;
    b. blood tests every 1-3 months, depending on her clinical stability, to monitor kidney function, tacrolimus levels, complete blood count, and glucose;
    c. urinalysis every month (although every 6-12 months is recommended by KDIGO and by a well cited review of kidney transplant clinical care in the American Journal of Transplant Review, as shown in the General Introduction section above);
    d. periodic renal ultrasound (4-5 times over her lifetime);
    e. medications, including prednisone (Deltasone) (5mg daily, or equivalent), mycophenolic acid (Myfortic or Cellcept) (roughly 3 tabs of 180mg, taken twice daily, or the equivalent), and tacrolimus (Prograf or Envarsus) (roughly 1 tab of 5mg, taken twice daily, or the equivalent);
    f. screening for BK virus and HLA antibodies at 1 year and then annually at transplant clinic visits;
    g. monitoring fasting lipid levels every 6 months (part of regular transplant clinic visits), and
    h. age-appropriate screening for cancer, including skin exams with a dermatologist annually.

Section 5) Responses to the report of Dr. Matthew Cooper.

There are many areas in the Specific Causation report by Dr. Cooper that I fully agree with, others where I am uncertain, and a few where I respectfully disagree. To start with areas of agreement, in Section V. of his report, Dr. Cooper writes that the deceased donor kidney transplant Mrs. Tukes received is expected to last about 13 years, which is true, on average. Dr. Cooper also writes that Mrs. Tukes will be negatively affected if she either loses her transplant due to rejection, or if she develops a recurrence of kidney cancer, which are also quite true. I also agree that if her transplant fails and she returns to hemodialysis, then all of the complications of dialysis would return, including increased risk of cardiovascular disease, decreased dietary flexibility, and decreased quality of life, all of which is discussed in the sections on hemodialysis under my General Introduction, section 2h, above. I agree that her transplant requires lifelong immunosuppression and close clinical monitoring, with roughly 14-20 blood draws in the 1st year. After 1 year, I have differences with Dr. Cooper's suggestions for required monitoring, as discussed below. Lasty, I agree with Dr. Cooper that Mrs. Tukes will have a risk of transplant medication side effects, and that compared to the General Population, she will have an increased risk of infections, cardiovascular disease, and cancers (particularly skin cancer), as outlined in the discussion of long-term complications of kidney transplantation at the end of Section 2h of the General Introduction to Kidney disease, above.

In section V, Dr. Cooper writes, based on her age, that Mrs. Tukes would "more likely than not be ineligible for another transplant." I am uncertain how healthy Mrs. Tukes will be in 10-12 years, and I am uncertain whether or not she might be a candidate for a 2nd transplant. There is no standard age limit for kidney transplantation, and if she remains quite healthy, she may be a good candidate. In the literature on kidney transplantation in older adults, "the consistent theme is that chronologic age is substantially less important than physiologic age and the nature and severity of any coexisting conditions."[34] At present, Mrs. Tukes has no diabetes, no known cardiovascular disease, and she had a much shorter duration of CKD plus dialysis compared to most patients who undergo kidney transplantation; in combination, this means her "comorbid conditions" are less than average for a 59 year-old transplant recipient. If she remains in good functional, physiologic health, with good diet and exercise, then it is more likely than not that she would be a candidate for repeat transplantation in 10-12 years, if needed.

More importantly, it is speculative to decide she will need repeat evaluation for a 2nd kidney transplant in 10-12 years, because I disagree with Dr. Cooper when he writes, in Section V, that "Mrs. Tukes will more likely than not need dialysis starting in under 12 years." This is an overstatement. If the median deceased donor kidney transplant graft lasts 13 years as Dr. Cooper states, and she is already finishing the most important first year after transplantation with excellent allograft function, then our expectation at this point is for her graft to last longer than the median before she might require a return to dialysis. The higher rate of transplant graft loss in the 1st year is shown on the previous page, Figure 3D, "Rate of Graft Loss, Deceased Donor," noting that the BLUE LINE is significantly higher than the other lines that represent transplant graft loss after 1 year. In other words, the median 13-year figure that Dr. Cooper cites includes a large number of kidney transplants that fail within the first year, which is not relevant to Mrs. Tukes's case.

[34] Knoll, GA "Kidney Transplantation in the Older Adult." Am J Kid Dis. 2013. 61(5):790-97. Kodali L and Turner A, "When are you too old to get a kidney transplant?" Curr Opin Nephrol Hyperten. 2019. 28:593-599.

While speculative, her kidney transplant is expected to do better than the median, as discussed in section 4c above regarding her kidney transplant.

Lastly, in section VI, and again in XII, Dr. Cooper briefly outlines the estimates of costs for future. I defer entirely to Dr. Cooper on all matters of surgical transplantation, but I disagree with some sections of the future cost-estimates. In section VI, Dr. Cooper writes that Mrs. Tukes will need monthly CMV testing, yearly echocardiograms, and yearly stress testing. These tests might be required for post-transplant patients with ongoing CMV viremia, or ongoing adverse cardiovascular events, but these tests are not part of routine care of the transplant patient as suggested in KDIGO clinical practice guidelines and in the review of post-transplant kidney care, as outlined with references in section 2h of the General Introduction to Kidney Disease.[35,36] See also the figure below regarding surveillance testing for cytomegalovirus from the KDIGO summary statement, which does not include monthly CMV monitoring.[37] Similarly, the cost estimates should not include ongoing need for Bactrim or Valcyte, since as of November, 2024, after 6 months, she had completed her full course for both medications. Additionally, Dr. Cooper forecasts future hemodialysis, echocardiogram, and support services in Mrs. Tukes's last years of life. Those needs are contingent on the failure of Mrs. Tukes's transplant at 13 years, and her ineligibility for a second transplant, which as explained above are both speculative and unlikely. Future care in assisted living is predicated on early loss of physical or mental fitness, but it is more likely than not that a 59- year-old with an excellent transplant kidney at 1 year post-surgery can maintain good physical and mental fitness for many years, by following a healthy diet, regular exercise, and medication compliance.

SELECT RECOMMENDATIONS FOR MANAGING INFECTION	
BK polyoma virus	Suggest screening all KTRs with NAT [R 13.1.1 (2C)]: • Monthly for the first 3 to 6 months after transplantation (2D), then every 3 months until the end of the first posttransplant year (2D) • Whenever there is an unexplained rise in serum creatinine (2D) • After treatment for acute rejection. (2D) Suggest reducing IS medications when BKV plasma NAT is persistently >10^7 copies/L. [R 13.1.2 (2D)]
Cytomegalovirus	Recommend KTRs receive chemoprophylaxis with oral ganciclovir or valganciclovir [R 13.2.1]: • For at least 3 months after transplantation (1B) • For 6 weeks after treatment with a T-cell-depleting antibody (1C) • Except when both donor and recipient have negative CMV serologies. In patients with CMV disease, suggest weekly monitoring of CMV by NAT or pp65 antigenemia. [R 13.2.2 (2D)]

Conclusions:

[35] Josephson, M "Monitoring and Managing Graft Health in the Kidney Transplant Recipient." CJASN. 2011. 6:1774-80.
[36] Hariharan, S. "Recommendations for Outpatient Monitoring of Kidney Transplant Recipients." 2006. AJKD 47(4) S22-S36.
[37] KDOQI US commentary on the 2009 KDIGO clinical practice guideline for the care of kidney transplant recipients. *Am J Kidney Dis*. 2010;56:189-218.

Plaintiff is seeking judgement against the USA on the basis that contaminated water from Camp Lejune caused kidney cancer, which resulted in bilateral nephrectomy, the need for dialysis, and eventually led to kidney transplantation. Mrs. Tukes is now nearly 1-year post-transplant. Based on the records made available to me and my training and experience as a nephrologist, I would characterize her transplant as extremely successful.

Any negative impacts to her life expectancy are, at this point, speculative. The major causes of death among transplant recipients in general are cardiovascular (heart attack and stroke) because the most common cause of kidney disease that requires kidney transplantation is diabetes, which causes high, chronic cardiovascular risk. Mrs. Tukes had no diabetes, so her life expectancy is expected to be better than the average kidney transplant patient. Very slowly progressive CKD also carries an increased risk of cardiovascular death, as described in the General Introduction, but Mrs. Tukes had very rapid progression from CKD 3a to ESRD at the time of her nephrectomy, which means she spent far less time with severe CKD than the average kidney transplant recipient; this also increases her life expectancy.

Any predictions for when her transplant might fail and require her to return to dialysis are also quite speculative. First, if her transplant were to fail prematurely, then more likely than not, she would be a good candidate for a second transplant based on the lower burden of vascular disease compared to the average transplant recipient. It is far too speculative to say she would never be a good candidate for repeat kidney transplant. It is also quite speculative to predict her transplant will fail in 13 years, at the median time cited by Dr. Cooper, because she is already faring superbly at close to 1-year post-transplant, which includes the most risky times for early transplant failure. At this point, her success at 1 year predicts that, more likely than not, her transplant will last significantly longer than the median.

She will require future medical care as described above—primarily immunosuppressant medications for her kidney transplant, regular doctor visits to monitor her transplant, and surveillance testing for the risks of hypertension, hyperlipidemia, diabetes post-transplantation, and cancer surveillance post-transplantation, as outlined for her future medical care needs. Future care in assisted living is quite speculative and is predicated on early loss of physical or mental function, which at this junction is less likely.

Duncan Johnstone

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