

Fabry Disease and Your Kidney Health

In this guide you will learn about:

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- How your kidneys work—and how Fabry Disease can affect kidney function over time

You and Your Kidney Health

- How your kidney function might decline over time if you are not on appropriate treatment for Fabry Disease*

Patient Perspectives

- What other individuals with Fabry Disease have to say about kidney health

Managing Your Kidney Health

- What clinical guidelines say about kidney health and managing Fabry Disease
- Resources where you can learn more about Fabry Disease

*This guide includes an optional activity you can use to track your estimated glomerular filtration rate (eGFR) results over time. If you have them handy, you can use your prior lab results to complete this exercise.

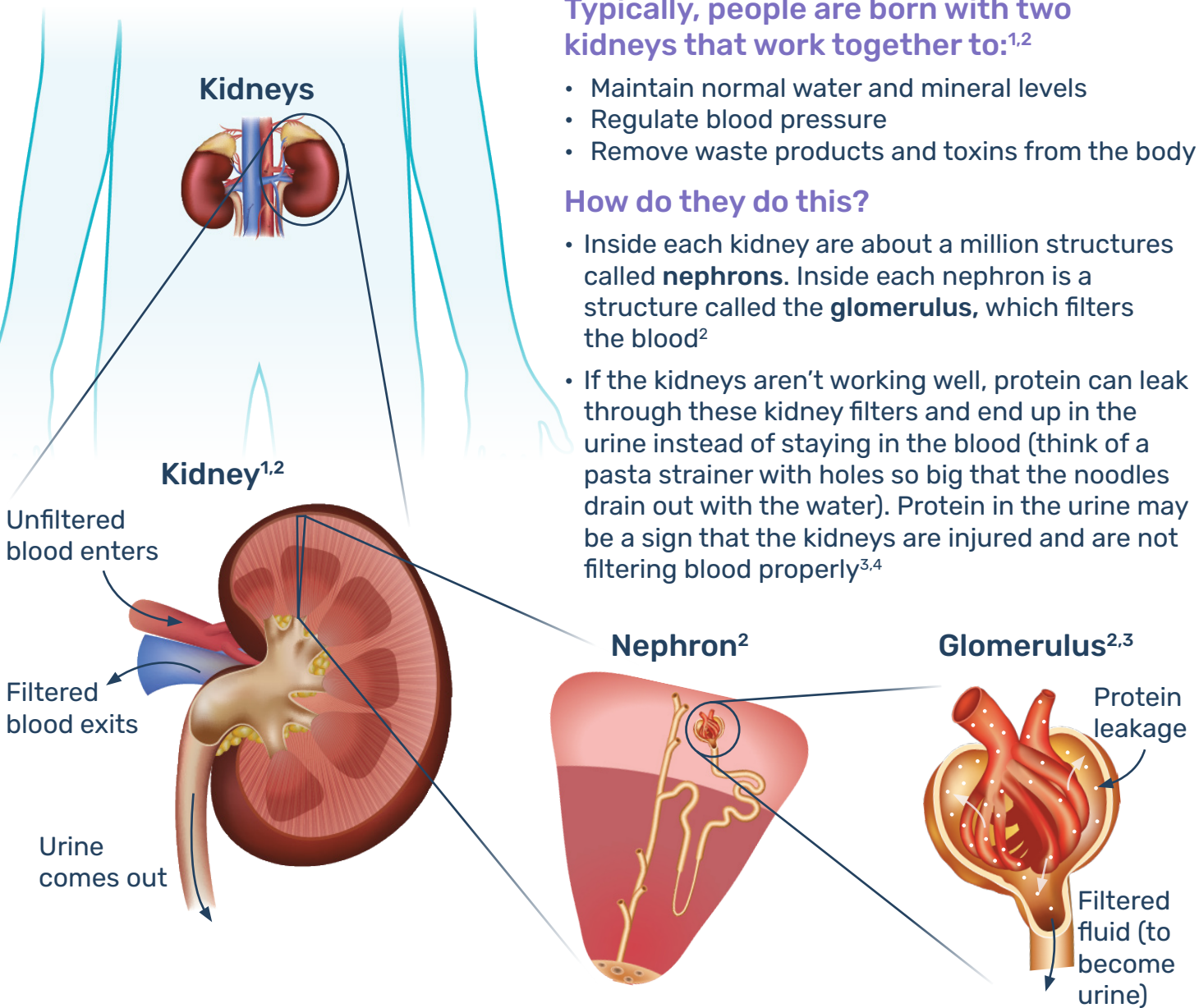
Your Kidneys are Vital Organs

Typically, people are born with two kidneys that work together to:^{1,2}

- Maintain normal water and mineral levels
- Regulate blood pressure
- Remove waste products and toxins from the body

How do they do this?

- Inside each kidney are about a million structures called **nephrons**. Inside each nephron is a structure called the **glomerulus**, which filters the blood²
- If the kidneys aren't working well, protein can leak through these kidney filters and end up in the urine instead of staying in the blood (think of a pasta strainer with holes so big that the noodles drain out with the water). Protein in the urine may be a sign that the kidneys are injured and are not filtering blood properly^{3,4}



The kidneys' ability to filter out waste products through each glomerulus is estimated by the eGFR, which is used to determine how well the kidneys are working^{2,5}

Fabry Disease Can Damage the Kidneys

- Fabry Disease is caused by a variant in the *GLA* gene. The *GLA* gene normally produces an enzyme that breaks down a fatty substance naturally produced by cells, called GL-3^{6,7}
- In patients with Fabry Disease, the *GLA* gene variant prevents normal enzyme production, causing GL-3 buildup in cells throughout the body. This includes the cells that make up the kidneys⁶
- Over time, buildup of GL-3 can progressively reduce the function of organs such as the kidneys, brain, and heart⁶

eGFR is Used to Monitor Your Kidney Function

- eGFR is calculated based on the levels of a substance called creatinine that is normally filtered out by the kidneys. eGFR levels vary based on your age, biological sex, and body size^{5,8}
- eGFR is **expressed as a number** followed by “mL/min/1.73m²”. It is obtained with a **basic blood test** and may **change over time**^{4,5,9,10}
- Higher eGFR numbers show that the kidneys are working well. **Lower, or declining, eGFR numbers may indicate kidney disease**¹¹
- Creatinine may be measured anywhere from once per month to once per year, based on your risk of worsening kidney disease.^{4,12} Talk to your healthcare provider to find out how often you should have your creatinine measured and eGFR calculated

Fabry Disease can eventually cause kidney failure if not managed appropriately. Kidney failure due to Fabry Disease may be irreversible, so it's important for patients with Fabry Disease to maintain and monitor their kidney health^{6,12}

What can you expect at different stages of chronic kidney disease (CKD)?^{4,11,13}

Stage	eGFR	Potential Signs and Symptoms	
1	>90	Patients may not have symptoms	Foamy urine, urinating at night, edema (swelling in the face and body), anxiety, anemia
2	60-89		
3a	45-59		
3b	30-44	Patients likely have symptoms	Edema in the legs, difficulty breathing, high blood pressure, constipation, slowed growth in children, anemia
4	15-29		<ul style="list-style-type: none"> • Worsening edema • Itching • Fatigue • Difficulty thinking, remembering, and concentrating
5	<15		<ul style="list-style-type: none"> • Changes in taste and smell • Reduced appetite • Nausea/vomiting • Daytime sleepiness • More significant anemia
		End-stage kidney/renal disease (ESKD/ESRD)*	
		<ul style="list-style-type: none"> • Worsening heart failure • Hiccups that won't go away • Bleeding • Dry skin • Lack of menstruation 	<ul style="list-style-type: none"> • Sexual problems • Bone changes • Spontaneous bone breaks • Weight changes • Muscle wasting • More significant anemia
Advanced kidney disease requires dialysis or kidney transplant			

Fabry Disease can cause organ damage throughout the body, and kidney disease is common in patients. However, not everyone with Fabry Disease will develop kidney disease.^{12,14} See last page for additional information.

*Patients at any stage of kidney disease may also have symptoms of earlier stages.¹¹

Chart Your Own Kidney Function Over Time by Following the Steps Below

Tracking Results

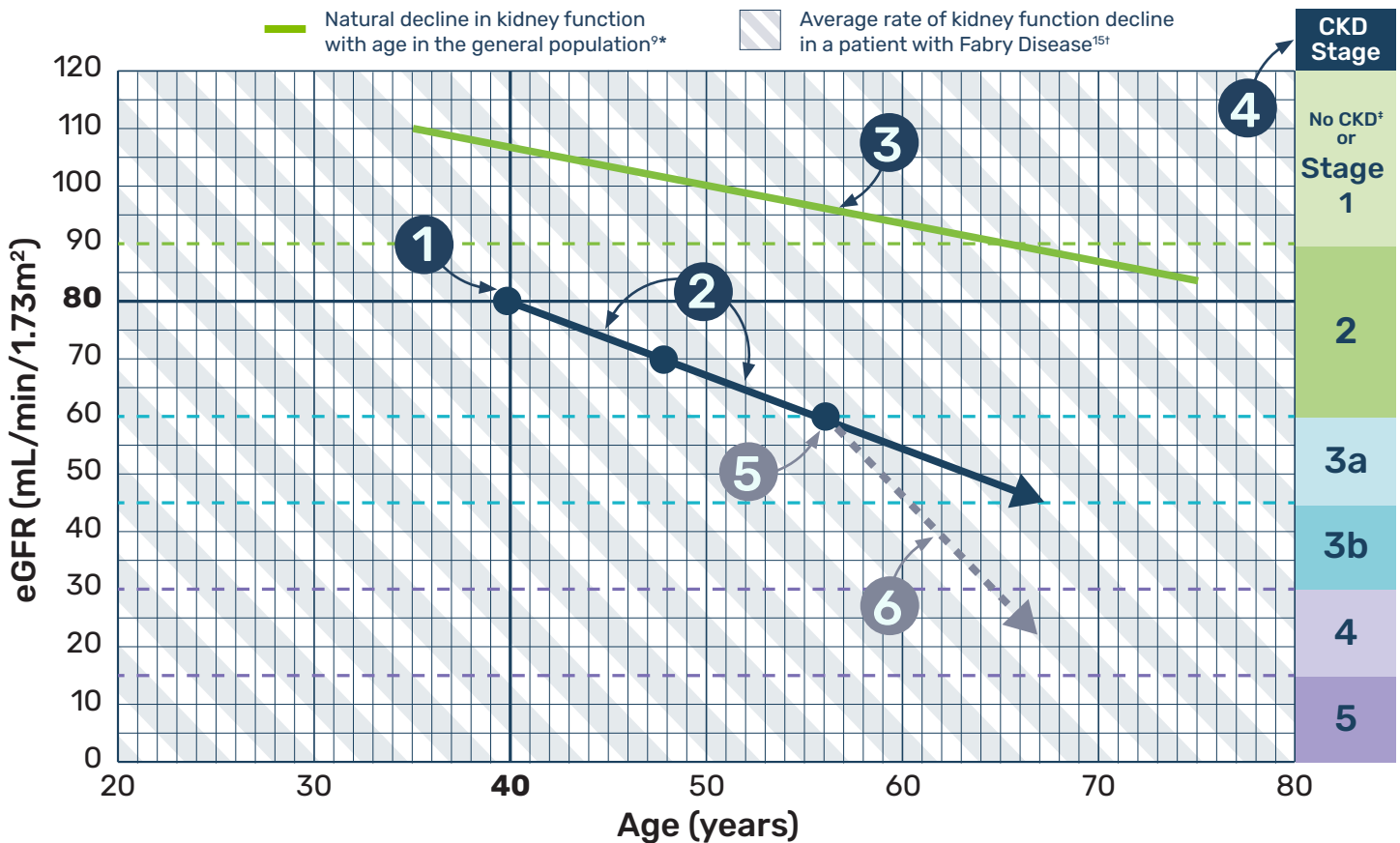
1 Find your eGFR on the left side of the graph and your age at the time of your test result on the bottom of the graph. Place a dot where the two values meet. For this example, age is 40 and eGFR is 80, which are bolded below

2 Repeat Step 1 for all eGFR results and connect the dots in age order

3 Compare your dot or line to the green line. If your dot or line closely follows the green line, your kidneys are declining at the same rate as the general population⁹

Understanding the Impact for CKD

4 Compare your latest eGFR dot to the colored bars on the right, which correspond to the different stages previously explained⁴



Understanding the Importance of Treatment

5 Note which thick white or gray line your latest eGFR dot falls on

6 Draw a line following the path of the white or gray line. This line represents the decline in kidney function you might have if your Fabry Disease was left untreated.¹⁵ Note how much faster that line drops compared to the green line. The steeper decline indicates a faster drop in kidney function over time. A goal of Fabry Disease treatment is to make that decline less steep⁶

*Average eGFR is about 110 mL/min/1.73m² in healthy young adults, and it typically begins to decline beginning at age 35 in the general population.⁹

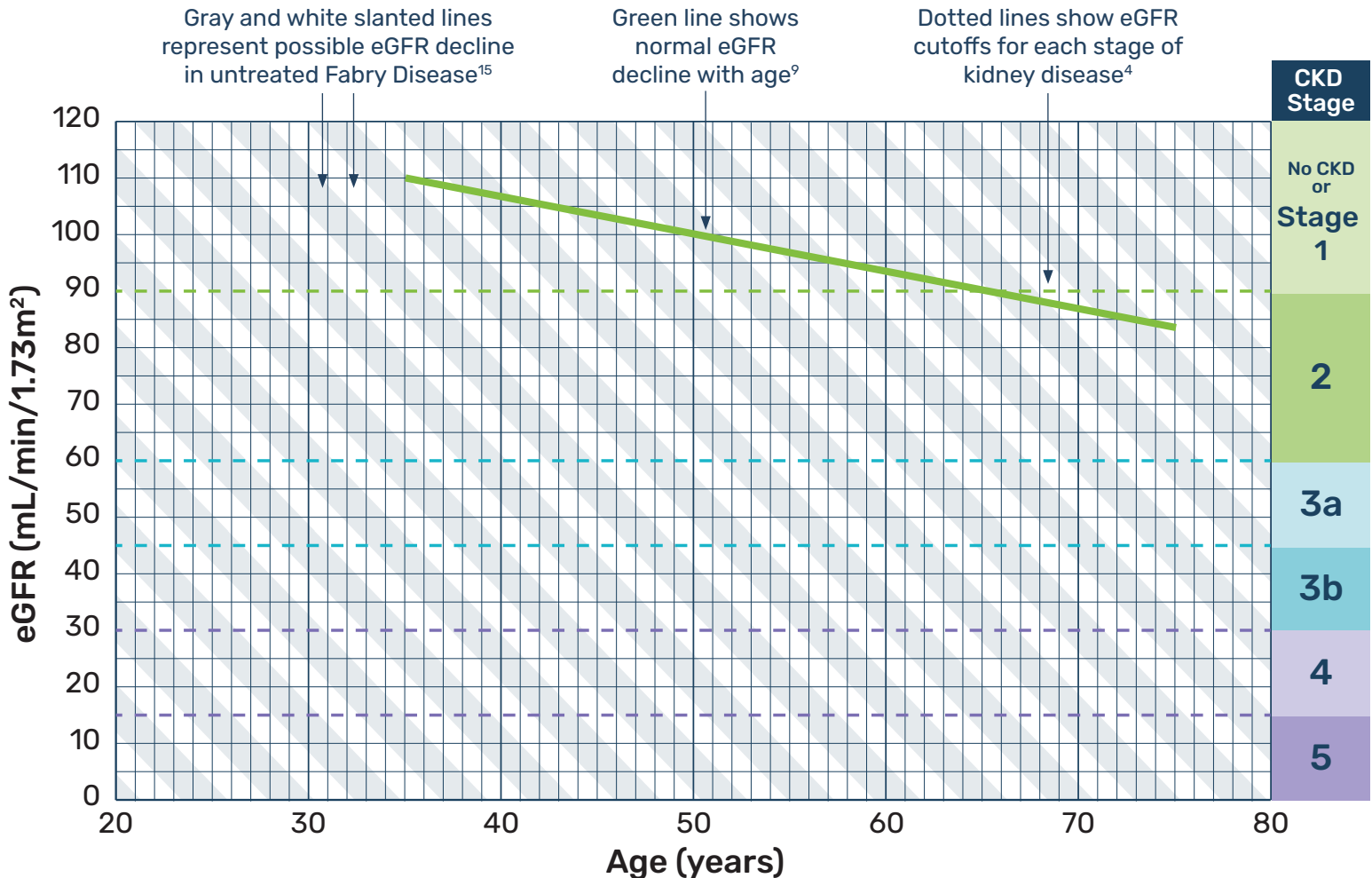
[†]The graph above is based on studies that evaluated kidney function in patients ages 35-75 in the general population and patients ages 17-65 with Fabry Disease.^{9,16,17} The gray lines for ages 66-80 have been extrapolated for the purpose of expanding the graph.

[‡]You may not have kidney disease today, but you may want to understand what can happen in the future with your Fabry Disease.

How Well Are Your Kidneys Working Today? How Well Might They Be Working Tomorrow?

eGFR naturally declines as you age; however, patients with Fabry Disease can have a much faster drop in kidney function. This decline may be even faster when you are not getting the right treatment.⁹ Use this chart to see how your kidney function is changing over time – and how it might decline if you do not manage your Fabry Disease appropriately.

Use the line above to title your graph based on what your results mean to you.



Follow the instructions on the previous page to graph your own kidney function over time, then ask yourself the following questions. It's easier than you think and may provide you with a sense of what your kidney function might look like without appropriate treatment.

Let's consider what your eGFR graph might mean for you



1. How does your rate of eGFR decline compare to the general population (green line)?
2. What stage of kidney disease do your eGFR values currently indicate?
 - As your kidney function declines over time, what might each of these stages mean for you?
 - How might kidney disease impact your life?
3. What action can you take today to help protect your kidney health in the future?
4. Do you have questions about your kidney function? Contact your healthcare provider. You can also receive additional background education by visiting CareConnectPSS.com to talk to a Patient Education Liaison (PEL)

Kidney Function Is an Important Consideration for Managing Your Fabry Disease



"It is so easy to not worry about test results, but some are too important to ignore. Following your eGFR numbers is vital to understanding kidney disease progression, which plays a role in overall Fabry disease impact." – Jack Johnson, *Living with Fabry Disease*



"Ask questions. Your doctor and nurse are aware of how everything can change with kidney disease... But ultimately, you have to go home with it. This is your thing. Don't just look at numbers like eGFR and assume they're OK... It's important to know yourself, how to read the results, what they mean, and what will make the levels change." – Christian Garza, *Living with Fabry Disease**

International guidelines recommend treatment with enzyme replacement therapy (ERT) for all patients with Fabry Disease who have signs and symptoms of organ damage, or laboratory evidence of organ damage. Below, see potential signs and symptoms of damage to some organs, among many, that can be affected by Fabry Disease.^{11,12}

Heart



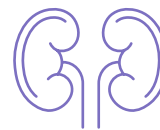
Enlarged heart, irregular heartbeat, heart failure, very slow heartbeat, difficulty exercising

Brain



Stroke, mini-stroke, blood clot

Kidneys



Protein in the urine, urinating at night, foamy urine, leg swelling, and shortness of breath

If you experience any of the above symptoms or have a personal or family history of organ damage, talk to your healthcare provider to ensure that your Fabry Disease is being treated appropriately.

Visit DiscoverFabry.com to learn more about Fabry Disease and connect with PELs and patient groups that can provide support.



Glossary

Creatinine – a substance that is normally filtered by the kidneys⁸

Estimated glomerular filtration rate (eGFR) – calculated number that approximately measures the ability of the kidneys to filter out waste products based on a patient's biological sex, age, body size, and blood creatinine levels⁵

Glomerulus – main structure inside the nephron that is responsible for filtering out waste products²

Nephron – structure inside kidneys that is responsible for filtering the blood⁵

*This patient was compensated for their time providing this quote.

1. Choudhary U, Kumar S, Jee K, Singh A, Bharti P. A cadaveric study on anatomical variations of kidney and ureter in India. *Int J Res Med Sci.* 2017;5(6):2358–2361. 2. Hoenig MP, Hladik GA. Overview of kidney structure and function. In: Gilbert S, Weiner D, eds. *National Kidney Foundation Primer on Kidney Diseases*. 7th edition. Elsevier;2017:2–18. 3. Russo LM, Sandoval RM, McKee M, et al. The normal kidney filters nephrotic levels of albumin retrieved by proximal tubule cells: retrieval is disrupted in nephrotic states. *Kidney Int.* 2007;71(6):504–513. 4. KDIGO 2012 Clinical Practice Guideline for the evaluation and management of chronic kidney disease. *Kidney Int Suppl.* 2013;3(1):1–150. Accessed June 9, 2023. https://kdigo.org/wp-content/uploads/2017/02/KDIGO_2012_CKD_GL.pdf 5. Inker LA, Levey AS. Assessment of glomerular filtration rate. In: Johnson RJ, et al, eds. *Comprehensive Clinical Nephrology*. 6th edition. Elsevier;2018:29–38. 6. Germain DP. Fabry Disease. *Orphanet J Rare Dis.* 2010;5(30):1–49. 7. Celi AB, Goldstein J, Rosato-Siri MV, Pinto A. Role of globotriaosylceramide in physiology and pathology. *Front Mol Biosci.* 2022;9:1–20. 8. Nankivell BJ, Nankivell LFJ, Elder GJ, Gruenewald SM. How unmeasured muscle mass affects estimated GFR and diagnostic inaccuracy. *EClinicalMedicine.* 2020;29:100662. 9. Waas T, Schulz A, Lotz J, et al. Distribution of estimated glomerular filtration rate and determinants of its age dependent loss in a German population-based study. *Sci Rep.* 2021;11(1):10165. 10. Qaseem A, Hopkins Jr. RH, Sweet DE, Starkey M, Shekelle P; Clinical Guidelines Committee of the American College of Physicians. Screening, monitoring, and treatment of stage 1 to 3 chronic kidney disease: a clinical practice guideline from the American College of Physicians. *Ann Intern Med.* 2013;159(12):835–847. 11. Kalantar-Zadeh K, Lockwood MB, Rhee CM, et al. Patient-centered approaches for the management of unpleasant symptoms in kidney disease. *Nat Rev Nephrol.* 2022;18(3):185–198. 12. Ortiz A, Germain DP, Desnick RJ, et al. Fabry Disease revisited: management and treatment recommendations for adult patients. *Mol Genet Metab.* 2018;123(4):416–427. 13. Stack AG, Alghali A, Li X, et al. Quality of care and practice patterns in anaemia management at specialist kidney clinics in Ireland: a national study. *Clin Kidney J.* 2018;11(1):99–107. 14. Mehta A, Clarke JTR, Giugliani R, Elliott P, Linhart A, Beck M, Sunder-Plassmann G. Natural course of Fabry Disease: changing pattern of causes of death in FOS – Fabry Outcome Survey. *J Med Genet.* 2009;46(8):548–552. 15. Ortiz A, Kanters S, Hamed A, et al. Agalsidase beta treatment slows estimated glomerular filtration rate loss in classic Fabry disease patients: results from an individual patient data meta-analysis. *Clin Kidney J.* 2020;14(4):1136–1146. 16. Eng CM, Guffon N, Wilcox W, et al. Safety and efficacy of recombinant human α -Galactosidase A replacement therapy in Fabry's Disease. *N Engl J Med.* 2001;345(1):9–16. 17. A study of the safety and efficacy of Fabrazyme (agalsidase beta) as compared to placebo in patients with advanced Fabry Disease. Clinicaltrials.gov Identifier: NCT00074984. Updated December 27, 2013. <https://clinicaltrials.gov/ct2/show/results/NCT00074984?term=NCT00074984&draw=2&rank=18&view=results>. Accessed June 14, 2023.