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High-Impact Trials Spotlight Advances in Therapies for IgA Nephropathy and Lupus

Insights on MRAs, Fish Oil Benefits, and Acute Dialysis Also Featured

By Bridget M. Kuehn

https://doi.org/10.62716/kn.002452025

The latest results from clinical trials of targeted agents for immunoglobulin A (IgA) nephropathy demonstrate strong kidney-protective effects that could help stave off kidney failure, according to presentations during the High-Impact Clinical Trials sessions at ASN Kidney Week 2025.

In addition to the latest results from a trio of trials of three potential new IgA nephropathy therapies, the High-Impact Clinical Trials sessions highlighted the potential of finerenone for patients with type 1 diabetes, the benefits of fish oil for preventing cardiovascular events in patients with kidney diseases, as well as significant advances in therapies for lupus nephritis and membranous nephropathy.

A trio of IgA therapies

Presenter Richard Lafayette, MD, professor of medicine (nephrology) at Stanford University Medical Center in Stanford, CA, noted that significant progress has been made in recent years in the treatment of IgA nephropathy. However, the goal of achieving a stable estimated glomerular filtration rate (eGFR), similar to that of individuals with healthy kidneys, had proved elusive. Studies revealing the role of immune system B cells in the disease have led to new B cell-targeted therapies aimed at protecting the kidneys. Lafayette presented results from the phase 3 ORIGIN trial (NCT04716231), which were published simultaneously in *The New England Journal of Medicine* (1).

Atacicept is a once-weekly self-injected therapy that binds to B cell autoantibodies B cell-activating factor and a proliferation-inducing ligand (APRIL). The treatment helps clear these autoantibodies from the circulation, protecting the kidneys from inflammation caused by the buildup of these molecules. The trial randomized 431 patients to atacicept or placebo and demonstrated a 40% to 50% reduction in proteinuria, a 20-fold higher rate of resolution of hematuria, and a two-thirds reduction of galactose-deficient

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Transplant Policy Takes Center Stage in 2025 and Beyond: Legislative and KidneyX Initiatives Focus on Organ Donation, Transplant System Reform Advances

By Bridget M. Kuehn

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Increasing access to organ transplantation and identifying opportunities to improve the US transplant system have been the focus of a flurry of national policy changes over the past year, a trend that will likely continue into 2026, according to policy leaders at ASN.

Over the past 6 months, the Center for Medicare and Medicaid Innovation (CMMI) began implementing its Increasing Organ Transplant Access (IOTA) model. The Department of Health and Human Services (HHS) and Health Resources and Services Administration (HRSA) have announced additional steps to modernize and increase accountability in the organ procurement and transplantation system, as part of HRSA's Organ Procurement and Transplantation Network (OPTN) Modernization initiative. ASN's policy committees are instrumental partners with the federal agencies to advance legislation aimed at boosting living organ donation by removing barriers for living donors. ASN is again partnering with HHS on the Kidney Innovation Accelerator (KidneyX) in 2026 with plans to support organ donation innovation projects.

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Inside

FABHALTA®
(iptacopan) 200 mg capsules

To reduce proteinuria in adults with primary IgAN at risk of rapid disease progression (generally a UPCR ≥1.5 g/g)[1]

TAKE ACTION WITH FABHALTA

This indication is approved under accelerated approval based on reduction of proteinuria. It has not been established whether FABHALTA slows kidney function decline in patients with IgAN. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial.[1]

Persistent proteinuria despite maximally tolerated RASi ± SGLT2i can signify the need for a different approach[2-4]

In APPLAUSE, a phase 3 clinical trial for adults with primary IgAN and elevated proteinuria, FABHALTA significantly reduced proteinuria at 9 months[1,5]

FABHALTA is a single capsule taken orally twice a day[1]

Scan to explore efficacy and safety data or visit FABHALTA-HCP.com/IgAN

Patient portrayal.

IMPORTANT SAFETY INFORMATION

WARNING: SERIOUS INFECTIONS CAUSED BY ENCAPSULATED BACTERIA

FABHALTA, a complement inhibitor, increases the risk of serious infections, especially those caused by encapsulated bacteria, such as *Streptococcus pneumoniae*, *Neisseria meningitidis*, and *Haemophilus influenzae* type b. Life-threatening and fatal infections with encapsulated bacteria have occurred in patients treated with complement inhibitors. These infections may become rapidly life threatening or fatal if not recognized and treated early.

- **Complete or update vaccinations for encapsulated bacteria at least 2 weeks prior to the first dose of FABHALTA, unless the risks of delaying therapy with FABHALTA outweigh the risk of developing a serious infection. Comply with the most current Advisory Committee on Immunization Practices (ACIP) recommendations for vaccinations against encapsulated bacteria in patients receiving a complement inhibitor.**
- **Patients receiving FABHALTA are at increased risk for invasive disease caused by encapsulated bacteria, even if they develop antibodies following vaccination. Monitor patients for early signs and symptoms of serious infections and evaluate immediately if infection is suspected.**

Because of the risk of serious infections caused by encapsulated bacteria, FABHALTA is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the FABHALTA REMS.

CONTRAINDICATIONS

- In patients with serious hypersensitivity to FABHALTA or any of the excipients.
- For initiation in patients with unresolved serious infection caused by encapsulated bacteria, including *Streptococcus pneumoniae*, *Neisseria meningitidis*, or *Haemophilus influenzae* type b.

WARNINGS AND PRECAUTIONS

Serious Infections Caused by Encapsulated Bacteria

- FABHALTA, a complement inhibitor, increases a patient's susceptibility to serious, life-threatening, or fatal infections caused by encapsulated bacteria, including *Streptococcus pneumoniae*, *Neisseria meningitidis* (caused by any serogroup, including nongroupable strains), and *Haemophilus influenzae* type b. Life-threatening and fatal infections with encapsulated bacteria have occurred in both vaccinated and unvaccinated patients treated with complement inhibitors. The initiation of FABHALTA is contraindicated in patients with unresolved serious infections caused by encapsulated bacteria.
- Complete or update vaccination against encapsulated bacteria at least 2 weeks prior to the start of FABHALTA, according to the current ACIP recommendations for patients receiving a complement inhibitor. Revaccinate patients in accordance with ACIP recommendations considering the duration of therapy with FABHALTA. Note that ACIP recommends an administration schedule in patients receiving complement inhibitors that differs from the administration schedule in the vaccine prescribing information. If urgent FABHALTA therapy is indicated in a patient who is not up to date with vaccines against encapsulated bacteria according to ACIP recommendations, provide the patient with antibacterial drug prophylaxis and administer these vaccines as soon as possible. The benefits and risks of treatment with FABHALTA, as well as the benefits and risks of antibacterial drug prophylaxis in unvaccinated or vaccinated patients, must be considered against the known risks for serious infections caused by encapsulated bacteria.

Please see additional Important Safety Information and Brief Summary of full Prescribing Information, including Boxed WARNING on the following pages.

IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS (continued)

Serious Infections Caused by Encapsulated Bacteria (continued)

- Vaccination does not eliminate the risk of serious encapsulated bacterial infections, despite development of antibodies following vaccination. Closely monitor patients for early signs and symptoms of serious infection and evaluate patients immediately if an infection is suspected. Inform patients of these signs and symptoms and instruct patients to seek immediate medical care if they occur. Promptly treat known infections. Serious infection may become rapidly life threatening or fatal if not recognized and treated early. Consider interruption of FABHALTA in patients who are undergoing treatment for serious infections, depending on the risks of interrupting treatment in the disease being treated.

FABHALTA REMS

- FABHALTA is available only through a restricted program under a REMS called FABHALTA REMS, because of the risk of serious infections caused by encapsulated bacteria.
- Under the FABHALTA REMS, prescribers must enroll in the program; counsel patients about the risks, signs, and symptoms of serious infections caused by encapsulated bacteria; provide patients with the REMS educational materials; ensure patients are vaccinated against encapsulated bacteria; prescribe antibacterial drug prophylaxis if patients' vaccine status is not up to date and treatment must be started urgently; and provide instructions to always carry the Patient Safety Card during treatment and for 2 weeks following the last dose of FABHALTA.
- Further information is available by telephone: 1-833-993-2242 or online at www.FABHALTA-REMS.com.

Hyperlipidemia

- FABHALTA may increase total cholesterol, LDL cholesterol, and serum triglycerides. Some patients required cholesterol-lowering medications.
- Monitor serum lipid parameters periodically during treatment with FABHALTA and initiate cholesterol-lowering medications, if indicated.

ADVERSE REACTIONS

- The most common adverse reactions (≥5%) in adults with IgAN receiving FABHALTA were upper respiratory tract infection, lipid disorder, and abdominal pain.

DRUG INTERACTIONS

- Concomitant use of CYP2C8 inducers (eg, rifampin) may decrease iptacopan exposure, which may result in loss of or reduced efficacy of FABHALTA. Monitor the clinical response and discontinue use of the CYP2C8 inducer if loss of efficacy of FABHALTA is evident.
- Concomitant use of strong CYP2C8 inhibitors (eg, gemfibrozil) may increase iptacopan exposure, which may result in an increased risk for adverse reactions with FABHALTA. Coadministration with a strong CYP2C8 inhibitor is not recommended.

USE IN SPECIFIC POPULATIONS

- Because of the potential for serious adverse reactions in a breastfed child, breastfeeding should be discontinued during treatment and for 5 days after the final dose.
- FABHALTA is not recommended in patients with severe hepatic impairment (Child-Pugh class C). No dose adjustment is required for patients with mild (Child-Pugh class A) or moderate (Child-Pugh class B) hepatic impairment.

INDICATION

FABHALTA is indicated to reduce proteinuria in adults with primary immunoglobulin A nephropathy (IgAN) at risk of rapid disease progression, generally a urine protein-to-creatinine ratio (UPCR) ≥1.5 g/g.

This indication is approved under accelerated approval based on reduction of proteinuria. It has not been established whether FABHALTA slows kidney function decline in patients with IgAN. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory clinical trial.

IgAN, immunoglobulin A nephropathy; RASi, renin-angiotensin system inhibitor; SGLT2i, sodium/glucose cotransporter-2 inhibitor; UPCR, urine protein-to-creatinine ratio.

References: 1. Fabhalta. Prescribing information. Novartis Pharmaceuticals Corp. **2.** Rovin BH, Adler SG, Barratt J, et al; Kidney Disease: Improving Global Outcomes (KDIGO) Glomerular Diseases Work Group. KDIGO 2021 clinical practice guideline for the management of glomerular diseases. *Kidney Int*. 2021;100(suppl 4):S1-S276. doi:10.1016/j.kint.2021.05.021 **3.** Medjeral-Thomas NR, Troldborg A, Constantinou N, et al. Progressive IgA nephropathy is associated with low circulating mannan-binding lectin–associated serine protease-3 (MASP-3) and increased glomerular factor H–related protein-5 (FHR5) deposition. *Kidney Int Rep*. 2018;3(2):426-438. doi:10.1016/j.ekir.2017.11.015 **4.** Lim RS, Yeo SC, Barratt J, Rizk DV. An update on current therapeutic options in IgA nephropathy. *J Clin Med*. 2024;13(4):947. doi:10.3390/jcm13040947 **5.** Data on file. APPLAUSE Sub Analysis. Novartis Pharmaceuticals Corp; July 2024.

Please see additional Important Safety Information on previous page and Brief Summary of full Prescribing Information, including Boxed WARNING on the following pages.

NOVARTIS

Novartis Pharmaceuticals Corporation
East Hanover, New Jersey 07936-1080

Printed in USA 7/25 FA-11460310

FABHALTA® (iptacopan) capsules, for oral use
Initial U.S. Approval: 2023

BRIEF SUMMARY: Please see package insert for full prescribing information.

WARNING: SERIOUS INFECTIONS CAUSED BY ENCAPSULATED BACTERIA

FABHALTA, a complement inhibitor, increases the risk of serious infections, especially those caused by encapsulated bacteria, such as *Streptococcus pneumoniae*, *Neisseria meningitidis*, and *Haemophilus influenzae* type b *[see Warnings and Precautions (5.1)]*. Life-threatening and fatal infections with encapsulated bacteria have occurred in patients treated with complement inhibitors. These infections may become rapidly life-threatening or fatal if not recognized and treated early.

- **Complete or update vaccination for encapsulated bacteria at least 2 weeks prior to the first dose of FABHALTA, unless the risks of delaying therapy with FABHALTA outweigh the risk of developing a serious infection. Comply with the most current Advisory Committee on Immunization Practices (ACIP) recommendations for vaccinations against encapsulated bacteria in patients receiving a complement inhibitor. See *Warnings and Precautions (5.1)* for additional guidance on the management of the risk of serious infections caused by encapsulated bacteria.**
- **Patients receiving FABHALTA are at increased risk for invasive disease caused by encapsulated bacteria, even if they develop antibodies following vaccination. Monitor patients for early signs and symptoms of serious infections and evaluate immediately if infection is suspected.**

Because of the risk of serious infections caused by encapsulated bacteria, FABHALTA is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the FABHALTA REMS *[see Warnings and Precautions (5.2)]*.

1 INDICATIONS AND USAGE

1.1 Paroxysmal Nocturnal Hemoglobinuria

FABHALTA is indicated for the treatment of adults with paroxysmal nocturnal hemoglobinuria (PNH).

1.2 Immunoglobulin A Nephropathy

FABHALTA is indicated to reduce proteinuria in adults with primary immunoglobulin A nephropathy (IgAN) at risk of rapid disease progression, generally a urine protein-to-creatinine ratio (UPCR) ≥1.5 g/g.

This indication is approved under accelerated approval based on reduction of proteinuria. It has not been established whether FABHALTA slows kidney function decline in patients with IgAN. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory clinical trial.

1.3 Complement 3 Glomerulopathy

FABHALTA is indicated for the treatment of adults with complement 3 glomerulopathy (C3G), to reduce proteinuria.

4 CONTRAINDICATIONS

FABHALTA is contraindicated:

- in patients with serious hypersensitivity to iptacopan or any of the excipients.
- for initiation in patients with unresolved serious infection caused by encapsulated bacteria, including *Streptococcus pneumoniae*, *Neisseria meningitidis*, or *Haemophilus influenzae* type b.

5 WARNINGS AND PRECAUTIONS

5.1 Serious Infections Caused by Encapsulated Bacteria

FABHALTA, a complement inhibitor, increases a patient's susceptibility to serious, life-threatening, or fatal infections caused by encapsulated bacteria, including *Streptococcus pneumoniae, Neisseria meningitidis* (caused by any serogroup, including non-groupable strains), and *Haemophilus influenzae* type b. Life-threatening and fatal infections with encapsulated bacteria have occurred in both vaccinated and unvaccinated patients treated with complement inhibitors. The initiation of FABHALTA treatment is contraindicated in patients with unresolved serious infections caused by encapsulated bacteria.

Complete or update vaccination against encapsulated bacteria at least 2 weeks prior to administration of the first dose of FABHALTA, according to the current ACIP recommendations for patients receiving a complement inhibitor. Revaccinate patients in accordance with ACIP recommendations considering the duration of therapy with FABHALTA. Note that ACIP recommends an administration schedule in patients receiving complement inhibitors that differs from the administration schedule in the vaccine prescribing information. If urgent FABHALTA therapy is indicated in a patient who is not up to date with vaccines against encapsulated bacteria according to ACIP recommendations, provide the patient with antibacterial drug prophylaxis and administer these vaccines as soon as possible. Various durations and regimens of antibacterial drug prophylaxis have been considered, but the optimal durations and drug regimens for prophylaxis and their efficacy have not been studied in unvaccinated or vaccinated patients receiving complement inhibitors, including FABHALTA. The benefits and risks of treatment with FABHALTA, as well as the benefits and risks of antibacterial drug prophylaxis in unvaccinated or vaccinated patients, must be considered against the known risks for serious infections caused by encapsulated bacteria.

Vaccination does not eliminate the risk of serious encapsulated bacterial infections, despite development of antibodies following vaccination. Closely monitor patients for early signs and symptoms of serious infection and evaluate patients immediately if an infection is suspected. Inform patients of these signs and symptoms and instruct patients to seek immediate medical care if these signs and symptoms occur. Promptly treat known infections. Serious infection may become rapidly life-threatening or fatal if not recognized and treated early. Consider interruption of FABHALTA in patients who are undergoing treatment for serious infections, depending on the risks of interrupting treatment in the disease being treated.

FABHALTA is available only through a restricted program under a REMS *[see Warnings and Precautions (5.2)]*.

5.2 FABHALTA REMS

FABHALTA is available only through a restricted program under a REMS called FABHALTA REMS, because of the risk of serious infections caused by encapsulated bacteria *[see Warnings and Precautions (5.1)]*.

Notable requirements of the FABHALTA REMS include the following:

- Prescribers must enroll in the REMS.
- Prescribers must counsel patients about the risk of serious infections caused by encapsulated bacteria.
- Prescribers must provide patients with the REMS educational materials.
- Prescribers must assess patient vaccination status for vaccines against encapsulated bacteria and vaccinate if needed according to current ACIP recommendations two weeks prior to the first dose of FABHALTA.
- Prescribers must provide a prescription for antibacterial drug prophylaxis if treatment must be started urgently, and the patient is not up to date with vaccines against encapsulated bacteria according to current ACIP recommendations at least two weeks prior to the first dose of FABHALTA.
- Pharmacies that dispense FABHALTA must be certified in the FABHALTA REMS and must verify prescribers are certified.
- Patients must receive counseling from the prescriber about the need to receive vaccinations against encapsulated bacteria per ACIP recommendations, the need to take antibiotics as directed by the prescriber, and the early signs and symptoms of serious infections.
- Patients must be instructed to carry the Patient Safety Card with them at all times during treatment and for 2 weeks following the last dose of FABHALTA.

Further information is available by telephone: 1-833-99FABHA (1-833-993-2242) or online at www.FABHALTA-REMS.com.

5.3 Monitoring of PNH Manifestations After FABHALTA Discontinuation

In PNH patients, after discontinuing treatment with FABHALTA, closely monitor patients for at least 2 weeks after the last dose for signs and symptoms of hemolysis. These signs include elevated lactate dehydrogenase (LDH) levels along with a sudden decrease in hemoglobin or PNH clone size, fatigue, hemoglobinuria, abdominal pain, dyspnea, major adverse vascular events (such as thrombosis, stroke and myocardial infarction), dysphagia, or erectile dysfunction. If discontinuation of FABHALTA is necessary, consider alternative therapy.

If hemolysis occurs after discontinuation of FABHALTA, consider restarting treatment with FABHALTA, if appropriate, or initiating another treatment for PNH.

5.4 Hyperlipidemia

FABHALTA may increase total cholesterol, LDL-cholesterol, and serum triglycerides *[see Adverse Reactions (6.1)]*.

Of the 54 FABHALTA-treated patients who had a normal total cholesterol level at baseline in APPLY-PNH, 43% developed Grade 1 hypercholesterolemia during the randomized treatment period. One FABHALTA-treated patient in APPLY-PNH experienced increased total cholesterol that worsened to Grade 2 from Grade 1 at baseline.

Of the 34 FABHALTA-treated patients who had a normal cholesterol level at baseline in APPOINT-PNH, 24% developed Grade 1 hypercholesterolemia during the core treatment period.

Of the 60 FABHALTA-treated patients who had LDL-cholesterol ≤ 130 mg/dL at baseline in APPLY-PNH, 17% developed LDL-cholesterol > 130-160 mg/dL, 8% developed LDL-cholesterol > 160-190 mg/dL, and 7% developed LDL-cholesterol > 190 mg/dL during the randomized treatment period. Of the 36 FABHALTA-treated patients who had LDL-cholesterol ≤ 130 mg/dL at baseline in APPOINT-PNH, 11% developed LDL-cholesterol > 130-160 mg/dL and 3% developed LDL-cholesterol > 160-190 mg/dL.

Of the 52 patients with normal triglyceride levels at baseline in APPLY-PNH, 23% developed Grade 1 elevated triglycerides during the randomized treatment period. Three FABHALTA-treated patients in APPLY-PNH experienced an increase in triglycerides from Grade 1 to Grade 2.

Of the 37 FABHALTA-treated patients who had a normal triglyceride level at baseline in APPOINT-PNH, 27% developed Grade 1 elevated triglycerides in the core treatment period.

Of the 102 FABHALTA-treated patients in APPLY-PNH and APPOINT-PNH, two patients required cholesterol-lowering medications.

Monitor serum lipid parameters periodically during treatment with FABHALTA and initiate cholesterol-lowering medication, if indicated.

6 ADVERSE REACTIONS

The following clinically significant adverse reactions are discussed in greater detail in other sections of the labeling:

- Serious Infections Caused by Encapsulated Bacteria *[see Warnings and Precautions (5.1)]*.
- Hyperlipidemia *[see Warnings and Precautions (5.4)]*.

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

Paroxysmal Nocturnal Hemoglobinuria (PNH)

The data described below reflects the exposure in adults with PNH who received FABHALTA (n = 62) or anti-C5 treatment (US-approved and non-US-approved eculizumab product or US-approved and non-US-approved ravulizumab product, n = 35) in APPLY-PNH [NCT04558918] and adults who received FABHALTA (n = 40) in APPOINT-PNH [NCT04820530] at the recommended dosing regimen for 24 weeks. In APPLY-PNH, serious adverse reactions were reported in 2 (3%) patients with PNH receiving FABHALTA. Serious adverse reactions included pyelonephritis, urinary tract infection and COVID-19. In APPOINT-PNH, serious adverse reactions were reported in 2 (5%) patients with PNH receiving FABHALTA. Serious adverse reactions included COVID-19 and bacterial pneumonia. The most common adverse reactions (≥ 10%) with FABHALTA

were headache, nasopharyngitis, diarrhea, abdominal pain, bacterial infection, viral infection, nausea, and rash.

Table 1 describes the adverse reactions that occurred in > 5% of patients treated with FABHALTA in the APPLY-PNH or APPOINT-PNH studies.

Table 1: Adverse Reactions Reported in > 5% of Patients Treated with FABHALTA in APPLY-PNH or APPOINT-PNH Studies (24-Week Treatment Period)

Adverse reactions	APPLY-PNH		APPOINT-PNH
	FABHALTA (N = 62) n (%)	Anti-C5 (Eculizumab or Ravulizumab) (N = 35) n (%)	FABHALTA (N = 40) n (%)
Headache[a]	12 (19)	1 (3)	11 (28)
Nasopharyngitis[b]	10 (16)	6 (17)	6 (15)
Diarrhea	9 (15)	2 (6)	3 (8)
Abdominal pain[a]	9 (15)	1 (3)	3 (8)
Bacterial infection[c]	7 (11)	4 (11)	2 (5)
Nausea	6 (10)	1 (3)	2 (5)
Viral infection[d]	6 (10)	11 (31)	7 (18)
Arthralgia	5 (8)	1 (3)	0
Thrombocytopenia[a]	4 (6)	0	0
Dizziness	4 (6)	0	1 (3)
Systemic hypertension[a]	4 (6)	0	0
Lipid disorder[e]	4 (6)	0	3 (8)
Rash[f]	2 (3)	0	4 (10)

[a]Includes similar terms.
[b]Nasopharyngitis contains: rhinitis allergic, upper respiratory tract infection, pharyngitis, rhinitis.
[c]Bacterial infection contains: pyelonephritis, urinary tract infection, bronchitis bacterial, bronchitis haemophilus, cholecystitis, folliculitis, cellulitis, arthritis bacterial, sepsis, klebsiella infection, staphylococcal infection, *Pseudomonas* infection, hordeolum, pneumonia bacterial.
[d]Viral infection contains: COVID-19, herpes zoster, oral herpes, nasal herpes, influenza A virus test positive, influenza.
[e]Lipid disorder contains: dyslipidemia, blood cholesterol increased, low density lipoprotein increased, hypercholesterolemia, blood triglycerides increased, hyperlipidemia.
[f]Rash contains: dermatitis allergic, acne, erythema multiforme, rash maculo-papular, rash erythematous.

Clinically relevant adverse reactions reported in less than or equal to 5% of patients includes urticaria in one patient (3%) in APPOINT-PNH.

Description of Select Adverse Reactions (graded per NCI CTCAE Version 4.03 unless noted otherwise)

Platelet Count Decreased
Of the 37 FABHALTA-treated patients who had normal platelet counts at baseline in APPLY-PNH, 43% experienced any Grade thrombocytopenia during the randomized treatment period. Three FABHALTA-treated patients in APPLY-PNH experienced decreased platelets that worsened to Grade ≥ 3 from baseline (one patient with normal platelets that worsened to Grade 4, one patient with baseline Grade 1 that worsened to Grade 4, and one patient with baseline Grade 3 that worsened to Grade 4).

Immunoglobulin A Nephropathy (IgAN)
The safety of FABHALTA was evaluated in APPLAUSE-IgAN, a randomized placebo-controlled, double-blind clinical study in adults with IgAN (eGFR ≥ 20 mL /min/1.73 m^2 at baseline).

The data below reflect FABHALTA exposure in 235 patients with IgAN (eGFR ≥ 20 mL/min/1.73 m^2 at baseline) with a median duration of 43 weeks (up to 104 weeks) in APPLAUSE-IgAN. Table 2 describes the adverse reactions that occurred in ≥ 3 % of patients treated with FABHALTA and were ≥ 2% higher in frequency than placebo. All of these adverse reactions were mild or moderate in severity.

Table 2: Adverse Reactions Reported in ≥ 3% of Adult Patients with IgAN (eGFR ≥ 20 mL /min/1.73 m^2) Treated with FABHALTA and ≥ 2% Higher in Frequency Than Placebo in APPLAUSE-IgAN

Adverse reaction	FABHALTA (N = 235) n (%)	Placebo (N = 235) n (%)
Upper respiratory tract infection	20 (9)	16 (7)
Lipid disorder[1]	15 (6)	10 (4)
Abdominal pain[1]	15 (6)	5 (2)
Nausea	8 (3)	2 (1)
Dizziness	7 (3)	2 (1)

[1] Includes similar terms.

Complement 3 Glomerulopathy (C3G)
The safety of FABHALTA was evaluated in APPEAR-C3G, a randomized, placebo-controlled, double-blind trial in adult patients with native kidney C3G. No new adverse reactions were identified during the 6-month placebo-controlled period of APPEAR-C3G, in which 38 patients were treated with FABHALTA and 36 patients were treated with placebo. The most common adverse reactions that occurred in ≥ 10% of patients treated with FABHALTA and were ≥ 5% higher in frequency than placebo were nasopharyngitis (11% in FABHALTA, 3% placebo) and viral infections (29% in FABHALTA, 22% placebo), mainly respiratory infections. One patient (3%) on FABHALTA and none on placebo had a serious adverse reaction of pneumonia and bacteremia secondary to an encapsulated organism (*S. pneumoniae*).

7 DRUG INTERACTIONS

7.1 CYP2C8 Inducers
Concomitant use of CYP2C8 inducers (e.g., rifampin) may decrease iptacopan exposure, which may result in loss of or reduced efficacy of FABHALTA. Monitor the clinical response and discontinue use of the CYP2C8 inducer if loss of efficacy of FABHALTA is evident.

7.2 Strong CYP2C8 Inhibitors
Concomitant use of strong CYP2C8 inhibitors (e.g., gemfibrozil) may increase iptacopan exposure, which may result in an increased risk for adverse reactions with FABHALTA. Coadministration with a strong CYP2C8 inhibitor is not recommended.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy
Risk Summary
Available data from clinical trials with FABHALTA use in pregnant women are insufficient to identify a drug-associated risk of major birth defects, miscarriage, or other adverse maternal or fetal outcomes. There are risks to the mother and fetus associated with untreated PNH, IgAN, or C3G in pregnancy *(see Clinical Considerations)*. The use of FABHALTA in pregnant women or women planning to become pregnant may be considered following an assessment of the risks and benefits.

In animal reproduction studies, oral administration of iptacopan to pregnant rats and rabbits during organogenesis at exposures 4- to 6-times the human exposure (based on AUC) at the maximum recommended human dose (MRHD) of 200 mg twice daily did not induce embryo or fetal toxicity *(see Data)*.

The estimated background risk of major birth defects and miscarriage for the indicated populations is unknown. All pregnancies have a background risk of major birth defects, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriages in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

Clinical Considerations
Disease-Associated Maternal and/or Embryo/Fetal Risk
PNH in pregnancy is associated with adverse maternal outcomes, including worsening cytopenias, thrombosis, infections, bleeding, miscarriages, increased maternal mortality, and adverse fetal outcomes, including fetal death and premature delivery.

IgAN in pregnancy is associated with adverse maternal outcomes, including increased rates of cesarean section, pregnancy-induced hypertension, pre-eclampsia and preterm delivery, and adverse fetal/neonatal outcomes, including stillbirth and low birth weight.

C3G in pregnancy may be associated with adverse maternal outcomes, in particular preeclampsia and miscarriage, as well as adverse fetal outcomes including prematurity and low birth weight.

Data
Animal Data
In an embryo-fetal development study in rats, oral administration of iptacopan during organogenesis did not cause embryo-fetal toxicity when given up to the highest dose of 1,000 mg/kg/day, which corresponds to 4-times the MRHD based on AUC.

In an embryo-fetal development study in rabbits, oral administration of iptacopan during organogenesis did not cause embryo-fetal toxicity when given up to the highest dose of 450 mg/kg/day, which corresponds to 6-times the MRHD based on AUC.

In a pre- and postnatal development study in rats, oral administration of iptacopan during gestation, parturition, and lactation did not cause adverse effects in offspring when given up to the highest dose of 1,000 mg/kg/day, which corresponds to 4-times the MRHD based on AUC.

8.2 Lactation
Risk Summary
There are no data on the presence of iptacopan or its metabolites in either human or animal milk, the effects on the breastfed child or on milk production. Since many medicinal products are secreted into human milk, and because of the potential for serious adverse reactions in a breastfed child, breastfeeding should be discontinued during treatment and for 5 days after the final dose.

8.4 Pediatric Use
Safety and effectiveness in pediatric patients with PNH, IgAN, or C3G have not been established.

8.5 Geriatric Use
There were 29 PNH patients 65 years of age and older in APPLY-PNH and APPOINT-PNH *[see Clinical Studies (14) in the full prescribing information]*. Of the total number of FABHALTA-treated patients during the 24-week treatment period in these studies, 21 (20.6%) were 65 years of age and older, while 7 (6.9%) were 75 years of age and older. There were 8 IgAN patients 65 years of age and older in APPLAUSE-IgAN *[see Clinical Studies (14) in the full prescribing information]*. Of the total number of FABHALTA-treated patients, 3 (2.4%) were 65 years of age and older. Clinical studies of FABHALTA did not include sufficient numbers of patients 65 years of age and older to determine whether they respond differently from younger patients.

8.7 Hepatic Impairment
The use of FABHALTA is not recommended in patients with severe hepatic impairment (Child-Pugh class C). No dose adjustment is required for patients with mild (Child-Pugh class A) or moderate (Child-Pugh class B) hepatic impairment *[see Clinical Pharmacology (12.3) in the full prescribing information]*.

Distributed by:
Novartis Pharmaceuticals Corporation
East Hanover, New Jersey 07936

For more information, visit www.FABHALTA.com or call 1-888-669-6682.

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High-Impact Trials Spotlight Advances in Therapies

Continued from cover

IgA-1 over 36 weeks in the atacicept group. Most importantly, he noted that patients had eGFR reductions comparable with people with healthy kidneys. The therapy was also well-tolerated, with 90% of patients who received the treatment remaining on it for the full 96 weeks of follow-up, with fewer dropouts than in the placebo group (2). There were no serious infections, and most injection-site reactions were mild to moderate.

Lafayette said that the data will help support an application to the US Food and Drug Administration (FDA) for accelerated approval of the therapy. "These are patients who are facing imminent dialysis or transplantation, and, in that journey, there are life-threatening complications," he said. "If you can show [atacicept] gets eGFR progression to 1 mil per minute per year or less, then you are talking about a lifetime without dialysis or transplant risk…. It's a major ray of sunshine for patients."

Vlado Perkovic, MBBS, PhD, FASN, professor and provost at the University of New South Wales in Sydney, Australia, presented 12-month data from the phase 3 VISIONARY trial (NCT05248646) of sibeprenlimab for IgA nephropathy, as well as interim safety results and prespecified subgroup analyses from the full 510 patient cohort (3). Previously, Perkovic presented 9-month data that showed a 51% reduction in proteinuria in the sibeprenlimab group versus placebo (4). At Kidney Week, he showed that the relative reduction in proteinuria had increased to 54% by 12 months, with indications that the reductions are continuing to increase over time. Additionally, 34% of patients in the sibeprenlimab group achieved remission compared with about 13% in the placebo group. The results were published simultaneously in *The New England Journal of Medicine*.

"The benefits appear consistent across all subgroups that we tested," he said. The complete safety analyses were also promising, with no deaths or increase in the risk of serious adverse events. An FDA decision on expedited approval for sibeprenlimab was expected by the end of November.

Jicheng Lv, MD, professor in the Renal Division at Peking University First Hospital in Beijing, China, presented the results of a phase 3 trial conducted in China of weekly subcutaneous injectable telitacicept. Telitacicept is a fusion protein that targets the B-lymphocyte stimulator and APRIL. At 9 months, the drug reduced proteinuria by 55% compared with placebo. There was also no difference in serious adverse events in the two groups, although injection-site reactions were more common in the telitacicept group (5). Final trial results are expected in 2026.

In all three trials, a substantial proportion of study participants also received sodium-glucose cotransporter-2 (SGLT2) inhibitors, suggesting that the drugs provided a benefit on top of existing therapies. "We now have an array of different treatment options, and a big challenge for us over the next few years is to figure out whether we should use them in combination, whether we should choose different drugs for different patients, and how we should think about different mechanisms," Perkovic said. He added that he expects B cell-targeting therapies to become foundational treatments for IgA nephropathy.

More autoimmune disease advances

Investigators also reported advances in therapies for other autoimmune forms of kidney diseases, including lupus nephritis, during the late-breaking trials. Results of a study that examined kidney biopsies from participants in the REGENCY trial (NCT04221477) suggest that patients with lupus nephritis may reap immunologic benefits from obinutuzumab even if they do not experience improvements in proteinuria. The FDA approved the use of obinutuzumab to treat lupus nephritis in October, based on the phase 3 results of the REGENCY trial, which showed that 46% of patients receiving the infusion therapy achieved a complete renal response compared with 33% in the standard therapy group (6).

To better assess the renal response beyond measuring biomarkers like proteinuria, lead author Brad Rovin, MD, FASN, professor of internal medicine at The Ohio State University Wexner Medical Center in Columbus, and his colleagues asked participants in the REGENCY trial if they would be willing to undergo a second biopsy at the end of the trial. Sixty-four participants volunteered for the second biopsy. Histologic analysis of the second biopsies revealed that 47% of patients achieved complete remission, and 66% had an activity index of less than one (7). Importantly, Rovin noted that 53% of patients in the obinutuzumab group who did not achieve complete renal remission based on renal biomarkers did achieve complete histologic remission.

"We can actually achieve much higher benefit for the kidney than we see in a complete renal response defined clinically only," he said. "We also do very well in depleting the B cells from the kidney parenchyma."

The results, Rovin said, may suggest that obinutuzumab offers a less-intense therapeutic alternative to chimeric antigen receptor T cell (CAR-T) therapies for patients with lupus nephritis. He explained that CAR-T therapies engineer patients' T cells and reinfuse them into patients. Although CAR-T therapy is very effective at removing B cells, it does require patients with lupus nephritis to stop their immunosuppressive therapy and undergo therapies that cause severe immunosuppression, which comes with serious infection risks. Patients must also be hospitalized for weeks to monitor for immune adverse effects. By comparison, obinutuzumab is an outpatient therapy. "We have a plethora of new therapies for lupus nephritis. [The question now] is how to choose the best one for a patient," Rovin said.

For example, he noted that therapies like belimumab, for which he also led clinical trials, might be a potential choice for maintenance therapy after induction therapy with an immune-targeted therapy, such as obinutuzumab or CAR-T. That might also give patients a break from chronic mycophenolate, which can cause fatigue and other adverse effects. He suggested that further studies might help guide those choices, as well as choices about which combinations of therapies or sequences of therapies may benefit patients.

"We are starting to think about how we can line these drugs up together to get the best benefit of the new therapies and maybe start to retire the older, less well-tolerated therapies," he said. "We just have to rethink how we're going to use these medications and put the trials together to prove it."

MRAs and SGLT2s

New details about which patients may benefit from mineralocorticoid receptor agonists (MRAs) or SGLT2 inhibitors were also presented during the meeting. Many clinical trials of these blockbuster medications left out key groups of patients, such as those with type 1 diabetes.

About 30% of people with type 1 diabetes develop chronic kidney disease (CKD), and having both diseases concurrently increases the risk of cardiovascular events or kidney failure, requiring dialysis or transplant, said Hiddo Heerspink, PhD, professor in the Department of Clinical Pharmacology at Rijksuniversiteit Groningen in the Netherlands. Yet, despite the flurry of clinical trials for new therapies for people with CKD and type 2 diabetes, there have been few trials focused on people with type 1 diabetes and CKD.

"Although the treatment for type 2 diabetes has advanced, we have left the [people with] type 1 behind," Heerspink said. "This illustrates the high need and our commitment and our responsibility to develop new therapies for type 1 diabetes as well."

Heerspink presented results of the FINE-ONE trial (NCT05901831), which showed that the MRA finerenone may benefit patients with CKD and type 1 diabetes (8). The phase 3 trial randomized 242 patients with CKD and type 1 diabetes to finerenone or placebo. Patients who received finerenone had a 13% reduction in albuminuria and a 25% reduction in the urine albumin-creatinine ratio (UACR) at 6 months. Adverse events were similar in the two groups. "The effect is robust and clinically meaningful because we know from clinical trials that a 25% reduction in UACR [will likely], in the long term, reduce the risk of kidney [failure and need for] transplantation," he said.

Heerspink said he is hopeful that the drug may be approved by FDA for type 1 diabetes in 2026. If finerenone is approved for type 1 diabetes, it would become the first new drug to be approved for the condition in decades.

He also presented results showing that MRA balcinrenone, in combination with the SGLT2 inhibitor dapagliflozin in patients with CKD, reduced albuminuria more than dapagliflozin alone, with minor effects on potassium levels (9). The trial randomized 324 patients to receive 15 mg of balcinrenone and 10 mg of dapagliflozin, 40 mg of balcinrenone and 10 mg of dapagliflozin, or placebo and 10 mg of dapagliflozin. Patients' UACR decreased 22.8% in the lower-dose combination therapy group and 32.8% in the higher-dose combination group compared with the dapagliflozin-alone group.

Other results

Other high-impact clinical trials at Kidney Week addressed topics as varied as transplant, fish oil supplementation, and acute dialysis, including the following:

- The Protection Against Incidences of Serious Cardiovascular Events Study (PISCES [ISRCTN00691795]) showed that daily fish oil supplementation with 400 mg eicosapentaenoic acid and 200 mg docosahexaenoic acid reduced serious cardiovascular events in patients on dialysis by 40%, even among those with a history of cardiovascular events. Event-free survival was also 27% higher in the supplement group (10).
- The Liberation From Acute Dialysis (LIBERATE-D) trial (NCT04218370) found a 13.8% increase in kidney recovery in patients who were hospitalized with acute kidney injury requiring dialysis who received dialysis only when indicated by metabolic or clinical factors, compared with patients who received standard three-times-per-week acute dialysis (11).
- The OPTIMIZE study (NCT03797196) showed that everolimus and reduced-dose tacrolimus immunosuppression did not increase transplant success rates for deceased donor kidney transplant recipients aged 65 years and older. Transplant outcomes were not statistically significant between patients receiving this combination or the more standard combination of corticosteroids, mycophenolate mofetil, and tacrolimus (12).
- A head-to-head comparison of tirzepatide and dulaglutide in patients who are high risk with kidney diseases, and with type 2 diabetes and cardiovascular disease, showed that patients treated with tirzepatide had a 33% lower risk of kidney events (13). ■

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Transplant Policy Takes Center Stage in 2025 and Beyond

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The ASN Transplant Policy Committee has been working to guide policy efforts in conjunction with the ASN Policy and Advocacy Committee and staff, who have been coordinating with legislators and federal agencies on transplant-focused initiatives and legislation. The goals of these efforts include improving patient care, ensuring fair access to kidney transplantation, and building the data infrastructure to support the US transplant system.

"ASN has been a key player working with agencies and legislators to keep transplant a priority," said Transplant Policy Committee Chair Roslyn Mannon, MD, FASN, professor, vice-chair for research, and associate chief of nephrology for research, University of Nebraska Medical Center in Omaha. Mannon credited 2021 ASN President-Elect Barbara Murphy, MD, MB, BAO, BCh, and 2023 ASN President Michelle Josephson, MD, FASN, for helping to increase the organization's focus on increasing transplant access (1).

Transplant system reform

The transplant system has undergone enormous change over the past 5 years, explained Jesse Schold, PhD, MS, MStat, MEd, professor of surgical epidemiology at the University of Colorado Anschutz School of Medicine in Aurora, who highlighted some of the key policy changes that have occurred in the transplant system over the past 5 years during a session at ASN Kidney Week 2025. He noted that there has been a 39% increase in organ procurement from deceased donors, including a doubling of donations from donors after circulatory death. But with more donor organs often traveling farther distances to transplant centers, the complexity of the system has also increased, as has acceptance times. More organs are also being accepted with higher risk scores. "We are trying to adapt to all of these big changes simultaneously," Schold explained.

Despite there being more potential donor organs available for transplant, there are more than 90,000 people on the waiting list for a kidney, and roughly 12 people die each day waiting. Yet, despite the ongoing need, about one-third of donor organs are not utilized. Additionally, more organs are used out of sequence on the waitlist, which can help increase the number of patients who receive a transplant but may also contribute to inequities, Schold noted.

The need to increase transplant access and allocation efficiency and to reduce inequities has galvanized bipartisan support for system-level reforms. Legislation passed in the past several years is now being implemented across several US agencies with the common goal of improving the US transplant system. President Trump's Advancing American Kidney Health Executive Order in 2019—which set goals of doubling the number of deceased donor kidneys for transplant by 2030, streamlining the kidney matching process, and reducing barriers to living donation—has also received renewed interest.

As already noted, CMMI began implementing its 6-year IOTA model on July 1, 2025, randomizing transplant centers, with half of the nation's donation service areas participating in the model, and the other half of transplant hospitals serving as the comparison group. The program incentivizes transplant centers to increase the number of kidney transplants completed each year. It aims to do so by providing centers with financial incentives for maximizing the use of deceased donor kidneys, increasing living donor transplants, and improving the quality of care for transplant recipients. Schold called it the largest-ever experiment in the transplant system. "We want transplant centers to do more and more, and we want [them] to do it in an efficient way," he said.

HRSA also took several steps in September to advance its OPTN Modernization initiative (2). During a September 18th briefing, HRSA Administrator Thomas J. Engels described several steps that the agency has taken as part of its modernization initiative, including seating an independent 34-member board to oversee the OPTN contractor. The agency also launched a dashboard to enable public monitoring of site-level and system-wide organ allocations, ensuring fairness and reducing discards.

Mannon said that out-of-sequence transplants are becoming more common for several reasons. She noted that organ procurement organizations have been working to increase organ availability by securing donor organs with higher risk scores, for example, donor organs from older patients or patients with underlying health conditions. She explained that organs with a higher likelihood of failure or potentially a shorter lifespan may not be appropriate for a younger patient with a longer lifespan at the top of the list, whereas they may be more appropriate for a patient further down the list. Additionally, some higher-volume transplant centers have a higher risk tolerance, whereas lower-volume programs may be more risk averse and may be less willing to take an organ with a higher risk score.

"[D]ashboards are helpful in raising awareness of the problem, but I'm not sure if it will tell us why it is happening," Mannon said. She noted that there have been many studies trying to tease apart the complex contributors (3, 4).

ASN has also advocated for a greater collection of prewaitlist and transplant data to help guide policymaking and improve transplant access. Now, HRSA is developing a new directive to collect such data. Schold noted that HRSA may include information on every patient referred or evaluated at a transplant center, and it will also collect more data on prospective donors.

"Transplantation is the optimal therapy for most people with kidney failure, and gaining access to the waitlist is a critical gateway step in the process," explained ASN President Prabir Roy-Chaudhury, MD, PhD, FASN, in a letter to Administrator Engels in July (5). "However, our understanding of how and why some people make it to the waitlist, and others do not is limited, restricting our ability to improve access to transplantation through either national policy or local practice changes. Obtaining this information is a significant step forward in understanding and intervening to address barriers and is pivotal in allowing the creation of a smooth, transparent patient journey through the transplant process."

Mannon noted a recent study showing that patients want more transparency in the waitlist process, especially about why they may have been turned down, wherease centers worry that sharing more information will harm the clinician-patient relationship or reduce efficiency (6).

During the September briefing, Engels also cited congressional actions to support modernization, including opening the OPTN system to competition and allowing HRSA to increase and collect OPTN fees. The agency has also instituted a new process for reporting misconduct and patient safety concerns in the organ collection, allocation, and transplant system. He noted that HHS Secretary Robert F. Kennedy Jr. has also directed that every organ procurement organization have a designated patient safety officer and report patient safety data to OPTN. HHS Deputy Secretary Jim O'Neill also announced $25 million in new funding for HRSA's Living Organ Donation Reimbursement Program to help reduce the financial burden on living donors by paying for eligible nonmedical expenses, such as lost wages, travel, lodging, meals, or dependent care costs.

Supporting living donors

Many of ASN's policy efforts have focused on increasing access to living donor transplants. Mannon explained that although the number of organs from deceased donors has increased, living donor rates have remained flat for decades. Often, financial barriers and other practical considerations make it impossible for many would-be donors.

"It's hard for those in front-line jobs to say, 'I'm going to take time off,'" she explained. Many employers are not supportive of living donors, and some existing policies are outdated. For example, Mannon noted that living donors' access to financial assistance is currently based on the recipient's income, not their own. She explained that it may have made sense if the donor was a spouse or another immediate family member, but it does not make sense if the donor is someone you know from social or religious circles or someone you met at a fundraiser.

ASN has advocated for two important bills intended to reduce these barriers: the Living Donor Protection Act, to increase protections from insurance discrimination for donors and to ensure that they have access to family medical leave during recovery, and the Honor Our Living Donors Act, to increase access to financial support for living donation. A third piece of legislation, the Removing Burdens From Organ Donation Act, is designed to improve electronic communication between hospitals and organ procurement organizations about organ donation. Suzanne Watnick, MD, FASN, ASN's Health Policy Scholar-in-Residence, chair of the Policy and Advocacy Committee, and professor of medicine in the Division of Nephrology at the University of Washington, Seattle, noted that some institutions still rely on telephone calls to relay information, which can require a dedicated nurse working full-time rather than a more streamlined electronic communication. "Everyone in the kidney community is supportive of this legislation," she said.

At press time, uncertainty hung over ASN's legislative efforts as the government shutdown was just ending. Mannon noted that ASN staff and Watnick were continuing to work with senatorial offices to shape policies on transplant modernization and quality initiatives.

Organ donations, including living donations, will likely be the focus of the next iteration of the KidneyX program, a public-private partnership between ASN and HHS. In 2025, the project received $5 million in appropriations. At press time, the total for 2026 was not yet confirmed. "Hopefully, we'll figure out ways to attract more people to give the gift of life, to make this a cost-neutral endeavor, and to ensure that kidney donors feel comfortable and safe," Watnick said.

Transplant policy is likely to remain a focus at both ASN and federal levels into 2026. The Centers for Medicare & Medicaid Services (CMS) is scheduled to update its organ procurement organization performance metrics. The metrics are designed to increase organ donations from deceased donors. Mannon noted that ASN staff had been meeting with CMS and HRSA prior to the shutdown to share the kidney communities' priorities. The Transplant Policy Committee has also been offering its guidance on a series of proposals from federal agencies, OPTN, and the United Network for Organ Sharing on multiorgan transplant policies, patient waitlist notification, and a living donor collective, Mannon said. She explained that those activities are vital because they not only help shape policy but also educate the wider nephrology community about issues shaping transplant care. ■

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Shaping Kidney Science and Scientists: The Work of Kurt Amsler

By Zach Cahill

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"If you put me on stage at the ASN, I bet 90% of that audience wouldn't know who I was." Curiosity is the foundation that spawns innovative treatments for kidney diseases, and this pipeline of basic research discoveries is increasingly jeopardized with threats of reduced funding. Kurt Amsler, PhD, retired this fall after 18 years at the New York Institute of Technology and is concluding his term as an inaugural cochair of KidneyCure's Pre-Doctoral Fellowship Program Review Panel, which evaluates applications of PhD students pursuing research careers. In a field dominated by patient care, contributions of catalytic research leaders, such as Amsler, need to be recognized, emphasized, and supported.

Starting in a different direction

Throughout his 50-year career, Amsler led a fight against kidney diseases from his laboratory. His pioneering work validating LLC-PK1 cells as a model for epithelial transport within the kidney created a simple and reliable way for others to conduct research. He further elucidated how kidneys reclaim glucose from filtrate, defining the mechanism for sodium-glucose cotransporter-2-inhibiting drugs that has revolutionized kidney care.

Amsler's career path started with research in a different field—nuclear physics. It changed direction when he first read that several Nobel Prize physicists earned their awards for their research conducted in the earliest part of their careers. At the time, Amsler thought he would unlikely be able to measure up, which is now ironic since he is highly regarded for the research he pursued in graduate school. As the younger Amsler was heading to the University of Sussex's Physics Department to let them know of his change of heart, he happened to pass the Biology Department.

Combining physics and biology was an unheard of concept in the 1970s. But the emerging field of quantum biology married experimental techniques and scientific theory, and Amsler's curiosity found a perfect application within epithelial cell transport. At that time, the kidney was largely a black box with limited understanding of how different compounds were transported within the kidney. Under the mentorship of Melvin Silverman, MD, a nephrologist with similar interests of bridging physics and biology, their research focused on answering a simple question: "How does the kidney keep all sugar in the body?" This led to groundbreaking research in quantum mechanical tunneling through biological membranes, the subject of Amsler's master's thesis. Even though that research identified the protein that mediates the sodium-dependent glucose transporter in the kidney, Amsler was more excited to have built a laboratory tool that others could apply in their research of cellular sugar transport pathways.

For his research doctorate, Amsler was mentored by John S. Cook, PhD, at the Oak Ridge National Laboratory, whose research on cellular-level membrane transport was similarly at the physics-biology intersection. When Amsler's project on cancer-related transport pathways ended prematurely, he happened to hear a talk at a meeting of The American Society for Cell Biology on kidney sugar transport in the LLC-PK1 cell line. This presentation was the spark that led to his numerous and notable career contributions as a successful kidney researcher.

Combining research and mentorship

In addition to his research training, Amsler emulates Cook's mentorship strategy. Cook used team discussions to guide each trainee and fellow without explicitly directing them, allowing them to define their research projects with ownership over successes and failures. These insights committed Amsler to a mentorship ethos of empowering trainees to pursue their own research interests: "That helped bring me from thinking I knew what I was talking about, to understanding I knew nothing about what I was talking about, to recognizing what I needed to learn." His rationale was really simple: "If you're interested in it, you'll work harder, you'll do more, you'll really make it work. If you're just doing what I tell you to do, you'll do a decent job, but your heart won't be in it in the same way."

Beyond the laboratory

Amsler acknowledges that basic scientists often contribute insights from, for example, a single cell line. His own interests in epithelial transport was "wherever it happens," whether in the kidney, intestine, lung, or a malignant tumor. Recognizing the opportunity for basic researchers to unveil the complexities underlying kidney function, Amsler collaborated with Ambra Pozzi, PhD, DrPh, to advocate that ASN provide grant funding to force early research trainees away from a "specific cell line" mentality to one of conducting a "kidney project." This led to KidneyCure's inaugural Pre-Doctoral Fellowship Program in 2018, which has funded 27 trainees to date. In addition to funding, Amsler notes that "ASN has made a real effort to bring more basic science into the mainstream of the society."

While the KidneyCure program and ASN's evolving culture are bright spots for kidney researchers, the broader US environment has been steadily decreasing its support for basic research. Reflecting on how the 1980s' research funding cuts were followed by a doubling of the National Institutes of Health's budget, Amsler is optimistic that this current phase will similarly pass and that basic researchers will survive until that change happens. His hope for KidneyCure's Pre-Doctoral Fellowship Program is that more basic scientists focus on the kidney because ASN "kept them alive when no one else did" through funding and a robust research environment, such as ASN Kidney Week.

While Amsler may be anonymous to the average Kidney Week participant, he thinks that "there is more recognition of and acceptance of basic science being an important part of nephrology and kidney research." Although Amsler recognizes that his best-known work may be his own research, he hopes that he is remembered more for his advocacy for a strong and curiosity-driven kidney research workforce and for the numerous research leaders who he has mentored along his own winding career path. ■

Zach Cahill is a program manager with KidneyCure, the philanthropic foundation of ASN.

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ASN President's Update

ASN President's Address at Kidney Week 2025

By Prabir Roy-Chaudhury

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The following is an edited version of the ASN President's Address presented by ASN President Prabir Roy-Chaudhury, MD, PhD, FASN, at Kidney Week 2025 in Houston, TX, on November 6, 2025.

Thank you, and welcome to ASN Kidney Week 2025. Kidney Week is when we share our stories, and so I, too, want to start by telling you a story.

The year was 1993, and I was a first-year nephrology fellow at Beth Israel Hospital. I clearly remember going to work on the subway and reading an article, which demonstrated that the use of the angiotensin-converting enzyme (ACE) inhibitor Captopril could prevent the progression of kidney diseases in people with type 1 diabetes. I remember feeling incredibly excited because I felt that nephrology now had a drug that we could call our own, and I just presumed that there would be a parade of new therapies coming into nephrology. How naïve….

What happened, in fact, was a quarter-century of therapeutic stagnation. ACEs and angiotensin II receptor blockers (ARBs) were the only therapies that we had because we did not have an innovation substrate in kidney care.

Today, in 2025, the dream of that young nephrology trainee from 1993 could, in fact, come true.

Momentum in kidney care

Because today, we have real momentum in kidney care. We now have an increasing number of new therapies across the entire continuum of care—from the glomerulonephritides to cardiovascular-kidney-metabolic (CKM) diseases to xenotransplantation and innovative kidney-replacement devices. It is not just new therapies; we also have new care-delivery pathways and payment plans, which are beginning to be aligned with value. All of this means that the vision my mentor, Ronald J. Falk, MD, FASN, shared in his 2012 ASN presidential address—when he first spoke about curing kidney diseases—could become a reality for the current generation of nephrologists.

Now, the fact that we have so many new therapies either available or soon to be available (10 for immunoglobulin A [IgA] nephropathy, 5 for CKM diseases, 4 for lupus nephritis, and 2 for C3 glomerulopathy) means that we now have a new set of challenges around how to use these therapies. For example:

- Do we use them sequentially or in combination?
- Do we need to adopt a more precision-based approach?
- Could some of these therapies be used to prevent kidney diseases in patients who are high risk?

I do not know the answers to these questions, but to me, these questions are not challenges; rather, they are wonderful opportunities for clinical investigation by today's generation of nephrologists.

I never want to go back to when all we had were ACEs and ARBs. It is exhilarating and, quite frankly, just a lot more fun to be part of a specialty that is pushing the envelope as nephrology is doing today.

To all of you, the largest gathering of kidney professionals in the world, but most of all to the young nephrologists, I want to say this loud and clear: There has never been a better time to be a nephrologist.

Accelerating the momentum

You may wonder: "Prabir, why is 2025 going to be different from your experience in 1993?" My answer would be that over the last 25 years, the kidney community has built an innovation substrate for kidney care that allows for original kidney science to be converted into new therapies and for these new therapies to get to patients.

What we have in 2025 that we did not have in 1993 is momentum. We have momentum in kidney science. We have momentum in innovation and investment in kidney diseases. We have momentum in new kidney therapies. And we have momentum in care delivery through value-based care and global payment systems.

But just having momentum is not enough. We must keep the momentum going. We must accelerate the momentum. Because if we do not, and if I were a person living with kidney disease, then I would say to all of you: "Shame on you for not rising to the occasion."

One example of how we can accelerate the momentum in kidney science is the National Institutes of Health (NIH)-funded Kidney Precision Medicine Project (KPMP), which links clinical, demographic, and kidney outcome data on patients with acute kidney injury and chronic kidney disease with the "omic" signatures from their kidney biopsies. KPMP will allow us to identify new mechanistic pathways that could be used as druggable targets for the next generation of kidney therapies and also as biomarkers for a more precision-medicine approach to kidney care. This will mean that we can get the right drug or the right clinical trial (since we now have so many of both) to the right patient at the right time and in the right way.

Another example of accelerating momentum in the areas of innovation and investment comes from a public-private partnership between ASN and the US Food and Drug Administration, called the Kidney Health Initiative (KHI). KHI's goal is to facilitate the passage of new therapies into kidney diseases by bringing the entire kidney community together. The best example of KHI's success comes from an IgA nephropathy project, which demonstrated that an early reduction in proteinuria at 9 months was an excellent surrogate endpoint for clinical trials in this field. This has shortened both the duration and the cost of clinical trials in IgA nephropathy, and the results are there for all of you to see at this meeting: multiple new therapies for IgA nephropathy; lots of new clinical trials; and, above all, a better future for people living with this disease.

Most importantly, both KPMP and KHI have kept the patient perspective front and center through active patient advisory panels. On behalf of all of us here today, I personally want to thank all the people living with kidney diseases in the audience and beyond for the urgency in their advocacy, because 50% of new patients starting hemodialysis today will not be alive in 5 years or less.

If you compare kidney innovation to a game of Snakes and Ladders (which is what I grew up with in India) or Chutes and Ladders (which is what my children grew up with in the United States), then we are just getting started. The kidney world is probably at square 15 or 20—much better than 10 years ago for sure, when we were likely at square number 3—but far behind specialties such as cardiology and oncology, which are probably up in the 70s. If we want to accelerate the momentum that we now have, we need to identify the ladders and avoid the snakes. And we need to particularly address the snakes—or the challenges—that are ahead of us.

Addressing the challenges

More than 50 years ago, Martin Luther King, Jr., said, "Of all the forms of inequality, injustice in health care is the most shocking and inhumane." Today, there are huge inequities and disparities in kidney care. We must do better. We must deliver the benefits of the new kidney therapies to regions with lower socioeconomic status, to inner cities, to rural areas, to border areas, and to wherever we have vulnerable populations who will likely benefit the most from these therapies.

A global problem

We must also never forget that kidney diseases are a global problem. The greatest benefit of generic versions of therapies, such as sodium-glucose cotransporter-2 inhibitors, will be in low- and middle-income countries, where access to therapies for kidney failure is often limited due to cost. We must also focus on finding a cause for chronic kidney disease of unknown etiology, which is both common and devastating in Central America and South Asia. It was, therefore, a very humbling experience for me to visit a village in India recently, where 25% of the houses in a single lane had patients on hemodialysis.

Talking about the global kidney community, I am so proud of the fact that ASN is the world's largest international kidney organization with almost 22,000 members from 142 countries. This reach is an important part of who we are. I am extremely proud of our partnerships with the International Society of Nephrology, the European Renal Association, and the Indian and Japanese Societies of Nephrology, for which we are jointly advocating

for global access to lifesaving kidney therapies and better education about kidney health. I also want to emphasize that the international origins of many US nephrologists (including myself), together with the presence of organizations such as the American Nephrologists of Indian Origin and the Chinese American Society of Nephrology, have made interactions with other countries both easier and more meaningful.

Research uncertainty

Another challenge that we face in the United States today is uncertainty in research funding for kidney diseases from NIH. Just last week, ASN released the Transforming Kidney Health Research report, which calls on the federal government to invest $1.8 billion annually into kidney health research over the next decade. In addition, I am proud to share with you that ASN has committed to $6 million of additional bridge funding over a 3-year period starting in January 2026 to fund kidney researchers impacted by these changes. I am also delighted to announce a $2 million gift from Satellite Healthcare, which ASN will match, to set up the Norman and Sandra Coplon Transition to Independence Grants. Thank you, Dovid Coplon and all the members of the Satellite Healthcare Board (Tom, Chris, and Glenn) for this generous gift.

Workforce opportunities

We also need to address the kidney workforce challenge, which I want to frame as an opportunity. We currently have a dichotomy in kidney care: a huge increase in innovation, interest, and investment but with a nephrology workforce pipeline that is relatively flat. That is exactly why we need to have an aggressive implementation of the new therapies, so that they can be the catalyst that will allow us to demonstrate the value of nephrology and nephrologists to governments, health care systems, insurers, and payors. This would allow us to get payment for the new therapies and for the value-add that we as nephrologists bring to the table. It would allow us as nephrologists to not only work hard but also work smart.

To set ASN and the kidney community on the path of demonstrating value, I want to recognize the Vertex Foundation and the chief executive officer of Vertex Pharmaceuticals, Reshma Kewalramani, MD, FASN (a nephrologist herself). Vertex Foundation has committed to a lead investment of $3 million—to which ASN will add $2 million—to initiate a comprehensive program that will train the kidney workforce in the implementation of the new immune-mediated therapies across a spectrum of conditions from glomerulonephritis to transplantation.

Making it happen

Can all of this really happen? I am certain that this can and will happen because of the strength, resilience, commitment, and passion of the entire kidney community, including people living with kidney diseases.

The best part of my year as ASN president by far has been the humbling opportunity to meet with so many people in the kidney community in this country and across the globe.

- People like Vishal Patel, MD, at The University of Texas Southwestern Medical Center, who never gave up on his dream of finding a cure for autosomal dominant polycystic kidney disease and who discovered that blocking microRNA 17 could reduce cyst formation, which has resulted in a new treatment for this condition
- People like Nichole Jefferson, who has lived with kidney disease for over 20 years but never abandoned her fight for equity and justice in health care for all people with kidney diseases
- People like Clarissa Tio, MD, FASN, MPH, who, while on a J-1 visa waiver at the University of Mississippi, put together a primer for both international medical graduate trainees and their training programs, which has allowed for better care for vulnerable populations
- Finally, people like Michelle Donnelly, PA-C, who chose to become an advanced practice provider in a second career and who has transformed the care of veterans with a kidney transplant at a North Carolina VA Medical Center

The end result of all of these interactions has always been the same: They have made me so proud to be a nephrologist.

We are truly holistic physicians; we are patient-centered; we follow the science; and we come from many countries, which gives us a diversity of thought and opinion and is good for our patients and for our field. Above all, we want to deliver better care for our patients. These are exactly the qualities that are needed to leverage the momentum from the new kidney therapies into a cure for kidney diseases.

In order to achieve this, each and every one of you needs to add your push to the momentum that we currently have. My challenge to all of you for the next 4 days and for when you leave Houston is:

- If you are a full-time clinician in community practice, participate in care-delivery pathways that will allow your patients rapid access to new kidney therapies, and also enroll your patients in clinical trials, because research can bring hope to patients.
- If you are a basic or translational science researcher, think about ways to translate your research into treatments so that your science gets to patients who are desperately waiting for your cutting-edge innovations.
- If you are a clinical trialist, encourage others to follow in your footsteps. We have so many questions to answer and so many studies to conduct.
- If you are an industry partner, work with other industry colleagues, academic institutions, and federal agencies to pool your clinical and biological data to develop an integrated and real-world, evidence-generating system for the benefit of the entire kidney community.
- Perhaps most importantly, if you are a fellow in training or a young nephrologist, know that this is your meeting, and this is your time. I wish I was starting my nephrology career today and not 1993!

Yes, we can...cure kidney diseases

I have been a nephrologist for over 25 years, and what I remember most of all are my patients. I remember my successes: the first transplant patient who I cared for as a young attending in 1998 in Cincinnati, OH, who tracked me down to thank me on the 25th anniversary of her successful kidney transplant. And I also remember my failures: the young woman who had tears of joy in her eyes when I told her that she was going to get a second kidney transplant but who then died when the kidney failed, and she ran out of vascular access.

The point that I want to make here is that the majority of my memories, both good and bad, are all about people with kidney failure. But that does not have to be the case in the future.

As a result of the new kidney therapies, we now have the ability to prevent kidney diseases, slow the progression of kidney diseases, and, yes, cure kidney diseases.

This will only happen if we can succeed in implementation. So, my final challenge to you, is for all us—health professional organizations, industry partners, federal agencies, patient organizations, and more, in the United States and around the world—to work together to accelerate the momentum so that the new therapies get to all of the people who will benefit from them.

If we can do that, then that is when we will be able to change my kidney story, your kidney story, and most importantly, the kidney stories of the 850 million people worldwide living with kidney diseases, from one of kidney *disease* to one of kidney *health*.

Thank you so much for your attention. It has truly been the greatest honor and privilege of my professional life to have served as your president. ■

The Dawn of the Aldosterone Synthase Inhibitors

By Milagros Flores Fonseca, Cristina Popa, and Swapnil Hiremath

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In nephrology, we have often talked, written, and read about the renin angiotensin system without including its cousin, aldosterone, and only purists properly allude to the renin angiotensin aldosterone system. Yet, aldosterone is not an innocent bystander. It drives cardiac fibrosis, vascular damage, and even worsening kidney function, especially in proteinuric diabetic kidney disease. Hence, to no one's surprise, mineralocorticoid receptor antagonists (MRAs)—such as spironolactone and eplerenone (in heart failure) and finerenone (in diabetic kidney disease and recently in heart failure with preserved ejection fraction)—have been demonstrated to be useful in clinical trials.

But an alternate method of ridding oneself of aldosterone is by inhibiting aldosterone synthesis with aldosterone synthase inhibitors (ASIs). Think of it as a world in which angiotensin receptor blockers were available and approved before angiotensin converting enzyme inhibitors. One of the main reasons that ASI development has taken so much time is that aldosterone synthase is closely related to the 11ß-hydroxylase enzyme, which is involved in cortisol synthesis. The development of an ASI required it to be specific for aldosterone synthase and to not inhibit glucocorticoid synthesis. Astute readers will note that some form of analysis of that pathway is included in ongoing regulatory trials of ASIs—of which there are quite a few in development: lorundrostat mostly in uncontrolled hypertension (1), vicadrostat for diabetic kidney disease (2), and baxdrostat in both conditions (3). However, it is known that MRAs already work in these conditions, so are ASIs really needed? Notably, these trials in hypertension and diabetic kidney disease do not have proven and indicated MRAs as comparators.

One indication that we have not discussed so far is using MRAs (or ASIs) in primary aldosteronism (PA). PA is the most common cause of secondary hypertension (excluding, for example, counting sleep apnea and chronic kidney disease as causing secondary hypertension). It is also the most underscreened, underdiagnosed, and undertreated hypertensive diagnosis; thus, testing is rare for recognizing and treating PA (4). All major hypertension guidelines have elevated the need for screening and have simplified screening guidelines (5). But beyond those screening issues, a minority of people with PA have unilateral disease, which can be cured or ameliorated with an adrenalectomy. For the vast majority of people with PA, an MRA for treatment is used. But in many people with PA, the doses required of an MRA are huge, for example, 200 mg of spironolactone (or 400 mg of eplerenone) or even higher. There is so much aldosterone that we need lots of MRAs to block it all, and we often do not succeed. Hence, an ASI makes much more sense to use in this area. Being a niche condition (mostly because PA is underdiagnosed), it has been hard to convince researchers to perform proper drug trials in this area. Indeed, eplerenone is often used off-label for PA.

Consequently, the hypertension community is likely pleased that a clinical trial was conducted with baxdrostat in PA (6). In this single-arm, phase 2 trial, 15 patients with PA received baxdrostat for 72 weeks. The initial dose was 2 mg for 4 weeks, escalating to 4 mg and 8 mg after that, based on the blood pressure (BP) response. By 12 weeks, the overall systolic BP decreased from a baseline of approximately 151 mm Hg by about 25 mm Hg, with normalization of serum potassium in 10 of the 15 patients. From a mechanistic point of view, of much more interest was that aldosterone (in plasma and 24-hour urine collections) plummeted, and there was a corresponding gradual increase in renin 6 times by week 72 (measured with plasma renin activity). There were some interesting changes noted in deoxycorticosterone levels (a biphasic rise and fall) and a smaller increase in plasma cortisol, which have an interesting anatomic and physiologic explanation (see pages 43–47 in the supplement) (6). Nevertheless, the 97% reduction in aldosterone makes one compare the effect of baxdrostat with the surgical treatment of PA—in this case, akin to a medical adrenalectomy.

Baxdrostat produced large BP reductions and marked biochemical responses in PA. Yet, this is a small, phase 2, single-arm trial with no control group and with no active comparator such as spironolactone. It is still very early to call this a clear "win." However, these are extremely promising data, and the use of ASIs in PA would be much more exciting than in undefined, uncontrolled hypertension or proteinuric kidney disease in which other options exist. If this succeeds, one may wonder whether the pharmaceutical muscle may help increase the low screening rates that remain in the doldrums despite our best efforts. The phase 3 clinical trial, BaxPA (NCT07007793), is currently recruiting to answer this question. ■

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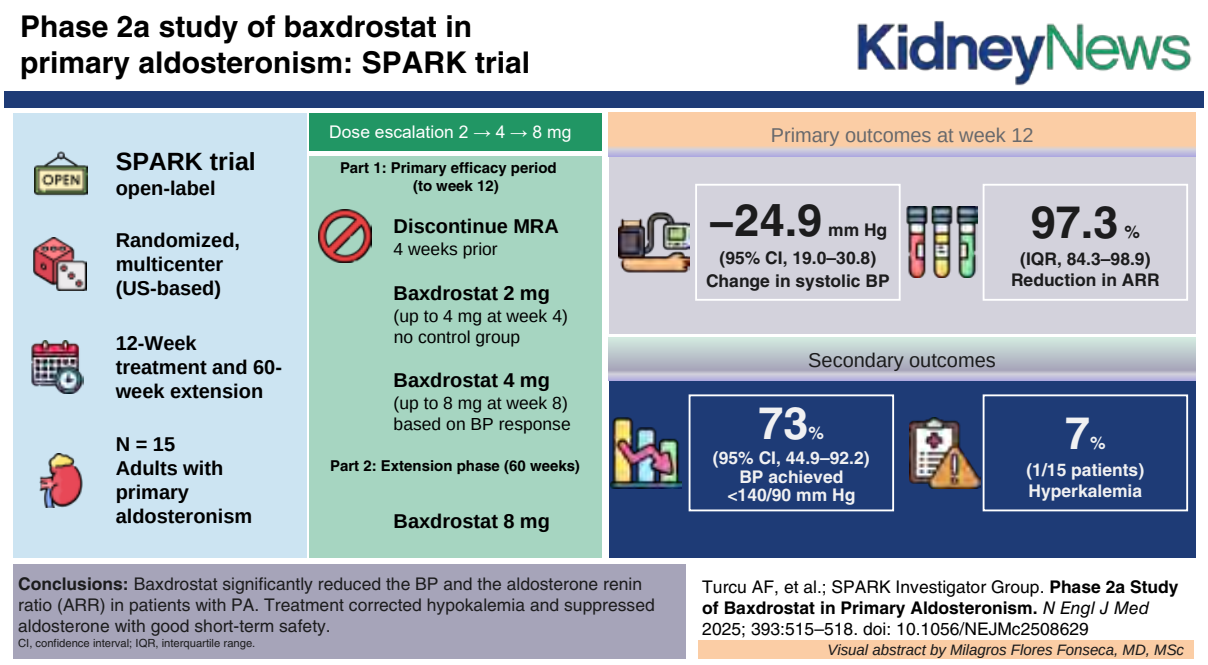
The authors report no conflicts of interest.



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ASN Advances "STAND" Policy Priorities in 2025

By Katherine Crowley

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This year, ASN continued to champion the policy interests of kidney health professionals and people with kidney diseases by advancing its policy priorities, embodied by the acronym STAND—a framework that prioritizes five key goals:

1) Start earlier to prevent, diagnose, and treat kidney diseases.
2) Transform kidney transplant to expand access to the optimal therapy.
3) Accelerate research, discovery, and innovation to advance American kidney health.
4) Nurture a nephrology workforce to meet patient needs.
5) Drive efficiency to deliver value in kidney health.

The STAND framework guides ASN's policy and advocacy efforts to promote research and innovation, address barriers to health care justice, and support the entire kidney health team. Amid the rise of kidney diseases globally as well as changes to American health care systems, ASN's policy efforts are affirmed by the leadership of the ASN Council and the engagement of the ASN Policy and Advocacy Committee, the ASN Quality Committee, the ASN Transplant Policy Committee, and the ASN Health Care Justice Committee. This article reflects on ASN's major policy accomplishments from this past year and considers policy priorities for 2026.

Start earlier to prevent, diagnose, and treat kidney diseases.

- Called on Congress to protect the independence and integrity of the US Preventive Services Task Force (USPSTF). ASN joined leading medical societies in emphasizing that USPSTF plays a vital role in ensuring access to evidence-based preventive care—particularly for people with or at risk for kidney diseases. The letter urged Congress to resist efforts to politicize the task force's work and instead uphold the rigorous, transparent review process that supports preventive health coverage under federal law. ASN will continue to monitor and address this issue in the upcoming year and beyond.
- Urged the Centers for Medicare & Medicaid Services (CMS) to reinstate the collection of race and ethnicity data on Form CMS 2728, the End Stage Renal Disease (ESRD) Medical Evidence Report, in partnership with the National Kidney Foundation and the American Nephrology Nurses Association. In the joint letter to the CMS administrator, the partners stressed that the collection of demographic data is critical for identifying and targeting differences in kidney disease incidence, access to care, and outcomes. This information is crucial for understanding and addressing disparities in kidney health, guiding equitable policy, and supporting high-quality care for every American with kidney failure. Without this data, CMS and the kidney community will lose a key tool for identifying at-risk populations earlier, advancing equity, and improving patient outcomes.

Transform kidney transplant to expand access to the optimal therapy.

- Submitted comments to the Health Resources and Services Administration (HRSA) that expressed strong support for the collection of pre-waitlisting referral and evaluation data through the Organ Procurement and Transplantation Network (OPTN). ASN emphasized that this information is essential to improving access to kidney transplantation and urged HRSA to adopt a phased-in approach, leverage technology upgrades such as batch reporting and application programming interfaces, reinstate key data fields, and align OPTN data with CMS's 2728 form to create a complete picture of the patient journey.
- Advocated for HRSA to receive $67 million in fiscal year (FY)2025 to implement the 2023 Securing the US OPTN Act.
- Supported the reintroduction of both HR 4582 and 4583, comprising the Living Donor Protection Act and the Senate companion bill S 1552. This legislation would support living donors by codifying family and medical leave for living donors; prohibit insurers from denying coverage based on a donor's decision to donate; and direct the Department of Health and Human Services to update educational materials on organ donation, expanding access to kidney transplant and protecting living donors.

Accelerate research, discovery, and innovation to advance American kidney health.

- Implored Congress to prioritize robust funding for the National Institutes of Health (NIH) in FY25 and, in that legislation, preserve existing protections against cuts to reimbursement for NIH grantee facilities and administrative costs. The letter advocates for NIH to receive at least a $1.77-billion increase in funding and supports the continuation of Section 224 of the FY24 Appropriations Act in the final FY25 appropriations bill, which prohibits changes to NIH facilities and administrative cost reimbursements.
- Released the Transforming Kidney Health Research (TKHR): A Research Agenda for the Future report (1). Developed in partnership with the American Association of Kidney Patients, the American Kidney Fund, the American Society of Pediatric Nephrology, and the National Kidney Foundation, the TKHR report outlines a bold, collaborative vision to improve patient outcomes and drive innovation by calling on the federal government to strengthen the research ecosystem and invest $1.8 billion per year over the next 10 years in kidney health research.
- Requested $25 million in FY25 appropriations to accelerate innovation in the prevention, diagnosis, and treatment of kidney diseases through the Kidney Innovation Accelerator (KidneyX).
- Submitted comments regarding the calendar year 2026 ESRD Prospective Payment System Proposed Rule, which included updates to the Quality Incentive Program. ASN called for reforms to support innovation in dialysis drugs, biologics, and devices. ASN continued to defend historic access to the ESRD benefit, while highlighting chronic underfunding and payment-forecasting errors that threaten dialysis facilities, patient access, and innovation in the kidney community.
- Submitted an official Statement for the Record (2) for the Senate Finance Committee's hearing on the president's 2026 Health Care Agenda that urged Congress to not only preserve access to vaccines but to sustain critical funding for scientific research and to strengthen data transparency and integrity.

Nurture a nephrology workforce to meet patient needs.

- Responded to several federal policies affecting international medical graduates. ASN believes non-US citizen international medical graduates play a critical role in alleviating the physician shortage by providing health care to many Americans, including the nearly 37 million living with kidney diseases. ASN swiftly urged the Department of Homeland Security (DHS) to lift its pause on J-1 visa provision and further responded to a DHS proposal to end the "duration of status" framework for J-1 physicians, warning that both would destabilize training programs, increase administrative burden, and worsen the stability of the US health care workforce (3). In addition, ASN urged DHS to reconsider two H-1B–related policies: first, to exempt physicians from a proposed $100,000 employer fee for new H-1B applications and second, to withdraw and reconsider a proposed weighted H-1B lottery system that could further exacerbate existing workforce shortages.
- Submitted formal comments in response to the proposed calendar year 2026 Medicare Physician Fee Schedule, calling attention to several issues: changes to practice expense methodology, proposed efficiency adjustments, and payment policies that may adversely affect nephrology practices. ASN urged CMS to ensure that any revisions maintain fair reimbursement that supports high-quality kidney care.

Drive efficiency to deliver value in kidney health.

- Received a $100,000 grant to support the ASN Health Care Justice Committee's "Encoding Equity: ASN eGFR [Estimated Glomerular Filtration Rate] Toolkit 2.0" project. The central goal of this project is to enhance the original ASN eGFR Toolkit to address persistent misconceptions about the removal of race from eGFR calculations by improving the use of race in clinical care.
- Submitted three letters to the OPTN for the Summer 2025 public comment. ASN commented on the following proposals: Require Patient Notification for Waitlist Status Changes, Establish Comprehensive Multi-Organ Allocation Policy, and Update and Improve Efficiency in Living Donor Data Collection. In the letters sent to OPTN's Transplant Coordinators Committee, Ad Hoc Multi-Organ Transplantation Committee, and Living Donor Committee, ASN advocated for improved transparency in patient notification of waitlist changes, encouraged greater representation of the kidney community on the Ad Hoc Multi-Organ Transplantation Committee, and expressed concern regarding proposed changes to living donor data collection. These changes to OPTN policy would promote patient needs and create efficient systems for practitioners.

ASN's policy efforts in 2025 represented the society's vision of a world without kidney diseases by advancing kidney health, promoting health care equity, and supporting innovation. From supporting legislation that promotes kidney health care and securing funding for NIH and KidneyX initiatives to a commitment to integrating health equity and promoting social justice in kidney care, ASN continues to make strides in improving the landscape of kidney care. As kidney diseases continue to be a major public health matter and amid changes in American health care norms, ASN's leadership and advocacy will remain diligent and committed to ensuring that patients receive the best care possible while supporting the kidney care workforce on all fronts.

To keep up with ASN's policy efforts, follow coverage in *Kidney News* and the ASN podcast feed, and visit ASN's policy webpage (www.asn-online.org/policy). For real-time updates from ASN Policy, follow @ASNAdvocacy on X. ■

Katherine Crowley is a temporary policy and government affairs associate at ASN.

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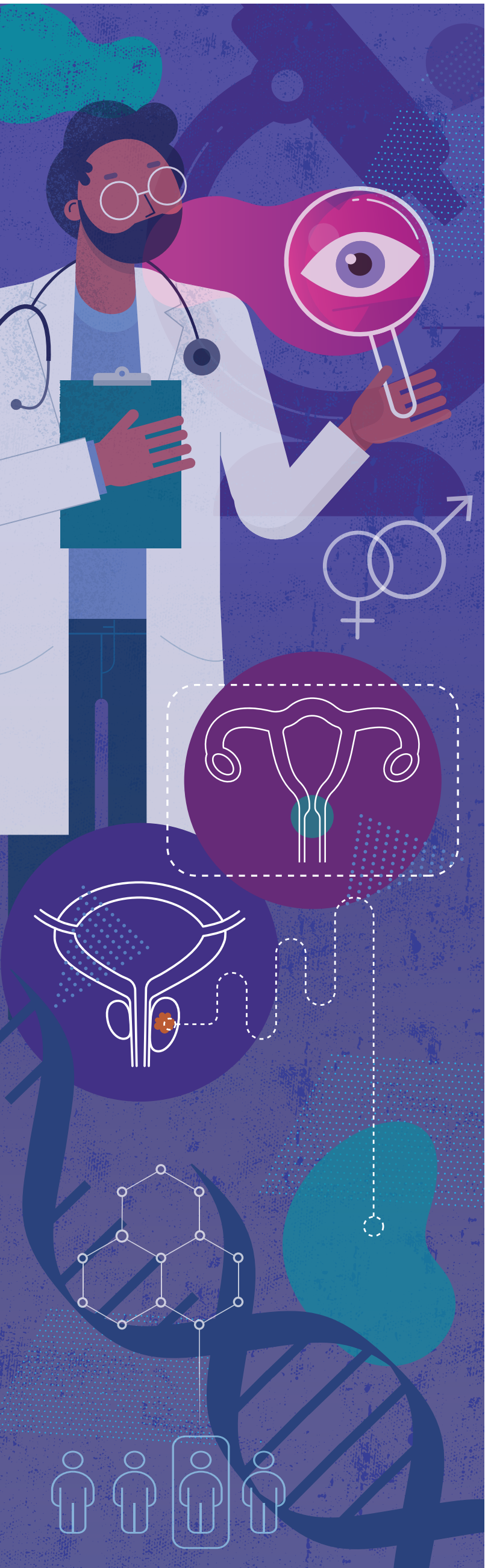

REPRODUCTIVE HEALTH AND KIDNEY DISEASES:

Time to Close the Knowledge Gap

By Jia Hwei Ng and Silvi Shah

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Reproductive health is rarely part of the nephrology conversation, yet it is inseparable from the lived experience of people with kidney diseases. From menstruation and fertility to pregnancy and sexual well-being, these issues shape quality of life, autonomy, and long-term health. This special issue of *Kidney News* brings reproductive health to the forefront, not as a secondary concern but as a core dimension of kidney care that requires attention, compassion, and scientific rigor.

In this issue, we cover topics spanning family planning, pregnancy in glomerulonephritis, reproductive health after transplant, sexual dysfunction, menstrual health, and the unique challenges faced by individuals with autosomal polycystic kidney disease. One common thread emerged: Our patients are navigating deeply personal, high-stakes reproductive choices without the comprehensive guidance or support they need.

Many of these gaps persist because reproductive health remains poorly integrated into nephrology practice. Nephrology training rarely includes reproductive health, and stigma or discomfort often limits such discussions with patients. In the article by Bathini and colleagues, menstrual health was described as "a vital sign too often ignored." Menstrual irregularities, heavy bleeding, and amenorrhea affect the majority of women with chronic kidney disease. These conditions are associated with anemia, transplant eligibility, and even cardiovascular risk. Yet these issues often go unaddressed in most clinics. Similar gaps extend to sexual health. As Lobo and Kattah note, three out of four men and up to 80% of women with chronic kidney disease report sexual dysfunction, but few are ever asked about it. Srinath and colleagues review sexual dysfunction in men with kidney diseases.

Pregnancy in kidney diseases presents both opportunities and challenges. Koubar highlights that with careful preparation, even women with glomerulonephritis can achieve healthy pregnancies. However, the risks remain substantial, particularly when disease activity, blood pressure, or proteinuria are not optimized beforehand. Gupta and colleagues remind us that after transplant, fertility often returns quickly. Thus, there is a need for timely contraceptive counseling and coordinated, multidisciplinary care. Anandh and coauthors review the importance of preconception counseling and family planning in individuals with kidney diseases. In addition, Ghozluojeh and colleagues' article on autosomal polycystic kidney disease underscores the complexity of reproductive decision-making in the context of genetic diseases, from preimplantation testing to pregnancy safety and postpartum planning.

Collectively, these contributions highlight that reproductive health is an essential aspect of kidney health. Future progress will require a coordinated effort on several fronts. First, investment should be made in education and research that center patients' experiences. Second, efforts to equip clinicians with the knowledge and confidence to address discussions about menstruation, sexual function, and pregnancy intentions in everyday clinical encounters should be implemented. And third, integration of reproductive counseling, development of national guidelines, and multidisciplinary collaboration into standard nephrology practice to ensure comprehensive support should be applied. Recognizing reproductive health as a core component of kidney care is essential to improving outcomes and advancing equitable, patient-centered practice. ■

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Navigating Reproductive Choices in CKD

By Urmila Anandh, Gayatri Pegu, and Priyadarshini John

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Kidney diseases have a significant impact on individuals' overall health and reproductive capabilities. Chronic kidney disease (CKD) affects about 0.5% to 9.0% of women of childbearing age and can present unique challenges during pregnancy. Women with kidney diseases face increased risks of complications like preeclampsia, preterm birth, and neonatal intensive care unit admission (1). Conversely, pregnancy can exacerbate kidney diseases, potentially leading to disease progression or flare of the kidney disease. The challenges of sexual and reproductive health in CKD depend on the estimated glomerular filtration rate (eGFR), proteinuria, and hypertension (2). Family planning, therefore, is of paramount importance and requires consideration in this population.

This editorial will explore the interplay between kidney diseases and family planning, addressing fertility challenges, the importance of preconception counseling, contraception, psychosocial considerations, and multidisciplinary care to optimize both maternal and fetal outcomes.

Pregnancy risks in CKD

The pathophysiologic impact of CKD on reproductive health is multifactorial. Women with CKD are often subfertile with disrupted menstrual cycles and multiple hormonal imbalances. In men, CKD impairs sperm production and motility. Dialysis further exacerbates these issues (3). Whereas pregnancy among people with kidney failure is rare, the number of pregnancies has been increasing worldwide from the beginning of the early part of this century. The Australia and New Zealand Dialysis and Transplant (ANZDATA) Registry showed an increase in pregnancy rates of 3.3 per 1000 in people on hemodialysis between 1998 and 2008 (it was 0.7 per 1000 women on hemodialyis between 1986 and 1995) (4). Various studies now report the frequency of conception in people with CKD to be between 0.3% and 7.0% per year (5–7). Conception is 10 times higher in successful kidney transplant recipients. Despite improvements in care, both maternal and fetal risks still continue to be high. Adverse effects on the pregnant individual during pregnancy was noted in one-third of cases.

Family planning: Role of counseling

Family planning is a complex and often emotional process for individuals with kidney diseases. The prospect of pregnancy can be both exciting and daunting, as individuals must weigh the potential risks and benefits of starting a family against the challenges posed by their kidney disease. Unplanned pregnancies may not only cause mental stress but also cause high maternal and fetal risks, including an accelerated decline in kidney function in the pregnant individual and preterm births in 40% and low birth weight in 90% of the pregnancies (8). In a study in India, stillbirths were noted in 15 of 51 pregnancies (9).

One of the key components of family planning for individuals with kidney diseases is preconception counseling. It should involve a detailed discussion about the potential risks and benefits of pregnancy, as well as the steps that can be taken to optimize the patient's health and minimize the risk to the self and the fetus (10). Conception should ideally occur when kidney function is stable. Proper contraception methods before conception that are compatible with the kidney condition, knowledge of potential risks of pregnancy, and achievement of optimal kidney function before conception should be part of counseling. Medications commonly used to treat kidney diseases, such as angiotensin-converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARBs), mycophenolate mofetil (MMF), and sodium-glucose cotransporter-2 (SGLT2) inhibitors, can have negative effects on pregnancy outcomes. These medications can cause birth defects, miscarriage, and other complications, making it important to adjust them before conception (11).

Contraception

Unplanned pregnancies can pose significant challenges for individuals with kidney diseases. Use of proper and effective contraception gives individuals control over their reproductive choices and ensures that they can start a family when the time is right for them (12). A range of contraceptive options, like the barrier method, hormonal contraception, and long-acting reversible contraception (LARC), such as intrauterine devices (IUDs) and implants, are available (Table). Contraceptive choice depends on many variables, like method efficacy, duration of action, type of contraceptive (hormonal), and timing of return of fertility. Additional concerns are the effect of the contraceptives on the disease progression and the presence of other coexisting medical conditions, all of which need to be balanced against the risk of unintended pregnancy (13).

Individuals with kidney diseases need to discuss their contraceptive options with their health care practitioner to find the method that best fits their needs and preferences.

For patients who desire long-acting or the most effective contraception, LARCs like IUDs and implants are preferable. Copper and levonorgestrel-releasing IUDs and etonogestrel implants are the types commonly used. They last for 3 to 10 years and have a failure rate of less than 1% depending on the device. LARCs are the most effective and safest for people living with CKD. Hormonal contraceptives like depot medroxyprogesterone acetate (DMPA), progestin-only oral pills, combined estrogen-progestin products like oral pills, transdermal patches, and vaginal rings are highly effective when short-duration contraception is required. However, use of hormonal agents is associated with increased risk of cardiovascular and venous thromboembolic events, osteopenia (DMPA), and accelerated hypertension. Use of combined estrogen-progestin pills is associated with a theoretical risk of progression of CKD by activating the renin-angiotensin system and increasing the risk of hypertension and microalbuminuria (14). Therefore, these drugs are to be used with caution and not recommended for people with uncontrolled hypertension.

By using effective contraception consistently and correctly, individuals with kidney diseases can prevent unintended pregnancies and better plan for their future family goals.

In conclusion, family planning decisions require a comprehensive approach that addresses both the potential risks and benefits of pregnancy, while also considering the patient's overall health and preferences. Patients need to be educated about the high risk of pregnancy, and a multidisciplinary team involving both a nephrologist and an obstetrician should be involved in the care. By addressing the unique challenges and considerations of family planning, health care practitioners can support patients in making informed decisions about starting a family and navigating the complex and emotional journey of pregnancy. ■

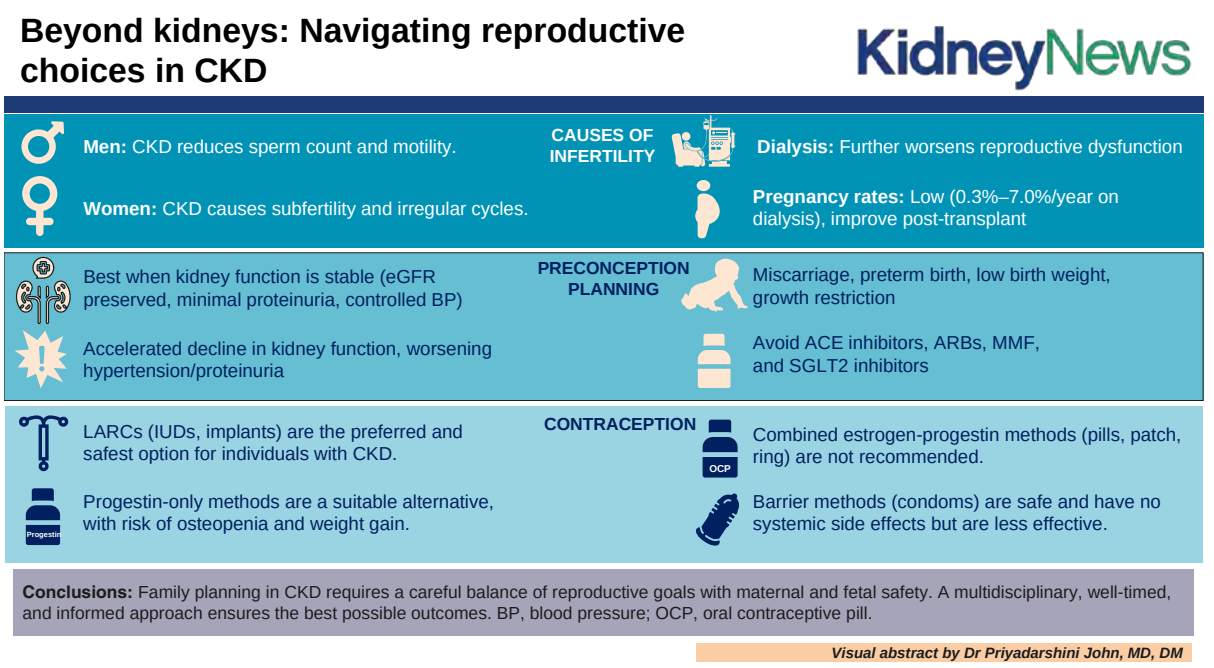

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Table. Various contraceptive methods

Method of contraception	Mechanism of action	Merit	Demerit	Contraindication
Hormonal				
Combined (progestin and estrogen) oral	Inhibits GnRH; blocks ovulation; alters endometrium; thickens cervical mucus; worsens albuminuria	Highly effective; failure rate, 0.3% (perfect use)–7.0% (typical use)	Thrombotic and cardiovascular risk. Progesterone increases the levels of CNIs, and CNIs reduce the efficacy of the pill.	Absolute: anti-phospholid syndrome; history of venous thromboembolism, breast cancer, and cardiovascular disease; smokers >35 years. Relative: diabetes; hypertension; proteinuric kidney disease
Progestin-only OCP	Inhibits GnRH; reduces endometrial thickness; modifies cervical mucus; alters tubal motility	No impact on coagulation and hypertension; failure rate, 9%–13% (typical use)	Weight gain; spotting; irregular menses; interaction with CNIs, as with estrogen-containing hormonal contraception	Absolute: none. Relative: SLE with anti-phospholipid antibodies; diabetes; hypertension
Progestin-only subdermal implant	Actions as above	Failure rate, 0.1%; long acting (3 years) and reversible	Side effects similar to progestin-only OCPs	Absolute: thromboembolic disease. Relative: SLE with anti-phospholipid antibodies; diabetes; hypertension; dyslipidemia; immunocompromised state
Injectable progestin-only	Actions as above	Long acting (2–3 months); failure rate, 0.2% (perfect use) and 4%–6% (typical use)	Weight gain; reduction in bone mineral density	Absolute: breast cancer; coagulation disorders. Relative: SLE ± anti-phospholipid antibodies; diabetes; hypertension; cardiovascular; osteoporosis; history of fractures; dyslipidemia; immunocompromised state
IUD				
Nonmedicated copper-containing	Foreign body in the endometrium induces local changes hostile to fertilization.	Long acting (5–10 years); useful as an emergency contraceptive if inserted within 5 days of sexual intercourse; can be considered in patients with obesity, diabetes, hypertension, and coagulation disorders; very low failure rate, 0.1%–0.6%; copper toxic to sperm	Higher incidence of pelvic infections; increased chances of extrauterine pregnancy; risk of IUD expulsion and rarely uterine rupture	Absolute: none. Relative: patients who are immunocompromised (kidney transplant recipients with complications); people on peritoneal dialysis
Medicated	Thickens mucus; prevents sperm motility; impairs ovulation	Very low failure rate, 0.1%–0.6%; high compliance; long acting (3–5 years)	Disadvantages similar to that of nonmedicated IUDs	Similar to that of nonmedicated IUDs
Barrier				
Condom/cervical cap/ sponge/diaphragm	Prevents direct contact between the spermatozoa and the ovum	No adverse effect; condoms protect against sexually transmitted diseases	High failure rate, as high as 20% across all barrier methods; increased risk of urinary tract infection with cervical caps and diaphragms (especially if spermicide is used concomitantly)	History of vaginal infections in recent childbirth; latex allergies; toxic shock syndrome in diaphragm users

CNIs, calcineurin inhibitors; GnRH, gonadotropin-releasing hormone; OCP, oral contraceptive pill; SLE, systemic lupus erythematosus.

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Reproductive Care in ADPKD: Moving Beyond Risk Talks to Supportive Choices

By Zohreh Gholizadeh Ghozluojeh, Amir Abdipour, and Sayna Norouzi

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Family planning in autosomal dominant polycystic kidney disease (ADPKD) poses a tremendous burden on patients; maternal and fetal risk are determined mainly by the chronic kidney disease (CKD) stage, proteinuria, and blood pressure (BP). The genotype (e.g., PKD1 vs PKD2) predicts lifetime disease severity and also informs the risk of disease severity in the next generation in case of transmission (1–3). Hence, family planning and pregnancy care can be overwhelming for patients. Nephrologists are often asked whether pregnancy is advisable. When information arrives late, uncertainty fills the space; patients often report anxiety and decisional conflict (4). With advances in maternal-fetal care and reproductive genetics, we can replace that uncertainty with a patient-centered approach. This editorial aims to outline reproductive care in ADPKD, spanning contraception, preconception, pregnancy, and postpartum, and to clarify where selective, risk-based evaluations (e.g., intracranial aneurysm [ICA]) fit within preconception counseling.

Preconception planning and counseling

Because estrogen exposure can accelerate polycystic liver disease (PLD) growth, women with significant PLD should preferentially use nonestrogen contraception (e.g., a copper intrauterine device, progestin-only options), with choices guided by bleeding pattern, thrombotic risk, and patient priorities (5, 6).

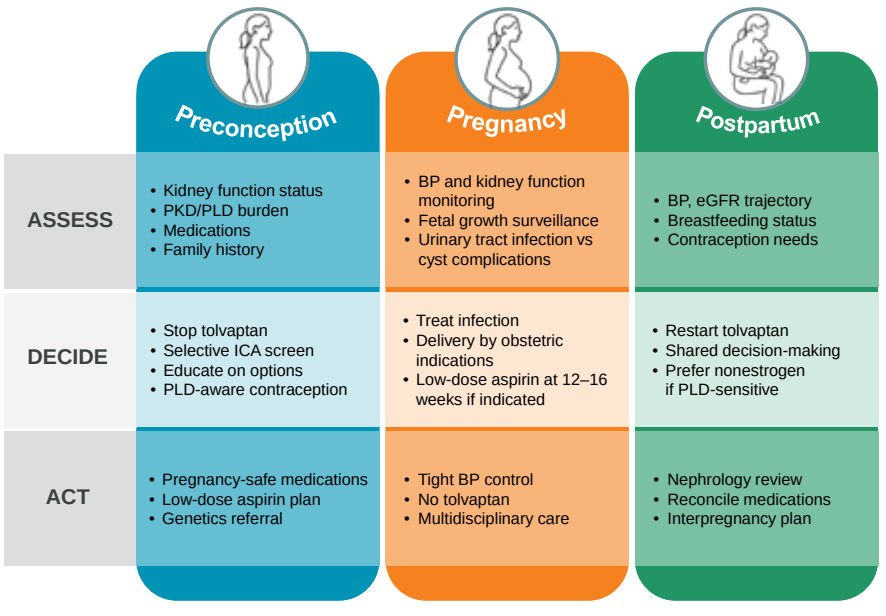
A structured review of the estimated glomerular filtration rate (eGFR) trajectory, albuminuria, hypertension, disease phenotype, and medication reconciliation should precede pregnancy. Tolvaptan should be discontinued at least 4 weeks before conception and avoided during pregnancy and breastfeeding, with effective contraception advised while on therapy and until an appropriate washout is complete per guidance (5, 7). It is important to counsel patients on in vitro fertilization (IVF) with preimplantation genetic testing (PGT), specifically PGT for monogenic conditions as an option (2, 8). Understanding the limitations of the process is critical in this particular situation. Although rare, PGT carries a small risk of embryo loss, which may require multiple IVF cycles to achieve pregnancy. There is a small possibility of a false-negative result as well. The ethical concerns around PGT, in addition to the high cost of IVF, which is often not covered by insurance, are major concerns.

According to Kidney Disease: Improving Global Outcomes (KDIGO), universal ICA screening is not recommended. Apply screening selectively in those with a personal or family history of ICA or subarachnoid hemorrhage, in certain high-risk occupational contexts, or when patient preference is strong after informed counseling. If pursued, screening should occur before pregnancy. Pregnancy itself is not a sufficient indication (5, 9).

Pregnancy management

Pregnancy should be managed by CKD principles with ADPKD nuance: Maintain tight BP control with pregnancy-safe agents, monitor for hypertensive disorders and fetal growth restriction, and treat urinary tract infection promptly, selecting pregnancy-safe antibiotics with cyst penetration when cyst infection is suspected (2, 3). The timing and mode of delivery should be guided by obstetric indications rather than by the presence of kidney or hepatic cysts, within a multidisciplinary team familiar with ADPKD (2, 3).

Figure. ADPKD reproductive choice architecture



Preconception, pregnancy, and postpartum pathway showing assess → decide → act steps.

Beyond the index pregnancy, counseling should also calibrate the expected long-term renal trajectory so that families understand not just how to manage this pregnancy but also what it may mean for kidney health over time (1, 5, 9) (Figure).

Postpartum care in ADPKD

Tolvaptan can be reintroduced once breastfeeding is stopped; make the restart decision via shared decision-making that integrates postpartum recovery, kidney disease stage, contraception planning, and possible future pregnancy plans (6, 7).

When counseling about future outcomes, anchor discussions in CKD-specific evidence: Mild CKD generally shows no long-term decline after pregnancy**,** whereas advanced CKD carries a higher risk of postpregnancy kidney function loss, especially with chronic hypertension. This stage- and BP-anchored framing of pregnancy outcomes should be applied to ADPKD counseling (1).

Changing the standard

These decisions land in real lives: How early and how well we inform, support, and coordinate care will shape outcomes (4). Qualitative studies highlight the need for earlier information, stronger psychosocial support, and tighter multidisciplinary coordination across nephrology, obstetrics, and genetics (4). In the Developing Intervention Strategies to Halt Progression of ADPKD (DIPAK) cohort, women were more likely to report that ADPKD influenced family size with more advanced disease (Mayo Clinical classification D or E) or with hypertensive pregnancy complications. In the DIPAK cohort, about one in four partnered adults, aged 27 years or older, without children, reported involuntary childlessness, and one in eight parents said that ADPKD curtailed their desired family size (10).

Reproductive care in ADPKD is a sequence of well-timed decisions: cessation of teratogens at the right moment, contraception tailored to hepatic phenotype, genetic testing and IVF options offered without coercion, pregnancy managed by CKD principles with ADPKD-specific nuance, and ICA screening reserved for those who benefit (2, 5, 8, 9). With advances in maternal-fetal medicine and reproductive genetics, nephrologists must ensure that reproductive care in ADPKD is delivered with rigor, personalization, and evidence literacy, consistently and as the standard rather than the exception (2, 5). ■

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Glomerulonephritis and Pregnancy

By Sahar H. Koubar

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"Children of women with renal disease used to be born dangerously or not at all—not at all, if their doctors had their way…. Obstetricians and physicians must batten down the hatches and prepare to ride out the storm together with those determined to set sail" (1).

Glomerulonephritis during pregnancy, even when in remission, is often associated with a high-risk profile (2, 3) and requires proactive counseling, close monitoring, and coordinated care between nephrologists and maternal-fetal medicine specialists. Encouragingly, advances in perinatal care and chronic kidney disease (CKD) management during pregnancy have led to improved live birth rates.

Unfortunately, routine kidney function testing before pregnancy is uncommon, and many women with glomerulonephritis receive their initial diagnosis during pregnancy. Furthermore, early glomerulonephritis may be overlooked during pregnancy due to the presence of physiologic proteinuria. Hence, vigilance is key, and any proteinuria exceeding the physiologic threshold from pregnancy-related hyperfiltration (>300 mg/day) should prompt thorough evaluation and close monitoring.

Diagnosis of glomerulonephritis during pregnancy is further limited by concerns about performing a kidney biopsy, as the procedure carries an increased risk of bleeding, especially in the late second trimester. The risk should always be carefully balanced against the potential benefits that could influence management decisions. Generally, the risk-benefit ratio is lower in early pregnancy (before 12 weeks) and higher after 30 weeks. In a systematic review by Piccoli et al., major bleeding occurred in 2% of cases, at a median gestational age of 25 weeks (range, 23–26 weeks) (4). A kidney biopsy may be technically easier to perform in kidney transplant recipients.

Women with glomerulonephritis face an increased risk of preeclampsia and preterm delivery (5). However, this risk can be mitigated when treatment is optimized prior to pregnancy, and the disease remains stable for at least 6 months before conception. Indeed, the key to a successful pregnancy in women with glomerulonephritis is careful preparation. Entering pregnancy with the lowest proteinuria possible (ideally, <1 g/day), well-controlled blood pressure, and quiescent inflammatory glomerulonephritis provides the best chance for favorable pregnancy outcomes (6).

Although most glomerulonephritides have been reported in pregnancy, the most common biopsy-proven glomerulonephritides in pregnancy or in the postpartum period are focal segmental glomerulosclerosis, immunoglobulin A nephropathy (IgAN), and lupus nephritis (LN). Due to its typically less-acute presentation and chronic course, IgAN seems to carry a lower risk of adverse pregnancy outcomes compared with other forms of glomerulonephritis (7, 8). However, this risk largely depends on the degree of kidney impairment (e.g., a reduced glomerular filtration rate and proteinuria) and blood pressure control. IgAN is rarely diagnosed during pregnancy unless it presents as nephrotic syndrome or rapidly progressive glomerulonephritis, in which case a kidney biopsy is usually warranted.

On the other hand, LN flare is well associated with poor pregnancy outcomes. Diagnosis of an LN flare during pregnancy usually relies on a combination of worsening serologic and biochemical markers alongside clinical symptoms; kidney biopsy is rarely required. Whether pregnancy triggers LN flares remains controversial. It is generally recommended to wait at least 6 months of disease quiescence on pregnancy-safe medications before conception. A reduced glomerular filtration rate (<60 mL/min/1.73 m^2) and proteinuria (>1 g/day) are linked to a higher risk of renal flare, whereas normal complement levels at conception and aspirin use have been associated with improved live birth rates (9). Pregnant women experiencing an LN flare face up to a 35% risk of preeclampsia, with a heightened likelihood of developing preterm preeclampsia (before 37 weeks of gestation). All individuals with systemic lupus erythematosus should be maintained on hydroxychloroquine during pregnancy. Frequent follow-up is essential during pregnancy and should be tailored to disease severity—ranging from every 1 to 2 weeks for people with CKD stages 4 to 5 or proteinuria more than 3 g to every 4 to 6 weeks for those in remission with CKD stage 1, no proteinuria, and normal blood pressure.

Differentiating glomerulonephritis from preeclampsia remains a challenge. Although a soluble fms-like tyrosine kinase 1/placental growth factor (sFlt-1/PlGF) ratio and PlGF biomarkers are showing promise in identifying preeclampsia in pregnant women, their interpretation in those with CKD remains complex, their cost-effectiveness is still under evaluation, and they are not yet widely adopted in the United States (10, 11). Vascular endothelial growth factor (VEGF) and PlGF are proangiogenic proteins that bind to the membrane receptor (VEGFR-1), activating signaling pathways crucial for vascular homeostasis and a healthy pregnancy, whereas sFlt-1 (also known as soluble VEGFR-1) is a soluble splice variant of VEGFR-1 that binds and sequesters VEGF and PlGF, thereby blocking their angiogenic activity. An increased sFlt-1/PlGF ratio reflects placental dysfunction and endothelial injury and serves as a key biomarker for preeclampsia and related adverse pregnancy outcomes. Superimposed preeclampsia on glomerulonephritis is usually "maternal" preeclampsia (i.e., occurring late in pregnancy [>34 weeks] with relatively preserved fetal growth).

General measures include limiting sodium intake to less than 4 g/day and shifting to plant-based protein. Loop and thiazide diuretics may be used during pregnancy, but overzealous use should be avoided. Aspirin (81–162 mg/day) is essential for preeclampsia prophylaxis (<12 to 34–36 weeks), together with low-molecular-weight heparin if serum albumin is less than 2.0 to 2.5 g/dL. Safe immunosuppression medications in pregnancy are summarized in the Table.

Glomerulonephritis in pregnancy remains challenging, and treatments are often limited for concern of fetal toxicity. Future efforts should focus on unique disease risk for a more personalized risk assessment to guide individualized counseling and care. Unfortunately, many women with pregnancy complications are lost to follow-up despite their increased risk of future cardiovascular disease. Hence, pregnancy should be viewed as a vital window into a woman's overall health and an opportunity to identify, address, and optimize long-term health outcomes in women.

Table. Safe immunosuppressive medications during pregnancy

Medications	Remarks
Steroids	• Oral or intravenous methyprednisone in induction doses may be justified, as the risk of a flare often outweighs the potential harms of steroid treatment to the mother and fetus. • The medication is relatively safe but can cause hypertension, weight gain, and diabetes.
Azathioprine	• The thiopurine methyltransferase level should be checked to determine myelosuppression risk. • The maximum dose in pregnancy is 2 mg/kg per day.
Calcineurin inhibitors (tacrolimus and cyclosporine)	• Voclosporin is discouraged given the alcohol component of the drug formulation.
Rituximab	• Avoid in second and third trimesters, as it is associated with neonatal lymphopenia. • Neonates exposed to rituximab are advised to avoid live vaccines until 6 months of age.

Mycophenolate mofetil, mycophenolic acid, cyclophosphamide, and methotrexate are contraindicated during pregnancy because of increased risk of early pregnancy loss and fetal malformations. They are also contraindicated during lactation.

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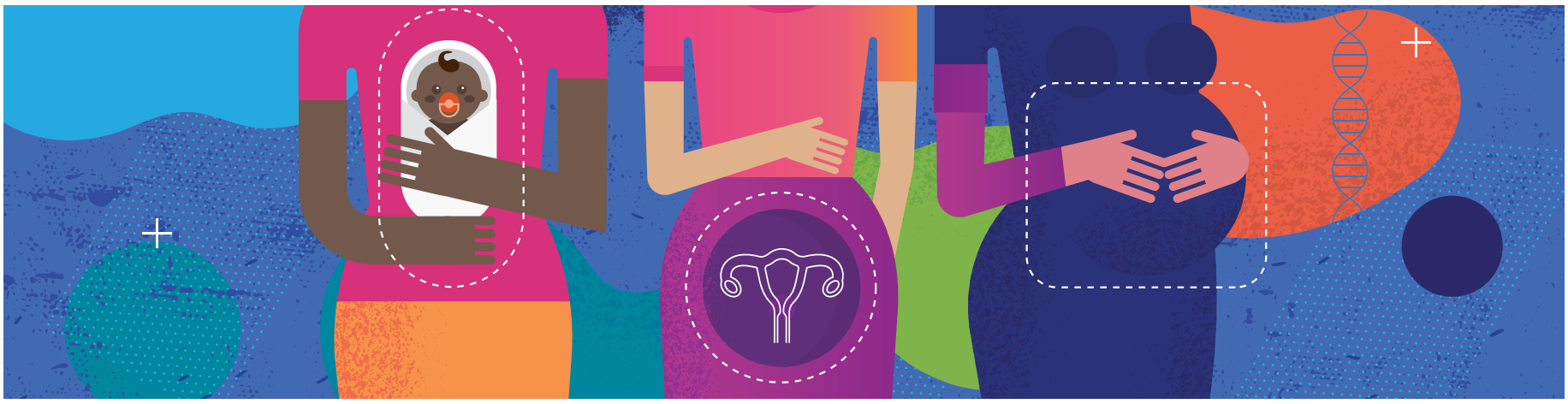

Reclaiming Reproductive Health in Kidney Transplantation: A Clinical Imperative

By Maitreyee Gupta, Hatem Najar, and Kiran Goli

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Kidney transplantation does not just save lives—it gives people their lives back. It improves survival, reverses kidney failure, and significantly boosts quality of life, including areas we often overlook, like reproductive health (1). For many patients, especially women of childbearing age, fertility can return after a transplant, creating both new possibilities and important clinical considerations.

As transplant outcomes continue to improve, it is time we fully recognize reproductive health as an essential part of transplant care. This editorial outlines key points related to reproductive health for both kidney transplant recipients and living donors and encourages a proactive, team-based, and patient-centered approach to care.

Preconception counseling

More than one-third of pregnancies among women who conceive after kidney transplant are unplanned. Fertility often returns within 6 weeks after transplant as hormone levels normalize, but most guidelines recommend postponing conception for at least 1 year to ensure graft stability and absence of recent rejection (2). This makes early contraceptive counseling essential to help prevent unplanned pregnancies during this vulnerable period.

The American Society of Transplantation emphasizes the need for access to routine and emergency contraception, as well as safe abortion care when indicated (3). Long-acting reversible contraceptives, including copper and hormonal intrauterine devices (IUDs), are generally safe and effective for transplant recipients, whereas estrogen-containing methods require individualized assessment due to thrombotic and cardiovascular risks (4, 5).

Mycophenolate mofetil and mammalian target of rapamycin (mTOR) inhibitors are teratogenic and should be discontinued 6 to 12 weeks before conception. A case series reports reassuring outcomes on belatacept, but data remain limited, and its safety is not yet well established (6). Due to the risk of fetal kidney injury, angiotensin-converting enzyme inhibitors and angiotensin II receptor blockers are contraindicated in pregnancy and should ideally be discontinued at least 6 weeks before conception (7).

Fertility is not affected in living kidney donors. Most studies show no significant differences in fetal or neonatal outcomes when comparing postdonation, predonation, and nondonor pregnancies (8). In general, donors go on to have healthy pregnancies and healthy babies. Although postdonation pregnancies carry a slightly higher risk of hypertensive disorders—such as gestational hypertension or preeclampsia—the overall risk remains low. In a large matched cohort study, these conditions occurred in 11% of donor pregnancies versus 5% in nondonors (odds ratio for donors, 2.4 [95% confidence interval, 1.2–5.0]; p = 0.01), with most pregnancies resulting in favorable outcomes (9).

Male kidney transplant recipients often experience meaningful improvements in sexual function, testosterone levels, and sperm quality after transplant. However, certain immunosuppressive medications—particularly sirolimus—may negatively impact fertility, highlighting the need for personalized counseling for men planning to father children (10) (Table).

Table. Reproductive health in kidney transplantation

Phase	Key considerations
Preconception	• Recognize possible return of fertility within weeks after transplant (typically ~6 weeks). • Delay pregnancy for at least 1 year after transplant. • Ensure stable graft function and absence of recent rejection. • Initiate early contraceptive counseling. • Avoid teratogenic medications (e.g., mycophenolate mofetil, mTOR inhibitors); switch to safer alternatives ≥3 months prior to conception. • Prefer long-acting reversible contraception (e.g., IUDs). • Counsel male recipients on fertility and the impact of immunosuppressants (e.g., sirolimus can impair spermatogenesis). • Evaluate vaccination status. • Assess psychosocial status.
During pregnancy	• Require comanagement by transplant nephrologist and maternal-fetal medicine specialist for high-risk pregnancy. • Continue safe immunosuppressants: tacrolimus, azathioprine, cyclosporine, and prednisone. • Avoid mycophenolate mofetil and mTOR inhibitors. • Monitor BP, kidney function, and calcineurin inhibitor levels closely. • Understand increased risk of preeclampsia, preterm birth, and fetal growth restriction. • Prefer vaginal delivery unless obstetric indications require cesarean delivery. • Recognize slight increased risk of gestational hypertension and preeclampsia but generally favorable outcomes among living donors.
Postpartum	• Monitor closely for graft dysfunction or acute rejection. • Encourage breastfeeding: safe with tacrolimus, cyclosporine, azathioprine, and prednisone. • Avoid breastfeeding with mycophenolate mofetil or mTOR inhibitors. • Reassess and plan for contraception prior to discharge. • Offer parenting and mental health support as part of comprehensive postnatal care.

Pregnancy management

Pregnancy after kidney transplant is high risk and requires coordinated care between transplant nephrologists and maternal-fetal medicine specialists, including medication adjustments, blood pressure (BP) control, immunosuppressant monitoring, and close fetal surveillance. Although live birth rates approach those of the general population, risks of preeclampsia, preterm delivery, low birth weight, and fetal growth restriction remain significantly elevated (11). The risk of pregnancy-induced hypertension in kidney transplant recipients was noted at 24%, and preeclampsia was

21% in a meta-analysis and systematic review of worldwide registries and single-center studies through 2017 (12).

Pregnant kidney transplant recipients should be comanaged by a high-risk obstetrician and transplant nephrologist. Although no formal monitoring guidelines exist, visits every 2 to 4 weeks are recommended to assess BP, preeclampsia, gestational diabetes, infection, and graft function (13, 14). Each visit should include BP checks (including home readings) and labs for creatinine, electrolytes, complete blood count, liver function, urinalysis with a protein-to-creatinine ratio, and tacrolimus or cyclosporine trough levels. Additional trimester-based tests, such as oral glucose tolerance and cytomegalovirus polymerase chain reaction, are recommended. Due to pregnancy-related pharmacokinetic changes, calcineurin inhibitor levels should be closely monitored and maintained at prepregnancy targets. This structured approach helps reduce maternal and graft-related risks. In the absence of transplant-specific targets, a BP goal of less than 140/90 mm Hg is advised, with antihypertensives initiated if exceeded. Vaginal delivery remains safe unless specific obstetric indications arise.

Postpartum considerations

Nephrologists should stay vigilant in the postpartum period—tracking kidney function, proteinuria, and BP as physiology resets. Immunosuppressant levels can shift with metabolic changes and breastfeeding, requiring fine-tuned dosing. Monitor individuals closely for anemia, fluid imbalance, and infections. Breastfeeding is encouraged: Tacrolimus, cyclosporine, azathioprine, and prednisone are compatible, whereas mycophenolate mofetil and mTOR inhibitors are not. Postpartum contraception must be proactively addressed to ensure safe spacing. Any changes in medication should be guided by a transplant nephrologist.

Conclusion

Reproductive health is a vital but often underemphasized component of comprehensive kidney transplant care. As patient survival continues to improve, transplant programs must evolve to address not only graft longevity but also patients' life goals, including parenthood. Multidisciplinary collaboration, anticipatory counseling, and individualized care plans are essential to support safe and successful reproductive outcomes. Addressing these needs proactively is not only a clinical responsibility but a moral imperative in delivering truly patient-centered transplant care. ■

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Sexual Dysfunction and Kidney Diseases: From Screening to Solutions

By Angie S. Lobo and Andrea G. Kattah

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In a routine clinic visit, we as nephrologists review labs and ask about symptoms, such as pruritus and sleep, but we too often ignore sexual health. Sexual dysfunction is common across the chronic kidney disease (CKD) spectrum yet rarely addressed in routine care. In men with CKD, erectile dysfunction affects approximately three-quarters of patients and improves—although does not normalize—after transplant (1). Among women with CKD, 30% to 80% report sexual symptoms (e.g., lack of desire, arousal, lubrication, or orgasm and pain) with substantial quality-of-life impact (2). These data argue for proactive screening and treatment as part of patient-centered kidney care.

Mechanisms span biology and context

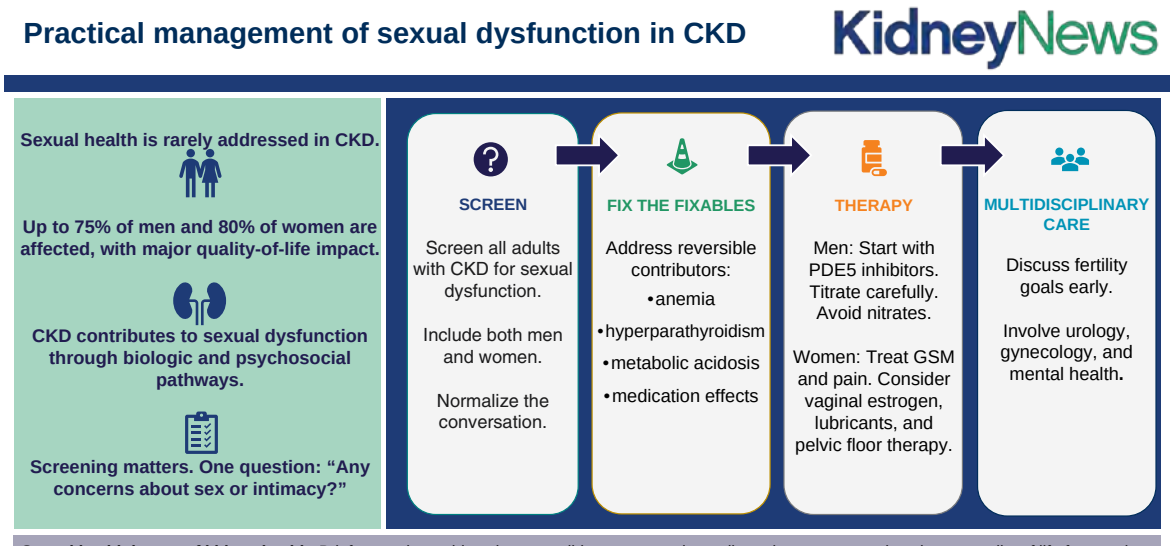
CKD impacts both biology and lived experience. It perturbs the hypothalamic–pituitary–gonadal axis, endothelial function, and neurotransmission; anemia, inflammation, uremic toxins, neuropathy, and polypharmacy compound the pathology. In men, hypogonadism and hyperprolactinemia track with falling glomerular filtration rate and abnormal semen parameters (3, 4). In women, anovulation, amenorrhea, and genitourinary syndrome of menopause (GSM) are more frequent, and symptom patterns can diverge from the general population (2, 5). Layered atop these biologic drivers are symptoms such as fatigue, pruritus, sleep disruption, and relationship stressors, with mood disorders further amplifying sexual dysfunction—underscoring a biopsychosocial model of disease (2, 4, 5). Medications can play a role (e.g., selective serotonin reuptake inhibitors, β-blockers, and spironolactone) (4), as can body image issues related to dialysis access (6).

Start with screening

Nephrologists should ask every adult with CKD about sexual health. The dialogue can start with one question: "Are there any concerns about sex or intimacy that you would like help with?" We can normalize the conversation, involve partners when appropriate, and document goals (e.g., comfort, intimacy, or fertility) to guide shared decision-making. When useful, apply brief, validated tools—the International Index of Erectile Function-5 for men and the Female Sexual Function Index for women—to standardize assessment and track change over time (2, 4).

Practical management

- **Fix the fixables**
  - Optimize anemia, mineral bone disease, volume/blood pressure, and glycemia.
  - Treat pruritus and sleep disturbance.
  - Screen and manage depression.
  - Review and, when possible, de-prescribe medications with sexual side effects.
  - Consider optimizing dialysis adequacy and reducing scheduling burdens.
  - Remind patients that relationship factors impact sexual health, and they may need to seek outside counseling (2, 4).
- **For men**
  - Begin treatment with phosphodiesterase-5 (PDE5) inhibitors. Randomized and prospective studies in hemodialysis and peritoneal dialysis show that sildenafil improves erectile function with acceptable safety (7, 8). Start at a low dose, and titrate as tolerated. Pharmacokinetic data show that sildenafil is not dialyzable and does not precipitate intradialytic hypotension. Avoid use with nitrates, and exercise caution with strong CYP3A4 modulators.
- **For women**
  - Focus on treating GSM and pain.
  - Incorporate low-dose vaginal estrogen, which effectively relieves vaginal dryness and dyspareunia. Large cohort studies show no increase in cardiovascular disease or cancer risk with this therapy (9).
  - Suggest local estrogen for women with CKD, which is generally appropriate after shared counseling.
  - Address pelvic pain, vaginismus, and lubrication issues with multimodal strategies, and consider gynecology/urogynecology referral.
  - Individualize treatment decisions because evidence guiding systemic hormone therapy in CKD remains limited (5, 9).
- **Fertility goals matter**
  - Discuss early and readdress often.
  - Explain that CKD-related endocrine disruption and prior cyclophosphamide exposure can affect reproductive plans.
  - Coordinate care with reproductive specialists (3, 10).



Sexual health is part of kidney health. Brief screening, addressing reversible causes, and coordinated care can greatly enhance quality of life for people with CKD. **If we do not ask, we cannot fix it.**

Visual abstract by Angie S. Lobo, MD, and Andrea G. Kattah, MD, MS

Bottom line

Sexual health is an important part of kidney health. Brief screening, attention to reversible drivers, judicious use of targeted therapies, and multidisciplinary collaboration can meaningfully improve quality of life for people living with CKD (1, 2, 5–8). If we do not ask, we cannot fix it (1–7). ■

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The authors report no conflicts of interest.

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Chronic Kidney Disease and Male Sexual Dysfunction

By Maya Srinath, Vinay Patel, and Gideon Richards

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Erectile dysfunction (ED) is defined as failure to achieve an erection sufficient for penetrative sexual intercourse. Men with ED face a broad range of experiences, from intermittent or incomplete erections to complete lack of turgidity. This range is reflective of the numerous psychologic and physiologic mechanisms that underlie erections. Approximately 50% of men over the age of 40 years have ED with increased prevalence with age. Chronic kidney disease (CKD) stages 1–5, as defined by estimated glomerular filtration rates, has a prevalence of 12% in men that also increases with age. The prevalence of ED among men with CKD is approximately 70% (1). The more advanced the CKD, the higher the rates of ED (2). In this article, we highlight some of the mechanisms hypothesized to account for the relationship between these processes (Figure) and discuss the evaluation and management of ED in this population.

Cardiovascular disease, diabetes, hypertension, obesity, tobacco use, and dyslipidemia are all risk factors for both CKD and ED. These comorbidities are associated with arteriopathy and endothelial dysfunction. Resultant small vessel blood flow changes decrease both glomerular filtration capacity and erectile blood flow. Although these risk factors account for a substantial part of the relationship between these entities, there is also evidence of direct and indirect negative effects of CKD on the erectile function of these men.

Abnormal endothelial function has been implicated in those with even mild CKD, regardless of the presence of arteriosclerosis, compared with individuals without CKD, suggesting that the uremia itself may contribute directly to endothelial dysfunction, which not only may result in development and progression of ED but also of cardiovascular disease (3).

Uremia has also been implicated in autonomic nervous system dysfunction, which has been correlated with abnormal nocturnal penile tumescence testing and decreased frequency of sexual activity in those with CKD (4).

CKD has also been found to increase the likelihood of depression, as well as result in hormonal changes in testosterone, luteinizing hormone prolactin, and erythropoietin, which are important factors in the psychologic and physiologic milieu that support both libido and erectile function (5–7).

Evaluation and diagnosis of men with ED are based primarily on history. Spontaneous reporting of erectile problems or direct questioning from the clinician will elicit the patient's subjective evaluation of their erectile function. Insufficient or unsatisfactory erections may prompt a referral to a urologist or further questioning, both intended to guide therapy.

There exist semiquantitative, validated instruments in the form of numerically scaled patient questionnaires—most notably, the Sexual Health Inventory for Men (8) and the International Index of Erectile Function (9). Although developed for research, these questionnaires can be used in the clinical setting. However, a simpler assessment of whether the patient has problems achieving an erection or maintaining an erection, whether they wake with erections, whether they consistently achieve better erections in certain situations than in others, and whether the desire for sexual activity (libido) remains preserved is generally sufficient to indicate the potential various contributing, underlying pathophysiologic mechanisms (vasculogenic, psychogenic, and hormonal factors).

A thorough evaluation of patient comorbidities, including metabolic conditions like diabetes and hypertension, as well as neurologic history (especially surgeries in the location of the pelvic plexus), should be undertaken. Examination and laboratory assessments are tailored to the history. For instance, a history of decreased libido would prompt hormonal evaluation (testosterone, thyroid-stimulating hormone testing), or similarly a history of absence of nocturnal erections or obesity would prompt testing for metabolic syndrome comorbidities (hemoglobin A_{1C}, blood lipid testing). When endocrine disorders or psychogenic factors are identified, referral to appropriate clinicians to aid in clinical management of these elements is warranted (e.g., endocrinologist or sexual psychologist).

Patients should be encouraged to address comorbidities as part of the first line of treatment. However, for people with concomitant CKD, the microvascular damage from these metabolic conditions may be too severe to recover erectile function with management of these conditions. Pharmacologic treatment with phosphodiesterase-5 inhibitors has been shown to improve erectile function including the subpopulation of men with CKD and ED (10). The intracavernosal use of injectable vasodilating agents, such as papaverine, phentolamine, and alprostadil (or more commonly, various combinations of these agents), has also been successful in people with CKD (11). Physical mechanisms may also be used in situations in which pharmacologic therapies are ineffective, contraindicated, or not preferred by the patient. Vacuum-constriction devices using negative pressure to pull blood into erectile tissue and then a veno-occlusive elastic ring around the penis to maintain rigidity have good mechanical efficacy, however, mixed reviews in patient satisfaction owning to the relatively cumbersome nature of their use. Finally, implantable penile prostheses are another effective mechanical intervention in those for whom pharmacologic therapy is not preferred. These devices replace the internal erectile tissue with inflatable or semimalleable cylinders that take up the shape of the penis and provide axial rigidity sufficient for penetration. These implants have excellent success in the treatment of ED in those with CKD (11).

ED is prevalent in those with CKD. There are numerous mechanisms that relate these disease processes. Identifying when they coexist affords the opportunity to provide these individuals with CKD referrals, evaluations, and/or treatments that may further improve the quality of their lives in addition to preservation and improvement of their kidney function. ■

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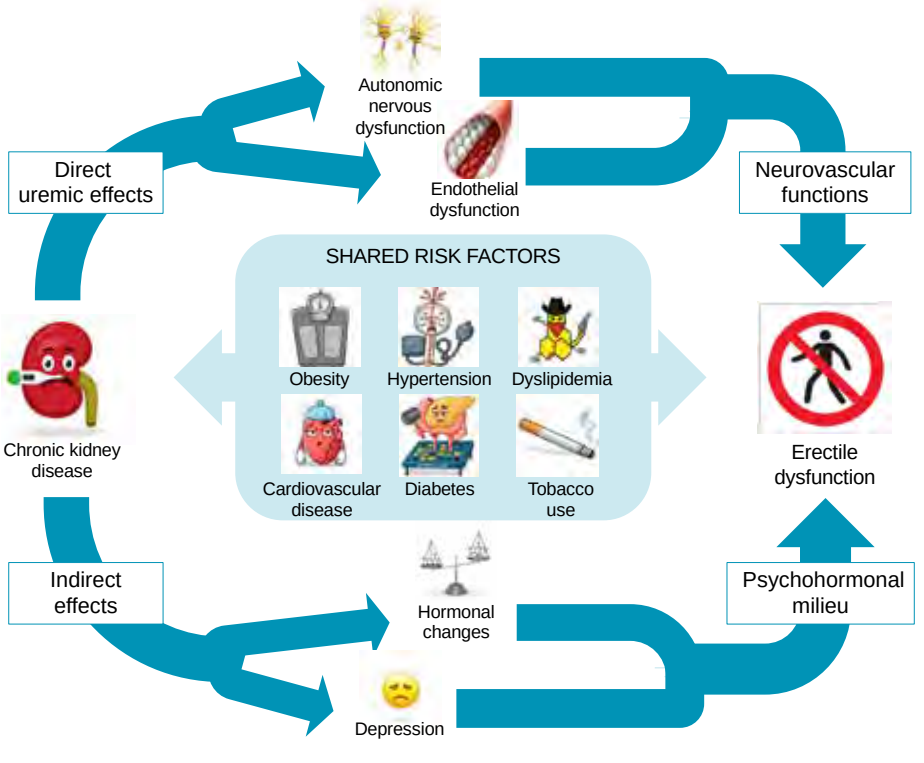
Figure. Relationship between psychologic and physiologic mechanisms underlying ED



Breaking the Silence on Menstrual Health in Chronic Kidney Disease

By Lavanya Bathini, Sandra Dumanski, and Sofia Ahmed

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Menstruation is a normal physiologic process and a vital sign of reproductive health. Yet for many individuals with chronic kidney disease (CKD), menstrual abnormalities remain under-recognized, underexplored, and undertreated (1). In nephrology clinics, menstrual health is inconsistently assessed and rarely discussed (2).

Menstrual abnormalities in CKD

CKD disrupts the hypothalamic–pituitary–ovarian axis function and has the potential to result in a range of menstrual abnormalities (3). Although early literature focused on those with kidney failure, newer studies suggest that abnormalities may occur even in earlier stages of CKD and worsen alongside CKD progression. A 2022 systematic review and meta-analysis found high rates of menstrual abnormalities—especially amenorrhea—in populations undergoing dialysis (4). In a recent international study of individuals with CKD, the vast majority reported current or past menstrual abnormalities, yet most reported that their menstrual health was overlooked and insufficiently addressed by their nephrology team (1).

Menstrual abnormalities are not benign. They adversely affect physical and psychosocial well-being and quality of life and have important personal and societal economic impacts. Importantly, in CKD, menstrual abnormalities contribute to iron deficiency and anemia, which can delay transplant eligibility by necessitating further investigation, transfusions, or optimization of hemoglobin levels before surgery. In the general population, menstrual abnormalities have been linked to shorter life expectancy and increased risk for cardiovascular disease and osteoporosis (5). In CKD, menstrual health intersects with multiple aspects of care—including anemia management, cardiometabolic risk, reproductive planning, and psychosocial well-being. This editorial highlights the prevalence, consequences, and clinical implications of menstrual abnormalities in CKD.

Influence on kidney health

Recognized as a vital sign by the American College of Obstetricians and Gynecologists and the American Academy of Pediatrics, menstrual health remains underprioritized in nephrology despite its association with life expectancy and CKD risk. A South Korean population-based study of over 8500 postmenopausal women found that later menarche and shorter reproductive lifespan were associated with markedly increased CKD risk, suggesting that reproductive milestones may both reflect and influence kidney health (6).

Heavy menstrual bleeding may further exacerbate CKD-related anemia and limit access to transplantation. In a mixed-methods study by Chang et al., the majority of menstruating individuals reported heavy menstrual bleeding, over one-third of women with CKD reported a history of blood transfusion, and one-half were using erythropoiesis-stimulating agents (1). Given the risks of alloimmunization with transfusions and thromboembolism or hypertension with erythropoieses-stimulating agent use, attention to menstrual bleeding is particularly important for patients receiving anticoagulation or hemodialysis with heparin.

Even kidney transplantation, which has been postulated to improve hypothalamic–pituitary–ovarian axis function, menstruation, and fertility, does not fully resolve reproductive health issues (7). Highlighting their conclusions from the Kidney Disease: Improving Global Outcomes (KDIGO) Controversies Conference on Women and Kidney Health, Piccoli et al. highlight persistent gynecologic symptoms and incomplete resolution of amenorrhea after kidney transplant and emphasize the need for integrated post-transplant reproductive care (8). However, in the event of normalization of menstruation for some individuals postkidney transplant, an increased risk of unintended pregnancy may be introduced, underscoring the importance of timely contraception counseling.

Period poverty

Menstrual health is also a health-equity issue. "Period poverty"—limited access to menstrual hygiene products—disproportionately affects individuals with chronic illness and limited income (9). In an international survey, 39% of menstruating individuals living with CKD reported current period poverty (1). This striking example highlights how the gendered experience of CKD remains vastly underexplored. Women on dialysis report higher overall symptom burdens than men, including fatigue, pain, and reduced quality of life, yet their sex- and gender-specific experiences—such as menstrual irregularities, heavy bleeding, or amenorrhea—remain underexplored and poorly addressed in routine care. The KDIGO Controversies Conference on Women and Kidney Health has recently called for greater integration of gynecologic and reproductive health into CKD management (8).

Despite these directives, menstrual health remains overlooked in CKD. A 2019 cross-border survey of Canadian and American nephrologists revealed that over 65% of respondents lacked confidence in women's health issues, including menstrual disorders (10). Similarly, an international survey of nearly 300 nephrologists and allied health professionals acknowledged the impact of CKD on sex hormones in women but found that sex hormone-related issues were infrequently discussed with patients (2). Silence stems from stigma, limited training, time constraints, and the misconception that reproductive health lies outside of nephrology.

Breaking the silence

Where do we go from here? First, we must normalize assessment of menstruation in nephrology practice. Menstrual history should be a routine part of intake—just like bowel habits or medication lists. Second, we need better evidence: longitudinal studies to map menstrual trajectories in CKD, research linking menstrual symptoms to kidney outcomes and quality of life, and trials of supportive interventions. Third, we must train the next generation of nephrologists to view reproductive and gynecologic health as core competencies—not ancillary concerns.

Above all, we must listen. For many patients, menstrual health is not a side issue—it is central to their well-being, transplant eligibility, and autonomy. By breaking the silence, we can begin to break down barriers to equitable kidney care. ■

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The authors report no conflicts of interest.

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CREATIVE CORTEX

Renal Rack

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This black and white photograph was taken in Copenhagen, Denmark, in July 2025 (iPhone 15). ■

Photograph by Brian Rifkin, MD, FASN. Rifkin is a general and interventional nephrologist in Hattiesburg, MS. In addition to photography, he also creates prints and watercolor, acrylic, and oil paintings. His art pieces often combine his love of medicine, nature, and humor. Rifkin sells his artwork at local craft fairs and art galleries, and he enjoys gifting pieces at medical conferences.

Improving CKD Care to Advance Health Equity

By Bridget M. Kuehn

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Earlier diagnosis of chronic kidney disease (CKD) and increased use of the growing armamentarium of CKD therapies that help prevent progression and reduce cardiovascular and other adverse events are key to achieving health equity in kidney care, according to speakers at ASN Kidney Week 2025.

The speakers, who participated in the session titled, "Bridging Gaps in CKD Care: Advancing Health Equity Through Policy, Practice, and Community Action," highlighted how innovations have improved access but have led to persistent global inequities in kidney care. However, new therapies for CKD, such as glucagon-like peptide-1 (GLP-1) agonists, sodium-glucose cotransporter-2 (SGLT2) inhibitors, and mineralocorticoid receptor antagonists; new targeted therapies for immunoglobulin A nephropathy and lupus; and new tools like race-free algorithms could help close those gaps in care.

"The time is now," said Cynthia Delgado, MD, FASN, professor of clinical medicine at the University of California, San Francisco, and a nephrologist at the Veterans Affairs Medical Center in San Francisco. "We have the clinical innovation. We also have the screening and prognostic common language to direct kidney care and improve health outcomes both within the practice of nephology and across all specialties, including our primary care colleagues."

Expanding access

Innovation and policy have long driven kidney care, according to Delgado. She noted that the emergence of chronic dialysis, at what is now known as the Northwest Kidney Centers, founded in Seattle, occurred in the early 1960s. However, access to the therapy was limited, and decisions about who would receive care were tied to the patient's contributions to society. Outcry about the limited access to dialysis and high costs for patients led Former President Nixon to create the Medicare End-Stage Renal Disease (ESRD) program in 1973, which dramatically expanded dialysis access. Additional clinical innovation and federal policy refinements have continued since then.

"We have definitely come a long way when it comes to dialysis care and having an organized system for managing [people with kidney failure]," she said. However, these advances focus on the roughly 131,000 people with kidney failure and leave out the 37 million living with CKD. She relayed that policy updates are needed to consider these individuals and hopefully prevent progression to a need for kidney failure care, which has high costs for both the ESRD program and personal costs for patients and their families.

Delgado noted that momentum is building for policies that shift the focus to preventing kidney failure and the need for dialysis. She highlighted President Trump's 2019 Advancing American Kidney Health Executive Order, which included calls for initiatives to reduce the rate of kidney failure by 25% by 2030 and increase access to home dialysis and transplantation (1).

Yet, shifting the focus to policy and care, even earlier in the pipeline to kidney failure, starting with earlier kidney disease screening and treatment, could prevent the need for dialysis or transplant, she explained. Already, Delgado noted that the Department of Health and Human Services has begun increasing its focus to kidney disease prevention, concentrating on risk factors like type 2 diabetes and hypertension and boosting routine testing and timely treatment.

She noted that the growing armamentarium of preventive therapies, which can often be used in combination to stave off kidney disease progression, is also helping. She relayed that a 2018 study found that managing risk factors like type 2 diabetes and hypertension by stage 3a or 3b could delay progression to kidney failure by several years (2). Adding newer therapies may further slow the progression of kidney diseases.

Delgado acknowledged that the costs of some newer therapies are high, and the uptake of both new and older therapies has been suboptimal. For example, the annual cost to treat a patient with a GLP-1 agonist for 1 year currently exceeds $5000, the annual cost of an SGLT2 inhibitor is more than $3000, and the cost of sacubitril and valsartan is approximately $3400 per year. Meanwhile, only about 6% of eligible patients are receiving GLP-1 agonists, about 7% are receiving SGLT2 inhibitors, and just 2% are receiving sacubitril and valsartan. Even older and less-costly medications like angiotensin-converting enzyme inhibitors and angiotensin II receptor blockers, which cost just $58 per year, have a less-than-optimal uptake, with fewer than 80% of Medicare and Medicaid beneficiaries with CKD and diabetes receiving these guideline-directed therapies and even fewer individuals with CKD without diabetes receiving this recommended care.

Chintan Dave, PharmD, PhD, assistant director of the Rutgers Center for Pharmacoepidemiology and Treatment Science, New Brunswick, NJ, highlighted geographic, racial and ethnic, as well as payor-based disparities in the use of SGLT2 inhibitors and GLP-1 agonists among eligible patients. He noted that drug-initiation rates vary fivefold, from 2.7% to 13.6% across US geographic regions, with more affluent areas having higher uptake and more socioeconomically disadvantaged communities lagging. Privately insured White patients were twice as likely to receive one of these drugs compared with their peers in other racial and ethnic groups, with use rates of 16% among White patients compared with 8% among others. Usage rates were more similar among patients covered by Medicare, with approximately 15% for White patients compared with 11% among other racial and ethnic groups. Overall, use among those covered by Medicaid was lower, at about 10%, but was consistent across groups.

Suboptimal use of preventive care leads to rising care costs for people with kidney diseases, Delgado noted, with costs escalating from $10,000 to $15,000 per year for stages 1 and 2 CKD, to $20,000 to $25,000 per year for people with advanced CKD, to $82,000 to $110,000 for people with kidney failure. Delgado argued that despite the high costs of some preventive medications, more optimal use of preventive therapies could reduce the costs of kidney care to Medicare and Medicaid. Although some audience members at Kidney Week questioned that assertion based on the high numbers of people with CKD, Delgado noted that increasing the number of individuals using newer therapies would help reduce drug costs, as has been the case with other therapies. She also emphasized that such cost-saving calculations do not consider how kidney failure reduces individuals' and their caregivers' productivity.

Delgado proposed expanding Medicare's ESRD program to cover care for people before they reach kidney failure, to delay or prevent the progression. She suggested that leveraging innovation and the current federal interest in kidney policy may help enact policy changes, and that better data about the potential cost savings and strong advocacy will be needed. She also highlighted the numerous advocacy groups across the United States for people with kidney diseases and the individuals living with CKD as potential allies in these efforts.

Going the last mile

Another speaker at the session, Elizabeth Montgomery, national vice president of Learning Strategies and Population Health Programs at the National Kidney Foundation (NKF), said NKF is currently developing an actuarial model to provide concrete data on the return on investment of earlier screening and care for CKD.

Montgomery also highlighted the work NKF's Intercept Team is doing to drive implementation of the race-free CKD-Epidemiology Collaboration (CKD-EPI) equation, recommended by a joint NKF and ASN task force (3). She explained that a previously widely used equation for calculating the estimated glomerular filtration rate (eGFR) relied solely on creatinine, an imperfect biomarker, and included a correction that artificially inflated results for Black individuals.

Yet, barriers to implementation remained, including the challenge of converting all of the clinical laboratories across the country to use the new equation and report results consistently. To overcome this challenge, NKF's Laboratory Engagement Workgroup developed an implementation tool kit for laboratories and pathology teams. "There was a unified voice; there was a unified language; there were unified tools," she said. The workgroup published a paper in 2022 shortly after the new equation was recommended that explained the rationale and provided tools and tricks for rapid deployment in laboratory systems (4). By May 2022, both of the largest laboratory systems in the country, Quest Diagnostics and Labcorp, had fully implemented the new equation (5).

"It was sort of like a moonshot moment," Montgomery said. "This was really amazing, how quickly the 'aircraft carrier' turned, because we had a group of people who were committed to driving change and making it easy for others to do the same." Since then, the team has been making the rounds at laboratory conferences across the country. "Every time we have an opportunity, we work to reinforce the message about why this equation matters," she said. That effort led to 60% of the laboratories across the country implementing it by 2023, a proportion that has since grown to 70% of US laboratories.

In the process, the workgroup has been able to identify factors holding up implementation. For example, Montgomery explained that large laboratory organizations did not initially account for desktop analyzers used in oncology or emergency medicine departments in their implementation plans. At some large academic institutions, she noted, this left 16% of analyses still using race-based equations. Smaller physician-owned laboratories, which may be less engaged with the larger laboratory community or have more limited resources for equipment updates, were also less likely to implement the change. Montgomery said she would love to talk with staff at academic centers who want advice on implementation. She noted that NKF also has grant funding to provide financial support and guidance to smaller institutions that are struggling with the update.

The shift to the race-free CKD-EPI equation is already having a positive impact on patients. The Organ Procurement and Transplantation Network implemented the change in 2022. By February 2025, 19,619 Black individuals had their waitlist time for a deceased donor kidney adjusted, resulting in an average reduction of 1.7 years in wait time. More than 6000 Black individuals had already received a transplant as a result.

Another 2025 article by the NKF team and its pharmacy partners recommended replacing the use of the Cockcroft-Gault equation with the race-agnostic 2021 CKD-EPI equation, which, they noted, provides a more precise method for estimating medication dosing for people with impaired kidney function (6). Now, NKF is working with the pharmacy community, including all pharmacy professional societies, on the implementation and rollout of an educational and pharmacist-engagement campaign in spring 2026. "We are working on a variety of deliverables the same way that we did for the laboratory community to make this transition as seamless and easy as possible," she said.

NKF is committed to "going the last mile" to ensure that all patients benefit from the equation, Montgomery said. The next step will be for NKF's CKD Intercept Team to

engage with primary care physicians to use the race-free CKD-EPI equation to recognize patients as early as possible and slow the progression of kidney diseases. She explained that 90% are undiagnosed in primary care settings, even though 80% have an eGFR in their electronic medical records that has not been acted upon effectively.

"The bottom line is that information is not being used to address the gaps we know exist," she said. To help, NKF has developed an implementation model for improving CKD care in primary care settings. It focuses on the importance of reducing cardiovascular risks, which is the leading cause of death in people with kidney diseases, and it emphasizes the system changes necessary to minimize the burden on clinicians.

The team is already working with 50 organizations in 23 states to help them improve CKD care in primary care. For example, they collaborated with Sanford Health, the largest rural health system in the United States, to extract data that would enable them to assess the quality of CKD care across the organization. The data were presented to organizational leaders, along with a discussion about the impact on emergency department visits, hospitalizations, and readmissions. Then, NKF helped them build an implementation plan, which focused on diabetes care.

The results, she relayed, were extraordinary. Between December 2023 and October 2024, the organization increased the number of patients tested for the urine albumin–creatinine ratio from about 13,000 to 88,000 by focusing on those with type 2 diabetes or laboratory evidence of CKD. By October 2024, the proportion of people with a CKD diagnosis had increased by 73%. There was also a fivefold increase in the use of SGLT2 inhibitors in these individuals living with CKD during this period. She said that NKF is currently seeking new partner institutions that would like to implement this model. ■

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Multifaceted Strategic Approaches Needed to Expand Kidney Care to Rural Areas

By Karen Blum

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After growing up in suburbia and completing medical training in inner-city Detroit, MI, Rebecca Schmidt, DO, FASN, said she was stunned to discover that her first patient at West Virginia University (WVU), where she began clinical practice, had driven 3 hours to see a nephrologist. The patient had been seen about 10 years prior but did not follow up because the drive was too long. Now, they had progressed to advanced chronic kidney disease (CKD) and promptly began dialysis. It marked the impetus of Schmidt's journey to try to improve rural health care for people with kidney diseases.

As chief of nephrology at WVU, Schmidt worked to expand access to kidney care across more than 24 counties in the state by establishing multiple decentralized clinics for CKD management. Now assistant dean for rural outreach and community engagement at WVU, she discussed her strategies in a presentation at ASN Kidney Week 2025.

Clinical impact

Between 2001 and 2020, Schmidt and colleagues developed 19 CKD clinics in north-central West Virginia and western Maryland. As the clinics grew, the drive time for more patients decreased, and the practice expanded from 3 to 15 nephrologists. In an era of shortages of specialty physicians in rural settings, the small team expanded by hiring advanced practitioners, Schmidt said, which allowed them to see more patients in rural settings and the main campus in Morgantown, WV.

During this time, the team managed 7000 rural clinic visits, saving an estimated 6.5 million driving miles for patients, she said.

"We started these clinics with the idea that patients who crashed into dialysis would be better served if we could go to them and see them in their own area," Schmidt said. Over time, Schmidt and colleagues observed a relationship between drive times and outpatient kidney replacement therapy; there was a 13% likelihood of having an outpatient start for every reduced hour in drive time to a rural clinic. By contrast, patients who lived farther away had a higher likelihood of starting as an inpatient.

They also analyzed the clinics' impact on home dialysis, finding a 40% higher chance that patients served by one of the rural clinics would start dialysis with a home program (1). Patients served by the rural clinics also had higher odds of vascular access and use of erythropoietin-stimulating agents prior to starting dialysis.

Multifaceted approach

Schmidt discussed several steps that helped the rural clinics take hold. She and her colleagues sought support from their institution to uphold their mission of serving the state. "Having a dedicated and engaged administrator is key," she noted. They also sought community advice and perspective. "The community has great insight into [its] own needs," she said. Schmidt and colleagues made sure to go where they were most needed, not in areas with a nearby nephrologist.

During the clinics' ramp-up, Schmidt's team used a multifaceted approach. In partnership with the National Kidney Foundation, they conducted 20 CKD screenings throughout the state, testing 1100 patients to raise awareness and educate people. They developed 12,000 educational packets, which they distributed to patients statewide, and held annual CKD conferences for local primary care practitioners to gain continuing medical education credits. They also invited Joe Manchin III, who served as governor of the state at the time, to a screening, which brought media attention to their efforts.

Their strategies also included the following:

- Engaging local leaders, including practitioners and hospital chief executive officers, about their needs and concerns regarding referrals and dispelling rumors that clinics would pilfer patients.
- Using available spaces. The first clinic was in the back of a primary care office with no telephone or copy machine. They also set up shop in a hospital emergency department for 1 year.
- Engaging local stakeholders, including senior centers, pharmacists, and primary care centers, in CKD screenings and distributing information packets.
- Developing and maintaining relationships with local clinicians and communicating assessments and recommendations. "Sometimes, a fast note or telephone call will do more than a world of good," Schmidt said.
- Recognizing social determinants of health in regional and local communities. Some patients live in food, pharmacy, and transportation deserts, so nephrologists tailor their recommendations whenever possible.
- Empowering and educating primary care physicians. Schmidt and colleagues developed a mobile app called NephRef to help practitioners know when and how to refer patients to the WVU experts.

Expansion is possible, despite hurdles

When expanding health care in rural and medically underserved areas, Schmidt advised that practitioners should be prepared to travel from their home location to satellites, expect a lack of physical space or infrastructure at a distant site, and anticipate kinks working through billing issues, as well as telemedicine regulatory limitations to adhere to, such as becoming licensed in neighboring states that feed the program. Operationally, practitioners need to find ancillary staff to work in the area when the clinician is present, and connectivity issues abound.

The literature is replete with information about barriers for trying to serve rural communities, said Schmidt, but "a dearth of information about what is actually being done." She highlighted several programs across the country, including hers, that make use of telemedicine, educating primary care physicians, partnering with community health centers, and engaging high school students in STEM (science, technology, engineering, and mathematics) careers as part of a strategy to improve care for rural communities.

"There's hope for these patients," Schmidt said. "There are a lot of global and regional considerations necessary to address the inadequacies of health care access in these areas, but a multifaceted, strategic approach tailored to the areas is key to improving outcomes." ■

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Point-of-Care Ultrasound in Nephrology: Benefits, Risks, and the Need for Standardized Training

By Christopher El Mouhayyar and Jonah Rubin

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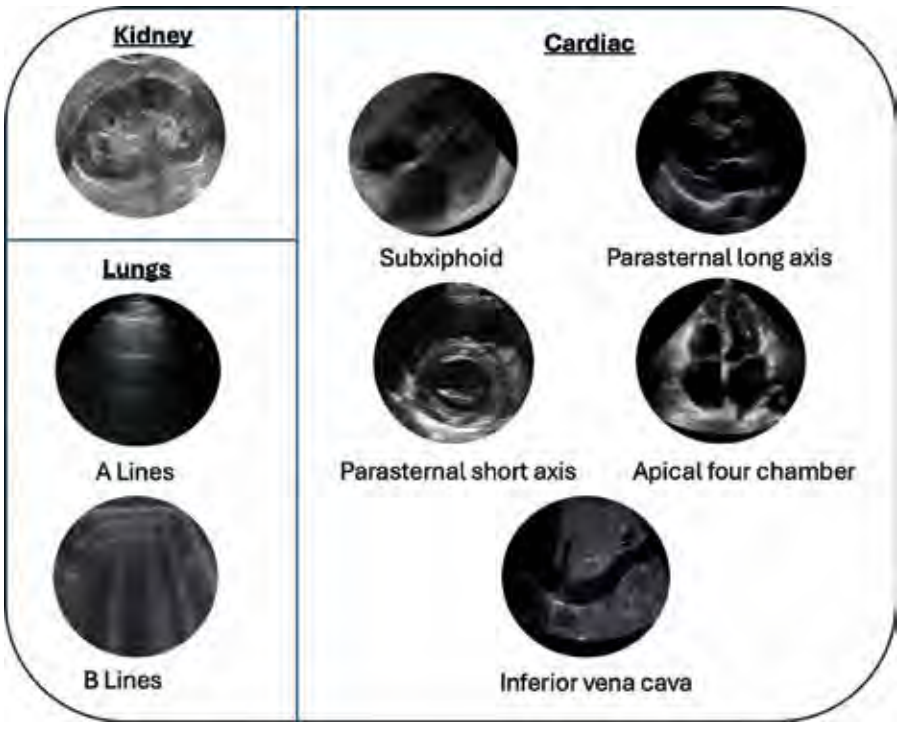
Point-of-care ultrasonography (POCUS) is an evolving tool in nephrology, allowing clinicians to perform bedside imaging to help address specific clinical questions. Historically, its use in nephrology was limited to procedural guidance for tasks such as dialysis catheter placement or kidney biopsy (1). However, POCUS is now being used for a wider range of diagnostic applications, including comprehensive hemodynamic assessments.

The utility of POCUS lies in its ability to supplement the traditional physical examination, providing greater sensitivity than traditional methods like auscultation and lower-extremity edema assessment (2). To help guide treatment decisions like diuresis or intravenous fluids administration, nephrologists often evaluate lung sounds, heart function, and signs of fluid overload such as jugular venous distension and pedal edema. However, POCUS has been shown to provide a more accurate diagnostic approach to these assessments compared with traditional methods (1) (Figure).

Benefits of POCUS

POCUS can help expedite diagnosis as well as optimize treatment. POCUS-trained clinicians can rapidly gather information that would otherwise require multiple imaging tests, such as a chest x-ray or cardiac and abdominal imaging, thus accelerating the diagnostic process. POCUS can also be used for follow-up assessments to evaluate a patient's response to treatment, such as tracking changes in B lines or venous waveforms. Furthermore, studies have shown that the use of POCUS often reduces the need for additional formal imaging studies and can lead to improved practical outcomes (3, 4). This not only streamlines patient care but also helps to lower health care costs.

Figure. POCUS findings and application



Risks of improper use

Although POCUS offers substantial benefits, its improper or untrained use can lead to patient harm and diagnostic errors. Without proper context, inaccurate assessment of the inferior vena cava (IVC) or lung can result in patient mismanagement. For instance, a small, collapsible IVC cannot distinguish between hypovolemia and euvolemia, and a plethoric IVC may indicate conditions other than hypervolemia, such as pericardial effusion or pulmonary hypertension (1). Similarly, B lines on a lung ultrasound are not specific to cardiogenic pulmonary edema and must be interpreted within the appropriate clinical context (5).

Training and competency

Mastering POCUS requires a significant time investment and a structured approach. Given that most practicing nephrologists have received minimal to no POCUS training, creating a comprehensive curriculum for fellowship programs is challenging. Key elements for successful POCUS integration include structured programs, expert oversight, and motivated learners. To address this, there is a call for nephrology societies to collaborate on universal training frameworks and certification processes (Table). This would ensure proper training, which is essential not only for safe clinical use but also for improving the quality of research in the field. It is important not to dismiss the value of POCUS based on a lack of mortality benefit in some studies. POCUS is a diagnostic tool, like a stethoscope, not a treatment. Its primary benefits are improving practical outcomes, such as reducing the time to diagnosis and decreasing the need for further imaging studies.

Table. POCUS resources

Source	Information
Alliance for Physician Certification & Advancement	POCUS certification academy
American College of Chest Physicians	POCUS workshops
American Society of Diagnostic and Interventional Nephrology	POCUS curriculum and certification
American Society of Echocardiography	Revision and workshops to assist with echocardiography boards
American Society of Nephrology	POCUS curriculum and workshops
Society of Hospital Medicine	Structured pathway with certification
Many home institutions	Workshops (usually led by emergency physicians)

Conclusion

With the rapidly evolving landscape of medicine, POCUS appears as a valuable, and increasingly important, diagnostic tool. By allowing for real-time, bedside imaging, POCUS enhances clinical decision-making and can significantly improve patient care. However, its improper or untrained use can pose risks to patients. Therefore, as the use of POCUS expands, the nephrology community must prioritize establishing rigorous, standardized training and certification. By fostering a culture of proper education and expert oversight, we can ensure the safe and effective application of POCUS, maximizing its utility in clinical practice and research to address patient care gaps. ■

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The authors report no conflicts of interest.

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Steady Dosing Wins the Race? Exploring CMV Prophylaxis With Letermovir in Kidney Transplantation

By Elisha Clark and Sam Kant

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Cytomegalovirus (CMV) provides a formidable challenge in kidney transplant. An inescapable β-herpes virus establishing lifelong latency in approximately 60% of adults (1), CMV can drive systemic insult, acute rejection, graft loss, and in severe cases, death—earning its reputation as "the troll of transplantation" (2). Despite decades of research, effective prophylaxis often remains difficult to achieve.

For over 2 decades, valganciclovir has been the established standard of care, although it has limitations: Myelotoxicity, emerging antiviral resistance, and renal elimination necessitate careful dosing (3, 4). In the early post-transplant period, in which kidney function is often fluctuant or impaired, achieving optimal dosing is a recurrent challenge. Recently, attention has turned to newer antivirals like letermovir, a CMV DNA terminase complex inhibitor. With a nonmyelosuppressive profile, hepatic metabolism, and fixed once-daily dosing, letermovir offers clear theoretic advantages—particularly in kidney transplant populations. In the phase 3 trial by Limaye et al., letermovir demonstrated noninferiority to valganciclovir for preventing CMV disease in kidney transplant recipients who were high risk, donor positive/recipient negative, with significantly lower rates of myelosuppression (5).

Building on these findings, Budde et al. conducted a post hoc analysis of a phase 3 trial (NCT03443869) exploring the impact of CMV prophylaxis on kidney function for over 200 days in 480 kidney transplant recipients who were donor positive/recipient negative (6). Participants were randomized 1:1 to receive valganciclovir (900 mg) with kidney-adjusted dosing or letermovir (480 mg) once daily. Letermovir dosing remained consistent across the spectrum of kidney function, whereas approximately 50% of valganciclovir recipients required intermittent regimens. Among the participants with reduced kidney function, adherence dropped substantially: 17.1% of participants receiving intermittent valganciclovir fell below 75% compared with 0.8% receiving fixed, once-daily prophylaxis.

Importantly, reduced adherence translated into differences in CMV DNAemia. By week 28, quantifiable DNAemia occurred in 2.1% of letermovir recipients compared with 8.9% of those receiving valganciclovir, a more than fourfold difference. In participants with creatinine clearance of 67 mL/min or less, CMV DNAemia rates were 1.7% with letermovir versus 13.1% with valganciclovir. Prophylaxis discontinuation was also lower with letermovir (4.3%) than with valganciclovir (17.0%), largely driven by myelotoxicity in the latter group.

These findings highlight the impact of regimen simplicity. In patients who are high risk, for whom dynamic kidney function complicates valganciclovir dosing, letermovir's fixed regimen provides superior adherence and fewer discontinuations. One might cautiously hypothesize that lower adherence reduces drug exposure, which increases CMV DNAemia, although confirmatory studies are needed, as the study did not measure valganciclovir plasma concentrations. Nonetheless, intermittent valganciclovir dosing presents undeniable disadvantages with extra clinic visits, frequent blood draws, and complicated dose schedules (6). Furthermore, this was a post hoc analysis of a controlled trial setting, and in real-world practice, alternative doses, dose frequencies, and less-frequent monitoring are seen. Long-term data on resistance, cost-effectiveness, and graft survival beyond 28 weeks are needed to further the case for letermovir, which remains a costly but promising alternative (7).

As demonstrated in this study, variability in kidney function remains a central challenge in CMV prophylaxis. Physicians have long relied on valganciclovir, but letermovir's efficacy, safety, and dosing simplicity challenge its dominance. Looking forward, if real-world data confirm these findings up to and beyond 28 weeks, letermovir could redefine CMV prophylaxis in transplant recipients, particularly those with fluctuating or reduced kidney function. ■

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Physician Well-Being: A Commentary and Call to Action

By Rakhi Khanna and Sarah Benington Sacha

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There is no question that the practice of medicine has changed over the last 20 years. The last 2 decades have seen the corporatization of medicine, rise of electronic medical records and artificial intelligence, less physician autonomy, and more oversight—contributors to decreased humanization of physicians. As physicians, we are often seen as robots. In many cases, administrators are far more interested in our relative value units than our well-being.

As "good physicians," we are held to superhuman standards. Delivering high-quality patient care often comes at the expense of clinicians' sleep, nutrition, exercise, and mental and spiritual health. Physician suicide rates are higher than those of the general population, due to increased workloads, the prevalence of medical errors, and the stigma surrounding mental health and asking for help (1). We are literally working ourselves to death.

We trained as osteopathic physicians and were taught to evaluate and treat patients across physical, mental, and spiritual dimensions. We understand that patients are not monolithic and that many things must be in our toolbox to assess and treat the whole person. Why do we not hold ourselves to the same standard? Our personal health should not be sacrificed in the name of professional duty.

Physician burnout is a well-documented phenomenon. In 2023, 45.2% of US physicians reported experiencing burnout, according to the American Medical Association (1). Admitting burnout is not a weakness but a natural response to unrelenting demands, often over which we have no control. Yet too often, the responsibility for combating burnout is placed back on us. Resilience training and meditation are the corporate answers to addressing this issue. Physicians often suffer through the unequal power structures within the corporate entities that now run health care, and we cannot or do not advocate for ourselves.

Given the current environment, physicians are retiring in large numbers, leaving the profession for other employment opportunities that align with their skill sets or pursuing career changes altogether. In residency programs, despite enacting duty-hour limits, resident burnout is at an all-time high—up to 75% in some specialties—forcing some residents to leave health care. This is exacerbating a crisis of a critical shortage of new physicians to replace those who are aging out of the system (2).

Burnout in nephrology

The nephrology community is not immune to this crisis. In the United States, 23.2% of nephrologists reported burnout in a 2022 national survey. This was driven by long work hours and the burden of managing electronic health records. Interestingly, those in academic centers with more patient care time reported lower burnout (3).

In fellowships, 30% of nephrology fellows reported burnout, with emotional exhaustion and depersonalization as the most common symptoms. Risk factors included poor work-life balance, gender disparities, and disruptive work environments (4).

Other factors: Malpractice and noncompete clauses

Physicians who face lawsuits frequently report depression, anxiety, and behavioral changes, including defensive medicine (5). Litigation can trigger trauma-like symptoms that persist long after the lawsuit resolution (6). One survey found that 56% of physicians who had been sued experienced significant psychological distress, and nearly half changed their practice defensively (5). Fear of malpractice nearly triples the odds of burnout in some populations (7).

Figure. Components of mental well-being

Noncompete clauses and restrictive covenants continue to undermine autonomy, disrupt continuity of care, and often force physicians to uproot their families and leave communities (8, 9). They foster job insecurity and moral distress, erode the therapeutic alliance with patients, and reinforce feelings of replaceability, fueling burnout. Eliminating or reforming noncompete clauses could restore autonomy, stabilize physician well-being, and improve patient access to consistent care.

Physician, heal thyself

Physicians dedicate themselves to healing others, but to sustain this mission, we must first and foremost care for ourselves. Physical rest, mental health, and spiritual fulfillment are not luxuries; they are essential to safe, compassionate, and effective patient care (Figure). Addressing systemic inefficiencies, improving communication with administrators, providing more autonomy, and reducing documentation burden and excessive work demands are crucial for cultivating mindfulness, purpose, and connection at an individual level.

As the saying goes: Physician, heal thyself. But true healing will only come when institutions, leaders, and physicians collectively commit to prioritizing physician well-being as the foundation of a healthier profession and a safer, more compassionate health care system. The era of blaming the physicians for their own burnout is over. It is time for us to reclaim the power that we have given away to institutions that sometimes have little to no concern for our well-being.

Systemic, organizational structures; staffing; and leadership play critical roles in mitigating stress. The Accreditation Council for Graduate Medical Education now formally recognizes well-being as a core competency. But barriers persist, and stigma continues to prevent physicians from seeking help for mental health concerns.

A call to action

We do not have many answers to these overarching problems. Recognizing that the experiences of physicians in rural areas are very different from those in larger cities and academic settings, we need to start having regional, state, and federal discussions regarding physician rights and what should be expected in practice. Some variations of unions—at a national level either within large hospital systems or through professional organizations—should be imperative. Unless we organize with leadership that advocates for physician well-being, our profession may become a shell of what it once was.

Many clinicians do not join professional societies or organizations because they feel there is little support or advocacy for change; however, such organizations should be the most vocal in promoting physicians' rights. We could take a page from our nursing colleagues on what this looks like and how we can ethically stand down from practice in protest while keeping our patients safe.

Reforms could also come in the form of mentorship programs, peer-support networks, and a cultural shift away from punitive responses when physicians ask for support. Protection through litigation reform—including early resolution, safe-harbor practices, and institutional support—could significantly improve mental well-being related to malpractice procedures.

We have moved too slowly and already given away too much. We have often been taken advantage of. By our nature, we work without considering how damaged we may have become, often until it is too late. We frequently complain, but there is no honest discussion moving the dialogue forward, and many problems may seem insurmountable. There is no one-size-fits-all solution, but doing nothing is no longer an option. ■

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From Launch to Legacy: Reflections From *Kidney360* Founding Editor-in-Chief Michael Allon

By Karen Blum

https://doi.org/10.62716/kn.002322025

Michael Allon, MD, has served as editor-in-chief of ASN's first online open-access journal, *Kidney360*, since 2019. During the past 6 years, Allon, professor of medicine, associate director for clinical affairs, and medical director of dialysis operations at The University of Alabama at Birmingham, said he worked hard to establish an impactful journal that nephrologists worldwide would want to read. As his term concludes at the end of the year, he shared his thoughts with *Kidney News* (*KN*).

KN: What interested you in taking on this inaugural role?

Allon: I had a fairly extensive history of participating in editorial activities. I had been a reviewer for numerous manuscripts for different medical and nephrology journals and had been associate editor for *CJASN* for 6 years. I felt that being editor-in-chief really provided this amazing opportunity to highlight new scientific papers and perspectives and reviews in a way that far exceeds what you can do as a single author. It was particularly exciting to be able to launch a brand new journal that hadn't even existed. Prior to *Kidney360*, ASN had two journals: *JASN* was inaugurated in 1990 and *CJASN* in 2006. There was an opportunity for a new journal to capture submissions that might not have fit with those and to offer an open-access option to authors. It was a formal application process, and I was really honored to be selected.

KN: What were your goals when you started?

Allon: They were fairly straightforward. I said this should be a journal that publishes papers that nephrologists want to read and furthermore, that provides a good experience to authors so that this is a journal that authors want to submit to. The third goal I had was to have some unique features that were not present in other nephrology journals to help us stand out from pretty crowded fields of probably 15 or 20 nephrology journals.

KN: What are some of the special features you added?

Allon: We introduced a new article type called Global Perspectives. When you practice nephrology in the United States, you have a kind of skewed view: These are the issues we have. This is how we solve them. But how these issues are handled and the practice and funding of things like dialysis and transplant are very different in different countries, depending on their health insurance, finances, and availability of dialysis and nephrologists. I thought it would be great to feature perspectives from different countries across the world. To date, we have published global perspectives from over 60 countries, from very high-income countries to very low-income, where resources are extremely limited. Every country has unique challenges and solutions that you wouldn't know about unless you were living and practicing there. This is a feature that is hard to find in other nephrology journals. I'm very proud that we've been able to carve a niche.

The second new article type is called Debates in Nephrology. We select different areas of controversy within the practice of nephrology. Each debate consists of three papers: One is pro—arguing in favor of a certain way to treat or a way to diagnose—and another one is con, and the third one is a moderator, which gives sort of a balanced perspective considering the pros and cons. We've had at least 40 debates on different topics since we launched it. They address issues that all of us struggle with as nephrologists, and they are quite popular among our readers.

The third new article type that we introduced is called Clinical Images in Nephrology and Dialysis. All of us see cases that may be unusual to diagnose in terms of how they look under an x-ray or a microscope. These are short presentations with a couple of pictures like a kidney biopsy or a radiologic finding or an unusual physical finding. This is submitted ahead of time for people to guess what the diagnosis is, and then in subsequent issues, the answer is provided. It is kind of fun for people to learn about unusual conditions or presentations of different conditions.

KN: How has the nephrology community embraced the journal?

Allon: Surprisingly well. It gives you a lot of heartburn when you start a new journal: Will anyone read it? Will anyone actually submit papers to it? Is it going to flop? One of the initial decisions I had was how often to publish. I decided to start right away doing it monthly.

It was fortuitous that we launched in 2020, at the onset of the COVID-19 pandemic. We featured some pretty important papers like how to handle outpatient dialysis with the COVID pandemic in terms of protecting the patients and staff while still providing lifesaving therapy and how to deal with a huge influx of hospitalized patients who had COVID but also required acute dialysis. We published two or three very important papers at that time in real time and very short turnaround. These were papers that we solicited, reviewed very quickly, and published within a month, because we thought it was important for nephrologists in this country, or across the world, to be aware of those issues.

Otherwise, it was a little bit of a struggle at the beginning. There were a lot of cold calls where I reached out to authors and encouraged them to submit their work. We established a reputation of having a fair and balanced but efficient review process. Our goal was to decide within 1 month whether to publish a manuscript. For the most part, we have been able to do that. After 2 years, we were indexed in PubMed. It's a big deal because when people are doing searches in different topics, if you're not indexed, then anything that's published in your journal, they're not even going to see. So a lot of people wouldn't even be aware of us unless they happen to be members of ASN. After 3 or 4 years, we established an impact factor, which is how often papers in your journal are cited in papers and other journals. We have seen quite a bit of growth in the submissions. Currently, we receive roughly 1000 original manuscripts per year. Obviously, it keeps us very busy.

KN: Why are open-access journals important?

Allon: The original model of medical journals was, in order to view the contents of the journal, you need a subscription. Or, for example, if you're a member of ASN, part of that membership would give you free access to ASN journals but not other journals. It can be quite expensive for a reader. If you're at an academic medical center, and your medical library has group subscriptions to certain journals, you can get them for free. But that's not true if you're out in the community or in many other countries. A 1-year subscription to some journals can easily be hundreds of dollars. The model for open access basically says that we charge the authors to publish the manuscript, and in exchange, it becomes open access. That means anyone in the world can access any of the contents in *Kidney360* for free. This is not the only open-access nephrology journal, but it's a novel model, and I think it's pretty attractive to people versus having to pay $35 to $50 for an individual article.

KN: What are you most proud of from your time as editor-in-chief?

Allon: I am really proud that we took a journal that didn't even exist before 2019, and we put it on the map. We have lots of people who read it. We have lots of people who submit to it. I think we have content that is interesting and up to date and some unique features that you don't get in other nephrology journals. After 6 years, I feel I'm handing my successor, Charuhas V. Thakar, MD, FASN, a solid, well-established journal with the opportunity to make it even better. ■

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Findings

Promising Results With Telitacicept in SLE

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Add-on therapy with telitacicept—an investigational recombinant fusion protein—improves the clinical response rate in systemic lupus erythematosus (SLE), reports a clinical trial in *The New England Journal of Medicine*.

The phase 3 trial enrolled 335 adults in China with active SLE. Eligibility criteria included a Safety of Estrogens in Lupus Erythematosus National Assessment–Systemic Lupus Erythematosus Disease Activity Index (SELENA-SLEDAI) score of 8 or higher, seropositivity for antinuclear or anti–double-stranded DNA antibodies, and at least 30 days on stable standard therapy. Nearly two-thirds of patients had kidney lesions; those with severe lupus nephritis were excluded.

Patients were randomly assigned to receive placebo or telitacicept (160 mg subcutaneously, once weekly for 52 weeks) added to standard therapy. The main efficacy outcome was a response on the modified SLE Responder Index 4 (SRI-4). That composite measure included at least a four-point reduction in the SELENA-SLEDAI score, with no new disease activity and no worsening on a physician's global assessment score.

At 52 weeks, the response rate on the modified SRI-4 was 67.1% in the telitacicept group versus 32.7% with the placebo group. The proportion of patients with at least a four-point reduction in the SELENA-SLEDAI score was 70.1% versus 40.5%, respectively.

Adverse events related to study treatments were more frequent with telitacicept: 74.9% versus 50.0%. Specific events associated with telitacicept included upper-respiratory infections, decreased serum immunoglobulin G and M, and injection-site reactions.

Telitacicept was designed as a novel treatment for autoimmune diseases, targeting two cytokines involved in B cell and plasma cell survival: B-lymphocyte stimulator and a proliferation-inducing ligand. Adding to results of a previous phase 2b trial, the new study shows a higher clinical response rate with telitacicept versus placebo. The researchers discuss possible explanations for the relatively high rate of placebo responses for some lupus manifestations, including renal lupus and vasculitis [van Vollenhoven RF, et al.; 18C010 Trial Investigators. A phase 3 trial of telitacicept for systemic lupus erythematosus. *N Engl J Med* 2025; 393:1475–1485. doi: 10.1056/NEJMoa2414719]. ■

AI Intervention for Diabetes Prevention Is Noninferior to Human Coaching

https://doi.org/10.62716/kn.002362025

For patients who are prediabetic, an artificial intelligence (AI)-led lifestyle intervention for diabetes prevention yields outcomes similar to those of human-led coaching, reports a randomized clinical trial in *JAMA*.

The pragmatic phase 3 trial included 368 adults with prediabetes and overweight or obesity who were considered at risk of diabetes. Patients were randomly assigned to the AI intervention, based on the diabetes prevention program (DPP), or a human coach-based DPP. The AI intervention was delivered by a mobile app and Bluetooth-enabled digital scale. Human coaching was delivered by synchronous distance learning. The two groups were compared for achievement of recommended thresholds for weight loss, hemoglobin A_{1c} (HbA_{1c}), and physical activity.

Among the patients, 71% were women, 27% were Black, and 61% were White. After referral, 93.4% of patients initiated the AI intervention, and 82.7% initiated human-led coaching. The primary outcome consisted of maintaining an HbA_{1c} of less than 6.5% throughout the study; weight loss of at least 5% or weight loss of at least 4% plus at least 150 minutes per week of moderate to vigorous physical activity; or an absolute HbA_{1c} decrease of at least 0.2 percentage points.

Rates of the composite outcome were almost identical between groups: 31.7% with the AI intervention and 31.9% with human-led coaching. Similar trends were observed for HbA_{1c}, weight loss, and physical activity level. Patients who completed their assigned program—37% of the AI group and 35% of the human-led coaching group—were more likely to achieve target outcomes.

The study adds new evidence that an AI-driven intervention provides outcomes noninferior to those of human-led DPP. "The asynchronous mobile delivery of personalized coaching may address barriers to implementation of human coach-based models," the researchers write [Mathioudakis N, et al.; AI-DPP Study Group. An AI-powered lifestyle intervention vs human coaching in the diabetes prevention program: A randomized clinical trial. *JAMA*, published online October 27, 2025. doi: 10.1001/jama.2025.19563]. ■

Palliative Care for Patients on Dialysis: New Insights

https://doi.org/10.62716/kn.002382025

More than half of patients undergoing dialysis receive palliative care during the last year of life—but usually not until the last few weeks before death, suggests a study in the *American Journal of Kidney Diseases*.

Using health data from Ontario, Canada, the researchers identified 18,452 recipients who underwent maintenance dialysis and died between 2012 and 2020. The median age at death was 71 years; 61.1% of patients were men. The median time from dialysis initiation to death was 2.5 years. Rates of physician-delivered palliative care during the last year of life were analyzed, along with sociodemographic and clinical factors associated with its use.

Overall, 52.2% of patients received at least one physician-delivered palliative care visit in the year before death. This percentage rose from 48.5% in 2012 to 58.2% in 2020. Patients received a median of three visits, although 28.4% received just one visit.

The initial palliative care visit occurred a median of 23 days before death. Most initial palliative care visits were provided by a family physician, including 60.9% from a generalist and 79.3% from a specialist. Across care settings, the number of visits increased during the last 2 months of life.

In regression analyses, women, older patients, and those with dementia or malignancy were more likely to receive physician-delivered palliative care. Palliative care visits were less likely for patients with heart failure, those on dialysis for over 1 year, those with lower income levels, and those living in more rural areas. Patients receiving palliative care were less likely to die in the hospital (odds ratio, 0.55).

The study adds to the limited evidence regarding physician-delivered palliative care for patients undergoing dialysis. Findings suggest that although more than half of decedents had received at least one palliative care visit, the initial visit most often occurred in the last 3 weeks of life. The researchers conclude: "This may represent a lingering perception of palliative care as exclusively end-of-life care and identifies a need to provide education about the value of timely integration of palliative care into dialysis care" [Bonares MJ, et al. Delivery of palliative care in the last year of life to individuals receiving maintenance dialysis: A population-level cross-sectional study. *Am J Kidney Dis* 2025; 86:594–604.e1. doi: 10.1053/j.ajkd.2025.06.012]. ■

Empagliflozin Improves Kidney Outcomes Across Subgroups

https://doi.org/10.62716/kn.002372025

Sodium-glucose cotransporter-2 (SGLT2) inhibitors have become the standard of care to reduce kidney failure and cardiovascular disease risks in people with kidney failure, chronic kidney disease (CKD), or heart failure, according to a meta-analysis in *The Lancet: Diabetes & Endocrinology*. However, questions remain about their effects in certain subgroups—including patients at lower risk of CKD progression or those at higher risk of sharp declines in estimated glomerular filtration rate (eGFR) on treatment initiation. Pooled data from recent clinical trials were analyzed to assess outcomes of empagliflozin therapy in key patient subgroups.

The meta-analysis included individual-level data on 23,340 patients from four placebo-controlled trials of empagliflozin: EMPA-REG OUTCOME (NCT01131676), EMPEROR-Reduced (NCT03057977), EMPEROR-Preserved (NCT03057951), and EMPA-KIDNEY (NCT03594110). A wide range of conventional and exploratory acute and chronic kidney outcomes were assessed, including potential variations based on the predicted size of the acute eGFR dip on treatment initiation and among key population subgroups.

The empagliflozin groups showed significant reductions in several key outcomes, including a marker of acute kidney injury: hazard ratio (HR), 0.80; acute kidney injury adverse events: HR, 0.73; CKD progression: HR, 0.70; and kidney failure: HR, 0.66. In further analyses, empagliflozin was associated with reductions in the chronic annual CKD rate and in an off-treatment, dip-free slope (HR, 0.36) for both outcomes.

Improvements in kidney outcomes were comparable in subgroups based on a predicted eGFR dip and regardless of diabetes, heart failure, kidney function, or albuminuria. Effects on the chronic eGFR slope were greater in patients with diabetes (74%) compared with those without diabetes (42%).

The assembled evidence suggests that empagliflozin reduces adverse kidney outcomes across a range of patient subgroups, including those at risk of large eGFR dips on treatment initiation. Empagliflozin appears beneficial in people with or without diabetes or heart failure and in subgroups defined by the cause of kidney diseases and markers of severity. The researchers conclude: "The findings support arguments for widespread early use of SGLT2 inhibitors to reduce the global burden of kidney disease, to simplify current guidance on whom to treat, and to discourage routine remeasurement of eGFR after initiation" [Herrington WG, et al. Effects of empagliflozin on conventional and exploratory acute and chronic kidney outcomes: An individual participant-level meta-analysis. *Lancet Diabetes Endocrinol*, published online October 10, 2025. doi: 10.1016/S2213-8587(25)00222-0]. ■

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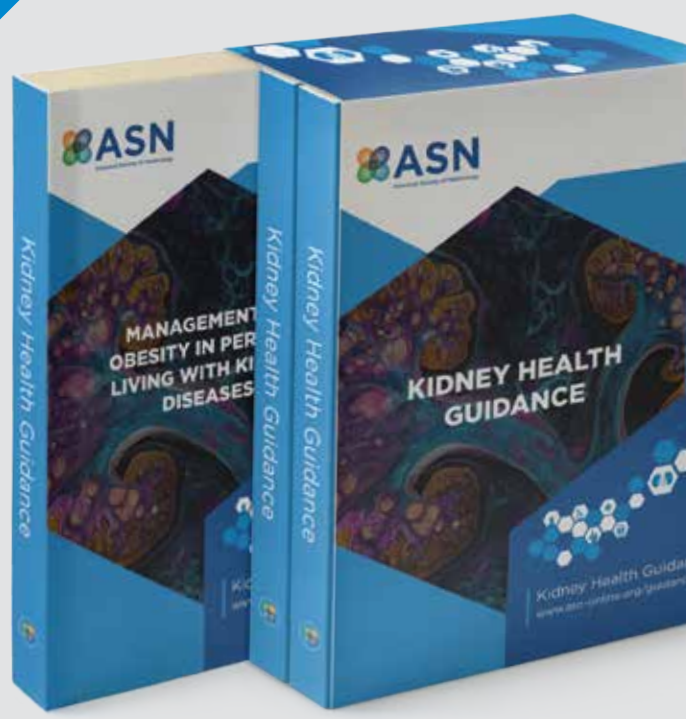

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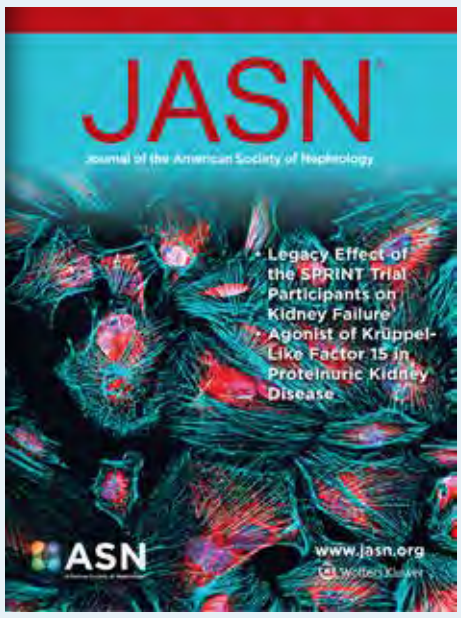

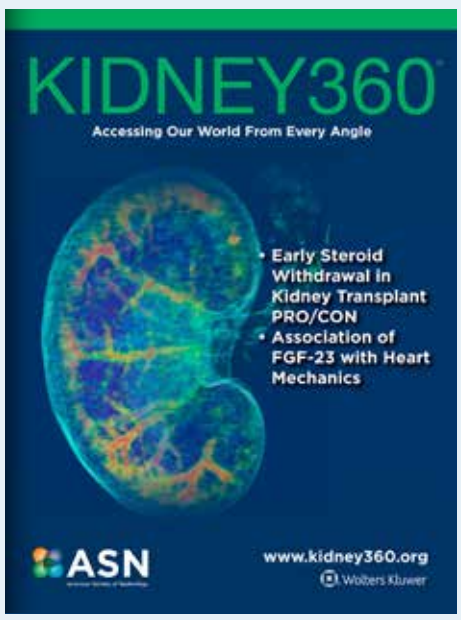

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High-Impact Trials Spotlight Advances in Therapies

Continued from page 7

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