W H I T E P A P E R

Chronic Kidney Disease

The Slow Path to Dialysis Dependency

CKD Stages 1-5 · ESRD · Dialysis · Transplantation · Xenotransplantation

A Complete Guide for Patients, Families, and Caregivers

Diagnosis · Medications · Dialysis · Transplant · 2026 Pipeline · Caregiver Support

Published July 2026 | Health Education Resource Center

Sources: NIH NIDDK, USRDS, KDIGO, National Kidney Foundation, FDA, CDC

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1. EXECUTIVE SUMMARY

Chronic kidney disease is one of the quietest catastrophes in American medicine. It develops silently over years or decades. Most patients feel fine until eGFR drops below 30 — at which point damage is already substantial and options are narrowing. By the time symptoms force a diagnosis, the trajectory toward dialysis is often set. For the family, the moment of recognition frequently comes not in a doctor's office but at a hospital admission: a routine surgery reveals kidney failure, or an emergency room visit for another problem uncovers a creatinine that should have been caught years earlier.

Today, approximately 35.5 million U.S. adults — about 14% of the adult population — have CKD. Roughly 9 in 10 do not know they have it. Around 808,000 Americans are living with end-stage renal disease (ESRD); the majority are on dialysis, and about 250,000 have functioning kidney transplants. Diabetes and hypertension together account for over 70% of new ESRD cases.

CKD is a dependency disease in three distinct ways. First, when it progresses to ESRD, in-center hemodialysis requires 3–4 hour sessions three days per week, indefinitely — a schedule that upends work, travel, and independent living. Second, transportation to and from dialysis becomes, for many families, a full-time caregiving job. Third, the cumulative effect of dialysis on frail older adults is severe: roughly 40% of adults 67 and older die within one year of starting dialysis, and most survivors experience significant functional decline in the first 12 months.

Key Facts at a Glance

- **Prevalence:** ~35.5 million U.S. adults with CKD (14%); ~9 in 10 undiagnosed. ~808,000 living with ESRD.
- **Leading causes:** Diabetes accounts for ~44% of new ESRD cases; hypertension ~29%. Together they drive over 70% of the pathway to dialysis.
- **Dialysis burden:** In-center hemodialysis is 3–4 hours × 3 days per week, indefinitely — plus travel time. Home dialysis (peritoneal, home hemo) offers more flexibility but requires trained caregiver support.
- **Older adult outcomes:** Approximately 40% of adults 67+ die within one year of starting dialysis; most survivors have significant ADL decline in the first year.
- **The 2026 pipeline is unusually rich:** Semaglutide (FLOW trial, FDA label expansion January 2025) is now the fourth pillar of CKD therapy alongside RAAS blockade, SGLT2 inhibitors, and finerenone. FDA-approved xenotransplantation clinical trials (United Therapeutics, eGenesis) began enrolling ESRD patients in late 2025 — the first genuine expansion of the transplant pool in decades.

> *The single most consequential fact about CKD is that it is largely silent until late. The families who fare best are the ones who screen at-risk relatives early, start SGLT2 inhibitors and finerenone when albuminuria is first detected, plan transplant workup years before dialysis is needed, and build the*

> *caregiving support system before — not after — dialysis begins.*

2. UNDERSTANDING CHRONIC KIDNEY DISEASE

Chronic kidney disease is defined as abnormalities of kidney structure or function present for more than three months. Function is measured primarily by two things: how well the kidneys filter the blood (glomerular filtration rate, or GFR) and whether they leak protein into the urine (albuminuria). Both matter independently. A patient with a normal GFR but heavy albuminuria has CKD; a patient with a moderately reduced GFR but no albuminuria also has CKD. The two together predict outcomes better than either alone.

The Scale of the Problem

35.5 million U.S. adults with CKD (~14% prevalence)

~9 in 10 people with CKD do not know they have it

808,000 Americans living with ESRD

~44% of new ESRD cases are caused by diabetes

~29% of new ESRD cases are caused by hypertension

CKD Staging — GFR Categories

Kidney function is staged by estimated glomerular filtration rate (eGFR), a calculated value based on serum creatinine, age, and sex. The 2021 CKD-EPI equation removed race as a variable — an important correction that had underestimated CKD severity in Black patients for years.

Stage	eGFR (mL/min/1.73 m²)	Description
G1	≥ 90	Normal or high — CKD only if albuminuria or structural damage
G2	60–89	Mildly decreased — CKD only if albuminuria or structural damage
G3a	45–59	Mildly to moderately decreased
G3b	30–44	Moderately to severely decreased
G4	15–29	Severely decreased — begin transplant evaluation, dialysis planning
G5	< 15	Kidney failure — dialysis or transplant required

Albuminuria Categories

Category	UACR (mg/g)	Description
A1	< 30	Normal to mildly increased
A2	30–300	Moderately increased (microalbuminuria)
A3	> 300	Severely increased (macroalbuminuria)

The combined GFR-albuminuria grid — the KDIGO heatmap — is the standard way to communicate CKD risk. A patient at G3a A2, for example, has a very different prognosis than a patient at G3a A3, even though both are labeled 'stage 3.' The albuminuria dimension is often the more actionable one, because most kidney-protective medications reduce albuminuria as a proximal effect.

The Major Causes

Diabetic Kidney Disease (DKD)

The leading cause of ESRD in the United States — approximately 44% of new cases. Persistent hyperglycemia damages the glomerular filtration barrier over years. Roughly 30% of patients with Type 1 diabetes and 40% of patients with Type 2 diabetes develop DKD. Classic progression: microalbuminuria → macroalbuminuria → declining eGFR → dialysis. Modern therapy (RAAS blockade, SGLT2 inhibitors, finerenone, and now semaglutide) has substantially slowed but not eliminated this pathway.

Hypertensive Nephrosclerosis

Long-standing, poorly controlled high blood pressure causes progressive damage to small renal arteries and glomeruli. Approximately 29% of new ESRD cases are attributed to hypertension. Non-Hispanic Black patients have disproportionately high rates of hypertensive kidney disease, driven in part by variants in the APOL1 gene.

Glomerulonephritis

A group of inflammatory glomerular diseases including IgA nephropathy (the most common primary glomerulonephritis worldwide), membranous nephropathy, focal segmental glomerulosclerosis (FSGS), minimal change disease, lupus nephritis, and ANCA-associated vasculitis. Together, glomerulonephritides account for roughly 8% of ESRD. Many are now treated with targeted immunosuppression.

Polycystic Kidney Disease (PKD)

Autosomal dominant polycystic kidney disease (ADPKD) affects approximately 1 in 400–1000 Americans. Kidney cysts progressively enlarge over decades, eventually destroying kidney function. Tolvaptan

(Jynarque), FDA-approved in 2018, slows ADPKD progression in appropriate patients but requires monitoring for hepatotoxicity.

Other Causes

- Interstitial nephritis (drug-induced, autoimmune, infectious)
- Obstructive uropathy (kidney stones, prostatic obstruction, tumors)
- Recurrent acute kidney injury — each episode leaves residual damage
- Congenital and hereditary disorders (Alport syndrome, Fabry disease)
- HIV-associated nephropathy
- Rarer glomerular diseases, myeloma, amyloidosis, atheroembolic disease

Demographics and Disparities

- Non-Hispanic Black Americans have approximately 3x the rate of ESRD compared to non-Hispanic white Americans
- Hispanic Americans have approximately 1.3x higher ESRD risk
- Native American and Alaska Native adults have elevated rates driven largely by diabetes
- Men develop CKD at slightly higher rates than women but progress to ESRD faster
- Prevalence rises sharply with age: over 30% in adults 65 and older meet CKD criteria

3. THE DEPENDENCY CASCADE

CKD produces dependency through several distinct mechanisms — some direct, some via the complications that accumulate as kidney function declines, and some via the treatments themselves. Below is the pathway by which a CKD diagnosis at age 55 becomes a supervised-living transition at age 78.

3.1 End-Stage Renal Disease and Dialysis

The defining dependency event in CKD is progression to ESRD and initiation of dialysis. In-center hemodialysis — the most common modality in the U.S. — requires 3–4 hour sessions, three days per week, indefinitely. Add travel time, waiting, and post-dialysis fatigue, and a dialysis day consumes 6–8 hours for the patient and, typically, a caregiver.

> *Dependency link: Older adults starting in-center hemodialysis experience a sharp decline in ADL function within the first 6–12 months. Approximately 40% of adults 67 and older die within one year of dialysis initiation; many survivors transition to skilled nursing or require substantial in-home support. The dialysis chair schedule alone often ends the ability to work, travel, or maintain the pre-dialysis lifestyle.*

3.2 Transportation Burden

Transportation to and from dialysis is one of the most invisible caregiving burdens in modern American medicine. Three sessions per week, indefinitely, mean roughly 150 round-trips per year. Patients who arrive by family car require a driver who is available for the full session (or who returns hours later). Patients dependent on medical transport face frequent scheduling problems, long waits, and cancellations. Weather, holidays, and driver availability all become emergencies. This is the single most common reason family members of dialysis patients report leaving jobs or reducing to part-time work.

3.3 Cardiovascular Disease

Cardiovascular disease is the leading cause of death in patients with CKD, and CV mortality risk increases exponentially as GFR declines. Patients with stage 4-5 CKD have roughly 10-20x the CV mortality of age-matched patients with normal kidney function. Heart failure, arrhythmias (particularly atrial fibrillation), coronary artery disease, and sudden cardiac death are all dramatically more common. Dialysis itself imposes recurrent hemodynamic stress on the heart.

> *Dependency link: Post-MI deconditioning, heart failure exacerbations, and stroke in a CKD patient all compound the underlying kidney disease. The combination of CKD plus heart failure is one of the most common presentations in elderly hospitalized patients — and one of the most frequent drivers of skilled nursing placement.*

3.4 Uremic Symptoms and Cognitive Impairment

As kidney function declines, uremic toxins accumulate. Symptoms — often blamed on aging rather than kidney disease — include fatigue, loss of appetite, nausea, sleep disturbance, restless legs, itching, cognitive slowing, and depression. Uremic encephalopathy in advanced CKD can present as confusion, agitation, or asterixis. Even sub-uremic CKD is independently associated with a 30–50% increased risk of cognitive impairment and dementia.

3.5 CKD-Mineral and Bone Disorder (CKD-MBD)

Failing kidneys cannot excrete phosphate or activate vitamin D. The result is a cascade: hyperphosphatemia, secondary hyperparathyroidism, low active vitamin D, and abnormal bone remodeling. Bone strength deteriorates, vascular calcification progresses, and fracture risk rises. Older CKD patients have approximately 2–4x the hip fracture rate of the general population. Post-fracture mortality in dialysis patients is particularly high — often 30–40% within one year.

3.6 Anemia of CKD

The kidneys produce erythropoietin — the hormone that signals the bone marrow to make red blood cells. As kidney function declines, erythropoietin production falls and anemia develops. Chronic anemia contributes to fatigue, exercise intolerance, cognitive impairment, and heart failure. Treatment uses erythropoiesis-stimulating agents (epoetin, darbepoetin), iron replacement, and — new to the class — hypoxia-inducible factor prolyl hydroxylase inhibitors (HIF-PHIs), including daprodustat (Jesduvroq), which was FDA-approved in 2023 for anemia in dialysis-dependent CKD patients.

3.7 Volume Overload and Pulmonary Edema

Failing kidneys cannot excrete excess sodium and water. Patients accumulate fluid — in the legs, in the abdomen, and — most dangerously — in the lungs. Recurrent pulmonary edema in advanced CKD is one of the most common reasons for emergency hospitalization. Each admission accelerates deconditioning and functional decline.

3.8 Electrolyte Disturbances

Advanced CKD produces hyperkalemia (life-threatening cardiac arrhythmias), metabolic acidosis (contributes to muscle wasting and bone loss), and hyperphosphatemia (contributes to vascular calcification and bone disease). Hyperkalemia is a common reason CKD patients cannot tolerate maximum doses of RAAS blockade — precisely the medications that would slow their progression.

3.9 Frailty and Sarcopenia

CKD accelerates muscle wasting through multiple mechanisms: metabolic acidosis, inflammation, uremic toxins, anorexia, reduced physical activity, and protein-energy wasting. Frailty is present in

approximately 15% of CKD stage 3 patients, rising to 60% or more of dialysis patients. Frailty is one of the strongest predictors of mortality and dependency in this population.

> *Dependency link: The combination of CKD-related fatigue, anemia, bone loss, cognitive slowing, muscle wasting, and hospitalization events produces a cumulative loss of function that often becomes irreversible. Recognizing frailty early and intervening — resistance exercise, nutrition optimization, medication review — can meaningfully change the trajectory.*

4. DIAGNOSIS AND ASSESSMENT

CKD is defined by persistent abnormalities of kidney function or structure for more than three months. Diagnosis rests on two central laboratory tests — serum creatinine (for eGFR calculation) and urine albumin-to-creatinine ratio — supported by imaging when structural disease is suspected, and by biopsy in selected cases.

Diagnostic Criteria (KDIGO)

CKD is present if one or more of the following persist for more than three months:

- eGFR below 60 mL/min/1.73 m^2
- Albuminuria (urine albumin-to-creatinine ratio ≥ 30 mg/g)
- Urine sediment abnormalities (persistent hematuria, casts)
- Electrolyte or other abnormalities due to tubular disorders
- Structural abnormalities on imaging
- Kidney transplantation history

Laboratory Testing

Test	What it Measures	Clinical Use
Serum creatinine + eGFR	Kidney filtration function	Foundational — calculated using 2021 CKD-EPI equation (race-free)
Cystatin C	Alternative filtration marker	Confirmatory when creatinine is unreliable (low muscle mass, athletes)
Urine albumin-to-creatinine ratio (UACR)	Glomerular protein leak	Best single early marker for kidney damage; risk stratification
Urinalysis with microscopy	Blood, protein, casts, cells	Detects glomerulonephritis, infection, stones
Basic metabolic panel	Sodium, potassium, bicarbonate, BUN	Monitors electrolyte disturbances and acidosis
Phosphorus, calcium, PTH, 25-OH vitamin D	CKD-mineral and bone disorder	Monitored starting at stage 3b
Complete blood count	Anemia detection	Monitor Hgb for erythropoietin deficiency anemia
Kidney ultrasound	Kidney size, obstruction, cysts	Rules out obstruction; assesses

Test	What it Measures	Clinical Use
		chronicity (small kidneys = chronic)
Kidney biopsy	Histologic diagnosis	Reserved for undiagnosed glomerulonephritis, nephrotic syndrome, unclear cases

Who to Screen

The 2024 U.S. Preventive Services Task Force and KDIGO both recommend screening in adults at increased risk:

- Diabetes — annual serum creatinine and UACR
- Hypertension — screening at diagnosis and periodically
- Cardiovascular disease
- Family history of kidney disease
- Age 60+ (increased incidence with age)
- Structural kidney disease, recurrent stones, urinary tract infections
- Prior acute kidney injury
- Use of nephrotoxic medications (long-term NSAIDs, lithium, some chemotherapies)

> *The single most important diagnostic point in modern CKD care: check UACR, not just serum creatinine. A patient with 'normal' creatinine but a UACR of 500 has albuminuric CKD and needs treatment. Most missed early CKD is missed because clinicians ordered creatinine alone.*

When to Refer to Nephrology

- eGFR persistently below 30 mL/min/1.73 m^2
- UACR persistently above 300 mg/g regardless of eGFR
- Rapid eGFR decline (more than 5 mL/min per year)
- Persistent hematuria of glomerular origin
- Resistant hypertension (uncontrolled on 3+ medications)
- Suspected glomerulonephritis, hereditary kidney disease, or complex electrolyte disorders
- Any patient approaching stage 4 CKD — for advance planning of dialysis or transplant

5. MEDICATIONS

The pharmacology of CKD has been transformed in the past decade. What was once a nearly inevitable one-way trajectory toward dialysis is now — for many patients — a slowly progressing condition that can be significantly modified. The modern CKD armamentarium is built around four pillars: RAAS blockade, SGLT2 inhibitors, non-steroidal mineralocorticoid receptor antagonists (finerenone), and — most recently — GLP-1 receptor agonists (semaglutide). Layered onto these are treatments for the complications of CKD: anemia, mineral-bone disorder, hyperkalemia, and acidosis.

5.1 Pillar 1 — RAAS Blockade

Angiotensin-converting enzyme inhibitors (ACE-I) and angiotensin receptor blockers (ARB) have been the foundation of CKD therapy for over 25 years. Both reduce intraglomerular pressure, decrease albuminuria, and slow eGFR decline in patients with albuminuric CKD. Common agents include lisinopril, ramipril, enalapril (ACE-I), and losartan, valsartan, olmesartan (ARB). Do not combine ACE-I with ARB — this doubles side effects without additional benefit.

Key monitoring: check potassium and creatinine within 1–2 weeks of initiation or dose change. An early creatinine rise of up to 30% is expected and does not require stopping the medication; larger rises require dose reduction or evaluation for renal artery stenosis. Hyperkalemia is the most common reason RAAS blockade is discontinued.

5.2 Pillar 2 — SGLT2 Inhibitors

Sodium-glucose cotransporter-2 inhibitors have fundamentally changed CKD care. Originally developed as glucose-lowering drugs for Type 2 diabetes, they were later shown to protect the kidneys in patients with and without diabetes. The landmark trials — CREDENCE (canagliflozin in DKD), DAPA-CKD (dapagliflozin in CKD with and without diabetes), and EMPA-KIDNEY (empagliflozin in CKD) — established SGLT2 inhibitors as standard of care.

Drug	FDA Kidney Indication	Key Trial
Canagliflozin (Invokana)	Diabetic kidney disease	CREDENCE — 30% reduction in composite kidney and CV outcomes
Dapagliflozin (Farxiga)	CKD (with or without T2D)	DAPA-CKD — 39% reduction in composite kidney outcome
Empagliflozin (Jardiance)	CKD (with or without T2D)	EMPA-KIDNEY — 28% reduction in kidney disease progression or CV death

Practical points: expect an acute drop in eGFR of 2–5 mL/min in the first month; this is hemodynamic, not damage, and reverses on discontinuation. Long-term slope is dramatically better. Watch for genital mycotic infections, euglycemic DKA (especially during illness or fasting), and volume depletion in older adults or those on diuretics.

5.3 Pillar 3 — Finerenone

Finerenone (Kerendia) is a non-steroidal mineralocorticoid receptor antagonist FDA-approved in 2021 for CKD associated with Type 2 diabetes. It works through a different mechanism than spironolactone or eplerenone, with less hyperkalemia and no anti-androgen effects. The FIDELIO-DKD and FIGARO-DKD trials demonstrated approximately 18% reduction in composite kidney outcomes and improvement in cardiovascular outcomes when added to standard therapy.

Finerenone is added on top of maximum-tolerated ACE-I or ARB, and increasingly on top of SGLT2 inhibitors in patients with persistent albuminuria. Starting dose is 20 mg daily if eGFR ≥ 60 or 10 mg daily if eGFR between 25 and 59. Serum potassium must be less than 5.0 mEq/L before initiation; recheck at 1 month and every 4 months thereafter. Hold or reduce dose for hyperkalemia.

5.4 Pillar 4 — GLP-1 Receptor Agonists (New in 2025)

The FLOW trial — published in the New England Journal of Medicine in 2024 — established GLP-1 receptor agonists as the fourth pillar of CKD therapy in patients with Type 2 diabetes. Once-weekly semaglutide 1.0 mg reduced the composite of major kidney disease events, cardiovascular death, and all-cause mortality by 24% compared to placebo. The trial was stopped early for clear benefit. The FDA approved a CKD label expansion for Ozempic in January 2025.

- Composite primary outcome (≥50% eGFR decline, kidney failure, kidney or CV death): HR 0.76 (24% reduction)
- All-cause mortality: HR 0.80 (20% reduction)
- Cardiovascular mortality: HR 0.71 (29% reduction)
- Annual eGFR decline: slowed by approximately 1.16 mL/min/1.73 m^2 per year
- Urine albumin-to-creatinine ratio: reduced by approximately 40% versus 3% with placebo
- Benefits consistent across CKD severity, age, and comorbidity subgroups

Semaglutide is now recommended alongside RAAS blockade, an SGLT2 inhibitor, and finerenone as part of comprehensive CKD care in Type 2 diabetes. The FLOW population was specifically patients with diabetes and CKD; benefit in non-diabetic CKD has not yet been established, and trials are underway. Whether tirzepatide (dual GIP/GLP-1) will show similar benefit is being studied.

> *Four-pillar therapy — ACE-I or ARB, SGLT2 inhibitor, finerenone, semaglutide — represents the most substantial advance in CKD care in a generation. Yet most eligible patients are not on all four. Working with a nephrologist to build up to comprehensive therapy — one drug at a time, watching*

> *potassium and volume status — is the single most important thing a patient with albuminuric diabetic kidney disease can do to delay dialysis.*

5.5 Managing Complications of CKD

Anemia

Erythropoiesis-stimulating agents (epoetin alfa, darbepoetin) have been the mainstay for decades. Iron replacement — oral or intravenous — is essential; most CKD anemia patients are iron-deficient. Newer hypoxia-inducible factor prolyl hydroxylase inhibitors (HIF-PHIs), including daprodustat (Jesduvroq, FDA-approved 2023 for dialysis patients), offer oral alternatives to injections.

Hyperkalemia

Two newer potassium binders — patiromer (Veltassa) and sodium zirconium cyclosilicate (Lokelma) — allow many CKD patients to continue RAAS blockade despite elevated potassium. Older-style sodium polystyrene sulfonate (Kayexalate) is used less because of poor tolerability and rare serious GI events.

Metabolic Acidosis

Sodium bicarbonate (typically 650 mg twice daily) or the newer agent veverimer (in development) treats CKD acidosis and appears to slow progression. Target serum bicarbonate 22–26 mEq/L.

CKD-Mineral and Bone Disorder

Phosphate binders (calcium acetate, sevelamer, lanthanum, iron-based ferric citrate and sucroferric oxyhydroxide) reduce dietary phosphate absorption. Active vitamin D analogs (calcitriol, paricalcitol) or calcimimetics (cinacalcet, etelcalcetide) treat secondary hyperparathyroidism. All require close monitoring of calcium, phosphate, and PTH.

ADPKD-Specific Therapy

Tolvaptan (Jynarque) is FDA-approved to slow ADPKD progression in adults at risk of rapid progression. It requires hepatic function monitoring (rare but serious hepatotoxicity) and produces marked polyuria — a demanding lifestyle change for patients who choose it.

6. DIALYSIS AND TRANSPLANTATION

When kidney function drops to a level where the kidneys can no longer sustain life — typically eGFR below 10–15 mL/min/1.73 m², or earlier if symptoms are severe — renal replacement therapy becomes necessary. There are four fundamental options: in-center hemodialysis, home hemodialysis, peritoneal dialysis, or kidney transplantation. A fifth option — supportive (conservative) care without dialysis — is increasingly recognized as appropriate for selected elderly and frail patients.

6.1 In-Center Hemodialysis

The most common modality in the United States — approximately 65% of ESRD patients. Blood is pumped from the patient through a dialyzer that removes waste products and excess fluid, then returned. Sessions are typically 3–4 hours, three days per week (Monday-Wednesday-Friday or Tuesday-Thursday-Saturday). Vascular access is required — ideally an arteriovenous fistula (AVF) created surgically 3–6 months before dialysis initiation, or an AV graft, or (least preferred) a tunneled central venous catheter.

> *Fistula-first: patients who begin dialysis with a working AVF have significantly better outcomes than those who start with a catheter. This is why nephrologists refer for vascular access surgery when eGFR reaches approximately 20 mL/min — long before dialysis is actually needed. Families should understand that the surgery is planning for a future need, not a signal that dialysis is imminent.*

6.2 Home Hemodialysis

Home hemodialysis has expanded substantially with newer, simpler machines (NxStage, Tablo). Patients are trained over 3–6 weeks, then perform dialysis at home — typically more frequently (5–6 short sessions per week) or with nocturnal dialysis (longer, slower sessions overnight). More frequent dialysis produces better blood pressure control, less post-dialysis fatigue, and improved quality of life. It requires a trained home partner (spouse, adult child, or paid caregiver) and adequate home space.

6.3 Peritoneal Dialysis (PD)

Peritoneal dialysis uses the patient's own peritoneum as the dialyzing membrane. Dialysate is instilled into the abdominal cavity via a permanent catheter, dwells for hours, and is then drained. Two modalities: continuous ambulatory PD (CAPD), with manual exchanges 4 times per day, or automated PD (APD), with a cycler machine that performs exchanges overnight while the patient sleeps.

Advantages: home-based, no vascular access needed, better preservation of residual kidney function, more schedule flexibility, no dietary restrictions as strict as hemodialysis. Disadvantages: peritonitis risk (1 episode per 24-36 patient-months on average), catheter-related complications, technique burden, gradual failure of peritoneal function over 5-10 years. PD is underused in the U.S. — approximately 12% of ESRD patients — but is more common in many other countries.

6.4 Kidney Transplantation

Kidney transplantation is the treatment of choice for most patients with ESRD who are medically suitable. Recipients of a kidney transplant live longer, have better quality of life, and require far less caregiving support than dialysis patients. Two graft sources:

Living Donor Transplant

A kidney from a healthy, willing donor — typically a family member, spouse, or altruistic donor. Living-donor grafts have better outcomes than deceased-donor grafts: half-life approximately 15-20 years versus 10-12 years for deceased-donor kidneys. Living-donor transplant can be scheduled electively, sometimes preemptively (before dialysis starts) — the best outcome pathway. Paired kidney exchange programs allow incompatible donor-recipient pairs to swap with other pairs to find compatible matches.

Deceased Donor Transplant

A kidney from an organ donor. Approximately 90,000 Americans are on the waiting list at any given time; median wait is 3–5 years and varies substantially by blood type, HLA sensitization, and region. Many older patients on the waiting list die before an organ becomes available. The 2014 Kidney Allocation System changed how kidneys are distributed to reduce racial disparities and improve matching.

Post-Transplant Immunosuppression

Standard modern regimen: tacrolimus (calcineurin inhibitor) + mycophenolate + prednisone, or steroid-avoidance protocols using tacrolimus + mycophenolate alone after induction. Newer agents (belatacept, iscalimab) offer alternatives with different side-effect profiles. Immunosuppression must continue for the life of the transplant. Long-term risks include infection, malignancy (particularly skin cancers and post-transplant lymphoproliferative disorder), diabetes, and cardiovascular disease.

6.5 Conservative Kidney Management (Non-Dialysis Care)

For selected patients — particularly frail elderly with multiple comorbidities and limited life expectancy — supportive care without dialysis is a legitimate and increasingly used option. Studies suggest that in patients over 80 with high comorbidity burden, dialysis may not extend life meaningfully and often reduces quality of remaining life. Conservative management focuses on symptom control, treatment of anemia and mineral disturbances, careful volume management, and palliative care support. This decision should be made in an informed, unhurried conversation with the patient, family, and nephrology team — ideally months before dialysis would otherwise be initiated.

7. CLINICAL TRIALS AND PIPELINE 2026

The 2026 CKD pipeline is unusually active. Three developments deserve particular attention: (1) FDA-approved xenotransplantation clinical trials (pig kidneys into human patients) that began enrolling in late 2025, (2) the emergence of GLP-1 receptor agonists as the fourth pillar of CKD therapy, and (3) the KDIGO 2026 diabetes-and-CKD guideline update reflecting these advances.

7.1 Xenotransplantation — Pig Kidneys in Humans

The organ shortage is the fundamental structural problem in transplantation: approximately 90,000 Americans on the kidney waiting list, roughly 25,000 kidney transplants performed each year, and thousands of patients dying annually before an organ becomes available. Xenotransplantation — using genetically modified pig kidneys — represents the first real prospect in decades of expanding the transplantable organ supply.

Timeline of the modern era: from January 2022 to January 2025, clinicians performed two pig heart and four pig kidney xenotransplants in living human patients under the FDA's Expanded Access (compassionate use) pathway. One eGenesis pig kidney survived nine months in a dialysis-dependent patient, bridging her to an eventual human kidney transplant.

Based on these early experiences, the FDA approved formal clinical trials in 2025. Three programs began enrolling ESRD patients in late 2025:

Sponsor	Product	Design
United Therapeutics	UKidney (10 gene edits)	EXPAND trial — Phase 1/2 in ESRD patients on dialysis
United Therapeutics	UThymoKidney (1 gene edit + thymus tissue)	Extend trial — thymus co-transplant to induce immune tolerance
eGenesis	EGEN-2784 (69 gene edits)	Enrolling 30 dialysis-dependent patients age 50+ awaiting a human kidney

The eGenesis program's gene-editing approach — 69 modifications to eliminate pig-specific glycans and endogenous retroviruses and to add human immune-regulatory transgenes — represents the most extensive genetic engineering to date. Primary endpoints in these Phase 1/2 studies focus on patient and graft survival at 24 weeks, glomerular filtration rate of the xenograft, and safety.

> *Xenotransplantation is not ready for routine clinical use. But the transition from compassionate-use single cases to formally approved clinical trials in 2025-2026 is a genuine inflection point. If early trials continue to show acceptable safety and graft survival, the transplant landscape could look*

> *meaningfully different by the early 2030s.*

7.2 GLP-1 Receptor Agonists — The Fourth Pillar Confirmed

The FLOW trial (semaglutide in Type 2 diabetes with CKD) is the most consequential CKD trial in a decade. See §5.4 above for the primary results. FLOW analyses published in JACC in June 2026 confirmed consistent kidney and survival benefit across subgroups including patients with established atherosclerotic cardiovascular disease, heart failure, and high total cardiovascular risk. Numbers needed to treat to prevent one primary kidney outcome at three years ranged from 13 to 22 across these high-risk groups.

Additional GLP-1 CKD trials underway or newly reported:

- Tirzepatide (Zepbound/Mounjaro) — dedicated CKD outcomes trials in progress; expected to show similar or greater benefit given its more potent glycemic and weight effects
- Semaglutide in non-diabetic CKD — dedicated trial (REMODEL) launched to test whether the FLOW benefit extends to patients without diabetes
- Combination trials of GLP-1 with SGLT2 inhibitor plus finerenone — dose-optimization and safety studies

7.3 KDIGO 2026 Guideline Update

The KDIGO 2026 Clinical Practice Guideline for Diabetes and Chronic Kidney Disease — released in public review draft in March 2026 — reflects the four-pillar era. Key updates include stronger recommendations for SGLT2 inhibitors as first-line therapy for cardiorenal protection (independent of glycemic control), formal incorporation of GLP-1 receptor agonists based on FLOW, expanded finerenone recommendations, and updated guidance on combination therapy sequencing.

7.4 Novel Anti-Fibrotic and Regenerative Approaches

Several early-stage strategies target kidney fibrosis directly — the final common pathway of CKD progression. Anti-fibrotic monoclonal antibodies targeting TGF-β, endothelin receptor antagonists (sparsentan approved for IgA nephropathy and FSGS in 2023), and cell-based therapies using autologous or allogeneic mesenchymal stem cells are in various stages of development. None yet has FDA approval for general CKD; sparsentan represents a real advance for its specific glomerular indications.

7.5 Wearable and Implantable Kidney Devices

Two long-running projects continue toward the goal of a wearable or implantable artificial kidney: the Kidney Project (an implantable bioartificial kidney combining hemofilter and cultured kidney cells) at UCSF/Vanderbilt, and various wearable hemodialysis prototypes. None is FDA-approved for routine use. These technologies represent a longer-term hope of freeing dialysis patients from the fixed-schedule burden that defines their lives today.

7.6 Anemia and Mineral Disorder Pipeline

HIF-PHI inhibitors continue to expand. Daprodustat (Jesduvroq) is FDA-approved for dialysis-dependent anemia; roxadustat and vadadustat are approved in other countries. Newer phosphate binders (tenapanor, an inhibitor of intestinal sodium hydrogen exchanger, approved 2023) offer alternatives to traditional binders.

8. CAREGIVER BURDEN AND PALLIATIVE CARE

Caring for someone with advanced CKD, and especially someone on dialysis, is one of the most demanding forms of family caregiving. Unlike diseases with acute crises followed by stable periods, dialysis caregiving is relentless — three sessions per week, indefinitely, plus the ordinary work of managing medications, appointments, nutrition, and complications.

The Practical Load

- Transportation — 150+ round-trips per year for in-center hemodialysis, plus appointments for nephrology, vascular access surgery, transplant workup, and other specialists
- Medication management — CKD patients typically take 10–15 daily medications; timing around dialysis and meals is complex
- Dietary support — sodium, potassium, phosphate, and fluid restrictions must be managed at every meal; grocery shopping and cooking often require re-training
- Access care — protecting an AVF or catheter site, watching for signs of infection or thrombosis, coordinating with the vascular access team
- Home dialysis training and execution — if the family has chosen PD or home hemo, the training period and ongoing technique burden are substantial
- Emergency response — access clotting, hyperkalemia, volume overload, hypotension after dialysis, and infections all can require urgent medical attention
- Emotional support — depression is present in approximately 25–40% of dialysis patients and correlates with worse outcomes

The Transportation Problem

Transportation to and from dialysis is the single most common caregiver-burden issue reported in surveys of dialysis family members. The pattern: three sessions per week for years, each session requiring several hours of family time (drop-off, waiting or return trip, pick-up, post-dialysis recovery time). Patients who cannot drive themselves — because of fatigue, medications, cardiovascular disease, or vision problems — depend on family, medical transport, or paid rides. Weather, holidays, driver illness, and scheduling conflicts become urgent problems. This is the caregiving burden that most commonly forces family members to reduce work hours or leave employment.

> *Practical strategies that help: use medical transportation benefits available through Medicare, Medicaid, or Medicare Advantage plans (many are underused); share transportation among family members with an explicit schedule; investigate ride-sharing programs run by dialysis centers or community organizations; and — for eligible patients — consider transitioning to home dialysis modalities to eliminate the transportation problem entirely.*

Caregiver Burnout

Approximately 40–50% of family caregivers of dialysis patients report significant emotional stress. Predictors include high caregiving hours per week, coexisting cognitive impairment in the patient, unpredictable schedules, and lack of respite. Depression rates in family caregivers exceed those in the general population by 2–3-fold. Physical health of caregivers deteriorates measurably over the years of caregiving.

> *Support strategies that work: joining a dialysis family support group (National Kidney Foundation, American Association of Kidney Patients), using respite services (adult day programs, short-term home health), sharing caregiving across multiple family members, and — critically — the caregiver's own primary care visits to screen for depression, hypertension, and sleep disorders.*

Palliative Care for Advanced Kidney Disease

Palliative care is not the same as hospice. Palliative care is expert symptom management and quality-of-life support for patients with serious chronic illness — at any point in the disease course. For CKD patients, palliative care teams can offer expert management of pruritus (uremic itching), pain, dyspnea, fatigue, restless legs, and depression. Palliative care can — and should — begin years before end-of-life discussions.

For patients who choose conservative kidney management (no dialysis), palliative care becomes the central medical framework. For dialysis patients approaching the end of life, or for those considering dialysis withdrawal (a legitimate and legally protected choice), palliative care and hospice teams provide comprehensive support.

Advance Directives

Every adult with CKD benefits from a completed advance directive and a durable power of attorney for health care. For CKD patients specifically, key decisions to think about in advance include: whether to initiate dialysis at all if cognitive function has declined; whether to continue dialysis if quality of life becomes unacceptable; preferences about aggressive intervention (mechanical ventilation, CPR) in the event of cardiovascular collapse during dialysis; and — for transplant candidates — preferences about the intensity of workup and post-transplant complications. These are decisions best made in unhurried conversations, not in the middle of a hospital crisis.

9. KEY RESOURCES AND WHERE TO GET HELP

The list below is organized by category. Every phone number and website has been checked as current at the time of publication.

Disease-Specific Organizations

Organization	Focus	Contact
National Kidney Foundation (NKF)	CKD patient education, advocacy, screening programs, professional education	kidney.org · 855-653-2273
American Association of Kidney Patients (AAKP)	Patient-led advocacy, education, dialysis patient support	aakp.org · 800-749-2257
American Kidney Fund	Financial assistance, education, patient advocacy	kidneyfund.org · 800-638-8299
National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK)	Federal research and patient education (Kidney Failure Risk Program)	niddk.nih.gov
PKD Foundation	Polycystic kidney disease patient support and research	pkdcure.org · 800-753-2873
NephCure Kidney International	Nephrotic syndrome, FSGS, IgA nephropathy	nephcure.org · 866-637-4287
Lupus Foundation of America	Lupus nephritis (kidney involvement in SLE)	lupus.org · 800-558-0121

Dialysis and Transplant Resources

Organization	Focus	Contact
Medicare Dialysis Facility Compare	Compare quality metrics of local dialysis facilities	medicare.gov/care-compare
Organ Procurement and Transplantation Network (OPTN/UNOS)	National transplant waiting list; patient education	optn.transplant.hrsa.gov · unos.org
National Kidney Registry	Paired kidney exchange program for incompatible living-donor pairs	kidneyregistry.org

Organization	Focus	Contact
Home Dialyzors United	Home hemodialysis and PD patient community	homedialyzorsunited.org
Kidney Transplant Recipients Support	Post-transplant patient community and education	Through NKF and AAKP local chapters

Caregiver and Community Support

Organization	Focus	Contact
Family Caregiver Alliance	Caregiver support, respite information, state-by-state resources	caregiver.org · 800-445-8106
National Alliance for Caregiving	Caregiving policy and family resources	caregiving.org
Eldercare Locator	Federal service connecting to local Area Agencies on Aging	eldercare.acl.gov · 800-677-1116
Meals on Wheels America	Home-delivered meals; useful for CKD dietary support	mealsonwheelsamerica.org · 888-998-6325
Well Spouse Association	Peer support for spousal caregivers	wellspouse.org · 800-838-0879
Rides in Sight	Transportation options database for older adults	ridesinsight.org · 855-607-4337

Government and Coverage Resources

Resource	Purpose	Contact
Medicare	Coverage for medical services, dialysis benefit, transplant coverage, enrollment	medicare.gov · 800-MEDICARE
Medicare ESRD Benefit	Medicare coverage for ESRD patients regardless of age	medicare.gov (ESRD section)
State Health Insurance Assistance Program (SHIP)	Free Medicare counseling in every state	shiphelp.org
National Council on Aging	Screening for federal and state	benefitscheckup.org

Resource	Purpose	Contact
BenefitsCheckUp	benefit programs	
ESRD Networks	Regional quality-improvement and patient-advocacy organizations for dialysis	esrdncc.org (National Coordinating Center)

Legal Planning

Resource	Purpose	Contact
National Academy of Elder Law Attorneys (NAELA)	Directory of elder-law attorneys for advance directives, powers of attorney, guardianship	naela.org
American Bar Association — Commission on Law and Aging	Educational resources for advance care planning	americanbar.org/groups/law_aging

> *The National Kidney Foundation's 1-800 helpline is staffed by trained kidney-disease educators who can answer clinical questions, connect callers to local resources, and help navigate the transplant process. Most patients and families do not use it until years into the disease. Call earlier.*

10. NEXT STEPS

CKD rewards early planning and punishes delay. The families who fare best move deliberately through the following sequence, adapted to the patient's stage of disease and personal preferences.

1. Know Your Numbers

Every adult should know their eGFR and their urine albumin-to-creatinine ratio. Ask your primary care physician to check both — not just creatinine. If either is abnormal, ask for repeat testing in 3 months to confirm chronicity. If CKD is confirmed, ask what stage and what category (G1-G5, A1-A3). Ask about the KDIGO risk category. These numbers are the foundation of every treatment decision that follows.

2. Aggressively Treat the Underlying Cause

Diabetes: aim for A1C in a range appropriate for your age and health status; use SGLT2 inhibitors, GLP-1 receptor agonists, and finerenone as clinical eligibility allows. Hypertension: target below 130/80 for most CKD patients; be willing to use 3-4 medications if needed. Glomerulonephritis: work with a nephrologist on appropriate immunosuppression. Polycystic kidney disease: discuss whether tolvaptan is appropriate. The underlying disease determines the trajectory.

3. Build Toward Four-Pillar Therapy

For patients with albuminuric diabetic kidney disease, the modern standard is comprehensive medical therapy: maximum-tolerated ACE-I or ARB, plus an SGLT2 inhibitor, plus finerenone, plus (for Type 2 diabetes) a GLP-1 receptor agonist such as semaglutide. Most eligible patients are not on all four. Ask your nephrologist and primary care team what pillars you are missing and why. One drug at a time, watching potassium and volume.

4. Get to a Nephrologist Early

Waiting until eGFR falls below 20 to see a nephrologist is a common — and costly — mistake. Earlier referral (eGFR under 30, or albuminuria over 300 regardless of eGFR) improves outcomes measurably. Nephrologists coordinate transplant workup, vascular access planning, medication optimization, and — for those who want it — conservative kidney management planning. Every one of these decisions is better made months to years before dialysis than in the middle of a crisis.

5. Plan Vascular Access Ahead of Time

If dialysis appears likely — eGFR approaching 20 mL/min with a downward trajectory — refer for arteriovenous fistula creation. The fistula takes 3–6 months to mature. Starting dialysis with a mature fistula is significantly better than starting with a catheter (lower infection risk, better long-term function, less hospitalization). Vascular access planning is the single most concrete example of a decision that must be made ahead of time.

6. Evaluate for Transplant Early — Ideally Preemptively

Kidney transplantation is the treatment of choice for most ESRD patients. Living-donor transplant, when possible, produces the best outcomes. Preemptive transplant (before dialysis is required) is the best outcome pathway of all. Begin transplant evaluation when eGFR reaches 20-25 mL/min; do not wait for dialysis to be underway. Discuss living donation with family early — willing donors often step forward when they understand the process, but only if the conversation happens.

7. Consider Home Dialysis

If dialysis is required and transplant is not immediately available, home modalities (peritoneal dialysis or home hemodialysis) offer better quality of life, more schedule flexibility, and less transportation burden than in-center hemodialysis. Home modalities require training, home space, and typically a family partner — but for patients and families able to commit to them, the impact on independence is substantial. Ask your nephrologist about eligibility.

8. Build the Caregiving Plan Before It Is Needed

Dialysis transforms family logistics. Identify who will drive to sessions, who will manage medications, who will monitor for complications. Investigate medical transportation benefits through Medicare, Medicaid, and Medicare Advantage plans. Contact the local Area Agency on Aging through the Eldercare Locator for in-home aide services, meal delivery, and respite programs. Do this before the first dialysis session, not after.

9. Complete Advance Directives

Every adult with chronic disease should have (1) an advance directive naming preferences for aggressive interventions, (2) a durable power of attorney for health care naming a decision-maker, and (3) — separately — a durable power of attorney for finances. For CKD patients, key preferences to document include whether to initiate dialysis if cognitive decline is significant, preferences about dialysis withdrawal, and preferences about mechanical ventilation and CPR. State-specific forms are available free through the Family Caregiver Alliance and each state's bar association.

10. Use Community Resources Proactively

Do not wait for crisis to call the National Kidney Foundation, the Eldercare Locator, or Family Caregiver Alliance. Transportation assistance, home-delivered meals, in-home aide services, adult day programs, and caregiver respite are available in every county in the United States through Area Agencies on Aging. Dialysis center social workers are one of the most underused resources in modern CKD care — they know the local landscape and can help families navigate it.

> *CKD dependency is not inevitable. It is a probability that shifts substantially based on how early the disease is detected, how aggressively the four pillars are used, how well vascular access and*

> *transplant are planned, how proactively the caregiving system is built, and how carefully advance care planning is completed. The clinical toolkit in 2026 — semaglutide, finerenone, SGLT2 inhibitors, xenotransplantation on the horizon — is better than at any point in history. But only if it is used.*

DISCLAIMER

This white paper is provided for educational purposes only. It does not constitute medical advice or legal advice. Information about clinical trials and medications is current as of July 2026 and may change. Consult qualified medical and legal professionals for guidance specific to your situation.

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