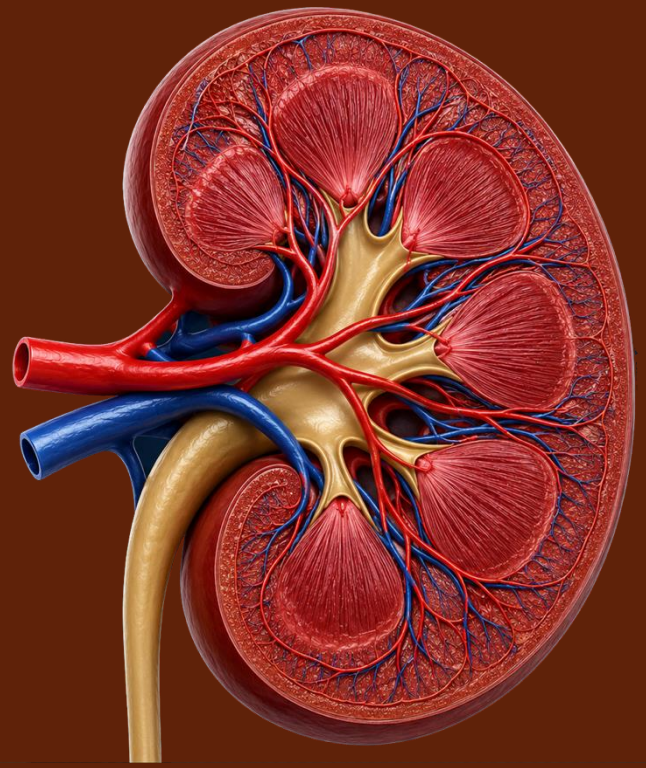
FOR PRIMARY CARE PHYSICIANS

Nephrology for the Non-Nephrologist

How to explain progression, protect remaining kidney function, and plan future kidney care



KIDNEY ASSOCIATES

OBJECTIVES

Detect

Use eGFR, albuminuria, urine sediment, imaging, and trajectory to recognize kidney disease early.

Explain

Teach the major progression loops: hyperfiltration, metabolic injury, vascular disease, fibrosis, and aging.

Protect

Layer lifestyle, blood pressure, RAS blockade, SGLT2 inhibition, diabetes therapy, and complication management.

Plan

Avoid crash starts by preparing for home PD or hemodialysis, access, transplant, conservative care, and urgent starts.

The literature map gives the backbone

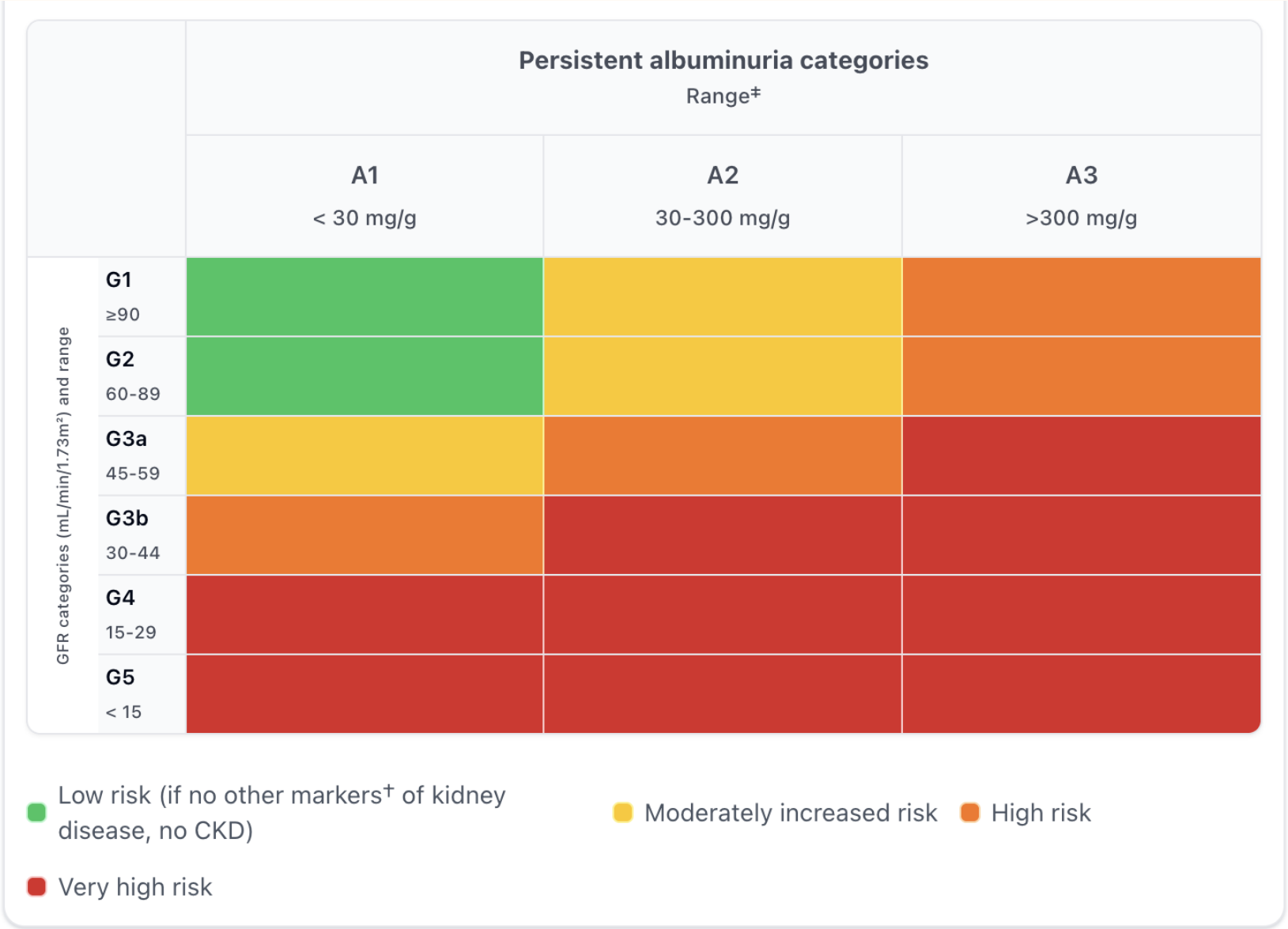
The course is organized around recurrent domains identified through large-scale CKD literature mapping using deep learning: detection and prognosis, progression biology, diabetes and vascular disease, aging, treatment response, kidney failure preparation, dialysis modalities, transplantation, and patient-centered care.

Detection	Progression	Diabetes
Vascular risk	Aging	Therapy
Dialysis	Transplant	Patient goals

CKD Heatmap

CKD is an abnormality of kidney structure or function that has been present for at least 3 months

CAUSES: Diabetes, hypertension, glomerular disease, obstruction, cystic disease, medication injury, systemic disease, and recurrent AKI.



Diagnosis

- ❑ Repeat elevations in serum creatinine
- ❑ Order urine ACR
- ❑ Urine microscopy can show hematuria, casts
- ❑ The ultrasound detects obstruction, cystic disease, small kidney size, cortical thinning, and/or echogenicity.
- ❑ Review for medications, NSAIDs, recent contrast, volume status, and recent illness.

The trap

A normal-looking creatinine can hide low GFR in older adults or low muscle mass.

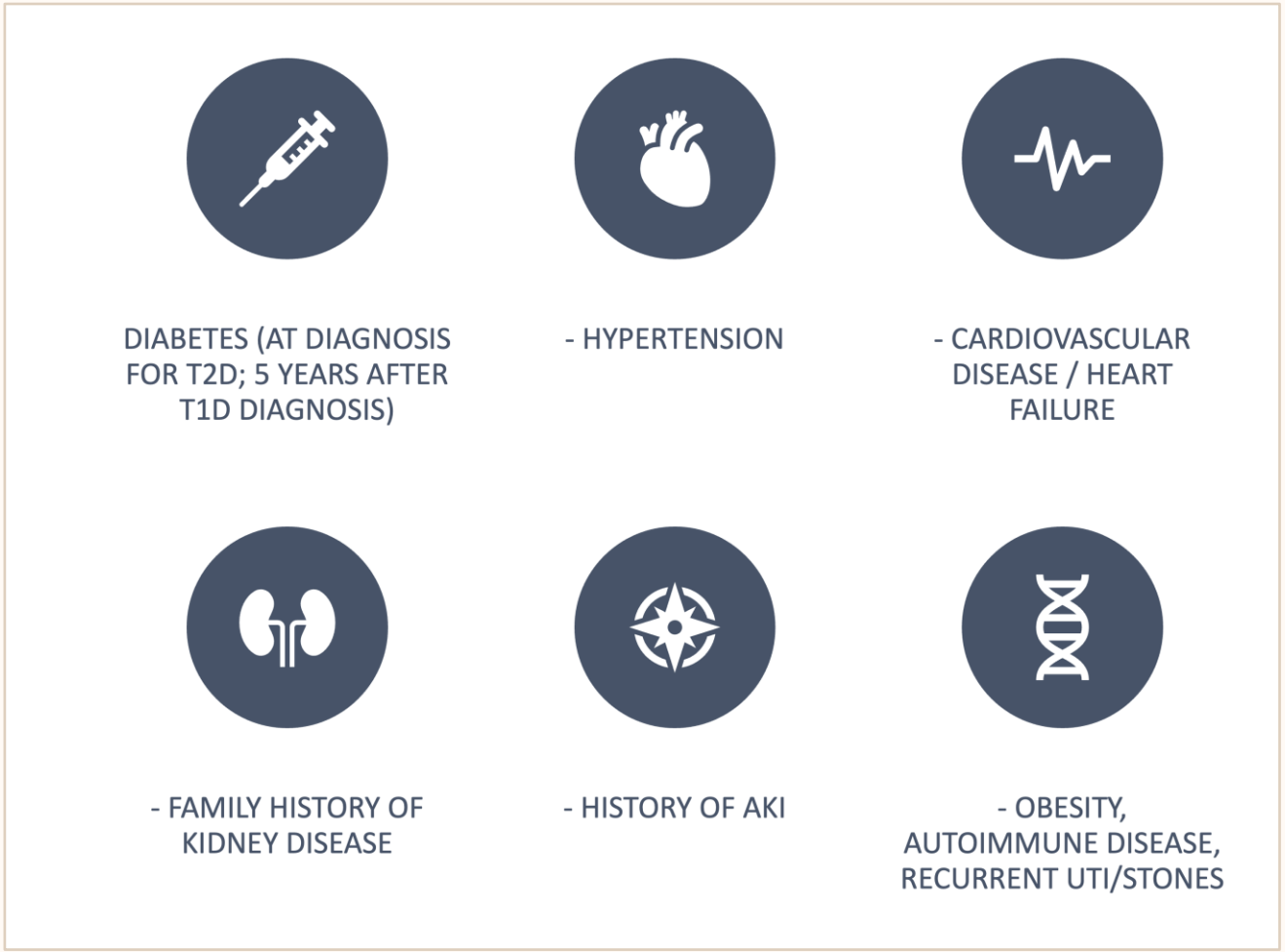
The clue

Albuminuria, active sediment, and trajectory often reveal the real risk earlier than eGFR alone.

The habit

Use single measurement to diagnose CKD

Who to screen (KDIGO 2024)



Bedside workflow

1 eGFR trend

Is this stable, acute, or progressive?

2 Urine ACR

Albuminuria changes prognosis and treatment.

3 Urine sediment

Casts or dysmorphic RBCs change the pathway.

4 Ultrasound

Obstruction, cysts, size, chronicity.

5 Medication review

NSAIDs, contrast, lithium, PPIs, supplements.

RED FLAGS

Urine sediment

RBC casts, dysmorphic RBCs, WBC casts, granular casts, or unexplained hematuria with proteinuria.

Rapid trajectory

eGFR fall that is faster than expected, especially with new proteinuria, systemic symptoms, or medication exposure.

Heavy albuminuria

ACR >300 mg/g or nephrotic-range proteinuria – consider a form of glomerulonephritis

Obstruction

Hydronephrosis is a reversible emergency until proven otherwise.

Stable diabetic CKD and hypertensive CKD are common, but active urine sediment, rapid decline in kidney function, or systemic features point to rapidly progressive glomerulonephritis

Signs and Symptoms

Stage	Typical Presentation	Key Findings
🟢 **Early CKD** *Stages 1–3*	Usually asymptomatic	• Lab abnormalities only • Foamy urine • Nocturia
🟡 **Moderate CKD** *Stages 3b–4*	Progressive symptoms	• Fatigue • ↓ Appetite • Edema • Pruritus • Urine changes
🔴 **Advanced CKD / Uremia** *Stage 5*	Multisystem uremia	• Nausea / vomiting • Metallic taste • Encephalopathy • Pericarditis • Volume overload • Cramps / restless legs

Mechanisms

Hyperfiltration

Surviving glomeruli carry more pressure and flow.

Sugar injury

Glycation, oxidative stress, podocyte injury, inflammation.

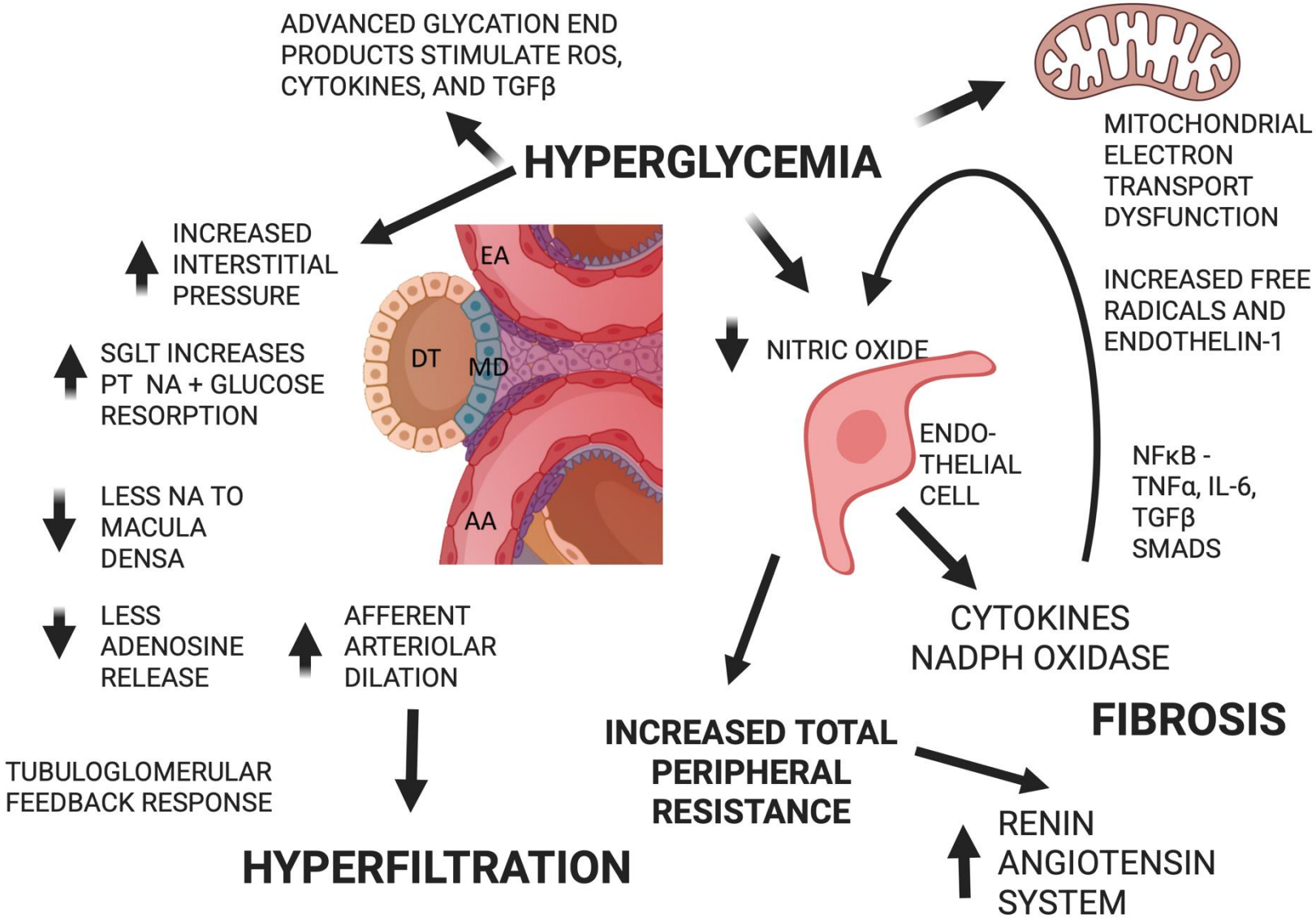
Vascular disease

Hypertension, stiffness, ischemia, heart failure, microvascular loss.

Fibrosis

Tubular stress, macrophages, fibroblast activation, matrix deposition.

Different diseases enter through different doors, but many converge on glomerular hypertension, endothelial injury, tubular stress, inflammation, and fibrosis.


ADVANCED GLYCATION END PRODUCTS STIMULATE ROS, CYTOKINES, AND TGFβ
HYPERGLYCEMIA
MITOCHONDRIAL ELECTRON TRANSPORT DYSFUNCTION
INCREASED FREE RADICALS AND ENDOTHELIN-1
INCREASED INTERSTITIAL PRESSURE
SGLT INCREASES PT NA + GLUCOSE RESORPTION
LESS NA TO MACULA DENSA
LESS ADENOSINE RELEASE
AFFERENT ARTERIOLAR DILATION
TUBULOGLOMERULAR FEEDBACK RESPONSE
HYPERFILTRATION
EA
DT
MD
AA
NITRIC OXIDE
ENDO-THELIAL CELL
NFκB - TNFα, IL-6, TGFβ SMADS
CYTOKINES NADPH OXIDASE
FIBROSIS
INCREASED TOTAL PERIPHERAL RESISTANCE
RENIN ANGIOTENSIN SYSTEM

Hyperfiltration is compensation that becomes injury

Loss of nephron number, obesity, diabetes, high sodium intake, and high intraglomerular pressure can make remaining glomeruli work harder. The patient may look stable until albuminuria and sclerosis reveal the price.

What helps

Lower intraglomerular pressure
ACEi/ARB,
SGLT2 inhibitor,
BP control,
Sodium reduction,
Weight strategy.

What hurts

NSAIDs
Dehydration
Excess sodium
Uncontrolled diabetes
Uncontrolled hypertension
Recurrent AKI

Diabetes injures the kidney through hemodynamics and metabolism

Tubuloglomerular feedback

More sodium-glucose reabsorption signals the kidney to hyperfilter.

Barrier injury

Albuminuria reflects glomerular and vascular stress.

Inflammation

Oxidative stress and fibrosis turn metabolic injury into scarring.

Glucose control alone is not enough.

Modern care layers SGLT2 inhibition, RAS blockade, GLP-1 receptor agonists, MRA , and lifestyle therapy.

CKD is often vascular disease wearing a kidney label

- Hypertension transmits pressure to the glomerulus and accelerates arteriosclerosis.
- Arteriosclerosis and arterial stiffness reduce renal reserve.
- Heart failure and venous congestion can lower effective filtration.
- Microvascular rarefaction makes the kidney less tolerant of acute illness.
- Albuminuria is both a kidney signal and a vascular risk signal.

CKD care is cardiovascular prevention: BP, statin, diabetes therapy, smoking cessation, sleep apnea, exercise, and volume control.

Resistant hypertension, unexplained hypokalemia, sudden creatinine rise after RAS blockade, or asymmetric kidneys should prompt secondary-cause thinking

Fibrosis is the final common pathway

Once injury becomes fibrosis, treatment shifts from cure to slowing loss, preventing complications, and preserving reserve. But fibrosis is not an excuse for nihilism: lowering ongoing injury still changes the slope.

The slope is the target: when you cannot reverse CKD, you can still slow it.

Aging lowers reserve but does not explain everything

Expected with age

Nephron loss, glomerulosclerosis, tubular atrophy, interstitial fibrosis, vascular stiffness, and reduced reserve during illness.

Clinical traps

Low muscle mass can hide low GFR. Polypharmacy and dehydration can mimic progression. Albuminuria is never just aging.

Best posture

Use trajectory, ACR, urine sediment, cystatin C when needed, frailty, nutrition, falls, goals, and time-to-benefit.

Do not undertreat older adults because they are old; do not overtreat them as if they were young.

Risk stratification: what should make you call nephrology?

- eGFR <30 ml/min/1.73m^2 or rapid sustained decline.
- ACR >300 mg/g, nephrotic-range proteinuria, or unexplained albuminuria.
- Active urine sediment, hematuria with proteinuria, suspected glomerulonephritis.
- Resistant hypertension, recurrent hyperkalemia, metabolic acidosis, anemia, CKD-MBD, or difficult volume.
- Unclear cause, hereditary disease, obstruction, cystic disease, or medication toxicity.
- Any patient approaching kidney failure who has not discussed modalities or transplant.

Modern CKD treatment is layered

Measures

eGFR trend
UACR
Sediment
BP

Lifestyle

Plant dominant
Restrict Na
Weight loss
Smoking cessation
Adequate sleep
Exercise

Vascular

BP control,
ACEi/ARB
MRA
Coming:
Endothelin agonists

Metabolism

SGLT2i,
Diabetes
Tx GLP-1
GLP-GIP

Complications

Anemia
acidosis
Potassium
Bone-mineral disease

Which combination best lowers kidney, cardiovascular, and treatment-burden risk for this person?


MANAGEMENT OVERVIEW
THE 4 PILLARS OF CKD
LIFESTYLE MODIFICATION
1
BLOOD PRESSURE CONTROL
2
KIDNEY-PROTECTIVE PHARMACO-THERAPY
3
COMPLICATION MONITORING & MANAGEMENT
4

PILLAR 1

LIFESTYLE MODIFICATION

- **Sodium 2,300 mg/day**
  (reduces BP and albuminuria)
- **Moderate exercise ≥150 min/week**
- **Smoking cessation**
- **Weight management**
- **Limit nephrotoxins: avoid NSAIDs**
- **Protein:** generally 0.8 g/kg/day
  in advanced CKD (discuss with nephrology)

ACEi and ARB: protect the filter by lowering pressure

Use for albuminuric CKD when tolerated.
Use the highest approved tolerated dose to match trial evidence.
Check creatinine and potassium 2-4 weeks after start or dose increase.
Manage hyperkalemia when possible rather than reflexively stopping therapy.
Continue unless creatinine rises >30% within 4 weeks or the clinical setting demands stopping.

Teaching phrase

A small creatinine rise can mean the medicine is lowering glomerular pressure, not damaging the kidney.

Safety phrase

Do not ignore potassium, dehydration, NSAIDs, renal artery stenosis clues, or a large creatinine rise.

SGLT2 inhibitors changed CKD from glucose care to kidney care

Mechanism

Restore tubuloglomerular feedback, lower intraglomerular pressure, reduce albuminuria, and improve cardiorenal outcomes.

Practice

Expect an early eGFR dip. Review volume status, genital infection risk, sick-day pauses, and perioperative holding.

Scope

Evidence now includes diabetic and non-diabetic CKD populations, especially albuminuric disease and heart failure.

Tell patients: "This is not just a diabetes drug. In kidney disease, it lowers pressure inside the filters and protects the heart-kidney system."

CREDENCE; DAPA-CKD; EMPA-KIDNEY

Diabetes add-ons: GLP-1 receptor agonists and finerenone

GLP-1 receptor agonists

For type 2 diabetes with CKD, obesity, and cardiovascular risk, GLP-1 RA therapy can support glycemic control, weight strategy, and cardiovascular risk reduction. FLOW added dedicated kidney outcome evidence for semaglutide.

Finerenone

For type 2 diabetes with persistent albuminuria despite maximally tolerated RAS blockade and acceptable potassium. Monitor potassium because hyperkalemia is the practical limiting toxicity.

CKD complications

Acidosis

Oral alkali or diet strategy when persistent metabolic acidosis is present.

Hyperkalemia

Diet review, diuretics, binders, and medication triage to preserve RASi when possible.

Anemia

Iron status first; ESA only when appropriate and with target discipline.

CKD-MBD

Calcium, phosphate, PTH, vitamin D, diet, binders, and avoiding excess calcium load.

Volume

Sodium, diuretics, heart failure management, and dialysis planning when diuretics fail.

Medication safety

Dose for eGFR, avoid NSAIDs, and teach sick-day holds.

The transition from CKD to ESKD

Scenario 1 – CRASHER - A patient with undiagnosed advanced kidney disease shows up in the emergency room in heart failure. A hemodialysis catheter is placed. The patient is dialyzed in the hospital and then discharged to a dialysis center.

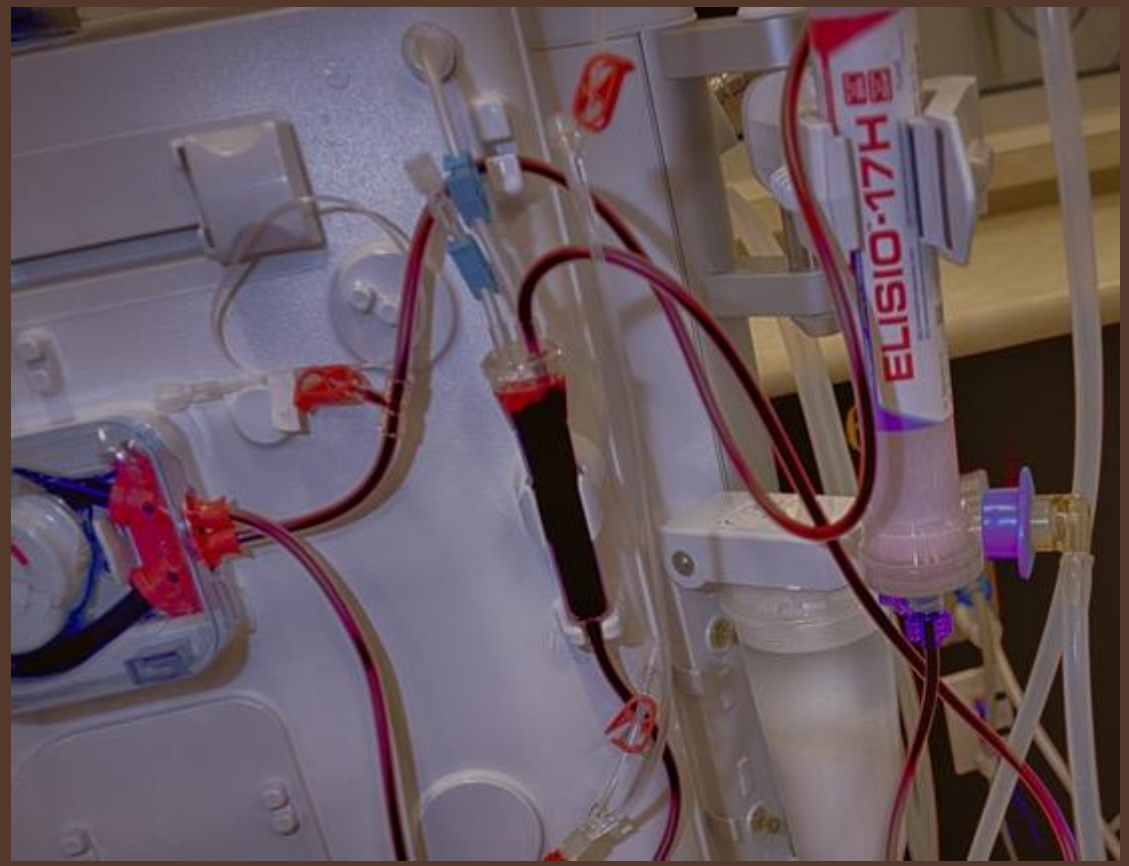
Scenario 2 – URGENT START - The patient has a peritoneal dialysis catheter placed and undergoes acute peritoneal dialysis in the hospital. The patient is then referred for PD training.

Scenario 3 – OPTIMAL START – The patient is jointly followed by an internist and a nephrologist. As the disease advances, they discuss choices, and the patient chooses home PD. An embedded PD catheter is placed. When the GFR reaches around 12 cc/min, the patient is sent for training. Hospitalization is avoided.

Timing is not eGFR alone. Symptoms, complications, trajectory, access, and readiness matter.

TWO TYPES OF DIALYSIS

HEMODIALYSIS



IN CENTER OR HOME

PERITONEAL

DONE AT HOME

Modality choice should start early

Transplant

Best survival option

Peritoneal dialysis

Home therapy using the peritoneal membrane; often flexible and autonomy-preserving.

Home hemo

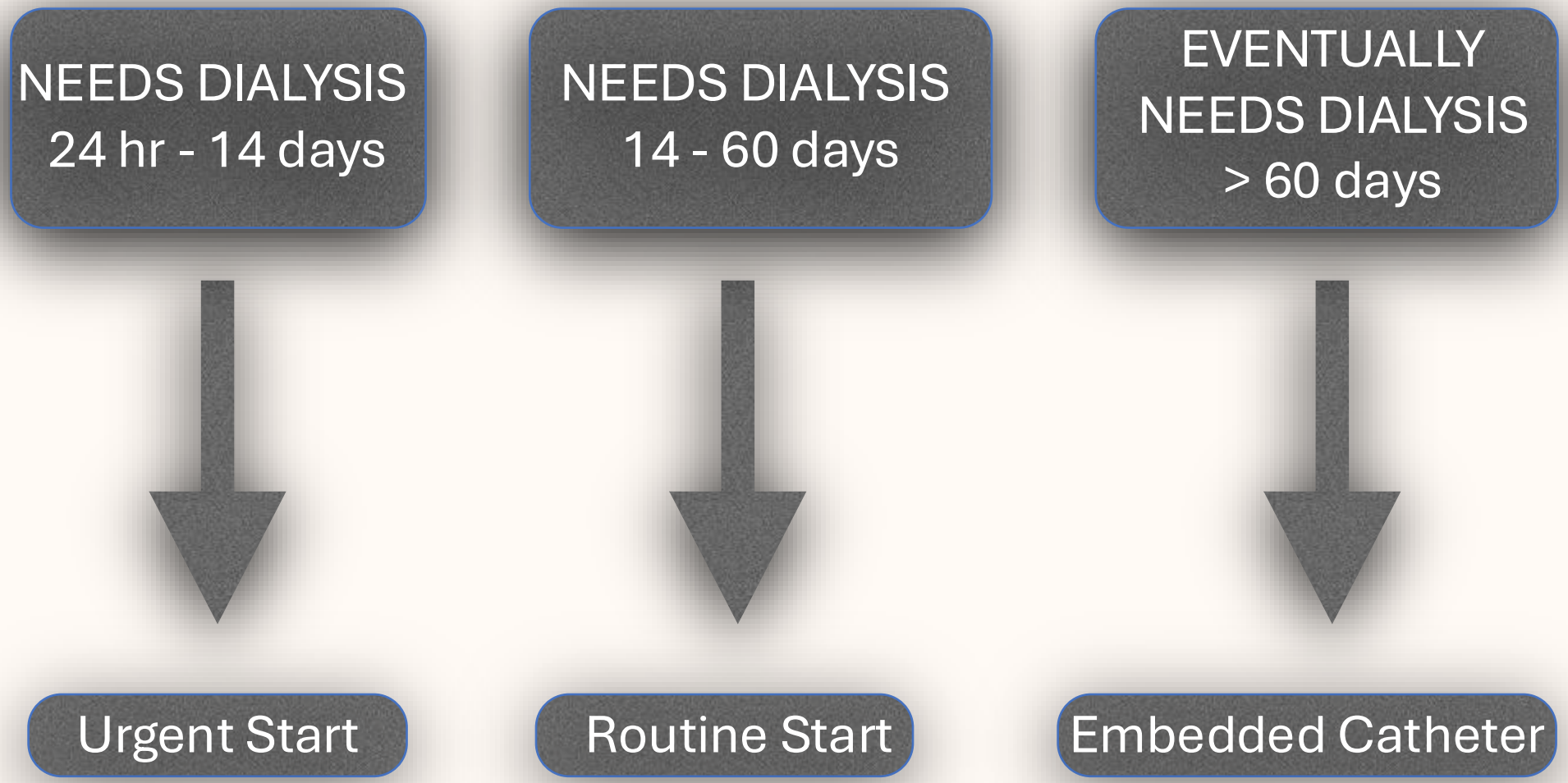
Flexible HD with training; can fit patients who want more control.

In-center HD

Staff-delivered therapy; plan fistula or graft early if this is the route.

Conservative care

Active symptom-focused care without dialysis; not "no care."

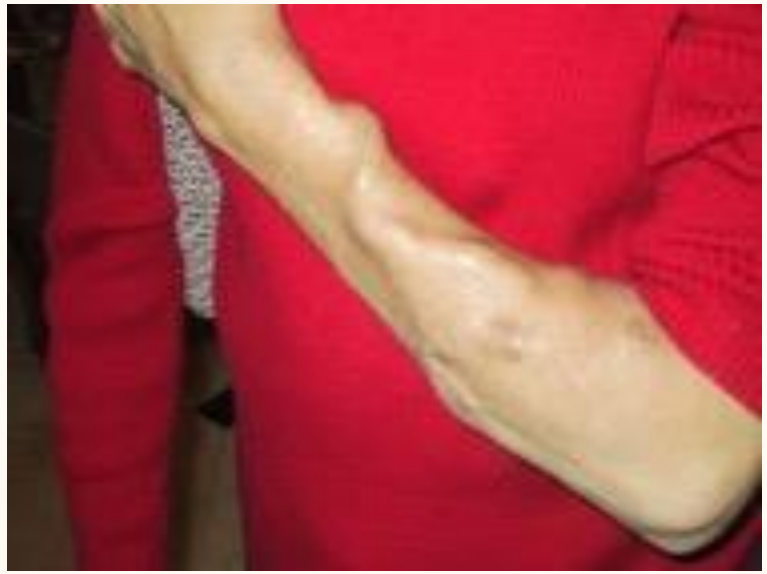

NEEDS DIALYSIS
24 hr - 14 days
NEEDS DIALYSIS
14 - 60 days
EVENTUALLY
NEEDS DIALYSIS
> 60 days
Urgent Start
Routine Start
Embedded Catheter

Why home is now preferred when feasible

- Home therapies (PD or Hemo) can reduce travel burden and preserve autonomy.
- Treatment can be integrated into work, family, sleep, and symptom patterns.
- PD and home HD require education, safety screening, training, and support.
- Home is a choice when the patient, home setting, and clinical situation fit.
- Every modality discussion should include transplant and conservative care.

Hemodialysis access is a timeline

- ❑ Education
- ❑ Vein preservation
- ❑ Mapping
- ❑ AV fistula placement
- ❑ Maturity
- ❑ Cannulation

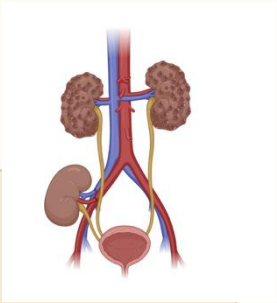


- ❑ Do not use forearm veins casually in advanced CKD. Preserve veins early if dialysis may be needed.
- ❑ Late referral leads to catheter starts, infections, centra vein stenosis, hospitalization, decreased home and transplant options

Myths

- You cannot do PD with
  - Obesity
  - Advanced Diabetes
  - Advanced Age
  - Prior Abdominal Surgery
- PD can’t be started immediately after catheter placement.
- PD can’t be resumed immediately after abdominal surgery.
- The moon is made of cheese.

Transplant and paired donation



Transplant-first

Eligible patients should be referred before dialysis when possible. Preemptive transplant avoids many dialysis complications.

Living donor

A living donor can shorten wait time and improve outcomes. Ask early and normalize the conversation.

Paired exchange

An incompatible donor may still help through a swap or chain. Incompatibility is not the end of the story.

Segev et al. JAMA 2005

Timeline, 1966-2005: making kidney care better

- 1945 – First dialysis by Willem .J. (Pim) Kolff in the Netherlands
- 1954 – First kidney transplant – Joseph Murray at The Brigham
- 1960 – First chronic hemodialysis – William Schribner in Seattle

1966	1976	1994	2001	2002	2005
Brescia-Cimino fistula	CAPD concept	MDRD	RENAAL / IDNT	AASK / HEMO	Paired donation

Timeline, 2010-2024: changing kidney outcomes

2010	**IDEAL**	Do not start dialysis early by eGFR alone.
2015	**SPRINT**	BP intensity enters CKD cardiovascular discussion.
2019	**CREDENCE**	SGLT2 kidney outcome trial in diabetic CKD.
2020	**DAPA-CKD**	SGLT2 benefit with and without diabetes.
2020	**FIDELIO**	Finerenone kidney and CV benefit in diabetic CKD.
2023	**EMPA-KIDNEY**	SGLT2 evidence broadens further.
2024	**FLOW / KDIGO**	GLP-1 kidney outcomes and updated CKD framework.

Take home message

CKD definition
Kidney disease means an abnormal kidney test or kidney structure problem that persists and matters for health.

SGLT2 inhibitor
This lowers pressure inside the filters and protects the heart-kidney system.

Transplant swap
An incompatible donor can still help through a swap or chain.

Albuminuria
Protein in the urine is a glomerular stress signal

Dialysis timing
We start when symptoms, safety, and readiness line up.

Conservative care
This is active kidney care focused on symptoms and goals without dialysis.

Primary care checklist

- ✓ Every CKD patient: eGFR trend, ACR, BP, diabetes status, medication safety, cardiovascular risk.
- ✓ Every albuminuric CKD patient: RAS blockade if tolerated, SGLT2 inhibitor eligibility, BP, and sodium strategy.
- ✓ Every Type 2 diabetic CKD patient: SGLT2 inhibitor, metformin appropriateness, GLP-1 RA discussion, finerenone eligibility if persistent albuminuria.
- ✓ Every advanced CKD patient: anemia, acidosis, potassium, bone-mineral disease, nutrition, vaccines, symptoms, modality education.
- ✓ Every kidney failure trajectory: transplant first if eligible, home options second, plan access, conservative care option.

Selected landmark sources

- 1994 — Modification of Diet in Renal Disease Study (MDRD) — eGFR equation
- 2002 — African American Study of Kidney Disease and Hypertension (AASK)-ACEi slows progression
- 2002 — HEMO Study — Higher dialysis dose ineffective
- 2005 — Kidney Paired Donation Study — Expanded incompatible transplant opportunities
- 2010 — IDEAL Trial — Early dialysis showed no benefit
- 2019 — CREDENCE Trial — SGLT2 inhibitors protect kidneys
- 2020 — DAPA-CKD Trial — Dapagliflozin reduced CKD progression
- 2020 — FIDELIO-DKD Trial — Finerenone reduced renal outcomes
- 2022 — Kidney 2023 — EMPA-KIDNEY Trial — Empagliflozin broadly preserved kidney function
- 2024 — FLOW Trial — Semaglutide improved kidney outcomes
- 2024 — Kidney Disease: Improving Global Outcomes CKD Guideline (KDIGO

Our mutual goals

- Identify risk early
- Protect the kidney-heart system
- Avoid preventable harm
- Early patient choice
- Avoid crashers

Recognize Protect Plan Refer wisely