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WHITE PAPER

The Importance of AI in the Management of Chronic Kidney Disease

Table of Contents

Executive Summary

Chronic Kidney Disease (CKD) is a complex, clinically dynamic, and progressive condition that despite being increasingly common, suffers from low awareness and treatment, fragmented care, poor health outcomes, and high healthcare costs.

Managing it successfully demands close surveillance and monitoring and that clinicians balance CKD's clinical, medical, and psychological effects while simultaneously avoiding its excess of potential adverse events.

CKD has traditionally been overlooked in many value-based care programs but in 2019, CMS announced five new payment models for kidney disease. The aim of these new models is to eliminate the traditional fragmentation of kidney care, incentivize and reward comprehensive care management, promote better outcomes and reduce healthcare costs. Such value-based programs can encourage the formation of comprehensive care management programs for CKD, which can have a significant impact on outcomes and costs.

AI-based models are ideally suited to enable such efforts. Data from EHRs, lab tests, and medical and pharmacy claims can be used in models designed to address CKD's specific challenges.

AI-Based Model Portfolio for Managing CKD

Care Mgt Goal	Model Focus	Specific Prediction
Promote Early Diagnosis	**At-Risk Diabetics**	Individuals likely to develop CKD in the near term
	Suspect CKD Patients	People likely to have undiagnosed CKD
Slow CKD Progression	**Rapid Progression**	Patients with CKD who are at risk of rapid progression in next 1-2 years
	Medication Adherence	Monitor medication adherence and predict adverse events due to poor adherence
Anticipate & Avoid Complications and Adverse Events	**CKD Complications**	Identify CKD patients at-risk for specific complications in the near term (e.g. hyperkalemia, anemia)
	Hospital-Acquired Complications	CKD patients who (if admitted) face a higher risk of hospitalacquired complications (e.g. surgical site infection, acute kidney injury, sepsis)
	Nephrotoxic Medications	CKD patients at-risk for complications from nephrotoxic medications

Integrating AI-based models with comprehensive CKD programs can catalyze the delivery of value-based care leading to better health outcomes, lower costs, and improved quality of life for patients living with chronic kidney disease.

Chronic Kidney Disease

Chronic kidney disease (CKD) is abnormal kidney function (or structure) that indicates the kidneys cannot work at their full capacity. It is characterized by the progressive loss of kidney function that leads to irreversible damage to the kidneys and begins with a decline in the glomerular filtration rate and/or albuminuria.

CKD raises a patient's risk for several life-threatening conditions and complications. If not treated, it can result in end-stage renal disease (ESRD), a severe complication often requires dialysis or renal transplant.

Kidney disease is measured and categorized using a blood test, the eGFR (estimated glomerular filtration rate) and a urine test, the ACR (albumin-tocreatinine ratio). Together, they define CKD stage and overall risk level.

- eGFR estimates how much blood is 'cleaned' by the kidneys in one minute. Because the average normal eGFR is 100, the eGFR it is a percent of normal kidney function.
- ACR looks for signs that protein is leaking into the urine (a condition called albuminuria or proteinuria). This is an important sign of kidney damage.

CKD often has no symptoms until the later stages. The most common causes of CKD are diabetes and hypertension, and 1 in 2 people with diabetes have CKD.

The Role of the Kidneys

The kidneys filter out the blood to produce urine which contains waste products, water, and electrolytes. The kidneys also make hormones that help with blood production, blood pressure regulation and hydration, and bone and mineral balance. They also regulate acid base, water, and electrolyte balance.

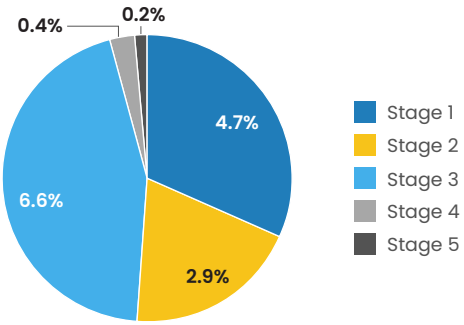
Prevalence of Chronic Kidney Disease

37 million people—15 percent of adults—are estimated to have CKD and another 20-25 million are at increased risk for developing it. The number of people with CKD has doubled each of the last two decades.

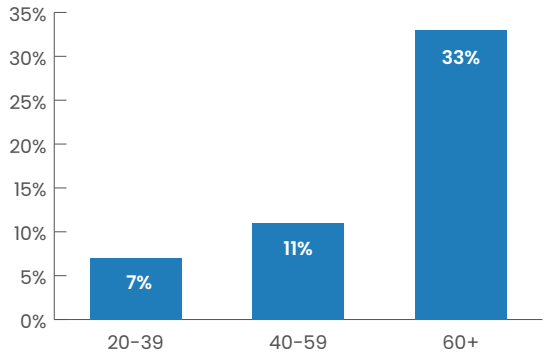
Stage	Description	GFR (mL/min/1.73 m2)
1	Normal kidney function but structural abnormalities or urine test results point to kidney damage	≥ 90
2	Mildly reduced kidney function	60-90
3a	Mild-to-moderate loss of function	45-60
3b	Moderate loss of kidney function	30-45
4	Severely reduced kidney function	15-30
5	Very severe or end stage renal failure	<15

Of CKD's five stages, Stage 3 is the most prevalent. While CKD can occur at any age, older adults are at higher risk. As CKD progresses, it may lead to kidney failure or end stage renal disease (ESRD). Nearly half a million people have kidney failure and require dialysis or kidney transplant to stay alive.

CKD Prevalence by Stage



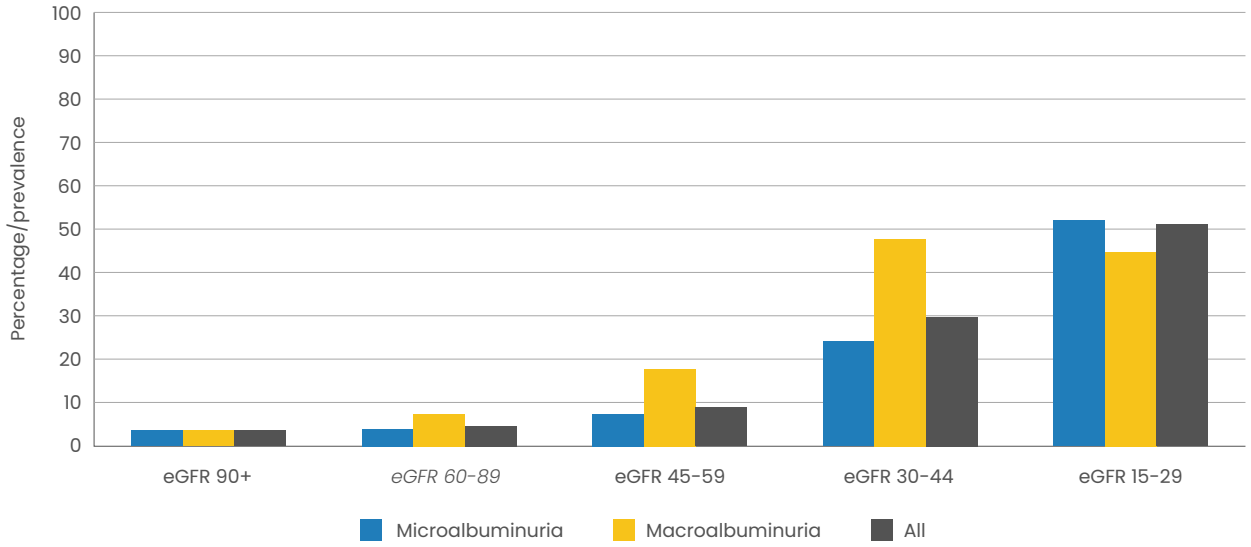
CKD Prevalence by Age



Low Awareness and Treatment of CKD

Despite increased prevalence, CKD remains under-recognized by providers and patients, especially in its early stages when patients are largely asymptomatic. Most (9 in 10) adults with CKD are not aware of their condition, and 1 in 2 people with extremely low kidney function (but not on dialysis) do not know they have CKD. This level of awareness is much lower than for other chronic illnesses. For example, with diabetes and hypertension, more than 70% of affected patients are aware of their diagnosis.

Percentage of People with CKD Who Were Aware of Their Disease by Severity of Their Disease (eGFR and Albuminuria), 1999-2012
National Health and Nutrition Examination Survey



Such widespread under-recognition of CKD leads to under-treatment. This is especially problematic since many of the adverse outcomes of CKD can be prevented or delayed with treatment and risk factor modification in the earlier stages of disease. Early detection of people suspected to have (or develop) CKD is paramount.

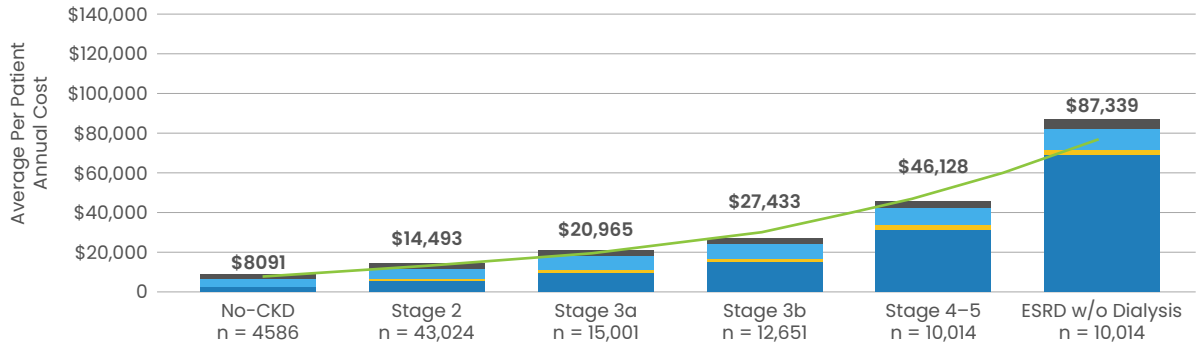
Health Economics and Outcomes

CKD is a complex co-morbid condition with a high mortality rate. Patients experience excess cardiovascular events and other adverse outcomes (even in early disease stages) and carry a heavy burden of morbidity, mortality, healthcare utilization, and costs.

Healthcare costs increase as CKD progresses with costs in later stages more than 5-10x higher than someone without CKD. These added costs are primarily due to hospitalizations, which reflect the severe complications that often accompany reduced kidney function.

Hospitalization rates rise dramatically with advanced disease, with the most frequent reasons for admission being hyperkalemia, heart failure, and volume overload. Should a patient be admitted, they then face higher rates of hospital-acquired complications and are more than twice as likely to experience a 30-day readmission. For Medicare, the annual costs to treat kidney disease are substantial; they consume 28 percent of Medicare's expenditures and are expected to increase in the coming years.

Medicare (aged ≥65 years)



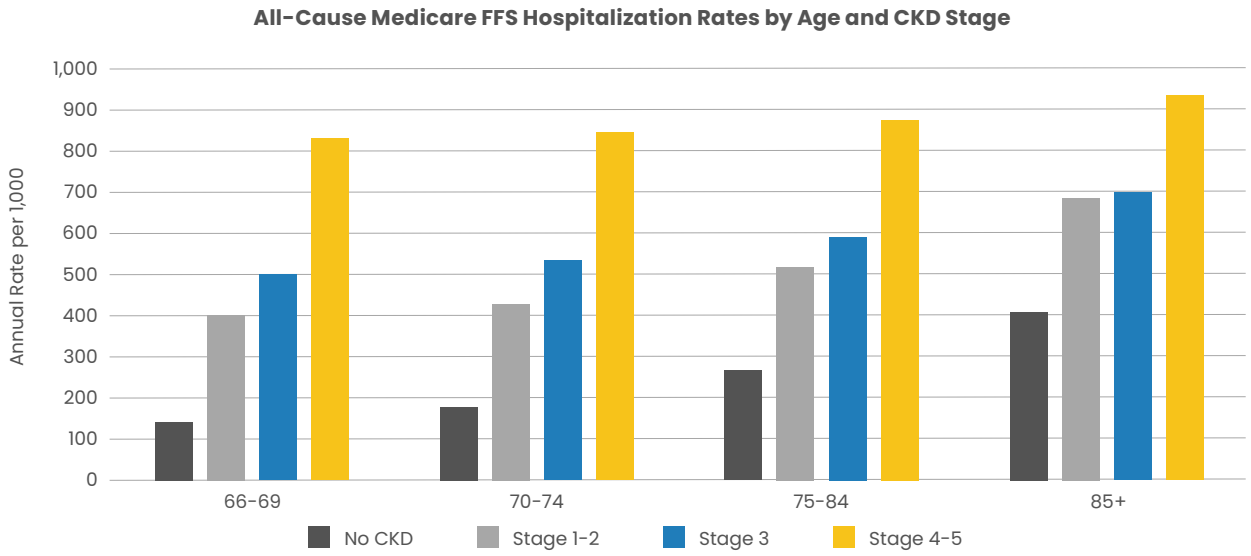
	No-CKD n = 4586	Stage 2 n = 43,024	Stage 3a n = 15,001	Stage 3b n = 12,651	Stage 4–5 n = 10,014	ESRD w/o Dialysis n = 10,014
Rx	$934	$2153	$2629	$2976	$3597	$4193
OP	$4689	$6426	$7386	$8043	$9169	$11,589
ED	$312	$605	$861	$1096	$1344	$1782
IP	$2156	$5309	$10,088	$15,319	$32,018	$69,775

CKD Stages

CKD Disease Progression

The course of CKD progression varies substantially by patient and is influenced by several individual and dynamic risk factors. Rapid progression is associated with worse clinical outcomes (e.g., cardiovascular events and death) independent of current eGFR levels.

A significant portion of patients with mild-tomoderate CKD do not progress in a predictable, slow linear pattern. Some barely progress while others have a much faster decline. In adults with mild-to-moderate CKD, rapid progression (i.e. within 2 years) occurs in ~ 1 in 4 patients with diabetes and ~ 1 in 7 without diabetes.



To avoid further loss of kidney function (and its accompanying adverse outcomes), it is vital to identify patients who are likely to progress more rapidly. Such patients would benefit from more frequent and intensive monitoring and intervention, but CKD's current staging system does not identify patients at greatest risk for rapid progression or complications.

Complications of CKD

Reduced kidney function affects almost every organ system. This is reflected in the complications that develop as CKD progresses, which often go unrecognized or are inadequately managed during the earlier stages and contribute to CKD's high morbidity and mortality and poor quality of life.

Complications and Effects of Progressive CKD	
Cardiovascular	Hypertension, congestive heart failure, pericarditis, atherosclerosis, arrhythmias, metastatic calcifications
Endocrine	Calcium-phosphorous imbalances, hyperparathyroidism, metabolic bone disease, thyroid function, carbohydrate metabolism, hypophyseal-gonadal dysfunction, decreased insulin metabolism, erythropoietin deficiency
Fluid & Electrolyte Imbalance	Fluid retention, hyperkalemia, hypermagnesemia, hyperphosphatemia, hypocalcemia, metabolic acidosis
Gastrointestinal	Anorexia, nausea, vomiting, delayed gastric emptying, GI bleeding, ulcers
Hematologic	Anemia, bleeding complications, immune suppression
Musculoskeletal	Renal bone disease, amyloidosis
Neurologic	Lethargy, tremor, asterixis, restless legs syndrome, seizures, motor weakness, peripheral neuropathy
Dermatologic	Pruritus, altered pigmentation
Psychological	Depression, anxiety, psychosis

For example, hyperkalemia (HK) is a challenging and not uncommon problem for clinicians caring for patients with CKD. Detected in more than 35% of patients and often asymptomatic, it is one of the more important clinical abnormalities, as it can lead to cardiac arrhythmias and sudden cardiac death. Its adverse impact is reflected in substantially higher healthcare costs; a study of CKD showed the annual costs for patients with HK were $56,002 as compared to $23,653 for a control cohort without hyperkalemia.

Treating and Managing CKD

The direct management of CKD focuses on using renin angiotensin aldosterone blockade (RAAS) inhibitors (which block a hormone system that can worsen kidney injury) and controlling blood pressure. Diuretics are also helpful to control blood pressure (along with water and salt retention) and patients sometimes need several blood pressure medications to get to goal.

Clinical management also includes addressing comorbid conditions such as diabetes and cardiovascular risk factors. Controlling diabetes is crucial to slowing CKD. Lowering the risk of heart disease is also vital since CKD is strongly associated with heart disease and they both influence each other.

Clinical management requires close monitoring and surveillance to avoid complications. For example:

- Hyperkalemia (serum potassium >5.0 mEq/L) is not only caused by the disease, it can also be brought on by the drugs used to treat it. Mortality rates are more than double in CKD patients with hyperkalemia than without it (24.9% vs 10.4%).
- Anemia is another widely recognized complication. Anemia is associated with increased cardiovascular disease, CKD progression, hospitalization, and mortality.

Monitoring and surveillance also includes medications. Several medications are nephrotoxic, meaning they can cause or worsen kidney dysfunction and should be avoided (including common over-the-counter medications and supplements, which can also cause nephrotoxicity).

As kidney dysfunction progresses, medications can need dose adjustments to prevent them from accumulating to high levels. Medications may also need stopped completely, as they can become very toxic (e.g. Metformin) or cause harm to kidneys if they are not dose adjusted (e.g. antibiotics).

Patient education and support for self-management are also essential with a multidisciplinary approach that includes nutritionists, renal dieticians, exercise physiologists, social workers, and life coaches.

A Continuum of Comprehensive CKD Care

Comprehensive CKD care begins with early detection. It allows low-cost interventions, patient education, and care management that can reduce comorbidities, limit adverse events, and reduce progression and the need for dialysis or kidney transplantation. And yet, earlier detection and management is a critical gap. Among Medicare beneficiaries, only 39% of diabetics and 6% of patients with hypertension had testing and only 40% with diabetes and hypertension had testing.

Collaboration between PCPs and nephrologists is also vital. It can result in reduced hospitalizations, fewer complications, avoidance of comorbidities, and delayed progression and dialysis. However, 041% of ESRD patients did not see a nephrologist before initiating dialysis, despite clinical practice guidelines.

For patients that progress to ESRD, planned initiation is crucial. Better outcomes and cost reductions can come from proper renal replacement therapy (RRT) preparation, greater use of Peritoneal Dialysis (PD), and pre-emptive transplant. Earlier preparation can also reduce initial hospital costs (including associated surgeries and complications) as well as other admissions and readmissions, which can be high during the first several months of dialysis. And yet, nearly two thirds of dialysis initiations occur in an inpatient setting.

Potential Health Economic Impacts

Effective interventions can improve outcomes and reduce healthcare costs in CKD patients. For example, a CKD intervention among Maryland beneficiaries of a health plan's PCMH program showed substantial decreases in admissions and readmissions. For CKD patients with stages 3-5, hospital admissions were reduced between 30 to 45% (depending on stage), readmissions declined by more than 70%, and healthcare costs declined by approximately 20%.

And among patients starting dialysis, intensive care coordination resulted in a 23% reduction in hospital admissions, 9% more patients selecting home dialysis, fewer missed treatments, and a 10% reduction in healthcare costs.

The Next Generation - Value-Based Care for CKD

CKD has traditionally been overlooked in value-based care programs. In part, this due to artificial boundaries that have traditionally segmented the management of kidney disease. It has also been challenging for payers to invest in long-term outcomes when beneficiaries leave before the economic impact of investments of better outcomes have been achieved.

In July of 2019 CMS announced the Advancing American Kidney Health initiative designed to increase transplantation, home dialysis, and value-based models starting in 2020. The initiative includes five new payment models aimed at transforming kidney care.

Healthcare organizations now have an opportunity to invest in broader kidney programs that cover a larger spectrum of the disease and creating comprehensive care delivery and population health management programs capable of generating better health outcomes.

Leveraging AI-Based Models in Value-Based Care for CKD

AI-based models are ideally suited to help clinicians and care teams in such programs. Data from electronic health records and medical and pharmacy claims can fuel CKD models designed to monitor key changes and anticipate and avoid specific adverse impacts.

Comprehensive CKD programs can use AI-based models tailored to the specific goals of their program and the needs of their populations:

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These models address CKD's specific challenges and fuel the delivery of comprehensive, value-based care that promotes health, reduces costs and leads to better quality of life for patients living with chronic kidney disease.

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Carol McCall is a health actuary and population health executive whose specialty is finding ways to combine innovations in health services, predictive modeling, and business models. Her aim is to rethink the traditional notions of care, accelerate the ability to learn what works, and catalyze sustainable value-based ecosystems and a culture of health.

Carol's experience spans actuarial work, health plan and PBM operations, innovations in health services, start-ups, predictive analytics and AI, health economics and outcomes research, the psychology of behavior change, personalized medicine diagnostics, national health information policy, and public health. Prior to joining ClosedLoop, Carol earned her MPH from George Washington University and served as a strategic advisor and consultant to health analytic, HIT companies and women-led health start-ups with Springboard Enterprises.

Carol also served as Chief Strategy and Product Officer for GNS Healthcare and as Chief Innovation Officer for Vanguard Health Systems. At Humana, Carol led R&D innovstion where she pioneered Humana's use of sophisticated analytics to build a portfolio of predictive, knowledge discovery, and simulation models. She also launched Humana's personalized medicine innovations and led their Health Services Research Center (HSRC). In other roles at Humana, Carol served as Chief Information Officer and as VP of Pharmacy Management.

In policy and advisory roles, Carol served a four-year term on the National Committee on Vital and Health Statistics and as co-chair of its Quality Workgroup; as a member of the HSRC's governing board; and as an advisor to the High-Risk Plaque Scientific Program Board. Carol is a Fellow of the Society of Actuaries, a member of the American Academy of Actuaries, and a member of the Golden Key International Honors Society.