EPH134

Impact of delayed or missing diagnosis of chronic kidney disease

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Objectives

To identify evidence on the current diagnosis patterns of chronic kidney disease (CKD), the long-term impact of delayed or missed diagnosis, and how early diagnosis and treatment could help mitigate the overall burden of CKD.

Background

- CKD is a progressive disease that represents a substantial clinical and economic burden. As the population ages, the burden of CKD is expected to increase further.
- Patients in the early stages of CKD often experience few or no symptoms and may therefore remain undiagnosed until their condition progresses. A lack of clinical diagnoses may delay initiation of treatment to slow progression.

Methods

- A search of Embase (via Ovid) and the gray literature was conducted to identify studies on the epidemiological, clinical, economic, and humanistic burden of CKD published between 2015 and 2024.
- Eligible studies reported on the screening and diagnosis rates of CKD, clinical and economic burden of delayed diagnosis, benefits of early treatment, and cost-effectiveness of CKD screening.

Results

- Current evidence suggests that the progression of CKD is significantly impacted by screening, diagnosis, and appropriate care, but that screening and diagnosis in current practice lags behind guideline recommendations (**Figure 1**).

Screening and diagnosis

- Between 19% and 33% of patients with hypertension, diabetes, and/or cardiovascular disease (CVD) did not receive timely renal testing.[1,2]
- Very few patients with early-stage CKD have clinical diagnoses (**Figure 2**).
- The median time from laboratory values confirming stage 3 CKD (ie, 2 estimated glomerular filtration rate [eGFR] measurements ≥30 and <60 taken 91–730 days apart) to diagnosis was nearly 5 years.[3]

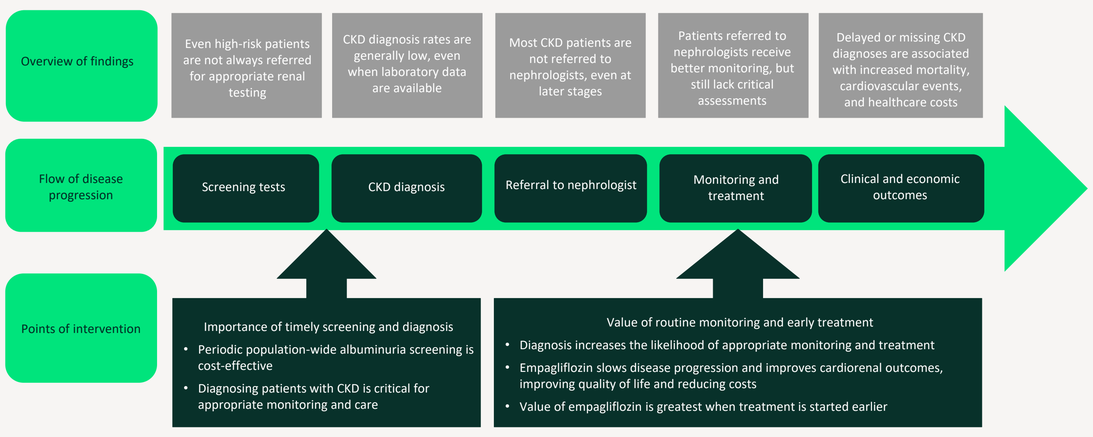
Burden of delayed diagnosis and benefits of early treatment

- Receiving a CKD diagnosis was associated with significantly increased rates of disease monitoring and prescription fill rates for both CKD and diabetes medications.
- A higher proportion of patients had stable eGFR (ie, increase or no change) after receiving a CKD diagnosis (46.6%) compared to before diagnosis (37.8%, *P*<0.001), while a lower proportion had a rapid decline (ie, annual eGFR decrease ≥4; 39.2% vs 47.1%, *P*<0.001).[4]
- Delayed diagnosis, which delays both appropriate nephrology referral and treatment, is associated with an increased risk of kidney failure,[4] cardiac events,[4] hospitalization,[4,5] and mortality[5,6] (**Table 1**).

Cost-effectiveness of population-wide CKD screening

- Recent economic models reported that population-wide CKD screening is cost-effective in the general population,[7-13] contradicting earlier models that did not incorporate newer, more effective treatments or cardiovascular outcomes (**Table 2**).
- One model reported that the addition of sodium-glucose cotransporter 2 (SGLT-2) inhibitors was more cost-effective than angiotensin-converting enzyme inhibitors (ACEIs)/angiotensin receptor blockers (ARBs) alone,[9] while another model reported that adding SGLT-2 inhibitors to the treatment regimen resulted in cost savings across age and frequency of screening.[13]
- Annual CKD screening decreases the lifetime incidence of CVD by 8%,[12] non-fatal myocardial infarction (MI) by 5%,[10] and non-fatal stroke by 4%.[10]

Figure 1. CKD progression framework: Overview of current evidence and points of intervention



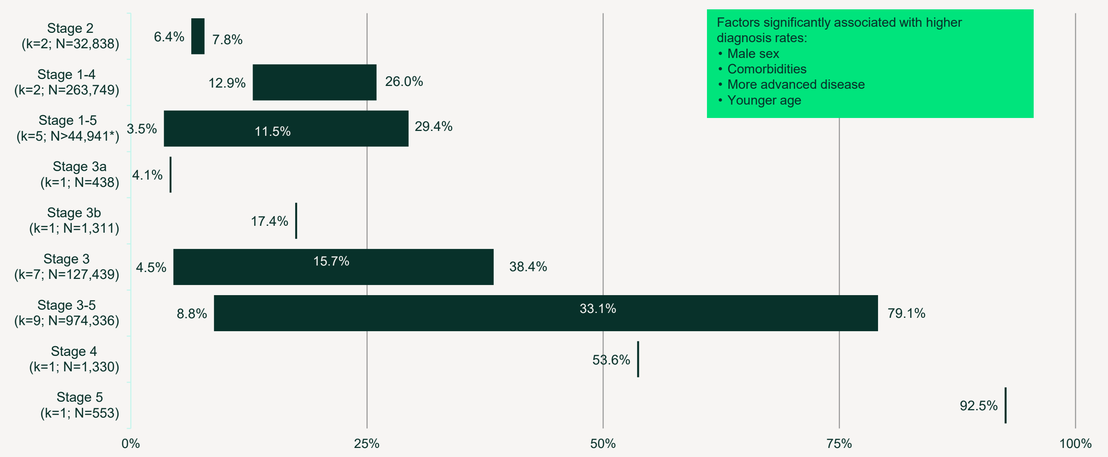
Key: CKD – chronic kidney disease.

Limitations

- Although this review sought to be comprehensive, it was not systematic. However, we were unable to identify any recent systematic reviews on this topic, and the recent advances in understanding the complex downstream consequences of undiagnosed CKD have resulted in an abundance of new research in a limited amount of time.
- Despite an increase in the studies assessing diagnostic rates of CKD, there is still somewhat limited evidence regarding the long-term clinical impacts of delayed or missing diagnoses. However, identified studies consistently reported that delayed or missing CKD diagnosis had a negative impact on key clinical outcomes, including kidney failure, cardiovascular outcomes, and mortality.

Results

Figure 2. Range and median diagnosis rate by stage of CKD



Values displayed are the minimum, median, and maximum diagnosis rates from the literature. If only 1 or 2 estimates are displayed, they represent the only identified estimates for that stage of disease.
Key: CKD – chronic kidney disease; k – number of separate analyses; N – total number of patients diagnosed with CKD.
* One study provided a weighted estimate of a 10.0% diagnosis rate but did not provide the raw number of patients diagnosed with CKD.
Sources: Stage 2[14,15]; stage 1-4[15,16]; stage 1-5[17-20]; stage 3a[15]; stage 3b[15]; stage 3[3,17]; stage 3-5[15,21-24]; stage 4[15]; stage 5[15]; and association by sex,[3,17,18,23,25] comorbidity,[3,19,22,23] more advanced disease,[3,19,23] and younger age.[3,23]

Table 1. Impact of delayed diagnosis and treatment on clinical outcomes in CKD patients

Reference	Country	Comparison	Stage	N	Outcome	Results
Tangri 2023[4]	US	1-year diagnostic delay, HR (95% CI)	Stage 3	26,851	Kidney failure	1.63 (1.23, 2.18)
					MI and/or stroke	1.08 (1.03, 1.13)
					MI, stroke, and/or HHF	1.08 (1.04, 1.13)
Molnar 2023[6]	Canada	Late vs timely CKD screening	Initiating dialysis	1,850	90-day mortality	16.8% vs 10.8%
Lonnemann 2017[5]	Germany	Late vs timely nephrology referral	Stage 3	11,861	Hospital admissions PPPY	2.07 vs 1.35, *P*=0.00001
					Mortality	23.1% vs 12.6%, *P*=0.006
			Stage 4	2,746	Hospital admissions PPPY	1.62 vs 1.16, *P*=0.025
			Stage 5	706	Hospital admissions PPPY	1.87 vs 1.69, *P*=0.11
			Dialysis	3,371		

Key: CI – confidence interval; CKD – chronic kidney disease; HHF – hospitalization for heart failure; HR – hazard ratio; MI – myocardial infarction; PPPY – per patient per year; US – United States.

Table 2. Cost-effectiveness of CKD screening in the general population

Reference	Country (perspective,[a] discount rate)	Type of screening[b]	Age	Screening interval	Added to ACEIs/ARBs[c]	Cost per QALY	WTP threshold
Kairys 2022[8]	Germany (3.5%)	UACR (2 tests at 1 follow-up)	Adults	2 years	None	€ 3,331.77 -€ 6,175.89[d]	NR
Cusick 2023[7]	US (3%)	UACR	35	One time	None	$64,100	$100,000; $150,000
				One time	SGLT2i	$95,800	
				10 years		$98,400	
				5 years		$183,700	
			45	One time	None	$55,600	
				One time	SGLT2i	$92,800	
				10 years		$93,100	
				5 years		$153,300	
			55	One time	None	$46,700	
				One time	SGLT2i	$86,300	
				10 years		$92,500	
				5 years		$121,100	
			65	One time	None	$55,700	
				One time	SGLT2i	$82,100	
				10 years		$89,800	
				5 years		$105,000	
			75	One time	SGLT2i	$82,200	
Konta 2024[9]	Japan (2%)	UACR vs UPCR	60	Repeated (unclear frequency)	None	¥1,966,433[e]	¥5 million
					SGLT2i	¥1,765,599[e]	
Pouwels 2024[10]	Netherlands (costs 4%, health outcomes 1.5%)	At-home UACR	45-85	One time	SGLT2i, statin, diuretic, and/or beta-blocker (based on risk)	€ 9,225.00	€ 20,000
			45-65			€ 7,946.00	
			65-85			€ 10,310.00	
Zafarnejad 2024[13]	US (NR, 3%)	Cumulative sum statistic of eGFR	30	2 years	None	$21,680.06	$50,000-$100,000
				1 year		$15,614.33	
			60	2 years		$49,792.88	
				1 year		$40,123.97	
			30 or 60	1 or 2 years	SGLT2i	Cost saving	
Wen 2025[12]	China (Societal, 3%)	UACR + SCr	45	One time	None	$18,980	$35,501
				10 years		$15,541	
				5 years		$15,160	
				2 years		$12,452	
				1 year		$10,588	
			55	One time		$18,421	
				10 years		$18,607	
				5 years		$15,191	
				2 years		$13,881	
				1 year		$13,081	
			65	One time		$17,977	
				10 years		$16,861	
				5 years		$16,620	
				2 years		$13,431	
				1 year		$11,463	
Tangri 2025[11]	International, 31 countries (Payer, specific to each country)	2 SCr tests	45	Annual for 10 years	None	Below WTP in all countries except Saudi Arabia	Specific to each country
			65			Below WTP in all countries	
		UACR + 2 SCr tests	45			Below WTP and SCr alone in all countries	
			65				

Key: ACEI – angiotensin-converting enzyme inhibitor; ARB – angiotensin receptor blocker; CKD – chronic kidney disease; eGFR – estimated glomerular filtration rate; QALY – quality-adjusted life-year; RRT – renal replacement therapy; SCr – serum creatinine; SGLT2i – sodium-glucose cotransporter 2 inhibitor; UACR – urine albumin-to-creatinine ratio; UPCR – urine protein-to-creatinine ratio; US – United States; WTP – willingness-to-pay.
[a] All studies used lifetime as the time horizon and the national healthcare system as the perspective unless otherwise stated.
[b] Comparator is usual care unless otherwise stated.
[c] All studies included ACEIs and/or ARBs in treatment received after screening. This column describes any additional treatments.
[d] Includes cost of testing and treatment minus saved costs from averted/delayed RRT.
[e] This study included only non-diabetic patients, rather than the general population. Because guidelines already indicate that screening is cost-effective and should be conducted in diabetic patients, this study of non-diabetic patients has been included alongside the other studies of screening in the general population.

Conclusions

- Earlier diagnosis of CKD allows timely intervention to slow progression, thereby improving clinical outcomes and decreasing costs.
- Most early-stage CKD patients, as well as many later-stage CKD patients, are not diagnosed, despite having relevant laboratory data available.
- Although data on the long-term impacts are sparse, evidence consistently suggests that earlier diagnosis is associated with improved clinical outcomes and decreased costs.
- Efforts should be made to increase albuminuria screening and diagnosis rates, facilitating earlier initiation of effective treatment.

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