

Clinical Practice Guideline

The Management of Chronic Kidney Disease not Requiring Renal Replacement Therapy in General Practice

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Summary

Background: Chronic kidney disease (CKD) is common in the German adult population, with a prevalence of 10%. This guideline, updated on the basis of current scientific evidence, contains recommendations for the management of CKD in general practice.

Methods: The updated guideline is based on a review and assessment of source guidelines and systematic reviews concerning individual questions. The recommendations were agreed upon in a moderated two-stage nominal group process by the mandate holders of the participating specialist societies, along with patient representatives.

Results: The risk of progression to renal failure requiring renal replacement therapy should be assessed with a risk score. Assessing this risk and determining the indication for treatment with SGLT2 inhibitors both require measurement of the urinary albumin-to-creatinine ratio. Pharmacotherapy is not recommended for

asymptomatic hyperuricemia. An initial ultrasonographic examination of the kidneys and urogenital system is now recommended for all patients. The vaccination recommendations that differ for people with CKD have been integrated into the guideline.

Conclusion: The risk assessment of CKD and the treatment options have been expanded. The updated guideline can improve primary care for patients with CKD and the selection of patients for interdisciplinary care.

Cite as:

Kiel S, Negnal M, Stracke S, Fleig S, Kuhlmann MK, Chenot JF: The management of chronic kidney disease not requiring renal replacement therapy in general practice. Dtsch Arztebl Int 2025; 122: 49–54. DOI: 10.3238/arztebl.m2024.0230

It is estimated that around 10% of adults in Germany, or 8–10 million people, have chronic kidney disease (CKD) (1, 2). Prevalence increases with age; in settings such as general practice it is around 30% (3), while in nursing homes it can be up to 50% (1, 2, 4). CKD is defined by a persistently reduced estimated glomerular filtration rate (eGFR) below 60 mL/min/1.73 m² for more than 3 months, or an increased albumin–creatinine ratio (UACR) above 30 mg/g creatinine in a random urine sample with or without structural changes to the kidneys and persisting for the same length of time. The Kidney Disease: Improving Global Outcome (KDIGO) organization classifies CKD into five stages (G1–5) based on GFR and three stages (A1–3) based on albuminuria (*Figure 1*) (5, 6). For a diagnosis of CKD, at least one finding must be abnormal: If eGFR is greater than 60 mL/min/1.73 m² without albuminuria and without structural changes, CKD is not present. Patients with structural changes (e.g., cystic kidneys), kidney function above 60 mL/min/1.73 m², and no albuminuria are in disease stages G1A1 and G2A1. The majority of those affected are mainly cared for by their general practitioner. Every year around 12 000 additional

patients require long term dialysis and around 2000 kidney transplants are carried out (7). For the individual patient, the risk of progression to kidney failure is relatively low, but if this does occur, it has a major impact on the individual and on health care costs. In Germany there are 1380 nephrologists providing outpatient care (as of 2023, National Association of Statutory Health Insurance Physicians [Kassenärztliche Bundesvereinigung]). Good care for all kidney patients requires coordinated, staged management. The aim of this guideline update is to provide evidence-based recommendations to general practitioners for the prevention, screening, diagnosis, and treatment of CKD not requiring renal replacement therapy in adults, and for referral to specialist nephrologists, so that progression to kidney failure or emergency dialysis and the occurrence of complications may be prevented, or at least delayed for as long as possible.

Figure 1

Low risk

Moderate risk

High risk

Very high risk

GFR categories*¹

G1

G2

G3a

G3b

G4

G5

Normal or high

Mildly reduced*²

Mildly to moderately reduced

Moderately to severely reduced

Severely reduced

Kidney failure

≥90

60–89

45–59

30–44

15–29

< 15

Persistent albuminuria categories*³

A1

A2

A3

Normal to mildly reduced

Moderately reduced

Severely reduced

<30 mg/g
<3 mg/mmol

30–300 mg/g
3–30 mg/mmol

>300 mg/g
>30 mg/mmol

0.04

0.31–0.44

0.72–0.8

0.04

0.15–0.29

1.9–2.68

0.28–0.88

1.6

5.88

2.24–2.96

11.76

30.52

17.32–41.76

42.24

91.44

KDIGO categories with color coding of the risk of kidney failure. The risk figures, which usually are not shown, are calculated from the data in the source publication (6) and indicate the risk of renal failure per 1000 patients over the period of 1 year.

*¹ Description and range of estimated glomerular filtration rate (eGFR, mL/min/1.73 m²)

*² Compared to a young adult.

*³ Description and range of urinary albumin–creatinine ratio (UACR)

Methods

For the German version of the guideline the adapted terminology by KDIGO which is recommended by the German Society of Nephrology (DGfN) is used. The guideline published in 2019 was based on a systematic review of guidelines (9). For the present update, a literature search for updated guidelines up to December 2023 was carried out. The National Institute for Health and Clinical Excellence (NICE) guideline published in 2021 (10) and the KDIGO guideline updated in 2024 (5) were used as primary source guidelines. For certain individual topics, a systematic literature search was carried out. Further details are given in the Methods Report (1). The recommendations were agreed by the delegated representatives of the participating medical specialist societies and patient representatives (*eBox*) in a moderated two-stage group process.

Symptom-related investigations and procedure on initial diagnosis

Kidney function (eGFR) screening is not recommended, but there are many situations when testing of kidney function is recommended: for example, on the initial diagnosis of diabetes or high blood pressure, before prescribing nephrotoxic drugs or drugs that can accumulate when kidney function is impaired (e.g., methotrexate). Where eGFR is reduced, a distinction must be made between acute kidney disease (AKD) and CKD; this is usually easy to do clinically. For a diagnosis of CKD, a second eGFR determination after 3 months is required. From the age of 40 onward, a drop in eGFR by around 0.5–1 mL/min per year

is physiological. Thus, aging processes cannot always be reliably distinguished from CKD. eGFR is subject to both measurement variation and biological variation (approx. 5%), which in the threshold range can tip the result into a higher stage of CKD. A drop in eGFR of 20%–25% from baseline is considered to indicate clinically important progression exceeding the measurement variation (10). Where AKD is suspected and symptoms such as shortness of breath and edema are present, the patient should be admitted directly to hospital. If AKD is suspected but there are no acute symptoms, a check-up after a few days to 2 weeks is recommended.

eGFR is insufficient for an assessment of kidney health: it provides information about renal clearance, but not about the condition of the glomerular “filter” that retains proteins and cells in the blood. If blood proteins such as albumin enter the urine, this is a strong indication of glomerular damage. For this reason, the presence of albuminuria, hematuria, and/or elevated blood pressure should also be recorded in an assessment of kidney health.

The semiquantitative determination of proteinuria by urine dipstick test is not reliable enough, as it will not detect small quantities of albumin (microalbuminuria). The test for proteinuria should therefore be the albumin–creatinine ratio (UACR) in a random urine sample. Determining the UACR is important for assessing the risk of kidney failure and deciding whether to prescribe a sodium-glucose cotransporter 2 (SGLT2) inhibitor. It is an expensive test in relation to the laboratory budget (€3.80 as of July 2024) and is still too rarely performed. Once albuminuria has been ruled out, it does

not need to be measured again unless for a specific reason. If albuminuria is detected, further investigation or referral to a nephrologist should be considered. A check-up after 1 to 2 years is recommended.

To rule out hematuria, a dipstick test is recommended, since examination under the microscope is not really feasible in practice. If the result is positive, a second test after a few days is recommended because of the high percentage of false positive results (11). In only a small percentage of cases (< 10%) is hematuria caused by kidney disease, e.g., glomerulonephritis. A urological disease is more likely. Hematuria should be interpreted in conjunction with any other findings. The first step in investigating macrohematuria must always be urological.

A summary of the initial diagnostic pathway is shown in *Figure 2*. When CKD is first diagnosed, high blood pressure and diabetes should also be ruled out, or, if present, their management should be checked. A review of all prescribed and over-the-counter medications should be carried out, which should then be repeated at regular intervals, e.g., annually. Information on any dosage adjustments required can be found at www.dosing.de (German-language website).

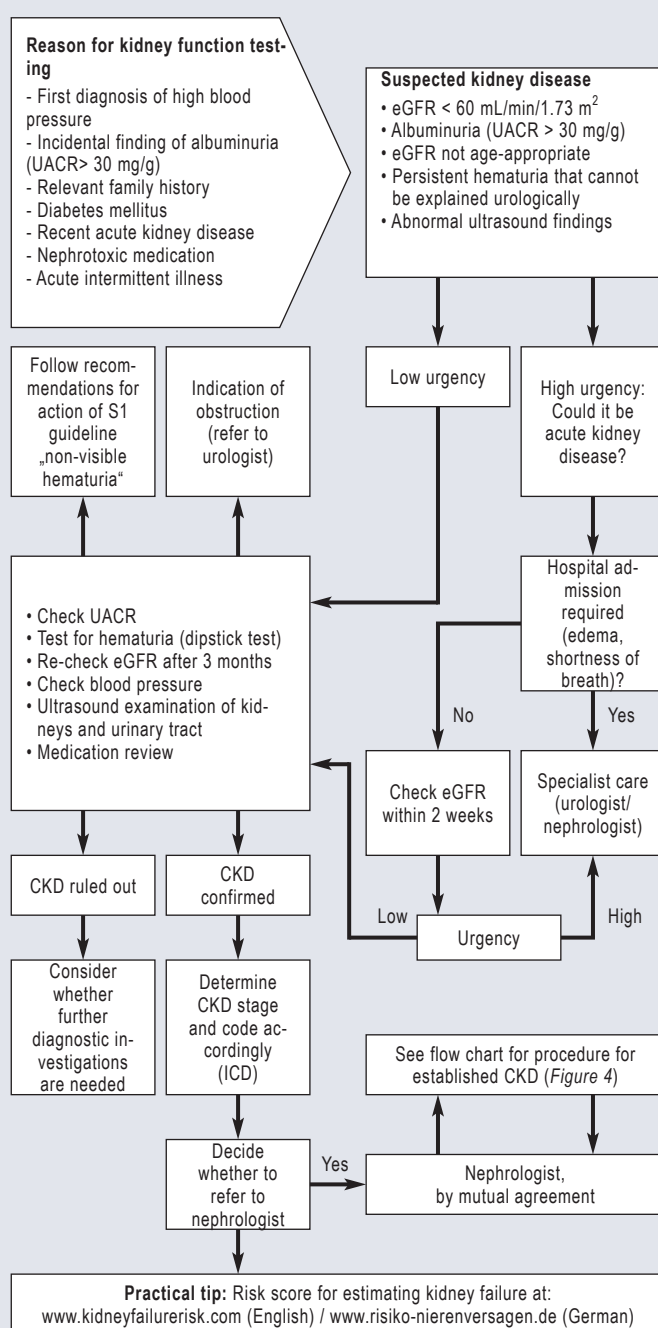
In the updated guideline, one ultrasound examination of the kidneys and efferent urinary tract, previously optional, is now recommended after the initial diagnosis. The size, shape, and structure of the kidneys can provide diagnostic information, and obstruction of the urinary tract or cystic kidneys can be ruled out. *Figure 3* from the guideline may help with the decision whether to refer the patient to a nephrologist. The decision should be made jointly with the patient based on the situation as a whole.

Another new recommendation is that the risk of progression to kidney failure be assessed using a suitable risk instrument. At present, the one best suited to this purpose seems to be the Kidney Failure Risk Equation (KFRE), which allows estimation of the risk of progression to kidney failure in the next 2 or 5 years on the basis of age, gender, eGFR, and UACR. This risk calculation can be done online using the calculator at the website www.risiko-nierenversagen.de (German) or at <https://kidneyfailure.risk.com> (English). The KFRE has been validated in many independent populations, including in Germany (12, 13). An evaluation of the predictive value of the KFRE in various kidney diseases, such as polycystic kidney disease or glomerulonephritis, also showed good discrimination (14). For CKD and diabetes, an alternative is the BEAt-DKD risk instrument developed in Germany (<https://beatdkd.shinyapps.io/shiny/>). It was developed and validated in a German population (15), but the website is available only in English. The advantage of estimating the risk of progression with a risk score is that—unlike in the KDIGO classification (*Figure 1*)—it is not five combined endpoints that are offered, but a single defined, understandable risk indication, given in absolute figures and taking age and gender into account, for the occurrence of kidney failure requiring renal replacement therapy within a defined prediction period.

Monitoring and treatment

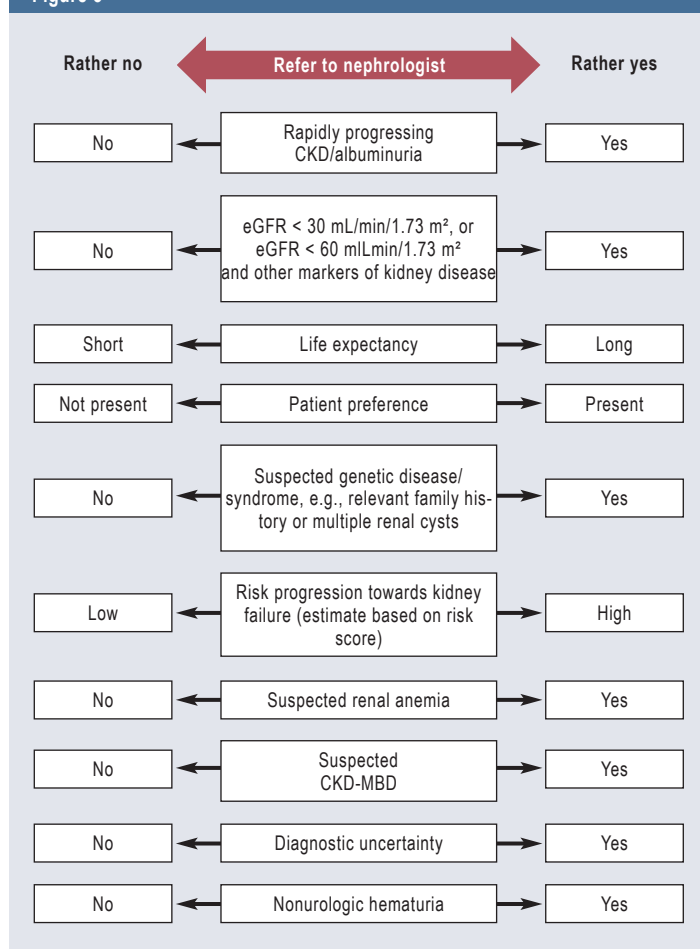
Figure 4 gives an overview of the treatment pathway once CKD has been confirmed (1). In addition to regular eGFR

Figure 2



Procedural flow chart for patients with suspected kidney disease (1)
 CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate;
 UACR, urinary albumin–creatinine ratio

Figure 3



Decision-making aid for referral to nephrologist (1)
CKD, chronic kidney disease; CKD-MBD, chronic kidney disease with mineral and bone disorder; eGFR, estimated glomerular filtration rate

measurements, monitoring CKD includes medication review, blood pressure monitoring, and lifestyle counseling. Monitoring intervals are agreed with the individual patient, as there is little scientific basis for a rational justification (*eFigure*). Check-ups at critical times, such as during medication changes or intercurrent illnesses, are more important. Life expectancy and the patient's wishes play an important part in decisions about monitoring and any referral to a nephrologist (*eFigure*). Consideration should be given to the question of whether a one-off referral to the specialist or ongoing shared care is desired.

All medications taken—including over-the-counter medications and dietary supplements—should be reviewed once a year. This allows dosage adjustments to be made and contraindications to be identified. Over-the-counter medications such as ibuprofen are contraindicated where eGFR is below 30 mL/min/1.73 m², and even where eGFR is higher, they should only be used for as short a time and at the lowest dose possible.

Blood pressure should be checked at all monitoring appointments. A target blood pressure of ≤140/90 mmHg is recommended. Based on a network meta-analysis, drug therapy with angiotensin-converting enzyme (ACE) inhibitors or angiotensin receptor blockers is recommended (1, 5, 10, 16). These medications reduce the odds ratio (OR) for a renal event (OR = 0.54; 95% confidence interval: [0.41; 0.73]) and all-

cause mortality (OR = 0.7 [0.66; 0.91]). Medications in these two drug groups should continue to be prescribed even where eGFR is below 30 mL/min/1.73 m², but they should not be combined. Lower target blood pressure values can be agreed with the individual patient, e.g., in the presence of albuminuria. The European Society for Hypertension (ESH) suggests the following age-dependent target values for blood pressure:

- Age 18–64 years: 130/80 mmHg,
- Age 65–79 years: 140/80 mmHg (if well tolerated, 130/80 mmHg),
- Age ≥80 years: 140–150/80 mmHg (if well tolerated, 140/80 mmHg).

As a rule, blood pressure should not be reduced below 120 mmHg systolic (17).

Individualized lifestyle advice, such as not smoking, and exercising regularly, allows patients to do something for their own health. The evidence in relation to renal endpoints is sparse. Dietary restrictions on protein and energy intake are not recommended due to the risk of sarcopenia. The recommendations for the general population apply. People with CKD should only follow a protein-restricted diet in consultation with a nephrologist. Advanced age, low BMI, or unintentional weight loss in a patient with CKD should suggest the possibility of malnutrition. In Germany, it is now increasingly possible to prescribe nutritional counseling under § 43 SGB V based on a doctor's certificate of need. Qualified nutritionists contact the health insurance companies for reimbursement. For patients at increased cardiovascular or renal risk, a low-salt, Mediterranean, high-fiber diet, avoiding highly processed foods such as ready meals and sweetened drinks, is recommended.

People with CKD have an increased cardiovascular risk. This risk should be estimated using a validated risk instrument, e.g., *arriba* (<https://arriba-hausarzt.de/>), if treatment with statins is not indicated because of underlying cardiovascular disease. The cardiovascular risk instruments validated in Germany do not include eGFR, which plays only a subordinate role in risk assessment (18). Consensus is lacking as to the risk thresholds above which lipid-lowering therapy is recommended in primary prevention; currently, the medication guideline requires a more-than-20% risk of a cardiovascular event. If the age-adjusted risk is classified as high, statin therapy is recommended. This has no advantage for kidney function (19). There is insufficient evidence about primary preventive lipid-lowering therapy in people over 75 years of age, so the decision needs to be weighed carefully (20). The indication for antiplatelet therapy is the same as in people without CKD and is based on cardiovascular risk (21).

Although the HbA_{1c} value is an important predictor of a drop in eGFR, a lower HbA_{1c} target value is not recommended for patients with diabetes and CKD (22). For treatment options, readers are referred to the German National Disease Management Guideline for Diabetes. Metformin must be adjusted to kidney function and discontinued if eGFR is below 30 mL/min/1.73 m². The Joint Federal Committee (Gemeinsamer Bundesausschuss) did not recognize any additional benefit for patients with diabetic nephropathy from finerenone, a nonsteroidal selective mineralocorticoid receptor antagonist,

because at the time very few renal patients were receiving an SGLT2 inhibitor, which at that time was not yet the established standard treatment. A study on semaglutide in CKD published after the research was completed showed an absolute risk reduction of 0.8% (4.7% versus 5.7%) for the endpoint kidney failure. Only 15% of the patients were receiving treatment with SGLT2 inhibitors (23).

Prescribing SGLT2 inhibitors is recommended for patients with CKD with albuminuria (UACR ≥ 300 mg/g) and/or eGFR below 45 mL/min/1.73 m² – even without diabetes or heart failure (1, 5, 10, 24–26). Currently, only dapagliflozin and empagliflozin are approved for this purpose in Germany. A meta-analysis found a lower relative risk (RR) of 0.62 [0.56; 0.68] for renal endpoints and for all-cause mortality (RR = 0.89 [0.85; 0.94]) (26).

When SGLT2 inhibitors are given, eGFR may initially drop by around 5 mL/min because of the inhibition of glomerular hyperfiltration. Over time, however, the rate of decline will slow. If eGFR is below 20 mL/min/1.73 m², treatment with an SGLT2 inhibitor should not be started, but if already ongoing it should not be stopped. The guideline provides a summary flow chart (Figure 5) for when an SGLT2 inhibitor could be prescribed.

As eGFR decreases, serum uric acid concentration rises. Recent studies have shown no benefit for the kidney of primary preventive treatment of asymptomatic hyperuricemia with a uric acid-lowering agent (allopurinol, febuxostat) (27).

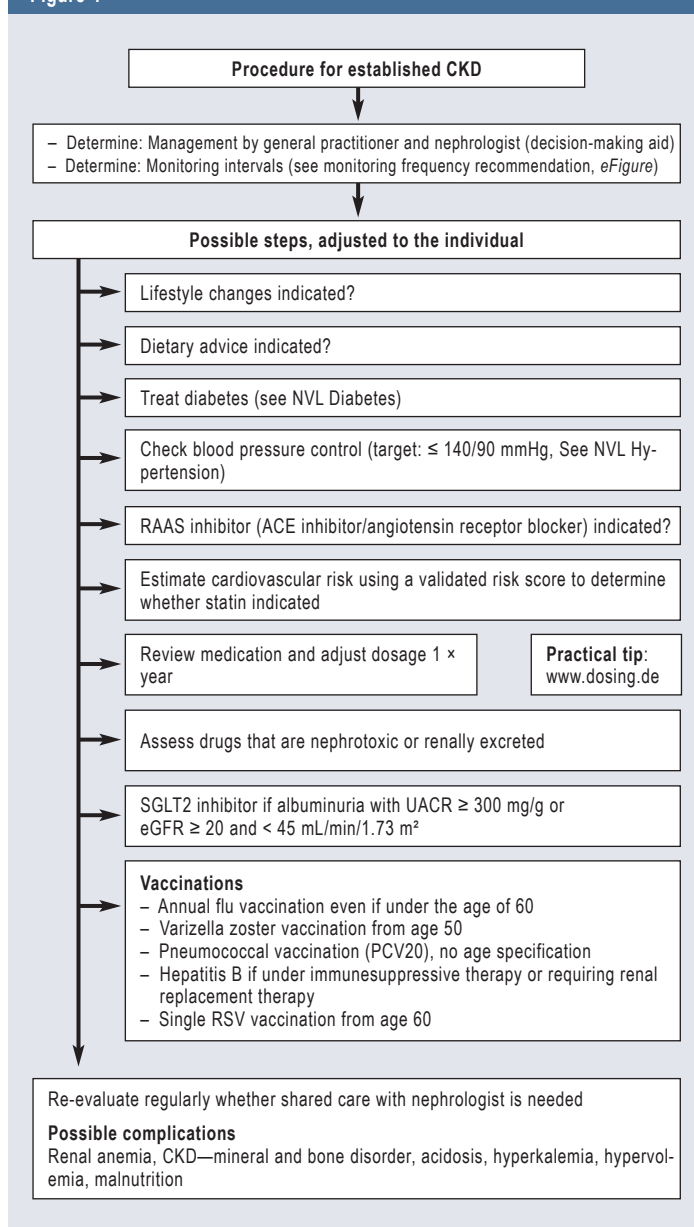
Changes in bone metabolism in patients with CKD usually only lead to symptoms from stage G4 onwards. From then on, calcium, phosphate, parathyroid hormone, and vitamin D should be monitored regularly. As vitamin D promotes phosphate and calcium absorption in the gut and can therefore trigger or exacerbate hyperphosphatemia and hypercalcemia, substitution should only be carried out in consultation with a nephrologist. In those with advanced CKD and kidney failure, hydroxylation of vitamin D precursors is no longer possible. Decisions regarding the treatment of CKD-MBD (chronic kidney disease—mineral and bone disorder), and whether to prescribe active vitamin D derivatives that do not require renal activation (e.g., calcitriol, alfacalcidol) or phosphate binders, should be made by a nephrologist.

The most common cause of anemia in a patient with CKD is iron deficiency. Persistent Hb <11 g/dL (6.8 mmol/L) should prompt suspicion of renal anemia if iron, vitamin B₁₂, and folic acid deficiency and bleeding have all been ruled out or treated. Treatment of renal anemia with erythropoiesis-stimulating agents (ESA) or hypoxia-inducible factor (HIF) stabilizers should be guided by a nephrologist (10).

For the first time, the guideline includes the STIKO (Ständige Impfkommision, Standing Committee on Vaccination) vaccination recommendations for people with CKD, which differ from those for the general population (28, 29):

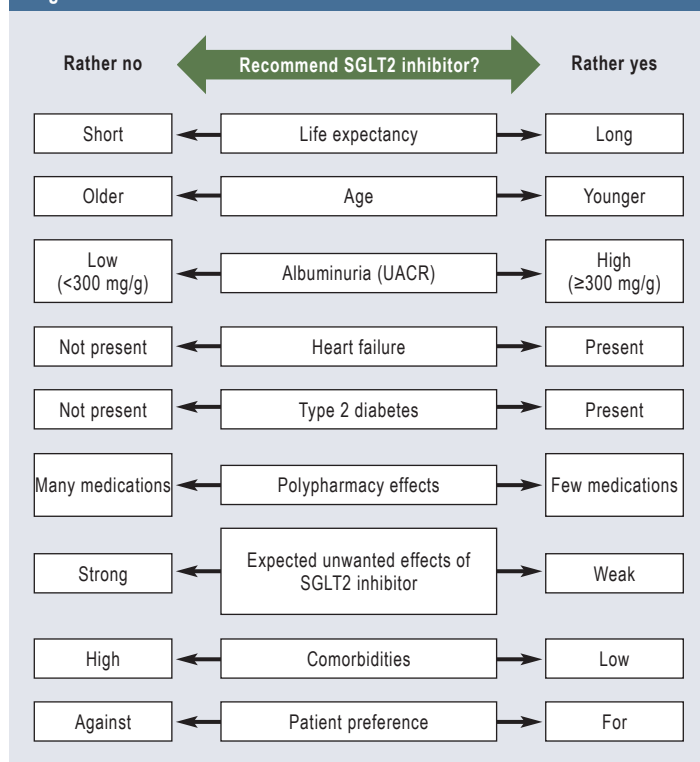
- Annual flu vaccination,
- Varicella zoster vaccination from age 50,
- Pneumococcal vaccination,
- Single respiratory syncytial virus vaccination from age 60.

Figure 4



Flow chart of procedure in patients with established CKD (1)
ACE, angiotensin-converting enzyme; CKD, chronic kidney disease;
eGFR, estimated glomerular filtration rate; NVL, German National Clinical Guideline (Nationale Versorgungsleitlinie);
RAAS, renin–angiotensin–aldosterone system; RSV, human respiratory syncytial virus; UACR, urinary albumin–creatinine ratio

Figure 5



Decision-making aid for prescribing an SGLT2 inhibitor (1)
UACR, urinary albumin–creatinine ratio; SGLT2, sodium glucose cotransporter 2

For patients under immunosuppression therapy or expected renal replacement therapy, hepatitis B vaccination with vaccines with a higher antigen content is recommended (28). A point of criticism is that the vaccination recommendations are based only on data from patients requiring renal replacement therapy.

Conclusion and outlook

Most people with CKD can be cared for by their general practitioner. This guideline provides assistance regarding treatment, monitoring, and the identification of people with CKD who will benefit from care shared with a nephrologist. To date, UACR measurement has not been employed widely enough: it is needed for reliable assessment and decisions on the further management of CKD. Supporting UACR measurement by introducing a laboratory exemption code allowing extrabudgetary billing would be helpful. Epidemiology data for CKD in Germany are incomplete. The value of the KFRE for guiding CKD care in general practice should be further investigated.

Support

This guideline was supported by the Innovation Committee of the Joint Federal Committee (Gemeinsamer Bundesausschuss) (grant number 01VSF22011).

Conflicts of interest

MN is a member of the German College of General Practitioners and Family Physicians (DEGAM, Deutsche Gesellschaft für Allgemeinmedizin und Familienmedizin) and the Mecklenburg-Vorpommern (MV) Association of General Practitioners.

SS has received lecture fees from AstraZeneca, Bayer Vital, Glaxo Smith Kline, Lilly, and CSL Vifor. She is a member of the Advisory Board of AstraZeneca. She is a member of the extended board of the German Society of Nephrology (DGfN, Deutsche Gesellschaft für

Nephrologie), the MV Society of Internal Medicine and the MV State Association for Nephrology as well as chair of the DGfN's Women and Kidney Commission and a representative on the Medical Advisory Board of the Kuratorium für Heimdialyse (KFH).

SF has received consultancy fees from AstraZeneca, Novartis, Medice/Medigital GmbH, and Stadapharm and lecture fees from Astra Zeneca, Akademie Niere a. V., VFED e. V., and StreamedUp! GmbH. She is chair of the renal nutrition working group of DGfN e.V.

MK has received consultancy fees from Böhlinger Ingelheim and Bayer Vital GmbH.

JFC has received seminar fees from IHF and medical associations and fees for expert opinions provided to courts, medical associations, and the medical service of health insurers. He is Vice President of DEGAM, a member of the Guidelines and Quality Management Section of DEGAM, and a member of the General Practitioners' Association of Mecklenburg-Western Pomerania.

SK declares that she has no conflict of interest.

Manuscript received on 24 September 2024, revised version accepted on 24 October 2024.

Clinical guidelines in the Deutsches Ärzteblatt, like those in many other specialist journals, are not subject to the peer review process because S3 guidelines are texts that have already been evaluated, discussed, and widely agreed by experts (peers).

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Supplementary material

Complete list of full references, eBox, eFigure:
www.aerzteblatt-international.de/m2024.0230

Supplementary material to accompany the article

The Management of Chronic Kidney Disease not Requiring Renal Replacement Therapy in General Practice

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eBox

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● **Participating medical specialty societies and patient representatives**

- German College of General Practitioners and Family Physicians (DEGAM, Deutsche Gesellschaft für Allgemeinmedizin und Familienmedizin) and German Society of Nephrology (DGfN, Deutsche Gesellschaft für Nephrologie), lead organizations
- German Society of Nutritional Medicine (DGEM, Deutsche Gesellschaft für Ernährungsmedizin)
- German Geriatrics Society (DGG, Deutsche Gesellschaft für Geriatrie)
- German Society of Internal Medicine (DGIM, Deutsche Gesellschaft für Innere Medizin)
- German Kidney Association (Bundesverband Niere e. V.), representing patients

eFigure

Persistent albuminuria categories*³

			A1	A2	A3
			Normal to mildly reduced	Moderately reduced	Severely reduced
			<30 mg/g <3 mg/mmoL	30–300 mg/g 3–30 mg/mmoL	>300 mg/g >30 mg/mmoL
G1	Normal or high	≥90	≤1 (if CKD present)	1	≥1
G2	Mildly reduced* ²	60–89	≤1 (if CKD present)	1	≥1
G3a	Mildly to moderately reduced	45–59	1	1	2
G3b	Moderately to severely reduced	30–44	≤2	2	≥2
G4	Severely reduced	15–29	2	2	3
G5	Renal failure	<15	4	≥4	≥4

Increasing risk

Increasing risk

Recommendations for monitoring frequency (number of check-ups per year) based on GFR and albuminuria category-based recommendations for number of monitoring checks per year modified according to NICE (1, 8)

*¹ Description and range of eGFR (mL/min/1.73 m²)

*² Compared to a young adult.

*³ Description and range of UACR.

CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; UACR, urinary albumin–creatinine ratio