Odesa National Medical University
Internal Medicine Dept. #2 with postgraduate education

Lecture

CHRONIC KIDNEY DISEASE

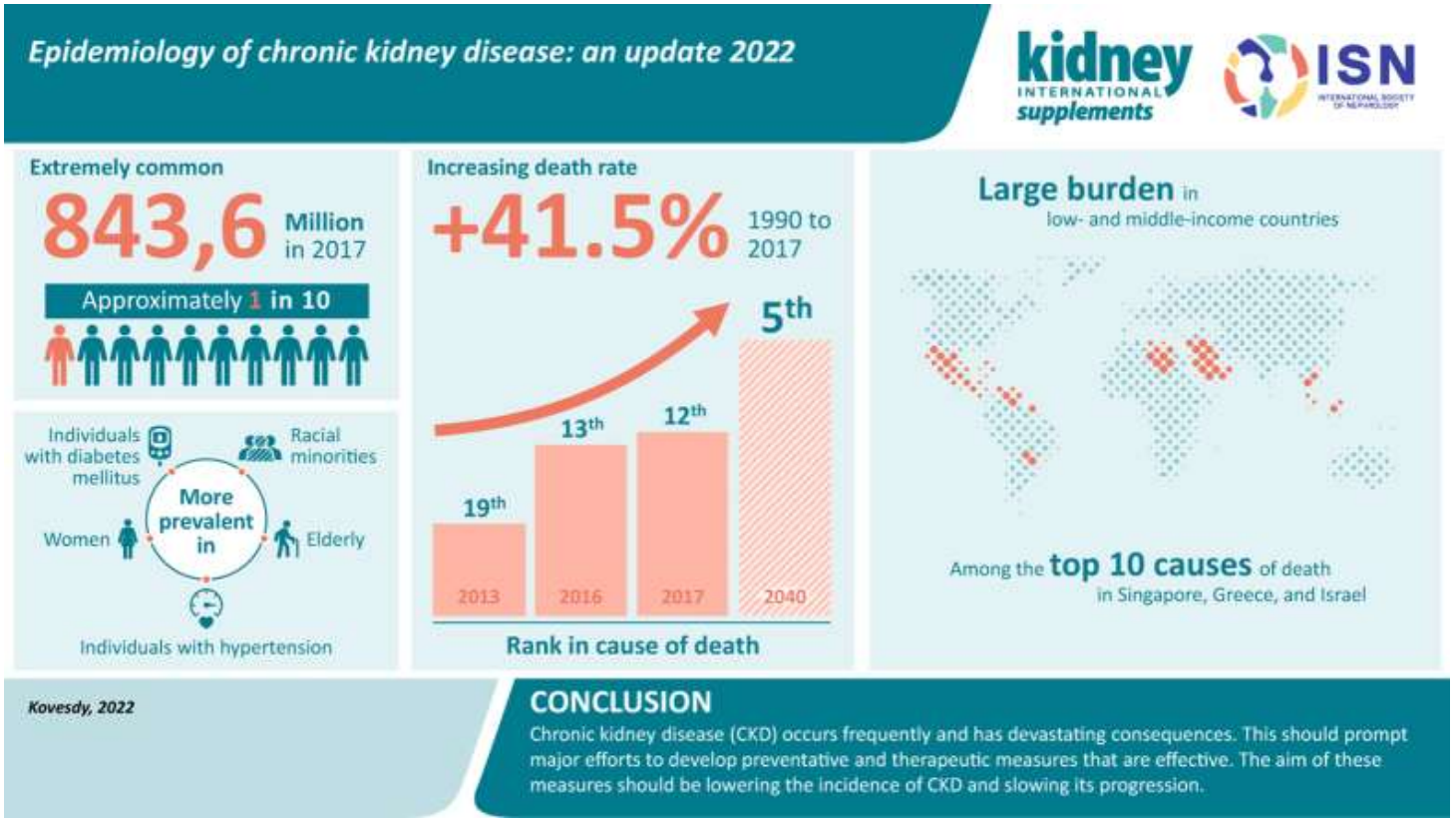
for 5th years students
2024-25 ed.y.

Lecturer:
Professor Susanna Tykhonova

Questions for consideration

- Epidemiology of chronic kidney disease (CKD)
- Present guidlines
- Definition and classification of CKD
- Classifying CKD
- Screening
- Evaluation of CKD
- CKD treatment and risk modification

CKD is a progressive condition that affects >10% of the general population worldwide, amounting to >800 million individuals



- **CKD is more prevalent in older individuals, women, racial minorities, and in people experiencing diabetes mellitus (DM) and hypertension (HTN)**
- CKD represents an especially large burden in low- and middle-income countries
- **CKD has emerged as one of the leading causes of mortality worldwide**, and it is one of a small number of non-communicable diseases that have shown an increase in associated deaths over the past 2 decades.

Kidney International Supplements (2022) 12, 7–11

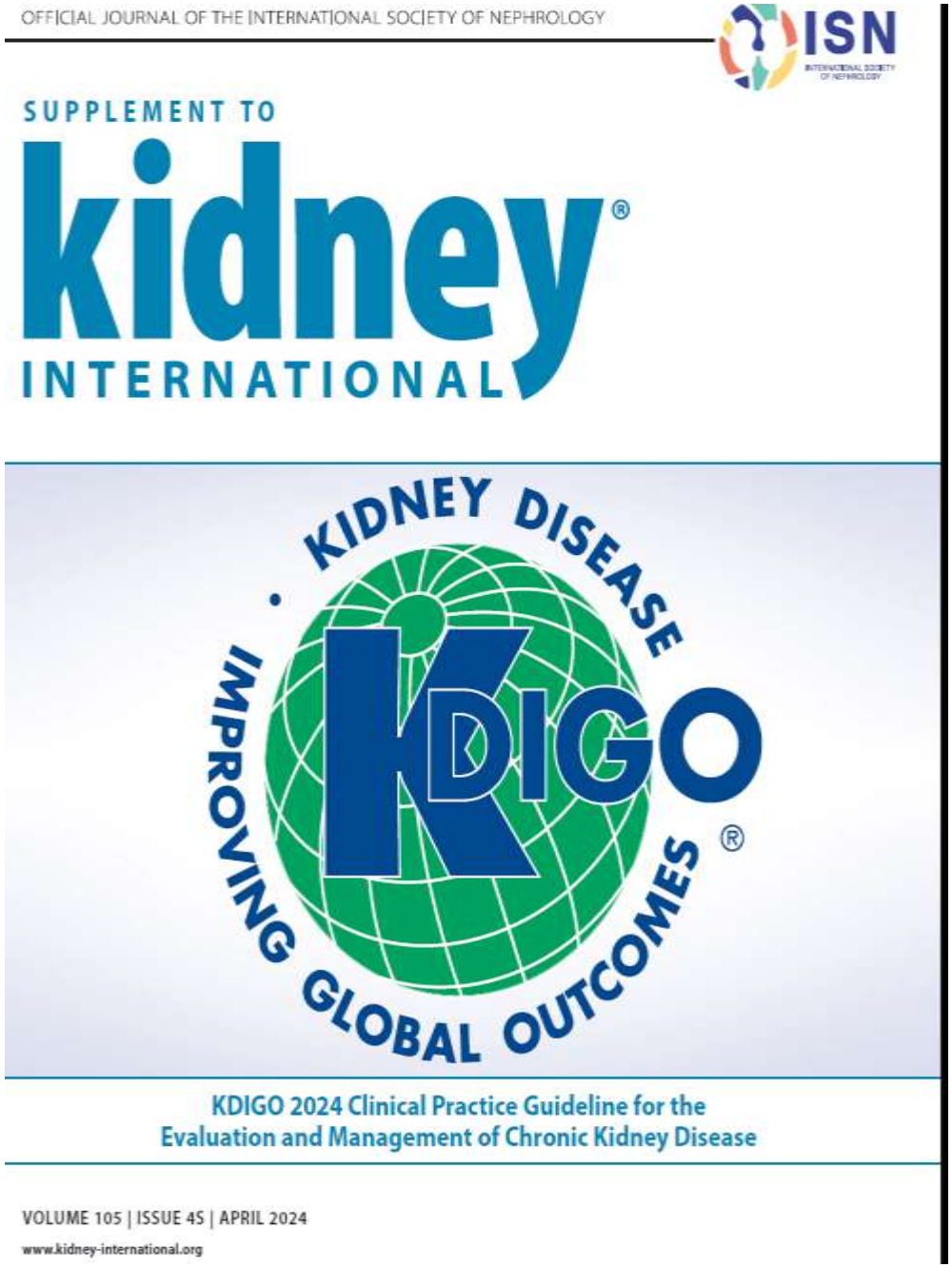
Risk factors for CKD

Domains	Example conditions
Common risk factors	Hypertension Diabetes Cardiovascular disease (including heart failure) Prior AKI/AKD
People who live in geographical areas with high prevalence of CKD	Areas with endemic CKDu Areas with the high prevalence of *APOL1* genetic variants Environmental exposures
Genitourinary disorders	Structural urinary tract disease Recurrent kidney calculi
Multisystem diseases/chronic inflammatory conditions	Systemic lupus erythematosus Vasculitis HIV

Risk factors for CKD

Iatrogenic (related to drug treatments and procedures)	Drug-induced nephrotoxicity and radiation nephritis
Family history or known genetic variant associated with CKD	Kidney failure, regardless of identified cause Kidney disease recognized to be associated with genetic abnormality (e.g., PKD, *APOL1*-mediated kidney disease, and Alport syndrome)
Gestational conditions	Preterm birth Small gestational size Pre-eclampsia/eclampsia
Occupational exposures that promote CKD risk	Cadmium, lead, and mercury exposure Polycyclic hydrocarbons Pesticides

AKD, acute kidney disease; AKI, acute kidney injury; *APOL1*, apolipoprotein L1; CKD, chronic kidney disease; CKDu, chronic kidney disease of undetermined origin; PKD, polycystic kidney disease.



The Kidney Disease: Improving Global Outcomes (KDIGO) organization was established in 2003 with the mission to improve the care and outcomes of people living with kidney disease worldwide

The development and implementation of global clinical practice guidelines is central to the many activities of KDIGO to fulfill its mission

There is update of the KDIGO Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease (CKD) to complement the existing 12 guidelines that address various other facets of kidney disease management.

CKD is defiined as abnormalities of kidney structure or function, present for a minimum of 3 months, with implications for health

Criteria for CKD (either of the following present for a minimum of 3 months)

Markers of kidney damage (1 or more)	Albuminuria (ACR ≥30 mg/g [≥3 mg/mmol])
	Urine sediment abnormalities
	Persistent hematuria
	Electrolyte and other abnormalities due to tubular disorders
	Abnormalities detected by histology
	Structural abnormalities detected by imaging
	History of kidney transplantation
Decreased GFR	GFR <60 ml/min per 1.73 m^2 (GFR categories G3a–G5)

ACR, albumin-to-creatinine ratio; GFR, glomerular filtration rate.

CKD is classified based on Cause, GFR category (G1–G5), and Albuminuria category (A1–A3), abbreviated as CGA

These 3 components of the classification system are each critical in the assessment of people with CKD and help enable determination of severity and risk.

GFR category	GFR (ml/min per 1.73 m^2)	Terms
G1	≥90	Normal or high
G2	60–89	Mildly decreased[a]
G3a	45–59	Mildly to moderately decreased
G3b	30–44	Moderately to severely decreased
G4	15–29	Severely decreased
G5	<15	Kidney failure

CKD, chronic kidney disease; GFR, glomerular filtration rate.

[a]Relative to the young adult level. In the absence of evidence of kidney damage, neither G1 nor G2 fulfills the criteria for CKD.

CKD is classified based on Albuminuria category (A1–A3)

Category	AER (mg/24 h)	ACR (approximately equivalent) (mg/mmol)	ACR (approximately equivalent) (mg/g)	Terms
A1	<30	<3	<30	Normal to mildly increased
A2	30–300	3–30	30–300	Moderately increased[a]
A3	>300	>30	>300	Severely increased

ACR, albumin-to-creatinine ratio; AER, albumin excretion rate.

[a]Relative to the young adult level.

CKD is defined as abnormalities of kidney structure or function, present for a minimum of 3 months, with implications for health. CKD is classified based on Cause, Glomerular filtration rate (GFR) category (G1–G5), and Albuminuria category (A1–A3), abbreviated as CGA.

KDIGO: Prognosis of CKD by GFR and albuminuria categories

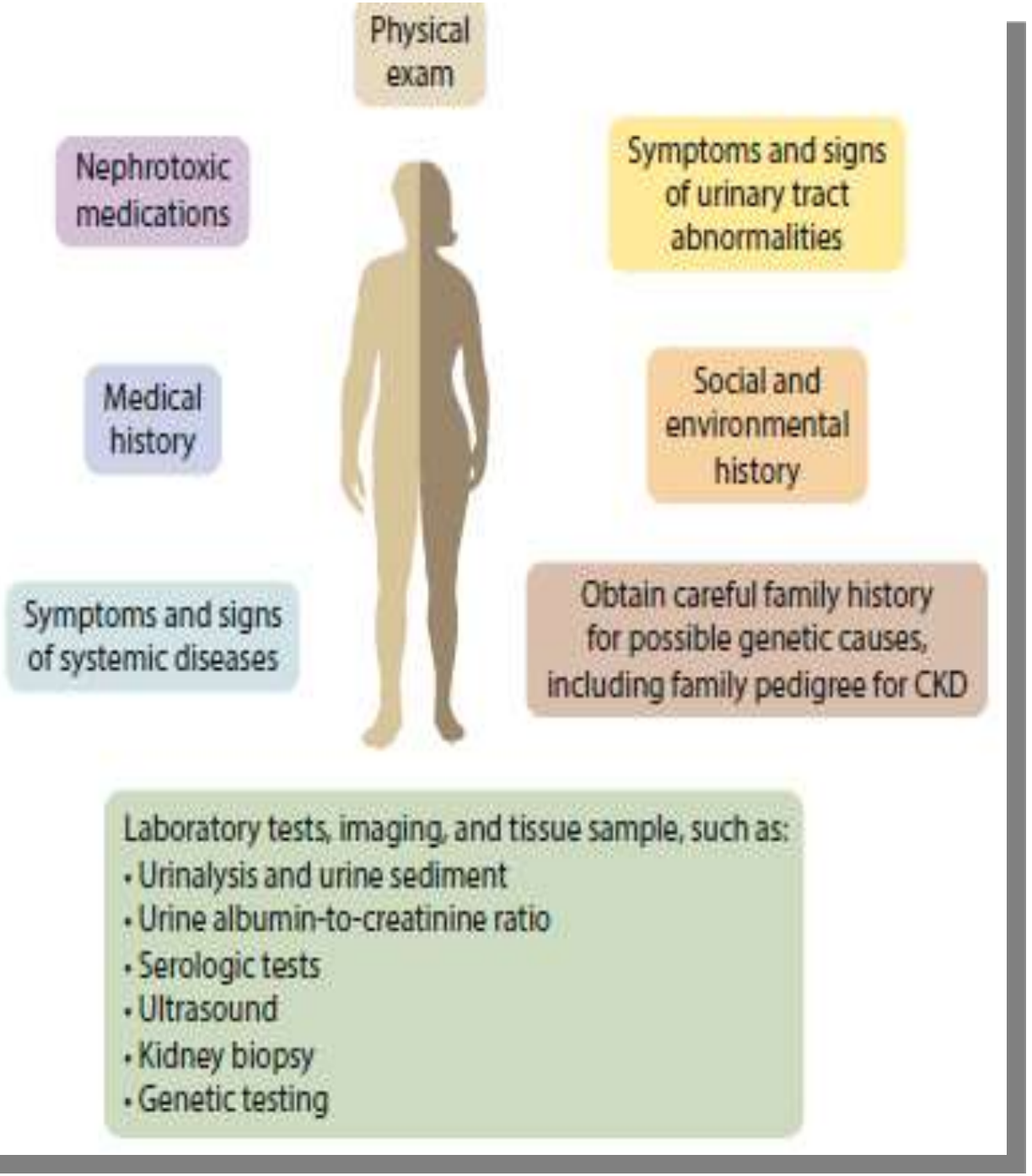
GFR categories (ml/min/1.73 m²) Description and range				Persistent albuminuria categories Description and range		
				A1	A2	A3
				Normal to mildly increased	Moderately increased	Severely increased
				<30 mg/g <3 mg/mmol	30–300 mg/g 3–30 mg/mmol	>300 mg/g >30 mg/mmol
	G1	Normal or high	≥90			
	G2	Mildly decreased	60–89			
	G3a	Mildly to moderately decreased	45–59			
	G3b	Moderately to severely decreased	30–44			
	G4	Severely decreased	15–29			
	G5	Kidney failure	<15			

Green: low risk (if no other markers of kidney disease, no CKD); Yellow: moderately increased risk; Orange: high risk; Red: very high risk. GFR, glomerular filtration rate.

CKD staging by eGFRcr and ACR and association with adverse events

Overall	Urine albumin-creatinine ratio, mg/g					Urine albumin-creatinine ratio, mg/g				
eGFRcr	<10	10–29	30–299	300–999	1000+	<10	10–29	30–299	300–999	1000+
	All-cause mortality: 82 cohorts 26 444 384 participants; 2 604 028 events					Myocardial infarction: 64 cohorts 22 838 356 participants; 451 063 events				
105+	1.6	2.2	2.9	4.3	5.8	1.1	1.4	2.0	2.7	3.8
90–104	ref	1.3	1.8	2.6	3.1	ref	1.3	1.6	2.2	3.2
60–89	1.0	1.3	1.7	2.2	2.8	1.1	1.3	1.6	2.2	3.1
45–59	1.3	1.6	2.0	2.4	3.1	1.4	1.7	2.0	2.8	3.7
30–44	1.8	2.0	2.5	3.2	3.9	1.9	2.0	2.4	3.2	4.3
15–29	2.8	2.8	3.3	4.1	5.6	2.7	3.1	3.1	4.2	5.1
<15	4.6	5.0	5.3	6.0	7.0	4.6	5.6	4.8	6.0	6.0
	Cardiovascular mortality: 76 cohorts 26 022 346 participants; 776 441 events					Stroke: 68 cohorts 24 746 436 participants; 461 785 events				
105+	1.4	2.0	3.0	4.1	5.4	1.2	1.6	2.2	3.1	4.3
90–104	ref	1.3	1.9	2.7	3.6	ref	1.3	1.6	2.4	3.1
60–89	1.0	1.4	1.7	2.4	3.2	1.1	1.3	1.7	2.2	3.0
45–59	1.4	1.7	2.2	2.8	3.8	1.4	1.6	1.9	2.3	2.9
30–44	2.0	2.3	2.8	3.7	4.6	1.6	1.7	2.0	2.4	3.0
15–29	3.2	3.1	3.5	5.0	6.5	1.8	2.1	2.1	2.7	3.0
<15	6.1	6.4	6.4	7.3	8.2	3.2	2.8	2.9	3.2	3.8

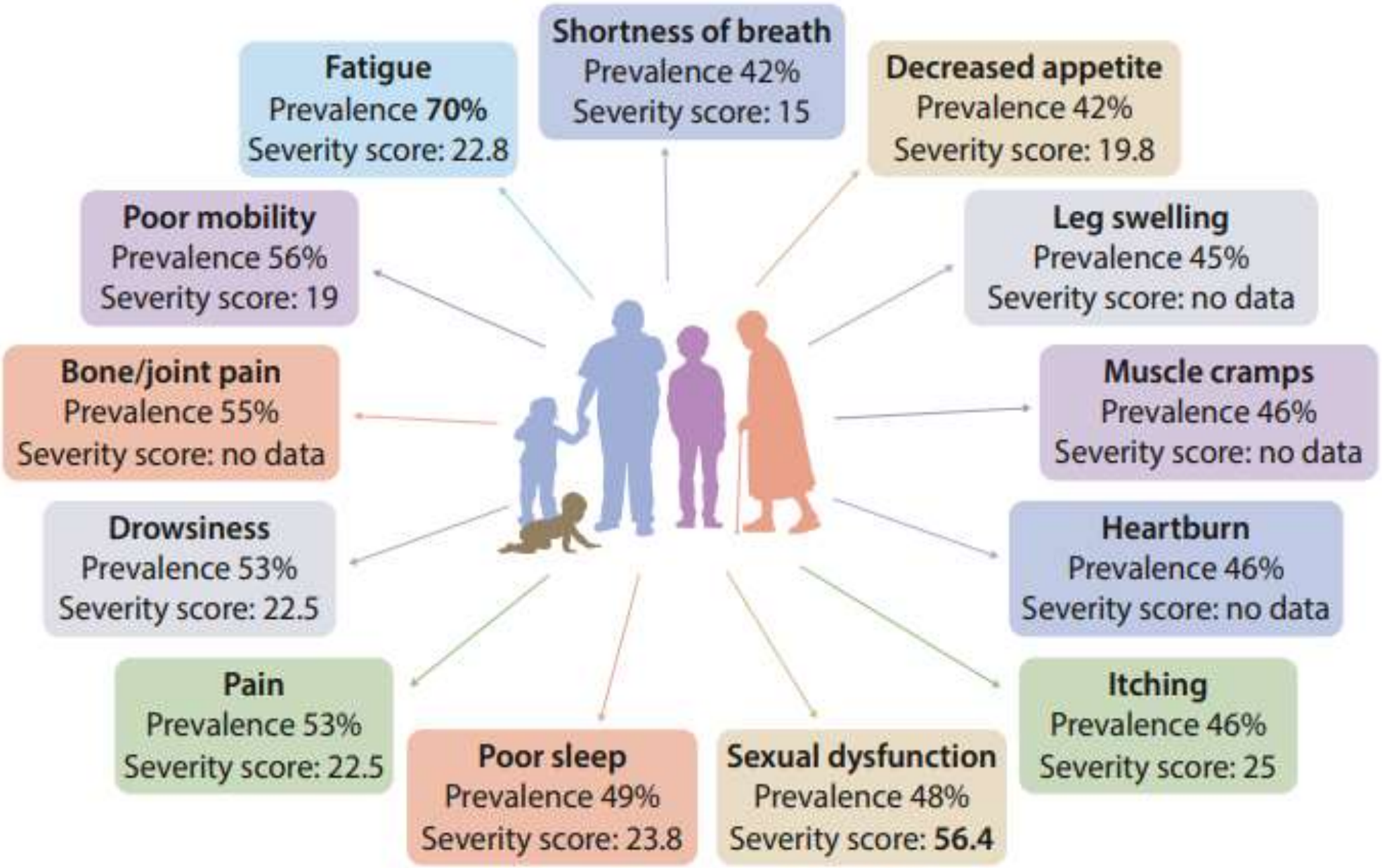
Evaluation of cause



Establish the cause of CKD using:

- clinical context
- personal and family history
- social and environmental factors
- medications
- physical examination
- laboratory measures
- imaging
- genetic & pathologic diagnosis

Common symptoms, prevalence, and severity in people with CKD



Adapted from Fletcher BR, Damery S, Aiyegbusi OL, et al. Symptom burden and health-related quality of life in chronic kidney disease: a global systematic review and meta-analysis. PLoS Med. 2022;19:e1003954.839 Copyright [a] 2022 Fletcher et al.

Screening and prevention

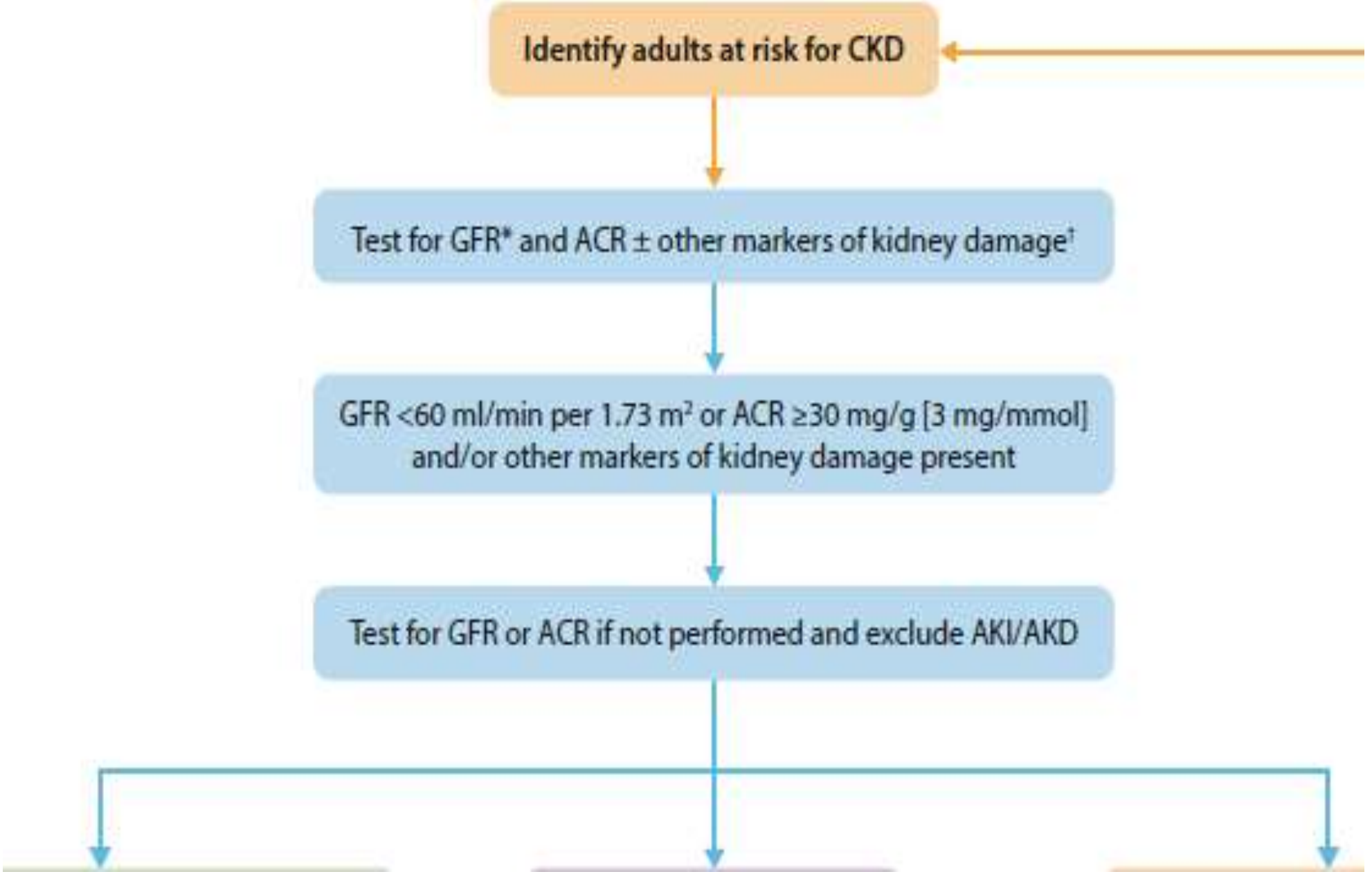
Education of both health personnel and **the populations at risk**, implementation of early kidney disease detection programs, and incorporation of evidence-based treatment of CKD and its associated conditions, such as BP and DM, are all essential components of a strategy to prevention

Globally people with HTN, DM, or CVD are at high risk for CKD

Other high-risk people may be identified through:

- genetic risk factors
- by varying exposure to environmental pollution, pesticides, water
- nephrotoxic medications including significant analgesic use and herbal medications

Simple algorithm
in settings such as primary care, cardiology, and endocrinology
could significantly improve the early identification and
treatment of CKD in adults



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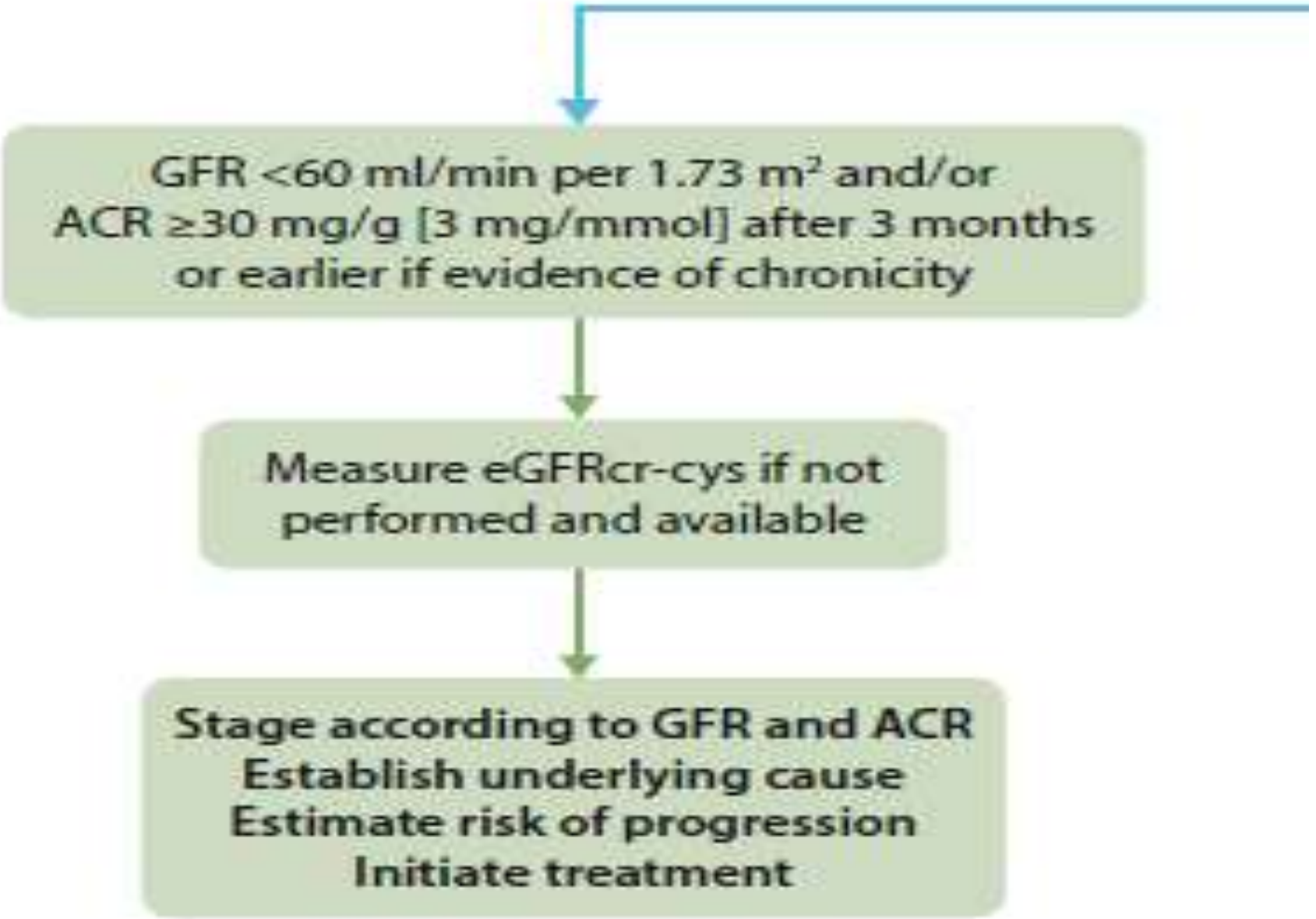

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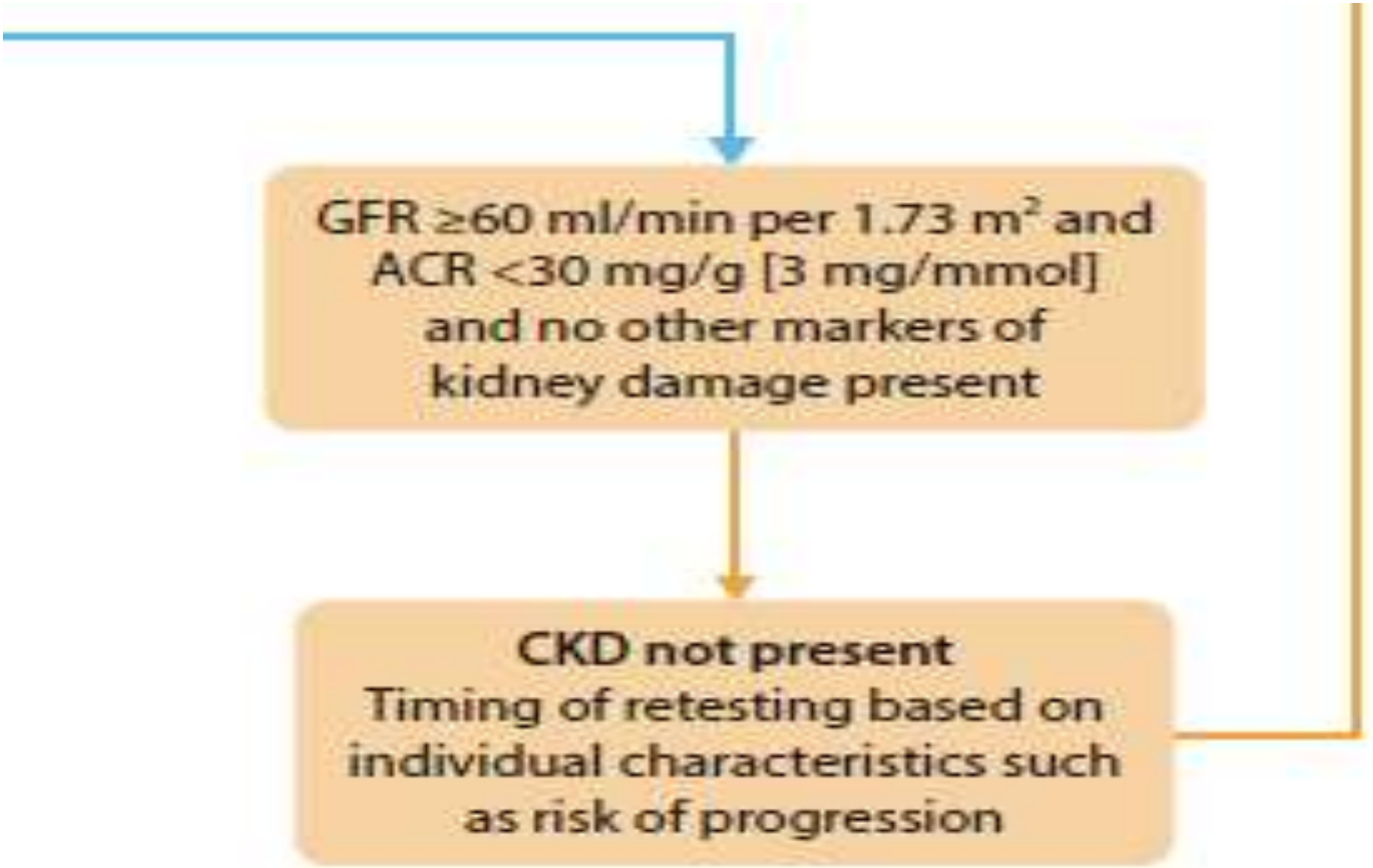


Evaluation of CKD

I. Step

In adults at risk for CKD, **it is recommend using creatinine-based estimated glomerular filtration rate (eGFRcr).**
If cystatin C is available, the GFR category should be estimated from the combination of creatinine and cystatin C (creatinine and cystatin C–based estimated glomerular filtration rate [eGFRcr-cys]) **(1B)**

Following incidental detection of **elevated urinary albumin-to-creatinine ratio (ACR), hematuria, or low estimated GFR (eGFR), repeat tests to confirm presence of CKD**

Evaluation of CKD

II. Step

Evaluation of chronicity: proof of chronicity (duration of a minimum of 3 months) can be established by:

(i) review of past measurements / estimations of GFR

(ii) review of past measurements of albuminuria or proteinuria and urine microscopic examinations

(iii) imaging findings such as **reduced kidney size and reduction in cortical thickness**

(iv) kidney pathological **findings such as fibrosis and atrophy**

(v) medical history, especially **conditions known to cause or contribute to CKD**

(vi) repeat measurements within and beyond the 3-month point

Evaluation of cause

Guidance for the selection of additional tests for evaluation of cause

Test category	Examples
Imaging	Ultrasound, intravenous urography, CT kidneys ureters bladder, nuclear medicine studies, MRI

Comment or key references
Assess kidney structure (i.e., kidney shape, size, symmetry, and evidence of obstruction) for cystic disease and reflux disease. Evolving role of additional technologies (e.g., 3D ultrasound)

Evaluation of cause

Guidance for the selection of additional tests for evaluation of cause

Kidney biopsy Ultrasound-guided percutaneous

Usually examined by light microscopy, immunofluorescence, and electron microscopy, and, in some situations, may include molecular diagnostics

Used for exact diagnosis, planning treatment, assessing activity and chronicity of disease, and likelihood of treatment response; may also be used to assess genetic disease

Evaluation of cause

Guidance for the selection of additional tests for evaluation of cause

Laboratory tests: serologic, urine tests	Chemistry including acid-base and electrolytes, serologic tests such as anti-PLA2R, ANCA, anti-GBM antibodies Serum-free light chains, serum, and urine protein electrophoresis/immunofixation Urinalysis and urine sediment examination
Genetic testing	*APOL1, COL4A3, COL4A4, COL4A5, NPHS1, UMOD, HNF1B, PKD1, PKD2*

Frequency of monitoring glomerular filtration rate (GFR) and albuminuria in people with CKD

CKD is classified based on: • Cause (C) • GFR (G) • Albuminuria (A)				Albuminuria categories Description and range		
				A1	A2	A3
				Normal to mildly increased	Moderately increased	Severely increased
				<30 mg/g <3 mg/mmol	30–299 mg/g 3–29 mg/mmol	≥300 mg/g ≥30 mg/mmol
GFR categories (ml/min/1.73 m²) Description and range	G1	Normal or high	≥90	Screen 1	Treat 1	Treat 3
	G2	Mildly decreased	60–89	Screen 1	Treat 1	Treat 3
	G3a	Mildly to moderately decreased	45–59	Treat 1	Treat 2	Treat 3
	G3b	Moderately to severely decreased	30–44	Treat 2	Treat 3	Treat 3
	G4	Severely decreased	15–29	Treat* 3	Treat* 3	Treat 4+
	G5	Kidney failure	<15	Treat 4+	Treat 4+	Treat 4+

Low risk (if no other markers of kidney disease, no CKD)

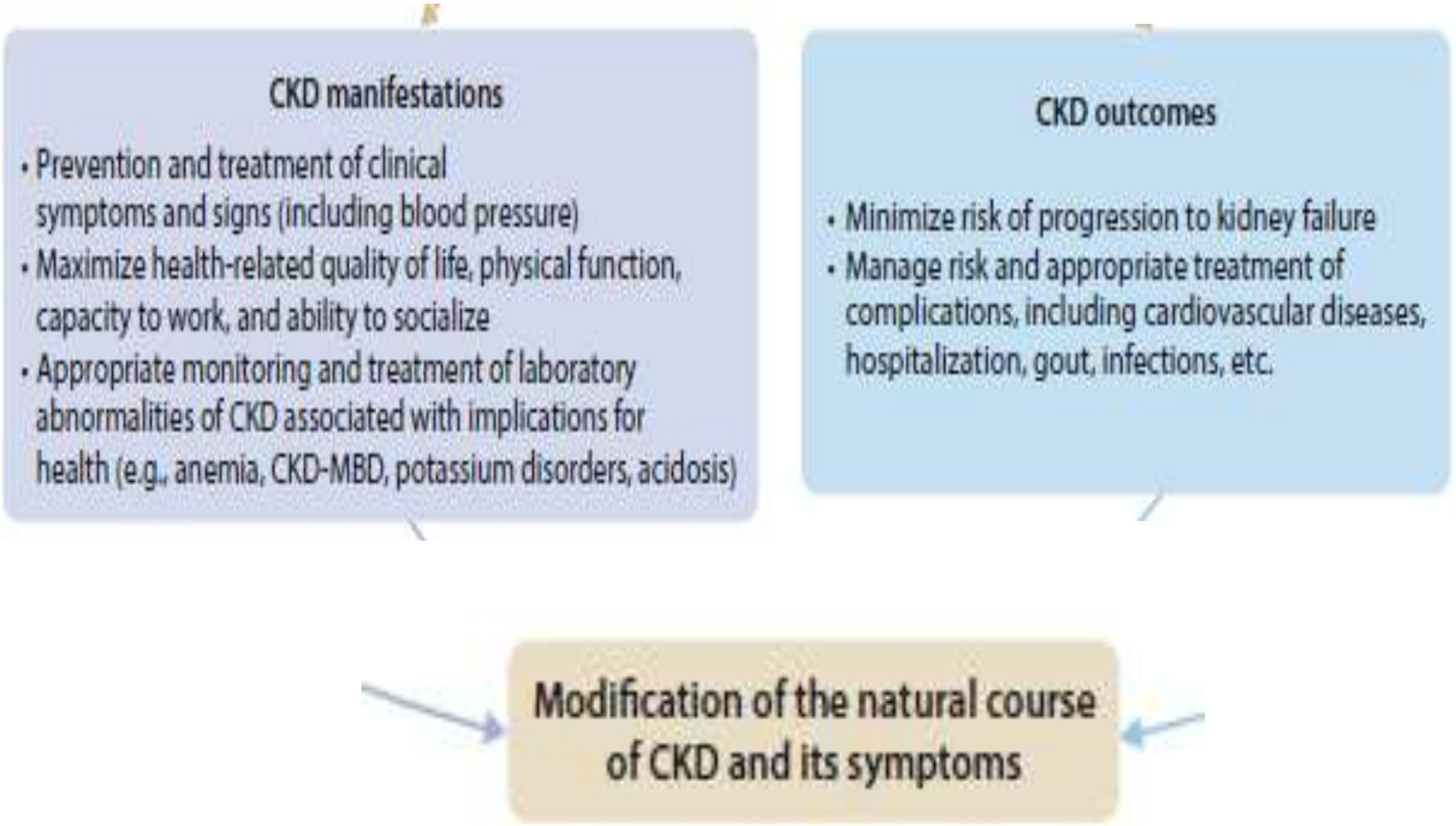
Moderately increased risk

High risk

Very high risk

CKD treatment and risk modification

Treat people with CKD with a comprehensive treatment strategy to reduce risks of progression of CKD and its associated complications



1D

3.2.2.1: We recommend that people with CKD be advised to undertake moderate-intensity physical activity for a cumulative duration of at least 150 minutes per week, or to a level compatible with their cardiovascular and physical tolerance (1D).

KDIGO 2024 Clinical Practice Guideline for Evaluation and Management Chronic Kidney Disease. Kidney Int. 2024

Lifestyle Modification in CKD

#NephJC

Physical activity should consider age/ ethnic background/presence of comorbidities and access to resources

People with CKD should be advised to avoid sedentary behavior

Encourage people with obesity and CKD to lose weight

People with CKD are advised to undertake moderate intensity physical activity for cumulative duration of atleast ***150 minute/ week***

Strength 1D

Avoid use of tobacco products

For people at higher risk of falls, healthcare providers should provide advice on the intensity and type of physical activity

Encourage children with CKD to undertake physical activity and achieve a healthy weight

- ✓ 1-5 years-≥***180 min daily***
- ✓ 5-17 years-≥***60 min daily***
- ✓ Limit sedentary/screen time

VA by:Jasmine Sethi @JasmineNephro

Protein intake

Maintaining a protein intake of **0.8 g/kg body weight/d** in adults with CKD G3-G5 **(2C)**

Avoid high protein intake (>1.3 g/kg body weight/d) in adults with CKD at risk of progression

In adults with CKD who are at risk of kidney failure, consider prescribing, under close supervision, **a very low–protein diet (0.3–0.4 g/kg body weight/d) supplemented with essential amino acids or ketoacid analogs (up to 0.6 g/kg body weight/d)**

Do not prescribe low- or very low–protein diets in metabolically unstable people with CKD.

3.3.2.1: We suggest that sodium intake be <2 g of sodium per day (or <90 mmol of sodium per day, or <5 g of sodium chloride per day) in people with CKD (2C).

KDIGO 2024 Clinical Practice Guideline for Evaluation and Management Chronic Kidney Disease. Kidney Int. 2024

Blood pressure (BP) **control**

Adults with high BP and CKD should be treated with a **target systolic blood pressure (SBP) of <120 mm Hg**, when tolerated, using standardized office BP measurement (**2B**)

Renin-angiotensin-system inhibitors (RASi) (**angiotensin-converting enzyme inhibitor [ACEi]** or **angiotensin II receptor blocker [ARB]**) for people with CKD and moderately-severely increased albuminuria (G1–G4, A3) with or without DM **(2C, 1B)**

We recommend avoiding any combination of ACEi, ARB, and **direct renin inhibitor (DRI) therapy in people with CKD, with or without diabetes (1B).**

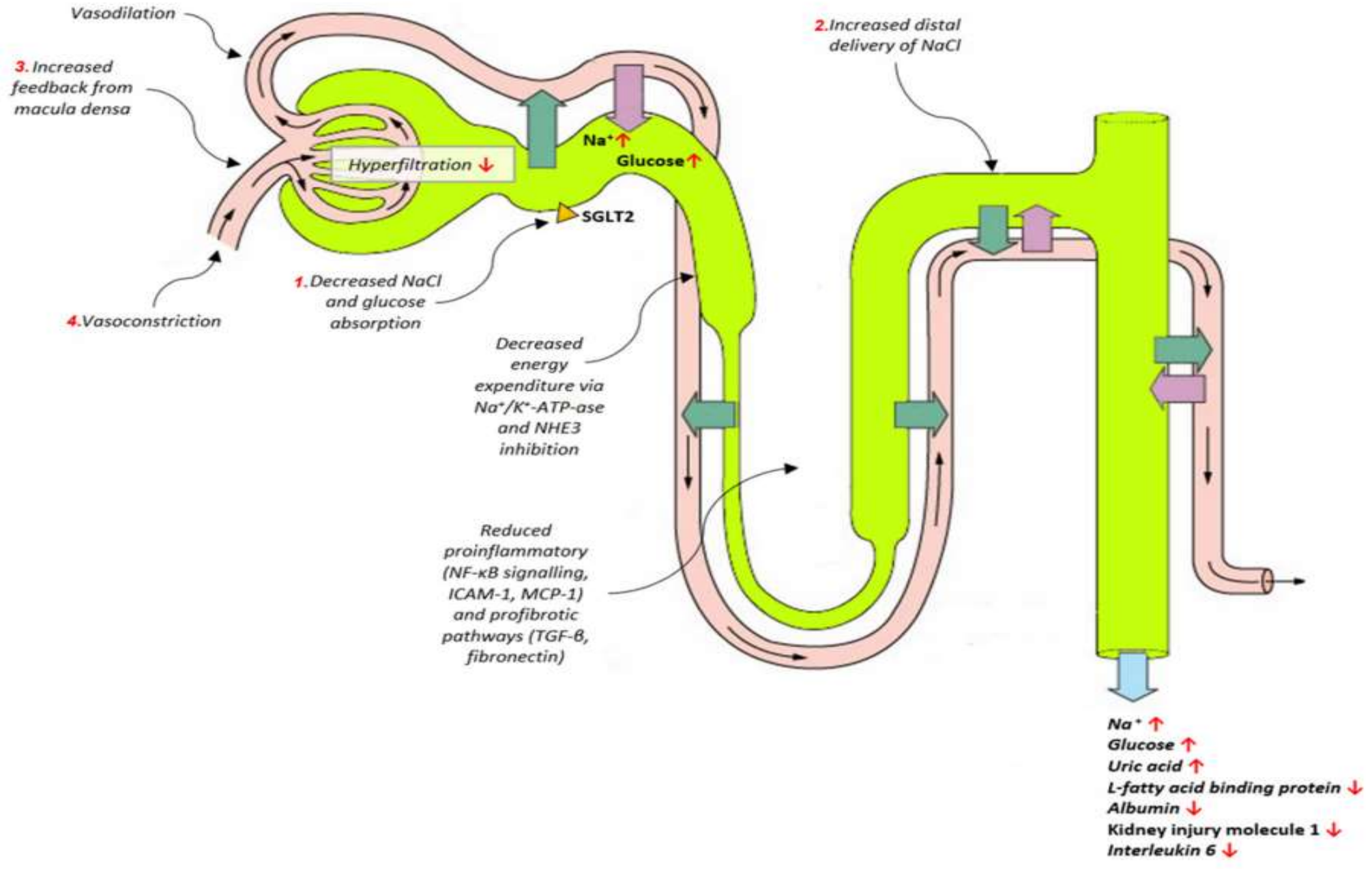
Sodium-glucose cotransporter-2 inhibitors (SGLT2i)

We recommend treating adults with CKD with an SGLT2i for the following (1A):

eGFR ≥ 20 ml/min per 1.73 m2 with urine ACR ≥ 200 mg/g (≥ 20 mg/mmol),

or heart failure, irrespective of level of albuminuria.

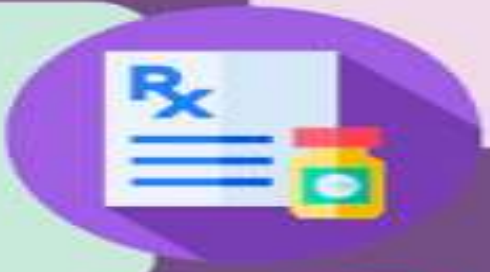
Direct mechanisms by which SGLT2 inhibitors exert renoprotective effects



What are the Steps to Prescribe SGLT2i?

1 Whom to prescribe?

- Proteinuric CKD ± T2DM
- eGFR > 20ml/min/1.73m2
- uACR > 200mg/gm
- Heart failure



2 Avoid use in the following

- Risk of genital infection
- Ketoacidosis
- Lupus nephritis
- Polycystic kidney disease

3 How to prescribe?

Use one dose with proven benefit.

- Canagliflozin 100mg
- Dapagliflozin 10mg
- Empagliflozin 10mg

Mineralocorticoid receptor antagonists (MRA)

The Work Group highlights a key recommendation and practice points from the KDIGO 2022 Clinical Practice Guideline for Diabetes Management in Chronic Kidney Disease

A nonsteroidal MRA *(FINERENONE)* with proven kidney or cardiovascular benefit for adults (2A):

- with DM 2 type
- an eGFR >25 ml/min per 1.73 m2
- normal serum potassium concentration
- albuminuria (>30 mg/g [>3 mg/mmol])

despite maximum tolerated dose of RAS inhibitor (RASi)

K^+ ≤4.8 mmol/l

- Initiate finerenone
  - 10 mg daily if eGFR 25–59 ml/min/1.73 m^2
  - 20 mg daily if eGFR ≥60 ml/min/1.73 m^2
- Monitor K^+ at 1 month after initiation and then every 4 months
- Increase dose to 20 mg daily, if on 10 mg daily
- Restart 10 mg daily if previously held for hyperkalemia and K^+ now ≤5.0 mmol/l

K^+ 4.9–5.5 mmol/l

- Continue finerenone 10 mg or 20 mg
- Monitor K^+ every 4 months

K^+ >5.5 mmol/l

- Hold finerenone
- Consider adjustments to diet or concomitant medications to mitigate hyperkalemia
- Recheck K^+
- Consider reinitiation if/when K^+ ≤5.0 mmol/l

Indications for the initiation of dialysis

Symptoms or signs attributable to kidney failure:

- neurological signs and symptoms attributable to uremia
- pericarditis
- anorexia
- medically resistant acid-based or electrolyte abnormalities
- intractable pruritus
- serositis-
- acid-base or electrolyte abnormalities

Inability to control volume status or BP

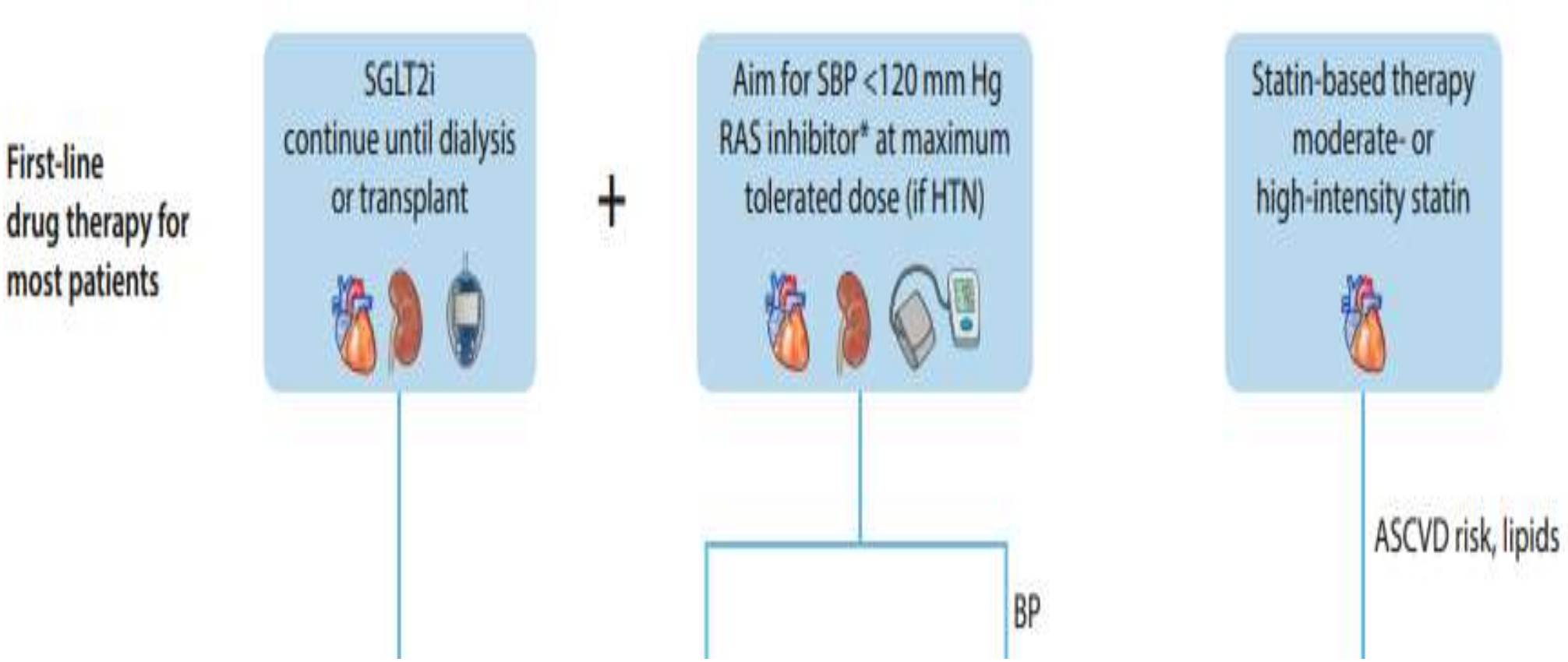
Progressive deterioration in nutritional status refractory to dietary intervention

Cognitive impairment

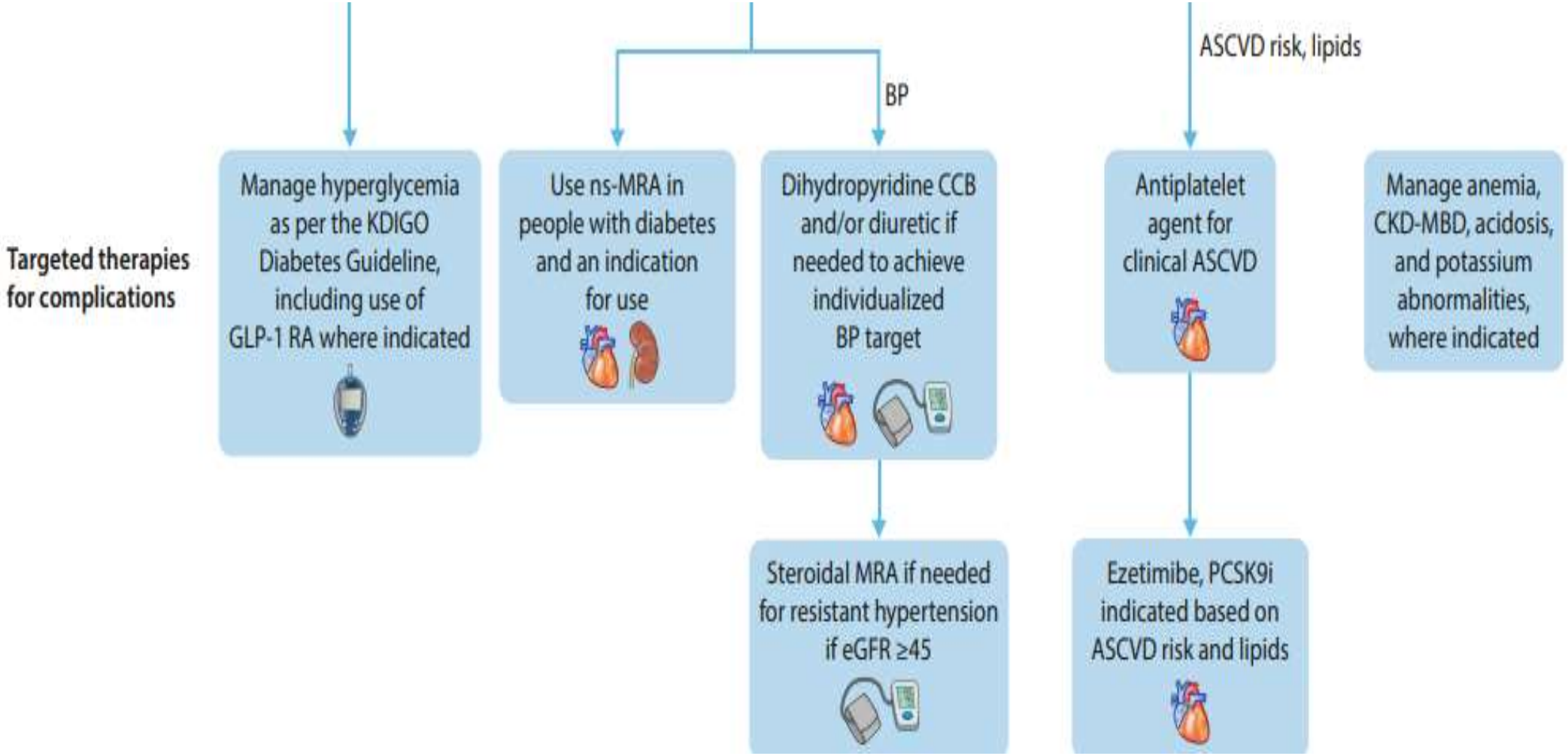
Holistic approach to CKD treatment and risk modification

Lifestyle

Holistic approach to CKD treatment and risk modification

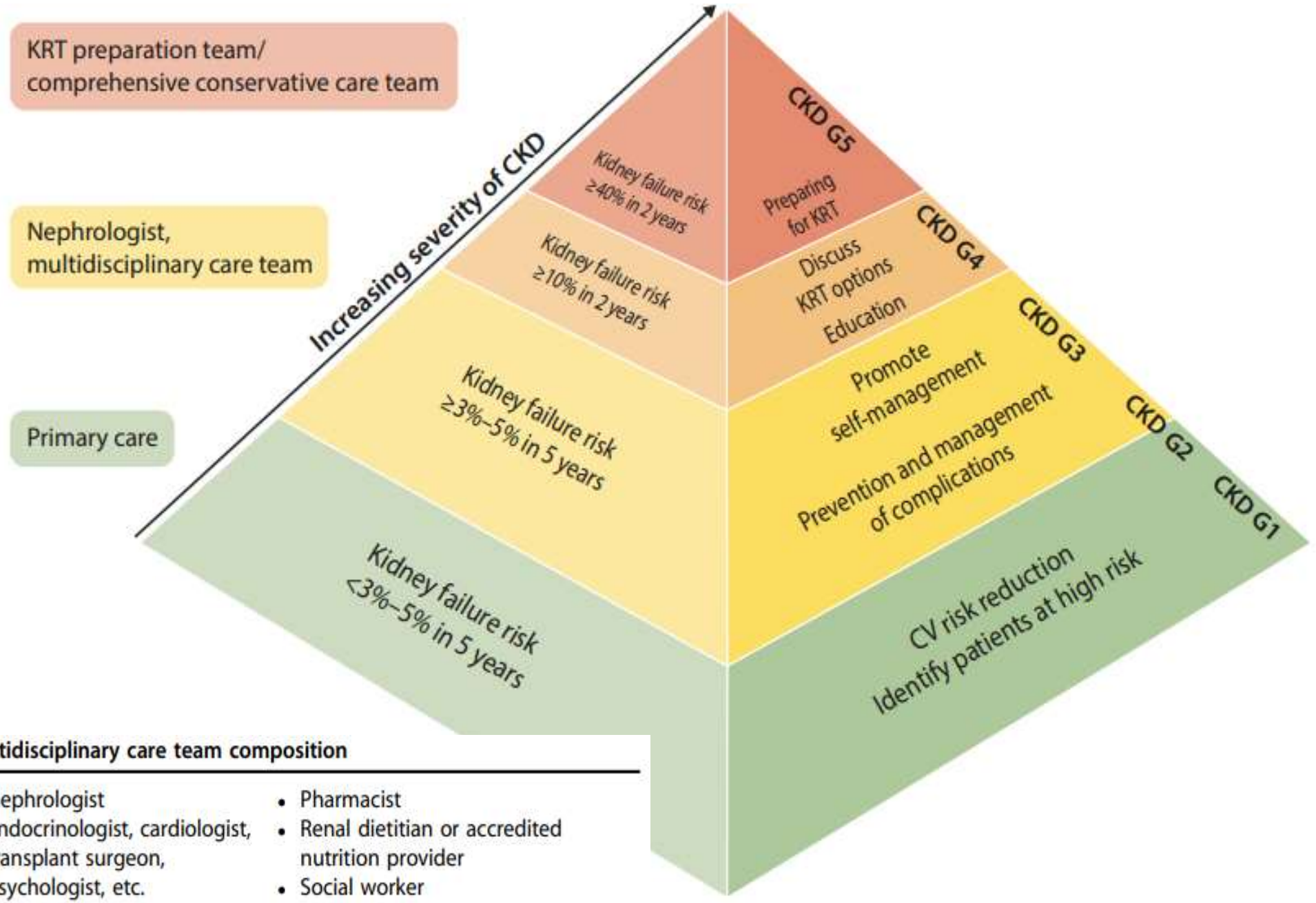


Holistic approach to CKD treatment and risk modification



Optimal care model by increasing severity of CKD

CV, cardiovascular; KRT, kidney replacement therapy



Multidisciplinary care team composition

- Nephrologist
- Endocrinologist, cardiologist, transplant surgeon, psychologist, etc.
- Nurse
- Pharmacist
- Renal dietitian or accredited nutrition provider
- Social worker

Clinical case: Anna, 54 y.o.

Complaints: headache, puffy face in morning, fatigue, thirst

Anamnesis:
Hypertension (HT) during 5 years
Obesity II grade, abdominal type during 8 years
Family anamnesis: patient's father died in 62 years from renal failure
Habits: smoker, sedentary lifestyle

Physical examination:
Pale face, paraorbital edema
BMI **32** kg/m2
BP **168 / 100** mm Hg
HR 88 bpm

ECG: sinus regular rythm, 86 bpm, **left ventricle hypertrophy**

Clinical case: Anna, 54 y.o.

Clinical diagnosis:

Hypertension II stage (LVH), 2 grade (168/100 mm Hg), risk 3 (high)

Obesity II grade, abdominal type

The patient has multiple risk factors of CKD:

- uncontroled hypertension
- obesity
- smoking
- family anamnesis by CKD

Thus, she need additional investigations to cardiovasculsr risk stratification and screening for CKD

Clinical case: Anna, 54 y.o.

Investigations:

- lipid profile
- serum creatinine and GFR calculation
- unrine analysis
- fasting glucose
- HbA1c

Cholesterol, mmol/l	**5,68**
LDL, mmol/l	**4,6**
Glucose fasting, mmol/l	**6,3**
Serum creatinine, μmol/l	**109**
eGFR, ml/min/1,73 m2	**50**
HbA1c, %	**6,0**
albumineuria	**300**

Has the patient CKD?

Clinical case: Anna, 54 y.o.

The patient has multiple risk factors of CKD:

- uncontroled hypertension
- obesity
- smoking
- family anamnesis by CKD

Thus, she need follow up in 3 months

Recommendation for Anna

1. **Weight control** (goal — BMI less 25,5 kg/m2)

- optimal exercise program
- diet: *cut down salt and protein intake*

2. Smoking cessation

3.**Medication:**

- fixed combination of antihypertensive drugs: Valsartan 160 mg + HCTZ 12,5 mg (goal — less 120 and 80)
- statins: atorvastatine 20 mg (goal — LDL less 1,8 mmol/l)

4. follow-up visit in 3 month to estimate eGFR

In 3 month

1. BMI 29 kg/m2
2. Creatinine 99 □mol/l, eGFR **56** ml/min/1,73m2
3. BP **138/88** mm Hg
4. LDL **2,8** mmol/l
5. albuminuria absent

Clinical diagnosis: HT III stage, high normal BP, risk 4.

CKD 3a stage (G3a), A1