Practical Approach to Detection and Management of Chronic Kidney Disease for the Primary Care Clinician

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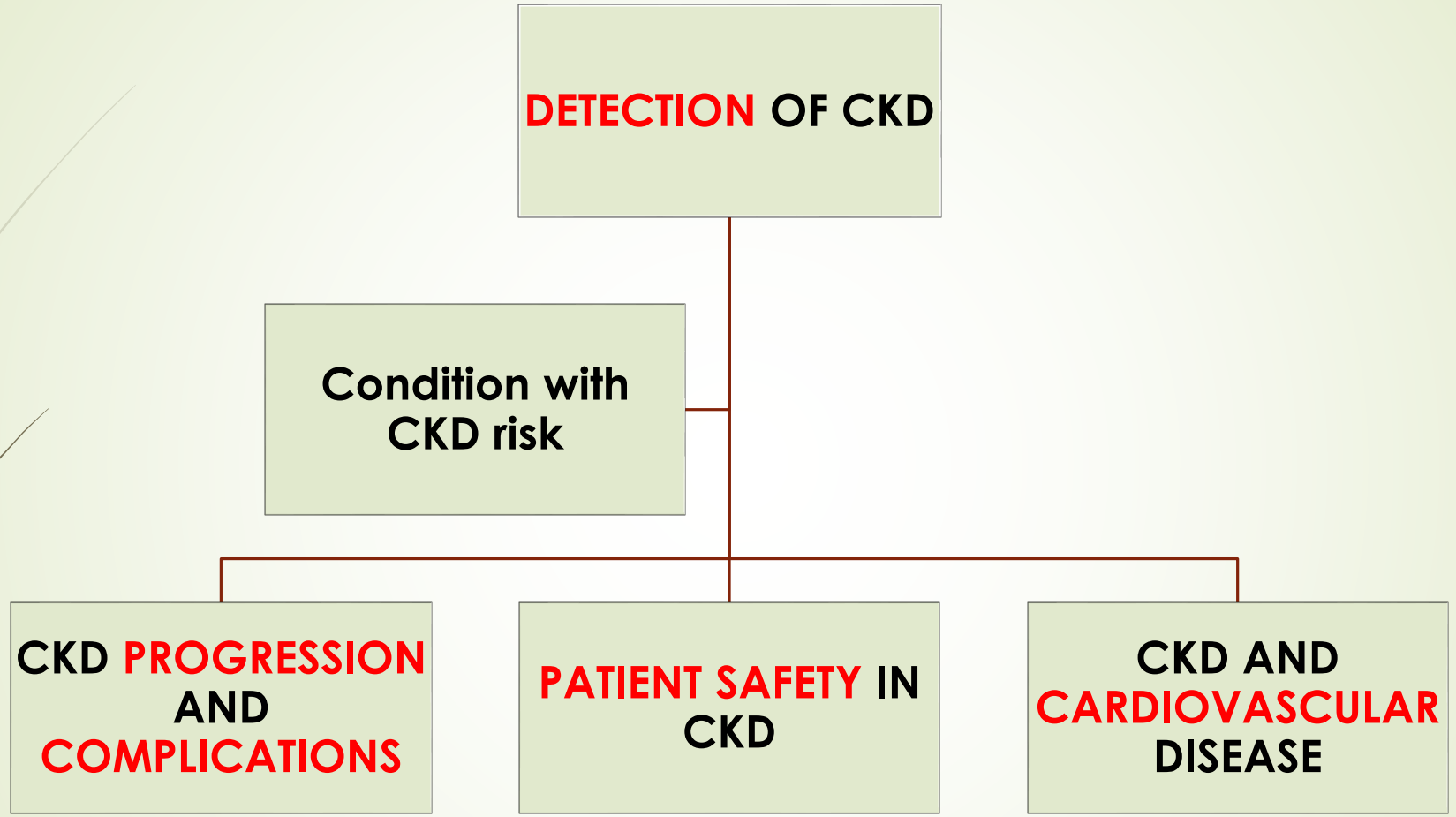

DETECTION OF CKD
Condition with CKD risk
CKD PROGRESSION AND COMPLICATIONS
PATIENT SAFETY IN CKD
CKD AND CARDIOVASCULAR DISEASE

Topic 1

- DETECTION OF CHRONIC KIDNEY DISEASE

Condition with ↑ CKD risk:

- ✓ DM
- ✓ HTN
- ✓ Cardiovascular disease
- ✓ Age>60
- ✓ Ethnics- racial
- ✓ Obesity
- ✓ Family history CKD
- ✓ AKI

- 2002, the National Kidney Foundation's Kidney Disease Outcomes Quality Initiative published the first guideline that defined CKD, independent of the cause, as based on **3 or more** months of either kidney damage (albuminuria, kidney biopsy findings or imaging abnormalities) **or** an eGFR <60 mL/min/1.73 m.

- In2012 the Kidney Disease Improving Global Outcomes released a new guideline for CKD that adds refinements based on cause, e GFR , and albuminuria categories .

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/1.73m^2) Description and range	G1	Normal or high	≥90	1 if CKD	Treat 1	Refer* 2
	G2	Mildly decreased	60-89	1 if CKD	Treat 1	Refer* 2
	G3a	Mildly to moderately decreased	45-59	Treat 1	Treat 2	Refer 3
	G3b	Moderately to severely decreased	30-44	Treat 2	Treat 3	Refer 3
	G4	Severely decreased	15-29	Refer* 3	Refer* 3	Refer 4+
	G5	Kidney failure	<15	Refer 4+	Refer 4+	Refer 4+

- Testing, risk stratification, and treatment plans differ according to eGFR and urinary Alb/Cr ratio.
- In practice, detection of CKD often occurs during routine care.
- The estimated prevalence of CKD in the general population exceeds 10%,

- In clinical practice the most common tests for CKD include GFR estimated from the serum creatinine concentration **(eGFR)** and **albuminuria** from the urinary albumin-to creatinine ratio.

- Assessment of eGFR and albuminuria should be performed for persons with diabetes and/or hypertension **but is not recommended for the general population**.

Kidney Function:

- Detection of CKD based on eGFR is a more accurate assessment of kidney function than serum creatinine alone.
- Two equations are used in practice to eGFR, the CKD Epidemiology Collaboration equation and the older Modification of Diet in Renal Disease Study equation.
- Recent studies have found that the CKD Epidemiology Collaboration equation more accurately predicts prognosis and is less biased than the older Modification of Diet in Renal Disease Study equation.
- One caveat is that any eGFR rate equation is inaccurate in the setting of acute kidney injury because kidney function is not in a steady state.

Urine Studies to Evaluate for Albuminuria or Proteinuria:

- Although quantification of albuminuria has been less widely adopted in clinical practice than assessment of eGFR,it is crucial to evaluating prognosis.
- A spot albumin-to-creatinine ratio is a more sensitive and specific marker of CKD than a spot urine protein/creatinine ratio, although both are predictive of clinical outcomes.
- Standardization of urine albumin measurement is ongoing but superior to urine protein that has much wider variability.
- A random or spot urine specimen quantifies albumin as milligrams per gram of creatinine (mg/g)

Cause of Chronic Kidney Disease

- Evaluation with imaging or serologic testing to identify the cause of CKD is not routinely required, particularly in the presence of diabetes or hypertension.
- Kidney and bladder ultrasound should be performed when there is a history of urinary tract stones or obstruction, frequent urinary tract infections, or a family history of polycystic kidney disease.
- Serologic workup is only required when a systemic or glomerular disease is suspected, such as myeloma or amyloidosis.

❑TOPIC 2:

CHRONIC KIDNEY DISEASE PROGRESSION AND COMPLICATIONS

Management of CKD includes

- ✓ reducing the patient's risk of CKD progression
- ✓ reducing the risk of associated complications, such as AKI and cardiovascular disease, anemia, and metabolic acidosis, as well as mineral and bone disorder.
- ✓ promote quality of life

- **Four interventions clearly delay CKD progression, including:**

- ✓ blood pressure <140/90 mm Hg
- ✓ use of angiotensin-converting enzyme inhibitors or angiotensin receptor blockers for patients with albuminuria and hypertension
- ✓ hemoglobin A1c 7% for patients with diabetes
- ✓ correction of CKD-associated metabolic acidosis.

Hypertension Management

- For the past 10 years, the Joint National Committee on hypertension (JNC) has recommended an office blood pressure target of 130/80 mm Hg or less for patients with chronic kidney disease.
- Recently, JNC 8 has loosened this target to 140/90 mm Hg, the same as for the general population under 60 years of age.
- This new recommendation reflects the lack of robust data supporting a lower blood pressure target.
- Accordingly, recent clinical practice guidelines for blood pressure management in CKD have suggested that a target of 130/80 mm Hg should be sough only in the context of severe albuminuria, but the evidence for this goal is of very low quality.

- **Sodium consumption** is an important consideration for blood pressure control in CKD. A diet high in sodium is a cause of resistance to hypertension medications, especially for patients with CKD.

- The average American consumes more than 3500 mg sodium daily.

- For patients with CKD current guidelines recommend less than 2000 mg of sodium per day; however, there is low quality evidence for this recommendation.

ACE-I or ARB:

- Treatment with ACE-I or ARB for hypertension in persons with CKD with or without diabetes who have A2 and A3 levels of albuminuria is supported by low-to high-level evidence, respectively.

- Although JNC 8 recommends a RAAS blocker for all patients with CKD, current evidence supports this treatment primarily for patients with albuminuria.

- Some CKD patients can develop hyperkalemia or a decreased eGFR rate after starting an ACE-I or an ARB.

- Monitoring should include assessment of serum potassium and eGFR several weeks after initiation or dose escalation.
- When hyperkalemia develops, outpatient management strategies include identification and restriction of dietary potassium, treatment of metabolic acidosis if appropriate , consideration of thiazide or loop diuretic use to increase potassium excretion, and treatment with a potassium-binding exchange resin.
- Discontinuation of the RAAS blocker should be considered only if these interventions fail.
- When the eGFR decreases more than 25% within 3 months of RAAS initiation, the patient deserves additional investigation for over diuresis or renal artery stenosis.

- Dual RAAS Blockade Combination therapy with an ACE-I plus an ARB should not be used for patients with chronic kidney disease and hypertension regardless of whether they have diabetes.
- Trials have shown greater complications, such as acute kidney injury and severe hyperkalemia, and no mortality or cardiovascular benefits with combination versus single-agent therapy.

Diuretic Therapy:

- Diuretics are generally necessary to manage extracellular fluid volume expansion and blood pressure control in CKD.
- Thiazides are used especially for patients with stages G1-3b CKD.
- A second-line option is a loop diuretic when the thiazide does not achieve volume control goals.
- Most patients with stage G4 CKD will require a loop diuretic, and furosemide, the most common drug, should be dosed twice daily for effective diuresis

Glycemic Control

- According to recent data regarding harms from overly intensive glycemic control, a target hemoglobin A1c (HbA1c) of approximately 7% has been recommended, with a higher target for those with a limited life expectancy or an elevated risk of hypoglycemia.

- In addition to cardiovascular risk reduction, the benefits of glycemic control in CKD include reduced progression of albuminuria and reduced loss of kidney function over time.

complication

CKD anemia:

- Measurement of hemoglobin (Hb) at least annually is recommended beginning with stage G3a CKD, because erythropoietin production decreases with low GFR.
- Evaluation :if Hgb<13 in men and Hgb<12for women

Treat iron deficiency anemia if present

treat with ESA if Hgb<10g/dl

Target Hgb 10-11.5

CKD mineral and Bone Disorder:

- Secondary hyperparathyroidism, hypocalcemia, hyperphosphatemia, decreased vitamin D, and vascular calcification typically begin in stage G3b.
- Serum calcium, phosphorus, intact parathyroid hormone, and total 25-hydroxy vitamin D should be measured at least once to document baseline levels.

CKD Metabolic Acidosis:

- Treatment of CKD associated metabolic acidosis with oral alkali to achieve a normal serum bicarbonate level has been shown in observational studies to slow CKD progression.
- When the bicarbonate level is less than 22 mmol/L, sodium bicarbonate (650 mg) should be prescribed 3 times daily.
- This dose corresponds to approximately 23 mEq daily of sodium and bicarbonate.

TOPIC 3:

- **PATIENT SAFETY IN CHRONIC KIDNEY DISEASE**

- Many commonly prescribed medications and/or their metabolites are excreted by the kidneys so dose adjustments based on eGFR reduce complications.
- Several medications can cause acute kidney injury that, in turn, can initiate and/or accelerate CKD progression.
- It may be prudent to discontinue or briefly withhold medications that may cause acute kidney injury (RAAS blockers, NSAIDs, diuretics) or those that can cause complications (eg, lactic acidosis due to metformin) when patients have an increased risk of volume depletion

NSAIDs:

- Nonsteroidal anti-inflammatory inhibitors can cause acute kidney injury by inhibiting vasodilatory prostaglandins, especially in the context of other factors that impair renal perfusion, such as dehydration and congestive heart failure.

- Other potential adverse effects of NSAIDS include allergic interstitial nephritis with or without minimal change disease, hyperkalemia, hypertension, and edema.

- Long-term use of NSAIDs can also increase the rate of progression of CKD.

- These drugs a available over the counter, so it is important that the clinician specifically inquire about their use and educate patients about potential harms.

- These medications should be avoided with an eGFR <30 mL/min/1.73 m2 and limited with an eGFR <60 mL/min/1.73 m2.

- Furthermore, they should be used with extreme cautionin patients with CKD and concomitant RAAS blocking agents and/or diuretic therapy.

- Early detection of CKD offers a valuate opportunity to avert complications before symptoms occur and to slow loss of kidney function over time.

- **Metformin** Although the US Food and Drug Administration has a black box warning for metformin use in patients with serum creatinine 1.5mg/dLin men and 1.4mg/dL in women owing to an increased risk for lactic acidosis, it is now recognized that this risk is extremely low.
- Many practice guidelines recommend discontinuing metformin use only when the eGFR is <30 mL/min/1.73 m2, and use with caution for patients with an eGFR of 30-45 mL/min/1.73 m2.

Iodinated Contrast

- The major risk factor for contrast-induced nephropathy is CKD.
- Use of N-acetylcysteine to prevent contrast-induced acute kidney injury is not consistently supported by clinical trial results, although the oral formulation has little risk.
- Other preventive strategies include minimizing the dose of contrast, volume expansion with intravenous isotonic saline or bicarbonate, and consideration of holding medications that increase risk of acute kidney injury or complications (eg, NSAIDs, diuretics, RAAS blockers, metformin).
- Most studies suggest hydration with isotonic fluids at a rate of 1 mL/kg/h, ideally started at least 1 hour before the procedure and continued for 3-6 hours afterwards.
- The kidney function should be measured 48-96 hours after exposure during the peak in the incidence of contrast-induced acute kidney injury.

TOPIC 4

- CKD and CVD

- Overview All people with CKD should be considered at increased risk for cardiovascular disease.
- In addition to well-known Framingham risk factors for cardiovascular disease, low e GFR and albuminuria have been reported to be independently predictive of cardiovascular disease and cardiovascular disease mortality in prospective cohort studies.
- Other CKD specific risk factors (anemia, mineral and bone disease, and vascular calcification) seem to also play a role in cardio vascular disease in patients with CKD.

Lipid Management:

- Statin-based therapies reduce vascular events in CKD.
- Fire and Forget Strategy in CKD Guidelines for lipid management in adults no longer mandate treating to a low-density lipoprotein cholesterol(LDL-C)target of 70 or 100 mg/dL, because it has not been shown to be beneficial in clinical trials.

Quick summary of the KDIGO recommendations for lipid-lowering treatment in adults with CKD

1. Rule out remediable causes of secondary dyslipidemia (eg, nephrotic syndrome, hypothyroidism, and certain drugs).
2. Establish the indication of treatment (YES or NO) and select agent and dose.
3. Treat according to a ‘‘re-and-forget’’ strategy: do not measure LDL-C unless the results would alter management.

This last step has been particularly controversial.

- Upon first presentation to establish the diagnosis of CKD, the nephrologist will obtain a full lipid prole as part of routine care.
- In case of referral and to conrm the CKD diagnosis, a full lipid prole may already be available.
- Results of the lipid prole should be used together with other clinical data to rule out remediable causes of secondary dyslipidemia.
- If excluded, the nephrologist will establish whether statin treatment is indicated (YES or NO) based on underlying cardiovascular risk.
- If the level of risk suggests that statin treatment is indicated, she/he will select a dose of a statin.
- that is available in her/his country and has been tested for safety in people with CKD.

- Measuring a lipid profile 6-12 weeks after initiating statins might be useful to ensure that an adequate (30%) decline in LDL-C is observed, and poor adherence or inadequate response should be considered if this goal is not achieved.
- Many believe that continued periodic monitoring is necessary to assess ongoing adherence and for lipid alterations associated with CKD progression.

- Randomized controlled trials of fixed-dose statin-based therapies in CKD have shown a reduced risk of primary and secondary atherosclerotic events, but no benefit has been demonstrated for all cause mortality or slower progression of CKD.
- The KDIGO Work Group does not recommend the treat-totarget strategy because it has never been proven benecial in any clinical trial. In addition, higher doses of statins have not been proven to be safe in the setting of CKD.
- Therefore, the Work Group recommends a ‘‘re-and-forget’’ strategy for patients with CKD (see Rationale for Recommendation 1.2). Physicians may choose to perform follow-up measurement of lipid levels in patients for whom these measurements are judged to favorably inuence adherence to treatment or other processes of care.
- Contemporary practice and other clinical practice guidelines emphasize the use of targets for LDL-C (e.g., 1.8 or 2.6mmol/l [70 or 100mg/dl]), which require repeated measurements of LDL-C and treatment escalation with higher doses of statin or initiation of combination lipid-lowering therapy (‘‘treat-to-target’’ strategy) when the LDL-C target is not met.

- Lipid-lowering therapy in persons with CKD who are aged 50 years should be based on assessing cardiovascular disease risk instead of an elevated LDL-C level.(All patient)
- Among adults with CKD aged 18-49 years, treatment with lipid-lowering therapy is indicated for those with known coronary disease (myocardial infarction or coronary revascularization); diabetes mellitus; prior ischemic stroke; or an estimated 10-year risk of coronary death or nonfatal myocardial infarction greater than 10%.

Antiplatelet Agents in CKD

- Adults with CKD should be advised to take low-dose aspirin for secondary prevention of cardiovascular disease unless the risk of bleeding outweighs the benefits.

- Unlike NSAIDs, low-dose aspirin is not associated with acute kidney injury or rapid CKD progression.

TOPIC 5

- REFERRAL TO NEPHROLOGISTS

- The main reasons to refer to nephrology specialists are;
- ✓ eGFR <30 mL/min/1.73 m2
- ✓ severe albuminuria
- ✓ Acute kidney injury.

- Primary care clinicians play a central role in referral to specialists and care coordination for patients with CKD.

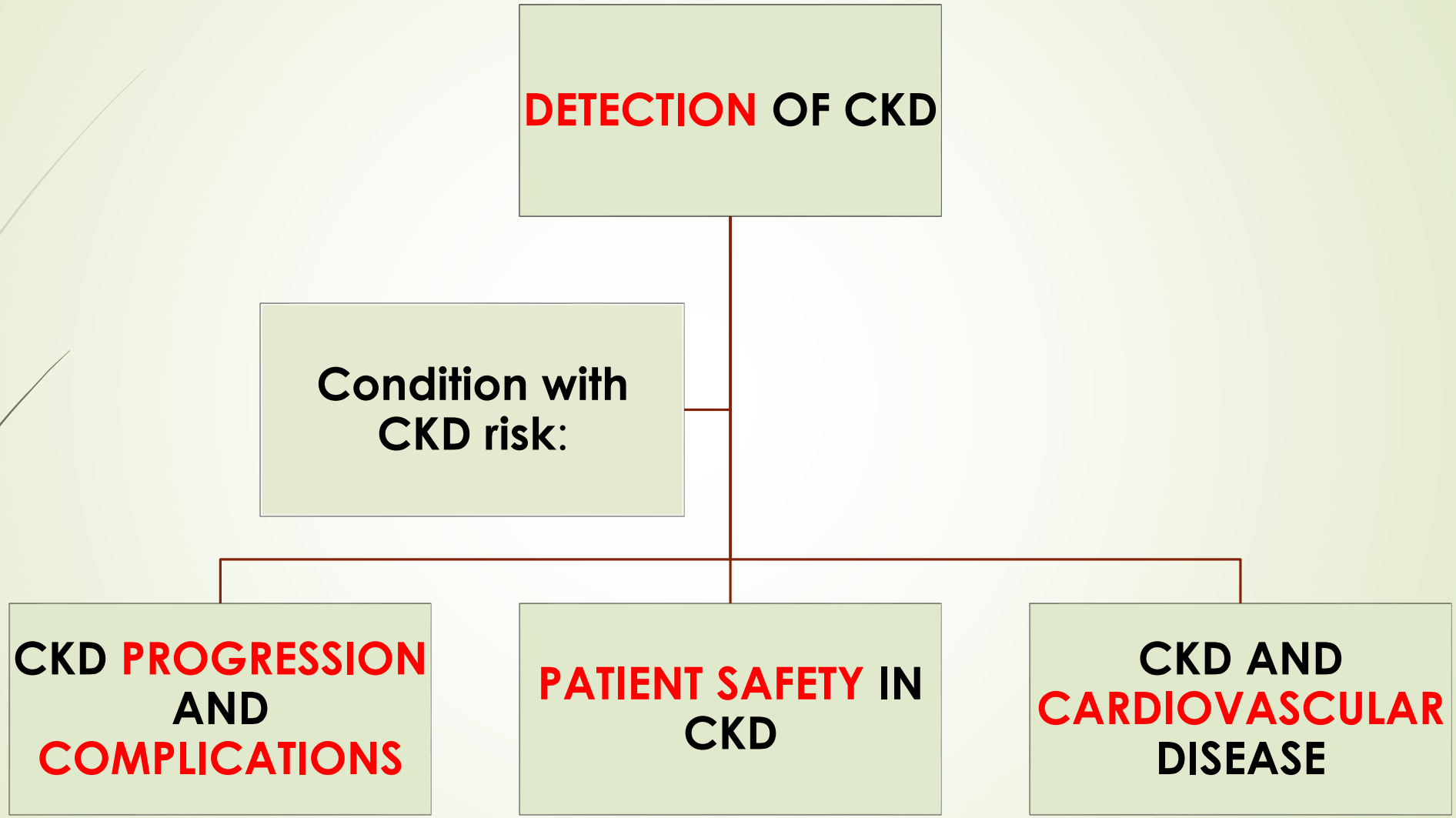
- The primary care clinician may choose not to refer many patients with severe albuminuria, especially those who have a clear etiology, such as diabetes.

- A common challenge for primary care clinicians is exemplified by a patient aged 65 years who has an estimated glomerular filtration rate of 45-60 mL/min/1.73 m2 but no albuminuria or urinalysis abnormalities.

- It is controversial whether this patient's kidney function reflects normal aging or CKD.

- These patients should be managed conservatively by avoiding NSAID and contrast exposures.

- Last, elderly with laboratory evidence of stage G3a CKD should be monitored closely for acute kidney injury after major surgical procedures, particularly cardiac surgery.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Thanks for your attention