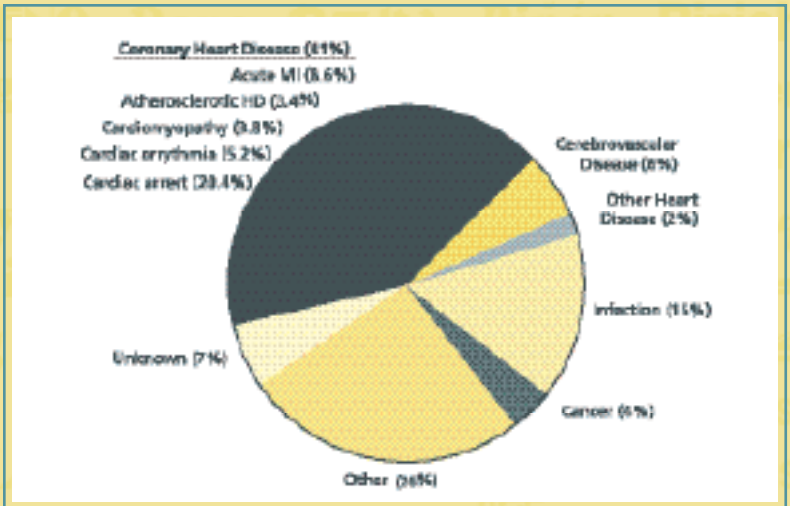


Managing Dyslipidemias in Patients With Chronic Kidney Disease



*Causes of Death Among Period Prevalent Patients,
1997-1999, Treated with Hemodialysis, Peritoneal
Dialysis or Kidney Transplantation*



Abbreviations: MI, Myocardial infarction, HD, heart disease

Based on recommendations contained in the *K/DOQI Clinical Practice Guidelines for Managing Dyslipidemias in Chronic Kidney Disease*

GUIDELINE 1

- 1.1 All adults and adolescents* with CKD should be evaluated for dyslipidemias. (B)**
- 1.2 For adults and adolescents with CKD, the assessment of dyslipidemias should include a complete fasting lipid profile with total cholesterol, LDL, HDL, and triglycerides. (B)
- 1.3 For adults and adolescents with Stage 5 CKD, dyslipidemias should be evaluated upon presentation (when the patient is stable), at 2-3 months after a change in treatment or other conditions known to cause dyslipidemias; and at least annually thereafter. (B)

GUIDELINE 2

- 2.1 For adults and adolescents with Stage 5 CKD, a complete lipid profile should be measured after an overnight fast whenever possible. (B)
- 2.2 Hemodialysis patients should have lipid profiles measured either before dialysis, or on days not receiving dialysis. (B)

GUIDELINE 3

Stage 5 CKD patients with dyslipidemias should be evaluated for remediable, secondary causes. (B)

Secondary Causes of Dyslipidemias

Medical Conditions	
Hypertension	Excessive alcohol consumption
Hypothyroidism	Liver disease
Diabetes	
Medications	
β ₂ -agonists	Anesthetics
Androgens/steroids	Oral contraceptives
Highly active anti-retroviral therapy	Corticosteroids
Diuretics	Cyclosporine
Beta-blockers	Statins

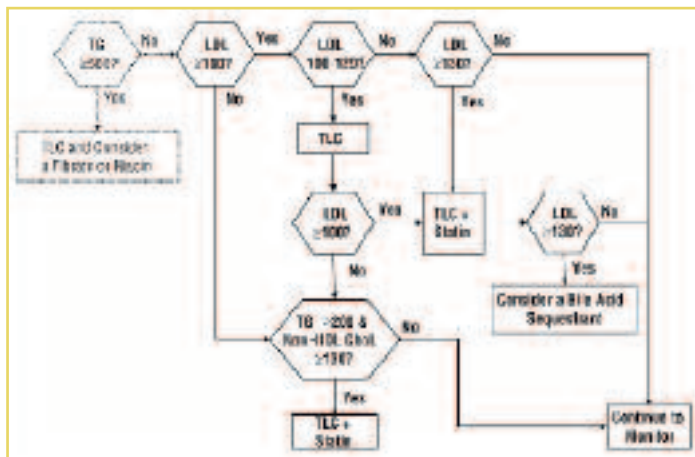
* Adolescent is defined by onset of puberty.

** (B) – It is recommended that clinicians routinely follow the guideline. There is moderate evidence that the practice improves net health outcomes.

GUIDELINE 4

- 4.1 For adults with Stage 5 CKD and fasting triglycerides ≥ 500 mg/dL (≥ 5.65 mmol/L) that cannot be corrected by removing an underlying cause, treatment with therapeutic lifestyle changes (TLC) and a triglyceride-lowering agent should be considered. (C)⁺
- 4.2 For adults with Stage 5 CKD and LDL ≥ 100 mg/dL (≥ 2.59 mmol/L), treatment should be considered to reduce LDL to < 100 mg/dL (< 2.59 mmol/L). (B)
- 4.3 For adults with Stage 5 CKD and LDL < 100 mg/dL (< 2.59 mmol/L), fasting triglycerides ≥ 200 mg/dL (≥ 2.26 mmol/L) and non-HDL cholesterol (total cholesterol minus HDL) ≥ 130 mg/dL (≥ 3.36 mmol/L), treatment should be considered to reduce non-HDL cholesterol to < 130 mg/dL (< 3.36 mmol/L). (C)

Treatment for Adults



Units for the figure above are in mg/dL. To convert mg/dL to mmol/L, multiply triglycerides by 0.01129 and LDL or non-HDL cholesterol by 0.02586. Abbreviations: TG, triglycerides; TLC, therapeutic lifestyle changes; LDL, low-density lipoprotein; HDL, high-density lipoprotein.

⁺ (C) It is recommended that clinicians consider following the guideline for eligible patients. This recommendation is based on either weak evidence, poor evidence or on the opinions of the Work Group and reviewers, that the practice might improve net health outcomes.

Key Features of the NKF-K/DOQI Guidelines That Differ from Those of the National Cholesterol Education Program Adult Treatment Panel III

NKF-K/DOQI Guidelines	Adult Treatment Panel III Guidelines
1. CKD patients should be considered to be in the highest risk category.	1. CKD patients are not managed differently from other patients.
2. Evaluation of dyslipidemia should occur at presentation with CKD, after a change status, and annually.	2. Evaluation of dyslipidemia should occur every 5 years.
3. Drug therapy should be used for LDL 100-129 mg/dL after 3 months of TLC.	3. Drug therapy is considered optional for LDL 100-129 mg/dL.
4. Initial drug therapy for high LDL should be with a statin.	4. Initial drug therapy for high LDL should be with a statin, bile acid sequestrant, or nicotinic acid.
6. Recommendations are made for patients <20 years old.	5. No recommendations are made for patients <20 years old.
8. Fibrates may be used in Stage 5 CKD a) for patients with triglycerides ≥ 500 mg/dL; and b) for patients with triglycerides ≥ 200 mg/dL with non-HDL cholesterol ≥ 150 mg/dL, who do not tolerate statins.	6. Fibrates are contraindicated in Stage 5 CKD.
7. Gemfibrozil may be the fibrate of choice for treatment of high triglycerides in patients with CKD.	7. No preferences are indicated for which a fibrate should be used to treat hypertriglyceridemia.
<p>To convert mg/dL to mmol/L, multiply triglycerides by 0.01129 and cholesterol by 0.02594.</p> <p>Abbreviations: NKF-K/DOQI, National Kidney Foundation Kidney Disease Outcomes Quality Initiative; CKD, chronic kidney disease; LDL, low-density lipoprotein cholesterol; HDL, high-density lipoprotein cholesterol; TLC, therapeutic lifestyle changes.</p>	

Management of Dyslipidemias in Adults with Chronic Kidney Disease

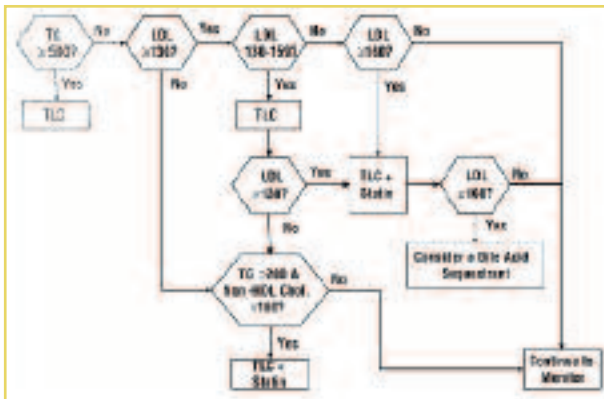
Dyslipidemia	Goal	Initiate	Increase	Alternative
TG \geq 500 mg/dL	TG <500 mg/dL	TLC	TLC + Fibrate or Niacin	Fibrate or Niacin
LDL 100-129 mg/dL	LDL <100 mg/dL	TLC	TLC + low dose Statin	Bile acid seq. or Niacin
LDL \geq 130 mg/dL	LDL <100 mg/dL	TLC + low dose Statin	TLC + max. dose Statin	Bile acid seq. or Niacin
TG \geq 200 mg/dL and non-HDL \geq 130 mg/dL	Non-HDL <130 mg/dL	TLC + low dose Statin	TLC + max. dose Statin	Fibrate or Niacin

To convert mg/dL to mmol/L, multiply triglycerides by 0.01129, and cholesterol by 0.02586.
Abbreviations: TG, triglycerides; LDL, low-density lipoprotein cholesterol; TLC, therapeutic lifestyle changes; seq., sequestrant.

GUIDELINE 5

- 5.1 For adolescents with Stage 5 CKD and fasting triglycerides \geq 500 mg/dL (\geq 5.65 mmol/L) that cannot be corrected by removing an underlying cause, treatment with therapeutic lifestyle changes (TLC) should be considered. (C)
- 5.2 For adolescents with Stage 5 CKD and LDL \geq 130 mg/dL (\geq 3.36 mmol/L), treatment should be considered to reduce LDL to <130 mg/dL (<3.36 mmol/L). (C)
- 5.3 For adolescents with Stage 5 CKD and LDL <130 mg/dL (<3.36 mmol/L), fasting triglycerides \geq 200 mg/dL (\geq 2.26 mmol/L), and non-HDL cholesterol (total cholesterol minus HDL) \geq 160 mg/dL (\geq 4.14 mmol/L), treatment should be considered to reduce non-HDL cholesterol to <160 mg/dL (<4.14 mmol/L). (C)

Treatment for Adolescents



Units for the figure above are in mg/dL. To convert mg/dL to mmol/L, multiply triglycerides by 0.01129 and LDL or non-HDL cholesterol by 0.02586. Abbreviations: TG, triglycerides; TLC, therapeutic lifestyle changes; LDL, low-density lipoprotein; HDL, high-density lipoprotein.

The *Clinical Practice Guidelines for Managing Dyslipidemias in Chronic Kidney Disease*, as well as all other K/DOQI guidelines, can be accessed on the Internet at www.kdoqi.org
Am J Kidney Dis 41:S1-S92, 2003 (suppl 3)

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The arrow below illustrates the audiences for KLS resources. Light-shaded boxes indicate the target audience(s) for this resource.



Key Features of the NKF-KDOQI Guidelines That Differ from Those of the National Cholesterol Expert Panel on Children

NKF-KDOQI Guidelines	Expert Panel on Children
1. Adolescents with CKD should be considered to be in the highest risk category.	1. Adolescents with CKD are not managed differently from other patients.
2. Evaluation of dyslipidemia should occur after presentation with CKD, after a change in kidney failure treatment modality, and annually.	2. Evaluation of dyslipidemia should occur every 6 years.
3. If LDL is 130-159 mg/dL, start TLC diet (if nutritional status is adequate), followed in 6 months by a statin ^a if LDL \geq 150 mg/dL.	3. If LDL >130 mg/dL, start TLC Step I AHA diet, followed in 3 months by Step II AHA diet if LDL >180 mg/dL.
4. If LDL \geq 160 mg/dL, start TLC plus a statin.	4. If LDL \geq 160 mg/dL and family history of CHD or two or more CVD risk factors, start drug therapy.

To convert mg/dL to mmol/L, multiply triglycerides by 0.01129 and cholesterol by 0.02596.
^aCurrently, atorvastatin is the only statin approved by the U.S. Food and Drug Administration for use in children.
 Abbreviations: NKF-KDOQI, National Kidney Foundation Kidney Disease Clinical Quality Initiative; CKD, chronic kidney disease; AHA, American Heart Association; LDL, low-density lipoprotein cholesterol; TLC, therapeutic lifestyle change; CHD, cardiovascular disease.

Therapeutic Lifestyle Changes (TLC) for Adults With Chronic Kidney

Diet (Consult a dietitian with expertise in chronic kidney disease)	Physical Activity
<p>Emphasize reduced saturated fat: Saturated fat: <7% of total calories Polyunsaturated fat: up to 10% of total calories Monounsaturated fat: up to 20% of total calories Total fat: 25%-35% of total calories Cholesterol: <200 mg per day Carbohydrate: 50%-60% of total calories</p> <p>Emphasize components that reduce dyslipidemia Fiber: 20-30 g per day emphasize 5-10 g per day viscous (soluble) fiber Consider plant stanols/sterols 2 g per day Improve glycemic control</p> <p>Emphasize total calories to attain/maintain standard NHANES body weight Match intake of overall energy (calories) to overall energy needs Body Mass Index 25-28 kg/m² Waist circumference Men <40 inches (102 cm) Women <35 inches (88 cm) Waist-Hip Ratio (Men <1.0; women <0.8)</p>	<p>Moderate daily lifestyle activities Use pedometer to attain/maintain 10,000 steps per day Emphasize regular daily motion and distance (within ability)</p> <p>Moderate planned physical activity 3-4 times per week 20-30 minute periods of activity Include 5-minute warm-up and cool-down Choose walking, swimming, supervised exercise (within ability) Include resistance exercise training Emphasize lean muscle mass and reducing excess body fat</p>
	<p>Habits Alcohol in moderation: limit one drink per day with approval of physician Smoking cessation</p>
	<p>Abbreviation: NHANES, National Health and Nutrition Examination Survey.</p>

Lipid-Lowering Medication Does Adjustments for Reduced Kidney Function

Agent	Adjust for Reduced GFR (mL/min/1.73 m ²)			Notes
	≥30	15-30	<15	
Atorvastatin	No	No	No	
Carvastatin	No	↓ to 50%	↓ to 50%	Withdrawn
Fenofibrate	?	?	?	
Lovastatin	No	↓ to 50%	↓ to 50%	
Pravastatin	No	No	No	
Simvastatin	?	?	?	
Nicotinic acid	No	No	↓ to 50%	34% kidney excretion
Cholestipol	No	No	No	Not absorbed
Cholestyramine	No	No	No	Not absorbed
Colesvelam	No	No	No	Not absorbed
Bezafibrate	↓ to 50%	↓ to 25%	Avoid	May ↑ serum creatinine
Ciclofibrate	↓ to 50%	↓ to 25%	Avoid	May ↑ serum creatinine
Cisfibrate	?	?	?	May ↑ serum creatinine
Fenofibrate	↓ to 50%	↓ to 25%	Avoid	May ↑ serum creatinine
Gemfibrozil	No	No	No	May ↑ serum creatinine

Abbreviations: GFR, glomerular filtration rate.

Recommended Daily Statin Dose Ranges^a

Statin	Level of GFR (mL/min/1.73 m ²)		With Cyclosporine
	≥ 30	<30 or dialysis	
Atorvastatin	10-80 mg	10-80 mg	10-40 mg
Fluvastatin	20-80 mg	10-40 mg	10-40 mg
Lovastatin	20-80 mg	10-40 mg	10-40 mg
Pravastatin	20-40 mg	20-40 mg	20-40 mg
Simvastatin	20-80 mg	10-40 mg	10-40 mg

^aAdult Treatment Panel III recommendations for GFR ≥30 mL/min/1.73 m². Most manufacturers recommend once daily dosing, but consider giving 50% of the maximum dose twice daily.

Effects of Cyclosporine on Blood Levels of Statins in Kidney Transplant Recipients

Statin	Increase in the Patient's AUC
Atorvastatin	8-fold
Carvastatin*	5-fold
Simvastatin	3-fold
Simvastatin	8-fold
Lovastatin	2-fold
Lovastatin	3-fold
Lovastatin	20-fold
Pravastatin	5-fold
Fluvastatin	2-fold [†]

*N=10, †N=10
Abbreviation: AUC, area under the concentration-time curve.

Bile Acid Sequestrant Dose

Agent	Dose Range (g per day)
Cholestyramine	4-16
Colestipol	5-20
Colesevelam	2.8-5.6

Relative Effect of Different Immunosuppressive Agents on Cardiovascular.

	AZA or MMF	Prednisolone	Cyclosporine	Tacrolimus	Silicic acid
Hypertension	—	↑↑	↑↑	↑	—
Dyslipidemia	—	↑↑	↑↑	—	↑↑↑
Diabetes	—	↑	↑	↑↑	—

Arrows offer a crude, semiquantitative comparison of the relative effect of each agent on cardiovascular disease risk factors. Abbreviations: AZA, azathioprine; MMF, mycophenolate mofetil.

Maximum Doses of Fibrates in Patients with Reduced Kidney Function

Fibrate	Dose (mg) by Level of GFR (mL/min/1.73 m ²)			
	>60	60-89	30-59	<15
Ezetimibe	200 tid	200 bid	200 qd	Avoid
Clofibrate	1,000 bid	1,000 qd	500 qd	Avoid
Ciprofibrate	200 qd	?	?	?
Fenofibrate	201 qd	134 qd	67 qd	Avoid
Gemfibrozil	600 bid	600 bid	600 bid	600 bid

Abbreviation: GFR, glomerular filtration rate.