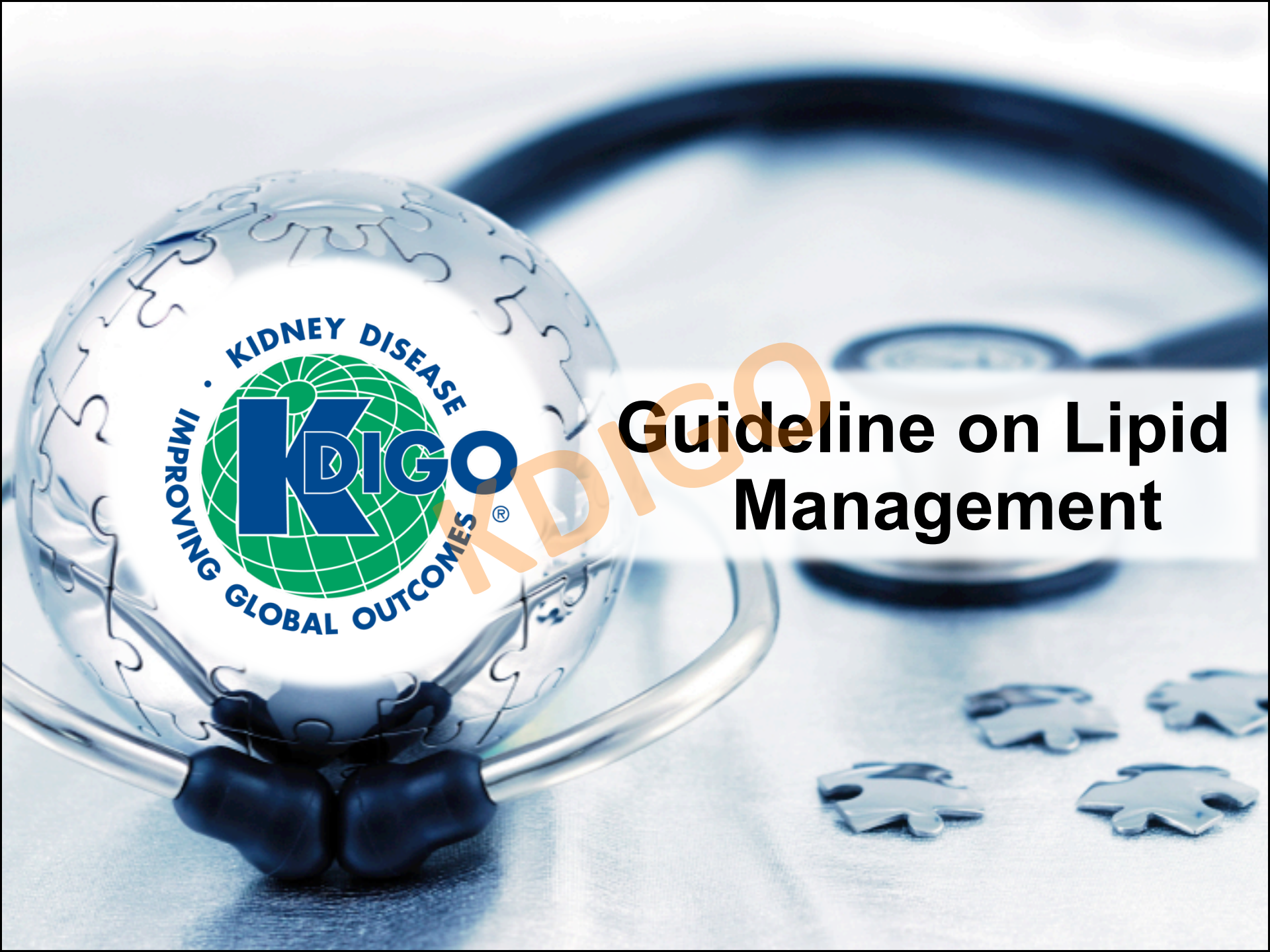
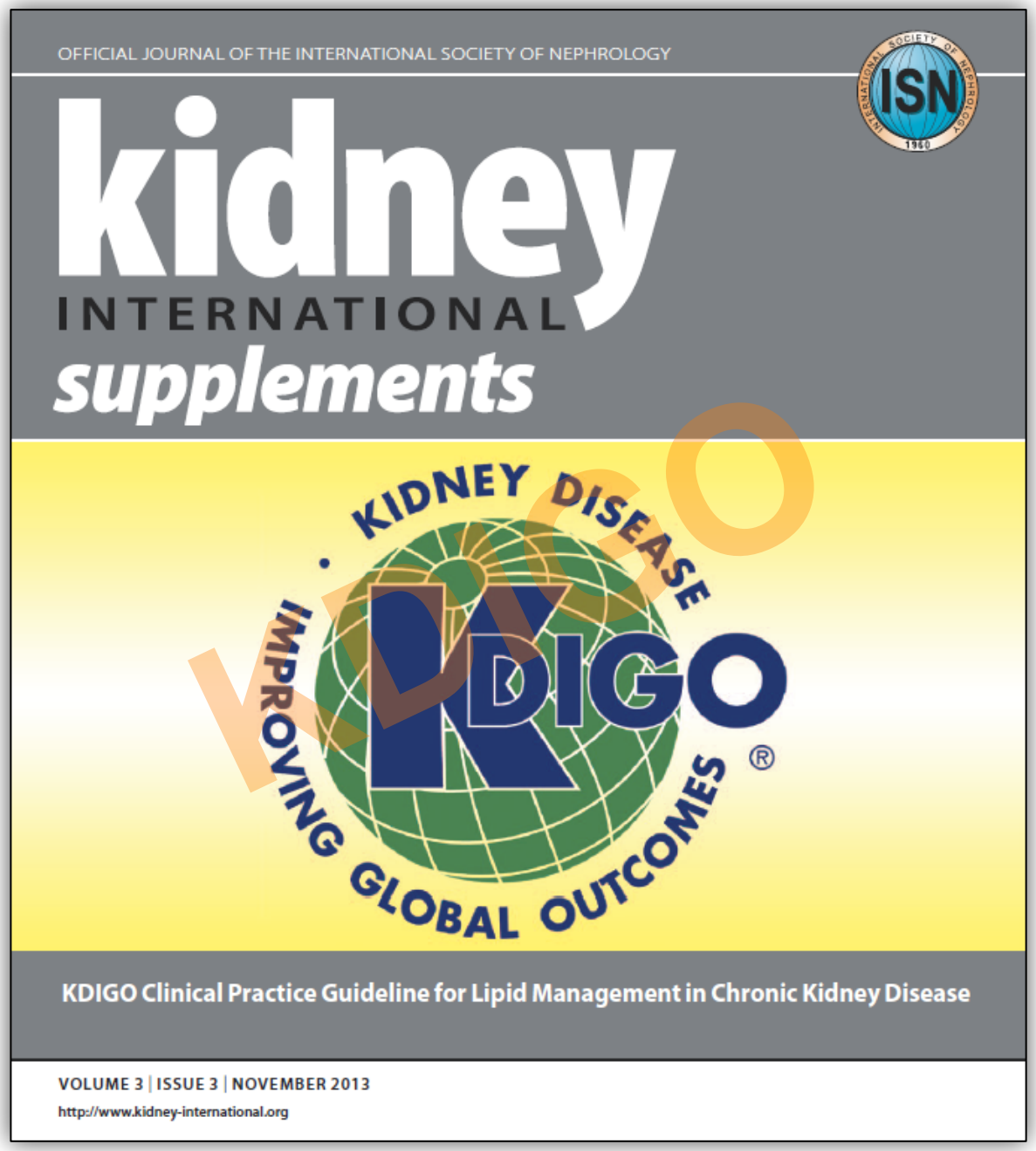


Guideline on Lipid Management

April 23-26, 2014 | Manila, Philipines
PSN 34th Annual Convention

Treat patients
&
stop measuring

but …….


OFFICIAL JOURNAL OF THE INTERNATIONAL SOCIETY OF NEPHROLOGY
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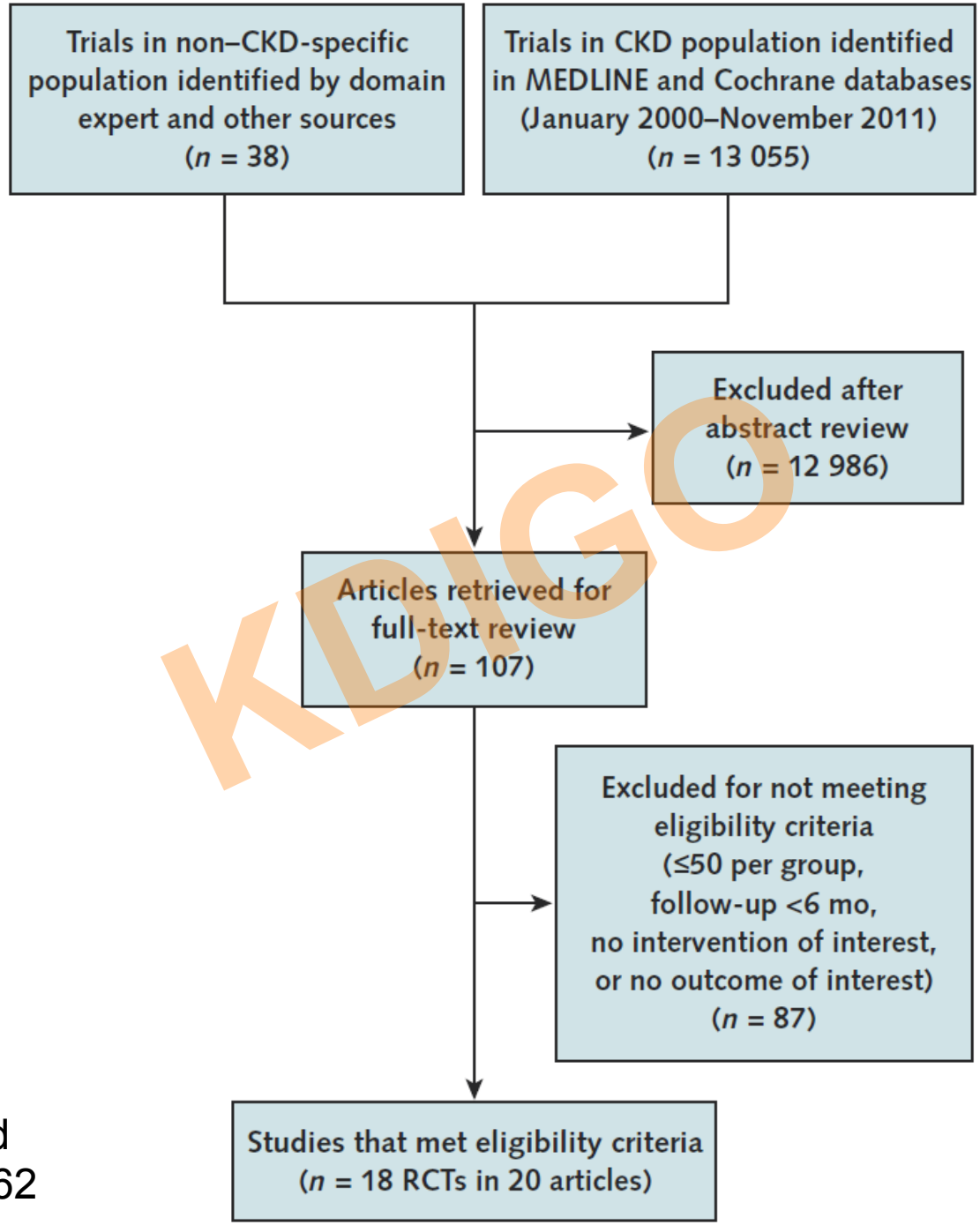
KDIGO
KDIGO Clinical Practice Guideline for Lipid Management in Chronic Kidney Disease
VOLUME 3 | ISSUE 3 | NOVEMBER 2013
http://www.kidney-international.org



Ann Intern Med
2012;157:251-262

A 58-y old non-smoking male (Mr N) is referred with a serum creatinine concentraion of 1,8 mg/dl (160 umol/l).

The history, classification and prognosis evaluation identifies a chronic kidney disease CGA categories G3bA3 :

A 58-y old non-smoking male (Mr S) is referred with a serum creatinine concentraion of **1.8 mg/dl** (160 umol/l).

The history, classification and prognosis evaluation identifies a chronic kidney disease CGA categories G3bA3 :

C) 10-years ago: biopsy profen IgA-nephropathy
G) CKD-EPI eGFR **43** (GFR category G3b 30-44 ml/min/1.73m^2)
A) UACR 1.1 g/g creatinine (Category A3). Measurement in a 24h urine specimen: protein 2.45 g and albumin 1.8 g)

Prognosis of CKD by GFR and Albuminuria Categories: KDIGO 2012

GFR categories (ml/min/ 1.73 m^2) 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			

At presentation no serum lipid profile is available. A fasting profile is ordered **(guideline *1.1*)**.

Why should we measure cholesterol ?

Total cholesterol 236 mg/dl, HDL-C 39 mg/dl, Triglyceride 165 mg/dl
LDL-C 142 mg/dl

Table 1 | Secondary causes of dyslipidemias

Medical Conditions	
Nephrotic syndrome	Excessive alcohol consumption
Hypothyroidism	Liver disease
Diabetes	
Medications	
13-*cis*-retinoic acid	Androgens
Anticonvulsants	Oral contraceptives
Highly active anti-retroviral therapy	Corticosteroids
Diuretics	Cyclosporine
Beta-blockers	Sirolimus

Kidney inter. Suppl. 2013; 3: 259–305

At presentation no serum lipid profile is available. A fasting profile is ordered **(guideline *1.1*)**.

1C

1.1: In adults with newly identified CKD (including those treated with chronic dialysis or kidney transplantation), we recommend evaluation with a lipid profile (TC, LDL-C, HDL-C, triglycerides)

1 = *we recommend*. Most patients should receive the recomended course of action.
C = *low quality of evidence.* The true effect may be substantially different from the estimate of the effect.

Can I ask you:

“Who wants to treat this patient ? “

A) Yes, I treat with a statin

B) I wait and treat at a later timepoint

C) No, I do not treat

I invest energies and resources into other treatments

Based on large observational studies (posthoc analysis of CKD patients included in RCTs) and on the SHARP study, the responsible physician is in favor of treatment (guideline *2.1.1*).

1A

2.1.1: In adults aged ≥50 years with eGFR <60 ml/ min/ 1.73 m^2 but not treated with chronic dialysis or kidney transplantation (GFR categories G3a-G5), we recommend treatment with a statin or statin/ ezetimibe combination.

1 = *we recommend*. Most patients should receive the recommended course of action.
A = *high quality of evidence.* We are confident that the true effect lies close to that of the estimate of the effect

SHARP
STUDY OF HEART AND RENAL PROTECTION

Am Heart J 2010;0:1-10.e10.

Lancet 2011;377:2181-2192

n=9.052

Hemodialysis	2.527
Peritonealdialysis	496
CKD	6.029
CKD3b	1.853
CKD4	2.565
CKD5	1.221

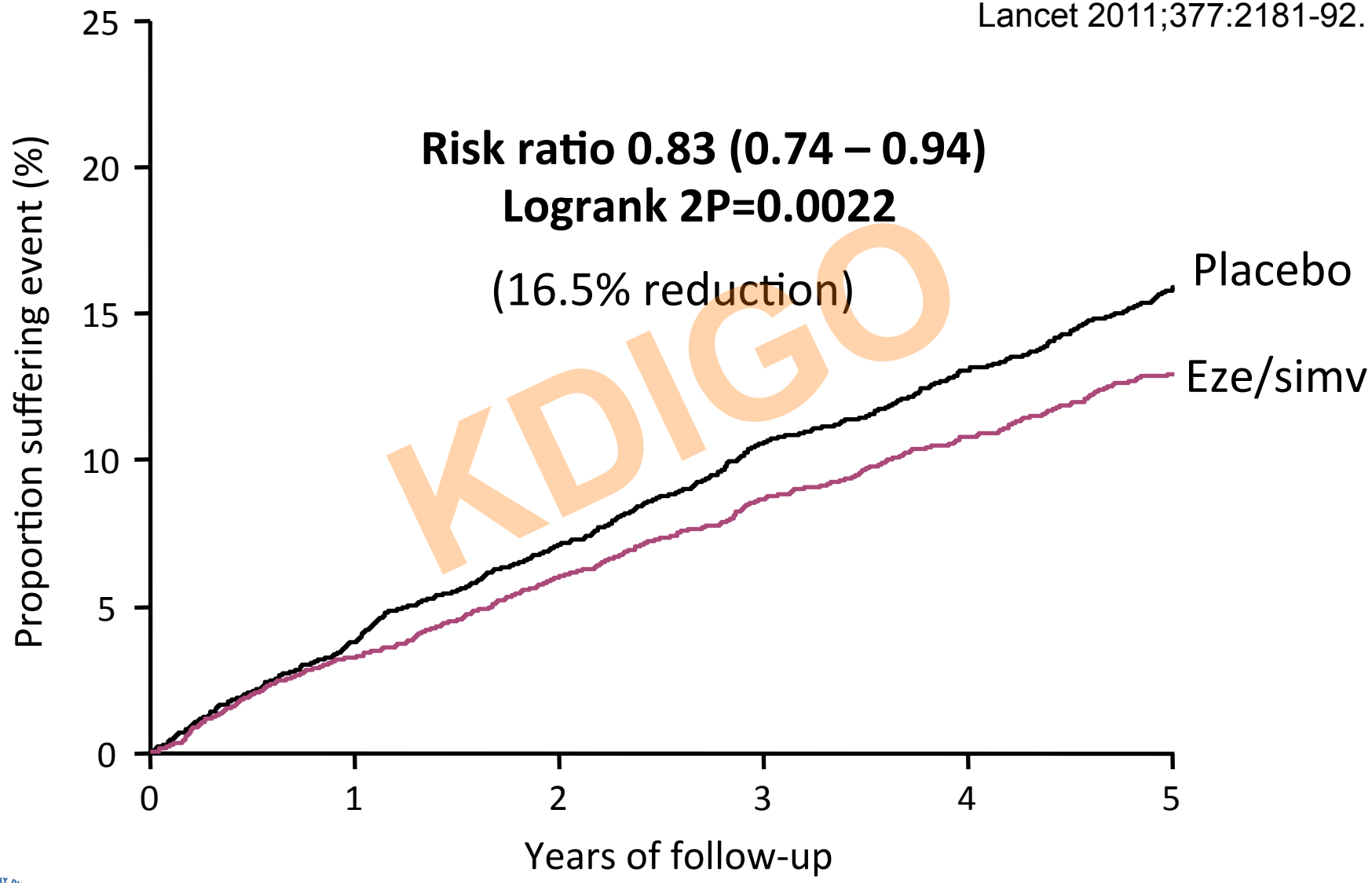
20 mg Simvastatin / 10 mg Ezetimibe

versus placebo, median follow-up 4.9 years

Patients: 62 years, 37% women, 23% diabetics, eGFR 27 ml/min/1.73m^2 in CKD stages 3-5

SHARP: Major Atherosclerotic Events

Lancet 2011;377:2181-92.



Other actions:

Blood pressure lowering medication is intensified.

A control visit is appointed in 3 month for monitoring of albumin excretion and specific serum parameter.

Implementation of the guideline in the Philippines ?

Treatment:

What statin or statin/ezitimibe combination is available ?

What dose of statin do you select for the patient ?

Table 4 | Recommended doses (mg/d) of statins in adults with CKD

Statin	eGFR G1-G2	eGFR G3a-G5, including patients on dialysis or with a kidney transplant
Lovastatin	GP	nd
Fluvastatin	GP	80[1]
Atorvastatin	GP	20[2]
Rosuvastatin	GP	10[3]
Simvastatin/Ezetmibe	GP	20/10[4]
Pravastatin	GP	40
Simvastatin	GP	40
Pitavastatin	GP	2

Lower doses than those used in major trials of statins in CKD populations may be appropriate in Asian countries.

1 ALERT, 2 4D, 3 AURORA, 4 SHARP

Kidney inter., Suppl. 2013; 3: 259–305

3 months later the patient is well and has tolerated the medication without adverse effects. He is reassuring that he has taken the lipid lowering medication on most days of the week. Thus we can assume that LDL-C has dropped by about 35% to below 100 mg/dl and we do not order another lipid profile (*guideline 1.2*).

not graded

1.2: In adults with CKD (including those treated with chronic dialysis or kidney transplantation), follow-up measurement of lipid levels is not required for the majority of patients.

Not graded was used, typically, to provide guidance based on common sense or where the topic does not allow adequate application of evidence.

Can I ask you:

Are you in agreement with this guideline ?

A) Yes, I am happy with this guideline
B) No, I am unhappy and want to remeasure

Why do other guidelines emphasize regular monitoring of LDL-cholesterol?

Circulation

JOURNAL OF THE AMERICAN HEART ASSOCIATION

2013 ACC/AHA Guideline on the Assessment of Cardiovascular Risk: A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines

David C. Goff, Jr, Donald M. Lloyd-Jones, Glen Bennett, Sean Coady, Ralph B. D'Agostino, Sr, Raymond Gibbons, Philip Greenland, Daniel T. Lackland, Daniel Levy, Christopher J. O'Donnell, Jennifer Robinson, J. Sanford Schwartz, Susan T. Shero, Sidney C. Smith, Jr, Paul Sorlie, Neil J. Stone and Peter W.F. Wilson

Circulation. published online November 12, 2013;

Why do other guidelines emphasize regular monitoring of LDL-cholesterol ?

ACC/AHA workgroup:

- (1) A lipid panel should be done 4-12 weeks after initiation of statin therapy to determine a patients adherence.
- (2) Down titrating statin dose due to unacceptable adverse effects when taking the recommended intensity of statin therapy (decide on new prescriptions and intensity of therapy).

KDIGO work group:

- random variation in TC on a single measurement is -0.8 to +0.8 mmol/l (-30 to +30 mg/dl)

2013 ACC/AHA Guideline on the Assessment of Cardiovascular Risk: A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines

Recommendations	NHLBI Grade
Treatment Targets	
1. The panel makes no recommendations for or against specific LDL–C or non-HDL–C targets for the primary or secondary prevention of ASCVD.	N (No recommendation)

Use moderate intensity statin therapy
Avoid high intensity statin therapy

Heart Failure and Hemodialysis	
1. The Expert Panel makes no recommendations regarding the initiation or discontinuation of statins in patients with NYHA class II–IV ischemic systolic heart failure or in patients on maintenance hemodialysis.	N (No Recommendation)

Further result of this visit:

Albuminuria decreased to < 0.5 g/g
Blood pressure is well controlled (130/80 mmHg).
S-creatinine increased by 0.2 mg/dl (eGFR 39 ml/min/1.73m^2).

Another visit was appointed 6 months later.

6 month later: Mr N. meanwhile has seen his GP, but „he has forgotten to measure cholesterol.“

We declare that a repeated measurement of 'cholesterol' is not necessary, because no further consequences arise (an increase in dose should not be done due to safety concerns). We are certain that the prescribed medication is effective.

Mr N. declares that he does not experience any effect and insists in knowing his cholesterol level, because otherwise he would not take a drug for nothing!

(***Rationale of guideline 1.2***): *"Physicians may choose to perform follow-up measurement of lipid levels in patients for whom these measurements are judged to favorably influence processes of care".*

The measurement resulted in:

TC	165 mg/dl
HDL-C	35
Triglyceride	189
LDL-C	92

Case 2: A 78 year old female patient has acute on chronic kidney failure and remains with ESRD. She did not take a statin in the past. Should we start statin therapy ?

2A

2.3.1: In adults with dialysis-dependent CKD we suggest that statins or statin/ezetimibe combination not be initiated.

2 = we suggest. Different choices will be appropriate for different patients. Each patients needs help to arrive at a management decision consistent with her or his values and preferences.

A = *high quality of evidence.* We are confident that the true effect lies close to that of the estimate of the effect

Case 2: A 78 year old female patient has acute on chronic kidney failure and remains with ESRD. She did not take a statin in the past. Should we start statin therapy ?

Can I ask you:

Do you want to treat this patient with a statin ?

A) Yes I will treat her with a statin
B) No I do not treat her

Case 2: A 78 year old female patient has acute on chronic kidney failure and remains with ESRD. She did not take a statin in the past. Should we start statin therapy ?

2A

2.3.1: In adults with dialysis-dependent CKD we suggest that statins or statin/ezetimibe combination not be initiated.

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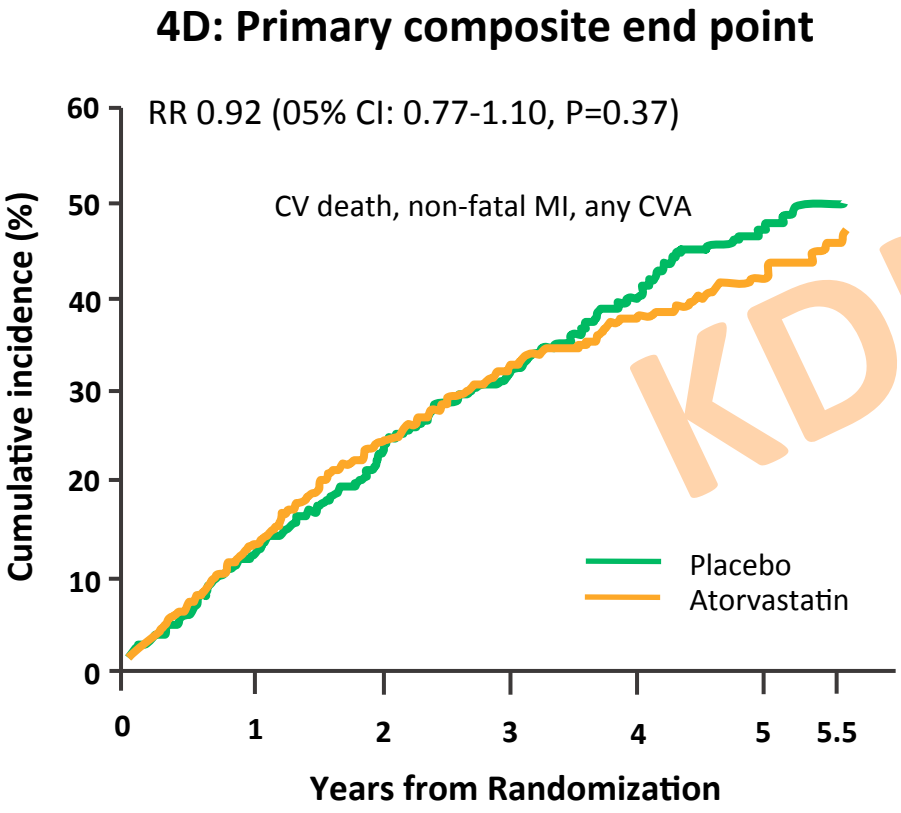
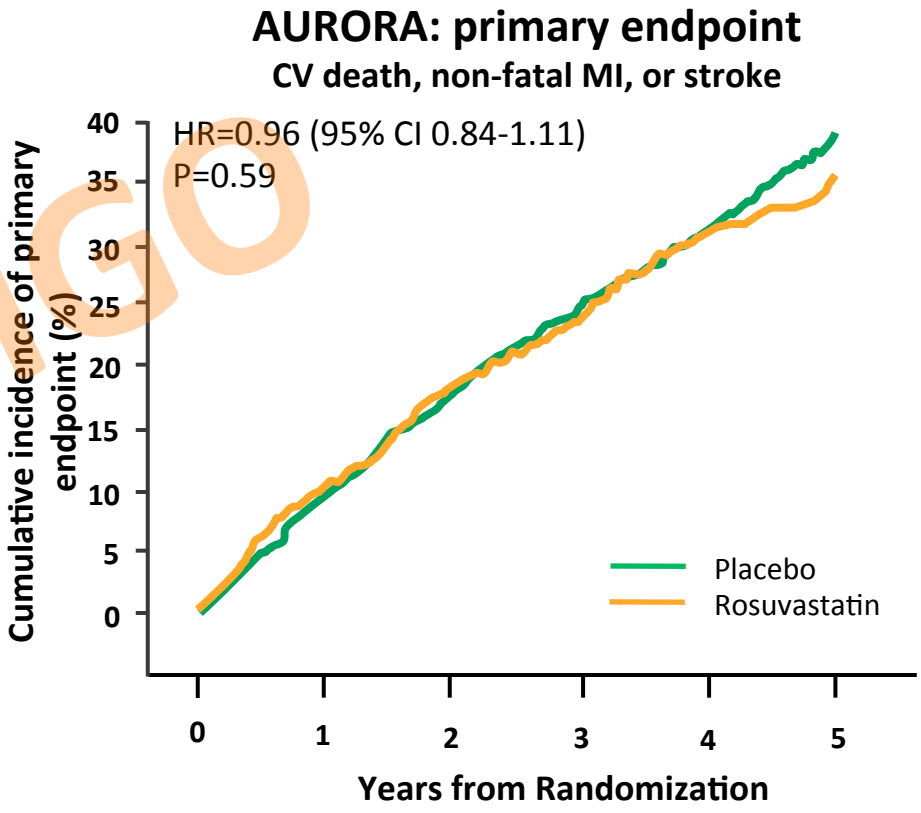
RCTs in hemodialysis patients have shown no benefits of statins





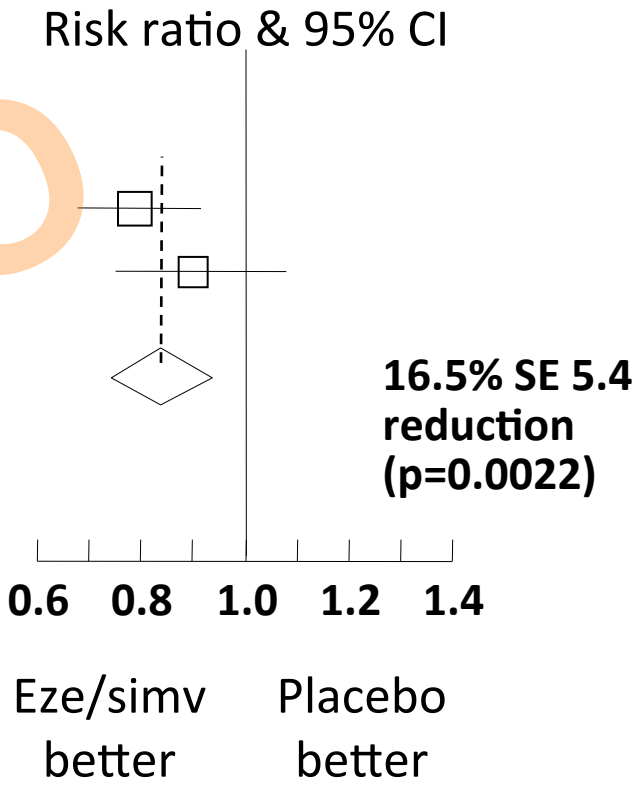
No. at risk:

Rosuvastatin	1390	1152	962	826	551	148
Placebo	1384	1163	952	809	534	153

Wanner et al, NEJM 2005; Fellström B et al, NEJM 2009

SHARP: Major Atherosclerotic Events by renal status at randomization

	Eze/simv (n=4650)	Placebo (n=4620)
Non-dialysis (n=6247) *	296 (9.5%)	373 (11.9%)
Dialysis (n=3023) **	230 (15.0%)	246 (16.5%)
Major atherosclerotic event	**526 (11.3%)**	**619 (13.4%)**



No significant heterogeneity between non-dialysis and dialysis patients (p=0.25)

* LDL-Reduction: 37 mg/dl (0,96 mmol/l)

** LDL-Reduction: 23 mg/dl (0,60 mmol/l)

Baigent et al, Lancet 2011

Mr. N will one day, most likely, progress to end-stage renal disease and will require renal replacement therapy.

2C

2.3.2: In patients already receiving statins or statin/ ezetimibe combination at the time of dialysis initiation, we suggest that these agents be continued.

2 = *we suggest*. Different choices will be appropriate for different patients. Each patients needs help to arrive at a management decision consistent with her or his values and preferences.

C = *low quality of evidence.* The true effect may be substantially different from the estimate of the effect.

2.3.2: Rationale

- SHARP, 4D and AURORA don't address this issue
- 2141 (34%) of SHARP participants in non-dialysis group initiated dialysis during follow-up
  - benefit observed in non-dialysis group for SHARP
- Reasonable to continue statins
  - recognize that benefits may be lower than in ND pts
  - could discontinue if patient preferences warrant it

1B

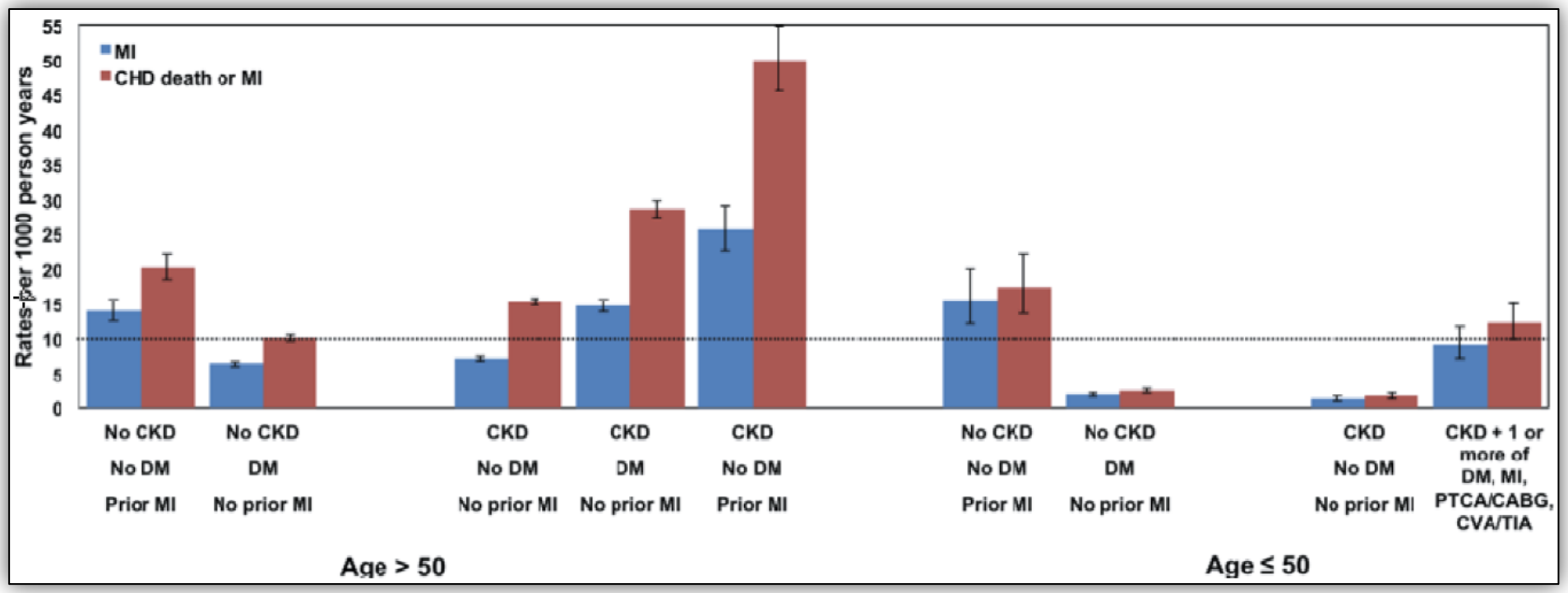
2.1.2: In adults aged ≥50 years with CKD and eGFR ≥60 ml/min/1.73 m^2 (GFR categories G1-G2) we recommend treatment with a statin.

2A

2.2: In adults aged 18-49 years with CKD but not treated with chronic dialysis or kidney transplantation, we suggest statin treatment in people with one or more of the following:

- known coronary disease (myocardial infarction or coronary revascularization)
- diabetes mellitus
- prior ischemic stroke
- estimated 10-year incidence of coronary death or non-fatal myocardial infarction >10%

Alberta Kidney Disease Kohorte (n=1,268.029)



CKD: eGFR 15-59,9 ml/min/1,73m^2

2A

2.4: In adult kidney transplant recipients, we suggest treatment with a statin.

2D

5.1: In adults with CKD (including those treated with chronic dialysis or kidney transplantation) and hypertriglyceridemia, we suggest that therapeutic lifestyle changes be advised.

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KDIGO is the world's only organization developing and implementing global guidelines in kidney disease.

It was founded on the principle that science is not regional or country specific. Rather it is global in nature; only implementation should be locally designed to take into account variations in practice and medication availability.

☺ Thank you for your attention !