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12-15 December 2023
Homa Hotel, Tehran

Management of Dyslipidemia in CKD

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TEHRAN 2023

Disclosure

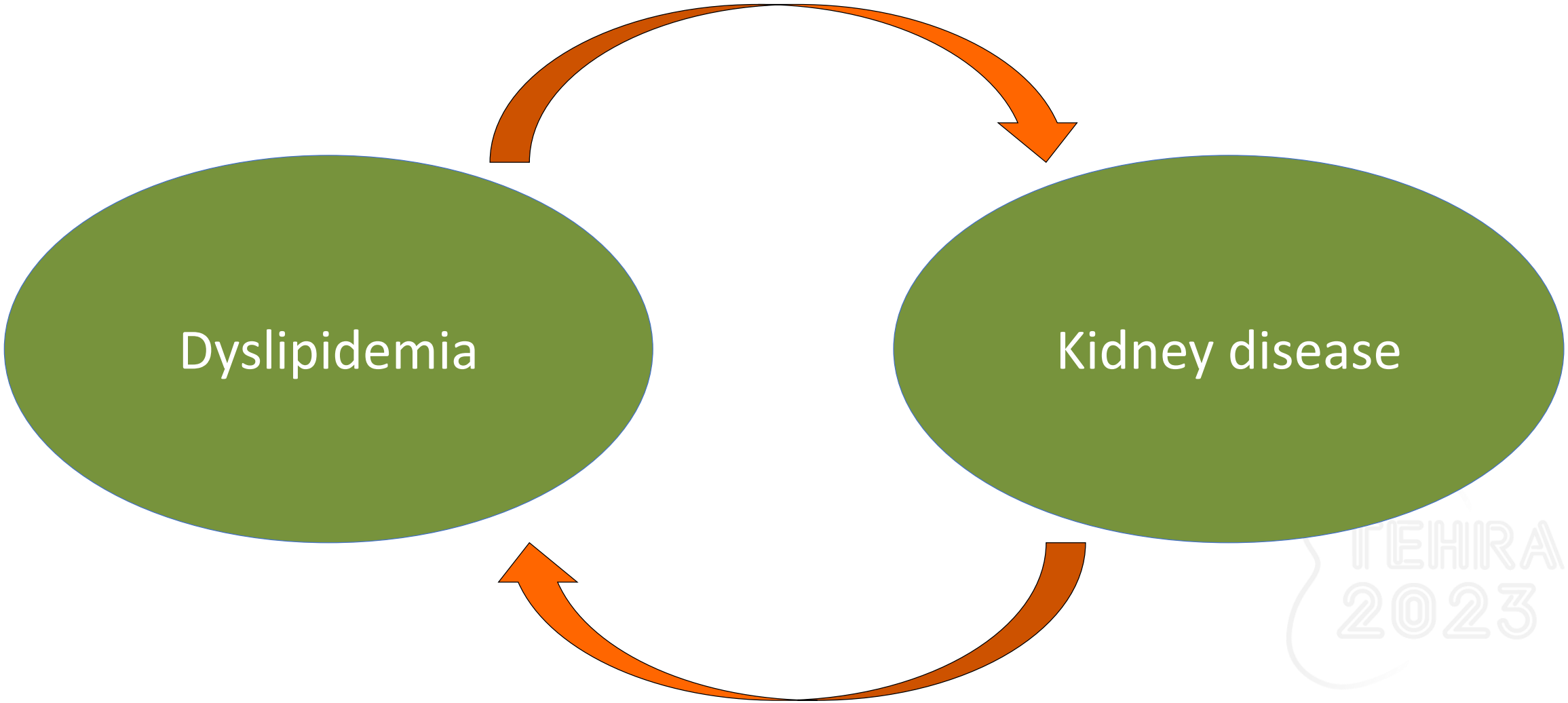
No conflict of interest

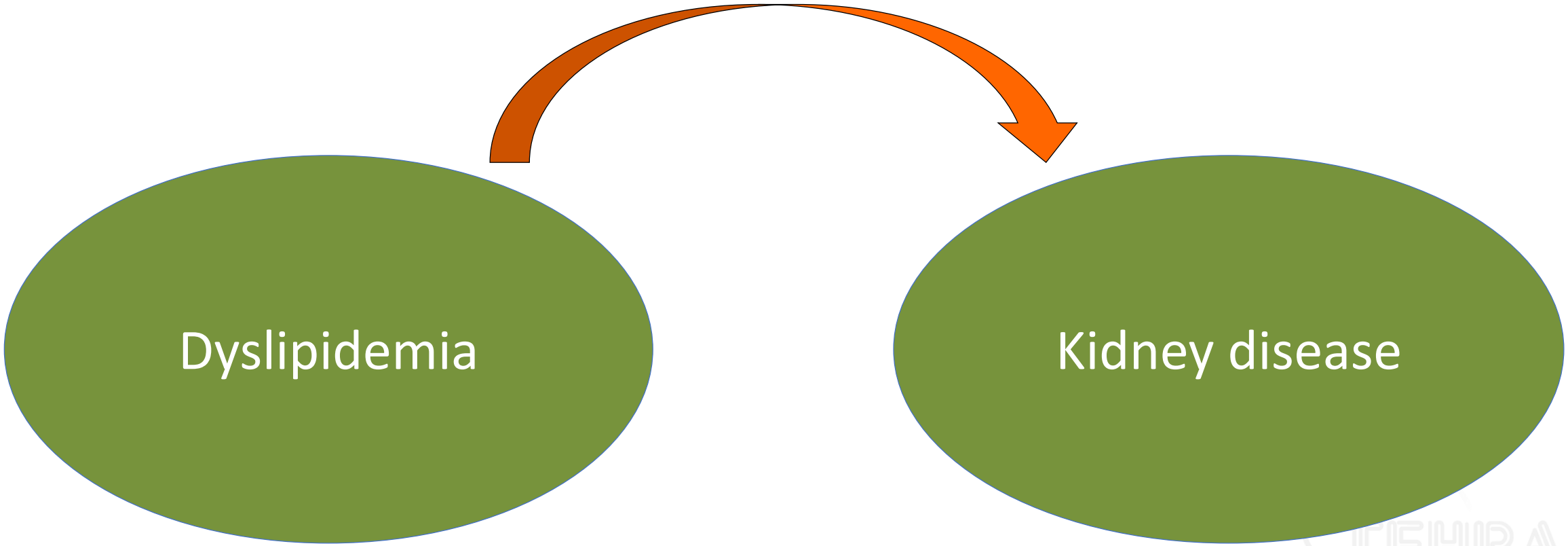
Outlines:

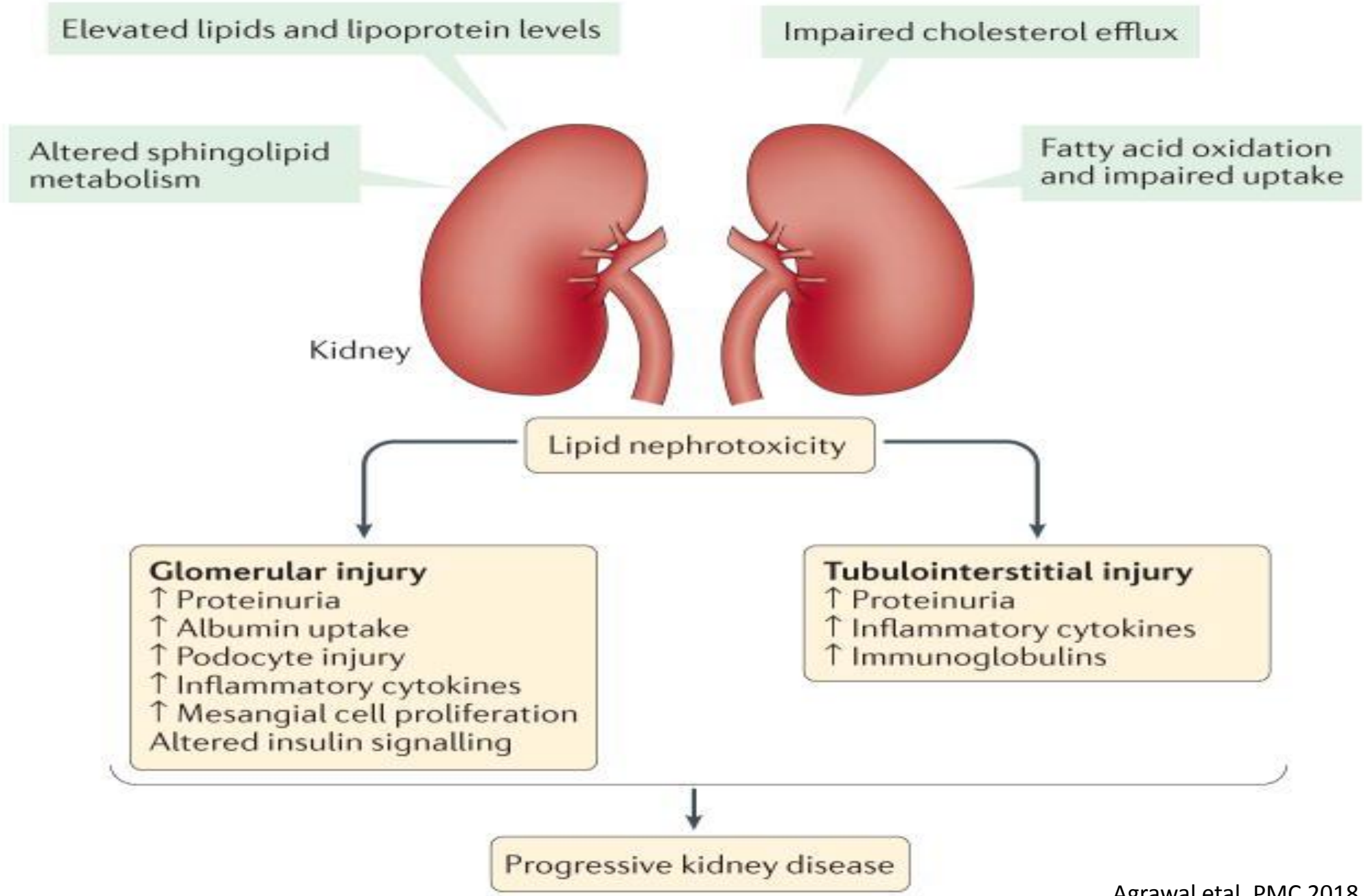
- ✓Lipid abnormalities and the kidneys
- ✓Guidelines for management of dyslipidemia in CKD
- ✓Role of statin on kidney function
- ✓Role of other lipid lowering agents and future therapeutic prospective

Dyslipidemia

Kidney disease

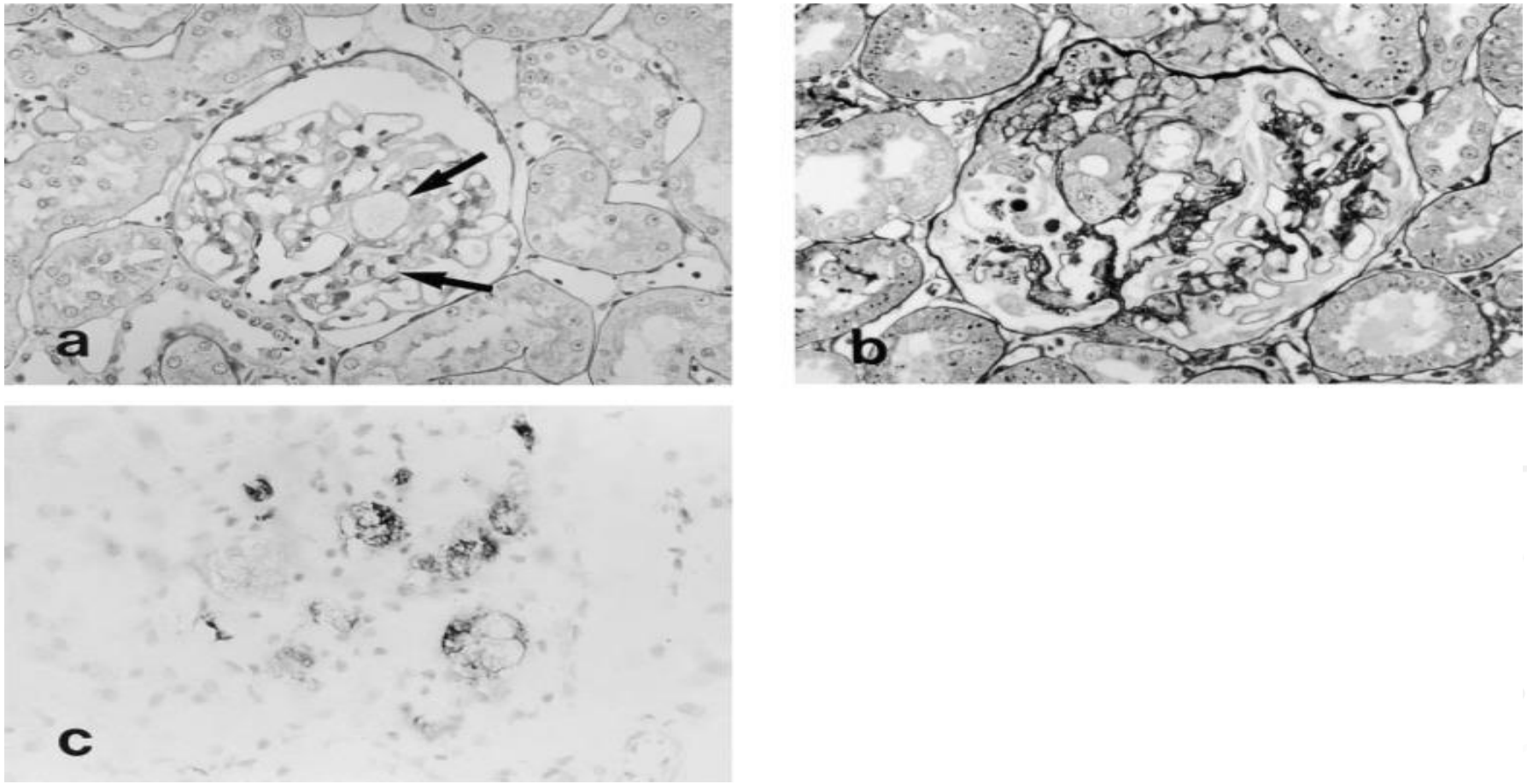

Dyslipidemia
Kidney disease


Dyslipidemia
Kidney disease



Agrawal etal. PMC 2018

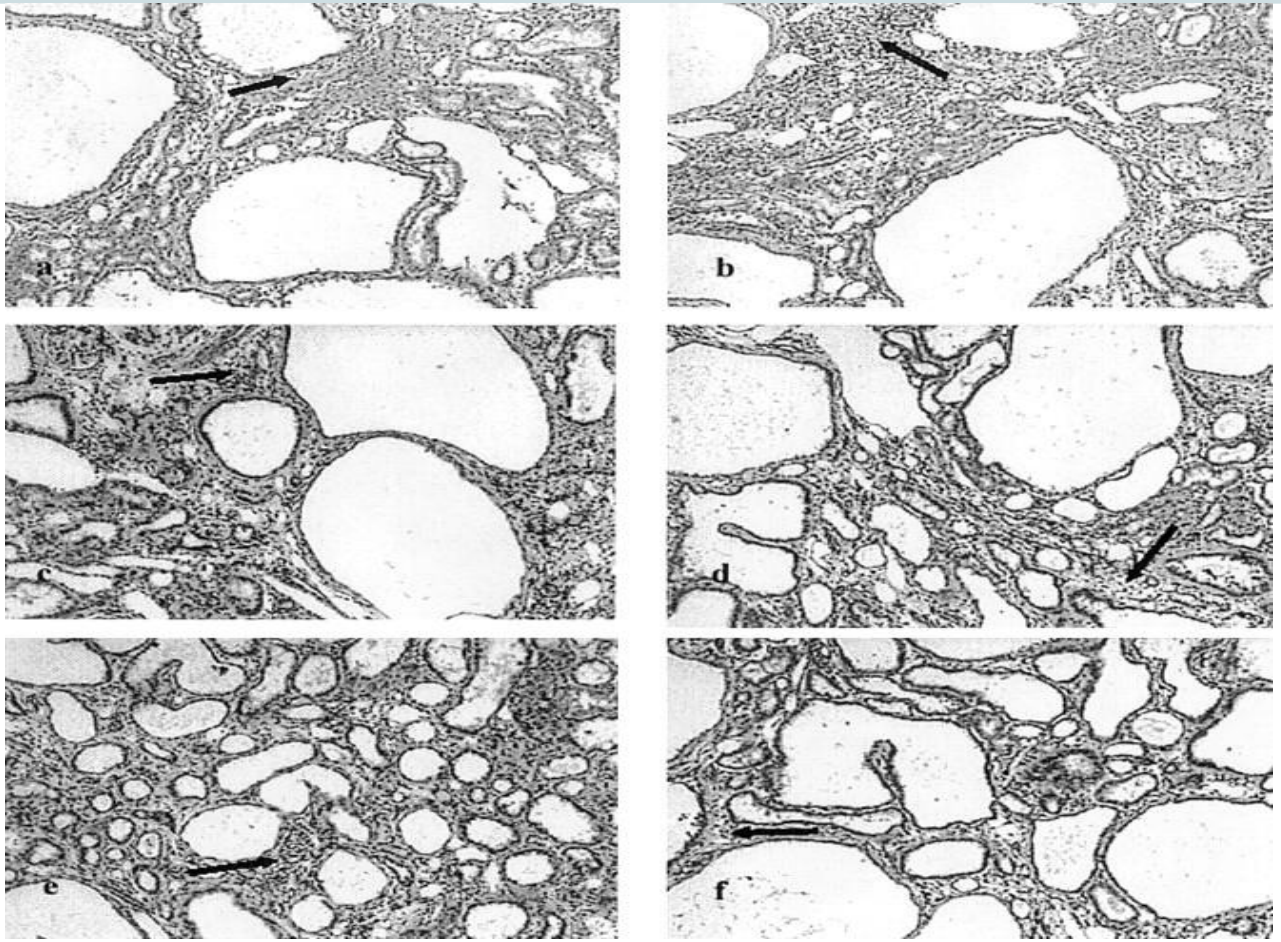
Mechanisms of glomerular macrophage infiltration in lipid-induced renal injury (animal model)



Motoshi Hattori et al, Kidney International
Volume 56 Pages S47-S50 (July 1999)

JN THE JOURNAL OF NUTRITION

Detrimental Effects of a High Fat Diet in Early Renal Injury Are Ameliorated by Fish Oil in Han:SPRD-*cy* Rats



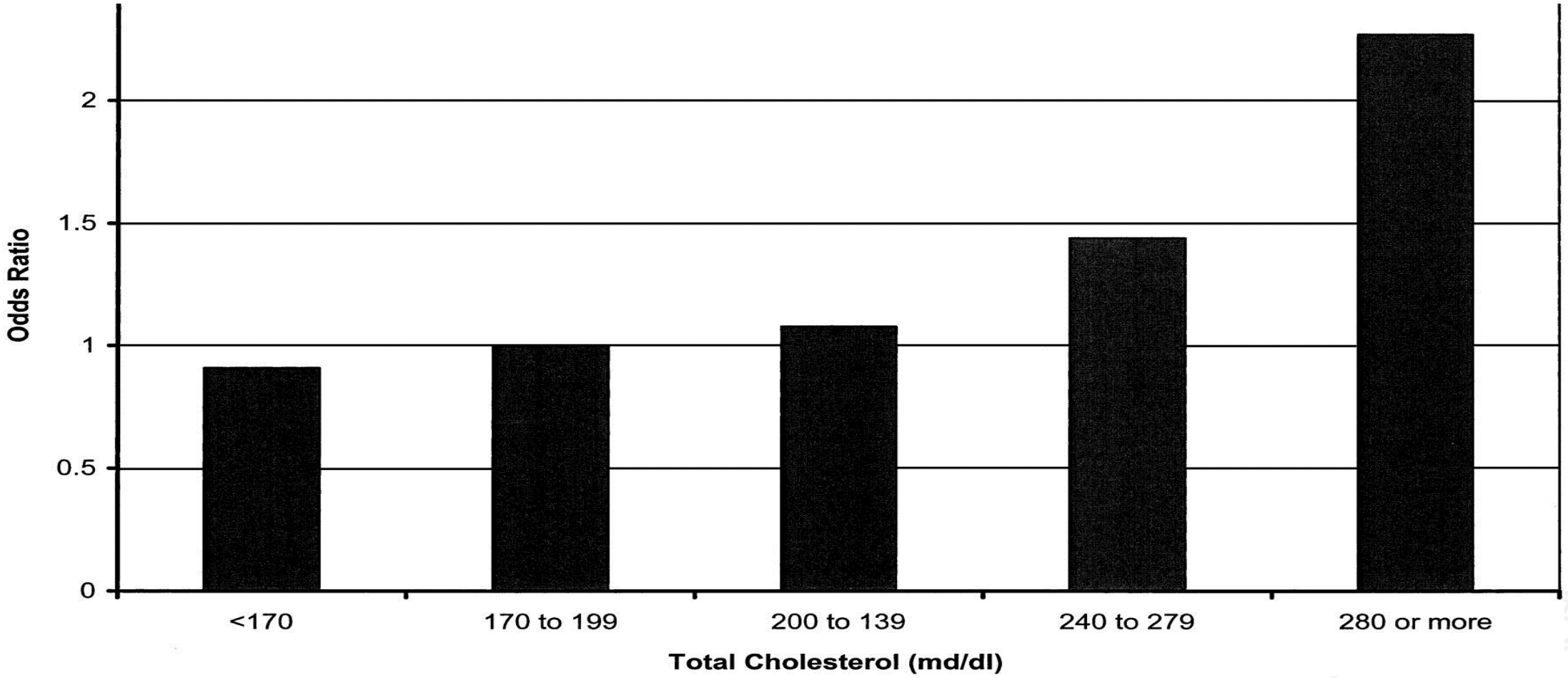
Renal interstitial inflammation in male Han:SPRD-cy rats fed 5 or 20 g of cottonseed (CO), menhaden (MO) or soyabean oil (SO)

OXFORD UNIVERSITY PRESS
J Nutr, Volume 133, Issue 1, January 2003, Pages 180–186,
https://doi.org/10.1093/jn/133.1.180

Cholesterol and the Risk of Renal Dysfunction in Apparently Healthy Men

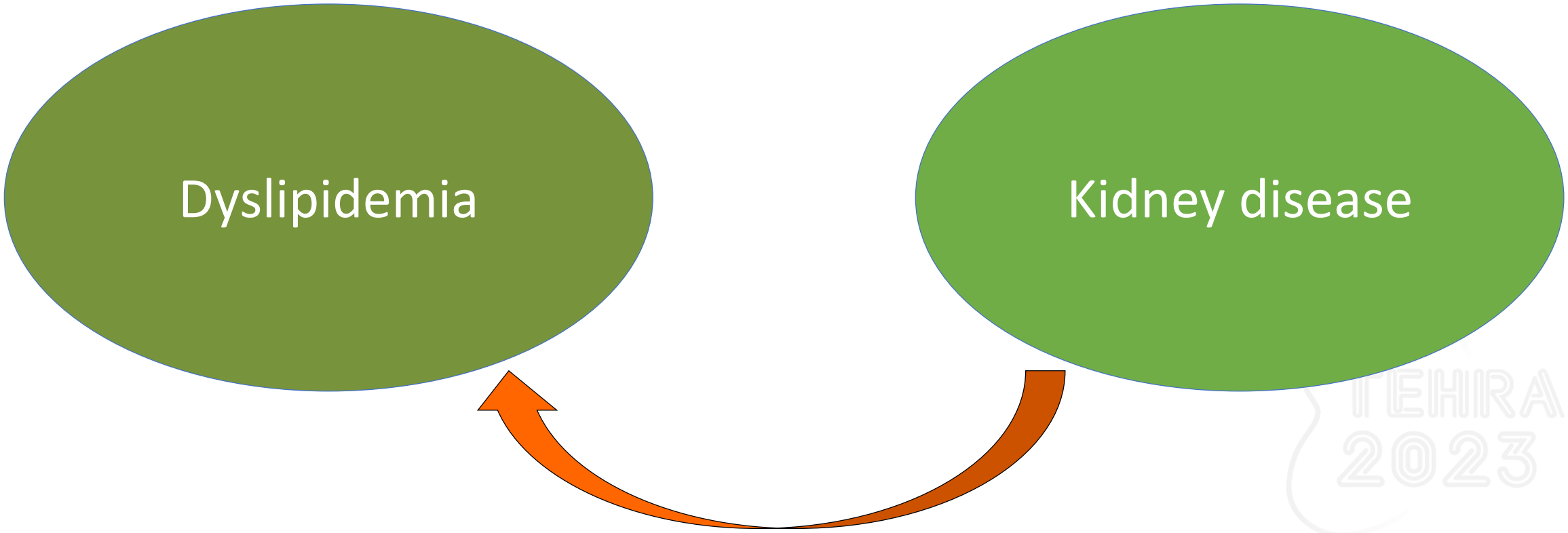
Elke S. Schaeffner, Tobias Kurth, Gary C. Curhan, Robert J. Glynn, Kathryn M. Rexrode, Colin Baigent, Julie E. Buring and J. Michael Gaziano

JASN August 2003, 14 (8) 2084-2091; DOI: https://doi.org/10.1681/ASN.V1482084

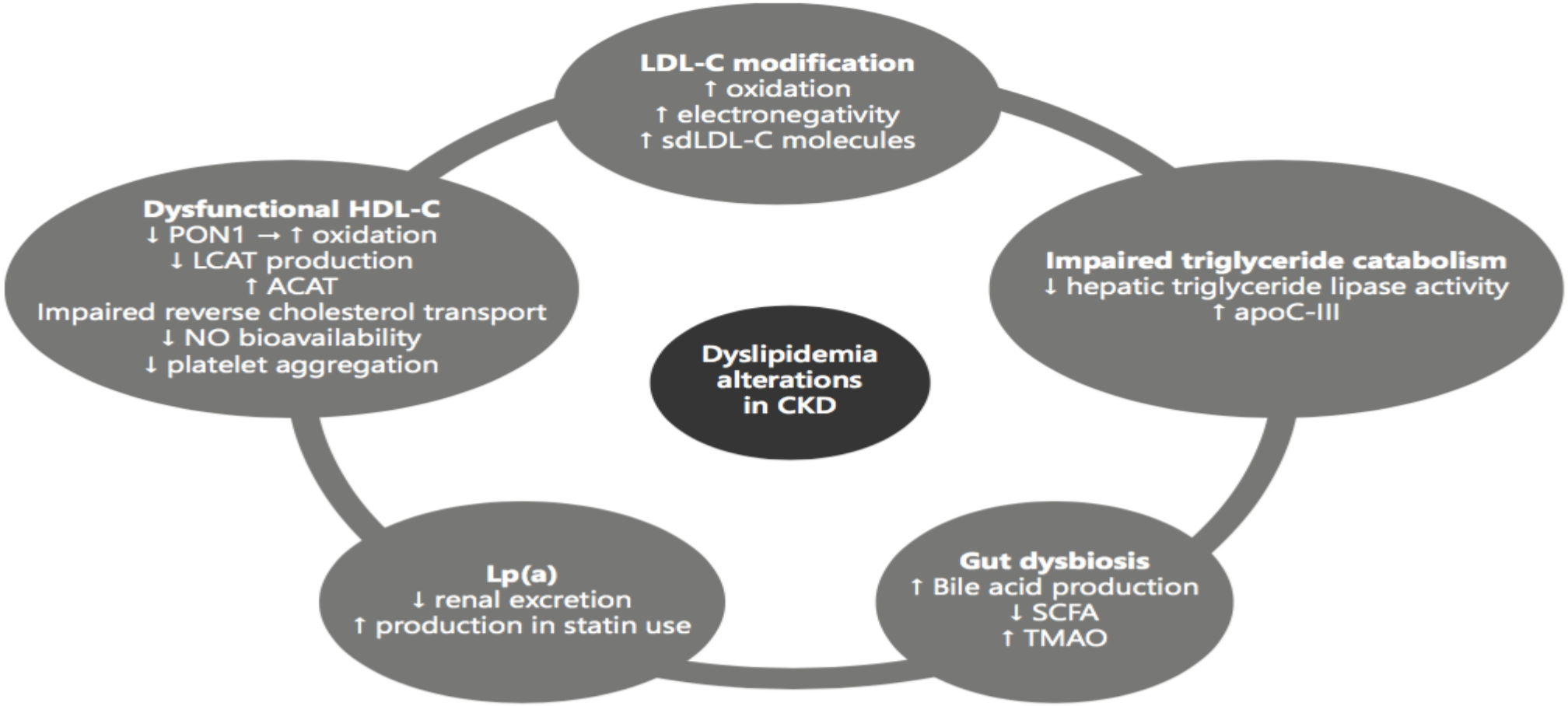


Association between total cholesterol categories and increased creatinine (≥1.5 mg/dl), adjusted for age (P for trend = 0.01).

JASN
JOURNAL OF THE AMERICAN SOCIETY OF NEPHROLOGY


Dyslipidemia
Kidney disease

Dyslipidemia in Chronic Kidney Disease: Contemporary Concepts and Future Therapeutic Perspectives



Theofilis p etal. Am J Nephrol 2021;52:693–701

Arteriosclerosis, Thrombosis, and Vascular Biology
Volume 37, Issue 10, October 2017; Pages 1971-1978
https://doi.org/10.1161/ATVBAHA.117.309920

CLINICAL AND POPULATION STUDIES

Lipoprotein(a) and Risk of Myocardial Infarction and Death in Chronic Kidney Disease

Findings From the CRIC Study (Chronic Renal Insufficiency Cohort)

Archna Bajaj, Scott M. Damrauer, Amanda H. Anderson, Dawei Xie, Matthew J. Budoff, Alan S. Go, Jiang He, James P. Lash, Akinlolu Ojo, Wendy S. Post, Mahboob Rahman, Muredach P. Reilly, Danish Saleheen, Raymond R. Townsend, Jinbo Chen, Daniel J. Rader, and the Chronic Renal Insufficiency Cohort (CRIC) Study Investigators*

Table 3. Event Rates of Study Participants for Myocardial Infarction, Death, and a Composite of Both Outcomes (Table view)

		Lipoprotein(a)				*P* Value
		Quartile 1, <9.8 mg/dL (n=936)	Quartile 2, 9.8–26.0 mg/dL (n=940)	Quartile 3, 26.1–61.3 mg/dL (n=935)	Quartile 4, >61.3 mg/dL (n=933)	
Myocardial infarction	Participants, no.	78	57	87	93	
	Event rate*	12.8 (10.3–16.0)	9.4 (7.3–12.2)	14.6 (11.8–18.0)	16.1 (13.2–19.7)	0.01
Death	Participants, no.	185	176	201	260	
	Event rate*	28.1 (24.4–32.5)	26.7 (23.0–31.0)	30.9 (26.9–35.5)	41.2 (36.4–46.5)	<0.001
Myocardial infarction or death	Participants, no.	230	204	242	304	
	Event rate*	37.9 (33.3–43.1)	33.7 (29.4–38.6)	40.6 (35.8–46.0)	52.7 (47.1–58.9)	<0.001

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- ✓Lipid abnormalities and the kidneys
- ✓Guidelines for management of dyslipidemia in CKD
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National Kidney Foundation®

KDOQI®
Kidney Disease Outcomes Quality Initiative

2003 recommendation

- No RCT

- ATP III guideline was adopted for CKD patients
  (CKD was classified as CHD risk equivalent)

- Target LDL-C (70-100mg/dl) (1.8-2.6mmol/L)

National Kidney Foundation® | KDOQI®
Kidney Disease Outcomes Quality Initiative

KIDNEY DISEASE IMPROVING GLOBAL OUTCOMES
KDIGO®

2003 recommendation

- No RCT
- ATP III guideline was adopted for CKD patients (CKD was classified as CHD risk equivalent)
- Target LDL-C (70-100mg/dl) (1.8-2.6mmol/L)

2013 recommendation

- Many RCT
- Cardiovascular risk stratification
- No longer recommended unless it alters your management

National Kidney Foundation® | KDOQI®
Kidney Disease Outcomes Quality Initiative

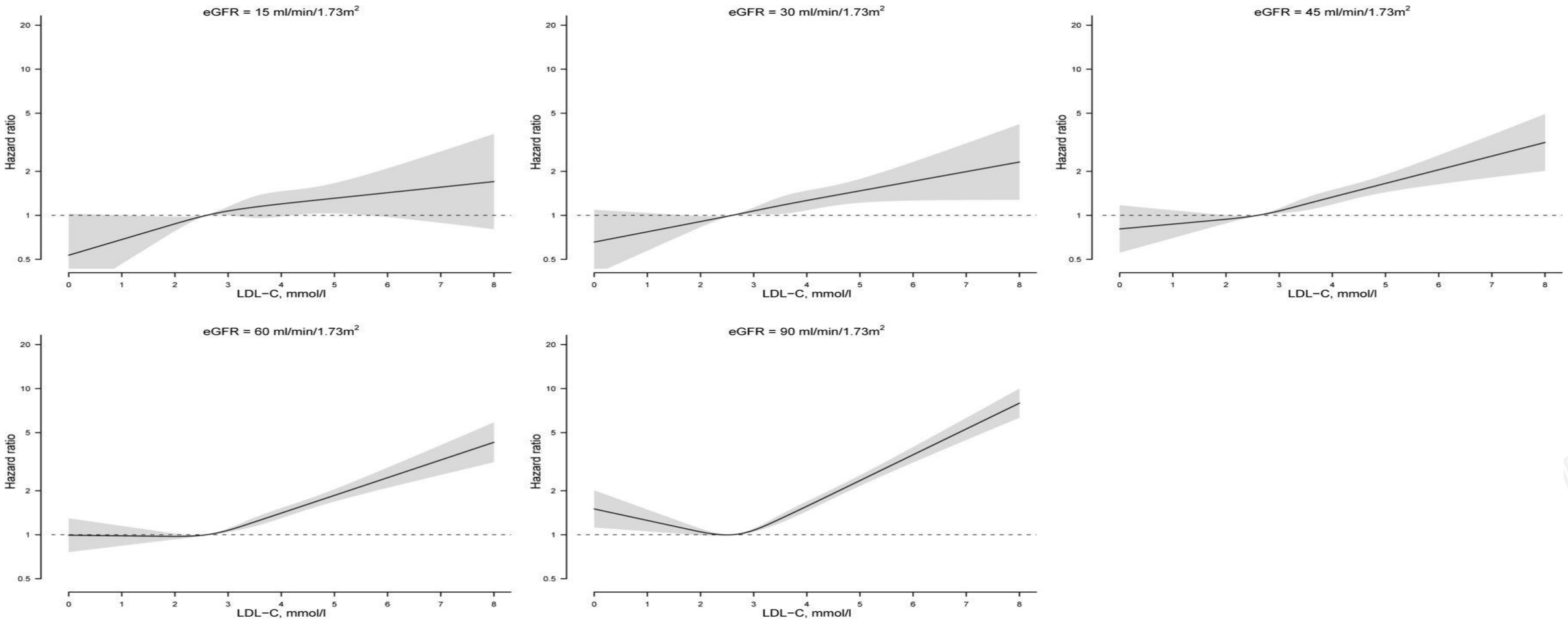
KIDNEY DISEASE IMPROVING GLOBAL OUTCOMES
KDIGO®

2003 recommendation

2013 recommendation

Association between LDL-C and Risk of Myocardial Infarction in CKD

JASN
JOURNAL OF THE AMERICAN SOCIETY OF NEPHROLOGY



Tonelli et al. JASN June 2013, 24 (6) 979-986

1C

In adults with newly identified CKD (including those treated with chronic dialysis or KT), we recommend evaluation with a lipid profile (TC, LDL-C, HDL-C, TG).

1: we recommend (most patients should receive the recommended course of action)

C: low quality of evidence (The true effect may be substantially different from the estimate of the effect)

1A

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)

Articles

Risk of coronary events in people with chronic kidney disease compared with those with diabetes: a population-level cohort study

THE LANCET

Dr Marcello Tonelli MD [a, b] ✉, Prof Paul Muntner PhD [c], Anita Lloyd MSc [a], Braden J Manns MD [d, e], Scott Klarenbach MD [a, b], Neesh Pannu MD [a], Matthew T James MD [d, e], Brenda R Hemmelgarn MD [d, e], for the Alberta Kidney Disease Network

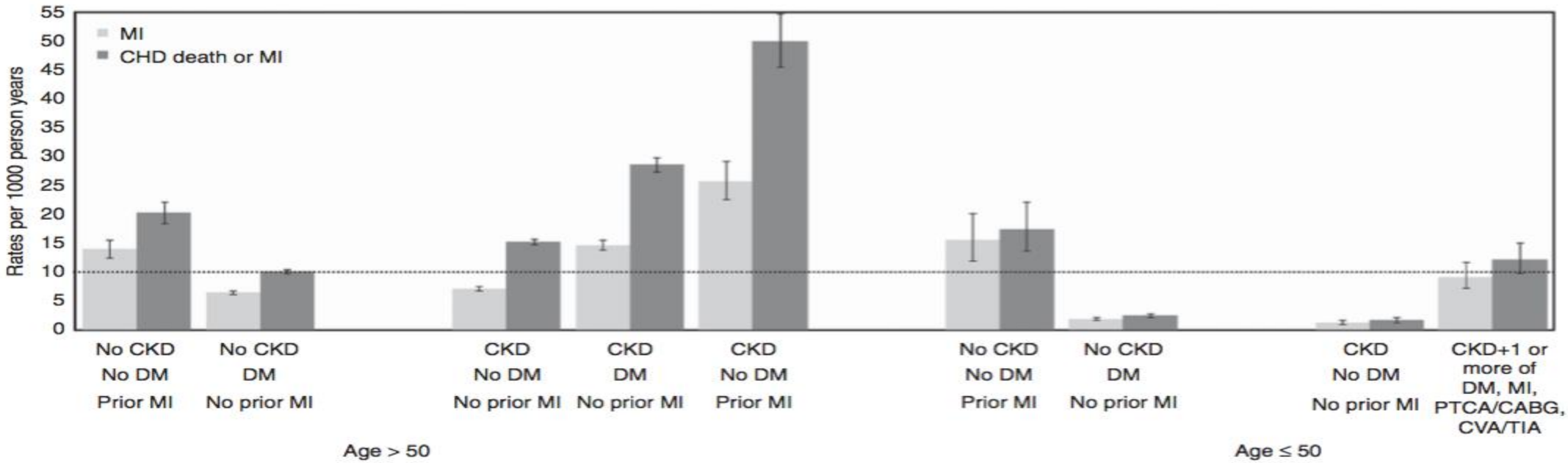


Figure 2 | Future 10-year coronary risk based on various patient characteristics. Data are unadjusted rates from 1,268,029 participants in the Alberta Kidney Disease cohort. CKD refers to eGFR 15-59.9 ml/min/1.73 m^2 or with proteinuria. CABG, coronary artery bypass grafting; CHD, coronary heart disease; CKD, chronic kidney disease; CVA, cerebrovascular accident; DM, diabetes mellitus; MI, myocardial infarction; PTCA, percutaneous transluminal coronary angioplasty; TIA, transient ischemic attack.

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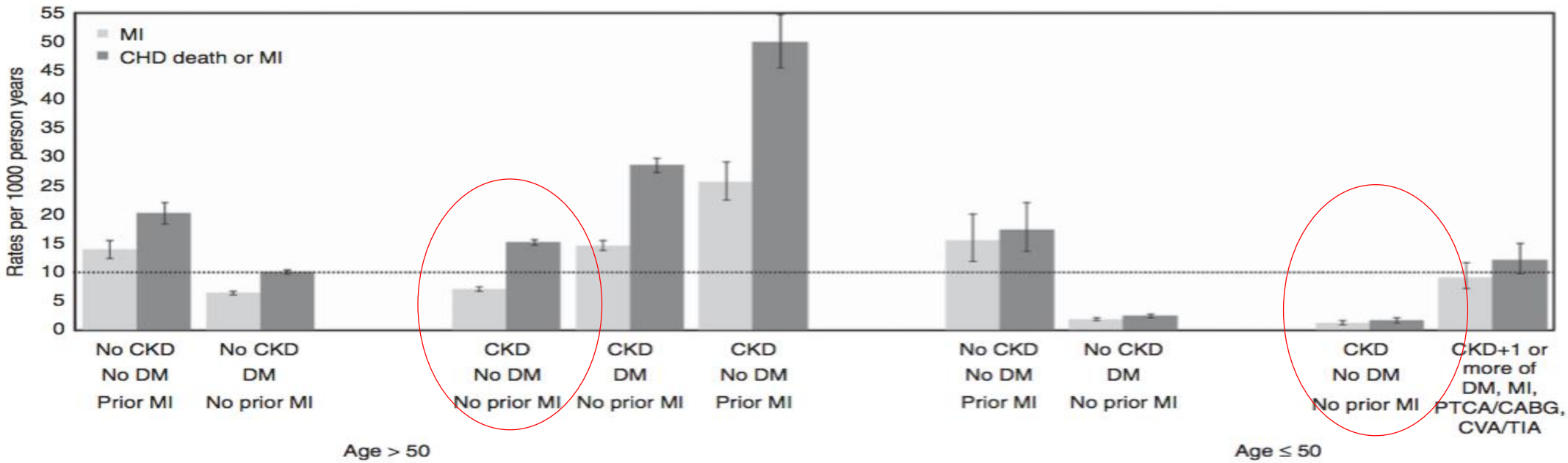

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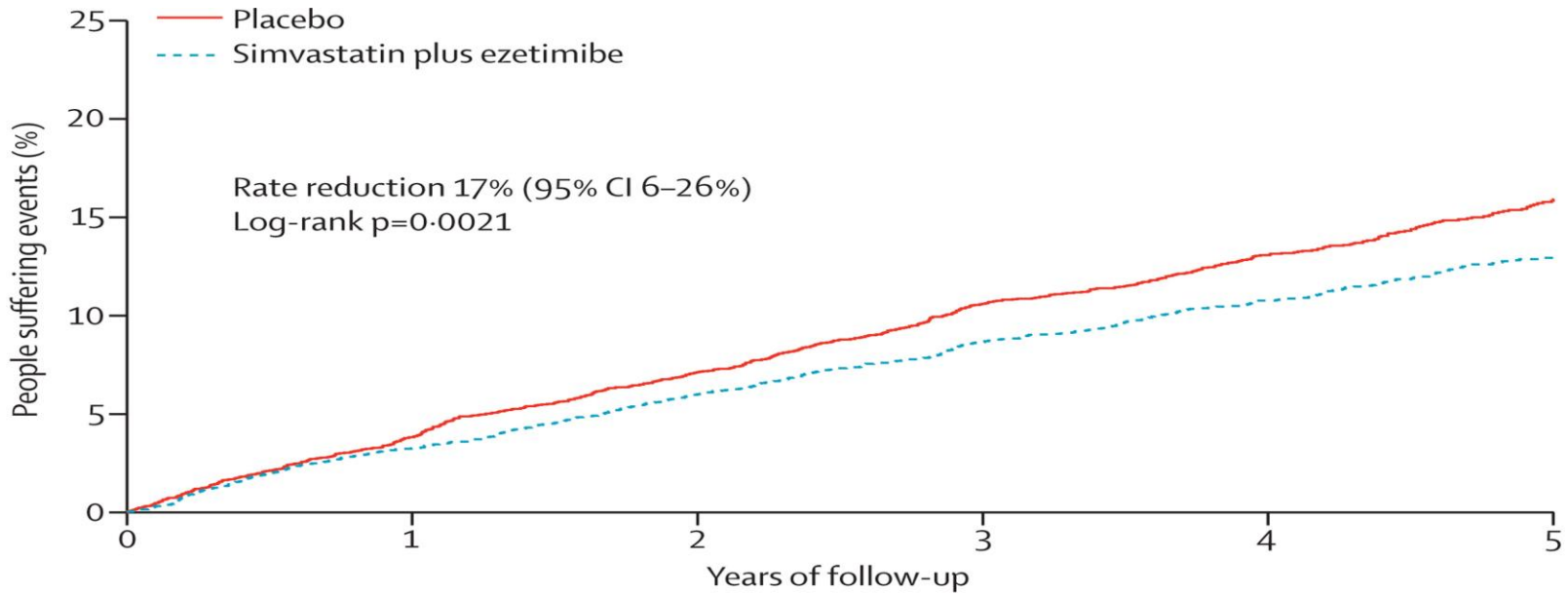
The effects of lowering LDL cholesterol with simvastatin plus ezetimibe in patients with chronic kidney disease (Study of Heart and Renal Protection): a randomised placebo-controlled trial

THE LANCET



Number at risk

Placebo	4620	4204	3849	3469	2566	1269
Simvastatin plus ezetimibe	4650	4271	3939	3546	2655	1265

Collin Baigent et al, *Lancet* 2011; 377: 2181–92
Published Online June 9, 2011

1B

In adults aged ≥ 50 years with CKD and eGFR ≥ 60 ml/min/1.73 m2 (GFR categories G1-G2) we recommend treatment with a statin.

1: we recommend (most patients should receive the recommended course of action)

B: moderate quality of evidence (The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different).

The New England
Journal of Medicine

VOLUME 335 OCTOBER 3, 1996 NUMBER 14

THE EFFECT OF PRAVASTATIN ON CORONARY EVENTS AFTER MYOCARDIAL INFARCTION IN PATIENTS WITH AVERAGE CHOLESTEROL LEVELS

FRANK M. SACKS, M.D., MARC A. PFEFFER, M.D., PH.D., LEMUEL A. MOYE, M.D., PH.D., JEAN L. ROULEAU, M.D., JOHN D. RUTHERFORD, M.D., THOMAS G. COLE, PH.D., LISA BROWN, M.P.H., J. WAYNE WARNICA, M.D., J. MALCOLM O. ARNOLD, M.D., CHUAN-CHUAN WUN, PH.D., BARRY R. DAVIS, M.D., PH.D., AND EUGENE BRAUNWALD, M.D., FOR THE CHOLESTEROL AND RECURRENT EVENTS TRIAL INVESTIGATORS*

2A

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 (MI or coronary revascularization)
- Diabetes mellitus
- Prior ischemic stroke
- e 10-years incidence of coronary death or non-fatal MI >10%

2: we suggest (Different choices will be appropriate for different patients. Each patient 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)

Articles

Risk of coronary events in people with chronic kidney disease compared with those with diabetes: a population-level cohort study

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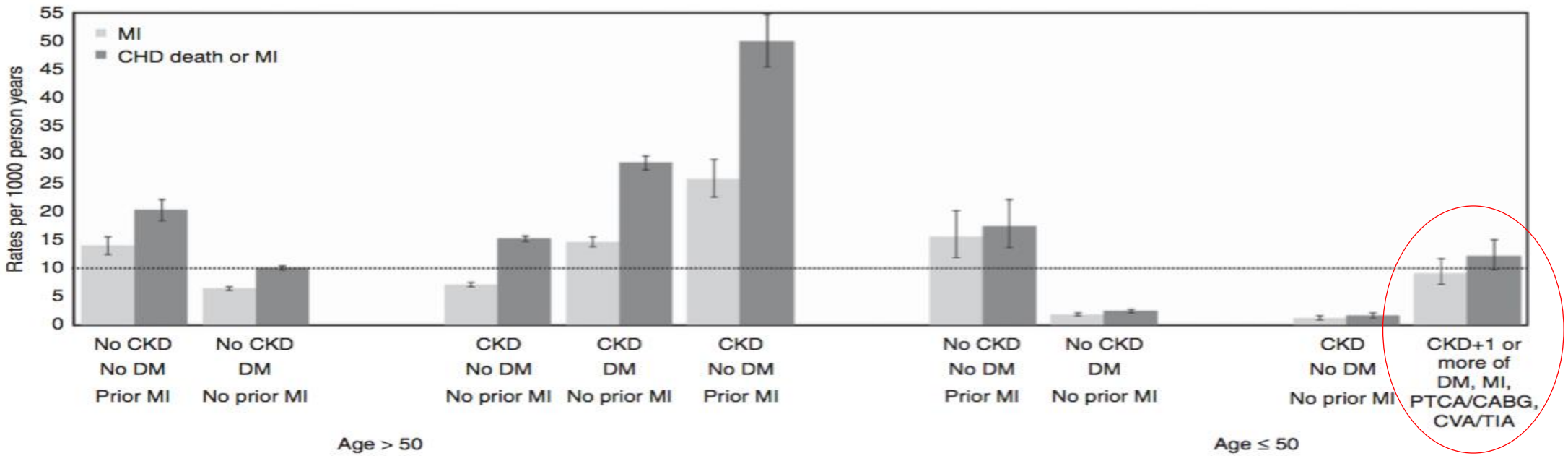

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2A

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 patient 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)

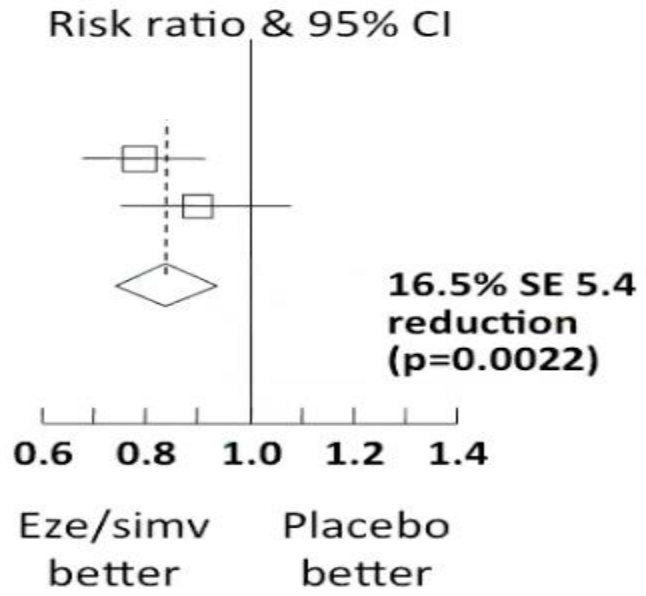
SHARP: Major Atherosclerotic Events by renal status at randomization

	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)

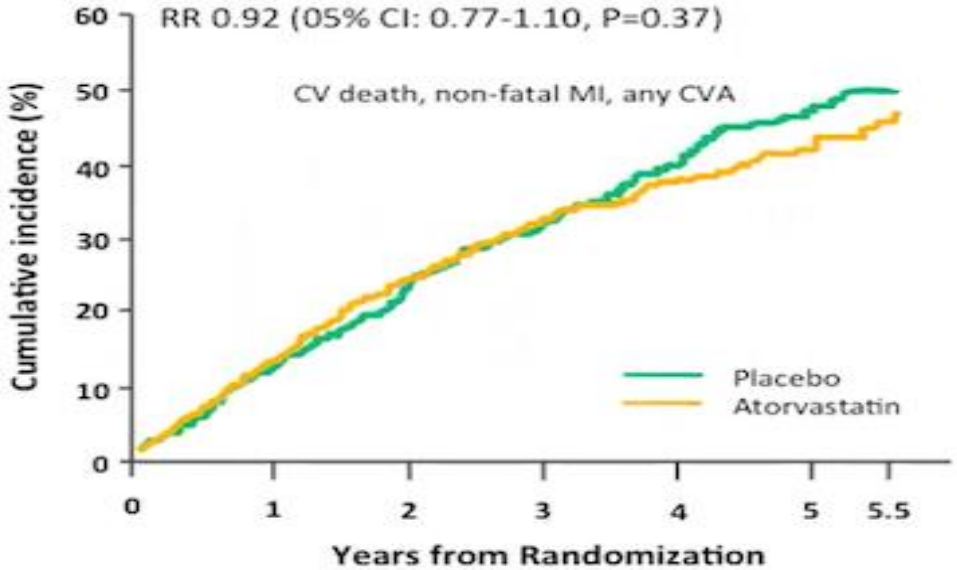
* LDL-Reduction: 37 mg/dl (0,96 mmol/l)

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



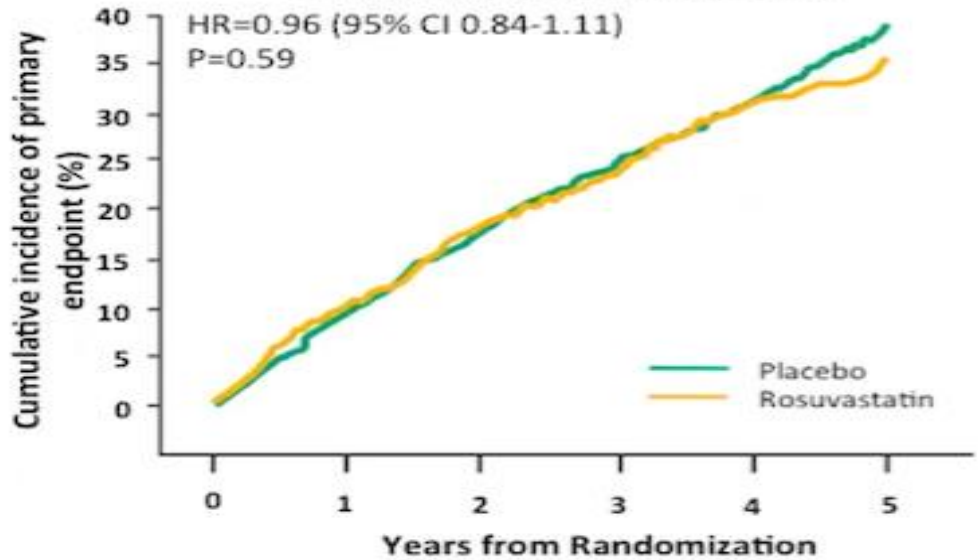
Baigent et al, Lancet 2011

4D: Primary composite end point



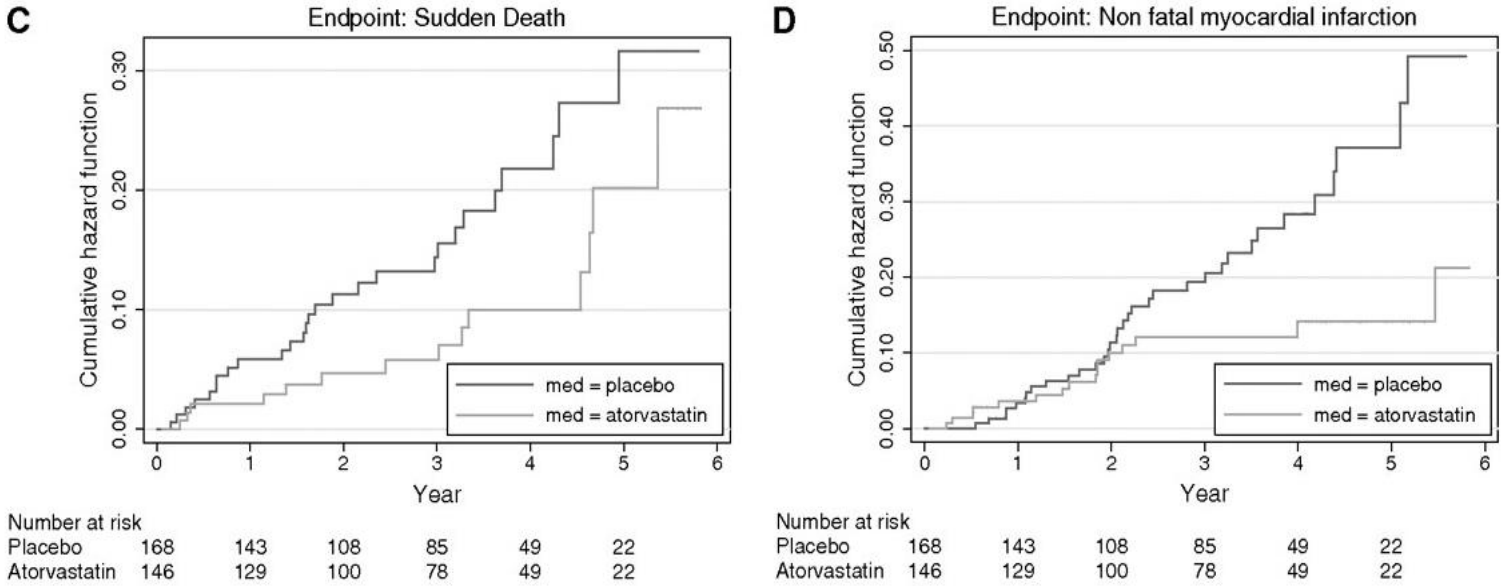
AURORA: primary endpoint

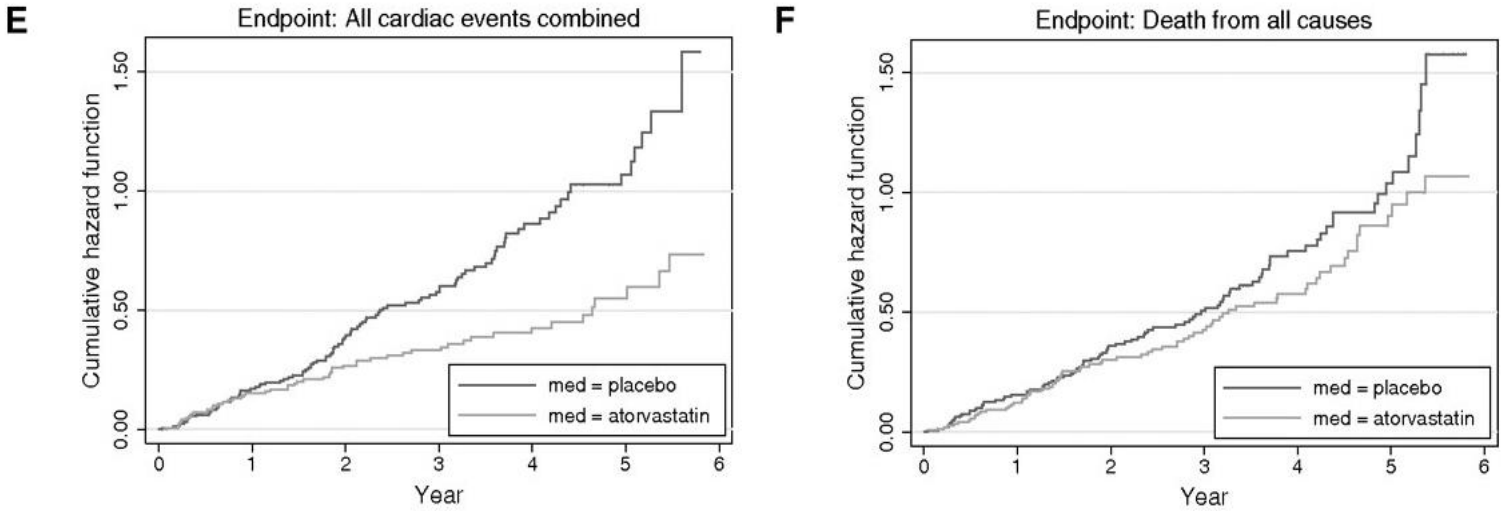
CV death, non-fatal MI, or stroke



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





Cumulative incidence of Cardiovascular events according To medication group in participants of the 4D study with an LDL-C in its fourth quartile at baseline (≥145 mg/dl, 3.76 mmol/L)

Marz Winfried etal. CJASN June 2011

2C

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 patient 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

2B

In adult kidney transplant recipients, we suggest treatment with a statin. (2B)

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

B: moderate (The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different).

Effect of fluvastatin on cardiac outcomes in renal transplant recipients: a multicentre, randomised, placebo-controlled trial

*Hallvard Holdaas, Bengt Fellström, Alan G Jardine, Ingar Holme, Gudrun Nyberg, Per Fauchald, Carola Grönhagen-Riska, Søren Madsen, Hans-Hellmut Neumayer, Edward Cole, Bart Maes, Patrice Ambühl, Anders G Olsson, Anders Hartmann, Dag O Solbu, Terje R Pedersen, on behalf of the Assessment of LEscol in Renal Transplantation (ALERT) Study Investigators**

Endpoint	Fluvastatin (n=1050)	Placebo (n=1052)	p	Risk ratio (95% CI)
Cardiac death	36 (3·4)	54 (5·1)	0·031	0·62 (0·40–0·96)
Definite non-fatal MI	46 (4·4)	66 (6·3)	0·050	0·68 (0·40–1·00)
Cardiac death or definite non-fatal MI	70 (6·7)	104 (9·9)	0·005	0·65 (0·48–0·88)
Cardiac death or definite or probable non-fatal MI	79 (7·5)	105 (10·0)	0·032	0·72 (0·54–0·97)
CABG	25 (2·4)	24 (2·3)	0·932	1·03 (0·58–1·81)
PCI	29 (2·8)	37 (3·5)	0·357	0·80 (0·49–1·30)
Cardiac death, definite or probable non-fatal MI, CABG/PCI	112 (10·7)	134 (12·7)	0·139	0·83 (0·64–1·06)
Fatal or non-fatal cerebrovascular events*	74 (7·0)	63 (6·0)	0·391	1·16 (0·83–1·63)
Non-cardiovascular deaths	77 (7·3)	65 (6·2)	0·288	1·20 (0·86–1·67)
All-cause death	143 (13·6)	138 (13·1)	0·848	1·02 (0·81–1·30)
Graft loss or doubling of serum creatinine	183 (17·4)	165 (15·7)	0·369	1·10 (0·89–1·36)

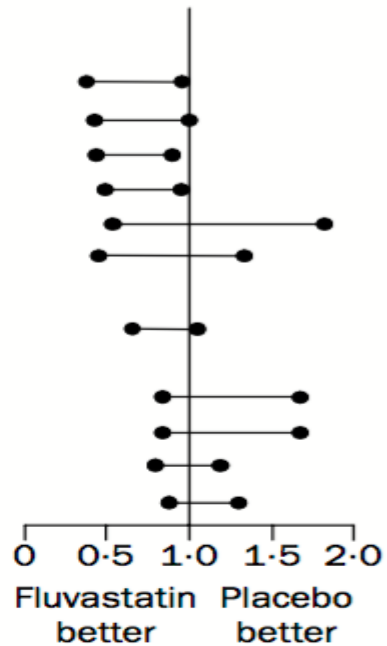


Figure 4: **Study endpoints in intention-to-treat population**
CABG=coronary artery bypass grafting. PCI=percutaneous coronary intervention. *Fatal or non-fatal stroke, transient ischaemic attack, reversible ischaemic neurological deficit, subarachnoid haemorrhage.

HMG CoA reductase inhibitors (statins) for kidney transplant recipients

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)
	Assumed risk	Corresponding risk			
	Placebo or no treatment	Statin			
Major cardiovascular events	**20 per 1000**	**17 per 1000** (13 to 21) **3 fewer** (7 fewer to 1 more)	**RR 0.84** (0.66 to 1.06)	2102 (1)	⊕⊕ **low**
All-cause mortality	**20 per 1000**	**22 per 1000** (12 to 37) **2 more** (8 fewer to 17 more)	**RR 1.08** (0.63 to 1.83)	2760 (6)	⊕⊕ **low**
Cardiovascular mortality	**5 per 1000**	**3 per 1000** (2 to 5) **2 fewer** (3 fewer to 0 more)	**RR 0.68** (0.45 to 1.01)	2322 (4)	⊕⊕ **low**

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: Confidence interval; **RR:** Risk Ratio

Palmer etal, Cochrane review, 2014

KDOQI US Commentary on the 2013 KDIGO Clinical Practice Guideline for Lipid Management in CKD

Table 1. Comparison of Guidelines for Lipids

	KDIGO[9]	ACC/AHA[5] (not CKD specific)	2014 ADA[61] (not CKD specific)	AACE[62] (not CKD specific)
LDL level required for treatment decision	Does not consider LDL in treatment decision	If CVD history, do not consider LDL; if LDL ≥ 190, treat; if LDL 70-189, depends on risk	LDL not used for treatment initiation, though there are target LDL levels on treatment	As part of risk assessment, recommend treat all adults at risk for CAD to reach optimal lipid values
Target LDL on treatment?	No	Reasonable to target 50% reduction if LDL ≥ 190, otherwise no	Without CVD, LDL < 100; with CVD, LDL < 70 is an option; can use reduction by 30%-40% as alternative target if on maximum statin	LDL < 100 with goal < 70 for very high risk, also targets HDL and triglycerides
Support combination pharmacologic therapy?	No	No	No	Yes if cholesterol markedly elevated and target not achieved with monotherapy, for mixed dyslipidemia, or to use lower doses of ≥2 drugs to decrease toxicity risk
Treatment of adults with DM (non-ESRD)	Treat all adults with statin or statin/ezetimibe (age 18-49 y: statin; age ≥ 50 y: statin or statin/ezetimibe)	Age 40-75 y: treat with statin; age 21-39 or >75 y: evaluate benefit vs risk and patient preferences (moderate- or high-intensity statin depending on CVD/risk)	Age > 40 y: treat with statin; age 18-39 y with CVD: few data but consider statin; age 18-39 y, no CVD: consider statin in addition to lifestyle if LDL remains > 100 or multiple risk factors	Treat to target lipid levels; statins drug of choice
Treatment of adults without DM (non-ESRD)	Age ≥ 50 y: treat with statin/ezetimibe; age 18-39 y: statin suggested if estimated 10-y incidence of coronary death or nonfatal MI > 10%	Age ≥ 21 y with CVD: treat (high or moderate intensity depending on age/tolerance); age 40-75 y, no CVD: treat if LDL 70-189 and 10-y ASCVD risk ≥ 7.5% (moderate- or high-intensity statin depending on CVD/risk); age 18-39 or >75 y without CVD: benefit uncertain, consider risk/benefit and patient preferences	Not applicable	If history of or at risk for CVD, treat to target LDL
Treatment of adults on dialysis[a]	Do not initiate, but continue statins if receiving at time of initiation of dialysis	Stated no recommendation as there was insufficient information for or against	Not discussed	Not discussed
Treatment of children	Do not initiate	AHA recommendations for children not revised with current update; prior AHA statement for high-risk pediatric patients (including CKD) recommends therapeutic lifestyle intervention; if age > 10 and LDL > 100 despite therapeutic lifestyle, treat with statin[43]	Age < 10 y: do not use statin; age ≥ 10 y: reasonable to consider statin if after diet and lifestyle changes, LDL > 160 or >130 with multiple risk factors (note only relevant to DM)	Recommend pharmacotherapy for age > 8 if do not respond sufficiently to lifestyle modifications, particularly if LDL ≥ 190 or ≥160 with risk factors

Note: LDL levels are reported in mg/dL.

Abbreviations: AACE, American Association of Clinical Endocrinologists; ACC/AHA, American College of Cardiology/American Heart Association; ADA, American Diabetes Association; ASCVD, atherosclerotic cardiovascular disease; CAD, coronary artery disease; CKD, chronic kidney disease; CVD, cardiovascular disease; DM, diabetes mellitus; ESRD, end-stage renal disease; HDL, high-density lipoprotein; KDIGO, Kidney Disease: Improving Global Outcomes; LDL, low-density lipoprotein; MI, myocardial infarction.

[a]KDIGO recommends statin for all transplant recipients; this population was not discussed in the other guidelines.

ESC European Society of Cardiology

European Heart Journal (2020) **41**, 111–188
doi:10.1093/eurheartj/ehz455

ESC/EAS GUIDELINES

2019 ESC/EAS Guidelines for the management of dyslipidaemias: *lipid modification to reduce cardiovascular risk*

The Task Force for the management of dyslipidaemias of the European Society of Cardiology (ESC) and European Atherosclerosis Society (EAS)

Table 30 Recommendations for lipid management in patients with moderate to severe chronic kidney disease

Recommendations	Class [a]	Level [b]	Ref [c]
Patients with stage 3–5 CKD have to be considered at high or very high CV risk.	I	A	388–392
The use of statins or statin/ezetimibe combination is indicated in patients with non-dialysis-dependent CKD.	I	A	393, 394, 397
In patients with dialysis-dependent CKD and free of atherosclerotic CVD, statins should not be initiated.	III	A	395, 396
In patients already on statins, ezetimibe or a statin/ezetimibe combination at the time of dialysis initiation, these drugs should be continued, particularly in patients with CVD.	IIa	C	
In adult kidney transplant recipients treatment with statins may be considered.	IIb	C	

CKD = chronic kidney disease; CV = cardiovascular.
[a]Class of recommendation.
[b]Level of evidence.
[c]Reference(s) supporting recommendations.

Table 31 Recommendations for the treatment of dyslipidaemia in transplant patients

Recommendations	Class [a]	Level [b]	Ref [c]
Global CV risk management strategies have to be developed in transplant patients.	I	C	
Statins should be considered as the first-line agents in transplant patients. Initiation should be at low doses with careful up-titration and with caution regarding potential drug–drug interactions, particularly for those on ciclosporin.	IIa	B	402
In patients who are intolerant of statins or those with significant dyslipidaemia and high residual risk despite a maximally tolerated statin dose, alternative or additional therapy may be considered: ezetimibe for whose where high LDL-C is the principal abnormality; or; fibrates for those where hypertriglyceridaemia and/or low HDL-C is the principal abnormality.	IIb	C	

CV = cardiovascular; HDL = high-density lipoprotein-cholesterol; LDL = low-density lipoprotein-cholesterol.
[a]Class of recommendation.
[b]Level of evidence.
[c]Reference(s) supporting recommendations.

Outlines:

- ✓Lipid abnormalities and the kidneys
- ✓Guidelines for management of dyslipidemia in CKD
- ✓Role of statin on kidney function
- ✓Role of other lipid lowering agents and future therapeutic prospective

JASN
JOURNAL OF THE AMERICAN SOCIETY OF NEPHROLOGY

Clinical Science Articles

Statins for Improving Renal Outcomes: A Meta-Analysis

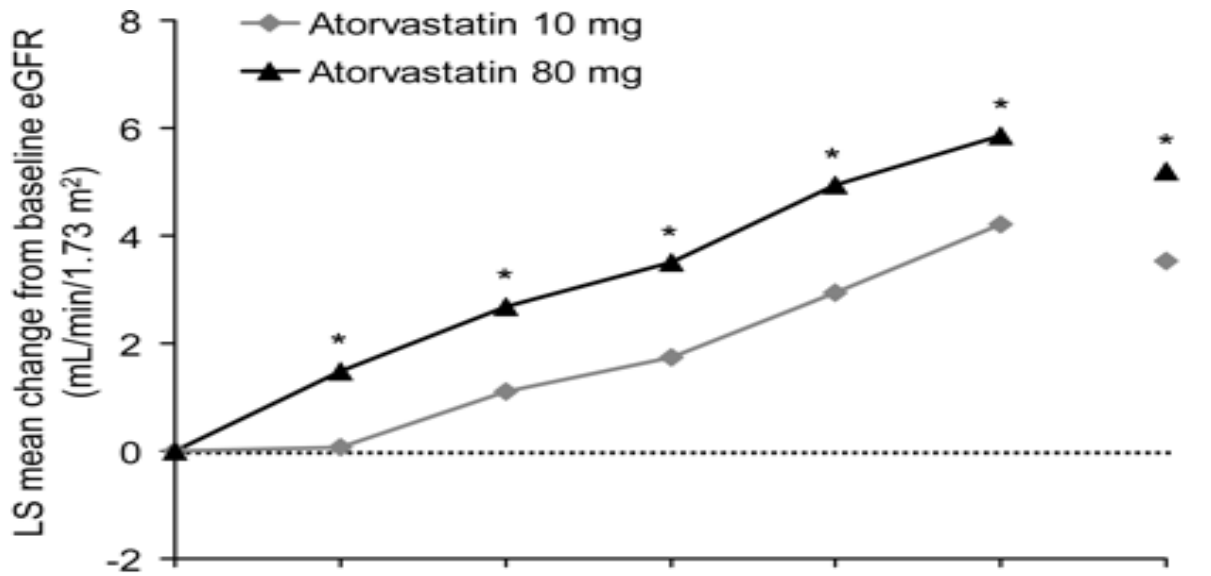
Sabrina Sandhu,* Natasha Wiebe,* Linda F. Fried,† and Marcello Tonelli*‡§‖

*Departments of *Medicine, ‡Critical Care, and §Public Health Sciences, University of Alberta, and ‖Institute of Health Economics, Edmonton, Alberta, Canada; and †Veterans Affairs Pittsburgh Healthcare System and Renal-Electrolyte Division, University of Pittsburgh, School of Medicine, Pittsburgh, Pennsylvania*

CJASN
Clinical Journal of the American Society of Nephrology

Effect of Intensive Lipid Lowering with Atorvastatin on Renal Function in Patients with Coronary Heart Disease: The Treating to New Targets (TNT) Study

James Shepherd,* John J.P. Kastelein,† Vera Bittner,‡ Prakash Deedwania,§ Andrei Breazna,‖ Stephen Dobson,¶ Daniel J. Wilson,** Andrea Zuckerman,** and Nanette K. Wenger,†† for the Treating to New Targets Investigators



*P<0.0001 vs atorvastatin 10 mg

AJKD
AMERICAN JOURNAL OF KIDNEY DISEASES

A controlled, prospective study of the effects of atorvastatin on proteinuria and progression of kidney disease

Stefano Bianchi, MD , Roberto Bigazzi, MD , Alberto Caiazza, MD , Vito M. Campese, MD. March 2003

HMG CoA reductase inhibitors (statins) for people with chronic kidney disease not requiring dialysis

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Quality of the evidence (GRADE)
	Assumed risk	Corresponding risk per year treated			
	Placebo or no treatment	Statins			
Major cardiovascular events	**20 per 1000**	**14 per 1000** (13 to 16 per 1000) 6 fewer (4 to 7 fewer)	**RR 0.72** (0.66 to 0.79)	36,033 (13)	⊕⊕⊕⊕ **high**
All-cause mortality	**25 per 1000**	**20 per 1000** (17 to 23 per 1000) 5 fewer (2 to 8 fewer)	**RR 0.79** (0.69 to 0.91)	28,276 (10)	⊕⊕⊕⊕ **high**
Cardiovascular mortality	**15 per 1000**	**12 per 1000** (10 to 13 per 1000) 3 fewer (2 to 5 fewer)	**RR 0.77** (0.69 to 0.87)	19,059 (7)	⊕⊕⊕⊖ **moderate**

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: Confidence interval; **RR:** Risk Ratio N38

Palmer etal, Cochrane review, 2014

The New England
Journal of Medicine

VOLUME 335 OCTOBER 3, 1996 NUMBER 14

THE EFFECT OF PRAVASTATIN ON CORONARY EVENTS AFTER MYOCARDIAL INFARCTION IN PATIENTS WITH AVERAGE CHOLESTEROL LEVELS

FRANK M. SACKS, M.D., MARC A. PFEFFER, M.D., PH.D., LEMUEL A. MOYE, M.D., PH.D., JEAN L. ROULEAU, M.D., JOHN D. RUTHERFORD, M.D., THOMAS G. COLE, PH.D., LISA BROWN, M.P.H., J. WAYNE WARNICA, M.D., J. MALCOLM O. ARNOLD, M.D., CHUAN-CHUAN WUN, PH.D., BARRY R. DAVIS, M.D., PH.D., AND EUGENE BRAUNWALD, M.D., FOR THE CHOLESTEROL AND RECURRENT EVENTS TRIAL INVESTIGATORS*

Effects of atorvastatin on kidney outcomes and cardiovascular disease in patients with diabetes: an analysis from the Collaborative Atorvastatin Diabetes Study (CARDS)

Helen M. Colhoun, D. John Betteridge, Paul N. Durrington, Graham A. Hitman, H. Andrew W. Neil, Shona J. Livingstone, Valentine Charlton-Menys, David A. DeMicco, John H. Fuller, CARDS Investigators

Research output: Contribution to journal › Article › peer-review

THE LANCET

Articles

SHARP trial

The effects of lowering LDL cholesterol with simvastatin plus ezetimibe in patients with chronic kidney disease (Study of Heart and Renal Protection): a randomised placebo-controlled trial

Outlines:

- ✓Lipid abnormalities and the kidneys
- ✓Guidelines for management of dyslipidemia in CKD
- ✓Role of statin on kidney function
- ✓Role of other lipid lowering agents and future therapeutic prospective

2D

In adult with CKD (including those treated with chronic dialysis or kidney transplantation) and hypertriglyceridemia, we suggest that therapeutic lifestyle changes be advised. (2D)

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

D: very low (The estimate of effect is very uncertain, and often will be far from the truth).

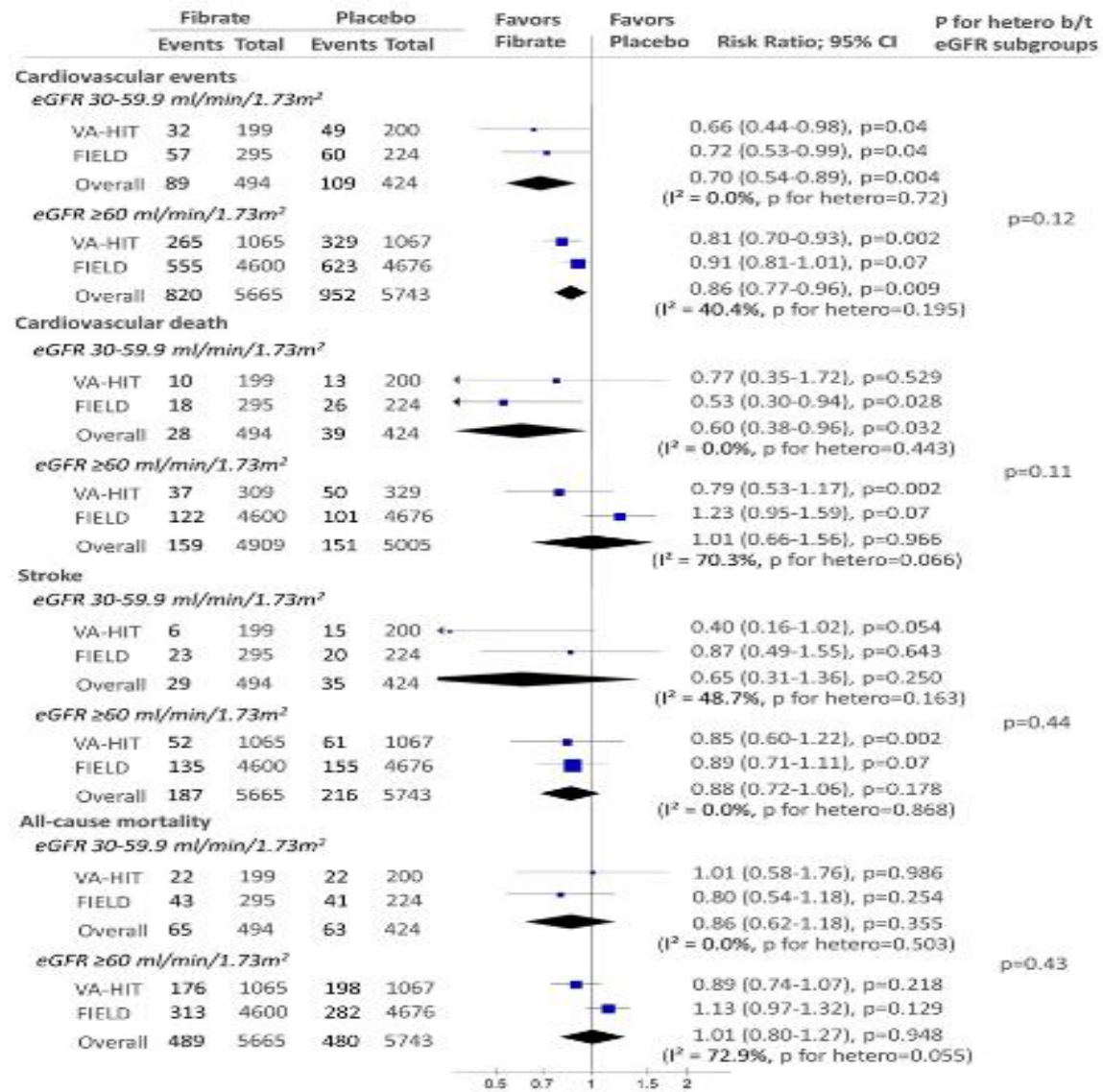
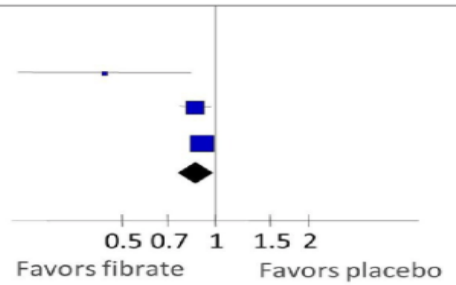
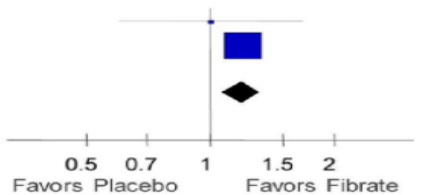


Figure 6 **Effect of Fibrates on Major Clinical Outcomes in Patients With CKD**

	Fibrate Events	Fibrate Total	Placebo Events	Placebo Total	Risk Ratio; 95% CI
Progression of albuminuria					
Ansquer 2005	12	155	28	159	0.44 (0.23-0.83)
Davis 2010	473	4249	557	4304	0.86 (0.77-0.97)
ACCORD 2010	1339	2765	1474	2753	0.90 (0.86-0.95)
Overall	1824	7169	2059	7216	0.86 (0.76-0.98), p=0.02 (I^2 = 63%, Q=5.47, p for hetero=0.06)
Regression of albuminuria					
Ansquer 2005	20	54	17	46	1.00 (0.60-1.67)
Davis 2010	475	1012	407	1040	1.20 (1.09-1.33)
Overall	495	1066	424	1086	1.19 (1.08-1.31), p=0.0005 (I^2 = 0.0%, Q=0.45, p for hetero=0.50)



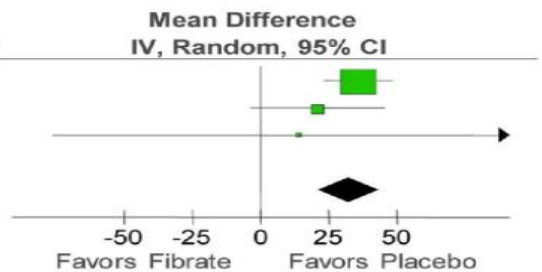


Serum creatinine & kidney function in kidney disease

Serum creatinine (µmol/L)

Study or Subgroup	Fibrate Mean	Fibrate SD	Fibrate Total	Placebo Mean	Placebo SD	Placebo Total	Weight	Mean Difference IV, Random, 95% CI
Barbir *et al* 1992	176	26	44	140	33	43	78.1%	36.00 [23.50, 48.50]
Bruce *et al* 1996	128	36	12	107	24	12	20.4%	21.00 [-3.48, 45.48]
Levin *et al 2000*	234	108	16	220	129	12	1.5%	14.00 [-76.15, 104.15]
Overall			**72**			**67**	**100.0%**	**32.61 [21.56, 43.66]**

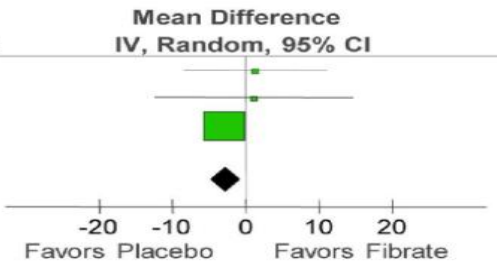
Heterogeneity: Tau² = 0.00; Chi² = 1.31, df = 2 (P = 0.52); I² = 0%
Test for overall effect: Z = 5.78 (P < 0.00001)



Glomerular filtration rate (ml/min/1.73m²)

Study or Subgroup	Fibrate Mean	Fibrate SD	Fibrate Total	Placebo Mean	Placebo SD	Placebo Total	Weight	Mean Difference IV, Random, 95% CI
Samuelsson *et al* 1997	35	13.8	28	33.7	22.8	29	4.8%	1.30 [-8.45, 11.05]
Levin *et al* 2000	43.6	19.9	16	42.5	16.4	12	2.5%	1.10 [-12.36, 14.56]
Tonelli *et al* 2004	54.36	10.97	199	57.34	11.61	200	92.7%	-2.98 [-5.20, -0.76]
Overall			**243**			**241**	**100.0%**	**-2.67 [-4.81, -0.54]**

Heterogeneity: Tau² = 0.00; Chi² = 1.01, df = 2 (P = 0.60); I² = 0%
Test for overall effect: Z = 2.45 (P = 0.01)



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Effects of Fibrates in Kidney Disease

A Systematic Review and Meta-Analysis

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Sydney, Australia; Hangzhou, China; and Edmonton, Alberta, Canada

N10

Fenofibrate Delays the Need for Dialysis and Reduces Cardiovascular Risk Among Patients With Advanced CKD

Chieh-Li Yen, Pei-Chun Fan, Ming-Shyan Lin, Cheng-Chia Lee, Kun-Hua Tu, Chao-Yu Chen, Ching-Chung Hsiao, Hsiang-Hao Hsu, Ya-Chung Tian, Chih-Hsiang Chang ✉

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Published: 02 March 2021 **Article history** ▾

Journal of Cellular Biochemistry

RESEARCH ARTICLE

Fenofibrate improves renal function by amelioration of NOX-4, IL-18, and p53 expression in an experimental model of diabetic nephropathy

Habib Yaribeygi, Mohammad T. Mohammadi ✉, Ramin Rezaee, Amirhossein Sahebkar ✉

First published: 15 May 2018 | https://doi.org/10.1002/jcb.27055 | Citations: 28

Dyslipidemia in Chronic Kidney Disease: Contemporary Concepts and Future Therapeutic Perspectives

Table 2. Potential therapeutic approaches against dyslipidemia in the setting of CKD

Study	Agent	CKD population	Outcome
PPAR agonism			
Yokote et al. [61]	Pemafibrate (PPARα agonist)	All eGFR ranges Dialysis patients not included	Correction of lipid abnormalities in CKD patients
Lin et al. [62]	Pioglitazone (PPARγ agonist)	Diabetics with ESRD	↓ MACCE-related death in the pioglitazone group with dyslipidemia compared with DPP4 inhibitors users
Yen et al. [63]	Pioglitazone (PPARγ agonist)	Diabetics with advanced CKD	↓ MACCE and all-cause mortality in the pioglitazone arm
PCSK9 inhibition			
Charytan et al. [64]	Evolocumab	eGFR ≥30 mL/min/1.73 m^2	Lipid-lowering and clinical efficacy maintained in CKD ↑ cardiovascular events reduction with worsening renal function
Lee et al. [65]	Evolocumab	All eGFR ranges + hemodialysis	Similar LDL-C reduction in severe renal dysfunction and hemodialysis
Tuñón et al. [66]	Alirocumab	eGFR >30 mL/min/1.73 m^2	↓ adverse cardiovascular outcomes across the different groups according to renal function
Wright et al. [67]	Inclisiran	CrCl ≥15 mL/min	Similar pharmacodynamics and pharmacokinetic effect in normal and impaired kidney function
Lp(a) inhibition			
Tsimikas et al. [68]	Pelacarsen	Not included	Dose-dependent reduction of Lp(a) in patients with cardiovascular disease
Gut microbiota modulation			
Han et al. [69]	Chickpea dietary fiber		↑ *Bacteroides* and *Lactobacillus* species Correction of lipid profile
Wang et al. [70]	Green tea leaf powder fiber		↑ *Blautia, Oscillibacter, Ruminiclostridium, Alloprevotella,* and *Butyrivibrio* species ↓ *Erysipelatoclostridium, Desulfovibrio,* and *Candidatus saccharimonas* species Prevention of high-fat diet-induced dyslipidemia
Zhang et al. [71]	Iodomethylcholine (TMAO inhibitor)	CKD model of apoE$^{-/-}$ mice	Favorable cardiovascular outcomes ↓ plasma cholesterol levels

Theofilis etal. Am J Nephrol 2021;52:693–701

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Theofilis etal. Am J Nephrol 2021;52:693–701

Conclusion

- ✓CKD patients should have CV-risk assessment irrespective of lipid profile.
- ✓Patients with CKD aged ≥50 or (<50 with risk factors) statin or statin/ezetimib should be given
- ✓For patients on dialysis if already on statin then continue if not then do not initiate.
- ✓Statin should be given to kidney transplant pts.
- ✓Statin may reduce albuminuria but its benefit on renal function is uncertain.
- ✓Fibrate can be given in isolated circumstances however, its safety has been questioned.
- ✓There are emerging evidences that PCSK9 & Lp(a) inhibitors are effective in reducing CV events.

Q1: 55 years old man with eGFR 35ml/min/1.73m^2 who is on statin.
Would measuring cholesterol level change your management?

A. Yes
B. No

Q2: 55 years old man with eGFR 35ml/min/1.73m^2 who is NOT on statin.
Would measuring cholesterol level change your management?

A. Yes
B. No

Q1: 55 years old man with eGFR 35ml/min/1.73m^2 who is on statin.
Would measuring cholesterol level change your management?

A. Yes
B. No

Q2: 55 years old man with eGFR 35ml/min/1.73m^2 who is NOT on statin.
Would measuring cholesterol level change your management?

A. Yes
B. No

Q1: 55 years old man with eGFR 35ml/min/1.73m^2 who is on statin.
Would measuring cholesterol level change your management?

A. Yes

B. No

Q2: 55 years old man with eGFR 35ml/min/1.73m^2 who is NOT on statin.
Would measuring cholesterol level change your management?

A. Yes

B. No

Q3: 45 years old man with eGFR 35ml/min/1.73m^2 who is smoker with DM and HTN. He is NOT on statin. Would measuring cholesterol level change your management?

A. Yes

B. No

Q4: 45 years old man with eGFR 35ml/min/1.73m^2 who is non-smoker without DM and HTN. He is NOT on statin. Would measuring cholesterol level change your management?

A. Yes

B. No

Q5: 45 years old man who is on dialysis and is NOT on statin. Do you think starting statin will improve his cardiovascular outcome?

A. Yes

B. No

Q3: 45 years old man with eGFR 35ml/min/1.73m^2 who is smoker with DM and HTN. He is NOT on statin. Would measuring cholesterol level change your management?

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B. No

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A. Yes

B. No

CKD and lipid

3 key points

- ✓Assess in everyone
- ✓Treat most of them
- ✓Follow up measures not needed

Sulaimanyah city

Thank you