Estatinas en el transplante renal

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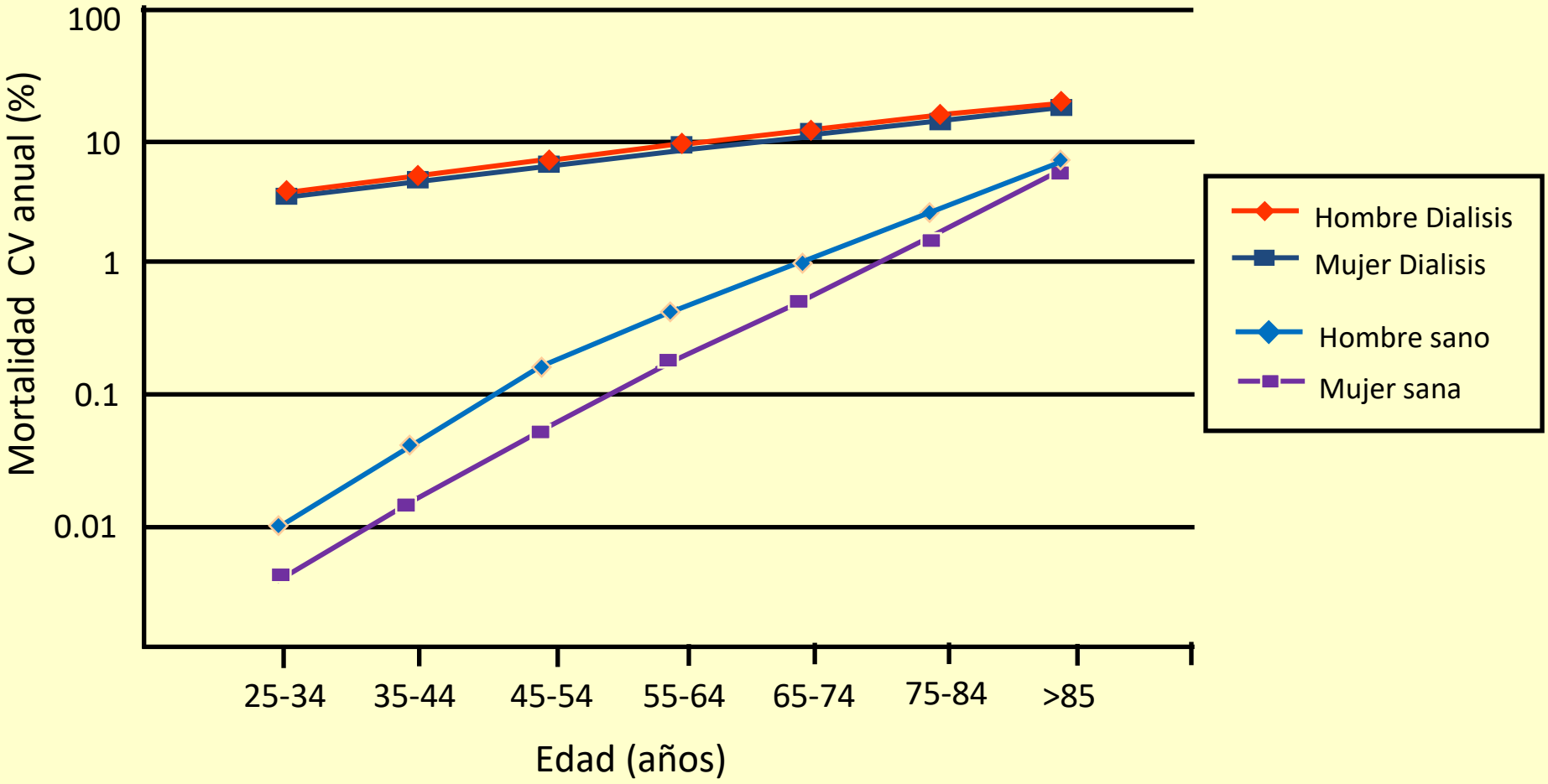
Proyecto PROMETEO. 2012

Outline

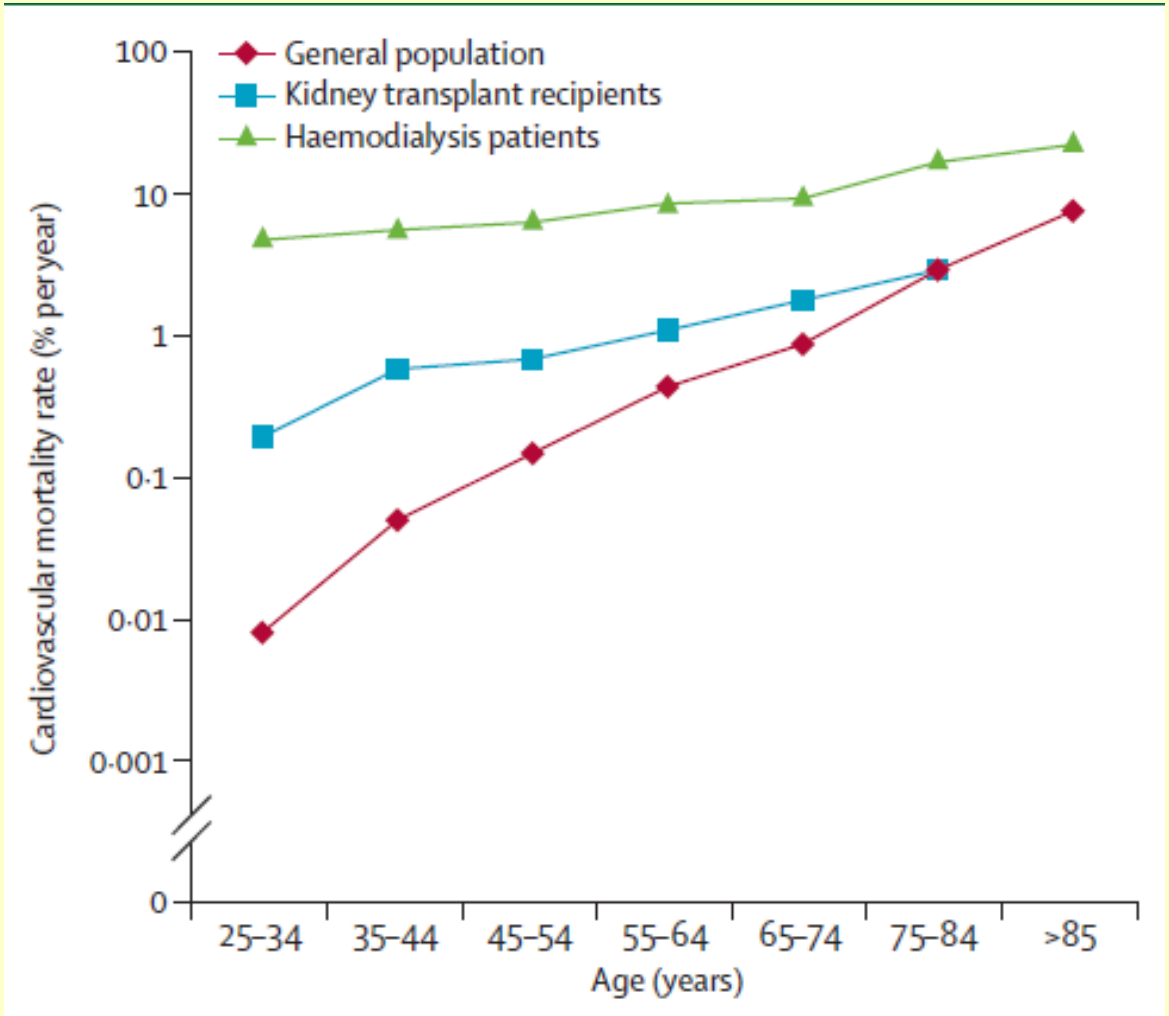
- CV mortality in CKD and transplantation
- Lipids and management of statins in CKD patients
- Evidence of beneficial effects of statins in general population
- Evidence of beneficial effects of statins in CKD
  - Post-hoc analysis of CKD patients included in major trials
  - Systematic reviews and meta-analysis (2009-2012)
  - ESC/EAS Guidelines for the management of dyslipidemia (2011)
  - European Guidelines on cardiovascular disease prevention (2012)
  - KDIGO on lipids in CKD (internal use, August 2012)
- Evidence of beneficial effects of statins in renal transplantation

Mortalidad cardiovascular en pacientes en hemodialisis vs población general



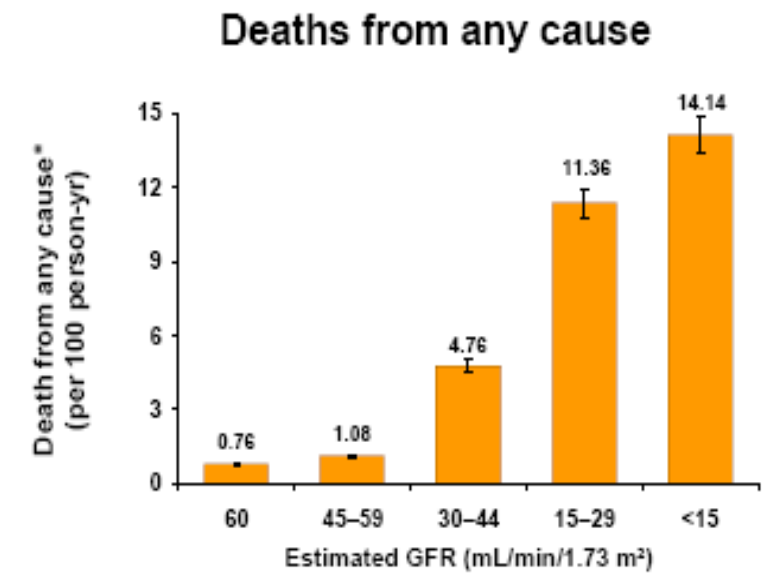
Foley et al. AJKD 1998;32:S112-9

Cardiovascular mortality rate by age group

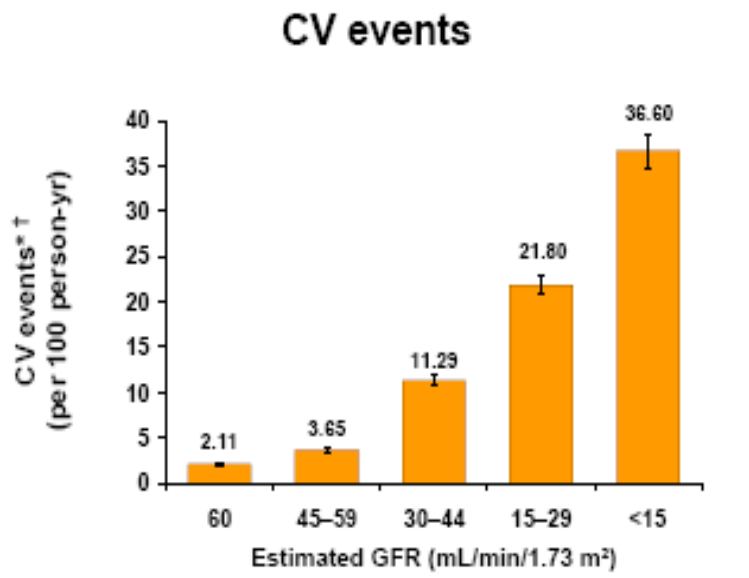


Jardine AG et al. Lancet 2011: 15;378:1419-27

Independent effects of CKD on CVD morbidity/mortality



No. of Events	25,803	11,569	7,802	4,408	1,842



No. of Events	73,108	34,690	18,580	8,809	3,824

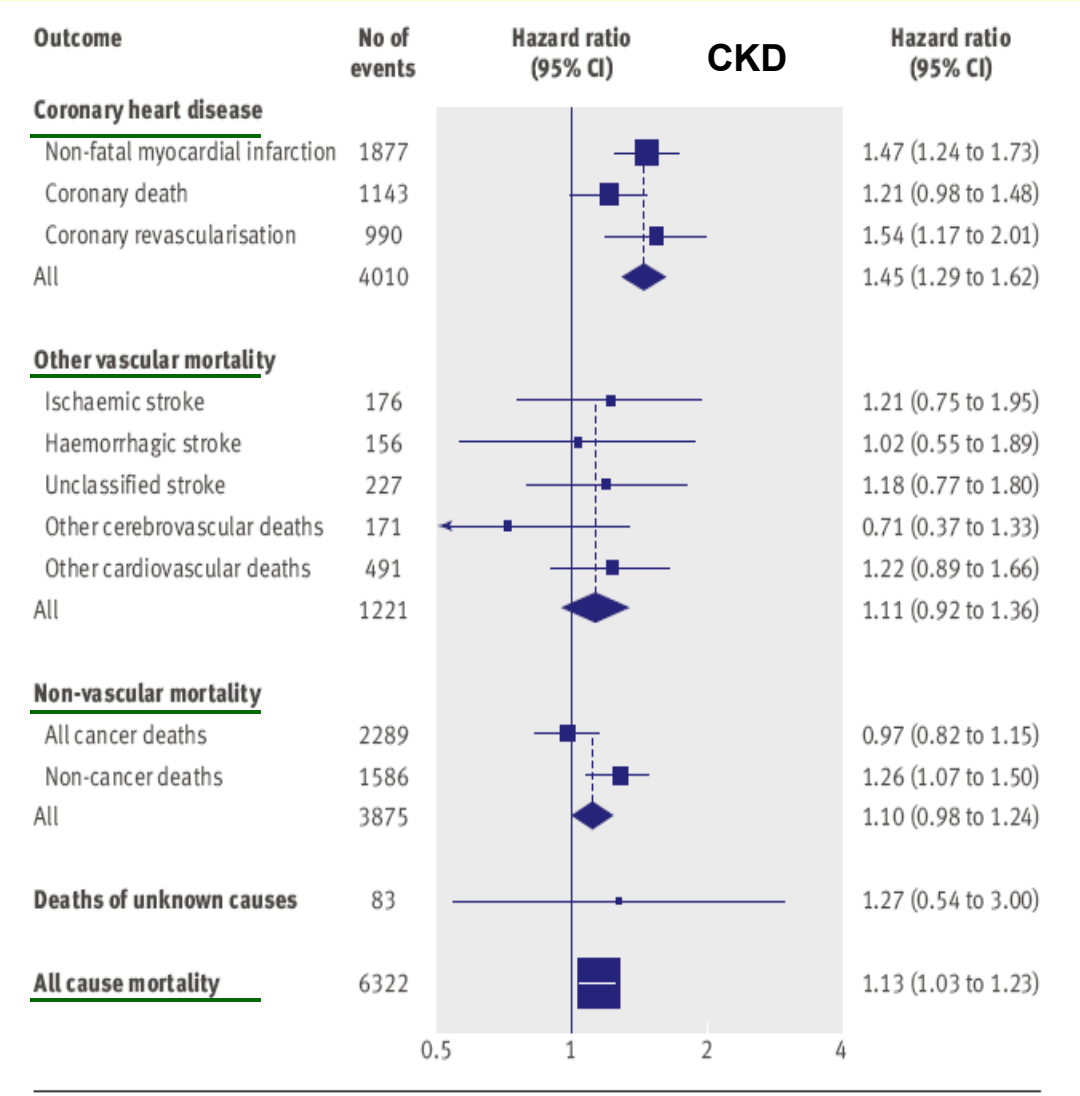
Go AS et al. N Engl J Med 2004;351:1296–305.

Chronic kidney disease and risk of major CV disease and non-vascular mortality

Prospective population based cohort study.

16,958 people aged 33-81 years without manifest vascular disease

1210 (7%) of participants had chronic kidney disease at entry and follow-up of 24 years

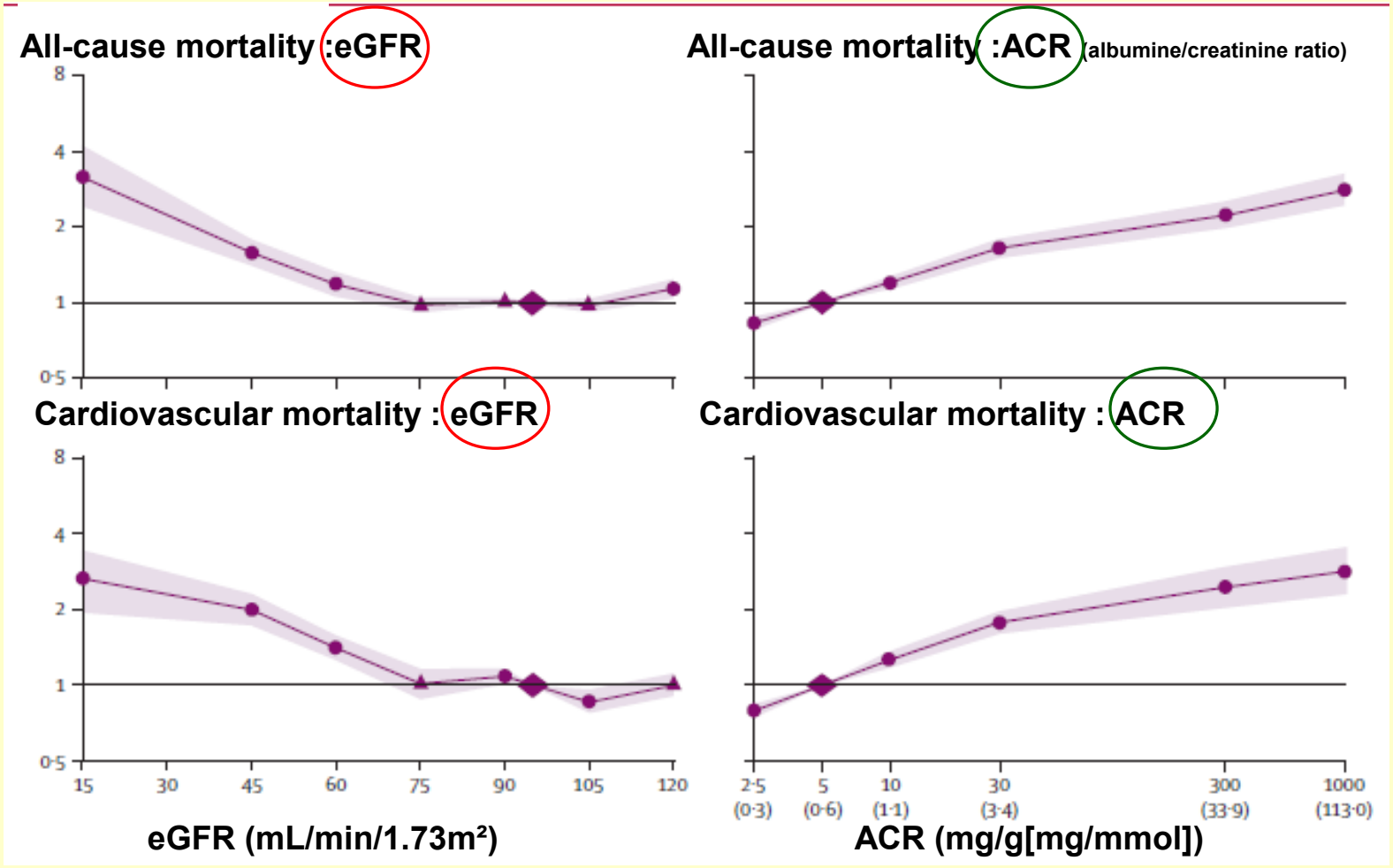


Di Angelantonio E et al. BMJ. 2010 30;341

Association of eGFR and albuminuria with all-cause and CV mortality in general population cohorts

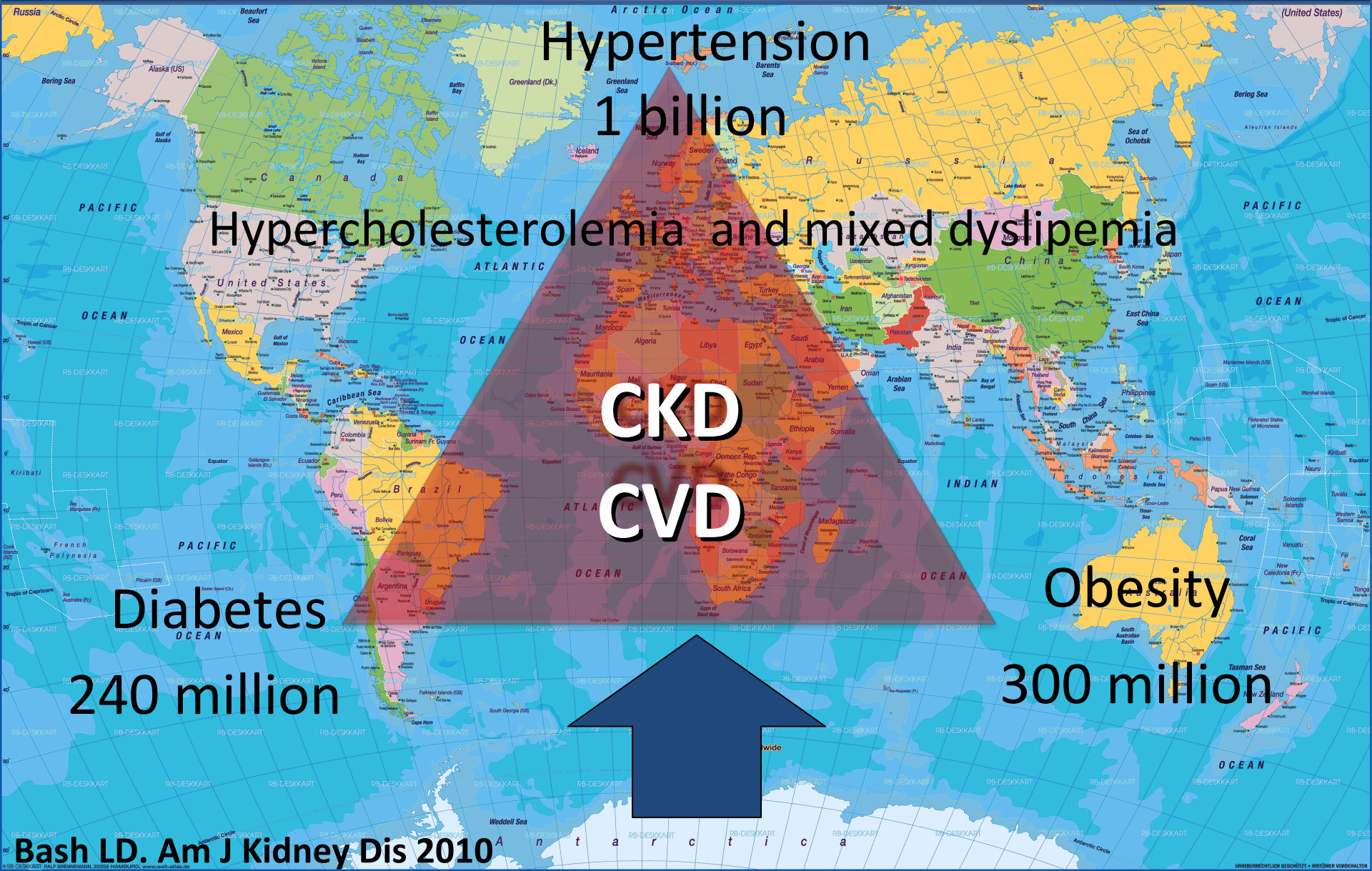
A collaborative metaanalysis

105,872 participants from 14 studies



Lancet 2010; 375: 2073–81

CKD and CVD, a global burden



Bash LD. Am J Kidney Dis 2010

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Traditional and non-traditional risk factors in patients with ESRD

TRADITIONAL RISK FACTORS	NONTRADITIONAL RISK FACTORS
Age	Anemia
Gender	Disturbances in calcium/phospate metabolism
Genetic factors	Chronic inflammation
Diabetes	Malnutrition
Hypertension	Uremic toxins
Smoking	Uremic dyslipidemia
Physical inactivity	Endothelial dysfunction
Obesity	Oxidative stress
High LDL	Hyperhomocystenemia
Low HDL	Autonomic dysfunction
High triglycerides	Immunosuppressive drugs

Dislipemia en pacientes con insuficiencia renal

-El perfil lipídico en pacientes con IR muestra cambios cuali y cuantitativos

-Dislipemia más acentuada a medida que progresa la IR

-Dislipemia urémica:

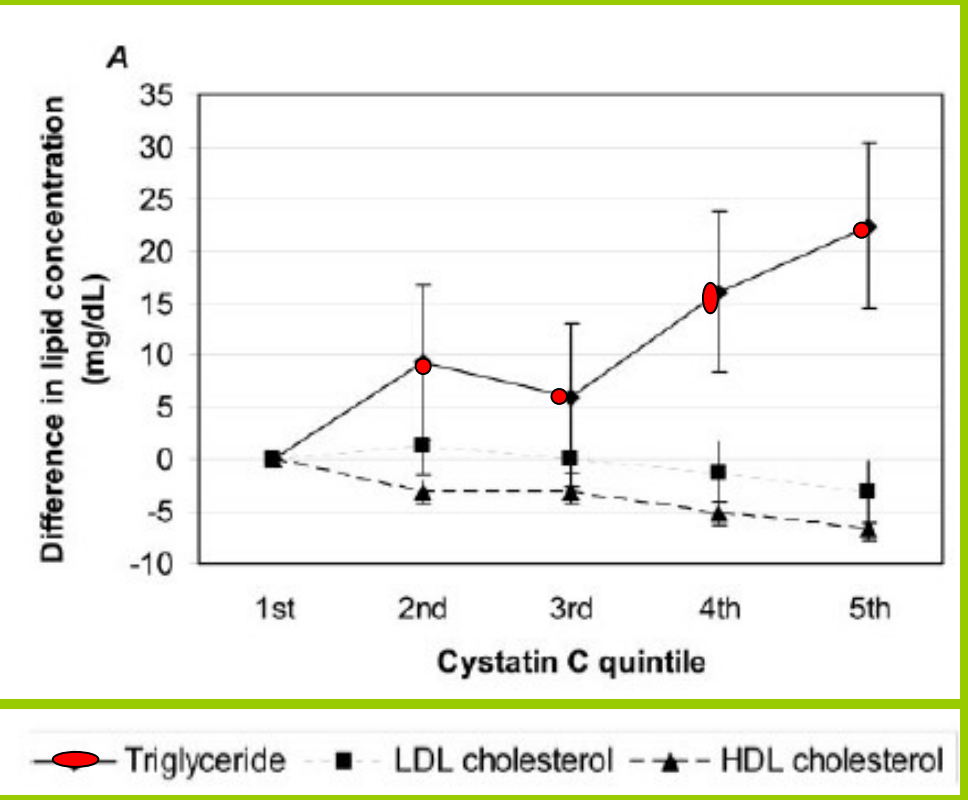
- ↑ Triglicéridos (aumento producción y descenso de catabolismo)
- ↓ HDL

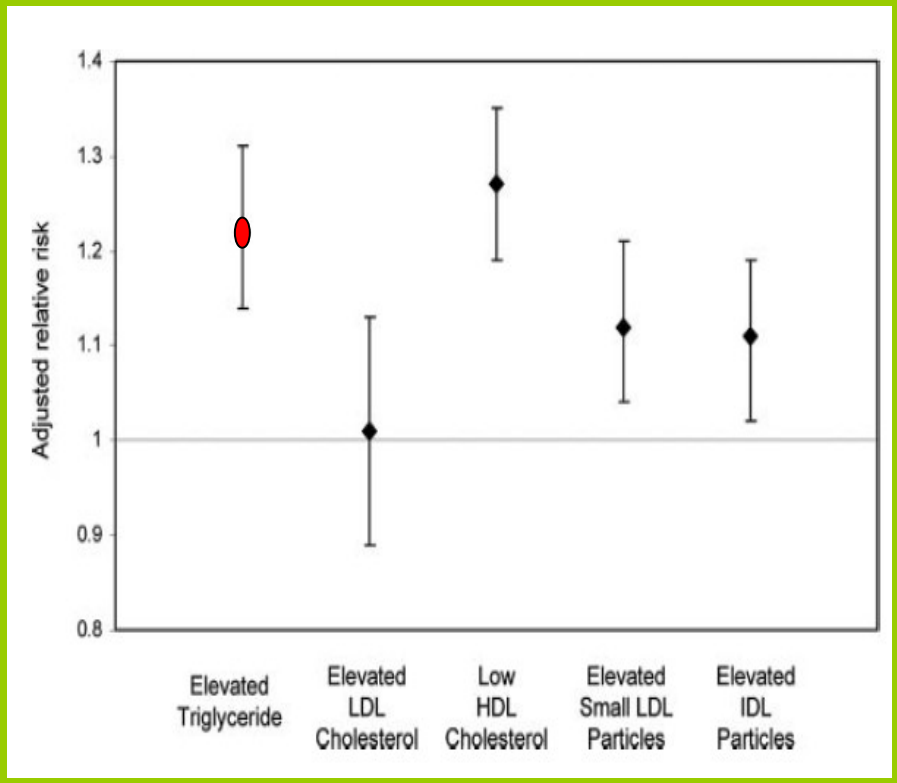
LDL: no cambios (estadio 1 y 2), aumento (estadio 3-5)

Partículas LDL pequeñas y densas (más aterogénicas)

Lipoprotein abnormalities are present with milder degrees of renal impairment

The Multi-Ethnic Study of Atherosclerosis: 5109 participants with GFR>60ml/min/1.73m2





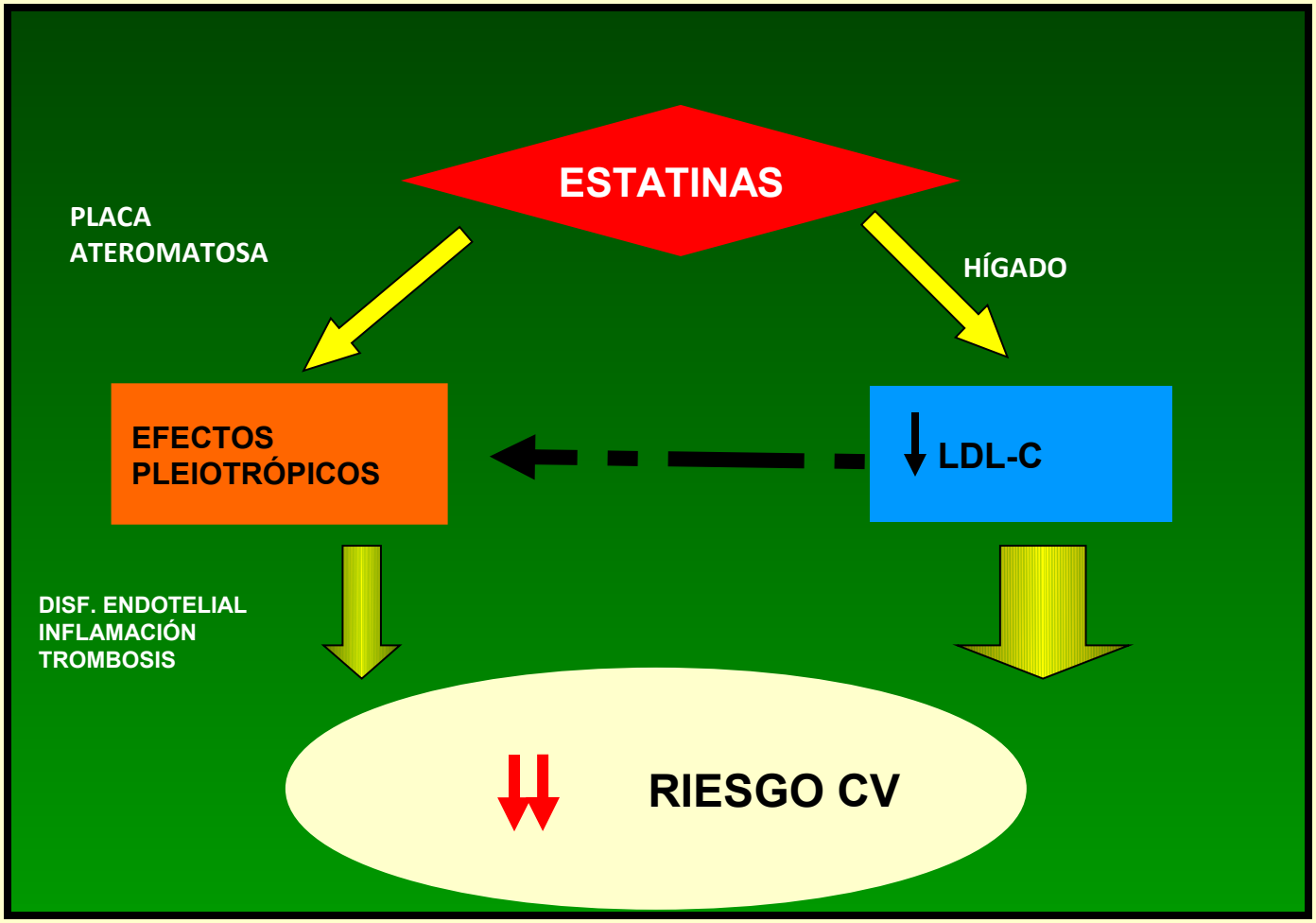
Clin J Am Soc Nephrol 3: 125–132, 2008

Dyslipidemia in CKD patients

	Predialysis	Hemodialysis	Kidney Transplant
Total cholesterol	Normal	Normal or decreased	Increased
HDL	Decreased	Decreased	Decreased
LDL	Normal or decreased	Normal or decreased	Increased
VLDL	Increased	Increased	Increased
Triglycerides	Increased	Increased	increased

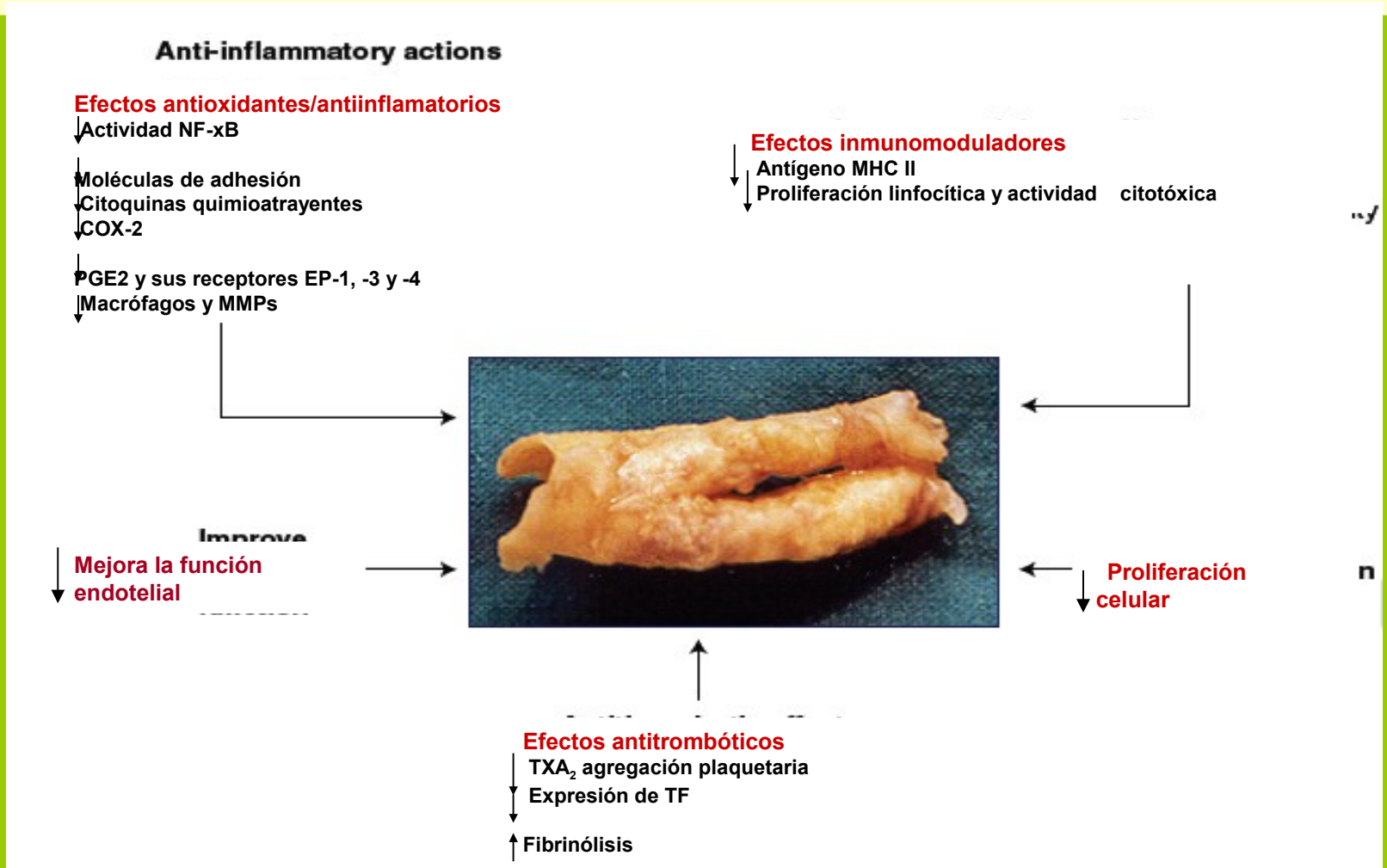
Clin J Am Soc Nephrol 6: 664–678, 2011

Los efectos beneficiosos de las estatinas se deben principalmente al descenso del colesterol y tambien a sus efectos pleiotrópicos



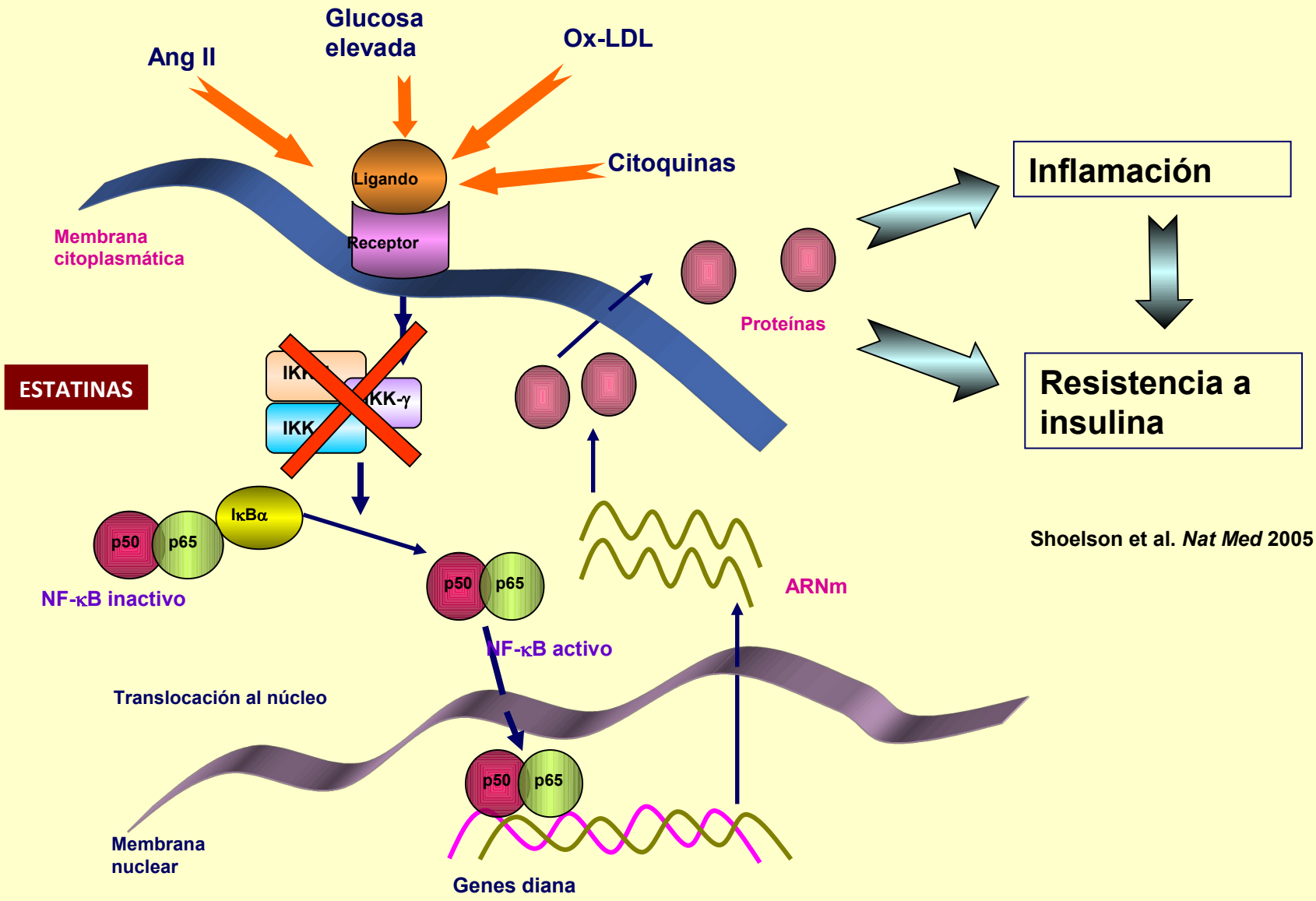
Guijarro C et al. Circ Res. 1998;83:490-500; Blanco-Colio LM et al. Atherosclerosis 2002;161:17-26 ; Blanco-Colio et al. Circulation 2003; 108:1506-1513

Efectos de estatinas sobre la aterotrombosis probablemente ligados a sus efectos pleiotrópicos



Tuñón J et al. Expert Opinion Ther. Target 2007; 11:273-278

El factor nuclear kappa-B (NF-kB) es la diana de las estatinas en sus acciones antinflamatorias



Shoelson et al. *Nat Med* 2005

Hernández-Presa et al. Circulation 1997; J Immunol 1998; Circ Res 2000; Am J Pathol 2001

Safety of lipid management in patients with CKD

The drug use should be based on GFR

Drugs eliminated mainly by the hepatic route should be preferred (●)

Avoid drug interaction through CYP3A4

Agent	GFR 60–90 ml/min/1.73 m^2	GFR 15–59 ml/min/1.73 m^2	GFR <15 ml/min/1.73 m^2	Notes
Statins				
Atorvastatin	No	No	No	
Fluvastatin ●	No	Not defined	Not defined	↓ dose to one-half at GFR <30 ml/min/1.73 m^2
Lovastatin	No	↓ to 50%	↓ to 50%	↓ dose to one-half at GFR <30 ml/min/1.73 m^2
Pravastatin ●	No	No	No	Start at 10 mg/day for GFR <60 ml/min/1.73 m^2
Rosuvastatin	No	5–10 mg	5–10 mg	Start at 5 mg/day for GFR <30 ml/min/1.73 m^2, max dose 10 mg/day
Simvastatin	No	No	5 mg	Start at 5 mg if GFR <10 ml/min/1.73 m^2
Nonstatins				
Nicotinic acid	No	No	↓ to 50%	34% kidney excretion
Cholestyramine	No	No	No	Not absorbed
Colesevelam	No	No	No	Not absorbed
Ezetimibe	No	No	No	
Fenofibrate	↓ to 50%	↓ to 25%	Avoid	May ↑ serum creatinine Fenofibrate not to be used with GFR<50ml/min/1.73m2
Gemfibrozil	No	No	No	NLA recommends a dose of 600 mg/day for GFR 15–59 ml/min/1.73 m^2 and avoiding use for GFR <15 ml/min/1.73 m^2
Omega-3 FAs	No	No	No	

Adapted from the K/DOQI clinical practice guidelines (29).

↓ = decrease; ↑ = increase; CKD = chronic kidney disease; FA = fatty acid; GFR = glomerular filtration rate; NLA = National Lipid Association.

● And pitavastatin

Statin dosages for dyslipidemias in patients with chronic kidney disease

Drug	CKD Stage			
	1 to 2	3	4 to 5	Transplant
Atorvastatin	10 to 80 mg	10 to 80 mg	10 to 80 mg	10 to 20 mg
Fluvastatin	20 to 80 mg	20 to 80 mg	10 to 80 mg	10 to 40 mg
Pravastatin	20 to 80 mg	20 to 40 mg	10 to 20 mg	10 to 40 mg
Rosuvastatin	10 to 40 mg	10 to 20 mg	5 to 10 mg	5 mg
Simvastatin	20 to 80 g	10 to 40 mg	10 to 20 mg	5 to 20 mg

The information in the table is adopted and modified from reference 4.

Clin J Am Soc Nephrol 6: 664–678, 2011

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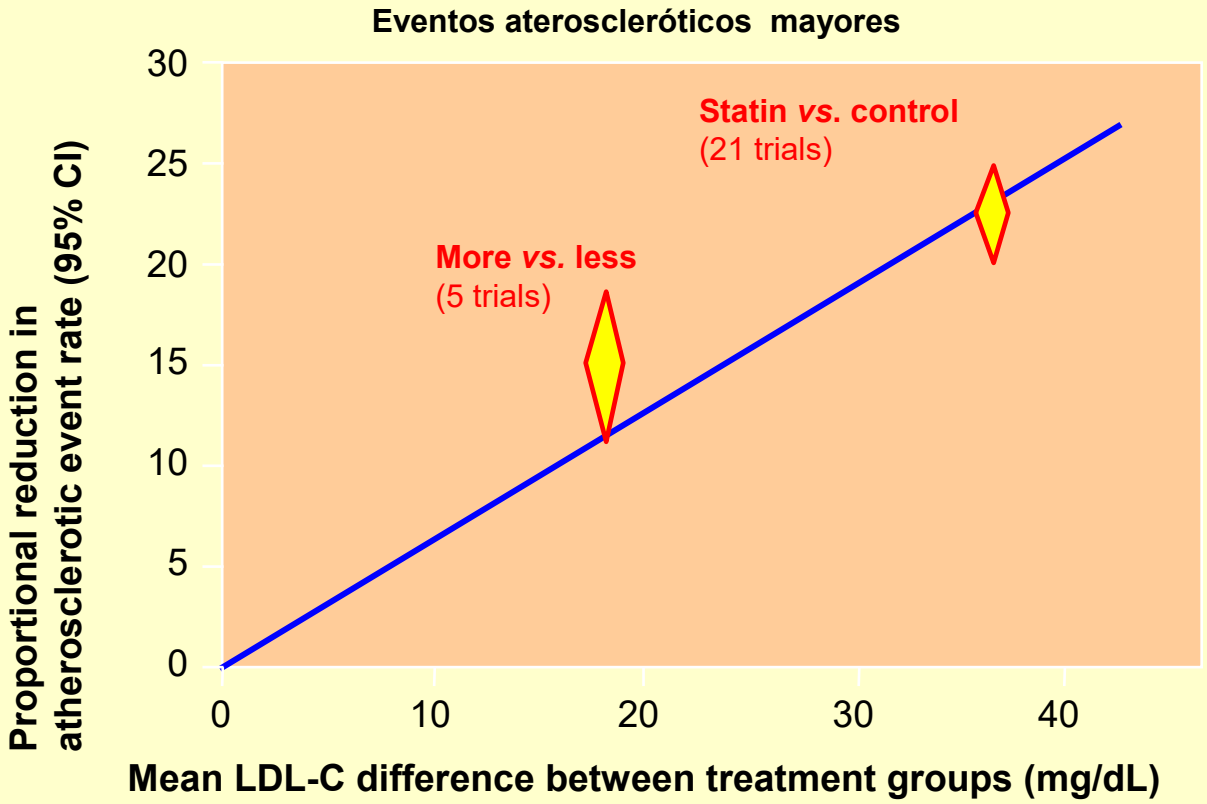
Eficacia del descenso del C-LDL con estatinas

Un meta-analisis de 90.056 participantes en 14 estudios clinicos de estatinas

- El tratamiento con estatinas reduce la incidencia a 5 años de eventos CV mayores, revascularizacion coronaria e ictus en un 20% por cada mmol/L (39mg/dL) independientemente del perfil lipídico inicial

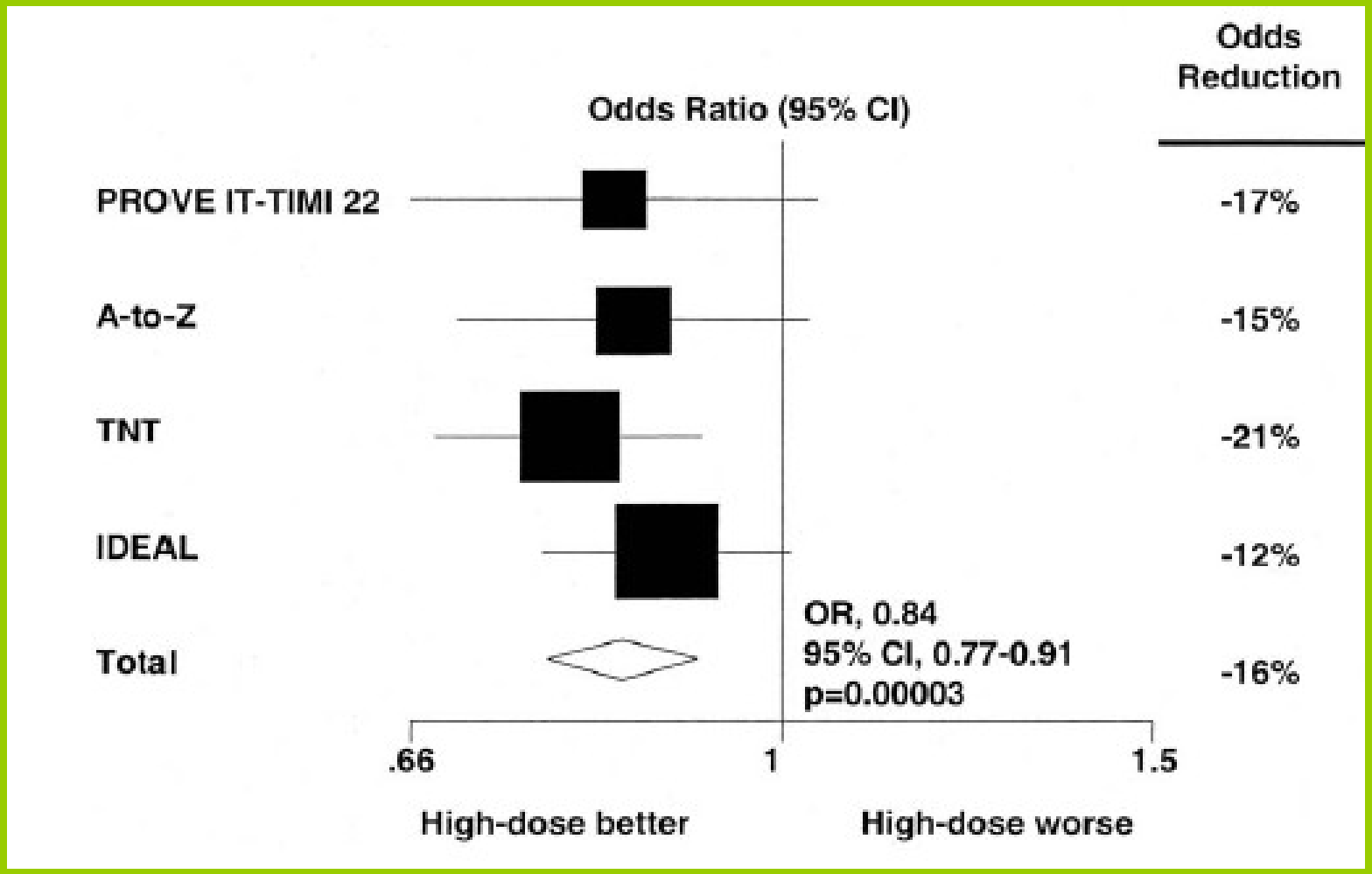
C-LDL % mg/dL	CV ↓
148	
↓	
109	20%
↓	↓
70	40%



Cholesterol Treatment Trialists' (CTT); Lancet 2005, 2010

El descenso intensivo del colesterol con altas dosis de estatinas proporciona un beneficio significativo sobre el tratamiento estándar en la prevención de eventos CV

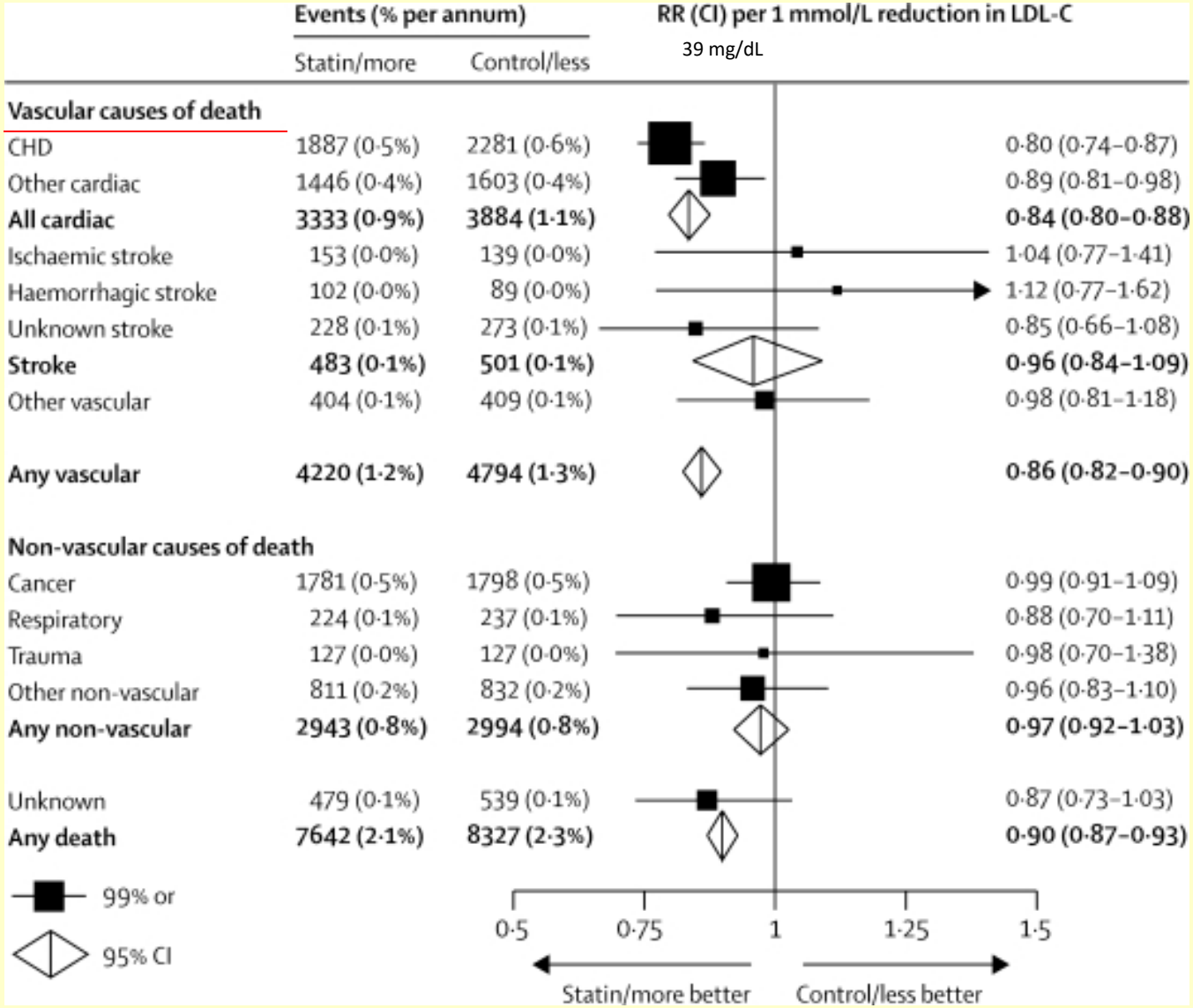
Un meta-análisis de 27.548 pacientes en 4 estudios clinicos



Canon CP et al; J Am Coll Cardiol 2006;48:438–45

Eficacia del descenso intensivo del C-LDL
Un meta-analisis de 170.000 participantes en 26 estudios clinicos aleatorizados

- **El tratamiento intensivo con estatinas produjo una reduccion significativa del 15% en los eventos CV mayores**



Cholesterol Treatment Trialists' (CTT); 376:. 2010. 1670–1681.

Cardiovascular Benefit of Magnitude of Low-Density Lipoprotein Cholesterol Reduction

Patients of all ages, including those 80 years or older , benefited the most from large reduction in LDL-c

Proportions of Subjects Who Had an Acute Myocardial Infarction or Underwent Revascularization, by LDL-C Reduction Category and Quartile of Age

Category of LDL-C Reduction	<61.1 y	61.1 to 69.3 y	69.3 to 75.3 y	≥75.3 y
Reference: <10 mg/dL, n (%)	489 (35.9)	403 (34.1)	340 (29.1)	283 (23.2)
Small: 10–40 mg/dL, n (%)	399 (27.7)	341 (22.2)	334 (20.4)	260 (15.7)
Moderate: 40–70 mg/dL, n (%)	267 (20.0)	240 (17.0)	211 (15.8)	189 (13.5)
Large: ≥70 mg/dL, n (%)	173 (19.7)	157 (16.8)	104 (12.4)	78 (10.0)

Circulation. 2009;120:1491-1497.

Necesidad de usar estatinas potentes para alcanzar objetivos terapeuticos en pacientes de alto/muy alto riesgo CV

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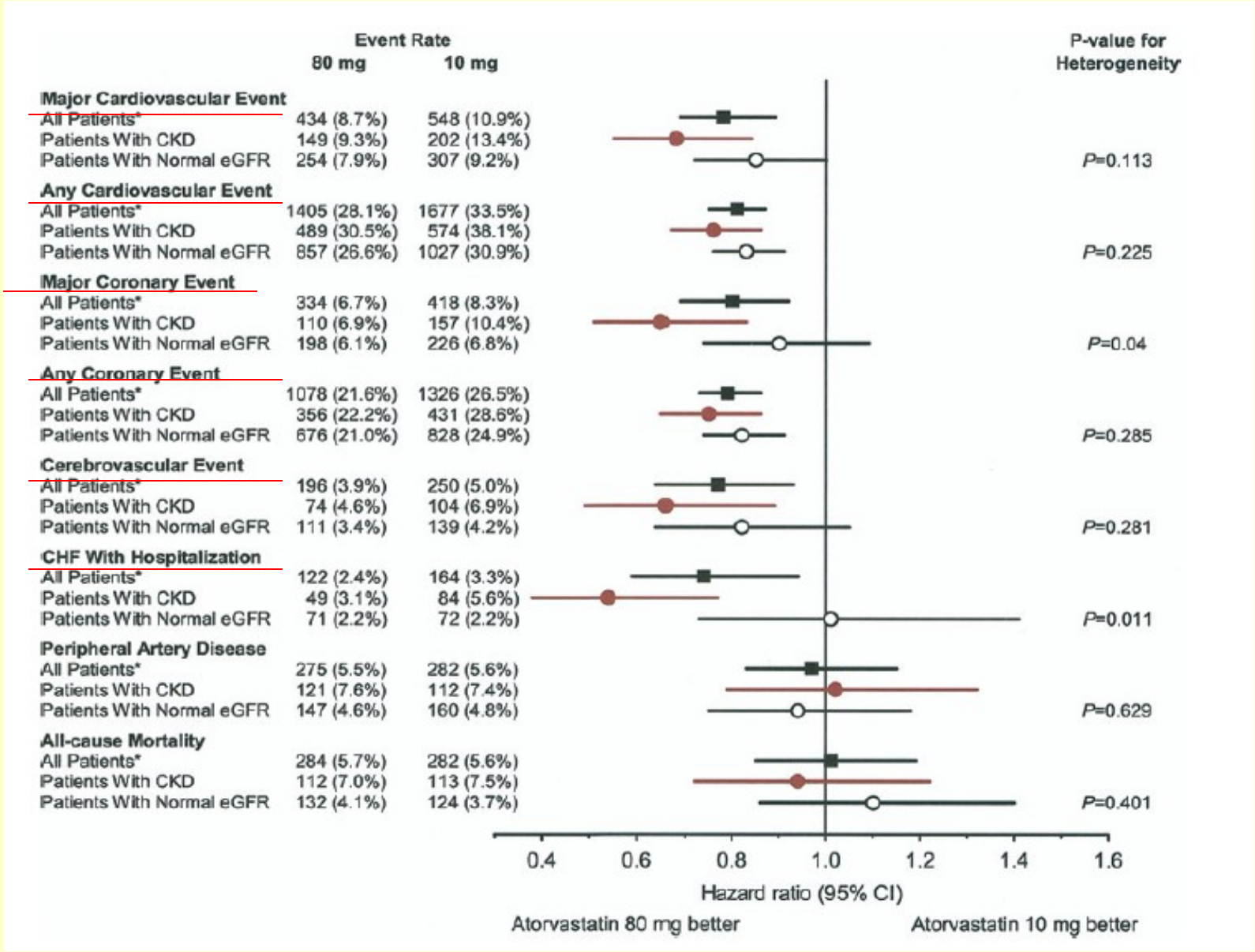
Post-hoc Analyses of CKD Patients (stages 2-3) in Major Statin Trials

Trial	Lipid-lowering Agent	Findings
CARE	Pravastatin	• Both statin and fibrate treatment result in reductions of LDL-C or triglyceride levels or both • Both statin and fibrate treatment reduce the relative risk of CHD and overall CVD morbidity to the same extent as in patients with normal renal function
HPS	Simvastatin	
VA-HIT	Gemfibrozil	
4S	Simvastatin	
AFCAPS/TexCAPS	Lovastatin	
TNT	Atorvastatin	

Adapted from Attman PO, *et al: Curr Opin Lipidol* 2009; 20(4):293-9.

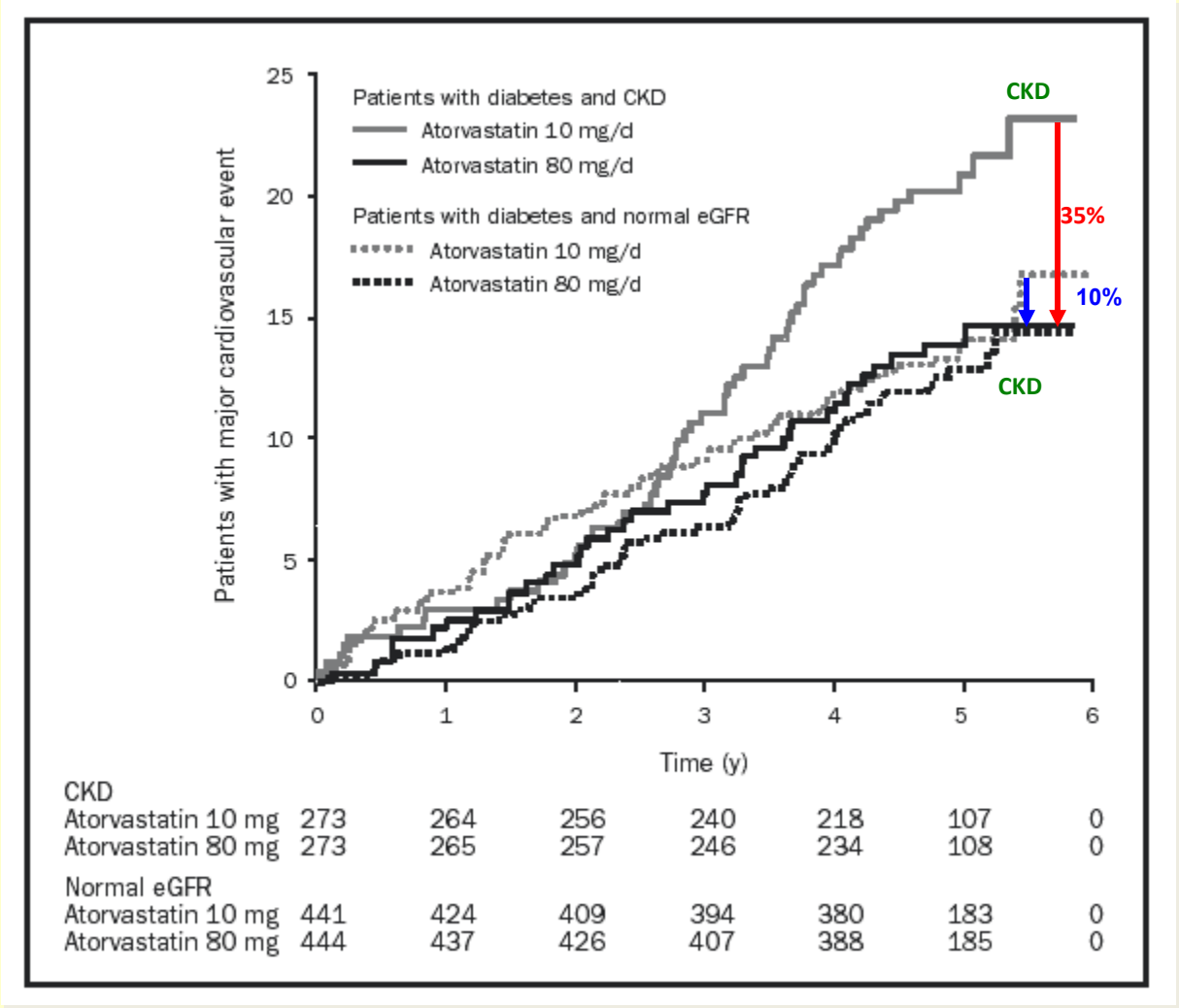
Aggressive lipid lowering was both safe and effective in reducing the excess of CV events in a high-risk population with CKD and CHD.

The TNT (Treating to New Target) Study .3,107 CKD vs 9,656 non CKD whith CHD



Shepherd et al J Am Coll Cardiol2008;51:1448–54

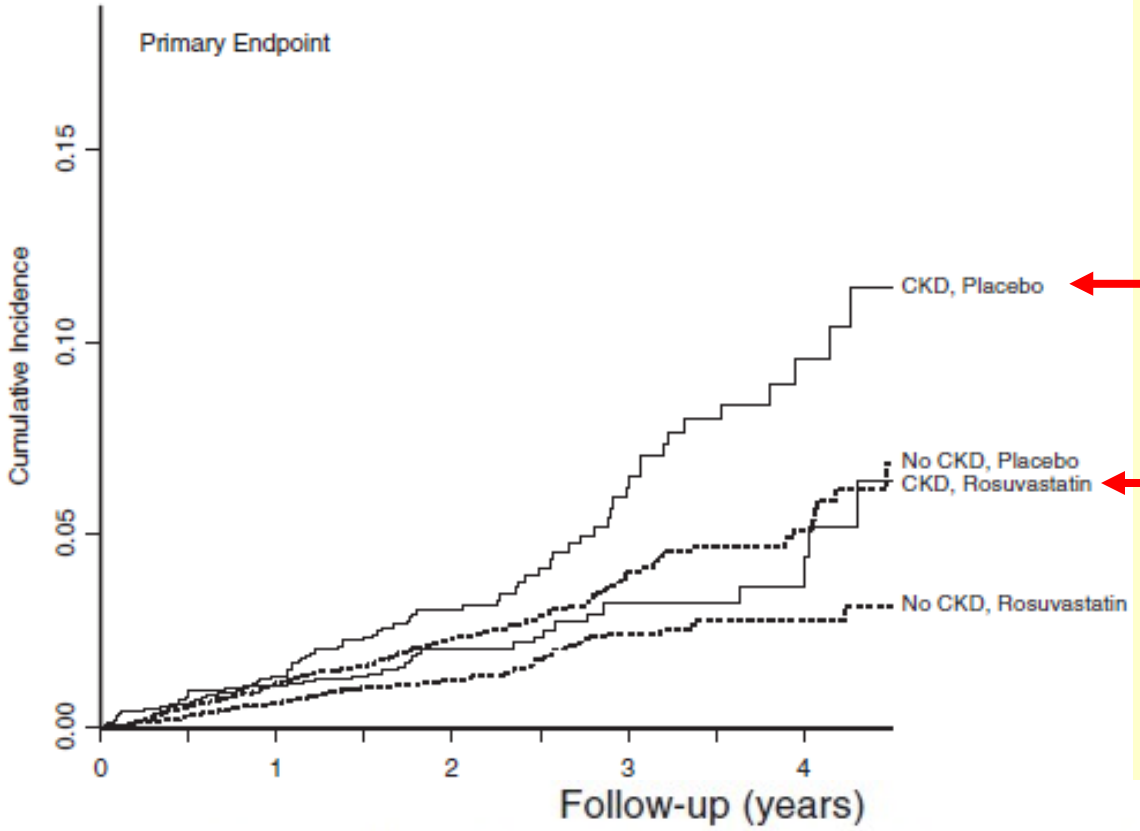
Los pacientes con diabetes y CKD en tratamiento intensivo con estatinas presentaron una mayor reducción del riesgo CV



Shepherd J et al Mayo Clin Proc.2008;83:870-879

Rosuvastatin reduces first cardiovascular events and all-cause mortality in subjects with moderate CKD and elevated C-reactive protein

A Secondary Analysis From the JUPITER



No. at Risk

CKD	Rosuvastatin	1,638	1,574	1,538	1,281	871	550	352	247	129	39
	Placebo	1,629	1,557	1,510	1,234	838	516	345	243	131	40
No CKD	Rosuvastatin	7,259	7,054	6,871	5,256	3,020	1,407	1,000	736	409	118
	Placebo	7,269	7,061	6,840	5,272	3,033	1,447	988	712	400	134

Ridker PM et al ,J Am Coll Cardiol 2010;55:1266–73

Estatinas en pacientes en hemodialisis

Estudio 4D, atorvastatina 20 mg vs placebo en 1.255 pacientes en hemodiálisis con diabetes tipo 2.

N. Engl J Med 2005:21:238-248

Estudio AURORA, rosuvastatina 10mg/d vs placebo en 2.776 pacientes en hemodiálisis

Reducción no significativa de los eventos CV

N. Engl J Med 2009:360:1395-1407

HMG CoA reductase inhibitors (statins) for people with chronic kidney disease not requiring dialysis Cochrane Database Syst Rev. 2009 Apr 15;(2):CD007784.

Twenty six studies (25,017 participants) comparing statins with placebo were identified.

- Statins significantly reduced the risk of all-cause and cardiovascular mortality in CKD patients who are not receiving renal replacement therapy
- They do not impact on the decline in renal function as measured by creatinine clearance, but may reduce protein excretion in urine
- Statins appear to be safe in this population

HMG CoA reductase inhibitors (statins) for dialysis patients.

Cochrane Database Syst Rev. 2009 Jul 8;(3):CD004289.

- Fourteen studies (2086 patients) compared statins versus placebo or other lipid lowering agents
- Statins decreased cholesterol levels in dialysis patients similar to that of the general population.
- With the exception of one study, studies were of short duration and therefore the efficacy of statins in decreasing the mortality rate is still unclear.
- Statins appear to be safe in this high-risk population
- Ongoing studies should provide more insight about the efficacy of statins in reducing mortality rates in dialysis patients.

Estatinas en pacientes en hemodialisis /CKD

Estudio SHARP (Study of Heart And Renal Protection)
Simvastatina 20mg + ezetimibe 10mg diarios vs placebo
9.270 pacientes con CKD (3.023 en diálisis y 6.947 no) sin historia conocida de infarto de miocardio o revascularización seguidos durante 4.9 años
17% reducción en eventos ateroscleróticos mayores
Lancet 2011:377:2181-2192

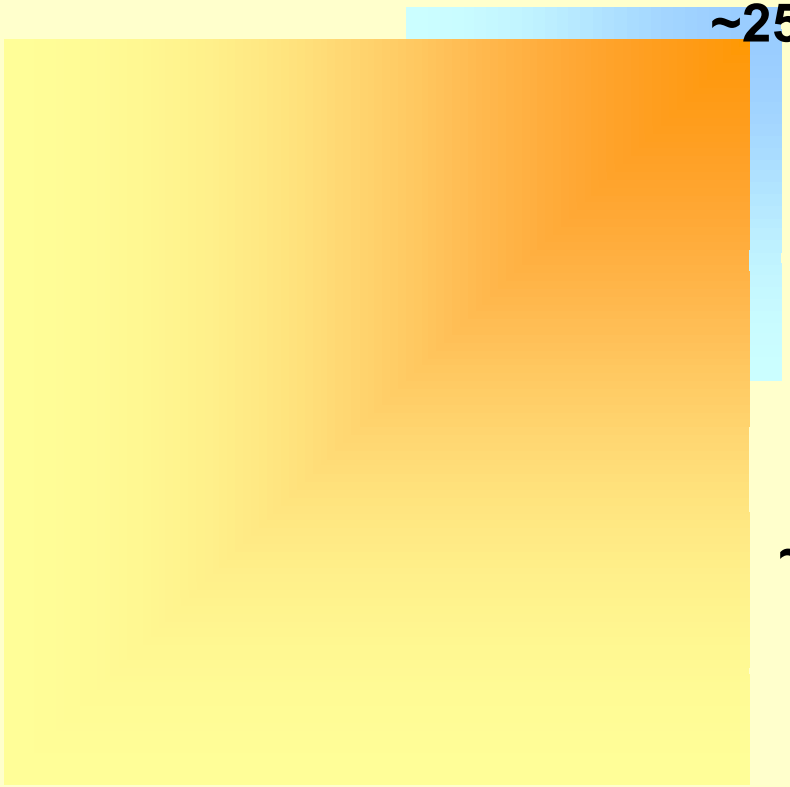
Es posible que solo puedan beneficiarse del uso de estatinas el subgrupo de pacientes con mayor carga aterosclerótica

La FDA recomendó el uso de simvastatina y ezetimibe para pacientes en estadios iniciales de CKD pero no para los que estaban en diálisis. (Nov. 2011)

Meses más tarde, revocó esa indicación. (Abril 2012)

Causes of CV Mortality in CKD

The pathobiology of CV disease is dominated by vascular calcification, cardiac hypertrophy and arterial stiffening.



~25%: Directly attributable to MI (potentially avoidable with cholesterol reduction)

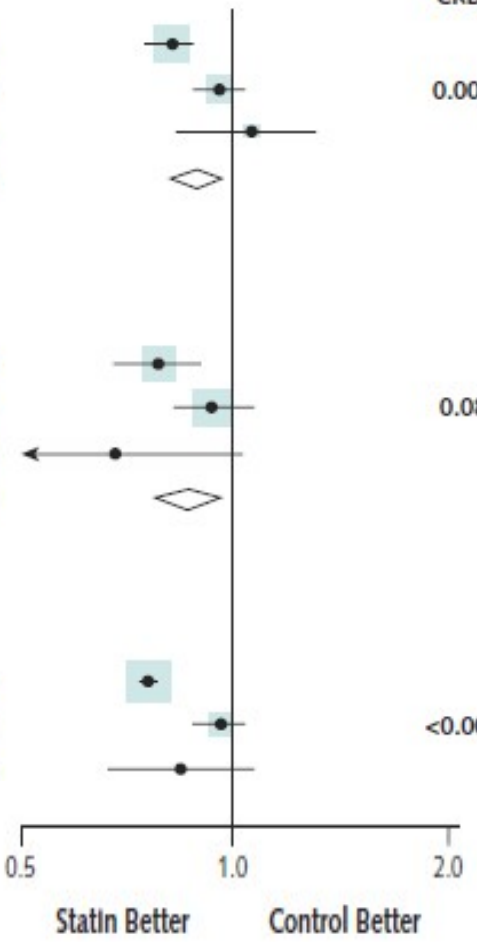
~75%: Other causes (cardiac arrest, arrhythmia, heart failure)
Not as dependent on cholesterol reduction

Adapted from Baigent C, *et al: Kidney Int Suppl* 2003; (84):S207-10.

Benefits of Statin Therapy for Persons With Chronic Kidney Disease
A Systematic Review and Meta-analysis

Eighty trials comprising 51,099 participants compared statin with placebo or no treatment

Category	Studies or Subsets, *n**	Statin, *n/N*	Control, *n/N*	Random-Effects Relative Risk (95% CI)	Random-Effects Relative Risk (95% CI)	*P* Value for Subgroup Difference (Stage of CKD)	Variance Explained by Stage of Kidney Disease, %
All-cause mortality							
CKD, not receiving dialysis	11	1005/14 063	1281/14 213	0.81 (0.74 to 0.88)			
Dialysis	13	938/2352	988/2353	0.96 (0.88 to 1.04)		0.009	89
Transplant	6	152/1382	144/1378	1.05 (0.84 to 1.31)			
All trials	32	3280/22 517	3575/22 637	0.89 (0.82 to 0.97)			
Heterogeneity across all trials: chi-square = 43.412; $P = 0.07$; $I^2 = 29\%$							
Cardiovascular mortality							
CKD, not receiving dialysis	8	439/9480	574/9579	0.78 (0.68 to 0.89)			
Dialysis	13	446/2311	1512/2312	0.94 (0.82 to 1.07)		0.08	100
Transplant	4	38/1161	56/1161	0.68 (0.45 to 1.02)			
All trials	27	1307/17 672	1512/17 745	0.86 (0.78 to 0.95)			
Heterogeneity across all trials: chi-square = 18.33; $P = 0.86$; $I^2 = 0\%$							
Major cardiovascular events							
CKD, not receiving dialysis	14	2525/17 912	3361/18 121	0.76 (0.73 to 0.80)			
Dialysis	4	852/3557	899/3527	0.95 (0.87 to 1.03)		<0.001	99
Transplant	1	112/1050	134/1052	0.84 (0.66 to 1.06)			
All trials	20	3495/22 589	4404/22 773	0.78 (0.72 to 0.8			
Heterogeneity across all trials: chi-square = 41.28; $P = 0.002$; $I^2 = 54\%$							

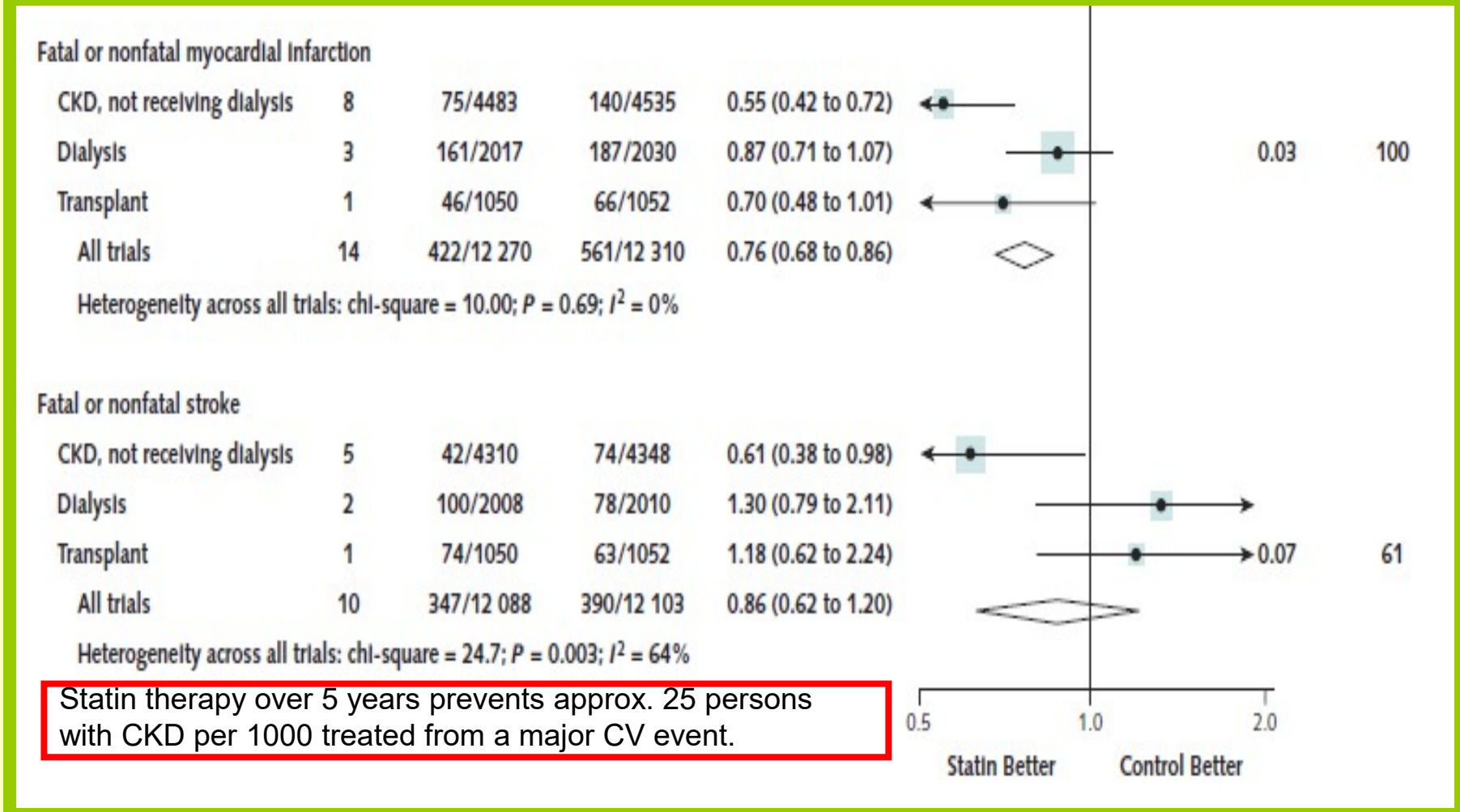


Palmer et al. *Ann Intern Med.* 2012;157:263-275.

Benefits of Statin Therapy for Persons With Chronic Kidney Disease

A Systematic Review and Meta-analysis

Eighty trials comprising 51 099 participants compared statin with placebo or no treatment



Statin therapy over 5 years prevents approx. 25 persons with CKD per 1000 treated from a major CV event.

Palmer et al. *Ann Intern Med.* 2012;157:263-275.

Patients with CKD are at very high CV risk

LDL-c and statins in patients with moderate to severe CKD (stages 2–4,GFR 89-15 mL/min/1.73 m2)

Recommendations	Class[a]	Level[b]
CKD is acknowledged as a CAD risk equivalent; in these patients LDL-C reduction is recommended as the primary target of therapy.	I	A
LDL-C lowering reduces CVD risk in CKD subjects and should be considered.	IIa	B
Statins should be considered to slow the rate of kidney function loss modestly and thus protect against the development of ESRD requiring dialysis.	IIa	C
Since statins have a beneficial effect on pathological proteinuria (>300 mg/day) they should be considered in patients with stage 2–4 CKD.	IIa	B
In moderate to severe CKD statins as monotherapy or in combination with other drugs should be considered to achieve LDL-C <1.8 mmol/L (less than ~70 mg/dL).	IIa	C

General agreement that a given treatment is useful

Data derived from multiple randomized clinical trial or metaanalysis

Evidence in favor of efficacy

Data from a single randomized CT

Small studies or retrospective

ESC/EAS guidelines for the management od dyslipidemia

European Heart Journal 2011. 32, 1769–1818

Recommendations for treatment of dyslipidemia in transplant patients

Recommendations	Class[a]	Level[b]	Ref[c]
Global CV risk management strategies are a priority 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	197
In patients who are intolerant of statins or those with significant dyslipidaemia and high residual risk despite a maximally tolerated dose of statin, alternative or additional therapy may be considered: ezetimibe for those where high LDL-C is the principal abnormality; fibrates or nicotinic acid for those where hypertriglyceridaemia and/or low HDL-C is the principal abnormality.	IIb	C	-

European Heart Journal 2011. 32, 1769–1818

The second objective in the management of mixed dislipidemia is the treatment of hipertrigliceridemia

Recommendations	Class[a]	Level[b]
In particular high risk patients (see above), lowering of HTG by using the following drugs:		
is recommended: fibrates	I	B
should be considered: nicotinic acid	IIa	B
nicotinic acid + laropiprant	IIa	C
n-3 fatty acids	IIa	B
statin + nicotinic acid[d]	IIa	A
statin + fibrate[d]	IIa	C
may be considered: combinations with *n*-3 fatty acids[e]	IIb	B

European Heart Journal 2011. 32, 1769–1818

Recommendations regarding other diseases with increased risk for cardiovascular disease

Recommendations	Class[a]	Level[b]	GRADE	Ref[c]
In patients with chronic kidney disease, risk factors have to be attended to in the same way as for very high-risk persons.	I	C	Strong	165, 166
All persons with obstructive sleep apnoea should undergo medical assessment, including risk stratification and risk management.	IIa	A	Strong	167, 168
All men with erectile dysfunction should undergo medical assessment, including risk stratification and risk management.	IIa	B	Strong	169

[a]Class of recommendation.
[b]Level of evidence.
[c]References.

European Guidelines on cardiovascular disease prevention in clinical practice (version 2012)

European Heart Journal 2012. 33, 1635–1701

KDIGO recommendations on lipids in CKD . August 2012

Assessment of lipid status in adults with CKD

- We recommend that adults with CKD should be evaluated with a lipid profile (TC, LDL-C, HDL-C, TG) when CKD is first diagnosed. (*1C*)
- Follow-up measurement of lipid levels is not required unless the results would alter treatment. (*2C*)

BACKGROUND

- *LDL-C is not suitable for identifying CKD patients who should receive pharmacological cholesterol-lowering treatment*

Associations between LDL-C and coronary artery disease in CKD 5D

- Dialysis patients with the highest and lowest levels of LDL-C and TC are at the highest risk of adverse outcomes such as all-cause and cardiovascular mortality

Associations between LDL-C and coronary artery disease in CKD 1-4

-As eGFR declines, the magnitude of the excess risk associated with increased LDL-C decreases.

KDIGO recommendations on lipids in CKD . August 2012

Pharmacological cholesterol lowering in adults

- In adults aged ≥40 years with CKD 3-5 ND, we recommend treatment with a statin or statin/ezetimibe combination regardless of LDL-C levels. (*1A*)
- In adults aged ≥40 years with CKD 1-2 we recommend treatment with a statin regardless of LDL-C levels. (*1B*)
- In adult kidney transplant recipients we recommend treatment with a statin regardless of LDL-C levels. (*1B*)
- In adults aged 18-40 years with CKD stage 1-5 ND, we suggest statin treatment in people with one or more of the following (*2A*):
  - 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%

KDIGO recommendations on lipids in CKD . August 2012

Pharmacological cholesterol lowering in adults

- **In adults with CKD stage 5D, we suggest that statins or statin/ezetimibe combination not be initiated, regardless of LDL-C levels. (*2A*)**
- **We suggest that statins or statin/ezetimibe combination be continued in patients already receiving them at the time of dialysis initiation, regardless of LDL-C levels. (*2C*)**

KDIGO recommendations on lipids in CKD . August 2012
Pharmacological triglyceride lowering in adults

- **We suggest that therapeutic lifestyle changes be recommended to adults with CKD 1-5 (including those on renal replacement therapy) and hypertriglyceridemia. (*2D*)**

Non-pharmacological treatment of high triglycerides

-If high fastinglevels of serum triglycerides (500 mg/dl) , **therapeutic lifestyle changes:**

Pharmacological treatment of high triglycerides:

-**Fibric acid** derivatives could be considered for the rare patients with CKD and markedly elevated fasting levels of serum triglyceride (>1000 mg/dl)(dose-adjusted for kidney function).

Concomitant therapy with both a fibric acid derivative and a statin is not recommended in patients with CKD due to the potential for toxicity

-**Nicotinic acid** has not been well studied in advanced CKD and therefore is not recommended for treatment of severe hypertriglyceridemia, given the risk of toxicity (especially flushing and hyperglycemia).

Outline

- CV mortality in CKD and transplantation
- Lipids and management of statins in CKD patients
- Evidence of beneficial effects of statins in general population
- Evidence of beneficial effects of statins in CKD
  - Post-hoc analysis of CKD patients included in major trials
  - Systematic reviews and meta-analysis (2009-2012)
  - ESC/EAS Guidelines for the management of dyslipidemia (2011)
  - European Guidelines on cardiovascular disease prevention (2012)
  - KDIGO on lipids in CKD (internal use, August 2012)
- Evidence of beneficial effects of statins in renal transplantation

Management of dyslipidemia in transplant recipients

Dyslipidemia	Goal	Initiate	Increase	Alternative
TG>500 mg/dL with LDL <100 mg/dL	TG<500 mg/dL	TLC	TLC + niacin	Fibrate or statin
LDL 100–129 mg/dL	LDL< 100 mg/dL	TLC	TLC + low-dose statin	Ezetimibe or niacin
LDL>130 mg/dL	LDL<100 mg/dL	TLC + low-dose statin (7,18)	TLC + 50% max dose statin	Ezetimibe or niacin
TG>200 mg/dL and non-HDL>130 mg/dL	Non-HDL <130 mg/dL	TLC + low-dose statin	TLC + 50% max dose statin	Ezetimibe or niacin

TG = triglycerides; LDL = low-density lipoprotein; HDL = high-density lipoprotein; therapeutic lifestyle changes (TLC) Non-HDL: TC minus HDL (surrogate for increased remnant lipoproteins in the setting of high TG); max. = maximum. To convert mg/dL to mmol/L, multiply triglycerides by 0.001129, and cholesterol by 0.02586.

KDIGO; Kasiske et al, *Am J Transplant* 2004; 4:13-53

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

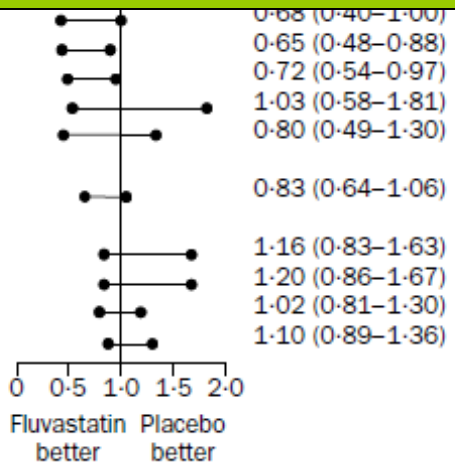
The ALERT Trial

Primary composite endpoints

Although cardiac deaths and non-fatal MI seemed to be reduced, fluvastatin did not generally reduce rates of coronary intervention procedures or mortality.

Overall effects of fluvastatin were similar to those of statins in other populations.

Definite non-fatal MI	46 (4·4)	66 (6·3)	0·050	0·68 (0·48–1·00)
Cardiac death or definite non-fatal MI (35% ↓)	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)



Holdaas et al. Lancet 2003; 361: 2024–31.

THE COCHRANE LIBRARY

Independent high-quality evidence for health care decision making

from The Cochrane Collaboration

HMG CoA reductase inhibitors (statins) for kidney transplant recipients

16 studies enrolling 3229 patients

Statins significantly reduced hyperlipidaemia and tended to reduce cardiovascular events in kidney transplant recipients, but no effect has yet been demonstrated for mortality outcomes.

Most of the data was derived from one large long-term study.

Considering the significant impact of statins on all-cause and cardiovascular mortality in the general and predialysis populations, more studies are needed in kidney transplant patients.

Cochrane Database Syst Rev. 2009, 15 Apr 15;(2)

Post Hoc analysis of the ALERT Trial

Metabolic syndrome and cardiovascular risk in renal transplant recipients: effects of statin treatment. Soveri I, et al. Clin Transplant. 2009 ;23:914-20.

Renal transplant recipients with MS have increased risk for CVD. Those patients are an easily identifiable group of patients who benefit from statin treatment.

In-Depth Reviews

Recent papers on CV disease , statins and kidney transplantation

-Prevention of cardiovascular disease in adult recipients of kidney transplants. Jardine AG, Lancet. 2011 ;378:1419-27.

-The efficacy and safety of statins in CKD, dialysis, and transplant patients. Olyaei et al .Clin J Am Soc Nephrol 6: 664–678, 2011

-Dyslipidemia and its therapeutic challenges in renal transplantation. Riella et al. American Journal of Transplantation 2012; 12: 1975–1982

Resúmen

- Las estatinas disminuyen los eventos cardiovasculares y la mortalidad en pacientes en los estadios iniciales de la enfermedad renal crónica.

  Evidencia de calidad moderada-alta

- La estatinas tienen poco o ningún efecto sobre la mortalidad total, mortalidad cardiovascular y eventos cardiovasculares mayores en pacientes en diálisis.

  Evidencia de calidad moderada-alta

- La evidencia para la administración de estatinas en los transplantados renales es limitada e incierta.

- Las estatinas tienen poco o ningún efecto sobre la incidencia de cáncer, mialgias, aumento de la CPK y aumento de transaminasas.

  Evidencia de baja calidad