Publicaciones de FRENA

1- *Clinical outcome in patients with peripheral artery disease. Results from a prospective registry (FRENA)*. **Eur J Intern Med 2008; 19: 192-197.**

2- *Secondary prevention of arterial disease in very elderly people. Results from a Prospective Registry (FRENA).* **Angiology 2008; 59: 427-434.**

3- *Clinical Outcome in Patients With Peripheral Artery Disease and Renal Artery Stenosis.* **Angiology 2010; 61: 58-65.**

4- *Body mass index and outcome in patients with coronary, cerebrovascular or peripheral artery disease: findings from the FRENA registry*. **Eur J Cardiovasc Prev Rehabil. 2009;16: 457-463.**

5- *Gender and Outcome in Patients with Coronary, Cerebrovascular or Peripheral Artery Disease. Findings from the FRENA Registry*. **Open Atheroscl Thromb J. 2009: 45-50.**

6- *Major bleeding events in stable outpatients with coronary, cerebrovascular or peripheral artery disease: findings from the FRENA registry*. **J Thromb Haemost. 2009: 1414-1416.**

7- *Differences in cardiovascular mortality in smokers, past-smokers and non-smoker. Findings from the FRENA registry*. **Eur J Intern Med. 2009: 522-526.**

8- *Treatment inertia in secondary prevention of cardiovascular disease. FRENA registry*. **Med Clin 2010; 134: 57-63.**

¿Se puede asociar clopidogrel con omeprazol?

- **Se pierde la eficacia del clopidogrel**

- **Se pierde la eficacia del omeprazol**

- **No interaccionan**

TABLA 2. Estudios clínicos sobre la asociación de clopidogrel e IBP

Estudios	Pacientes	Comentarios	Resultados
Pezalla, et al. 2008[9]	4.800 pacientes <65 años con IAM reciente	Bases de datos de farmacia	Mayor incidencia de reinfarto, proporcional a la duración del tratamiento con IBP
Ho, et al. 2009[11]	8.205 pacientes con IAM o angina inestable recientes	Cohorte retrospectiva	Mayor incidencia de muerte por cualquier causa y de reingreso por síndrome coronario agudo
Juurlink, et al. 2009[10]	4.800 pacientes >65 años con IAM reciente	Estudio de casos y controles	Mayor incidencia de reinfarto
Simon et al. 2009	2.208 pacientes con IAM reciente	Registro prospectivo	Ninguna diferencia
O'Donoghue et al. 2009	13.608 pacientes con síndrome coronario agudo	Subgrupo de un ensayo clínico aleatorizado	Ninguna diferencia

IBP: inhibidores de la bomba de protones; IAM: infarto agudo de miocardio.

¿Se puede asociar clopidogrel con omeprazol?

- **En Abril de 2009 había 2.788 pacientes en FRENA, procedentes de 14 hospitales.**

- **1230 (44%) tomaban clopidogrel.**

- **527 (43%) tomaban clopidogrel e IBPs: omeprazol 452, pantoprazol 52, lansoprazol 23.**

¿Se puede asociar clopidogrel con omeprazol?

- En Abril de 2009 había 2.788 pacientes en FRENA, procedentes de 14 hospitales.

- 1230 (44%) tomaban clopidogrel.

- 527 (43%) tomaban clopidogrel e IBPs: omeprazol 452, pantoprazol 52, lansoprazol 23.

- Tras 15 meses (rango, 2-72), 131 (11%) tuvieron 139 eventos:

- IAM 44,

- AVC 40,

- isquemia crítica en EE.II. 55 (17 amputaciones).

- De ellos, 17 (13%) murieron en 15 días (IAM 4, AVC 7, isquemia crítica 6).

Diferencias entre pacientes

	IBPs	No IBPs	p
Pacientes, N	*519*	*703*	
Edad (años±SD)	68±11	64±12	<0.001
Cáncer	7.3%	3.7%	0.005
ClCr. (mL/min)	71±31	78±30	<0.001
Colesterol total (mg/dL)	172±38	180±37	0.001
LDL-colesterol (mg/dL)	101±31	107±31	<0.001
Anticoagulantes	10%	7.1%	0.069
Diuréticos	41%	31%	<0.001
Calcio-antagonistas	32%	23%	0.001
Estatinas	85%	79%	0.017
Insulina	20%	14%	0.006

seguimiento medio: 14 meses

	PPIs	No PPIs	RR (95% CI)	p
CAD patients, N	**247**	**348**		
Myocardial infarction	6.8 (4.3-10)	2.0 (0.9-3.8)	3.4 (1.5-8.2)	0.002
Ischemic stroke	0.6 (0.1-2.0)	0.5 (0.08-1.6)	1.3 (0.1-12)	0.827
Critical limb ischemia	0.9 (0.2-2.5)	0.2 (0.01-1.2)	3.8 (0.4-98)	0.269
Overall death	4.7 (2.7-7.5)	1.5 (0.6-3.1)	3.2 (1.2-8.8)	0.014
CVD patients, N	**142**	**187**		
Myocardial infarction	1.7 (0.4-4.7)	0	-	0.079
Ischemic stroke	8.5 (4.9-14)	5.9 (3.3-9.8)	1.5 (0.7-3.3)	0.294
Critical limb ischemia	3.5 (1.4-7.3)	1.8 (0.6-4.3)	2.0 (0.6-8.1)	0.288
Overall death	6.3 (3.3-11)	3.9 (1.9-7.2)	1.6 (0.7-4.0)	0.298
PAD patients, N	**130**	**168**		
Myocardial infarction	3.2 (1.2-7.1)	3.8 (1.7-7.6)	0.9 (0.3-2.8)	0.817
Ischemic stroke	5.2 (2.4-9.8)	0.5 (0.03-2.6)	10 (1.6-225)	0.009
Critical limb ischemia	15 (9.5-22)	11 (6.6-16)	1.2 (0.6-2.2)	0.640
Overall death	8.2 (4.5-14)	4.2 (2.0-8.0)	1.9 (0.8-4.9)	0.142
All patients, N	**519**	**703**		
Myocardial infarction	4.6 (3.1-6.5)	1.8 (1.1-2.9)	2.5 (1.3-4.8)	0.003
Acute ischemic stroke	3.8 (2.5-5.6)	2.0 (1.2-3.1)	1.9 (1.03-3.7)	0.039
Critical limb ischemia	4.8 (3.3-6.8)	3.0 (2.0-4.3)	1.6 (0.95-2.8)	0.077
Overall death	6.0 (4.3-8.1)	2.8 (1.8-4.1)	2.2 (1.3-3.7)	0.003

seguimiento medio: 14 meses

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CAD patients, N	*247*	*348*		
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Critical limb ischemia	4.8 (3.3-6.8)	3.0 (2.0-4.3)	1.6 (0.95-2.8)	0.077
Overall death	6.0 (4.3-8.1)	2.8 (1.8-4.1)	2.2 (1.3-3.7)	0.003

*eventos por 100 pacientes y año

multivariante	Hazard ratio (95% CI)	p
Age >70 years	1.6 (1.1-2.4)	0.016
Diabetes mellitus	1.8 (1.3-2.7)	0.029
Coronary artery disease	1.0 (Ref.)	-
Cerebrovascular disease	2.0 (1.2-3.3)	0.008
Peripheral artery disease	3.3 (2.0-5.3)	<0.001
Clopidogrel and PPIs	1.8 (1.2-2.6)	0.003
Antiacoagulants	2.7 (1.7-4.5)	<0.002
Diuretics	1.5 (1.0-2.2)	0.040
Clopidogrel and PPIs	1.8 (1.3-2.7)	0.002
Propensity score	0.1 (0.03-0.7)	0.014

Los pacientes diabéticos con hemoglobina glicada <7.0% tienen:

- menos eventos isquémicos
- igual eventos isquémicos
- más eventos isquémicos

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Articles

Effect of intensive control of glucose on cardiovascular outcomes and death in patients with diabetes mellitus: a meta-analysis of randomised controlled trials

Dr Kausik K Ray MD[a, b], ✉, Sreenivasa Rao Kondapally Seshasai MD[a, ‡], Shanelle Wijesuriya BA[a, ‡], Rupa Sivakumaran BA[a, ‡], Sarah Nethercott BA[a, ‡], David Preiss MRCP[c], Sebhat Erqou MD[a] and Prof Naveed Sattar FRCPath[c]

33.040 pacientes

Table 2. Event rates for cardiovascular outcomes of intensive glucose-lowering versus standard treatment[§]

	Non-fatal myocardial infarction		Coronary heart disease		Stroke		All-cause mortality	
	Intensive treatment	Standard treatment	Intensive treatment	Standard treatment	Intensive treatment	Standard treatment	Intensive treatment	Standard treatment
UKPDS[47]	7·2	9·1	12·8	16·7	4·5	5·0	16·2	19·5
PROactive[18-20*†]	15·9	19·0	21·9	26·7	11·5	14·1	23·6	24·6
ADVANCE[5]	5·5	5·6	11·1	12·1	8·5	8·8	17·9	19·1
VADT[21,22]	12·8	15·5	15·4	17·9	5·6	7·2	20·4	18·9
ACCORD[8]	10·4	13·1	11·4	13·8	4·2	4·0	14·3	11·3
Overall[‡]	10·0	12·3	14·3	17·2	6·8	7·7	18·3	18·6

Data are rates per 1000 person-years. [*] Non-fatal strokes only.

[†] Coronary heart disease includes cardiac mortality.

[‡] Calculated by pooling study specific rates with a random-effects model meta-analysis.

[§] Event rates were calculated with the total person-years in each study group, which was estimated from the average follow-up in each study.
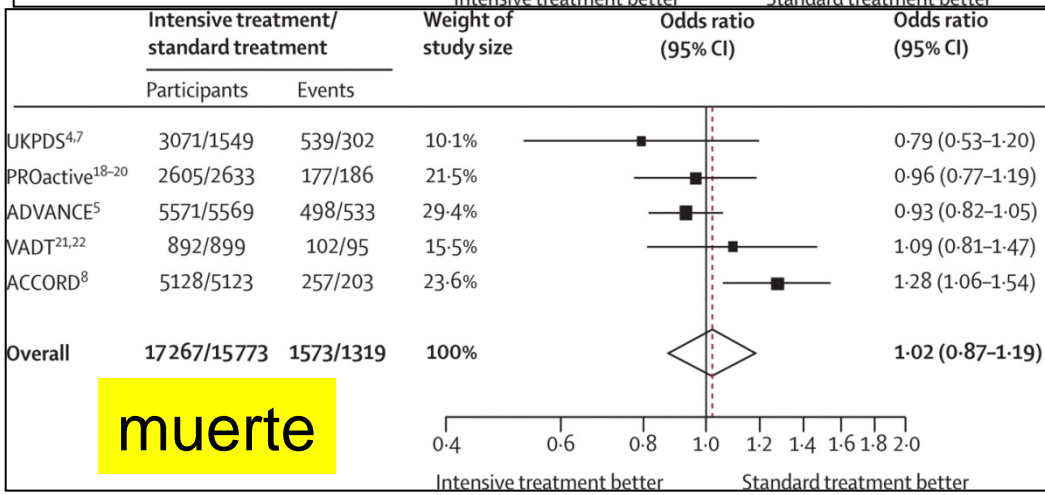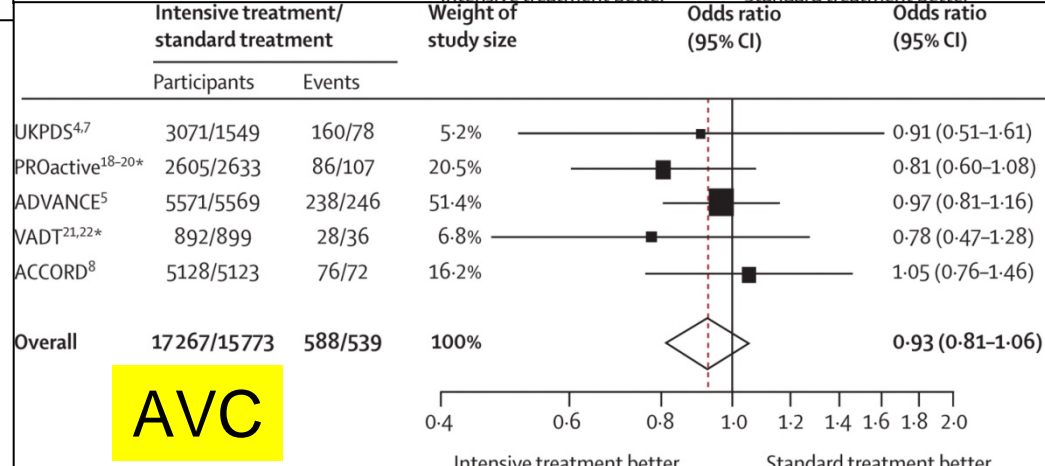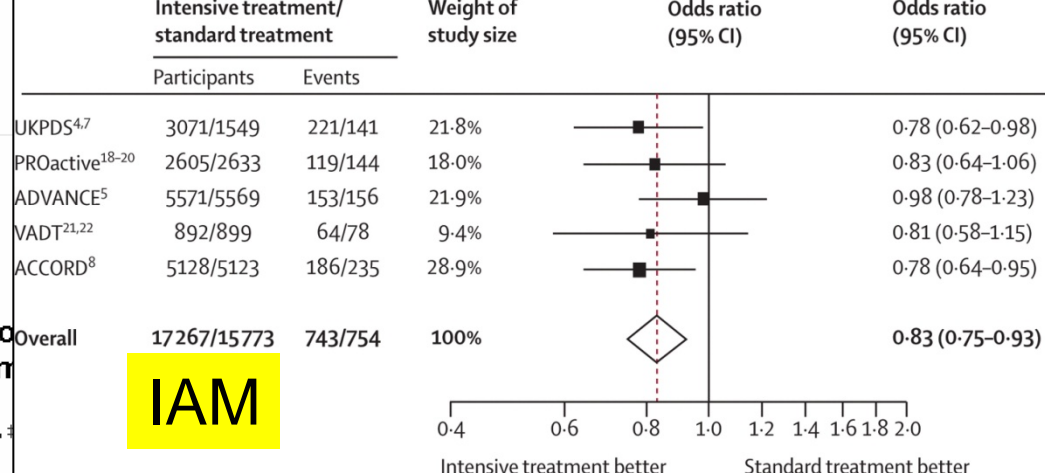
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Effect of intensive control of glucose on cardiovascular o
patients with diabetes mellitus: a meta-analysis of random

Dr Kausik K Ray MD[a, b], Sreenivasa Rao Kondapally Seshasai MD[a, ‡], Shanelle Wijesuriya BA[a, ‡]
Nethercott BA[a, ‡], David Preiss MRCP[c], Sebhat Erqou MD[a] and Prof Naveed Sattar FRCPath[c]

	Intensive treatment/ standard treatment		Weight of study size	Odds ratio (95% CI)	Odds ratio (95% CI)
	Participants	Events			
UKPDS[4,7]	3071/1549	221/141	21·8%		0·78 (0·62–0·98)
PROactive[18–20]	2605/2633	119/144	18·0%		0·83 (0·64–1·06)
ADVANCE[5]	5571/5569	153/156	21·9%		0·98 (0·78–1·23)
VADT[21,22]	892/899	64/78	9·4%		0·81 (0·58–1·15)
ACCORD[8]	5128/5123	186/235	28·9%		0·78 (0·64–0·95)
Overall	17 267/15 773	743/754	100%		0·83 (0·75–0·93)

IAM

0·4 0·6 0·8 1·0 1·2 1·4 1·6 1·8 2·0
Intensive treatment better   Standard treatment better

	Intensive treatment/ standard treatment		Weight of study size	Odds ratio (95% CI)	Odds ratio (95% CI)
	Participants	Events			
UKPDS[4,7]	3071/1549	160/78	5·2%		0·91 (0·51–1·61)
PROactive[18–20]*	2605/2633	86/107	20·5%		0·81 (0·60–1·08)
ADVANCE[5]	5571/5569	238/246	51·4%		0·97 (0·81–1·16)
VADT[21,22]*	892/899	28/36	6·8%		0·78 (0·47–1·28)
ACCORD[8]	5128/5123	76/72	16·2%		1·05 (0·76–1·46)
Overall	17 267/15 773	588/539	100%		0·93 (0·81–1·06)

AVC

0·4 0·6 0·8 1·0 1·2 1·4 1·6 1·8 2·0
Intensive treatment better   Standard treatment better

	Intensive treatment/ standard treatment		Weight of study size	Odds ratio (95% CI)	Odds ratio (95% CI)
	Participants	Events			
UKPDS[4,7]	3071/1549	539/302	10·1%		0·79 (0·53–1·20)
PROactive[18–20]	2605/2633	177/186	21·5%		0·96 (0·77–1·19)
ADVANCE[5]	5571/5569	498/533	29·4%		0·93 (0·82–1·05)
VADT[21,22]	892/899	102/95	15·5%		1·09 (0·81–1·47)
ACCORD[8]	5128/5123	257/203	23·6%		1·28 (1·06–1·54)
Overall	17 267/15 773	1573/1319	100%		1·02 (0·87–1·19)

muerte

0·4 0·6 0·8 1·0 1·2 1·4 1·6 1·8 2·0
Intensive treatment better   Standard treatment better

¿qué pacientes se benefician más de un buen control glucémico?

- los pacientes con cardiopatía isquémica
- los pacientes con isquemia cerebral
- los pacientes con arteriopatía periférica

974 pacientes

	HbA1c <7%	HbA1c >7%	p
Patients, N	*480*	*494*	
Mean age (years±SD)	69±9.5	67±9.5	0.016
Hypertension	82%	76%	0.023
Cerebrovascular disease	33%	25%	0.004
Peripheral artery disease	35%	41%	0.051
Mean SBP levels (mm Hg)	138±16	137±21	0.008
Total cholesterol (mg/dL)	172±34	181±40	<0.001
LDL-cholesterol (mg/dL)	100±28	104±32	0.016
Triglycerides (mg/dL)	137±78	165±126	<0.001
Glucose (mg/dL)	125±26	164±43	<0.001
Glycated haemoglobin (%)	6.2±0.6	8.1±1.0	<0.001
Beta-blockers	35%	42%	0.027
Insulin	21%	55%	<0.001
Oral antidiabetics	75%	68%	<0.001

	HbA1c levels < 7%	HbA1c levels > 7%	Rate ratio (95% CI)	p value
CAD patients, N	*152*	*168*		
Myocardial infarction	4.3 (2.2-7.8)	8.9 (5.3-14)	0.5 (0.2-1.1)	0.074
Acute ischemic stroke	0.4 (0.02-2.1)	2.5 (0.9-5.5)	0.2 (0.01-1.2)	0.086
Critical limb ischemia	0.4 (0.02-2.1)	2.5 (0.9-5.4)	0.2 (0.01-1.3)	0.090
Subsequent ischemic events	5.3 (2.9-8.9)	13 (8.9-19)	0.4 (0.2-0.8)	0.007
Overall death	2.1 (0.8-4.7)	4.9 (2.5-8.7)	0.4 (0.1-1.3)	0.131
CVD patients, N	*159*	*122*		
Myocardial infarction	1.0 (0.2-3.3)	2.1 (0.5-5.7)	0.5 (0.1-3.2)	0.445
Acute ischemic stroke	4.1 (1.9-7.8)	4.1 (1.7-8.5)	1.0 (0.3-2.1)	0.995
Critical limb ischemia	2.5 (0.9-5.6)	1.3 (0.2-4.4)	1.9 (0.4-14)	0.477
Subsequent ischemic events	6.8 (3.8-11)	7.9 (4.1-14)	0.9 (0.4-2.0)	0.725
Overall death	2.5 (0.9-5.5)	5.4 (2.5-10)	0.5 (0.1-1.4)	0.178
PAD patients, N	*169*	*204*		
Myocardial infarction	2.9 (1.2-6.0)	2.2 (0.8-4.8)	1.3 (0.4-4.7)	0.648
Acute ischemic stroke	2.4 (0.9-5.4)	1.7 (0.5-4.1)	1.5 (0.4-5.9)	0.627
Critical limb ischemia	10 (6.3-15)	14 (9.9-20)	0.7 (0.4-1.2)	0.209
Subsequent ischemic events	14 (10-21)	18 (13-24)	0.8 (0.5-1.3)	0.440
Overall death	4.7 (2.4-8.4)	6.0 (3.4-9.8)	0.8 (0.3-1.8)	0.582
All patients, N	*480*	*494*		
Myocardial infarction	2.8 (1.7-4.4)	4.4 (2.9-6.4)	0.6 (0.3-1.2)	0.147
Acute ischemic stroke	2.2 (1.3-3.6)	2.6 (1.5-4.2)	0.9 (0.4-1.8)	0.672
Critical limb ischemia	4.1 (2.7-5.9)	6.7 (4.8-9.1)	0.6 (0.4-1.01)	0.055
Subsequent ischemic events	8.6 (6.5-11)	14 (11-17)	0.6 (0.4-0.9)	0.012
Overall death	3.1 (1.9-4.7)	5.4 (3.8-7.6)	0.6 (0.3-0.99)	0.045

seguimiento medio: 14 meses

	HbA1c <7%	HbA1c >7%	Rate ratio (95% CI)	p
CAD patients, N	*152*	*168*		
Myocardial infarction	4.3 (2.2-7.8)	8.9 (5.3-14)	0.5 (0.2-1.1)	0.074
Acute ischemic stroke	0.4 (0.02-2.1)	2.5 (0.9-5.5)	0.2 (0.01-1.2)	0.086
Critical limb ischemia	0.4 (0.02-2.1)	2.5 (0.9-5.4)	0.2 (0.01-1.3)	0.090
Subsequent ischemic events	5.3 (2.9-8.9)	13 (8.9-19)	0.4 (0.2-0.8)	0.007
All patients, N	*480*	*494*		
Critical limb ischemia	4.1 (2.7-5.9)	6.7 (4.8-9.1)	0.6 (0.4-1.01)	0.055
Subsequent ischemic events	8.6 (6.5-11)	14 (11-17)	0.6 (0.4-0.9)	0.012
Overall death	3.1 (1.9-4.7)	5.4 (3.8-7.6)	0.6 (0.3-0.99)	0.045

*eventos por 100 pacientes y año

multivariante	Relative Risk (95% CI)	p
Age <70 years	0.6 (0.4-0.9)	0.012
Mean HbA1c levels >7%	1.0 (ref)	-
Mean HbA1c levels <7%	0.6 (0.4-0.9)	0.013
Mean CrCl levels >60 mL/min	0.7 (0.4-1.0)	0.040
Statins	0.6 (0.4-0.9)	0.011