HTA Vasculorrenal aterosclerótica:

Colocación de stent frente a tratamiento médico en la estenosis de arteria renal aterosclerótica

The NEW ENGLAND JOURNAL of MEDICINE

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Stenting and Medical Therapy for Atherosclerotic Renal-Artery Stenosis

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Estudio CORAL: Métodos

- Ensayo clínico multicéntrico, controlado, abierto, con asignación aleatoria (1:1), llevado a cabo en pacientes con estenosis de arteria renal y elevación de la presión arterial (PA sistólica ≥ 155 mm Hg), a pesar der estar tomando 2 o más antihipertensivos, enfermedad renal crónica o ambos.

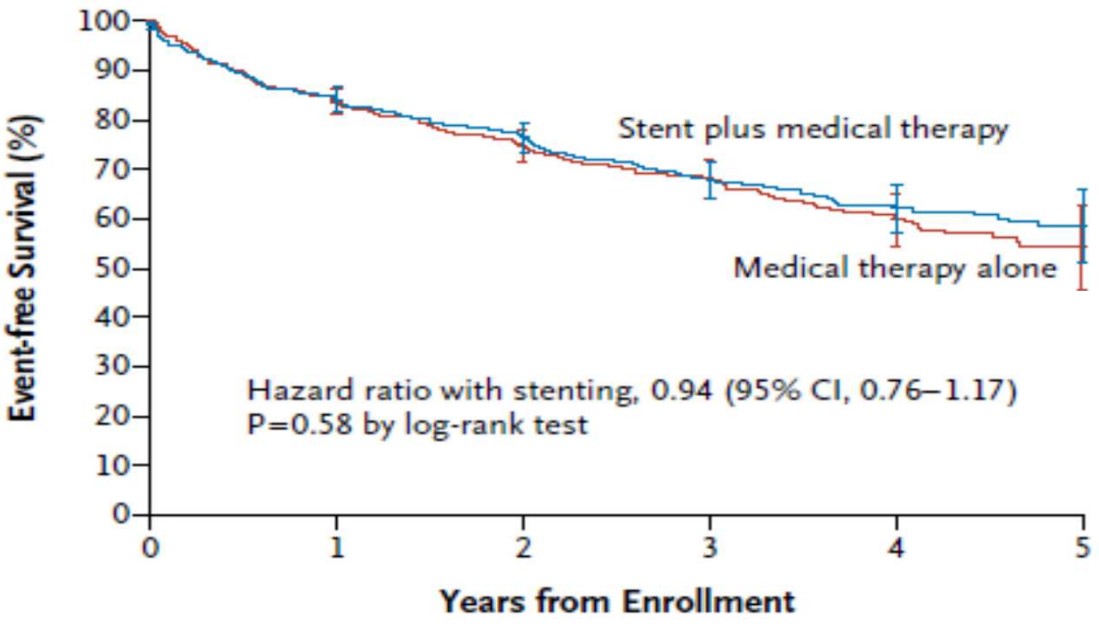
- Se comparó el tratamiento médico solo frente a la colocación de un stent + tratamiento médico

- Se definió la estenosis de arteria renal angiográficamente, como
  - Una estenosis de ≥ 80%, pero < del 100% de diámetro de la arterial
  - O una estenosis ≥ 60% con un gradiente de presión sistólica de al menos 20 mm Hg.

- Criterios de exclusión:
  - Estenosis de arteria renal debido a displasia fibromuscular
  - Enfermedad renal crónica distinta a la isquémica
  - Creatinina > 4,0 mg/dL (354 umol/l)
  - Tamaño renal < 7 cm
  - Lesión que no pudiese ser tratada con un solo stent.

- **Objetivo primario:** Incidencia de eventos cardiovasculares o renales : End point compuesto de mortalidad de causa cardiovascular o renal, infarto de miocardio, ictus, hospitalización por insuficiencia cardiaca, insuficiencia renal progresiva o necesidad de tratamiento renal sustitutivo

Estudio CORAL: Resultados del objetivo primario



No. at Risk

Medical therapy alone	472	371	314	214	115	40
Stent plus medical therapy	459	362	318	224	131	59

Figure 2. Kaplan–Meier Curves for the Primary Outcome.

Survival curves are truncated at 5 years owing to instability of the curves because few participants remained in the study after 5 years.

Cooper CJ et al. N Engl J Med 2014;370:13-22

Estudio CORAL: CONCLUSIONES

- *La colocación de un stent en pacientes con estenosis arteriosclerótica significativa de arteria renal e hipertensión arterial o enfermedad crónica, no confiere beneficio con respecto a la prevención de eventos clínicos, cuando se hace un tratamiento médico multifactorial*
- *El número de eventos observado durante el seguimiento (20%) fue la mitad de lo que se esperaba (40%).*

Cooper CJ et al. N Engl J Med 2014;370:13-22

Uso concomitante de diuréticos, inhibidores del sistema renina angiotensina (IECAS o ARA2) y antiinflamatorios.

BMJ

BMJ 2013;346:e8525 doi: 10.1136/bmj.e8525 (Published 8 January 2013)

- **Objetivo:** Valorar si un doble tratamiento con Inhibidores del sistema renina angiotensina y diuréticos con AINES se asociaban a un aumento del daño renal.
- **Diseño:** Estudio de cohorte retrospectivo usando una análisis de casos controles.
- **Participantes:** Cohorte de 487.372 sujetos con tratamiento antihipertensivo.

Lapi F et al. BMJ 2013;346:e8525

Uso concomitante de diuréticos, inhibidores del sistema renina angiotensina (IECAS o ARA2) y antiinflamatorios.

- **Resultados:** Seguimiento medio de 5,9 (DE 3,4) años, se identifcaron 2.215 casos de daño renal agudo (tasa de incidencia de 7/10.000 personas/año.

- El uso de doble tratamiento no se asoció con un aumento significativo de daño renal.

- El uso de triple terapia se asoció con un aumento del riesgo de daño renal agudo : 1,31, IC 95% 1,12-1,53. El riesgo mayor se observó durante los 30 días primeros de su uso: tasa de 1,82, IC 95% 1,35.2,42

What this paper adds

Double therapy combinations consisting of addition of NSAIDs to diuretics, ACE inhibitors, or ARBs did not generally increase the risk of acute kidney injury

A triple therapy combination consisting of addition of NSAIDs to diuretics and ACE inhibitors or ARBs was associated with an increased risk of acute kidney injury

The risk of acute kidney injury with triple therapy was particularly elevated during the first 30 days of use

Lapi F et al. BMJ 2013;346:e8525

Tratamiento de la HTA: Metaanálisis

Reducción de la PA y eventos cardiovasculares en sujetos con y sin enfermedad renal crónica

Blood pressure lowering and major cardiovascular events in people with and without chronic kidney disease: meta-analysis of randomised controlled trials

OPEN ACCESS

Blood Pressure Lowering Treatment Trialists' Collaboration

BMJ 2013;347:f5680 doi: 10.1136/bmj.f5680 (Published 3 October 2013)

- **Objetivo:** Definir los efectos cardiovasculares de la reducción de la presión arterial en sujetos con enfermedad renal crónica.

- **Participantes:** 26 ensayos clínicos (152.290 participantes), de los cuales 30.925 presentaban una reducción del FGe < 60 mL/min/m2

Tratamiento antihipertensivo: Metaanálisis

Reducción de la PA y efectos cardiovasculares mayores en sujetos con y sin enfermedad renal crónica

- **Resultados:**

  - En relación al placebo, la reducción de la PA redujo las complicaciones cardiovasculares mayores: aproximadamente 1/6 por cada 5 mm Hg de reducción de la PAS: HR 0,83 (IC 95% 0,76-0,90) en los sujetos con enfermedad renal crónica y HR 0,83 (IC 95% 0,79 a 0,88) en los que no tenían enfermedad renal crónica. La diferencia no fe significativa, pero el beneficio absoluto fue mayor en los sujetos con enfermedad renal crónica, por ser de riesgo más elevado.

  - No se observaron diferencias en relación al tratamiento antihipertensivo.

What this study adds

The proportional reductions of cardiovascular complications in risk with lowered blood pressure are similar in people with and without chronic kidney disease, but people with kidney disease gain much larger absolute benefits because their baseline risk is higher

There is little evidence to support the preferential choice of particular drug classes for the prevention of cardiovascular events in people with chronic kidney disease

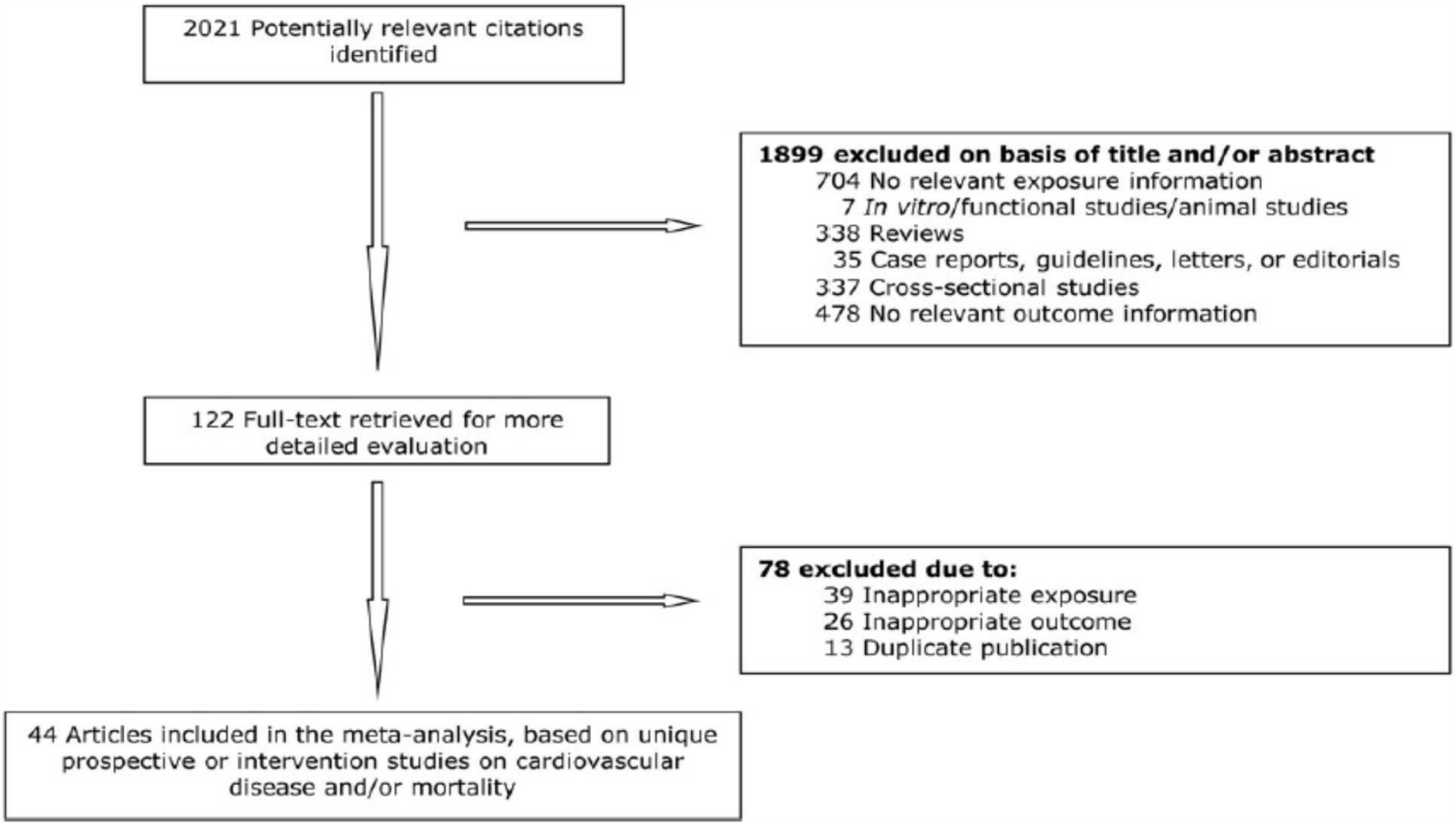
Blood Pressure Lowering Treatment Trialists' Collaboration BMJ 2013;347:f5680

Adherencia al tratamiento cardiovascular

Metaanálisis de la prevalencia y consecuencias clínicas

European Heart Journal (2013) **34**, 2940–2948
doi:10.1093/eurheartj/eht295

CLINICAL RESEARCH
Prevention and epidemiology



Adherencia al tratamiento cardiovascular

Prevalencia según el tipo de mediación cardiovascular

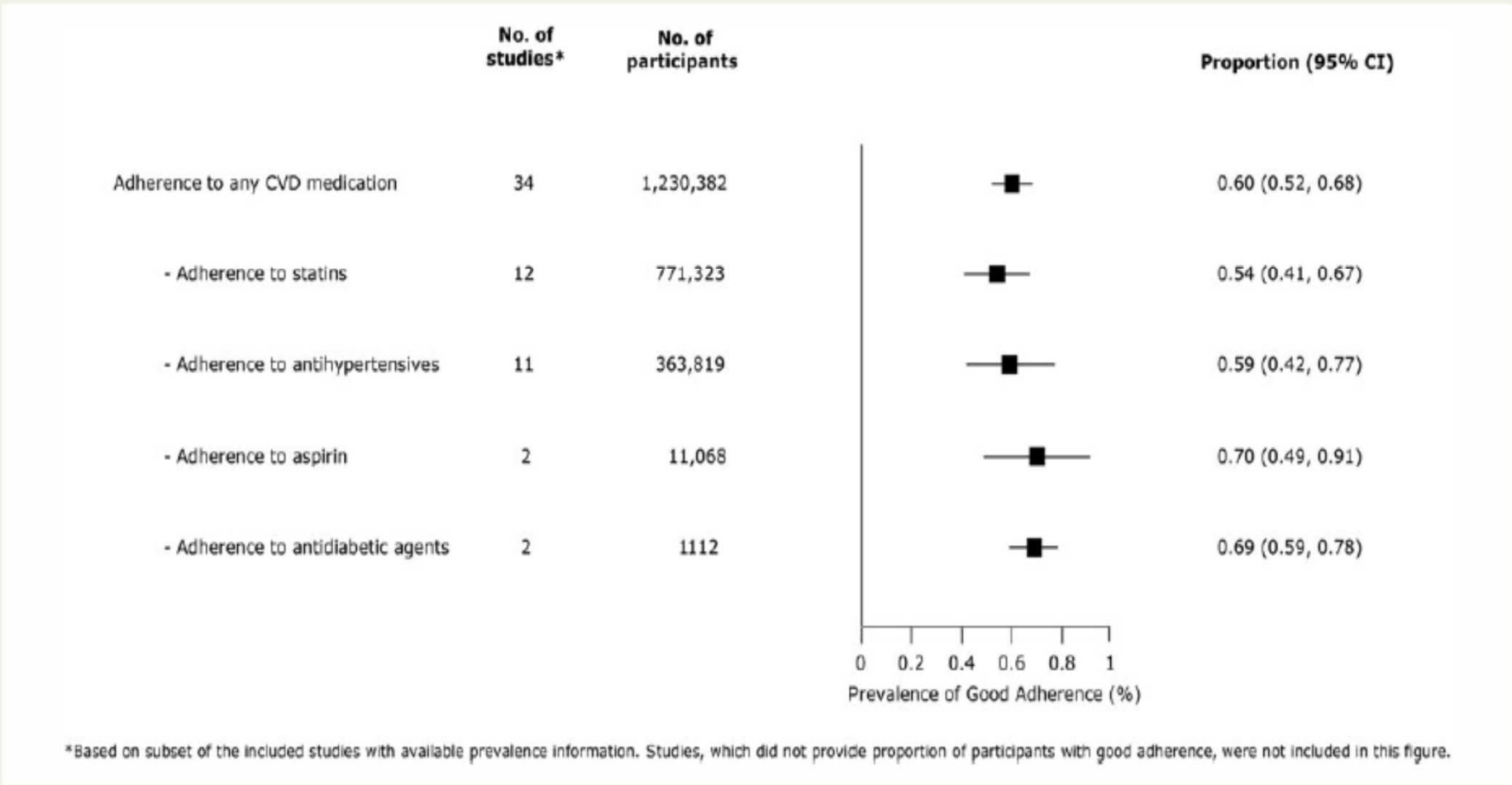


Figure 2 Prevalence (95% CI) of good adherence to cardiovascular medications among participants in prospective studies with available information.

Chowdhury R et al Eur Heart J 2013;34:2940-2948

Adherencia al tratamiento cardiovascular

Riesgo relativo de mortalidad total en función de la adherencia

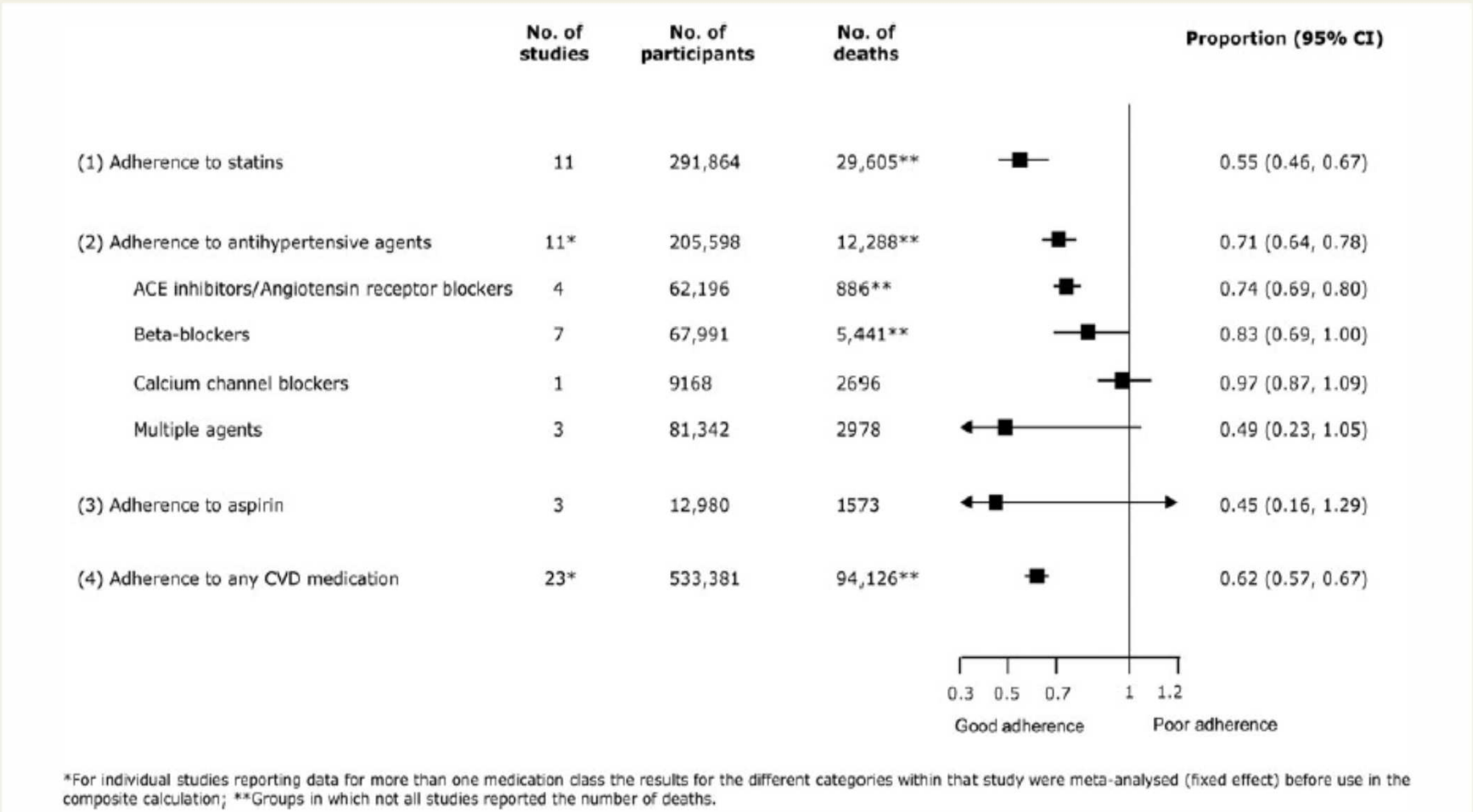


Figure 4 Relative risks for all-cause mortality in good vs. poor adherence to major cardiovascular medications.

Chowdhury R et al Eur Heart J 2013;34:2940-2948

Meta terapéutica de la presión arterial en pacientes con ictus lacunar reciente: Estudio SPS3

Blood-pressure targets in patients with recent lacunar stroke: the SPS3 randomised trial

*The SPS3 Study Group**

Summary

Background Lowering of blood pressure prevents stroke but optimum target levels to prevent recurrent stroke are unknown. We investigated the effects of different blood-pressure targets on the rate of recurrent stroke in patients with recent lacunar stroke.

Methods In this randomised open-label trial, eligible patients lived in North America, Latin America, and Spain and had recent, MRI-defined symptomatic lacunar infarctions. Patients were recruited between March, 2003, and April, 2011, and randomly assigned, according to a two-by-two multifactorial design, to a systolic-blood-pressure target of 130–149 mm Hg or less than 130 mm Hg. The primary endpoint was reduction in all stroke (including ischaemic strokes and intracranial haemorrhages). Analysis was done by intention to treat. This study is registered with ClinicalTrials.gov, number NCT 00059306.

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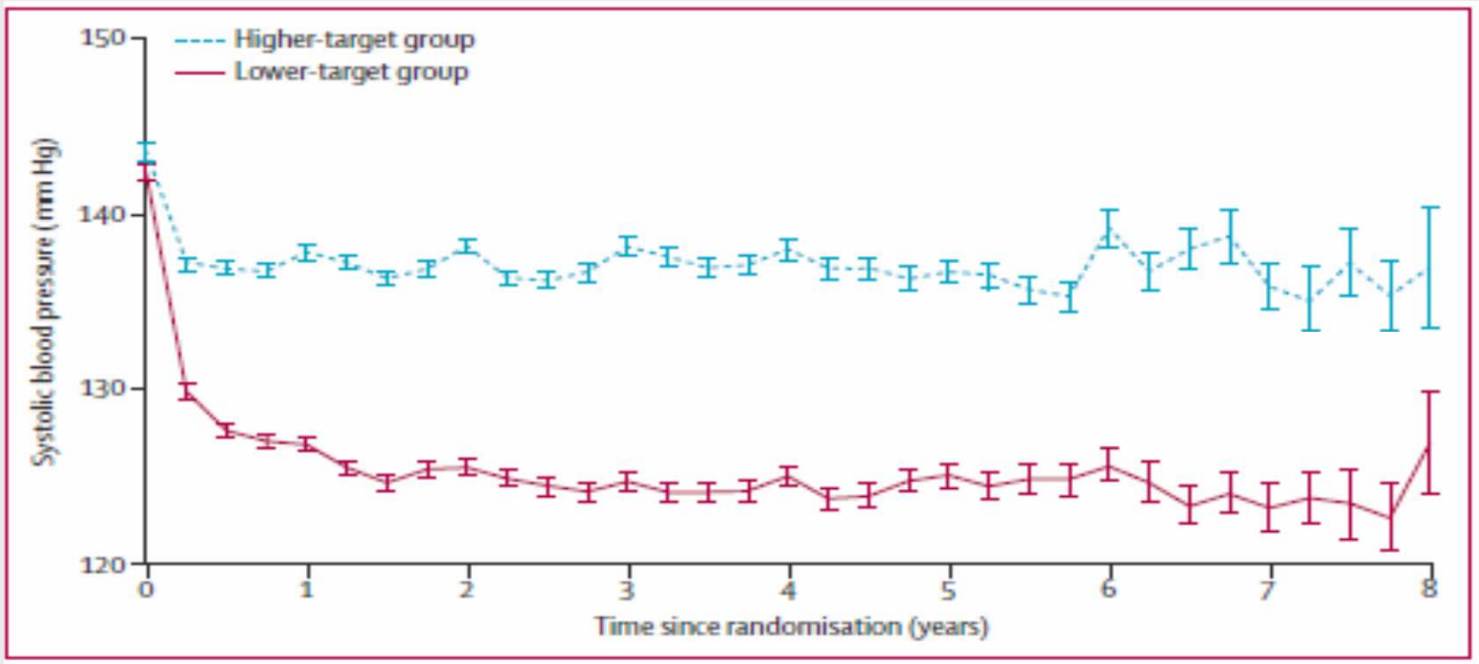
- **Encefalopatía hipertensiva**
- **Aterotrombosis de grandes arterias**
  - Enfermedad carotidea oclusiva
  - Enfermedad vertebrobasilar oclusiva
- **Enfermedad de vaso pequeño**
  - Lesiones isquémica cerebrales: Infartos lacunares
  - Lesión de sustancia blanca: leucoaraiosis
  - Microsangrados cerebrales
  - Espacios perivascualres prominentes
  - Hemorragia intracerebral

The SPS3 Study Group. Lancet 2013;382:507-15

Meta terapéutica de la presión arterial en pacientes con ictus lacunar reciente: Estudio SPS3



Interpretation

We assessed blood-pressure targets in survivors of MRI-defined lacunar stroke. A reduced rate of all stroke was observed in patients with a target systolic blood pressure lower than 130 mm Hg compared with a target of 130–149 mm Hg, but this difference was not significant. The intervention was safe and well tolerated. Interpreted in the context of previous randomised, controlled trials of blood-pressure lowering after stroke, our results suggest that management of systolic to levels lower than 130 mm Hg is likely to reduce the risk of recurrent stroke in patients with recent lacunar stroke.

The SPS3 Study Group. Lancet 2013;382:507-15

Meta terapéutica de la presión arterial en pacientes con ictus lacunar reciente: Estudio SPS3

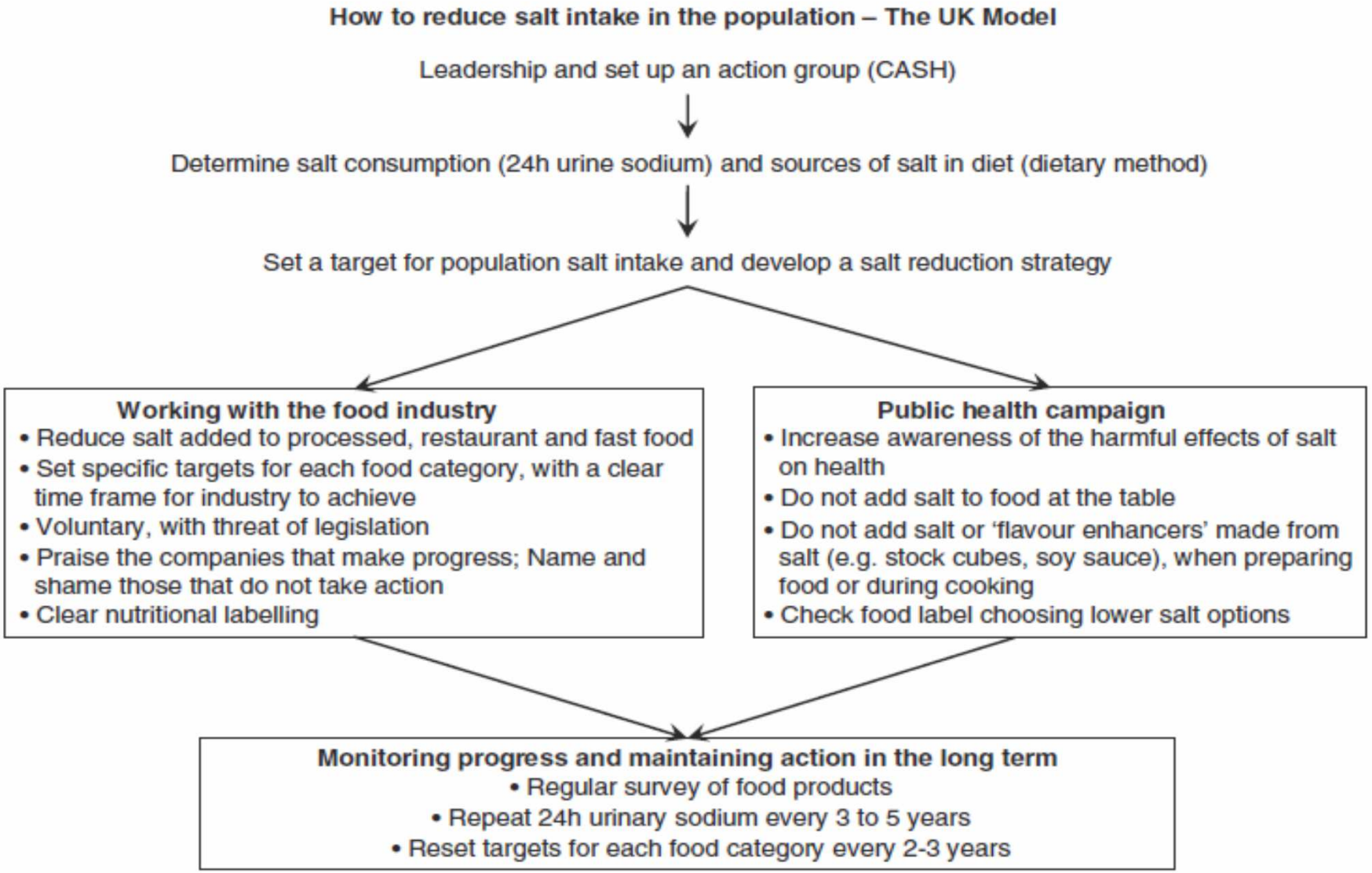
	Higher-target group (n=1519)		Lower-target group (n=1501)		Hazard ratio (95% CI)	p value
	Number of patients	Rate (% per patient-year)	Number of patients	Rate (% per patient-year)		
Stroke						
All stroke	152	2·77%	125	2·25%	0·81 (0·64–1·03)	0·08
Ischaemic stroke or unknown	131	2·4%	112	2·0%	0·84 (0·66–1·09)	0·19
Intracranial haemorrhage						
All	21*	0·38%	13†	0·23%	0·61 (0·31–1·22)	0·16
Intracerebral	16	0·29%	6	0·11%	0·37 (0·15–0·95)	0·03
Subdural or epidural	5	0·091%	6	0·11%	1·18 (0·36–3·88)	0·78
Other	2	0·036%	4	0·072%	1·97 (0·36–10·74)	0·43
Disabling or fatal stroke‡	49	0·89%	40	0·72%	0·81 (0·53–1·23)	0·32
Myocardial infarction	40	0·70%	36	0·62%	0·88 (0·56–1·39)	0·59
Major vascular event*	188	3·46%	160	2·91%	0·84 (0·68–1·04)	0·10
Deaths						
All	101	1·74%	106	1·80%	1·03 (0·79–1·35)	0·82
Vascular death	41	0·70%	36	0·61%	0·86 (0·55–1·35)	0·52
Non-vascular	35	0·60%	40	0·68%	1·12 (0·71–1·76)	0·62
Uncertain	25	0·43%	30	0·51%	1·18 (0·69–2·00)	0·55

The SPS3 Study Group. Lancet 2013;382:507-15

Programa de reducción en el consumo de sal en la población general

Journal of Human Hypertension (2013), 1–8

www.nature.com/jhh



He FJ et al. J Hum Hypertens 2014; 28:345-352

Reducción (15%) en el consumo de sal en la población general en un periodo de 7 años

Table 1. UK strategy for reducing salt intake

Salt intake		*Reduction needed*	*Target intake (g per day)*
Source	*g per day*		
Table/cooking (15%)	1.4 g	40% reduction	0.9 g
Natural (5%)	0.5 g	No reduction	0.5 g
Food industry (80%)	7.6 g	40% reduction	4.6 g
	Total: 9.5 g		Target: 6.0 g

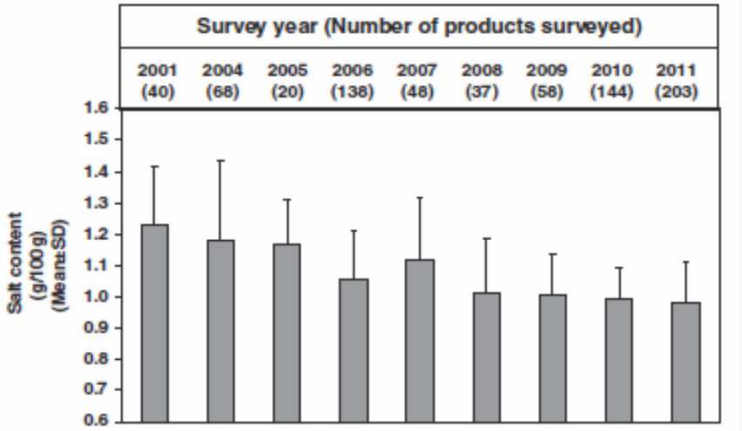


Figure 2. Changes in salt content of bread sold in the UK supermarkets from 2001 to 2011.

Table 3. Salt intake as measured by 24-h urinary sodium excretion in adult population from 2000/2001 to 2011

	2000/2001[a]		*2005/2006*[a]		*2008*[a]		*2011*[a]	
	N	*Mean ± s.d. (g per day)*	N	*Mean ± s.d. (g per day)*	N	*Mean ± s.d. (g per day)*	N	*Mean ± s.d. (g per day)*
Men								
19–34	214	11.3 ± 5.21	33	10.3 ± 3.87	46	10.0 ± 4.21	43	9.5 ± 4.03
35–49	170	11.1 ± 4.83	67	10.1 ± 3.90	111	9.50 ± 4.06	84	10.0 ± 3.86
50–64	183	10.5 ± 4.95	88	10.2 ± 4.19	137	9.30 ± 3.00	123	8.2 ± 4.79
All men	567	11.0 ± 5.02	188	10.2 ± 3.98	294	9.68 ± 4.10	250	9.3 ± 5.76
Women								
19–34	189	8.8 ± 4.60	49	8.6 ± 2.99	61	8.3 ± 3.38	43	7.1 ± 3.23
35–49	203	8.0 ± 3.42	99	7.9 ± 2.7	157	7.41 ± 2.86	101	6.8 ± 3.07
50–64	187	7.5 ± 3.45	112	6.8 ± 2.8	180	6.97 ± 3.00	153	6.6 ± 3.47
All women	580	8.1 ± 3.88	262	7.7 ± 2.8	398	7.66 ± 4.77	297	6.8 ± 3.59
All								
19–34	403	10.2 ± 5.08	71	9.3 ± 3.58	107	9.2 ± 4.24	86	8.3 ± 4.06
35–49	373	9.4 ± 4.40	119	9.0 ± 3.5	268	8.44 ± 3.87	185	8.5 ± 4.02
50–64	370	9.0 ± 4.51	179	8.5 ± 3.9	317	8.12 ± 3.31	276	7.4 ± 5.30
All	1147	9.5 ± 4.71	350	9.0 ± 3.7	692	8.64 ± 4.39	547	8.1 ± 5.79

[a]The 2000/2001 survey was carried out in a random sample of adults in Great Britain, the 2008 survey was in a random sample of adults in the United Kingdom, and the 2005/2006 and 2011 surveys were random samples of adults in England.

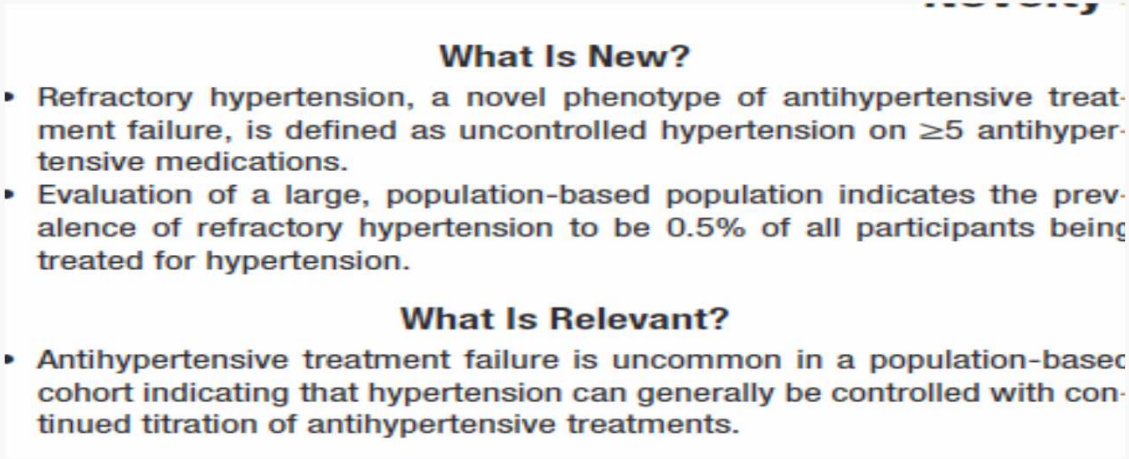
He F J et al. J Hum Hypertens 2014;28:345-352

Hipertensión arterial refractaria versus HTA resistente
Datos del estudio REGARDS

- **Resultados:**

  - La prevalencia de HTA refractaria fue del 3,6% entre los sujetos con HTA resistente (n =2.144) y del 41,7% entre los participantes con ≥ 5 antihipertensivos.

  - En comparación con los sujetos con HTA resistente, los que presentaban HTA refractaria eran más frecuentemente de raza negra (HR 3,00, IC 95% 1,69-5,37) y presentaban con mayor frecuencia albuminuria: HR 2,22 (IC 95% 1,40-3,52) y diabetes mellitus: HR 2,09 (IC 95% 1,32-3,31).



What Is New?

- Refractory hypertension, a novel phenotype of antihypertensive treatment failure, is defined as uncontrolled hypertension on ≥5 antihypertensive medications.
- Evaluation of a large, population-based population indicates the prevalence of refractory hypertension to be 0.5% of all participants being treated for hypertension.

What Is Relevant?

- Antihypertensive treatment failure is uncommon in a population-based cohort indicating that hypertension can generally be controlled with continued titration of antihypertensive treatments.

Calhoun DA et al, Hypertension 2014;63:451-458

Hipertensión arterial refractaria versus HTA resistente
Datos del estudio REGARDS

- **Objetivo:** Utilizar una amplia base poblacional para determinar la prevalencia de HTA refractaria e identificar los factores asociados a la misma, y estimar su riesgo coronario a los 10 años.
- **Definición de HTA resistente:** HTA no controlada (< 140/90 mm Hg) con ≥ 3 antihipertensivos o controlada con ≥ 4 fármacos.
- **Definición de HTA refractaria:** Hipertensos tratados con 5 o más antihipertensivos.
- **Participantes:** Estudio REGARDS; cohorte de base poblacional n=30.239).

Calhoun DA et al, Hypertension 2014;63:451-458

HTA Resistente
SYMPLICITTY-HTN3

The NEW ENGLAND JOURNAL of MEDICINE

N ENGL J MED 370;15 NEJM.ORG APRIL 10, 2014

ORIGINAL ARTICLE

A Controlled Trial of Renal Denervation for Resistant Hypertension

Deepak L. Bhatt, M.D., M.P.H., David E. Kandzari, M.D., William W. O'Neill, M.D., Ralph D'Agostino, Ph.D., John M. Flack, M.D., M.P.H., Barry T. Katzen, M.D., Martin B. Leon, M.D., Minglei Liu, Ph.D., Laura Mauri, M.D., Manuela Negoita, M.D., Sidney A. Cohen, M.D., Ph.D., Suzanne Oparil, M.D., Krishna Rocha-Singh, M.D., Raymond R. Townsend, M.D., and George L. Bakris, M.D., for the SYMPLICITY HTN-3 Investigators*

METHODS

We designed a prospective, single-blind, randomized, sham-controlled trial. Patients with severe resistant hypertension were randomly assigned in a 2:1 ratio to undergo renal denervation or a sham procedure. Before randomization, patients were receiv-

least three drugs, including a diuretic. The primary efficacy end point was the change in office systolic blood pressure at 6 months; a secondary efficacy end point was the change in mean 24-hour ambulatory systolic blood pressure. The primary safety end point was a composite of death, end-stage renal disease, embolic events resulting in end-organ damage, renovascular complications, or hypertensive crisis at 1 month or new renal-artery stenosis of more than 70% at 6 months.

Resultados Symplicity-HTN 3

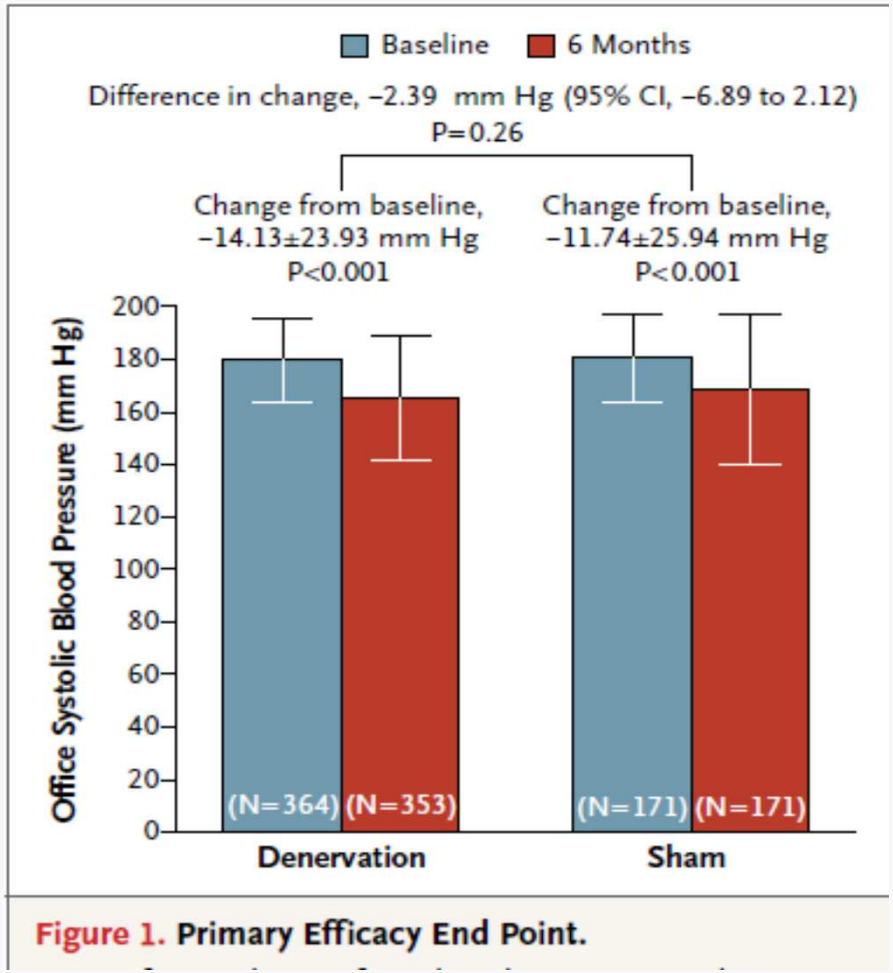


Figure 1. Primary Efficacy End Point.

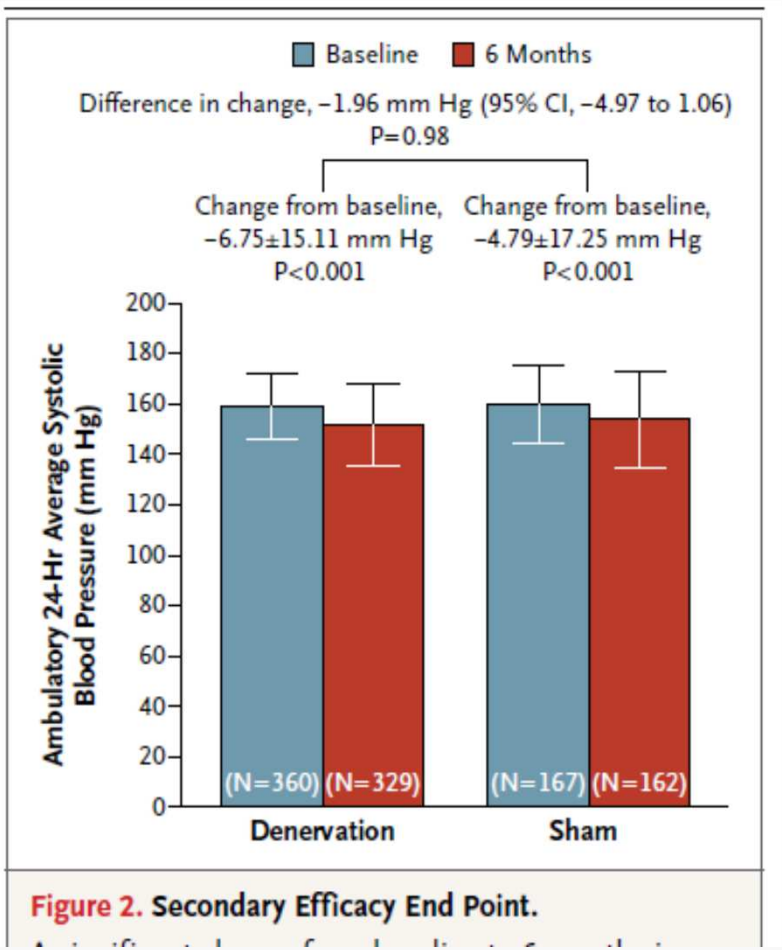
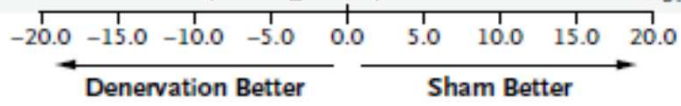


Figure 2. Secondary Efficacy End Point.

Bhatt DL et al. For the SYMPLICITY HTN-3, N Engl J Med 2014; 370:1393-1401

Resultados Symplicity-HTN 3
Análisis por subgrupos

Subgroup	Denervation	Sham	Between-Group Difference in Change in Office Systolic Blood Pressure (95% CI)	P Value	P Value for Interaction
	no. of patients		*mm Hg*		
All patients	353	171	−2.39 (−6.89 to 2.12)	0.26	
Diabetes mellitus					0.82
Yes	169	68	−4.53 (−11.51 to 2.46)	0.20	
No	181	101	−3.46 (−9.55 to 2.62)	0.26	
Sex					0.37
Male	208	108	−2.30 (−7.63 to 3.03)	0.40	
Female	142	61	−6.64 (−14.94 to 1.65)	0.12	
Black race					0.09
Yes	85	49	2.25 (−7.27 to 11.78)	0.64	
No	264	120	−6.63 (−11.81 to −1.44)	0.01	
Body-mass index					0.77
<30	91	42	−2.77 (−11.47 to 5.93)	0.53	
≥30	259	126	−4.36 (−9.76 to 1.03)	0.11	
Receiving aldosterone antagonist at baseline					0.36
Yes	76	47	−8.05 (−17.63 to 1.52)	0.10	
No	274	122	−3.24 (−8.42 to 1.93)	0.22	
Estimated GFR					0.31
<60 ml/min/1.73 m^2	68	38	0.54 (−8.29 to 9.37)	0.90	
≥60 ml/min/1.73 m^2	282	131	−5.22 (−10.51 to 0.06)	0.05	
Age					0.27
<65 yr	246	128	−5.73 (−11.06 to −0.40)	0.04	
≥65 yr	104	41	0.09 (−8.80 to 8.99)	0.99	
Any medication change					0.68
Yes	132	70	−5.41 (−13.49 to 2.67)	0.19	
No	218	99	−3.44 (−8.83 to 1.96)	0.21	



Bhatt DL et al. For the SYMPLICITY HTN-3, N Engl J Med 2014; 370:1393-1401