

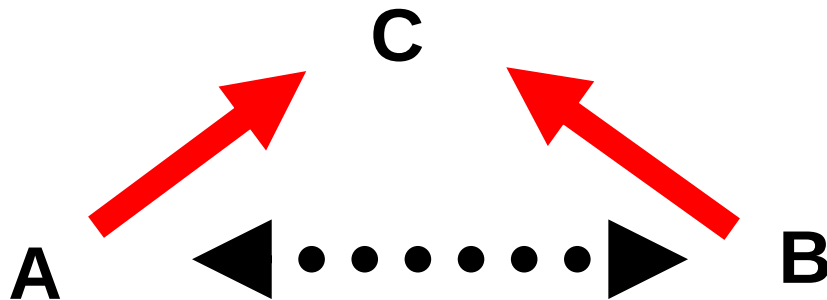
Comparaciones Indirectas y metanálisis



Dr. Pere Ventayol

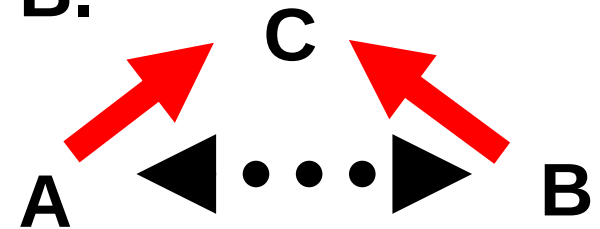
¿Qué es una Comparación Indirecta?

- Los ECA frente a placebo son suficientes para obtener la aprobación de las agencias reguladoras
- No se dispone de ECAs frente al comparador de interés/referencia
- Métodos que permiten realizar una estimación indirecta entre 2 tratamientos frente a un comparador común

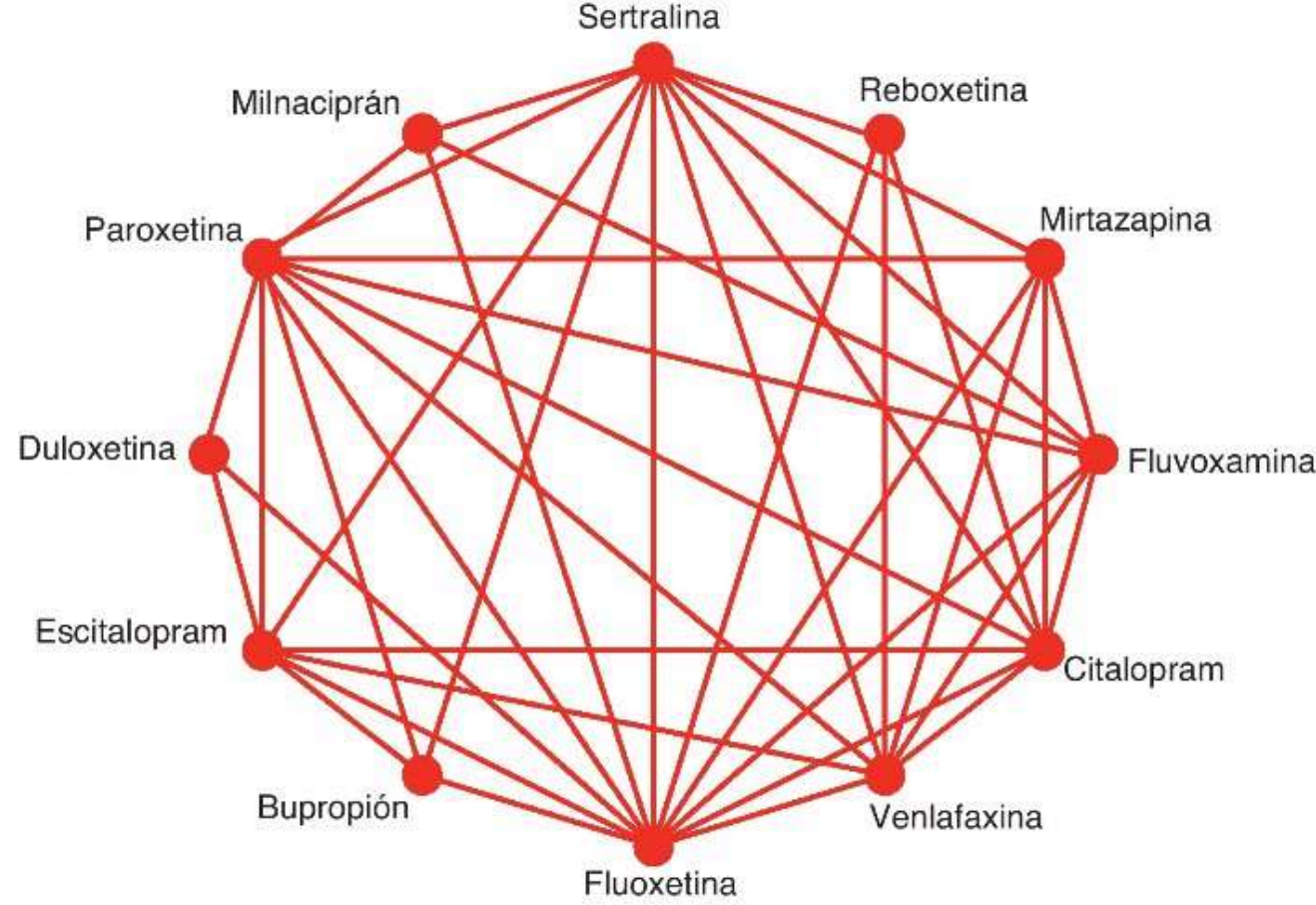


Niveles de complejidad

1. **Situación más simple: un solo ensayo de A vs C y B vs C que combinados proveen una estimación indirecta de A vs B.**



2. **Uno de los brazos o ambos son un metanálisis**
3. **Comparaciones múltiples entre distintos tratamientos**



¿Es necesario realizar comparaciones indirectas?

La información comparativa es crítica para la toma de decisiones

Incluso existiendo ECAs comparativos directos en ocasiones es útil la evidencia indirecta



¿Son válidas las comparaciones indirectas?

¿Como lo podríamos saber?

Validity of indirect comparison for estimating efficacy of competing interventions: empirical evidence from published meta-analyses

Fujian Song, Douglas G Altman, Anne-Marie Glenny, Jonathan J Deeks

Results 44 published meta-analyses (from 28 systematic reviews) provided sufficient data. In most cases, results of adjusted indirect comparisons were not significantly different from those of direct comparisons. A significant discrepancy ($P < 0.05$) was observed in three of the 44 comparisons between the direct and the adjusted indirect estimates. There was a moderate agreement between the statistical conclusions from the direct and adjusted indirect comparisons (κ 0.51). The direction of discrepancy between the two estimates was inconsistent.



¿Tipos de Comparaciones Indirectas?

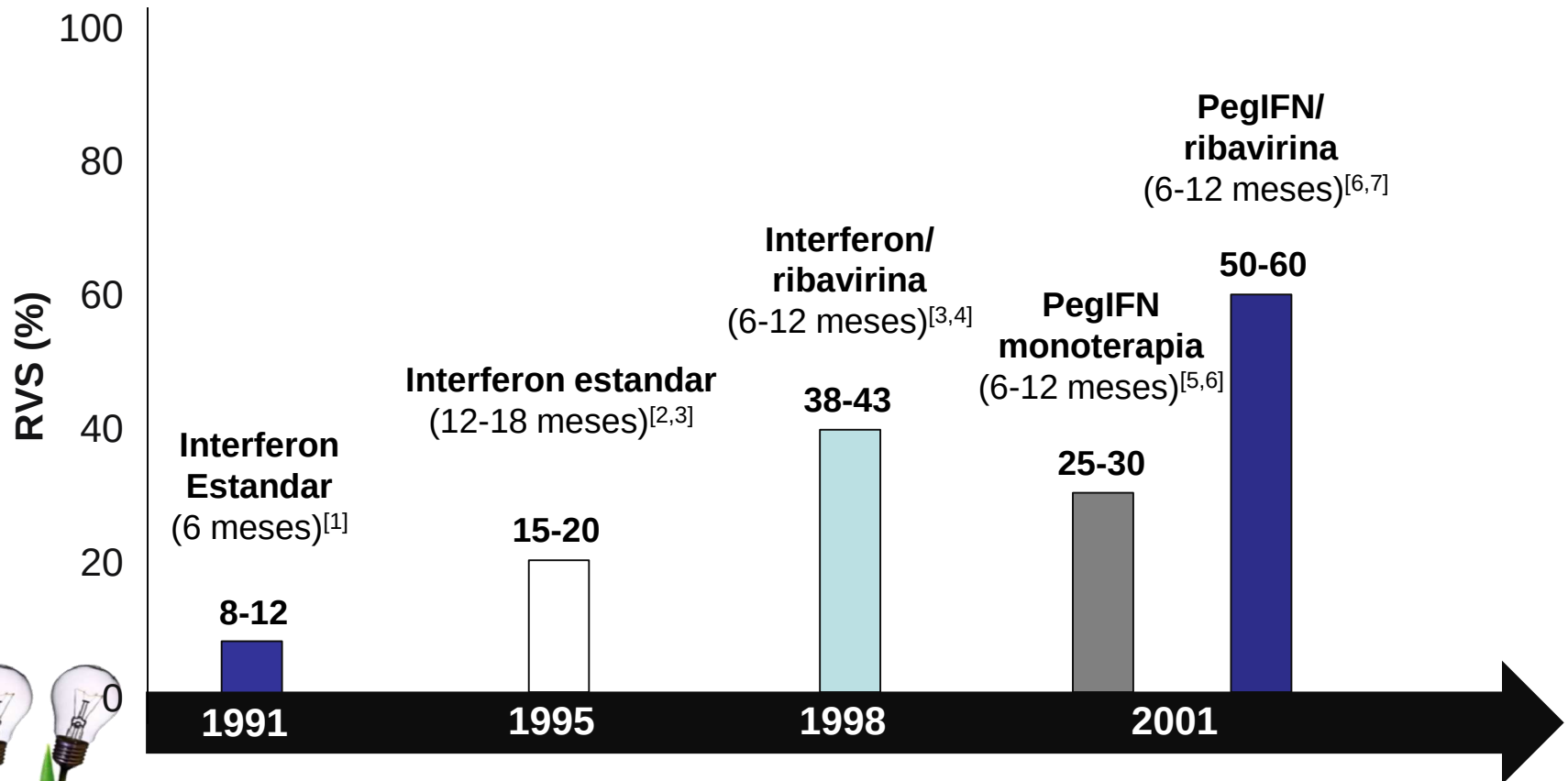


1.Naïve

2.Informales

3.Ajustadas

Comparaciones Indirectas Naïve



1. Carithers RL Jr., et al. Hepatology. 1997;26(3 suppl 1):83S-88S. 2. Zeuzem S, et al. N Engl J Med. 2000;343:1666-1672. 3. Poynard T, et al. Lancet. 1998;352:1426-1432. 4. McHutchison JG, et al. N Engl J Med. 1998;339:1485-1492. 5. Lindsay KL, et al. Hepatology. 2001;34:395-403. 6. Fried MW, et al. N Engl J Med. 2002;347:975-982. 7. Manns MP, et al. Lancet. 2001;358:958-965.

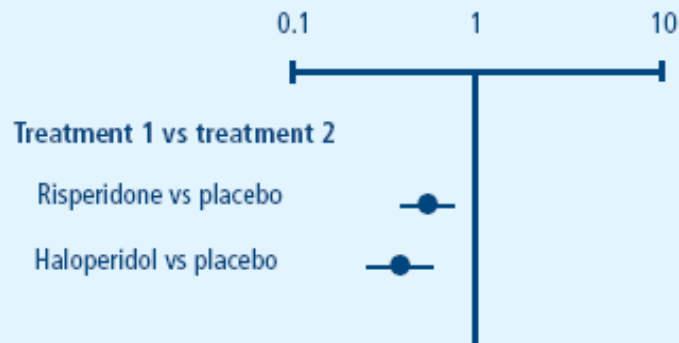


Comparaciones Indirectas informales o no ajustadas

Table 1. Meta-analyses of risperidone versus haloperidol for schizophrenia: number of patients without clinical improvement²

Comparison	Number of trials	Log odds ratio (SE)	Odds ratio (95% CI)	I ² %
Placebo controlled trials				
Risperidone vs placebo	3	-0.909 (0.218)	0.40 (0.26, 0.62)	37%
Haloperidol vs placebo	9	-1.707 (0.318)	0.18 (0.10, 0.34)	11%

Odds ratio (95% CI)



Lectura: estar sin mejora clínica es malo



Comparaciones Indirectas informales o no ajustadas

[Scandinavian Journal of Rheumatology 2007; 36, \(6\): 411 - 417](#)

The number needed to treat for adalimumab, etanercept, and infliximab based on ACR50 response in three randomized controlled trials on established rheumatoid arthritis: a systematic literature review

Authors: L. E. Kristensen ^a; R. Christensen ^b; H. Bliddal ^b; P. Geborek ^a; B. Danneskiold-Samsøe ^b; T. Saxne ^a

Affiliations: ^a Department of Rheumatology, Lund University Hospital, Lund, Sweden

^b The Parker Institute, Musculoskeletal Statistics Unit, Frederiksberg Hospital, Frederiksberg, Denmark

Objective: To compare the efficacy of adalimumab, etanercept, and infliximab in patients with established rheumatoid arthritis (RA) taking concomitant methotrexate (MTX) by calculating the number needed to treat (NNT) using three different methods.

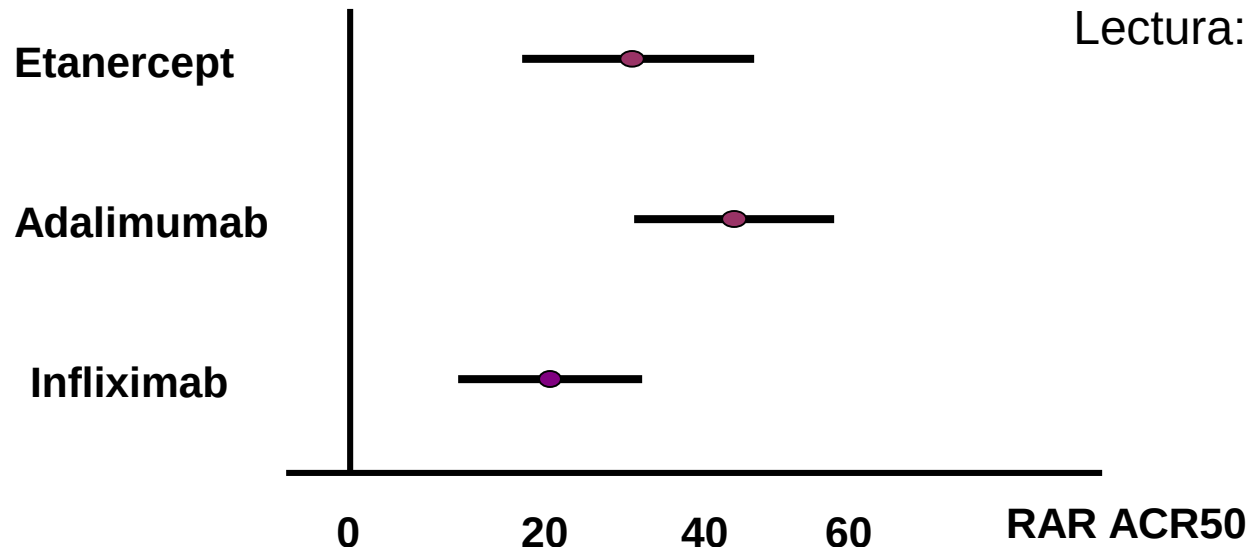
Methods: A systematic literature search of the Cochrane Library, MEDLINE, and EMBASE was conducted from inception to 30 June 2006. Two pairs of investigators, a Danish and a Swedish pair, independently conducted a structured literature review. The reviewers selected any published randomized, double-blind, MTX controlled study of adalimumab, etanercept, and infliximab, presenting the American College of Rheumatology 50% response (ACR50) after 12 months in RA patients with a mean disease duration of at least 5 years. The two review groups independently extracted the estimates necessary to calculate the NNT.

Results: The reviewers consistently selected the same three randomized, controlled trials (RCTs), one for each of the drugs, and extracted equal data for the number of patients completing the 12-month intervention, and the corresponding number of ACR50 responding patients after therapy. Some baseline differences were noted: patients in the etanercept trial had a shorter disease duration and did not receive MTX prior to inclusion; patients in the adalimumab study had lower Health Assessment Questionnaire (HAQ) scores. The calculated NNTs varied slightly depending on the method used. The fully adjusted NNTs (95% confidence intervals) for adalimumab, etanercept, infliximab standard dosage and infliximab double dosage were 4 (3-6), 4 (3-6), 8 (4-66), and 4 (3-11) patients, respectively.

Conclusion: This study indicates equal efficacy of the three anti-tumour necrosis factor (TNF) therapies.

Comparaciones Indirectas informales o no ajustadas

	RAR ACR50
Etanercept+MTX (Weimblatl 1999)	35,65 (21,60-49,70)
Adalimumab+MTX (ARMADA)	45,70 (31,80-59,60)
Infliximab +MTX (Maini 1999)	21,70(11,20-32,30)

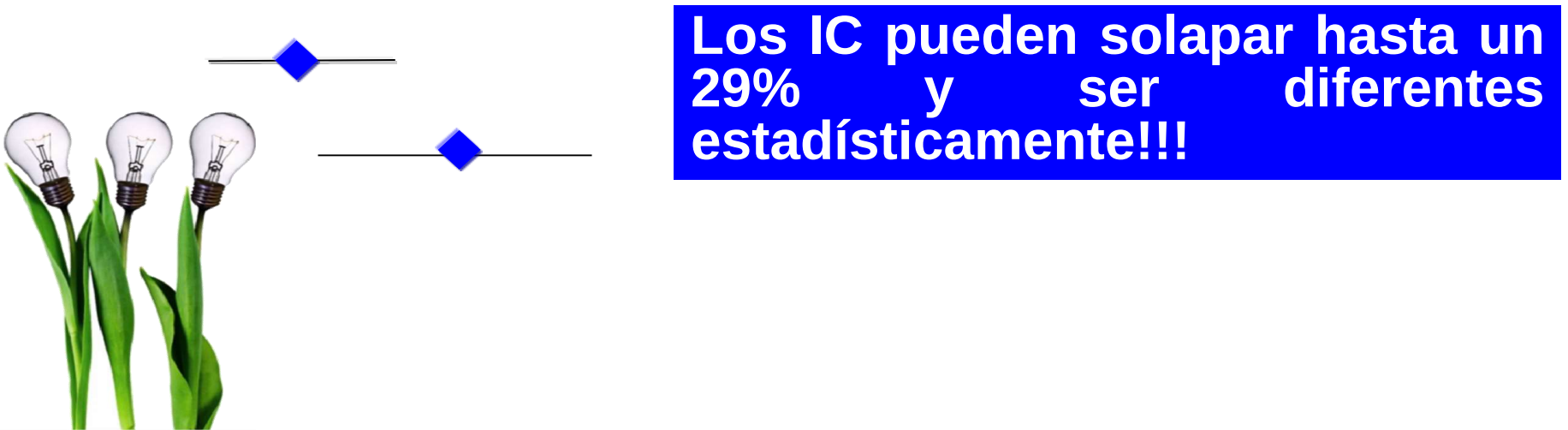


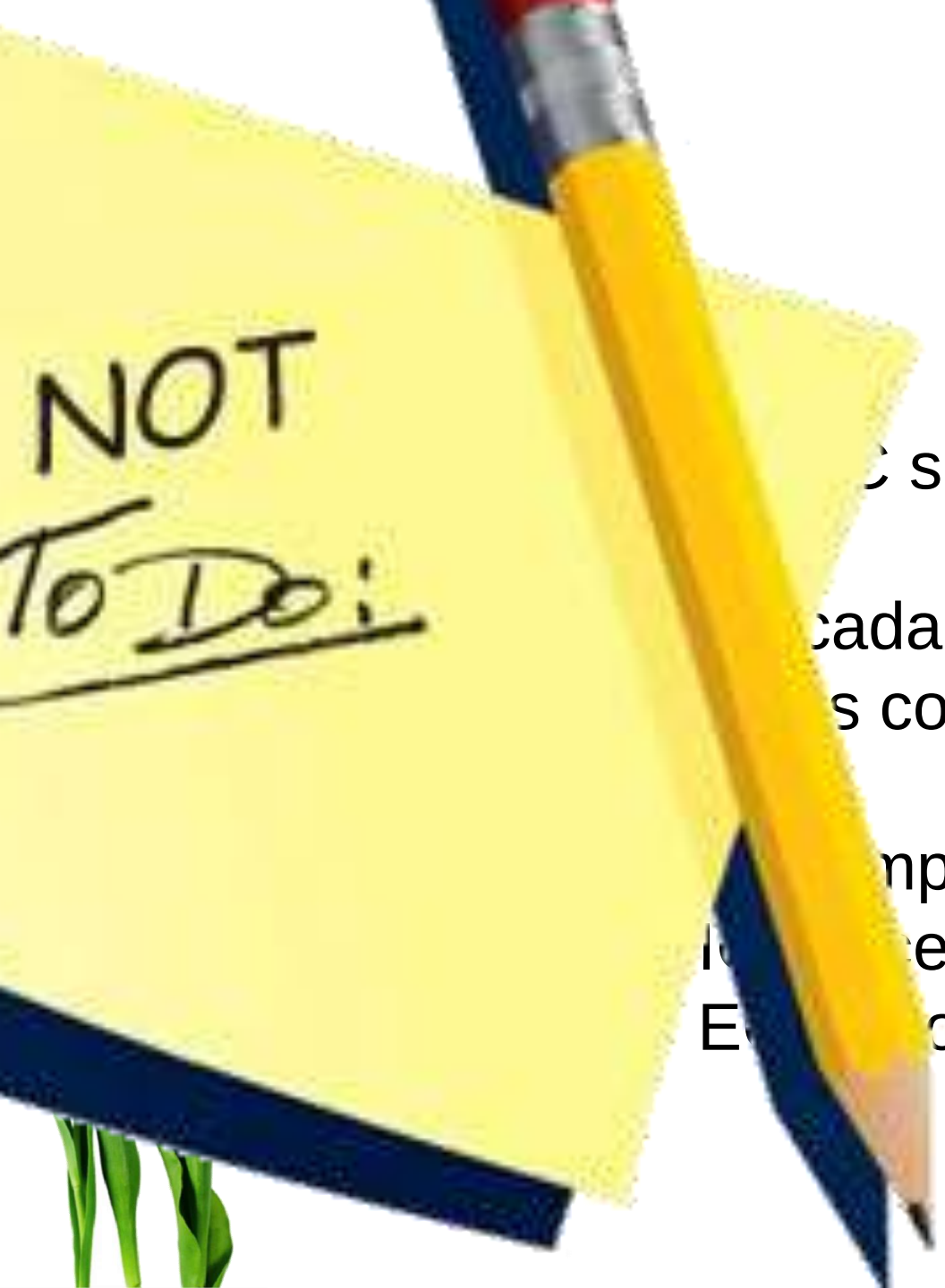
Lectura: Conseguir ACR es +



CI no ajustadas: cuidado con los IC!!

Porcentaje de solapamiento del IC	0%	5%	10%	15%	20%	25%
Valor de P	0.0056	0.0085	0.0126	0.0185	0.0266	0.0376





NOT
To Do:

son demasiado amplios

Para cada ECA se obtienen los
valores correspondientes a cada IC

Comparación de dos o más
grupos procedentes de distintos
Ecosistemas es un test estadístico

Comparaciones Indirectas ajustadas



What is indirect comparison?

Fujian Song
BMed MMed PhD
Reader in Research
Synthesis, Faculty
of Health, University
of East Anglia

- **Adjusted indirect comparison** (including mixed treatment comparison) is an indirect comparison of different treatments adjusted according to the results of their direct comparison with a common control, so that the strength of the randomised trials is preserved. Empirical evidence indicates that results of adjusted indirect comparison are usually, but not always, consistent with the results of direct comparison.



Ensayos diferentes frente a un tercer comparador común

Anti-TNF-α

Table 1 Characteristics of patients enrolled in placebo controlled, double blind, randomised controlled trials of the addition of tumour necrosis factor α blocking agents to methotrexate in patients with active rheumatoid arthritis

First author	Treatment group	RF(+) (%)
Weinblatt ²¹	Etanercept	86
Maini ¹⁹	Infliximab	81
Weinblatt ²²	Adalimumab	NS
Keystone ²³	Adalimumab	79

NS, not stated; RF, rheumatoid factor
*Combined treatment group
10 mg/kg every 8 weeks
†Treatment group that

Table 2 Adjusted indirect comparisons of the efficacy of TNFα blocking agents in placebo controlled, randomised, double blind trials in patients with active rheumatoid arthritis with an incomplete response to methotrexate

Comparison	Relative risk (95% CI)	
	ACR 20	ACR 50
Etanercept v adalimumab	1.10 (0.57 to 2.12)	2.60 (0.35 to 19.0)
Infliximab v adalimumab	1.07 (0.66 to 1.73)	1.35 (0.47 to 3.85)
Etanercept v infliximab	1.03 (0.49 to 2.18)	1.92 (0.22 to 17.0)

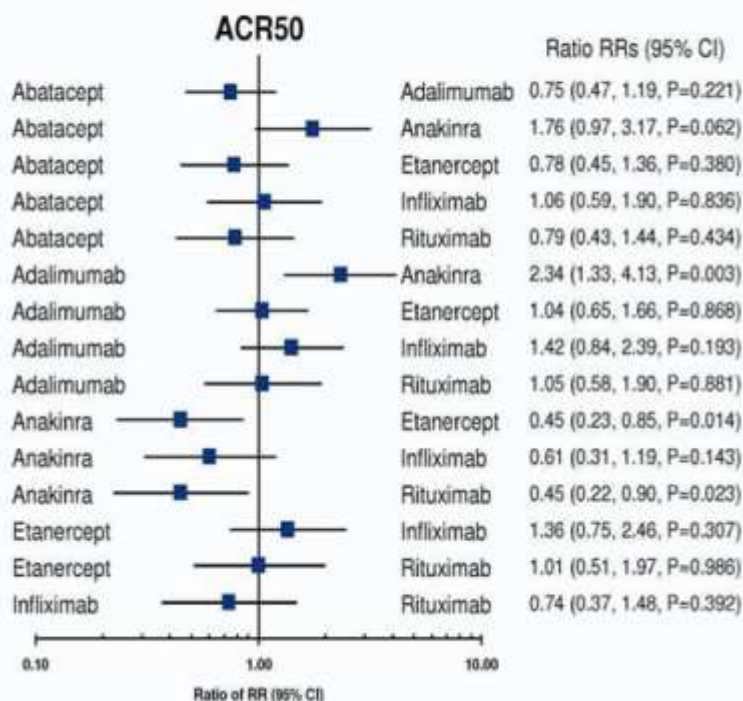
ACR, American College of Rheumatology; CI, confidence intervals.

weeks,

Biologics for rheumatoid arthritis: an overview of Cochrane reviews (Review)

DISCUSSION

Singh JA, Christensen R, Wells GA, Suarez-Almazo E, Tanjong Ghogomu E, **Summary of main results**



This is the first overview of Cochrane systematic reviews of biologic DMARDs for RA. We included updated reviews of six biologic DMARDs, including abatacept, adalimumab, anakinra, etanercept, infliximab and rituximab in recommended approved doses only.

Five of the six biologics were statistically significantly better than placebo in achieving ACR50, the main efficacy variable, as opposed to anakinra which was no different than placebo. The likelihood of achieving ACR50 varied with different biologic DMARDs. On the nominal level, all biologics had similar efficacy for ACR50 in indirect comparisons; it was evident that anakinra was half as efficacious as adalimumab, etanercept, and rituximab. This is an important observation, in the absence of direct comparisons of these biologic DMARDs in RCTs. While we noted that different types of patient populations were treated with different biologic DMARDs, with some biologics being used more in patients with longer disease duration and more DMARD failures than others, we are also aware of the limitations of such analyses, even when they were pre-specified. Most RCTs reported mean duration of RA (used for defining early, established and late RA), which may lead to ecological fallacy. Additionally, while these definitions of RA duration may not be universally accepted, these were perhaps the only clinically acceptable definitions available to us from the published literature available in existing Cochrane

Ens

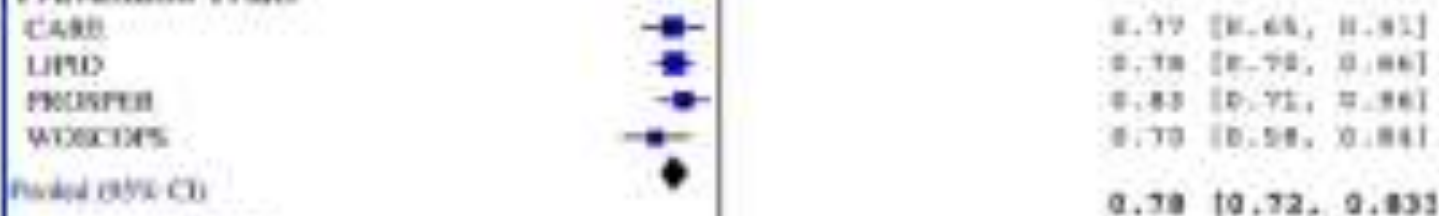
Est:

Major Coronary Events (fatal CHD, non-fatal MI)

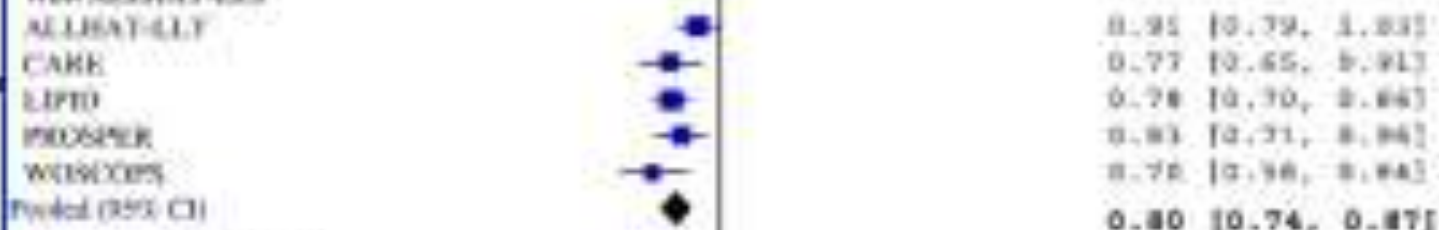
Simvastatin Trials



Pravastatin Trials



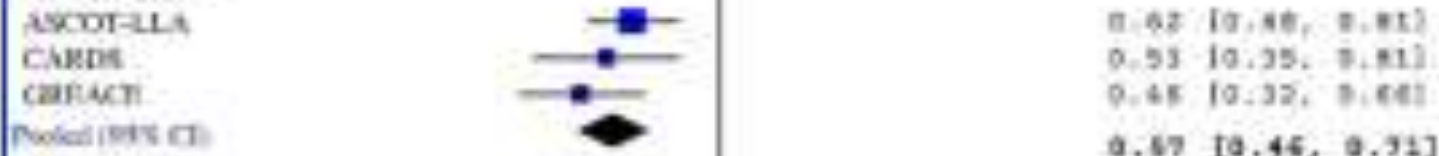
With ALTERNATE



Atorvastatin Trial



With GREACE



0.2 0.5 1 2 5

Favours Statin Favours Control

RR and 95% CI based on a random-effects model

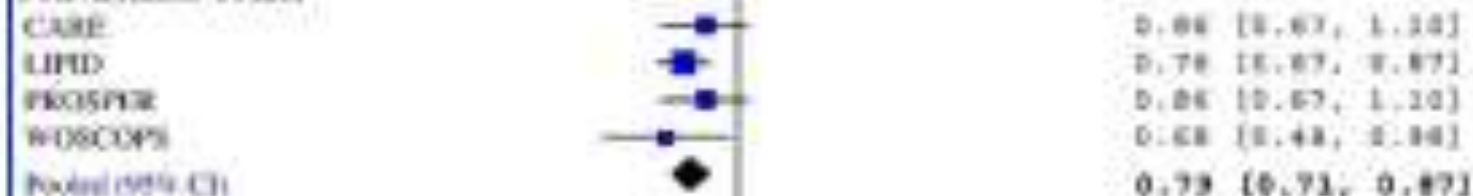
Major Cerebrovascular Events (fatal, non-fatal strokes)

All-Cardiovascular Death (coronary and cerebrovascular)

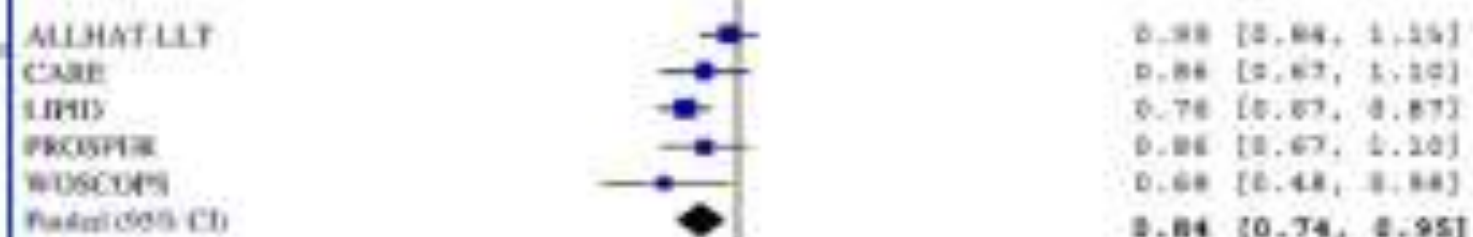
Simvastatin Trials



Pravastatin Trials



With ALLHAT-LLT



Atorvastatin Trial*



0.2 0.5 1 2 5
Favours Statin Favours Control
RR and 95% CI based on a random-effects model

(* Number of all cardiovascular death events not reported in the original publication of the GREACE trial)

All-Cause Mortality

En

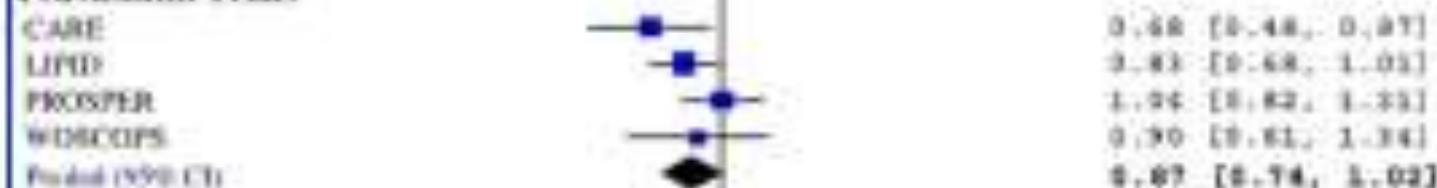
Es

Major Cerebrovascular Events (fatal, non-fatal strokes)

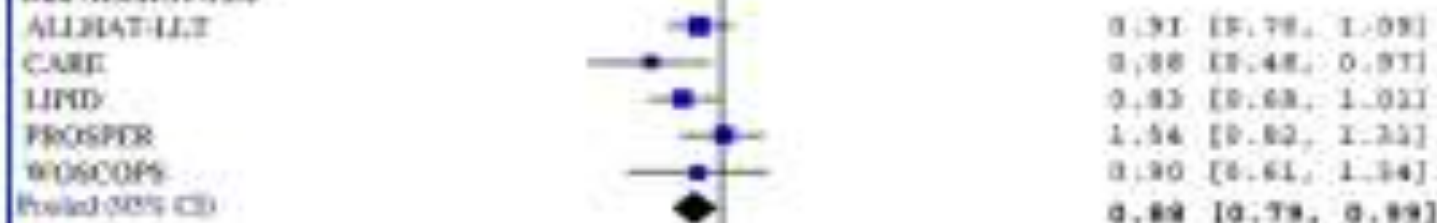
Simvastatin Trials



Pravastatin Trials



With ALLIAT-ALL



Atorvastatin Trial



With GREEK



0.2 0.5 1 2 5

Favours Statin Favours Control

RR and 95% CI based on a random-effects model

All-Cause Mortality

Simvastatin Trials

4S	0.71 [0.59, 0.85]
HPS	0.88 [0.82, 0.94]
Pooled (95% CI)	0.81 [0.65, 0.99]

Pravastatin Trials

CARE	0.82 [0.76, 1.11]
LIPID	0.78 [0.79, 0.88]
PROSPER	0.98 [0.84, 1.14]
WOSCOPS	0.78 [0.61, 1.01]
Pooled (95% CI)	0.86 [0.76, 0.98]

With ALHAT-LLT

ALHAT-LLT	0.89 [0.89, 1.09]
CARE	0.92 [0.76, 1.11]
LIPID	0.78 [0.70, 0.88]
PROSPER	0.98 [0.84, 1.14]
WOSCOPS	0.78 [0.61, 1.01]
Pooled (95% CI)	0.89 [0.80, 1.00]

Atorvastatin Trial

ASCOT-LLA	0.87 [0.71, 1.05]
CARDS	0.73 [0.53, 1.01]
Pooled (95% CI)	0.81 [0.70, 0.98]

With GREACE

ASCOT-LLA	0.87 [0.71, 1.05]
CARDS	0.73 [0.53, 1.01]
GREACE	0.58 [0.35, 0.95]
Pooled (95% CI)	0.78 [0.64, 0.95]

0.2 0.5 1 2 3

Favors Statin Favors Control

Ensayos diferentes frente a un tercer comparador común

Estatinas

Table II. Adjusted indirect comparisons between statins for different outcomes

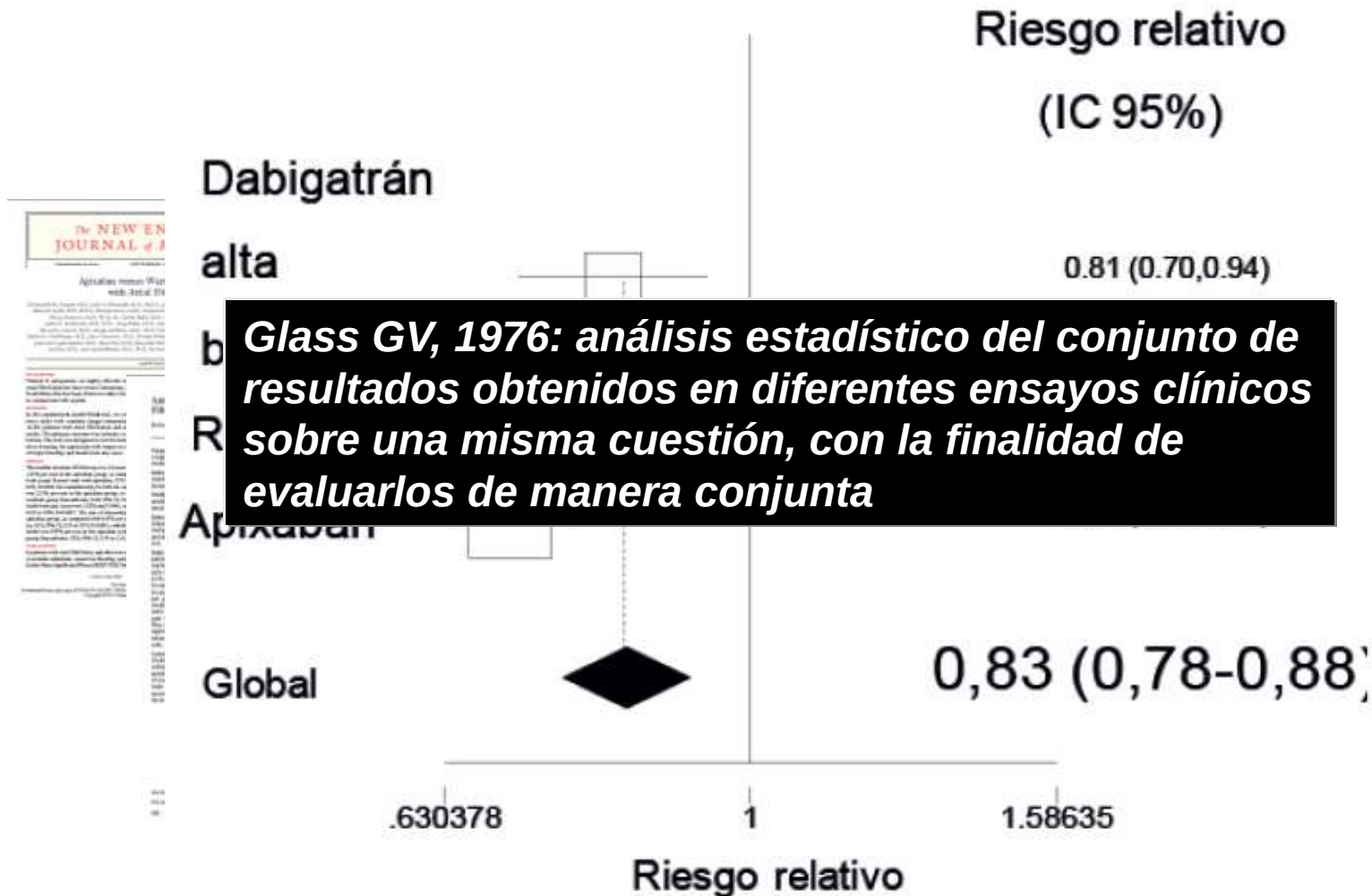
	Point estimate of relative effect (95% CI)	P*
Major coronary events (fatal CHD and nonfatal MI)		
Simvastatin vs pravastatin	0.93 (0.84-1.03)	.18
Atorvastatin vs simvastatin	0.84 (0.66-1.08)	.18
Atorvastatin vs pravastatin	0.79 (0.61-1.02)	.06
Major cerebrovascular events (fatal, nonfatal stroke)		
Simvastatin vs pravastatin	0.87 (0.71-1.07)	.18
Atorvastatin vs simvastatin	0.90 (0.68-1.20)	.47
Atorvastatin vs pravastatin	0.78 (0.57-1.07)	.12
All-cardiovascular death (coronary and cerebrovascular)		
Simvastatin vs pravastatin	0.96 (0.75-1.23)	.73
Atorvastatin vs simvastatin	1.10 (0.77-1.58)	.61
Atorvastatin vs pravastatin	1.05 (0.78-1.42)	.74
All-cause death		
Simvastatin vs pravastatin	0.93 (0.73-1.19)	.57
Atorvastatin vs simvastatin	1.03 (0.79-1.35)	.82
Atorvastatin vs pravastatin	0.96 (0.78-1.18)	.71

Conclusion Evidence from published statin randomized placebo-controlled trials suggests that pravastatin, simvastatin, and atorvastatin, when used at their standard dosages, show no statistically significant difference in their effect on long-term cardiovascular prevention. (Am Heart J 2006;151:273-81.)

¿Qué criterios ha de cumplir una CI ajustada?



Los mismos que los metanálisis



metanálisis

Sin protocolo de búsqueda



Revisión Narrativa



Revisión

Con protocolo de búsqueda



Revisión sistemática



Análisis Estadístico



Meta-análisis

metanálisis



metanálisis

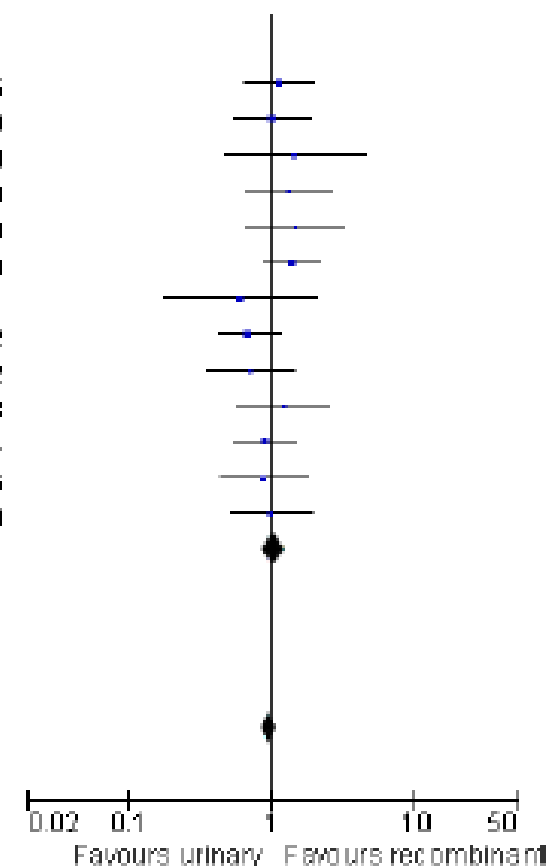
1.1.3 rFSH versus FSH-HP

Bergh 1997	40	119	36	116	4.0%	1.12 [0.65, 1.94]	1996
Frydman 2000	25	139	25	139	3.2%	1.00 [0.54, 1.84]	2000
Nardo 2000	12	75	4	35	0.9%	1.44 [0.46, 4.47]	2000
Lenton 2000	27	83	20	75	2.6%	1.32 [0.67, 2.61]	2000
Franco 2000	21	60	16	60	2.0%	1.47 [0.68, 3.19]	2000
Schats 2000	56	247	43	249	6.1%	1.40 [0.90, 2.18]	2000
Hugues 2001	7	56	6	32	0.8%	0.61 [0.18, 2.07]	2001
Belman 2002	41	134	52	133	4.7%	0.69 [0.42, 1.14]	2002
Dickey 2002	14	58	37	119	2.5%	0.71 [0.36, 1.42]	2002
Dickey 2003	24	60	21	60	2.2%	1.24 [0.59, 2.58]	2003
Cheon 2004	50	131	50	123	4.7%	0.90 [0.55, 1.49]	2004
Mohamed 2006	18	129	20	128	2.5%	0.88 [0.44, 1.74]	2006
Baker 2009	29	76	29	76	2.8%	1.00 [0.52, 1.92]	2009
Subtotal (95% CI)		1367		1345	39.0%	1.03 [0.86, 1.22]	

Total events 364 359
Heterogeneity: $\text{Chi}^2 = 8.64$, $\text{df} = 12$ ($P = 0.73$); $I^2 = 0\%$
Test for overall effect: $Z = 0.29$ ($P = 0.77$)

Total (95% CI) 3796 3543 100.0% 0.97 [0.87, 1.08]

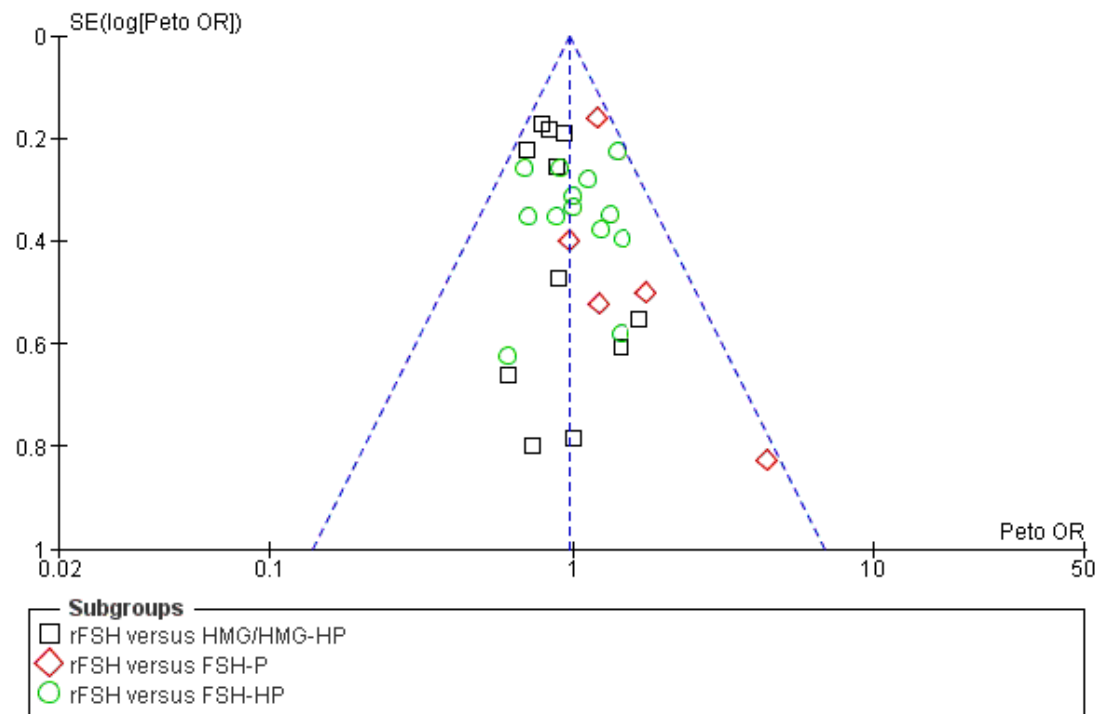
Total events 894 868
Heterogeneity: $\text{Chi}^2 = 22.50$, $\text{df} = 28$ ($P = 0.76$); $I^2 = 0\%$
Test for overall effect: $Z = 0.50$ ($P = 0.62$)
Test for subgroup differences: $\text{Chi}^2 = 8.81$, $\text{df} = 2$ ($P = 0.03$), $I^2 = 70.6\%$



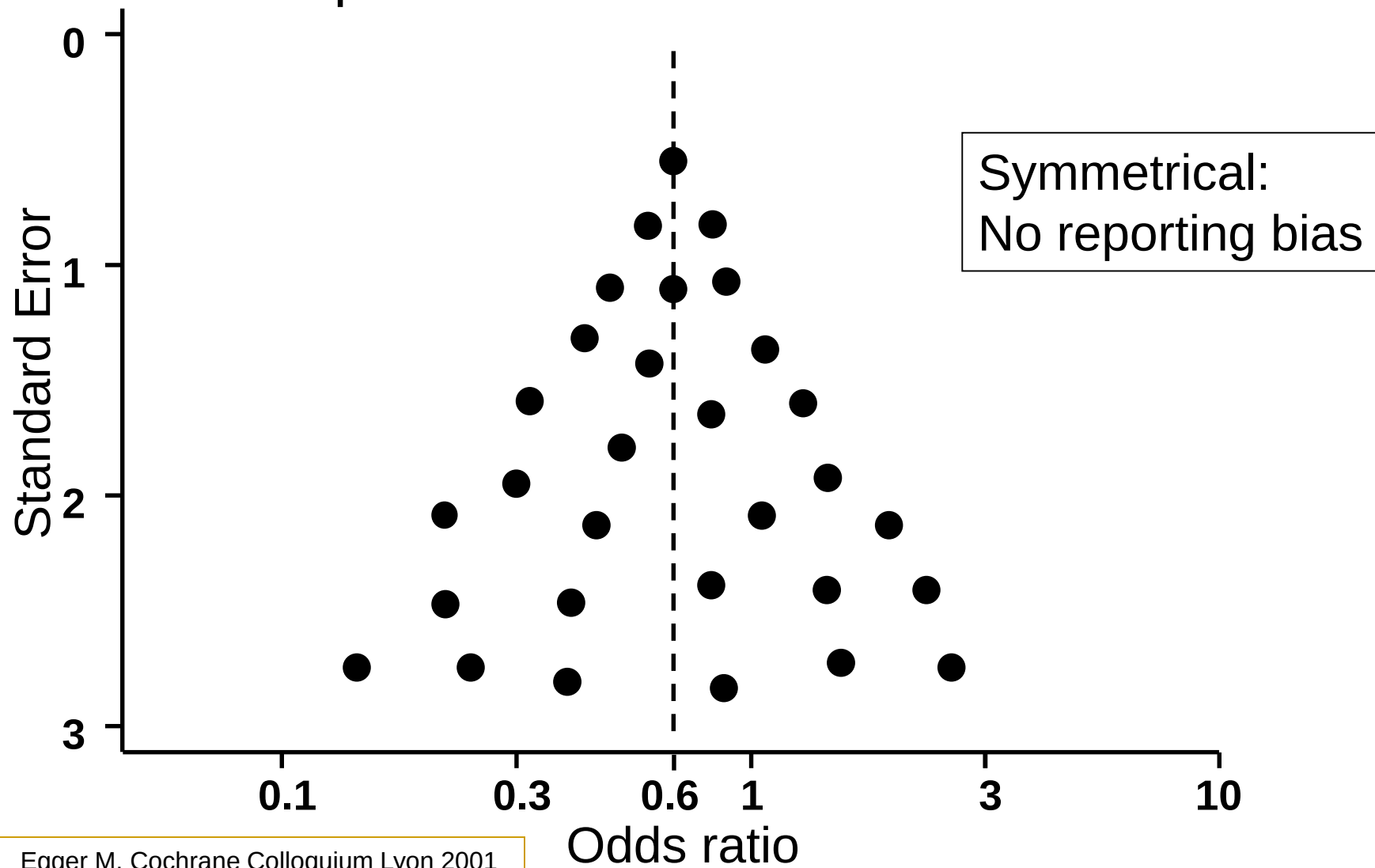
Herramientas de metanálisis.

Sesgos

Figure 3. Funnel plot of comparison: 1 rFSH versus urinary gonadotrophins, outcome: 1.1 Live birth (or pregnancy ongoing beyond 20 weeks).

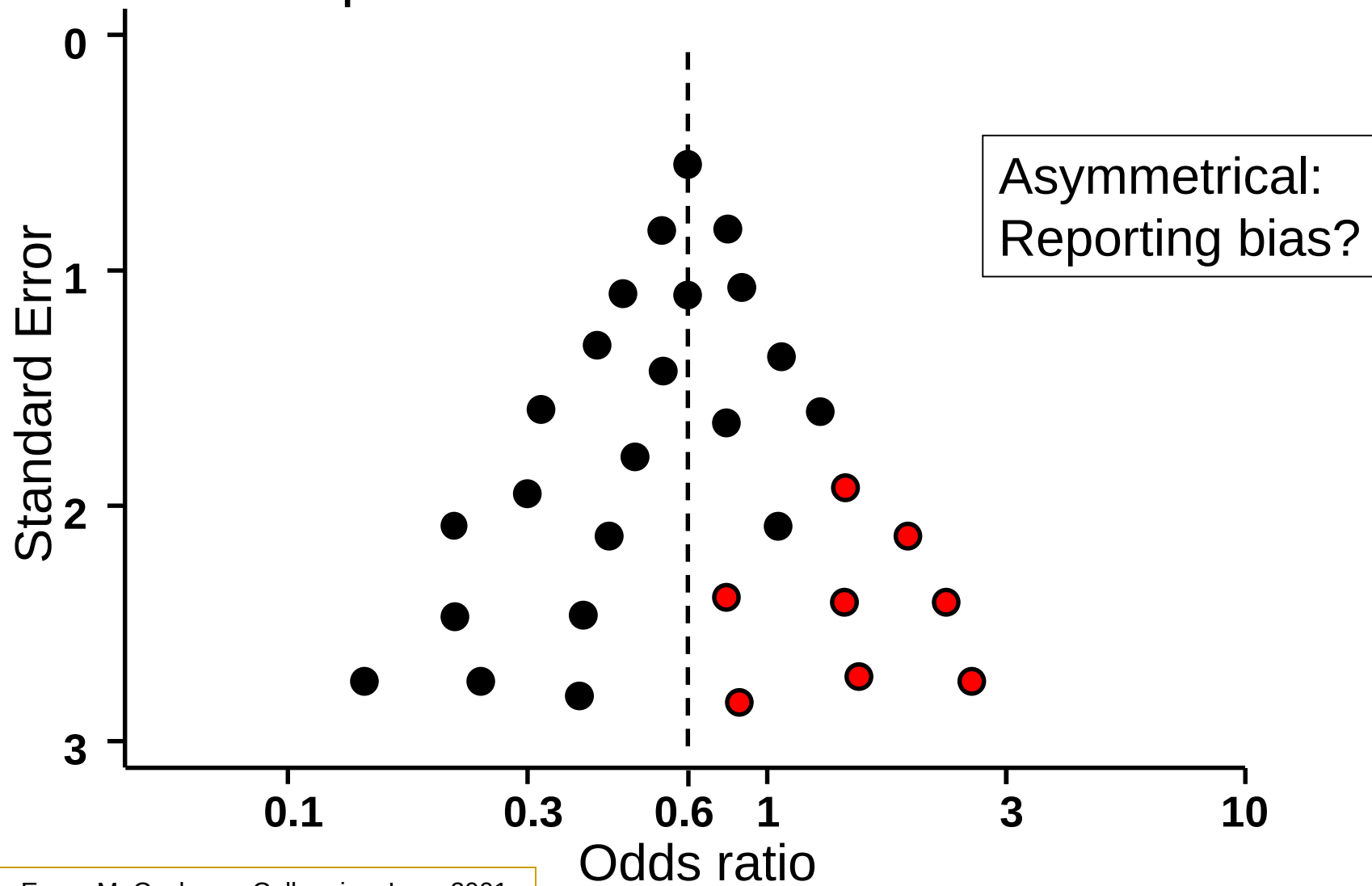


Funnel plot



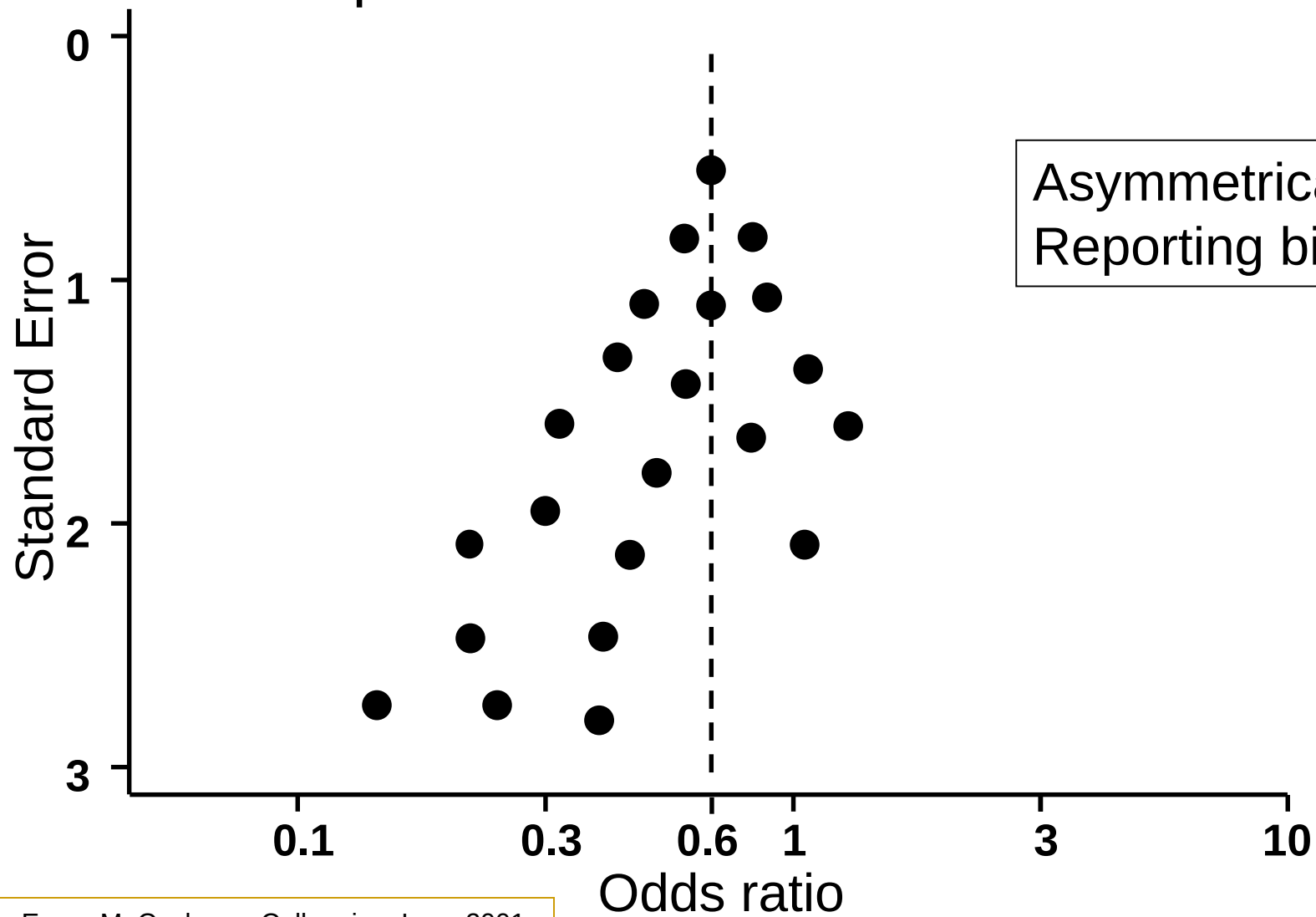
Egger M, Cochrane Colloquium Lyon 2001

Funnel plot



Egger M, Cochrane Colloquium Lyon 2001

Funnel plot



Asymmetrical:
Reporting bias?

Criterios de las comparaciones indirectas ajustadas



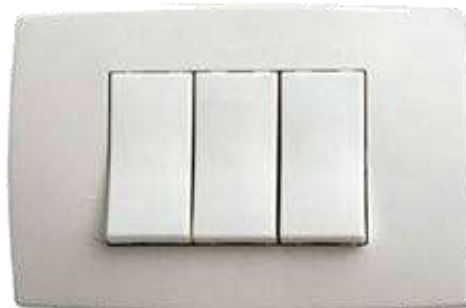
Homogeneidad



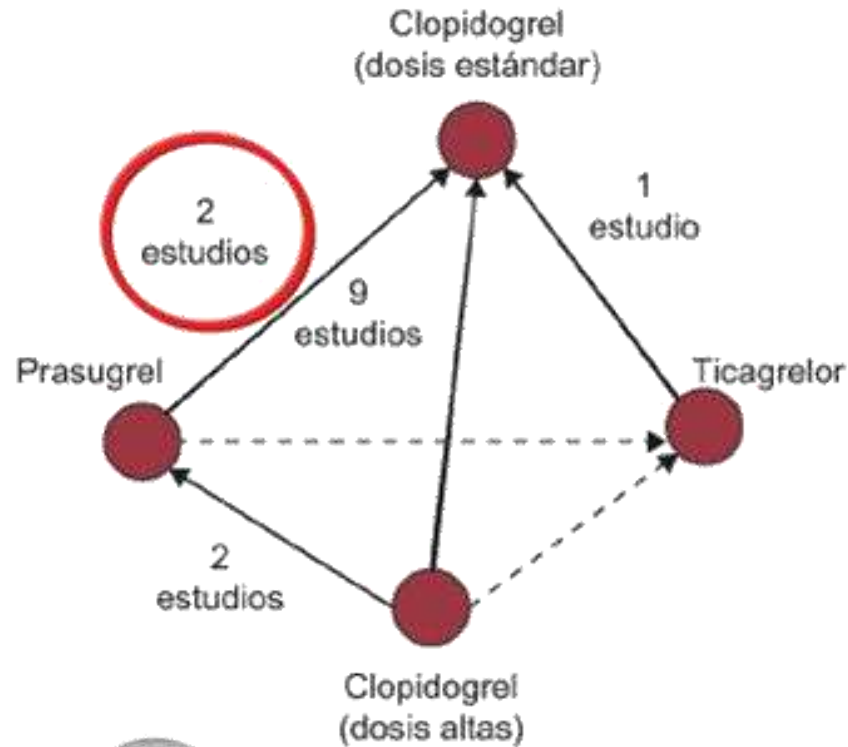
Semejanza



Consistencia



Homogeneidad



When multiple trials are available for a given comparison, the results from multiple trials *can* be pooled in meta-analyses before an adjusted indirect comparison is conducted



Homogeneidad

- Solo si hay varios estudios en la misma rama de la CI
- Variabilidad entre los resultados de los estudios en un meta-análisis
- Metodología bien establecida y relativamente sencilla (CASPe)



Measuring inconsistency in meta-analyses Julian P T Higgins, Simon G Thompson, Jonathan J Deeks, and Douglas G Altman *BMJ*, Sep 2003; 327: 557 – 560
Quantifying heterogeneity in a meta-analysis. Higgins JPT, Thompson SG. *Stat Med* 2002; 21:1539–58.

Homogeneidad

Se cuantifica a partir de:

Test I² (proporción de la variación de cada estudio respecto a la variación total)

Valores:

<25% puede ser no importante

25-50% heterogeneidad moderada

>75% heterogeneidad considerable



Semejanza

Grado de certeza en que el efecto del tratamiento en un brazo (de la CI) debería poderse generalizar a los pacientes del otro brazo

1. Clínica y demográfica

Edad, sexo, severidad de la enfermedad, comorbilidades, medicación coexistente, tiempo de respuesta, duración del tratamiento, dosis de fármaco, tiempo de seguimiento ...

2. Metodología

Aleatorización, Ocultación secuencia, enmascaramiento, tipo de análisis, pérdidas de seguimiento, abandonos.



Semejanza

“Si los pacientes en ambos brazos no son similares la diferencia (o igualdad) detectada a través de la CI puede ser debidas precisamente a ello”



“Similaridad en subgrupos de pacientes”



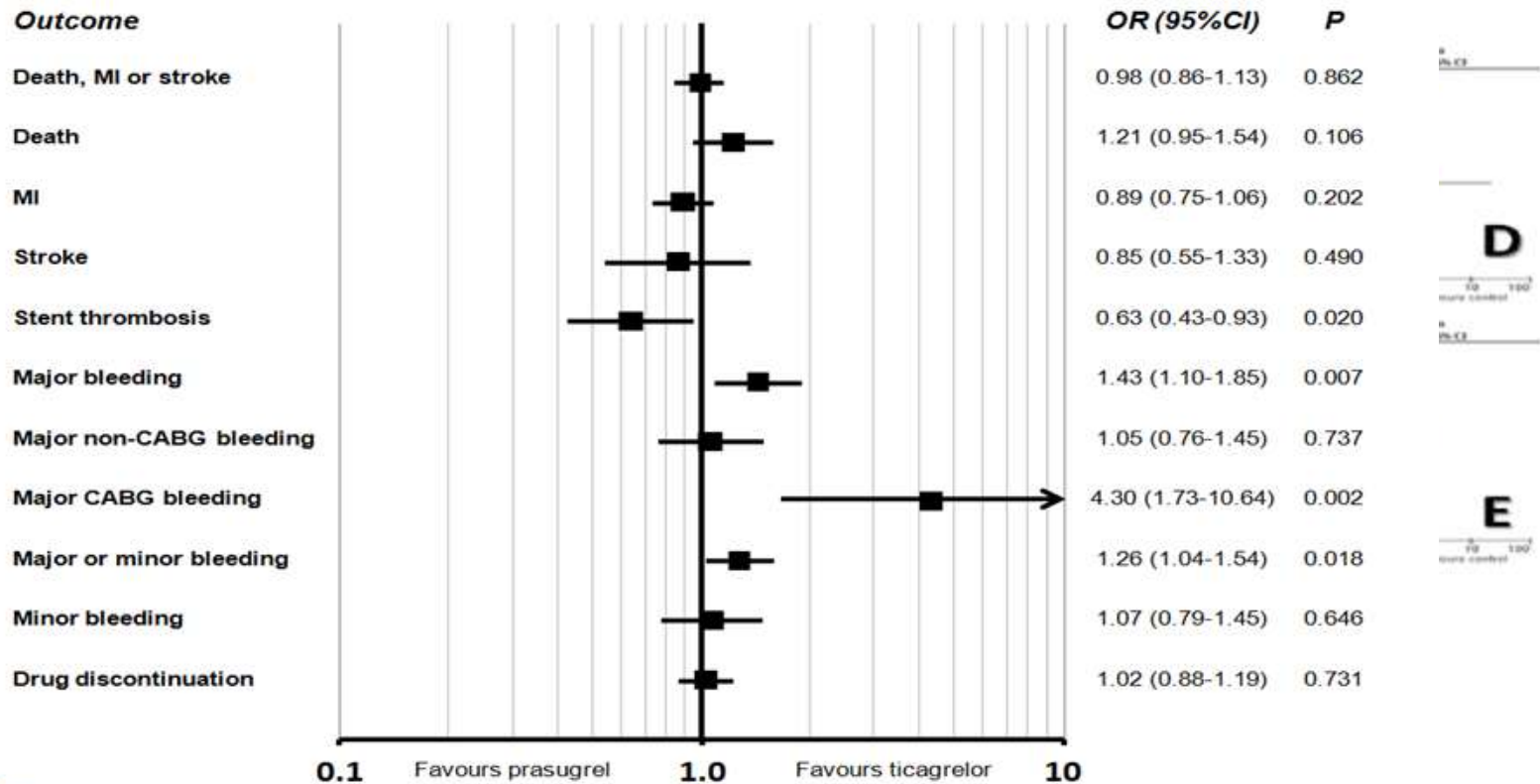
Semejanza

- No hay un método numérico
- Revisión exhaustiva de los estudios.
- Es clave para la validez de la CI



Fi. CI DI ΔTΔ fronte TRITON

Indirect comparison of prasugrel vs. ticagrelor



Funnel plots comparing prasugrel vs. ticagrelor for the risk of key clinical events. Odds ratios (OR) <1.0 favor prasugrel, whereas odds ratios >1.0 favor ticagrelor.

Funnel plots comparing prasugrel or ticagrelor vs. clopidogrel for the risk of: death, myocardial infarction or stroke (A); death (B); myocardial infarction (C); stroke (D); definite or probable stent thrombosis (E).

Consistencia

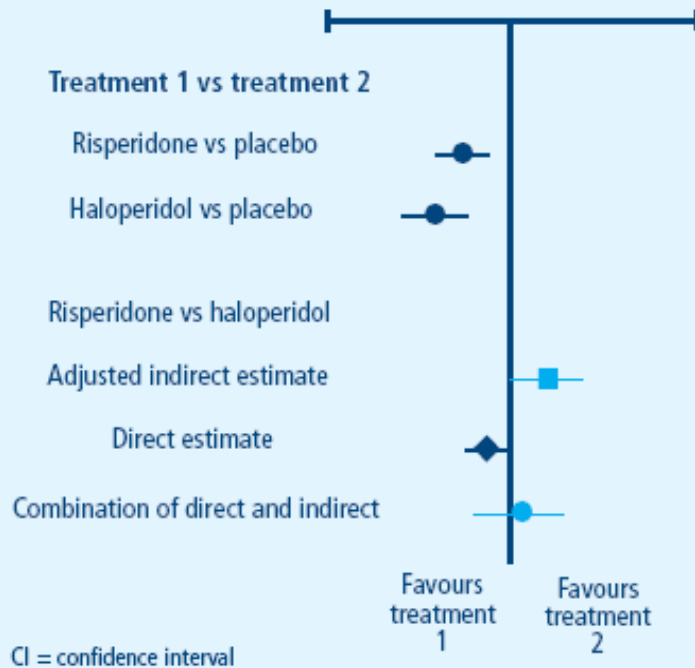
Table 1. Meta-analyses of risperidone versus haloperidol for schizophrenia: number of patients without clinical improvement²

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Risperidone vs placebo	3	-0.909 (0.218)	0.40 (0.26, 0.62)	37%
Haloperidol vs placebo	9	-1.707 (0.318)	0.18 (0.10, 0.34)	11%
Risperidone vs haloperidol				
Direct comparison	10	-0.262 (0.142)	0.77 (0.5	
Adjusted indirect comparison	3/9	0.798 (0.386)	2.22 (1.0	
Combination of direct and indirect estimates	10+(3/9)	0.207 (0.527)	1.23 (0.4	

NB Random-effects model was used in meta-analyses of trials and for the combination of indirect estimates. Odds ratio = EXP(log odds ratio).

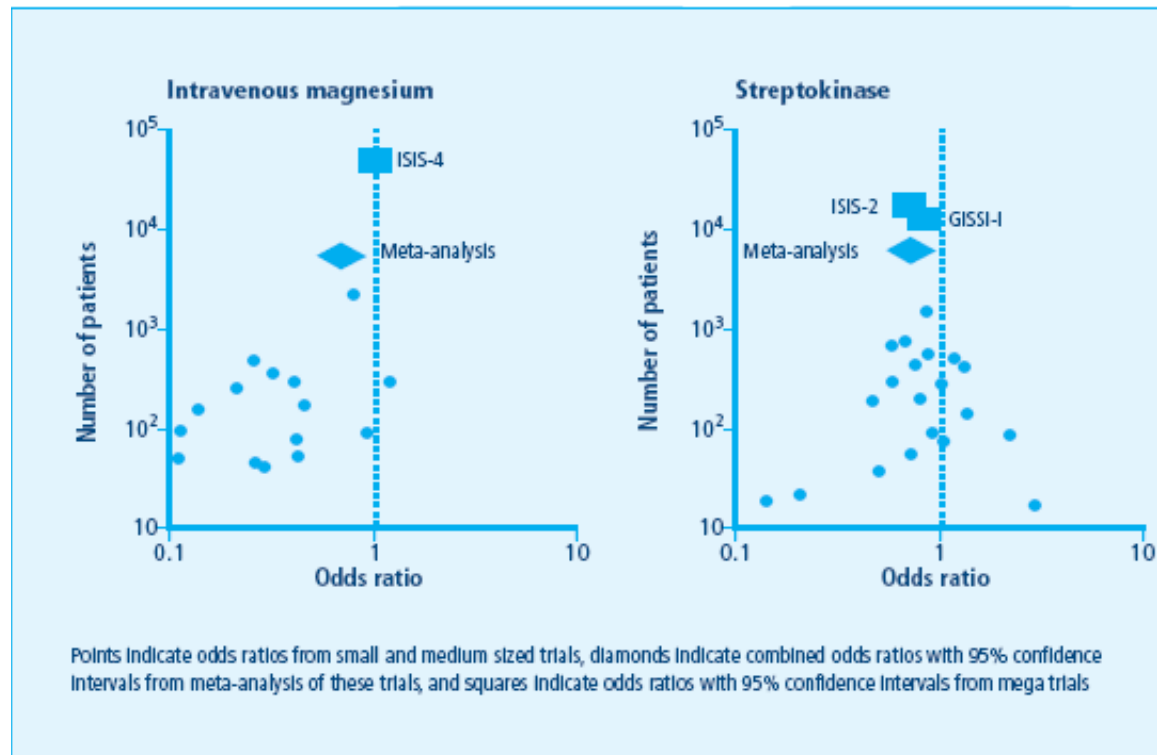
CI: confidence interval; SE: standard error

Lectura: estar sin mejora clínica es -



Validez de Metanálisis

- Válidez: Comparación resultado de metanálisis con resultado de gran ensayo clínico evaluando la misma cuestión



Validez de Metanálisis

- Se estima entre un 80%-90% la congruencia entre metanálisis y grandes EECC
- Una comparación de 12 metaanálisis con ensayos de gran tamaño reveló que a pesar de que se encontró congruencia en la dirección del efecto en un 80% de los casos, los resultados del metaanálisis hubieran conducido a la adopción de un tratamiento inefectivo en un 32% de los casos y a rechazar un tratamiento efectivo en un 33%

Validez de Metanálisis

No siempre se es congruente

- Los clínicos no recomiendan algunos tratamientos incluso 10 años después de que se haya demostrado su eficacia (*ej. tratamiento trombolítico*)
- Los clínicos continúan recomendando algunos tratamientos hasta 10 años después de que se haya demostrado su inutilidad (*ej. lidocaína profiláctica*)



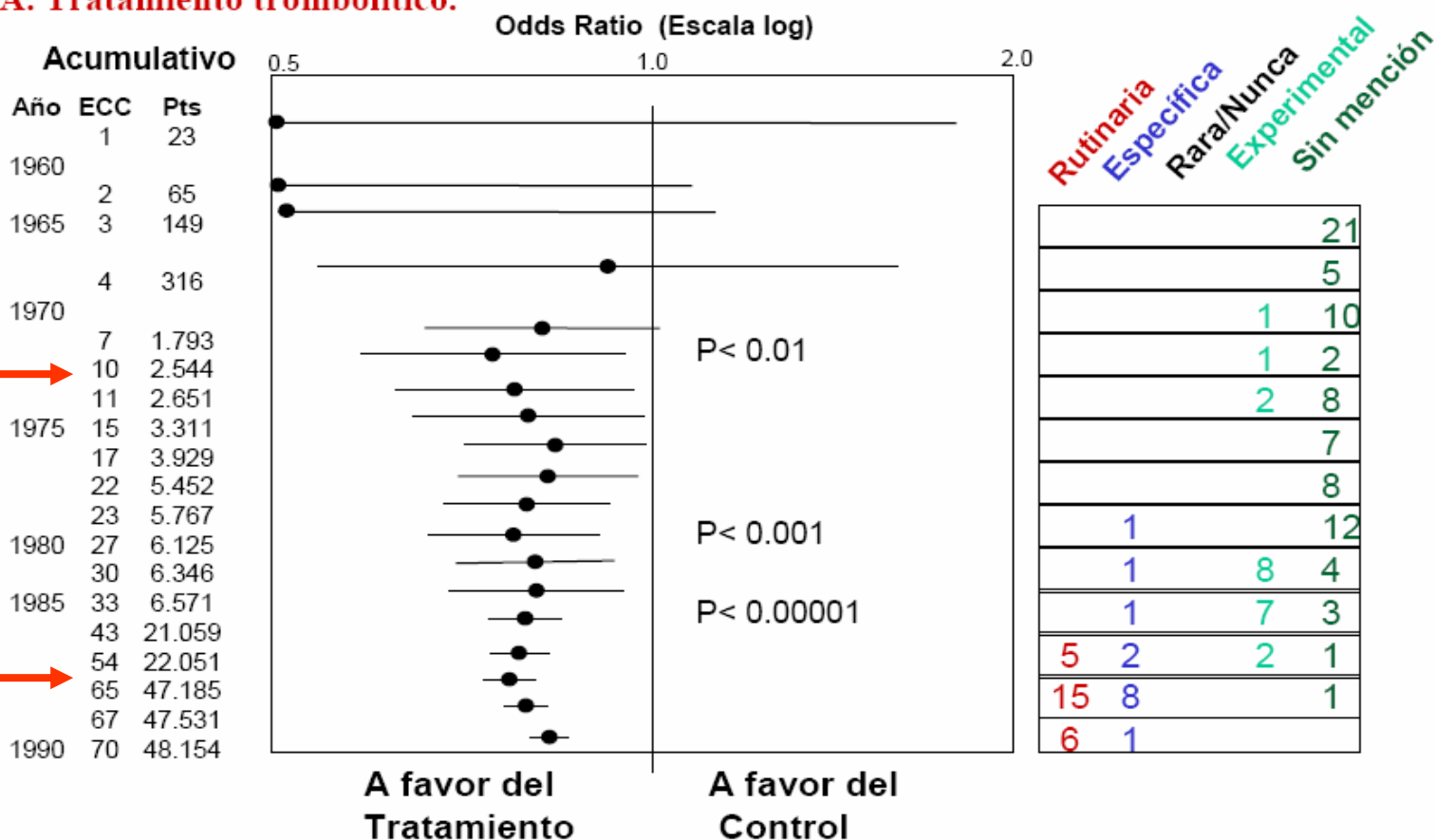
Antman E, Lau J, Kupelnick B, Mosteller F, Chalmers T.

Comparación de los resultados del metaanálisis sobre ensayos clínicos controlados (ECC) y recomendaciones de los expertos clínicos.

Tratamiento del infarto de miocardio. JAMA 1992; 2: 240.

A. Tratamiento trombolítico.

Texto / Revista
Recomendaciones





Antman E, Lau J, Kupelnick B, Mosteller F, Chalmers T.

Comparación de los resultados del metaanálisis sobre ensayos clínicos controlados (ECC) y recomendaciones de los expertos clínicos.

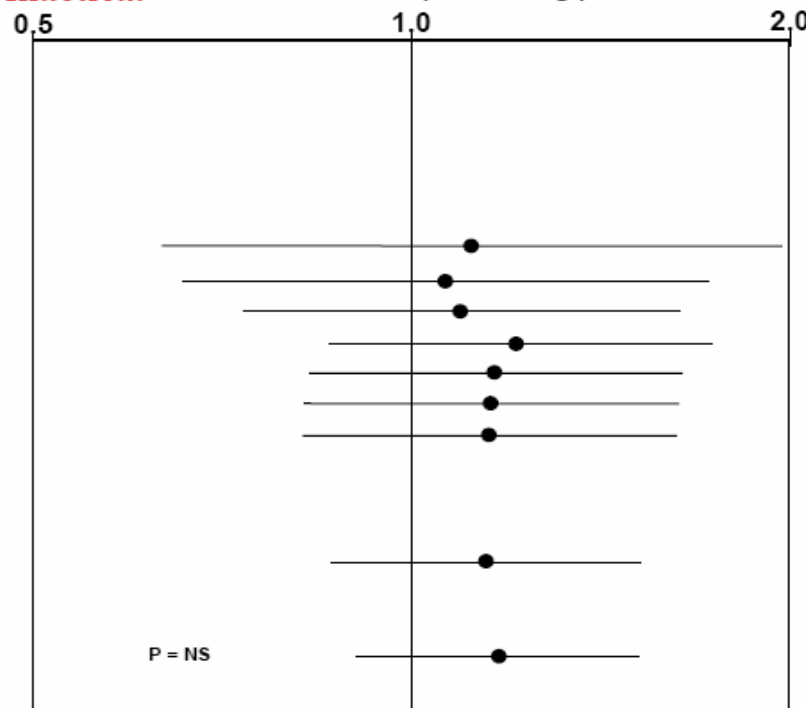
Tratamiento del infarto de miocardio. JAMA 1992; 2: 240.

B. Lidocaína profiláctica.

Acumulativo
Año ECC Pts

1960
1965
1970 2 304
5 647
6 850
8 1.239
9 1.451
1975 11 1.696
12 1.966
1980
1985 14 8.412
1990 15 8.745

Odds Ratio (Escala log.)



A favor del
Tratamiento

A favor del
Control

Texto / Revista
Recomendaciones

Rutinaria
Específica
Rara / Nunca
Experimental
Sin Mención

17	4
4	1
2 7 7	1
3	
8	2
1 4	2
4 2	1 1
4 8	1
5 6	2
3 5	3
4 8	1 3
5 9	4 6
1 3 2	1

Herramientas de metanálisis.

Calculadora

N° de estudios: 6						Grupo experimental			Grupo control			RR	IC 95%	z	p	Peso (%)
		Evento	No evento	Total		Evento	No evento	Total								
1		69	25,0	94		56	25,0	81		1,06	0,88 a 1,28	0,32	0,74546	47,2		
2		19	4,0	23		21	3,0	24		0,94	0,74 a 1,20	0,18	0,85453	16,1		
3		14	4,0	18		14	1,0	15		0,83	0,63 a 1,10	0,46	0,64218	12,0		
4		11	5,0	16		15	4,0	19		0,87	0,58 a 1,30	0,36	0,71895	10,8		
5		10	8,0	18		9	6,0	15		0,93	0,52 a 1,66	0,16	0,87031	7,7		
6		8	1,0	9		8	1,0	9		1,00	0,72 a 1,39	0,00	1,00000	6,3		
7																
8																
9																
10																
11																
12																
13																
14																
15																
16																
17																
18																
19																
20																
21																
22																
23																
24																
25																
26																
27																
28																
29																
30																
Total:		131,0	47,0	178,0		123,0	40,0	163,0								
Conceptos		Peto	OR MH	OR IV	OR DL	RR MH	RR IV	RR DL	DR MH	DR IV	DR DL	DPM IV	DPM DL	DEM Hedges	DEM Cohen	

Herramientas de CI ¿Como hacerlas?



The screenshot shows a software window titled 'Indirect Treatment Comparisons'. It has several sections: 'Effect measure:' with radio buttons for Relative Risk (RR), Odds Ratio (OR), Risk Difference (RD), Mean Difference (MD), and Hazard Ratio (HR); 'Number of Treatments:' with a dropdown menu set to 10; a table for inputting data; a 'Calculate' button; and a section for displaying results including 'Indirect Estimate: Treatments (1,8)', 'Effect measure:', 'Estimate:', '95% confidence interval:', and 'Test of association:'. The table has columns for 'Estimate', '95% LCL', '95% UCL', and 'Reverse'. The first row of the table is highlighted in yellow.

	Estimate	95% LCL	95% UCL	Reverse
(1,2)				☐
(2,3)				☐
(3,4)				☐
(4,5)				☐
(5,6)				☐
(6,7)				☐
(7,8)				☐
(8,9)				☐
(9,10)				☐



<http://www.cadth.ca>

Implicaciones

1. PIT
2. ATE
3. Económica
 - Estudios de minimización de costes
 - Concursos y Subastas públicas



Journal of
Clinical Pharmacy and Therapeutics
Journal of Clinical Pharmacy and Therapeutics, 2013 doi: 10.1111/jcpt.12048

Review Article

Direct and indirect comparison of the efficacy and safety of adalimumab, etanercept, infliximab and golimumab in psoriatic arthritis

S. Fénix-Caballero* PharmD, E. J. Alegre-del Rey* PharmD, R. Castaño-Lara† PharmD, F. Puigventós-Latorre‡ PharmD, J. M. Borrem-Rubio* PharmD and J. F. López-Vallada§ PharmD

*Pharmacy Department, Puerto Real University Hospital, Cádiz; †Pharmacy Department, Costa University Hospital, Costa; and ‡Pharmacy Department, San Espasa University Hospital, Palma de Mallorca, Spain



Implicaciones

	<u>% Ahorro</u>
■ Heparinas de BPM	80-100
■ Antieméticos 5-HT3	60-80
■ Factores Eritropoyéticos	40-60
■ Contrastes yodados no iónicos	40-60
■ G-CSF	30-40
■ Interferón alfa pegilado	30-50
■ IBP intravenosos	40-60
■ Agalsidasa alfa y beta	20-25
■ Equinocandinas	20-30

Take home message!!!



Las comparaciones indirectas permiten aportar evidencia en aquellos casos en los que las comparativas directas no están disponibles

La semejanza en la población analizada es una característica fundamental y necesaria

La CI naïves e informales no son suficientes para establecer conclusiones válidas

Take home message!!!



Las CI y los MA presentan puntos en común
El uso de ambas no es contradictorio, Δ las posibilidades posicionamiento

Los MA reducen amplias cantidades de información en porciones manejables
Permiten desarrollar GPC, el uso eficiente de los recursos

Δ el poder y la precisión
Limitan sesgos y mejoran exactitud