Análisis estadístico: medidas de asociación e impacto

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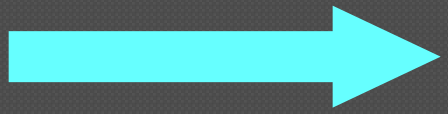
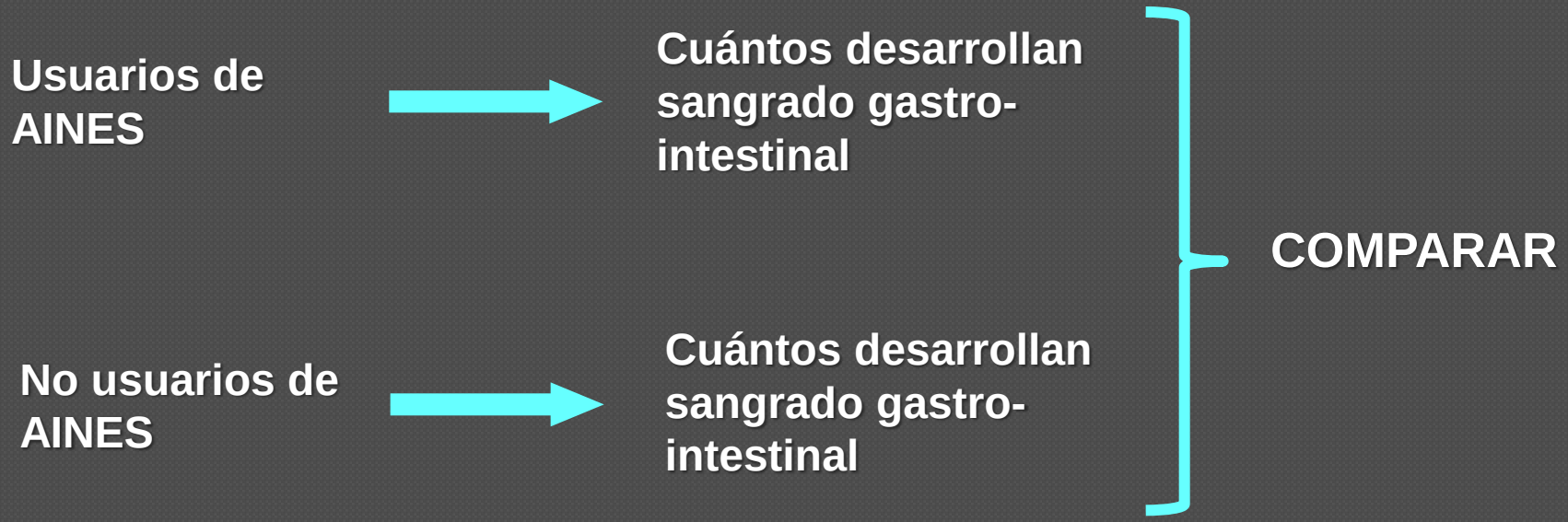
Riesgo

Es la probabilidad de enfermar o morir por estar expuesto a un determinado factor.

¿El uso de AINES incrementa el riesgo de sangrado gastro-intestinal?

Uso de AINES  **Sangrado gastro-intestinal**

Para responder esta pregunta la epidemiología utiliza un recurso metodológico: COMPARAR



La epidemiología es comparar

Comparar implica medir las diferencias y determinar si una variable está asociada a otra; o si la exposición a una variable afecta a otra.

La epidemiología es comparar

Usuarios de AINES → Cuántos desarrollan sangrado gastro-intestinal

No usuarios de AINES → Cuántos desarrollan sangrado gastro-intestinal

COMPARAR

Si hay más sangrado gastro-intestinal entre los usuarios de AINES

El uso de AINES estaría asociado al sangrado gastro-intestinal

Upper gastrointestinal bleeding among users of NSAIDs: a population-based cohort study in Denmark

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Aims It is well-known that use of nonsteroidal anti-inflammatory drugs (NSAIDs) increases the risk of upper gastrointestinal bleeding (UGIB), but characteristics of the association and quantification of excess risk at the population level require clarification.

Methods All users of nonaspirin prescription NSAIDs in North Jutland County, Denmark during 1991–95 were identified in the regional Pharmaco-Epidemiologic Database. Using the Hospital Discharge Register, all hospitalizations for UGIBs were identified among the 156 138 users of NSAIDs and compared with the number of expected based on the North Jutland population who did not receive NSAID prescriptions.

Table 2 Observed (Obs) and expected (Exp) number and O/E ratios of UGIB associated with current and former NSAID use among persons with at least one NSAID prescription recorded in the North Jutland County Pharmaco-Epidemiologic Prescription Database, 1991–95. Exposure window is 90 days for all drugs considered.

Periods of drug use	*Number of persons*	*Person-years*	*UGIB*			
			Obs	*Exp*	*O/E*	*95% CI*
Current use of NSAID	156 138	107 305	515	124.9	4.12	3.8, 4.5
NSAID only	152 882	94 987	365	101.2	3.61	3.3, 4.0
NSAID + glucocorticoids	17 875	5908	58	8.0	7.24	5.5, 9.4
NSAID + glucocorticoids + other drug (not anticoagulants)	1593	464	7	1.1	6.41	2.6, 13.2
NSAID + anticoagulants	1001	340	8	0.7	11.46	4.9, 22.6
NSAID + anticoagulants + other drug (not glucocorticoids)	178	35	0	0.1	–	–
NSAID + glucocorticoids + anticoagulants ± other drugs	154	29	1	0.1	18.74	0.2, 10.4
NSAID ± lowdose aspirin ± highdose aspirin	10 246	5542	76	13.8	5.52	4.3, 6.9
Former use of NSAID	145 877[1]	314 278	370	264.4	1.40	1.3, 1.5
Non use of any other drug[2]	144 584	294 676	267	224.9	1.19	1.0, 1.3
Current use of other drug[2] (not NSAID)	28 455	19 602	103	39.6	2.60	2.1, 3.2

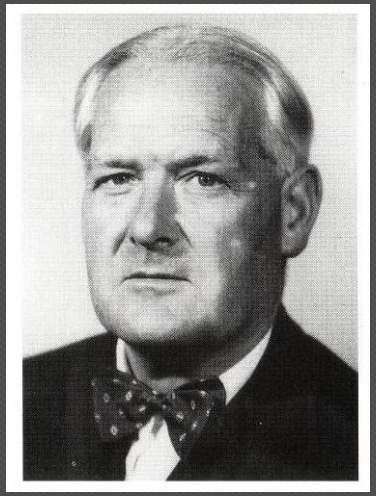
[1]Among the 156 138 NSAID users, 145 877 were followed during periods of non use 90 or more days after a nonrenewed prescription.
[2]The category includes drugs suspected to predispose to UGIB (low- and high dose aspirin, anticoagulants and glucocorticoids).

¿Qué es una asociación causal?

- Cuando se encuentra que un factor explica la aparición o exacerbación de un situación dada, hablamos de la existencia de una asociación causal.

- Para poder determinar relación causal se tiene que cumplir con determinados criterios.

Criterios de Hill



Sir Austin Bradford Hill propuso, en 1965, una serie de criterios a tener en cuenta para distinguir entre asociaciones causales y no causales:

Fuerza de Asociación, Consistencia, Especificidad, Temporalidad, Gradiente Biológica, Plausibilidad, Coherencia, Evidencia Experimental y Analogía.

Medidas de fuerza de asociación

Las medidas que nos ayudan a obtener esta información son:

Riesgo relativo (RR)
Odds ratio (OR).

Riesgo Relativo (RR)

El RR es una razón que relaciona el riesgo absoluto (incidencia) en dos grupos de población que difieren por el grado de exposición a un factor determinado.

Indica cuantas veces es mayor la probabilidad de sufrir una enfermedad entre quienes están expuestos al factor, respecto a los no expuestos.

Riesgo Relativo (RR)

$$\text{Riesgo Relativo (RR)} = \frac{\text{Incidencia entre los expuestos}}{\text{Incidencia entre los no expuestos}}$$

Riesgo Relativo (RR)

Exposición	Enfermedad: Presente	Enfermedad: Ausente	Total
Presente	a	b	a + b
Ausente	c	d	c + d

$$\text{Riesgo Relativo} = \frac{a / (a + b)}{c / (c + d)}$$

Riesgo Relativo (RR)

Uso de AINES	Sangrado digestivo: Sí	Sangrado digestivo: No	Total
Sí	20	1480	1500
No	5	1695	1700

$$\text{Riesgo Relativo} = \frac{20 / 1500}{5 / 1700} = \frac{0.0133}{0.0029} = 4.53$$

Odds Ratio (OR)

No siempre es posible calcular la incidencia en los estudios de investigación. Se calcula entonces la Odds Ratio (razón de ventaja, razón de chances, razón de momios, razón de productos cruzados).

Para un evento E, que ocurre con probabilidad P, la Odds se define como:

$$P / (1 - P)$$

Es decir, la probabilidad de “éxito” entre la probabilidad de “no éxito”.

Odds Ratio (OR)

$$\text{Odds Ratio (OR)} = \frac{\text{Odds entre los expuestos}}{\text{Odds entre los no expuestos}}$$

Odds Ratio (OR)

Exposición	Enfermedad: Presente	Enfermedad: Ausente	Total
Presente	a	b	a + b
Ausente	c	d	c + d

$$\text{Odds Ratio} = \frac{a/(a+b)}{b/(a+b)} \Big/ \frac{c/(c+d)}{d/(c+d)} = \frac{a}{b} \Big/ \frac{c}{d} = \frac{ad}{bc}$$

Odds Ratio (OR)

Exposición	Enfermedad: Presente	Enfermedad: Ausente
Presente	a	b
Ausente	c	d
Total	a + c	b + d

$$\text{Odds Ratio} = \frac{a / (a+c)}{c / (a+c)} \Big/ \frac{b / (b+d)}{d / (b+d)} = \frac{a}{c} \Big/ \frac{b}{d} = \frac{ad}{bc}$$

Odds Ratio (OR)

Uso de AINES	Hemorragia digestiva: Sí	Hemorragia digestiva: No
Sí	40	23
No	10	27
	50	50

$$\text{Odds Ratio} = \frac{40 \times 27}{23 \times 10} = 4.70$$

¿Cuándo el OR es un buen estimador del RR?

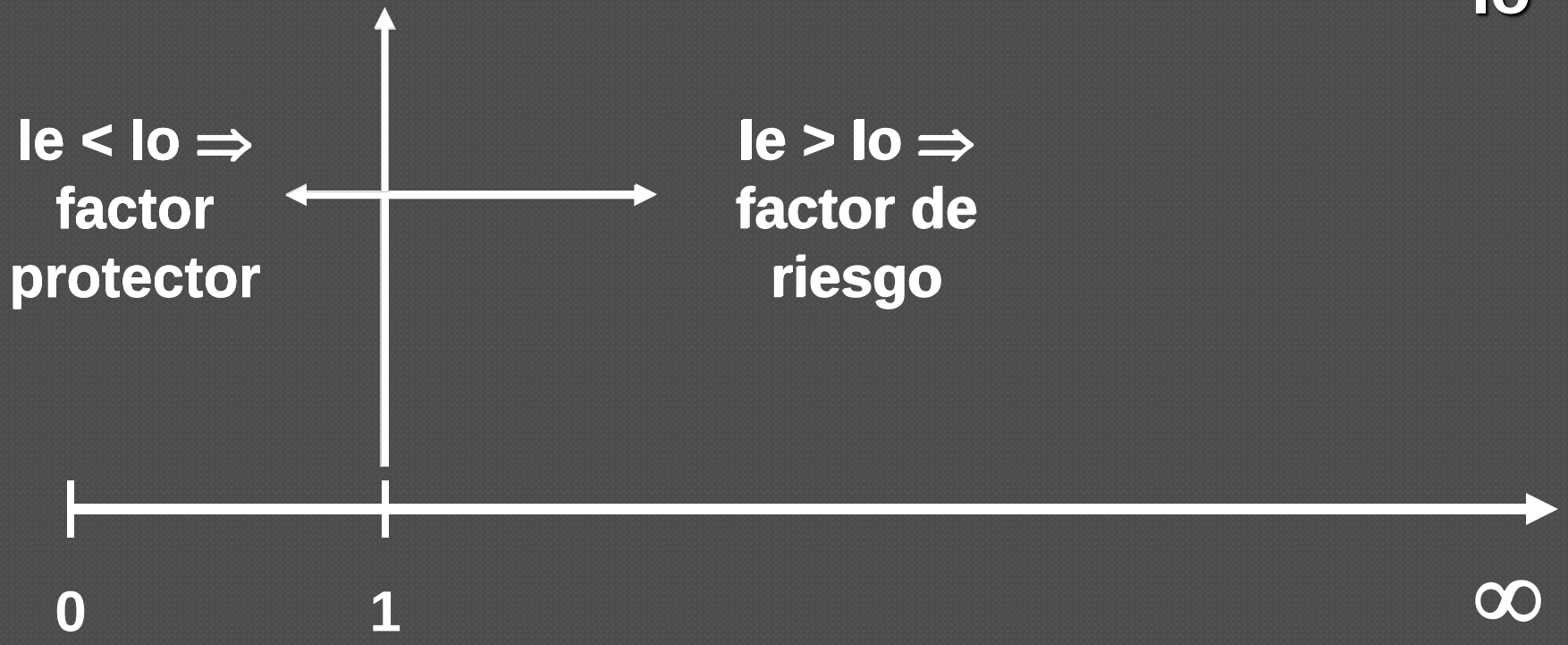
1. Cuando los “casos” son representativos, en relación a la historia de exposición, de todas las personas con la enfermedad en la población de la cual los casos son seleccionados.
2. Cuando los “controles” son representativos, en relación a la historia de exposición, de todas las personas sin la enfermedad en la población de la cual los casos son seleccionados.
3. ***Cuando la enfermedad es rara.***

Riesgo (Incidencia)	Odds ((riegso/(1-riesgo))
0.001	0.001
0.005	0.005
0.010	0.010
0.050	0.053
0.100	0.111
0.200	0.250
0.300	0.429
0.400	0.667
0.500	1.000
0.750	3.000
0.900	9.000
0.950	19.000
0.990	99.000

Interpretación del RR y OR

Ie = Io ⇒ Sin efecto

$$OR \approx RR = \frac{Ie}{Io}$$



Interpretación del RR y OR

Rango de RR y OR	Interpretación
0 – 0.3	Beneficio grande
0.4 – 0.5	Beneficio moderado
0.6 – 0.8	Beneficio leve
0.9 – 1.1	Sin efecto
1.2 – 1.6	Riesgo leve
1.7 – 2.5	Riesgo moderado
> 2.6	Riesgo elevado

Interpretación del RR y OR

Al reportar los valores de RR y OR, deben estar acompañados de sus intervalos de confianza.

Si el RR u OR incluye la unidad (1), el RR u OR encontrado no es significativo.

BMJ

BMJ 2012;344:e2697 doi: 10.1136/bmj.e2697 (Published 24 April 2012)

RESEARCH

Angiotensin receptor blockers and risk of cancer: cohort study among people receiving antihypertensive drugs in UK General Practice Research Database

Krishnan Bhaskaran *lecturer in statistical epidemiology*[1], Ian Douglas *lecturer in pharmacoepidemiology*[1], Stephen Evans *professor of pharmacoepidemiology*[2], Tjeerd van Staa *head of GPRD research*[3 4], Liam Smeeth *professor of clinical epidemiology*[1]

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Table 3| **Rate of any and specific cancers by treatment and crude and adjusted hazard ratios in people with hypertension taking angiotensin receptor blocker (ARB) or angiotensin converting enzyme (ACE) inhibitor**

	Total cancers	Total person time	Rate per 1000 person years (95% CI)	HR (95% CI)		P value†
				Crude	Adjusted*	
Any cancer						
Ever used ARB	5077	385 101	13.2 (12.8 to 13.6)	0.99 (0.96 to 1.02)	1.03 (0.99 to 1.06)	0.10
ACE inhibitor use only	15126	1 157 222	13.1 (12.9 to 13.3)	1.00‡	1.00‡	
Lung cancer						
Ever used ARB	422	385 101	1.1 (1.0 to 1.2)	0.72 (0.65 to 0.80)	0.84 (0.75 to 0.94)	0.003
ACE inhibitor use only	1722	1 157 222	1.5 (1.4 to 1.6)	1.00‡	1.00‡	
Breast cancer						
Ever used ARB	780	221 072	3.5 (3.3 to 3.8)	1.11 (1.02 to 1.21)	1.11 (1.01 to 1.21)	0.02
ACE inhibitor use only	1631	523 186	3.1 (3.0 to 3.3)	1.00‡	1.00‡	
Prostate cancer						
Ever used ARB	700	164 029	4.3 (4.0 to 4.6)	1.14 (1.05 to 1.24)	1.10 (1.00 to 1.20)	0.04
ACE inhibitor use only	2325	634 035	3.7 (3.5 to 3.8)	1.00‡	1.00‡	
Colon cancer						
Ever used ARB	384	385 101	1.0 (0.9 to 1.1)	0.99 (0.88 to 1.11)	1.02 (0.91 to 1.16)	0.70
ACE inhibitor use only	1132	1 157 222	1.0 (0.9 to 1.0)	1.00‡	1.00‡	

*Adjusted for age, sex, BMI, smoking, alcohol, diabetes (with or without metformin/insulin use), hypertension, heart failure, statin use, index of multiple deprivation score, calendar year.

†From Cox model with angiotensin receptor blocker/ACE inhibitor status treated as time updated covariate. Estimates from Cox model (for any cancer) suggested that only male sex (1.42, 1.38 to 1.47, older age (5.55, 5.23 to 5.88, for ≥75 *v* 18-54), smoking (1.49, 1.43 to 1.55), and history of heart failure (1.14, 1.08 to 1.19) were significantly associated with increased cancer risk. There was also evidence of variation by calendar year (P<0.001).

‡Reference category.

Conclusions Use of angiotensin receptor blockers was not associated with an increased risk of cancer overall. Observed increased risks for breast and prostate cancer were small in absolute terms, and the lack of association with duration of treatment meant that non-causal explanations could not be excluded.

Rheumatology 2003;42:1477–1485
doi:10.1093/rheumatology/keg398, available online at www.rheumatology.oupjournals.org
Advance Access publication 16 July 2003

A randomized placebo-controlled trial of arthroscopic lavage versus lavage plus intra-articular corticosteroids in the management of symptomatic osteoarthritis of the knee

M. D. Smith, M. Wetherall, T. Darby, A. Esterman[1], J. Slavotinek[2], P. Roberts-Thomson[3], M. Coleman[4] and M. J. Ahern

Objective. To assess the efficacy of intra-articular steroid injections following arthroscopy and joint lavage in symptomatic OA of the knee.
Methods. Seventy-seven patients with OA of the knee were randomized to receive either 120 mg methylprednisolone acetate (MPA) or placebo following arthroscopy. Clinical assessments included severity of pain on movement and at rest,

TABLE 3B. Presence of effusions

Time (weeks)	Presence of effusion (%)		Unadjusted RR	95% CI	Adjusted RR[a]	95% CI
	Active ($n=38$)	Placebo ($n=33$)				
0	19 (50)	20 (39)	–	–	–	–
2	2 (5.3)	9 (27)	0.193	0.045–0.831	0.082	0.012–0.558
4	6 (15.8)	11 (33)	0.474	0.196–1.140	0.275	0.080–0.948
8	6 (15.8)	11 (33)	0.474	0.196–1.140	0.213	0.063–0.724
12	9 (23.7)	9 (36)	0.651	0.315–1.348	0.566	0.211–1.520
24	10 (26.3)	12 (36)	0.724	0.360–1.454	0.338	0.126–0.911

[a]Adjusted for X-ray severity and baseline effusion.

Medición del Impacto

Si se establece una asociación estadística entre un factor y un problema de salud, se debe investigar entonces el impacto que tendrá dicho factor, ya sea desde el punto de vista de riesgo o beneficio.

Medición del Impacto

Impacto positivo:

- Reducción absoluta del riesgo
- Reducción relativa del riesgo
- Número necesario a tratar

Impacto negativo:

- Riesgo atribuible
- Fracción etiológica de riesgo
- Número necesario para dañar (perjudicar)

Reducción absoluta del riesgo

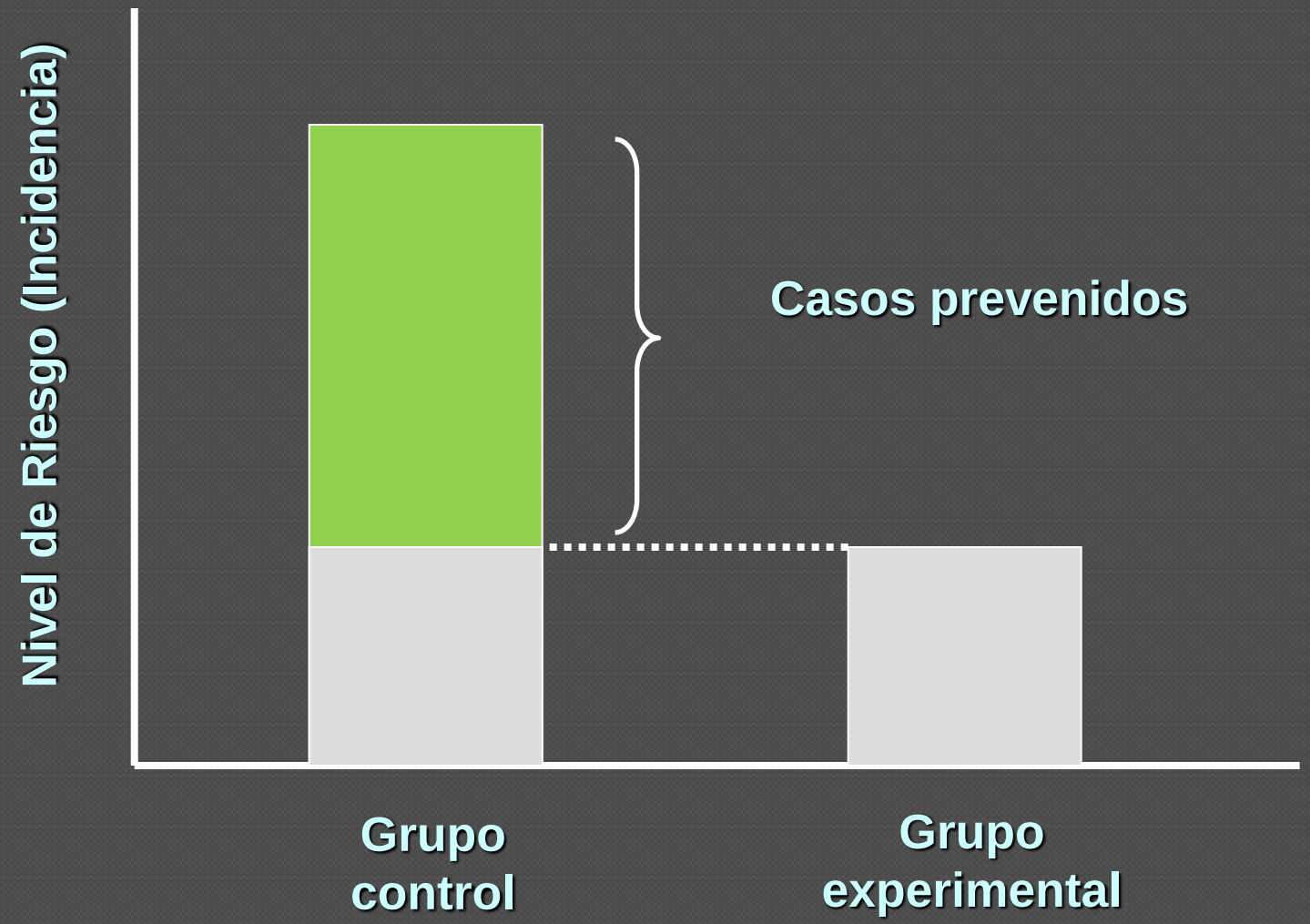
La RAR es la diferencia en riesgo entre el grupo control y el grupo experimental:

$$RAR = I_{control} - I_{experimental}$$

Mide el número de casos prevenidos por el tratamiento experimental frente al control.

Se expresa en las mismas unidades que la incidencia.

Reducción absoluta del riesgo



Prevention of Nosocomial Infection in Cardiac Surgery by Decontamination of the Nasopharynx and Oropharynx With Chlorhexidine Gluconate

A Randomized Controlled Trial

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Ron G. H. Speekenbrink, PhD
Dirk T. Ubbink, PhD
Marc L. van Ogtrop, PhD
Bas A. de Mol, MD, PhD

Context Nosocomial infections are an important cause of morbidity and mortality after cardiac surgery. Decolonization of endogenous potential pathogenic microorganisms is important in the prevention of nosocomial infections.

Objective To determine the efficacy of perioperative decontamination of the nasopharynx and oropharynx with 0.12% chlorhexidine gluconate for reduction of nosocomial infection after cardiac surgery.

Design, Setting, and Participants A prospective, randomized, double-blind, placebo-controlled clinical trial conducted at the Onze Lieve Vrouwe Gasthuis, Amsterdam, the Netherlands, between August 1, 2003, and September 1, 2005. Of 991 patients older than 18 years undergoing elective cardiothoracic surgery during the study interval, 954 were eligible for analysis.

Intervention Oropharyngeal rinse and nasal ointment containing either chlorhexidine gluconate or placebo.

Main Outcome Measures Incidence of nosocomial infection, in addition to the rate of *Staphylococcus aureus* nasal carriage and duration of hospital stay.

NOSOCOMIAL INFECTIONS AFter open heart surgery are recognized as an important cause of mortality, morbidity, prolonged hospital stay, increased need for antimicrobial therapy, and higher concomitant costs. Nosocomial infections also decrease patients' quality of life.[1-9] Incidence rates of more

Nosocomial Infection

A total of 96 patients (19.8%) in the chlorhexidine gluconate group were diagnosed with 116 nosocomial infections compared with 123 patients (26.2%) with 164 nosocomial infections in the placebo group (ARR, 6.4%; 95% CI, 1.1%-11.7%; $P = .002$). The incidence of LRTI in the chlorhexidine gluconate and placebo groups was 9.3% and 15.8%, respectively, resulting in an ARR of 6.5% (95% CI, 2.3%-10.7%; $P = .002$), with an

Reducción relativa del riesgo

El RRR es el cociente de la RAR entre el riesgo en el grupo control:

$$RRR = \frac{(I_{control} - I_{experimental})}{I_{control}} \times 100$$

Mide en que proporción se ha reducido el riesgo por el tratamiento experimental frente al control.

JJCO Japanese Journal of Clinical Oncology

Jpn J Clin Oncol 2011;41(3)417–423
doi:10.1093/jjco/hyq221
Advance Access Publication 1 December 2010

Efficacy and Safety of Dutasteride on Prostate Cancer Risk Reduction in Asian Men: The Results from the REDUCE Study

Hideyuki Akaza[1,*], Hiroshi Kanetake[2], Taiji Tsukamoto[3], Naoto Miyanaga[1], Hideki Sakai[2], Naoya Masumori[3], Hiroomi Nakatsu[4], Kazuyuki Sagiyama[5], Sadaaki Sakamoto[6], Yukihiro Endo[7] and Takayoshi Yamanouchi[7] on behalf of the REDUCE Study Group

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Received October 11, 2010; accepted November 1, 2010

Objective: A *post hoc* analysis of Asian men in the REDUCE study was conducted to investigate whether the outcomes were in line with those of the overall population.
Methods: REDUCE was a 4-year international, multicenter, randomized, double-blind, placebo-controlled, parallel-group study. Inclusion criteria were men between 50 and 75 years of age, a serum prostate-specific antigen level of 2.5–10.0 ng/ml (50–60 years) or 3.0–10.0 ng/ml (>60 years), and a single, negative prostate biopsy (6–12 cores) within 6 months before enrollment. The primary endpoint was biopsy-detectable prostate cancer. This *post hoc* analysis included subjects who were recorded as Asian.

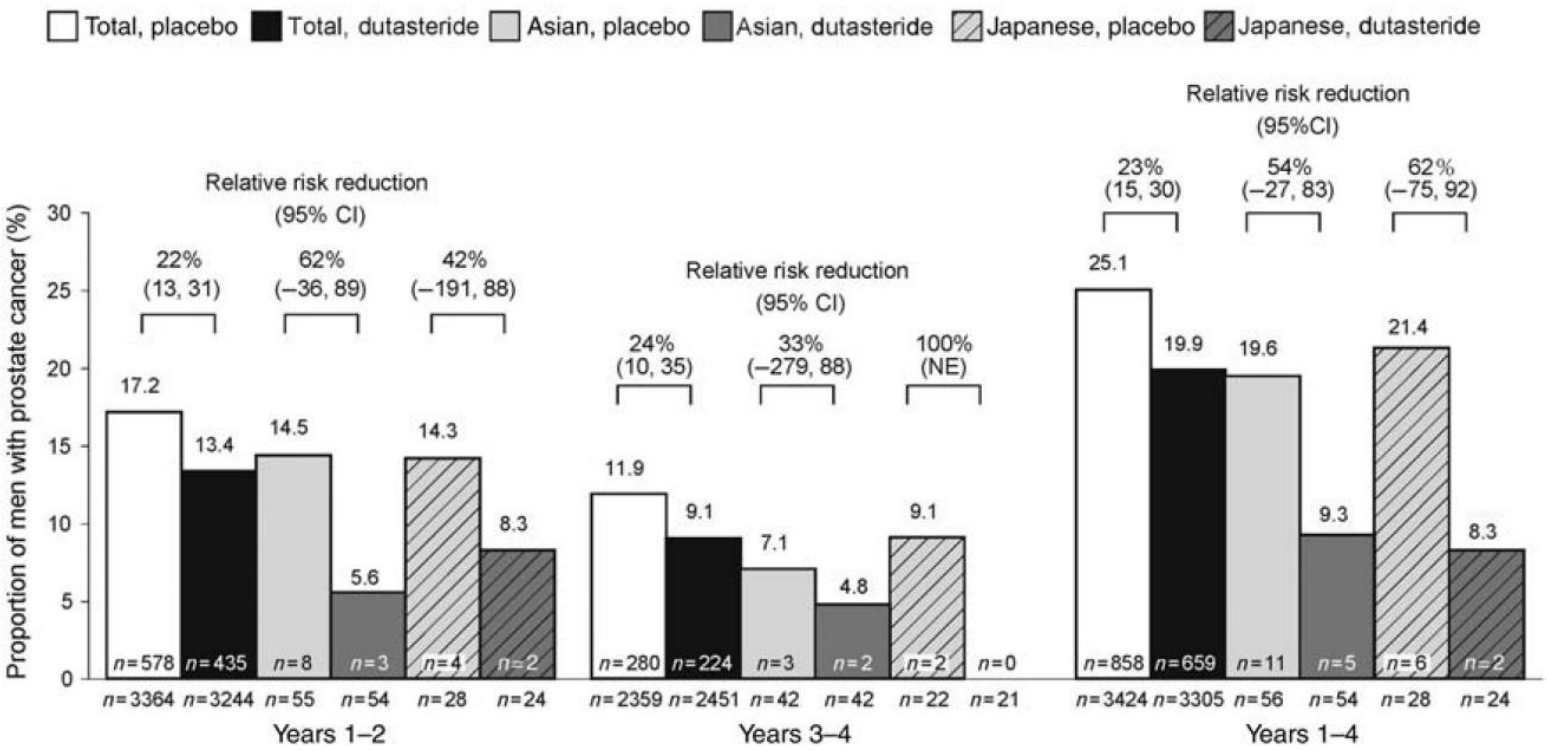

Figure 2. Proportions of men with a biopsy-detectable prostate cancer by the treatment period and the treatment group in the efficacy population. The occurrence of biopsy-detectable prostate cancer was calculated by using a restricted crude rate approach (men with at least one post-baseline biopsy). The numbers in and under the bars are the numbers of subjects. CI, confidence interval; NE, not estimable.

Número necesario a tratar

Representa el número de pacientes que necesitan ser tratados en un período de tiempo específico para lograr un resultado favorable ***adicional***, en relación al tratamiento de comparación (control).

Se calcula como el inverso del RAR:

$$NNT = 1 / RAR$$

Effects of Fenofibrate Treatment on Cardiovascular Disease Risk in 9,795 Individuals With Type 2 Diabetes and Various Components of the Metabolic Syndrome

The Fenofibrate Intervention and Event Lowering in Diabetes (FIELD) study

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ANTHONY KEECH, MB BS, FRACP, MSC(EPID)[4]
ON BEHALF OF THE FENOFIBRATE INTERVENTION AND EVENT LOWERING IN DIABETES (FIELD) STUDY INVESTIGATORS*

OBJECTIVE — We explored whether cardiovascular disease (CVD) risk and the effects of fenofibrate differed in subjects with and without metabolic syndrome and according to various features of metabolic syndrome defined by the Adult Treatment Panel III (ATP III) in subjects with type 2 diabetes in the Fenofibrate Intervention and Event Lowering in Diabetes (FIELD) study.

RESEARCH DESIGN AND METHODS — The prevalence of metabolic syndrome and its features was calculated. Cox proportional models adjusted for age, sex, CVD status, and baseline A1C levels were used to determine the independent contributions of metabolic syndrome features to total CVD event rates and the effects of fenofibrate.

metabolic syndrome features are present. The highest risk and greatest benefits of fenofibrate are seen among those with marked hypertriglyceridemia.

Diabetes Care 32:493–498, 2009

Subjects with metabolic syndrome have a higher risk for future cardiovascular disease (CVD) events and are more likely to develop diabetes (1). The various components of metabolic syndrome (abdominal obesity, dyslipidemia, hypertension, and glucose deregulation) confer differential risk for CVD based on the extent to which they deviate from healthy normality. The guidelines most commonly used clinically to define

mary prevention (Table 2). Indeed, the overall effect of fenofibrate in the presence of marked dyslipidemia was larger than that in all other groups, with borderline significance of treatment by group interaction: marked dyslipidemia group: 27% risk reduction (adjusted HR 0.73 [95% CI 0.58–0.91], $P = 0.005$); all others: 6% risk reduction (0.94 [0.83–1.06], $P = 0.321$; $P_{\text{interaction}} = 0.053$) (Fig. 2). The absolute risk reduction in the presence of marked dyslipidemia was 4.3% (from 17.8 to 13.5%), compared with 0.8% (from 13.0 to 12.2%) in its absence (Fig. 2). This corresponds to a number needed to treat of 23 compared with 143, respectively. The effects of treatment ac-

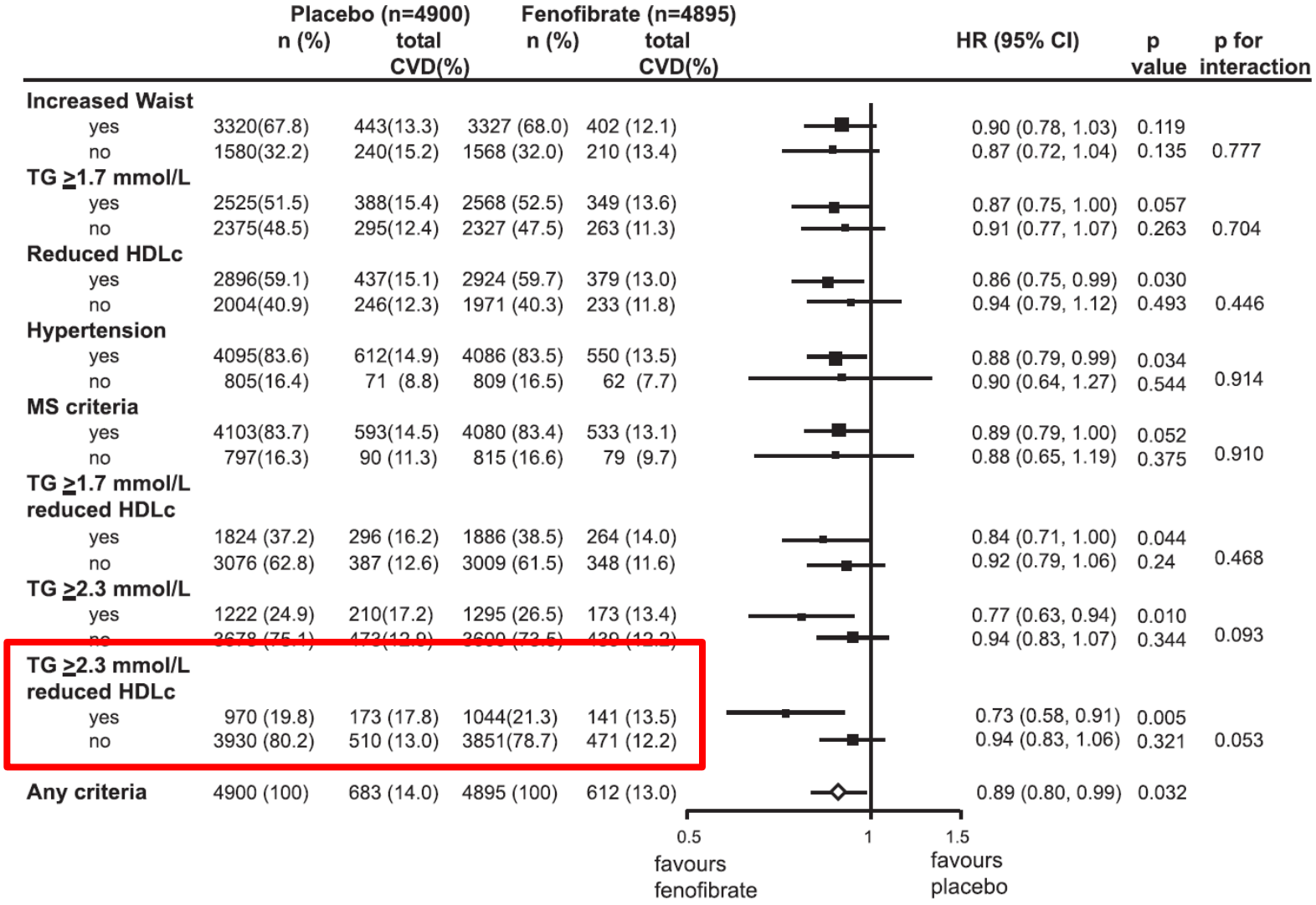


Figure 2—*Forest plot of effects of fenofibrate on cardiovascular events adjusted for sex, prior CVD, age at visit 1, and baseline A1C (HR and 95% CI): ATP III waist circumference criteria (men >102 cm and women >88 cm), raised triglyceride levels (TG) (≥1.7 mmol/l or ≥2.3 mmol/l), reduced HDL cholesterol (HDLc) levels (men <1.03 mmol/l and women <1.29 mmol/l), and ATP III metabolic syndrome (MS) criteria (diabetes and two others).*

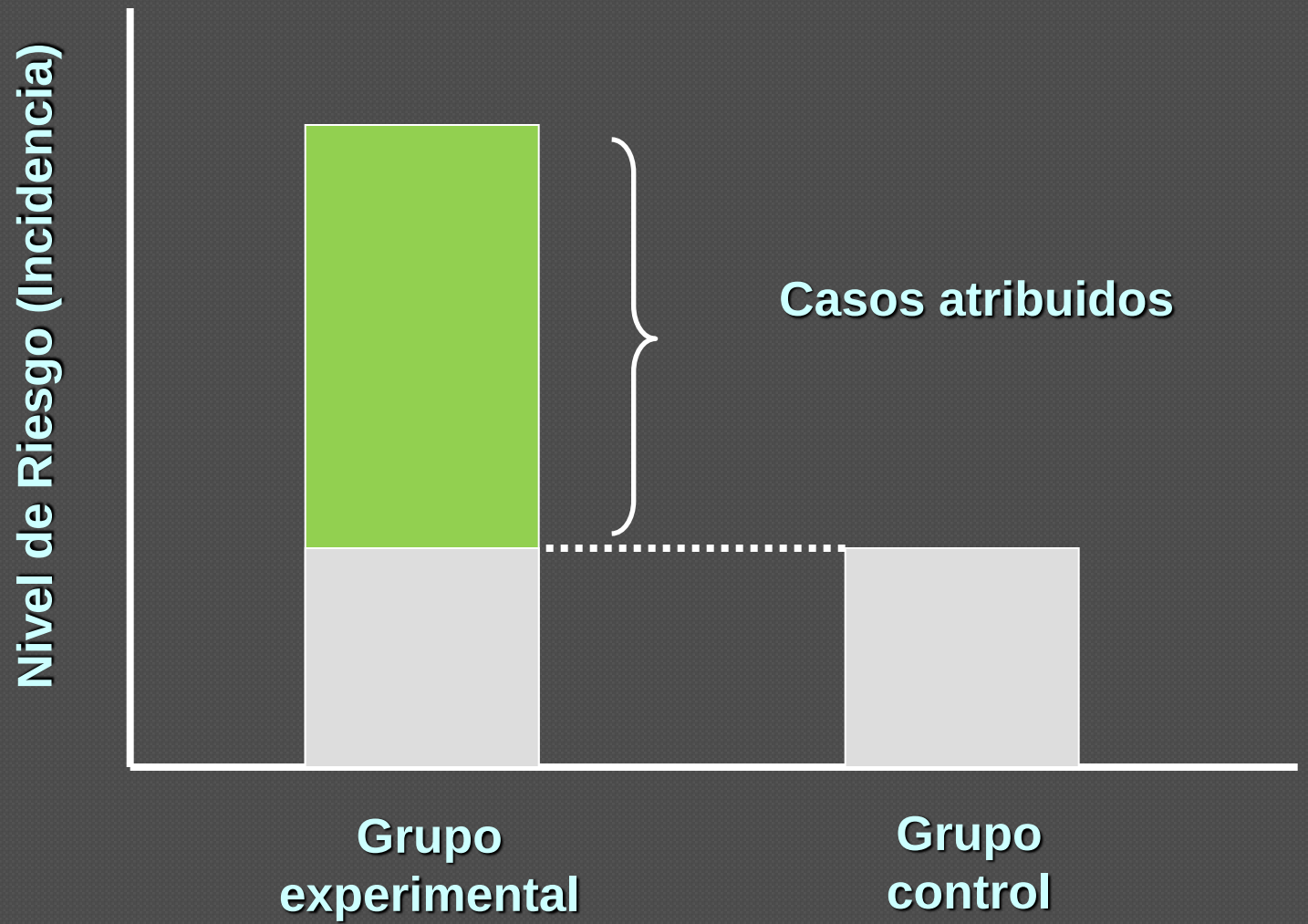
Riesgo atribuible

El RA es la diferencia de riesgo (incidencia) entre el grupo experimental y el grupo control:

$$RA = I_{experimental} - I_{control}$$

Mide los casos de eventos adversos que pueden atribuirse al tratamiento experimental.

Riesgo atribuible



BMC Medicine

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Cardioprotective aspirin users and their excess risk of upper gastrointestinal complications

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Published: 20 September 2006

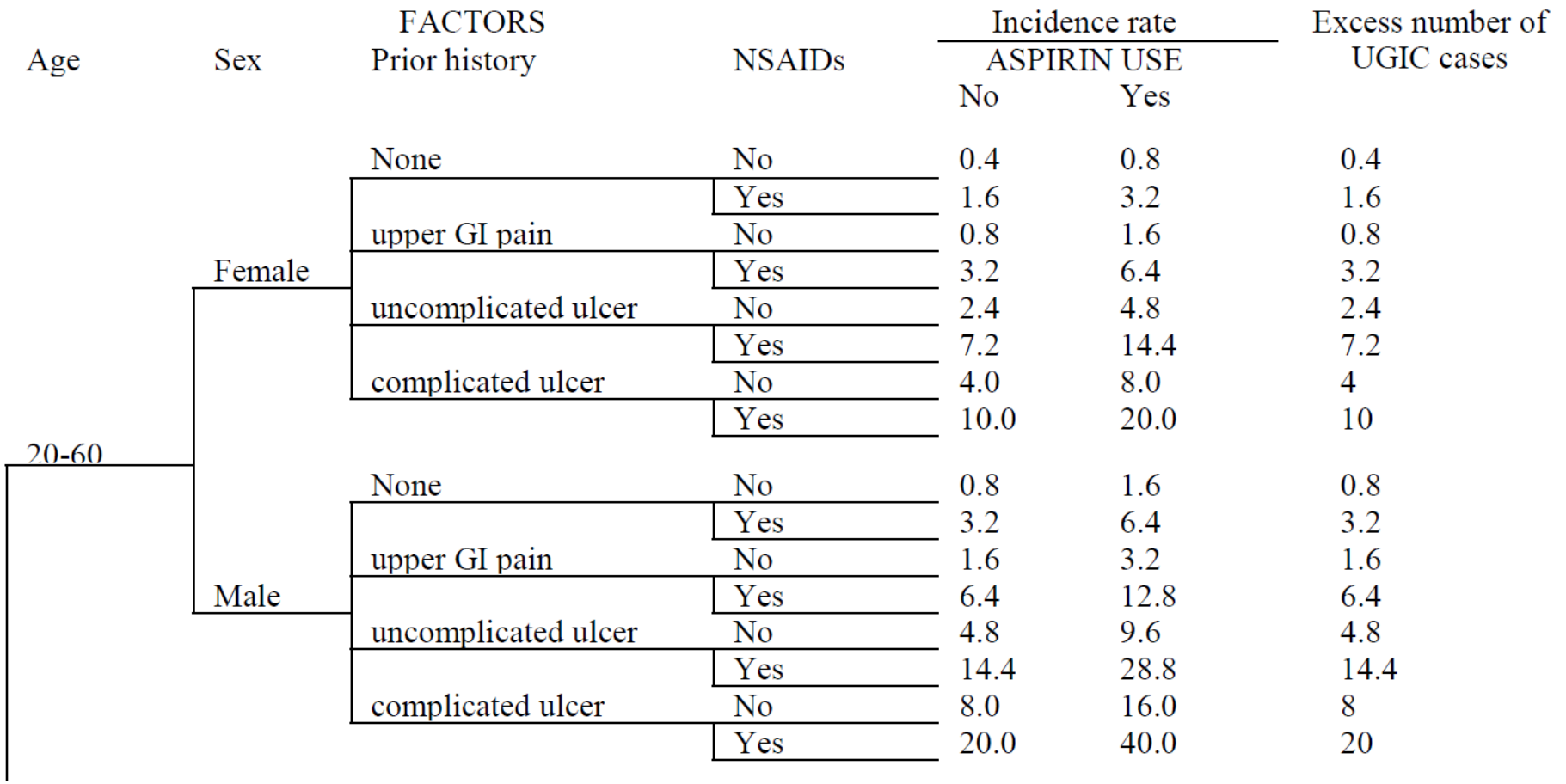
BMC Medicine 2006, **4**:22 doi:10.1186/1741-7015-4-22

Received: 01 May 2006
Accepted: 20 September 2006

This article is available from: http://www.biomedcentral.com/1741-7015/4/22

Abstract

Background: To balance the cardiovascular benefits from low-dose aspirin against the gastrointestinal harm caused, studies have considered the coronary heart disease risk for each individual but not their gastrointestinal risk profile. We characterized the gastrointestinal risk profile of low-dose aspirin users in real clinical practice, and estimated the excess risk of upper gastrointestinal complications attributable to aspirin among patients with different gastrointestinal risk profiles.



Age	Sex	FACTORS Prior history	NSAIDs	Incidence rate ASPIRIN USE No	Yes	Excess number of UGIC cases
20-60	Female	None	No	0.4	0.8	0.4
			Yes	1.6	3.2	1.6
		upper GI pain	No	0.8	1.6	0.8
			Yes	3.2	6.4	3.2
		uncomplicated ulcer	No	2.4	4.8	2.4
			Yes	7.2	14.4	7.2
		complicated ulcer	No	4.0	8.0	4
			Yes	10.0	20.0	10
	Male	None	No	0.8	1.6	0.8
			Yes	3.2	6.4	3.2
		upper GI pain	No	1.6	3.2	1.6
			Yes	6.4	12.8	6.4
		uncomplicated ulcer	No	4.8	9.6	4.8
			Yes	14.4	28.8	14.4
		complicated ulcer	No	8.0	16.0	8
			Yes	20.0	40.0	20

Figure 3

Estimated incidence rate of upper gastrointestinal tract complications (UGIC) per 1,000 person-years and estimated excess number of cases per 1,000 cardioprotection aspirin users per year attributable to aspirin within levels of gastrointestinal risk factors.

Fracción etiológica de riesgo

El FER es el cociente de la RA entre el riesgo en el grupo experimental:

$$FER = \frac{(I_{experimental} - I_{control})}{I_{experimental}} \times 100$$

Mide que proporción del riesgo se atribuye al tratamiento experimental frente al control.

Alimentary Pharmacology & Therapeutics

Hospitalization for gastrointestinal adverse events attributable to the use of low-dose aspirin among patients 50 years or older also using non-steroidal anti-inflammatory drugs: a retrospective cohort study

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SUMMARY

Background

Use of aspirin with non-steroidal anti-inflammatory drugs increases the risk of gastrointestinal ulcers; however, it is not clear if this risk varies with the non-steroidal anti-inflammatory drug used.

Aim

To assess the risk of gastrointestinal hospitalizations attributable to aspirin in patients 50 years or older also using non-steroidal anti-inflammatory drugs.

Table 6. Risk of GI hospitalization attributable to the use of aspirin* with COX-2 inhibitors, Ns-NSAIDs or acetaminophen

	Hazard ratio (95% CI)	Risk attributable to aspirin
Rofecoxib with aspirin vs. rofecoxib	2.4 (2.0, 2.9)	0.6 (0.5, 0.7)
Celecoxib with aspirin vs. celecoxib	2.6 (2.2, 3.1)	0.6 (0.5, 0.7)
Diclofenac with aspirin vs. diclofenac	1.9 (1.5, 2.5)	0.5 (0.3, 0.6)
Ibuprofen with aspirin vs. ibuprofen	1.5 (0.7, 3.2)	0.3 (−0.4, 0.7)
Naproxen with aspirin vs. naproxen	0.9 (0.7, 1.2)	−0.2 (−0.6, 0.2)
Piroxicam with aspirin vs. piroxicam	1.3 (0.4, 4.2)	0.2 (−1.4, 0.8)
Other NSAIDs with aspirin vs. other NSAIDs	1.2 (0.9, 1.8)	0.2 (−0.2, 0.4)
Acetaminophen with aspirin vs. acetaminophen	1.5 (1.4, 1.7)	0.3 (0.3, 0.4)

Ns-NSAID, non-selective non-steroidal anti-inflammatory drug; COX, cyclo-oxygenase; GI, gastrointestinal.

* Risk attributable to aspirin = (adjusted hazard ratio − 1)/adjusted hazard ratio.

Número necesario para dañar

Representa el número de pacientes que necesitan ser tratados en un período de tiempo específico para esperar un efecto adverso ***adicional***, en relación al tratamiento de comparación (control).

Se calcula como el inverso del RA:

$$NNH = 1 / RA$$

BMJ

RESEARCH

Long term treatment with metformin in patients with type 2 diabetes and risk of vitamin B-12 deficiency: randomised placebo controlled trial

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ABSTRACT

Objectives To study the effects of metformin on the incidence of vitamin B-12 deficiency (<150 pmol/l), low concentrations of vitamin B-12 (150-220 pmol/l), and folate and homocysteine concentrations in patients with type 2 diabetes receiving treatment with insulin.

Design Multicentre randomised placebo controlled trial.

Setting Outpatient clinics of three non-academic hospitals in the Netherlands.

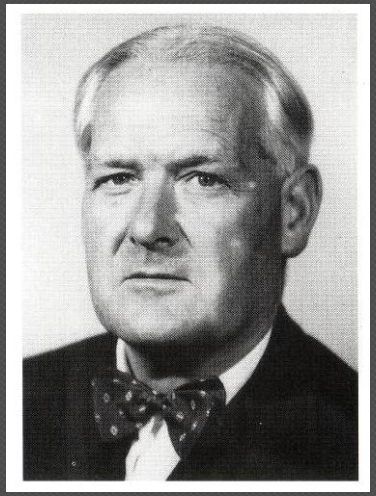
Participants 390 patients with type 2 diabetes receiving vitamin B-12) for patients with a normal vitamin B-12 concentration (>220 pmol/l).

Conclusions Long term treatment with metformin increases the risk of vitamin B-12 deficiency, which results in raised homocysteine concentrations. Vitamin B-12 deficiency is preventable; therefore, our findings suggest that regular measurement of vitamin B-12 concentrations during long term metformin treatment should be strongly considered.

Trial registration Clinicaltrials.gov NCT00375388.

The risk for vitamin B-12 deficiency at study end was 7.2 percentage points higher in the metformin group than in the placebo group (95% CI 2.3 to 12.1; P=0.004), with a number needed to harm of 13.8 per 4.3 years (95% CI 43.5 to 8.3). The risk difference at study end for a low vitamin B-12 concentration was 11.2 percentage points higher in the metformin group (95% CI 4.6 to 17.9; P=0.001), with a number needed to harm of 8.9 per 4.3 years (95% CI 21.7 to 5.6). The hazard ratio for developing vitamin B-12 deficiency when treated with metformin was 5.5 (95% CI 1.6 to 19.1; P=0.01), and the hazard ratio for a low vitamin B-12 concentration was 3.0 (95% CI 1.3 to 6.6; P=0.007).

Criterios de Hill



Sir Austin Bradford Hill propuso, en 1965, una serie de criterios a tener en cuenta para distinguir entre asociaciones causales y no causales:

Fuerza de Asociación, Consistencia, Especificidad, Temporalidad, Gradiente Biológica, Plausibilidad, Coherencia, Evidencia Experimental y Analogía.

Asociación estadística y asociación causal

La asociación estadística sólo establece que dos hechos aparecen en forma simultánea. No significa necesariamente que el hecho este relacionado con el proceso de causalidad.

Una asociación estadísticamente significativa no implica necesariamente que sea clínicamente relevante.

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Cincuenta años de la Medicina Tropical en el Perú
1963-2013

Gracias por su atención

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