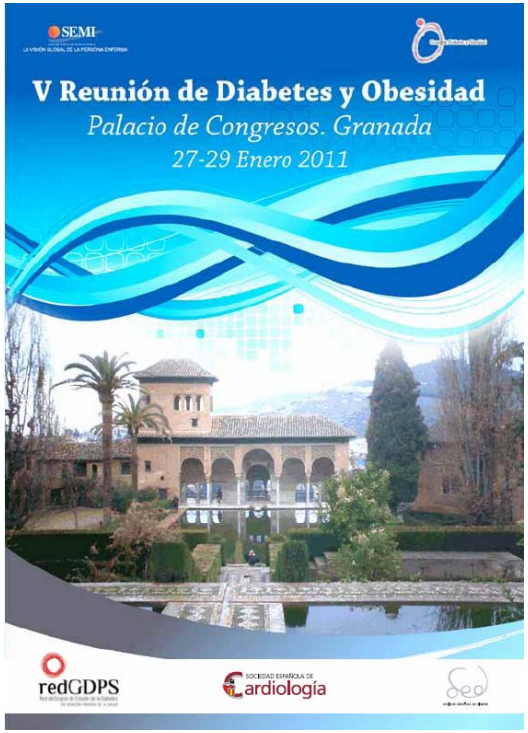

Pulmón y diabetes

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Medicina Interna. Hospital Royo Villanova. Zaragoza
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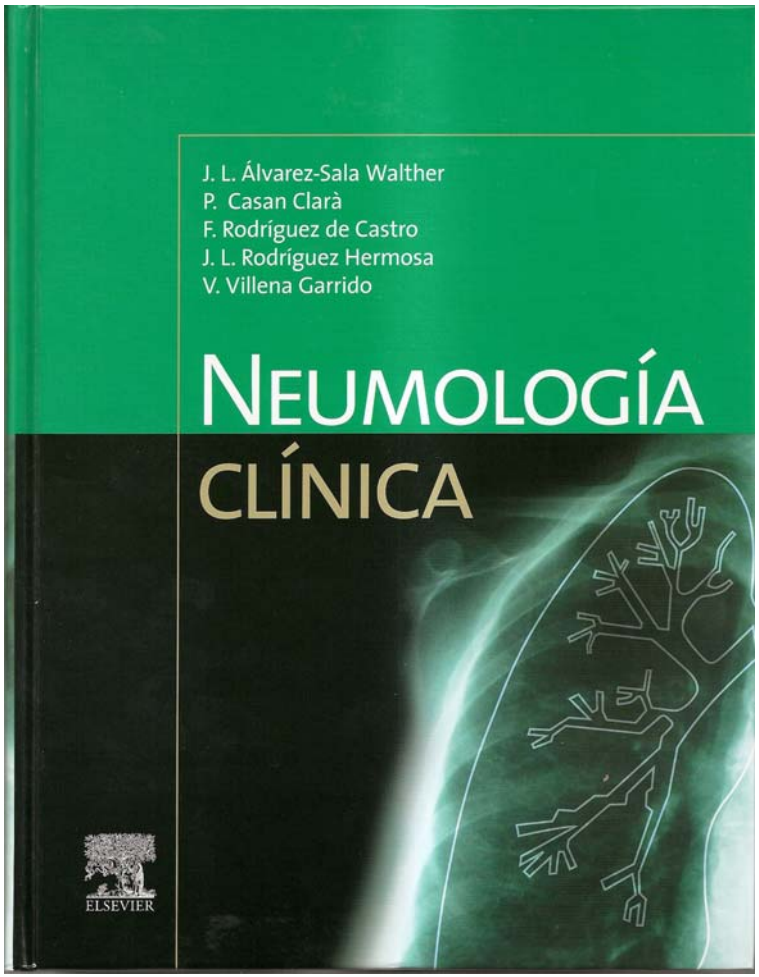
Mesa Redonda 3. Comorbilidades olvidadas en el diabético tipo 2

¿Pulmón y diabetes?



ALTERACIONES PULMONARES ASOCIADAS A LAS ENFERMEDADES ENDOCRINAS SISTÉMICAS

Diabetes mellitus

La complicación pulmonar más frecuente en la diabetes mellitus (DM) es la infección, en especial por hongos (aspergilosis invasiva y mucormicosis), micobacterias (*Mycobacterium tuberculosis*), *Staphylococcus aureus* y bacterias gramnegativas (sobre todo en los episodios de cetoacidosis).

Las pruebas de función pulmonar muestran en estos casos una reducción de la DLCO, de la capacidad vital forzada, del volumen espiratorio forzado en el primer segundo y de la capacidad pulmonar total. También parece existir una disminución de la fuerza de los músculos inspiratorios.

ISSN: 0014-2565

Incluida en Medline/Index Medicus, Science Citation Index Expanded, Journal Citation Reports y Embase/Excerpta Medica

Revista Clínica Española

Volumen 210
Número 10
Noviembre
2010

Publicación Oficial de la Sociedad Española de Medicina Interna

e Material adicional disponible on-line.

confundentes, lo que sugiere que la disminución de volúmenes pulmonares y la limitación al flujo aéreo pueden ser complicaciones crónicas de la DM2. Además, la limi-

La evidencia científica disponible no permite, en mi criterio, afirmar ni rechazar la asociación entre EPOC y diabetes mellitus tipo 2 (DM2)[1]. Es cierto que la DM2 figura, junto con

Pulmón y diabetes

- ¿Existe una neumopatía diabética?
- ¿Cómo influye la diabetes en la enfermedad pulmonar crónica?
- ¿Cómo influye la enfermedad pulmonar crónica en la diabetes?

CHEST Original Research

PULMONARY FUNCTION IN DIABETES

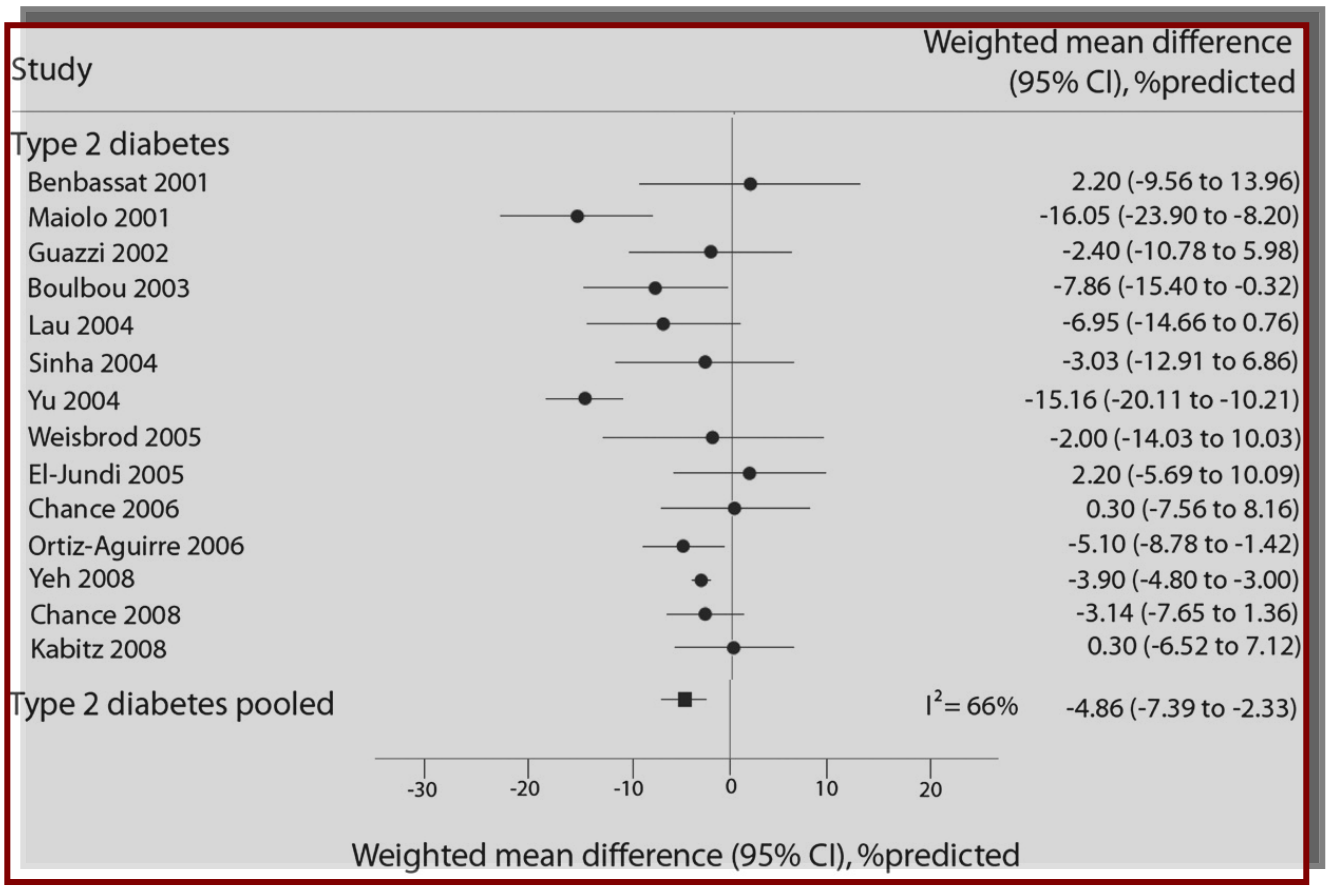
Pulmonary Function in Diabetes

A Metaanalysis

Bram van den Borst, MD; Harry R. Gosker, PhD; Maurice P. Zeegers, PhD; and Annemie M. W. J. Schols, PhD

Función pulmonar en DM2

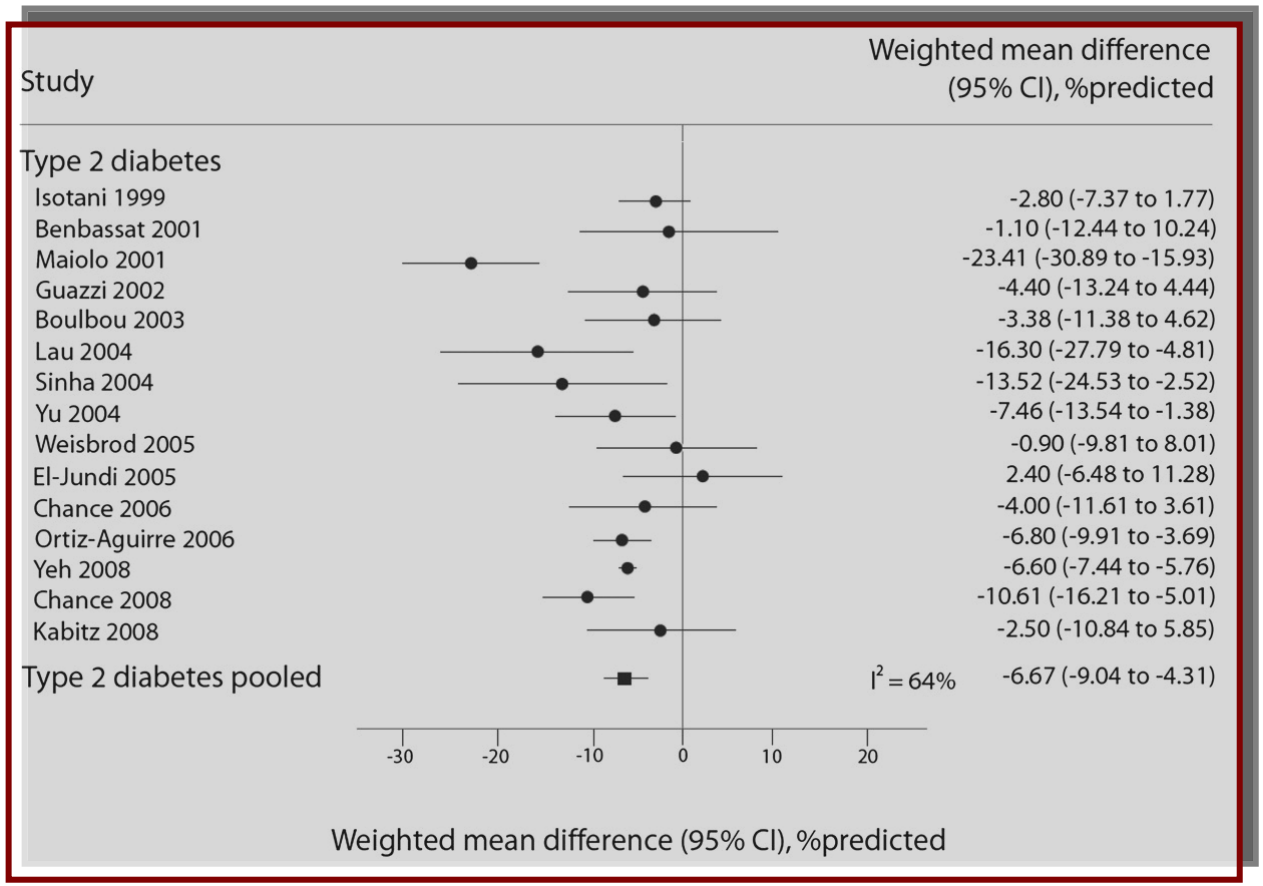
Descenso en el FEV1



van den Borst B et al. Chest 2010;138:393-406

Función pulmonar en DM2

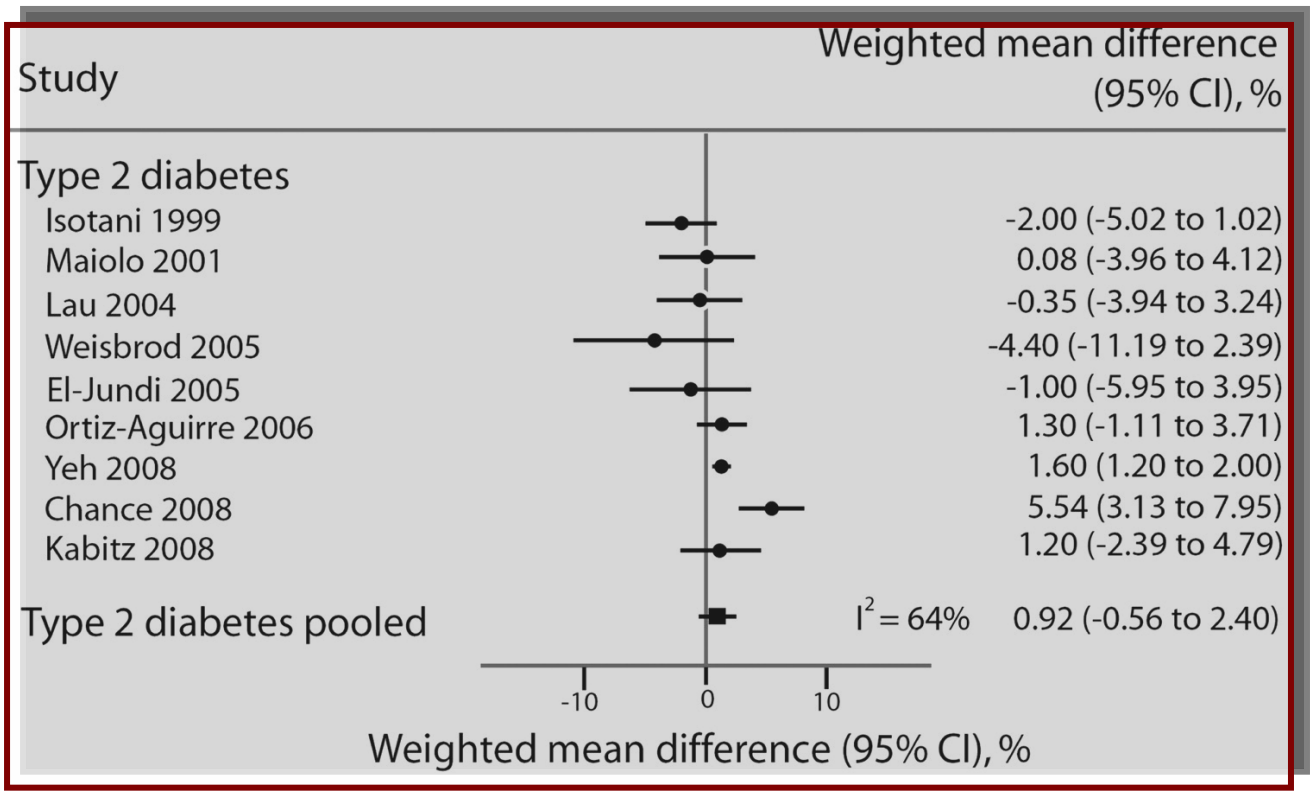
Descenso en la FVC



van den Borst B et al. Chest 2010;138:393-406

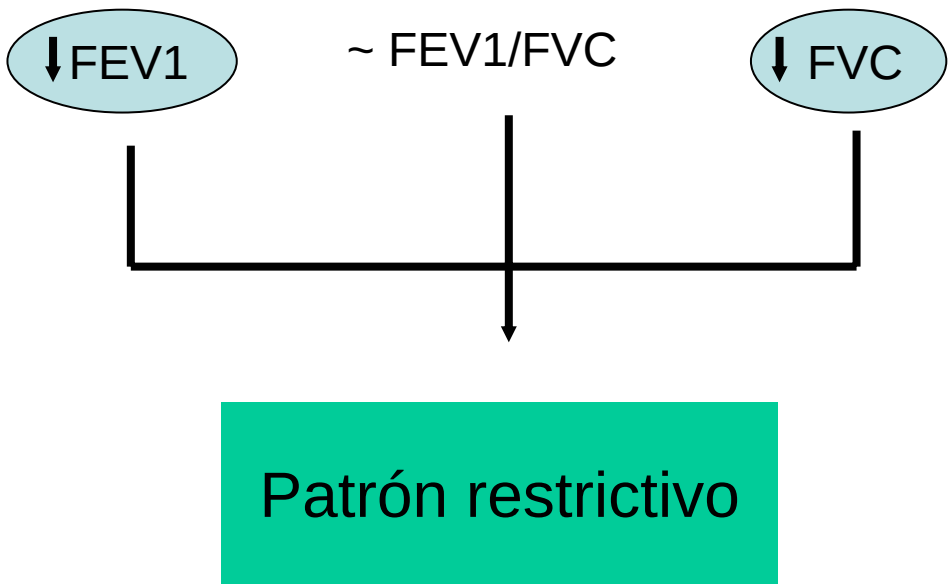
Función pulmonar en DM2

FEV1/FVC



van den Borst B et al. Chest 2010;138:393-406

Función pulmonar en DM2



Función pulmonar en DM2

Deterioro progresivo en el tiempo

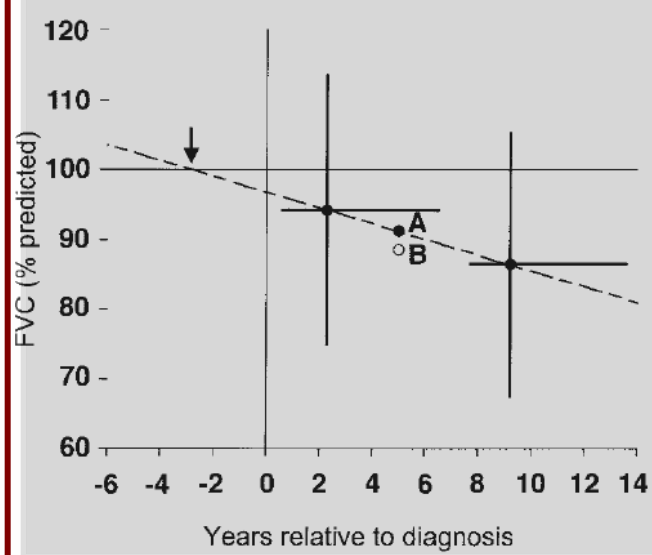


Figure 1—*FVC percentage-predicted values (mean ± SD) at both baseline and follow-up (median and interquartile range) using the predictive equations of Knudson and coworkers (see text). The trend line intersects the 100% FVC value at a point corresponding to −2.8 years on the x-axis. Point A is the FVC percentage-predicted value interpolated to a duration of diabetes of 5.0 years in the prospective cohort. Point B is the FVC percentage-predicted value in cross-sectional study patients who were not followed but who had a median duration of diabetes of 5.0 years.*

Table 2—*Lung function measures as absolute values and as percentage of predicted values*

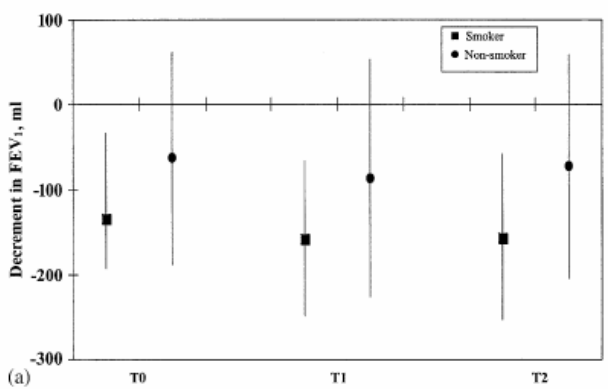
	Absolute measures			Percentage predicted			
	Baseline	Follow-up	Change	Equation	Baseline	Follow-up	Change
FVC	3.20 ± 0.89	2.72 ± 0.83*	−0.48 ± 0.51	Knudson	94.3 ± 19.3	86.4 ± 18.9*	−7.7 ± 17.8
				Busselton	90.1 ± 16.9	83.4 ± 17.7*	−6.7 ± 16.2
FEV_1	2.58 ± 0.78	2.08 ± 0.70*	−0.50 ± 0.51	Knudson	94.7 ± 22.0	83.7 ± 22.1*	−10.8 ± 20.5
				Busselton	94.2 ± 21.3	84.5 ± 22.2*	−9.7 ± 21.1
VC	3.15 ± 0.79	2.54 ± 0.85*	−0.58 ± 0.66	Knudson	92.9 ± 17.7	81.6 ± 20.1*	−10.9 ± 19.4
PEF	378 ± 129	260 ± 122*	−118 ± 109	Knudson	87.7 ± 24.6	66.2 ± 26.8*	−21.5 ± 26.8

Data are means ± SD. Absolute units of measurement were liters for FVC, FEV_1, and VC and liters per minute for PEF. For FVC and FEV_1, the percentage of predicted values are shown for both the Knudson and Busselton equations. *$P < 0.001$ versus baseline.

Davis WA et al. Diabetes Care 2004; 27:752-757

Función pulmonar en DM2

El deterioro aparece antes del diagnóstico de diabetes



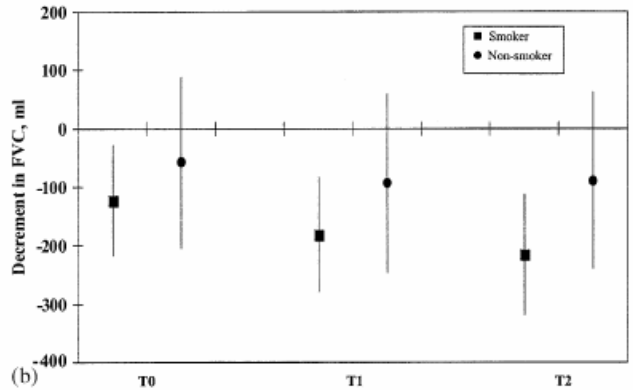


Table 2 Multiple linear regression models for lung function change/year.*

	T0–T1 β (SE)	*P*-value	T1–T2 β (SE)	*P*-value
ΔFEV_1: mL/year				
Intercept	−131.2 (55.5)	0.02	−86.2 (65.3)	0.2
Age	1.2 (0.2)	0.0001	0.6 (0.3)	0.02
Smoking status				
Never	—		—	
Current	9.7 (4.6)	0.03	11.8 (6.5)	0.07
Former	−0.3 (4.6)	0.9	3.0 (5.1)	0.6
Diabetic	1.1 (3.7)	0.8	1.1 (4.5)	0.8
Model R^2	0.10		0.07	
ΔFVC: mL/year				
Intercept	−206.3 (57.7)	0.0004	81.3 (63.7)	0.2
Age	1.4 (0.2)	0.0001	1.1 (0.3)	0.0001
Smoking status				
Never	—		—	
Current	12.6 (4.7)	0.008	14.6 (6.4)	0.02
Former	4.5 (4.8)	0.3	7.5 (4.9)	0.1
Diabetic	3.7 (3.8)	0.3	05.4 (4.4)	0.2
Model R^2	0.14		0.09	

*All models additionally adjusted for baseline height and weight.

Litonjua AA et al. Respir Med 2005; 99:1583-1590

Función pulmonar y control de glucemia

TABLE 6. Association between various clinical definitions of diabetes* and forced expiratory volume in 1 second, Third National Health and Nutrition Examination Survey, 1988–1994

Definition of diabetes and glucose tolerance	Model 1†		Model 1† with additional adjustment for body mass index‡ and waist:hip ratio	
	β (ml)	95% CI§	β (ml)	95% CI
Fasting plasma glucose level				
Normal (<110 mg/dl) (*n* = 3,877)	0		0	
Impaired (110–125.99 mg/dl) (*n* = 262)	−75.2	−109.4, −41.1	−60.8	−95.7, −25.8
Diabetic (≥126 mg/dl) (*n* = 118)	−126.2	−160.1, −92.3	−93.8	−127.4, −60.2
Glucose level 2 hours post-glucose-load				
Normal (<140 mg/dl) (*n* = 1,258)	0		0	
Impaired (140–199.99 mg/dl) (*n* = 250)	−60.5	−134.8, 13.9	−34.3	−114.5, −45.9
Diabetic (≥200 mg/dl) (*n* = 104)	−154.5	−265.6, −43.4	−108.8	−217.3, −0.3
Hemoglobin A1c concentration				
<7% (*n* = 4,196)	0		0	
≥7% (*n* = 61)	−110.3	−269.7, 49.0	−75.0	−231.0, 80.9

* According to the World Health Organization (19).
† Results were adjusted for sex, age, height, race/ethnicity, and smoking (status and pack-years).
‡ Weight (kg)/height $(m)^2$. Modeled as a categorical variable (<20, 20–24.9, 25–29.9, >30).
§ CI, confidence interval.

McKeever TM et al. Am J Epidemiol 2005;161:546-556

Función pulmonar y control de glucemia

TABLE 7. Association between known diagnosis of diabetes and forced expiratory volume in 1 second, Third National Health and Nutrition Examination Survey, 1988–1994

Comparison	Model 1*		Model 1* with additional adjustment for body mass index† and waist:hip ratio	
	β (ml)	95% CI‡	β (ml)	95% CI
Diabetes status				
No diabetes ($n = 4,257$)	0		0	
Diabetes ($n = 512$)	−119.1	−161.5, −76.6	−78.8§	−118.7, −38.8
Level of control of diabetes				
No diabetes ($n = 4,196$)	0		0	
Well-controlled diabetes (hemoglobin A1c <7%) ($n = 253$)	−91.6	−157.4	−54.5¶	−116.2, 7.3
Poorly controlled diabetes (hemoglobin A1c ≥7%) ($n = 395$)	−144.9	−200.5, −89.2	−100.1#	−155.3, −44.9

* Results were adjusted for sex, age, height, race/ethnicity, and smoking (status and pack-years).
† Weight (kg)/height $(m)^2$. Modeled as a categorical variable (<20, 20–24.9, 25–29.9, >30).
‡ CI, confidence interval.
§ $n = 489$.
¶ $n = 218$.
# $n = 259$.

McKeever TM et al. Am J Epidemiol 2005;161:546-556

Función pulmonar y control metabólico

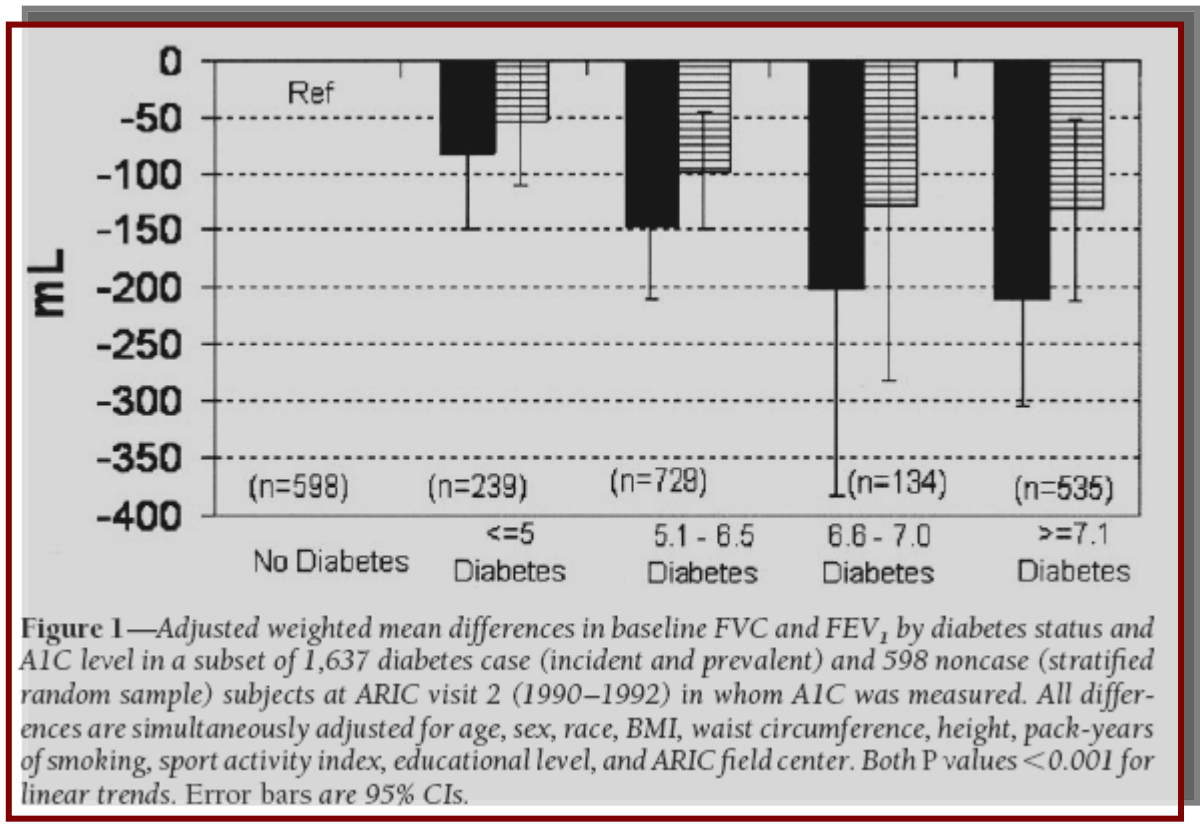


Figure 1—*Adjusted weighted mean differences in baseline FVC and FEV_1 by diabetes status and A1C level in a subset of 1,637 diabetes case (incident and prevalent) and 598 noncase (stratified random sample) subjects at ARIC visit 2 (1990–1992) in whom A1C was measured. All differences are simultaneously adjusted for age, sex, race, BMI, waist circumference, height, pack-years of smoking, sport activity index, educational level, and ARIC field center. Both P values <0.001 for linear trends.* Error bars *are 95% CIs.*

Yeh HC et al. Diabetes Care 2008;31:741-746

Función pulmonar y duración de la diabetes

Table 3—*Adjusted changes in FVC, FEV_1, and FEV_1-to-FVC ratio over 3 years of follow-up by diabetes status at baseline*

	ΔFVC (ml/year)	Δ FEV_1 (ml/year)	Δ FVC % predicted (%/year)	Δ FEV_1 % predicted (%/year)	Δ FEV_1-to-FVC ratio (%/year)
No diabetes	↓ 58 (56–59)	↓ 47 (45–48)	↓ 0.96 (0.9–1.0)	↓ 0.7 (0.7–0.8)	↓ 0.1 (0.07–0.1)
Diabetes	↓ 64 (59–69)	↓ 49 (46–53)	↓ 1.1 (1.0–1.3)	↓ 0.9 (0.7–1.0)	↓ 0.05 (−0.02–0.1)
P value	0.01	0.13	0.009	0.08	0.22
Diabetes by fasting glucose					
<140 mg/dl	↓ 63 (53–72)	↓ 49 (42–56)	↓ 1.1 (0.8–1.3)	↓ 0.8 (0.6–1.0)	↓ 0.1 (−0.03–0.2)
140–199 mg/dl	↓ 61 (52–69)	↓ 47 (40–53)	↓ 1.1 (0.9–1.3)	↓ 0.8 (0.6–1.0)	↓ 0.1 (−0.1–0.2)
200+ mg/dl	↓ 56 (46–65)	↓ 47 (40–54)	↓ 0.9 (0.7–1.2)	↓ 0.8 (0.5–1.0)	↓ 0.2 (0.01–0.3)
P_{trend}*	0.59	0.89	0.65	0.88	0.83
Diabetes by duration					
≤5 years	↓ 57 (48–67)	↓ 45 (38–52)	↓ 1.0 (0.7–1.3)	↓ .7 (0.5–1.0)	↓ 0.1 (−0.1–0.1)
6–9 years	↓ 63 (47–79)	↓ 52 (40–63)	↓ 1.1 (0.7–1.5)	↓ 0.9 (0.5–1.3)	↓ 0.1 (−0.3–0.1)
≥10 years	↓ 68 (57–79)	↓ 50 (41–58)	↓ 1.3 (1.0–1.6)	↓ 0.9 (0.6–1.2)	↑ 0.03 (−0.1–0.2)
Unknown	↓ 65 (59–72)	↓ 51 (46–56)	↓ 1.2 (1.0–1.3)	↓ 0.9 (0.7–1.1)	↓ 0.1 (−0.2–0.0)
P_{trend} in known duration*	0.07	0.42	0.05	0.31	0.11
Diabetes by medications					
No medication	↓ 63 (57–69)	↓ 48 (44–53)	↓ 1.1 (0.9–1.3)	↓ 0.8 (0.7–1.0)	↓ 0.1 (−0.02–0.1)
Oral agents	↓ 57 (48–66)	↓ 50 (43–57)	↓ 1.0 (0.7–1.2)	↓ 0.9 (0.6–1.1)	↓ 0.2 (0.1–0.3)
Insulin (alone or with oral)	↓ 79 (68–90)	↓ 52 (44–61)	↓ 1.5 (1.2–1.9)	↓ 0.9 (0.6–1.2)	↑ 0.2 (−0.4 −0.1)
P_{trend}*	0.001	0.40	0.001	0.33	0.0003

Data are means (95% CI) adjusted for baseline age, sex, race, height, BMI, waist circumference, pack-years of smoking, sport activity index, education level, baseline lung function, BMI change from baseline to year 3, waist change from baseline to year 3, incident asthma or chronic lung disease or use of medications for the conditions at 3-year follow-up, and ARIC center. **P* values correspond to tests for linear trend across categories.

Yeh HC et al. Diabetes Care 2008;31:741-746

Función pulmonar y duración de la diabetes

Table 2—*Baseline spirometry by diabetes status and adjusted differences in adults with diabetes versus without diabetes at baseline*

	FVC (ml)	FEV_1 (ml)	FVC % predicted	FEV_1 % predicted	FEV_1-to-FVC ratio (%)
No diabetes	3,873 (3,863 to 3,882)	2,911 (2,904 to 2,919)	102.8 (102.6 to 103.1)	96.5 (96.3 to 96.8)	75.4 (75.3 to 75.5)
Diabetes	3,740 (3,711 to 3,769)	2,839 (2,856 to 2,863)	98.3 (98.5 to 100.1)	94.1 (93.3 to 94.9)	76.2 (75.8 to 76.5)
Diabetes vs. no diabetes	−133 (−163 to −103)	−72 (−97 to −47)	−3.6 (−4.4 to −2.7)	−2.4 (−3.2 to −1.6)	0.8 (0.4 to 1.1)
P value	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001
Diabetes, by fasting glucose					
<140 mg/dl vs. no diabetes	−109 (−155 to −63)	−66 (−105 to −29)	−2.9 (−4.1 to −1.7)	−2.3 (−3.5 to −1.0)	0.4 (−0.1 to 0.9)
140–199 mg/dl vs. no diabetes	−147 (−202 to −93)	−81 (−127 to −36)	−3.8 (−5.3 to −2.4)	−2.6 (−4.1 to −1.1)	0.9 (−0.2 to 0.1)
200 + vs. no diabetes	−155 (−216 to −94)	−69 (−120 to −19)	−4.2 (−5.7 to −2.6)	−2.4 (−4.1 to −0.8)	1.3 (0.6 to 1.9)
P_{trend}*	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001
Diabetes, by duration					
≤5 years vs. no diabetes	−105 (−166 to −43)	−27 (−78 to 24)	−2.8 (−4.5 to −1.2)	−1.1 (−2.7 to 0.6)	1.3 (0.7 to 2.0)
6–9 years vs. no diabetes	−153 (−249 to −56)	−77 (−158 to 3)	−3.9 (−6.4 to −1.4)	−2.5 (−5.1 to 0.1)	1.0 (−0.02 to 2.1)
≥10 years vs. no diabetes	−155 (−224 to −86)	−86 (−144 to −29)	−4.0 (−5.8 to −2.2)	−2.8 (−4.7 to −0.9)	0.8 (0.01 to 1.5)
Unknown vs. no diabetes	−135 (−175 to −95)	−84 (−118 to −51)	−3.7 (−4.7 to −2.6)	−2.8 (−3.9 to −1.8)	0.5 (0.05 to 0.94)
P_{trend} in known duration*	<0.0001	0.0005	<0.0001	0.0005	0.0002
Diabetes, by medications					
No medication vs. no diabetes	−112 (−154 to −77)	−70 (−100 to −36)	−3.0 (−4.0 to −2.0)	−2.2 (−3.2 to −1.1)	0.5 (0.1 to 1.0)
Oral agents vs. no diabetes	−141 (−198 to −84)	−56 (−103 to −9)	−3.7 (−5.2 to −2.2)	−2.0 (−3.5 to −0.4)	1.3 (0.7 to 1.9)
Insulin (alone or with oral) vs. no diabetes	−187 (−257 to −117)	−112 (−170 to −53)	−5.3 (−7.1 to −3.4)	−4.0 (−5.9 to −2.1)	0.9 (0.1 to 1.6)
P_{trend}*	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001

Data are means (95% CI) adjusted for baseline age, sex, race, height, BMI, waist circumference, pack-years of smoking, sport activity index, education level, and ARIC center. **P* values correspond to tests for linear trend across categories.

Yeh HC et al. Diabetes Care 2008;31:741-746

Función pulmonar, diabetes e inflamación

Table 5 QUINTILES OF HBA_{1c} VALUES AND RELATION WITH RESIDUAL LUNG FUNCTION (*) AND MEAN INFLAMMATORY MARKER LEVELS

	1 < = 6.60 n = 107	2 6.61-7.50 n = 92	3 7.51 - 8.60 n = 103	4 8.61 - 10.40 n = 97	5 > 10.40 n = 96	*p* VALUE
$rFEV_1$ (ml)	-82.73	-96.05	-130.78	-224.63	-186.30	0.0848
rFVC (ml)	-128.72	-133.01	-219.96	-314.23	-270.11	0.0324
C-RP	1.55	1.94	1.94	3.71	2.94	0.0155
FERRITIN	119.58	146.24	150.96	193.65	161.43	0.0056
FIBRINOGEN	424.89	420.60	444.27	438.56	461.67	0.0830
IL-6	3.55	3.71	3.88	4.03	3.88	0.8806
TNF	8.08	8.31	8.67	9.48	9.16	0.3050

(*) Mean residuals for FEV_1 and FVC adjusted by differences in age, height, sex, and smoking history.
C-RP: C-reactive protein; TNF: Tumor necrosis factor.

Dennis RJ et al. BMC Pulmonary medicine 2010;10:38

Función pulmonar y resistencia a la insulina

Table 3. Age-adjusted and multivariable associations of measures of lung function with insulin resistance, components of the insulin resistance syndrome and diabetes among women who were life-long non-smokers and were either single or had partners who were life-long non-smokers

	Number[a]	Change[b] adjusted for nurse, age and height squared (95% CI)	Fully[c] adjusted change[b] (95% CI)
Exposure = 1 standard deviation log FEV1			

The main findings of our study were that FEV1 and FVC are inversely associated with insulin resistance and with Type 2 diabetes. These associations were still evident after adjustment for important adult confounding factors, and were also similar in a group of women with little or no lifetime exposure to cigarette smoke. FEF25–75 was not associated with insulin resistance or Type 2 diabetes.

[a] Number with complete data on all variables included in fully adjusted model

[b] Change = regression coefficients [absolute difference for HDLc and systolic blood pressure and proportionate (%) change for HOMA score and triglycerides] for continuous variables and odds ratio for diabetes prevalence for a one standard deviation increase in log FEV1, log FVC and log FEF25–75
One standard deviation of log FEV1=0.29, one standard deviation of log FVC=0.25, one standard deviation of log FEF25–75=0.55

[c] Fully adjusted = adjusted for examining nurse, age, height squared, physical activity, BMI, WHR, white cell count, respiratory medication, adult social class, childhood social class
FEV1, forced expiratory volume in one second; FVC, forced vital capacity; FEF25–75, forced expiratory flow rate in mid-phase of expiration; HDLc, HDL cholesterol, HOMA, homeostasis model assessment

Lawlor DA et al. Diabetologia 2004; 47: 195-203.
British Women´s Heart and Health Study

Función pulmonar y síndrome metabólico

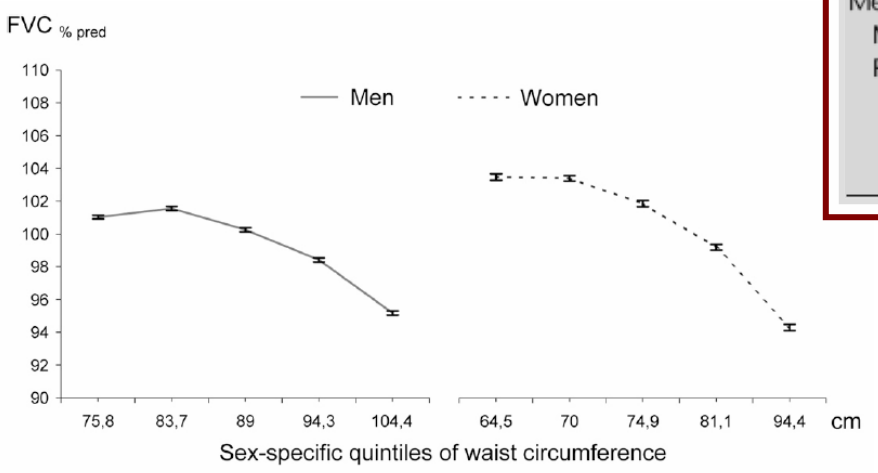


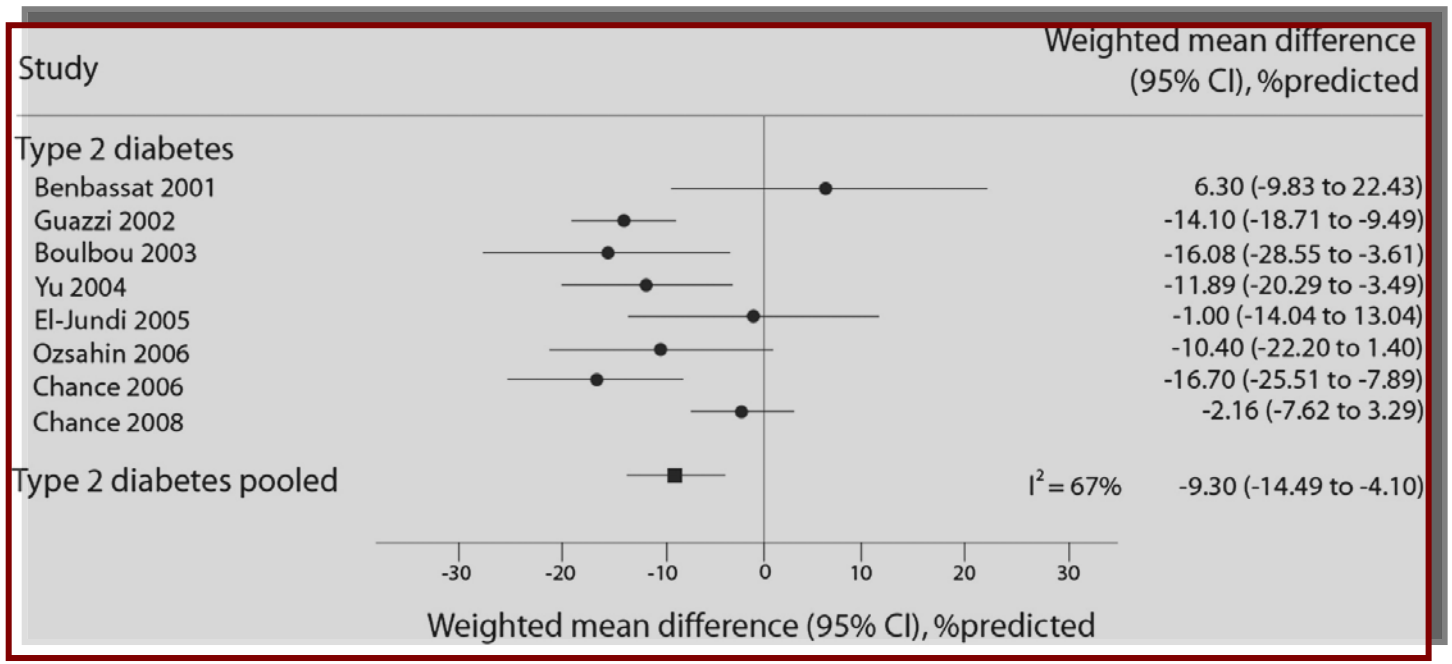
TABLE 6. ASSOCIATION BETWEEN METABOLIC SYNDROME, FACTORS FROM FACTOR ANALYSIS, AND VENTILATORY PATTERNS

	Normal	Obstructive Pattern*	Restrictive Pattern†
	OR	OR_a (95% CI)‡§	OR_a (95% CI)‡§
Whole cohort			
Metabolic syndrome	1 (Ref.)	0.94 (0.88–1.02)‡	1.40 (1.31–1.51)‡
Factors			
Lipids	1	0.96 (0.89–1.02)§	1.18 (1.10–1.26)§
Glucose–blood pressure	1	0.96 (0.91–1.02)	1.29 (1.21–1.38)
Abdominal obesity	1	1.13 (1.04–1.22)	2.13 (1.96–2.32)
Women			
Metabolic syndrome	1	0.92 (0.79–1.08)‡	1.33 (1.16–1.52)‡
Factors			
Lipids	1	0.94 (0.83–1.07)§	1.15 (1.01–1.30)§
Glucose–blood pressure	1	1.03 (0.92–1.16)	1.27 (1.12–1.44)
Abdominal obesity	1	1.19 (1.03–1.38)	2.37 (2.05–2.74)
Men			
Metabolic syndrome	1	0.96 (0.88–1.04)‡	1.46 (1.34–1.60)‡
Factors			
Lipids	1	0.96 (0.89–1.04)§	1.20 (1.10–1.31)§
Glucose–blood pressure	1	0.95 (0.89–1.01)	1.31 (1.21–1.41)
Abdominal obesity	1	1.11 (1.01–1.22)	2.03 (1.83–2.26)

Leone N et al. AJRCCM 2009; 179: 509-516.

Función pulmonar en DM2

DLCO



van den Borst B et al. Chest 2010;138:393-406

DLCO y diabetes

El descenso de la difusión pulmonar de monóxido de carbono (DLCO) en la diabetes se ha relacionado con:

- Microalbuminuria.

- Retinopatía

Pulmón y diabetes

- ¿Existe una neumopatía diabética?

  Sí, y se caracteriza por un patrón restrictivo con disminución de la capacidad de difusión.

Mecanismos fisiopatológicos

- Glicación no enzimática del colágeno y la elastina aumentando la rigidez del tórax y el parénquima pulmonar.
- Daño microvascular ➡ microangiopatía.
- Neuropatía frénica.

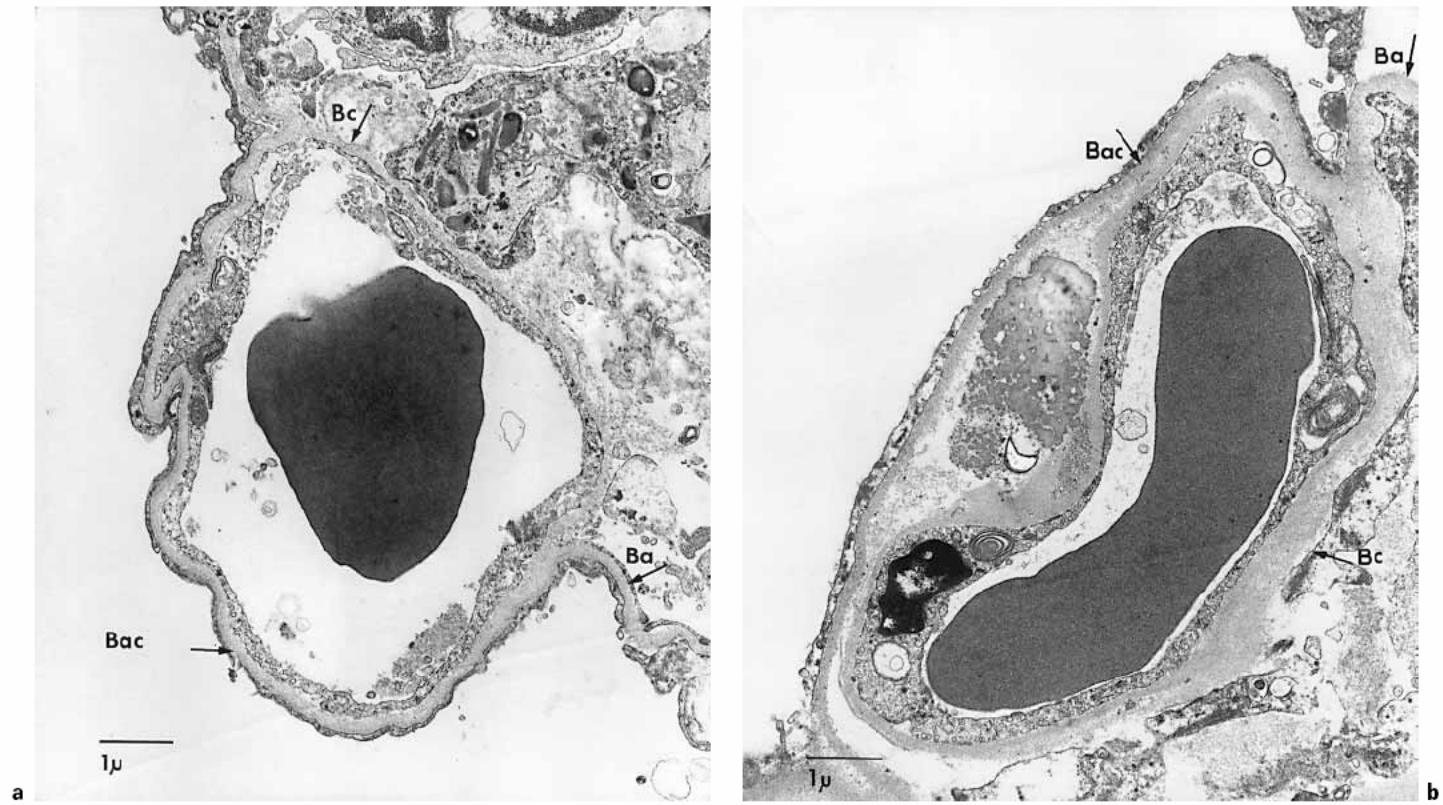
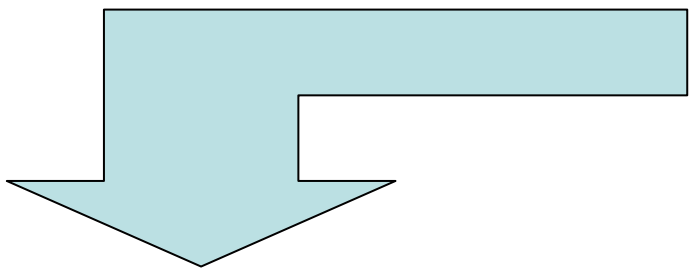
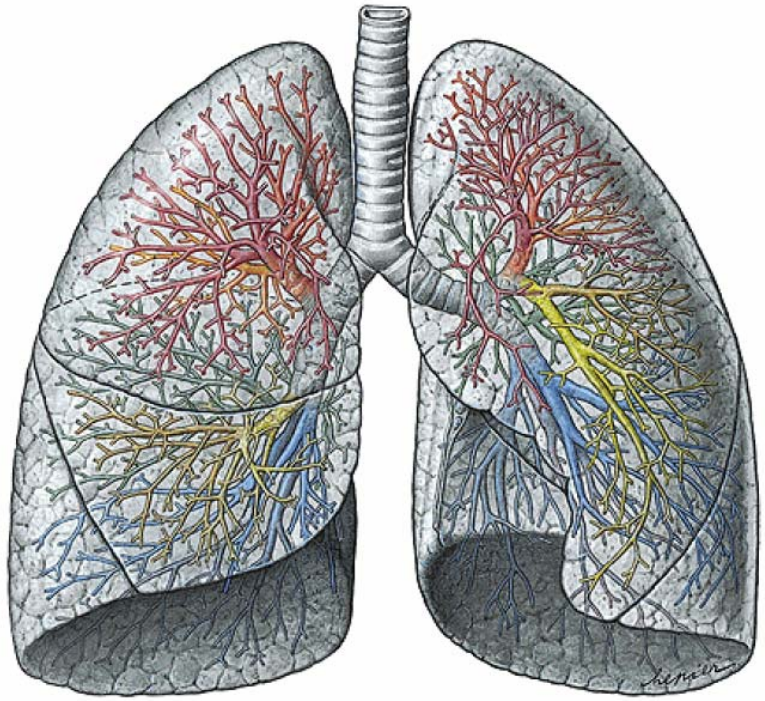
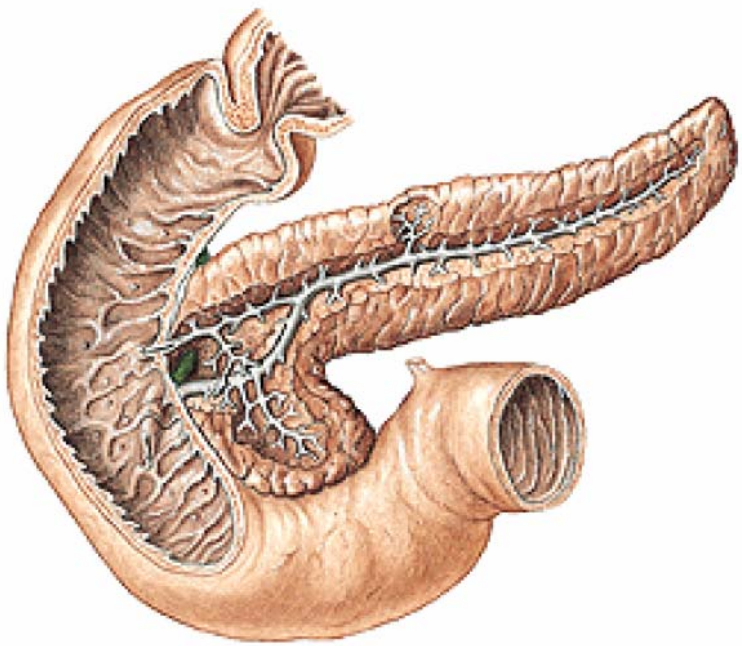


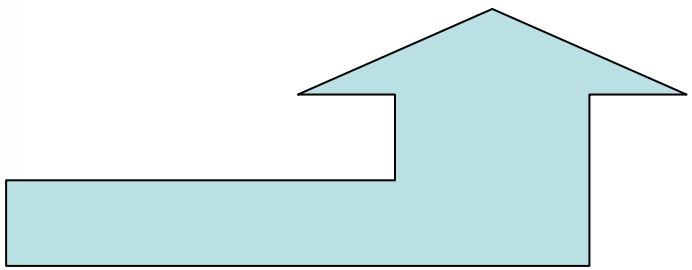
Fig. 1. Alveolar epithelium (Ba), alveolar capillary basal lamina (Bc) and both fused (Bac) in a control subject (**a**) and in a diabetic subject (**b**).

Weynand B et al. Respiration 1999;66:14-19.

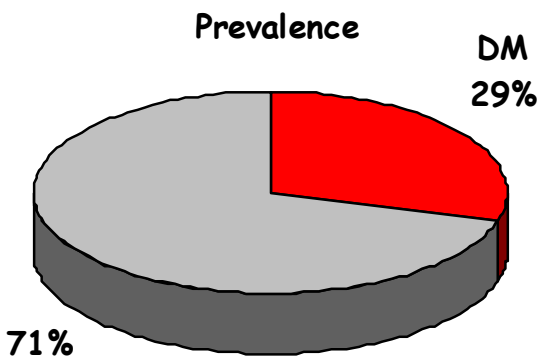


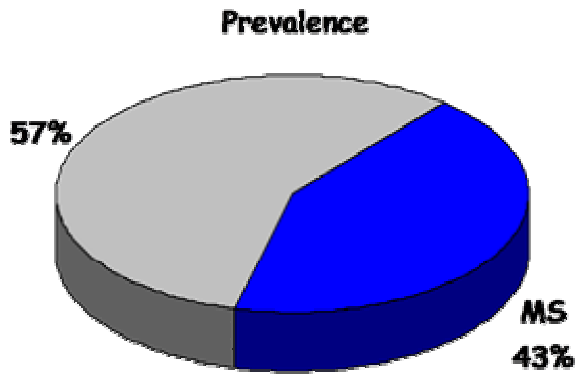






Estudio ECCO





MS component	GOLD stage II (n=127)	GOLD stage III (n=201)	GOLD stage IV (n=47)	p
Obesity	34 (26.8)	41 (20.4)	8 (17.0)	0.27
High blood pressure	97 (76.4)	142 (70.6)	25 (53.2)	0.01
Hyperglycemia	99 (77.9)	160 (79.6)	40 (85.1)	0.58
Hypertriglyceridemia	41 (32.3)	53 (26.4)	12 (25.5)	0.46
Low HDL	19 (31.5)	63 (31.3)	9 (19.1)	0.23
Data are presented as N (%)				

Riesgo de enfermedad pulmonar en la diabetes

Table 2—*Age- and sex-adjusted incidence rate (per 1,000 person-years) of each pulmonary outcome in all KPNC members aged ≥18 years, by diabetes status*

	Full cohort	Survey responder
Pneumonia*		
No diabetes	2.27 (2.24–2.29)	1.96 (1.85–2.08)
Diabetes	5.88 (5.56–6.21)	5.76 (5.40–6.11)
Asthma*		
No diabetes	0.22 (0.21–0.23)	0.16 (0.12–0.21)
Diabetes	0.48 (0.36–0.61)	0.41 (0.31–0.53)
COPD*		
No diabetes	0.60 (0.59–0.62)	0.52 (0.47–0.58)
Diabetes	0.91 (0.80–1.04)	0.87 (0.75–0.98)
Fibrosis*		
No diabetes	0.09 (0.09–0.10)	0.10 (0.07–0.13)
Diabetes	0.14 (0.12–0.16)	0.13 (0.11–0.16)
Lung cancer†		
No diabetes	0.51 (0.50–0.52)	0.66 (0.60–0.73)
Diabetes	0.47 (0.44–0.50)	0.66 (0.62–0.71)

Data are age- and sex-adjusted rates (95% CI). *Listed as the primary discharge diagnosis or underlying cause of death in the Kaiser Permanente databases. †Identified through the KPNC Cancer Registry.

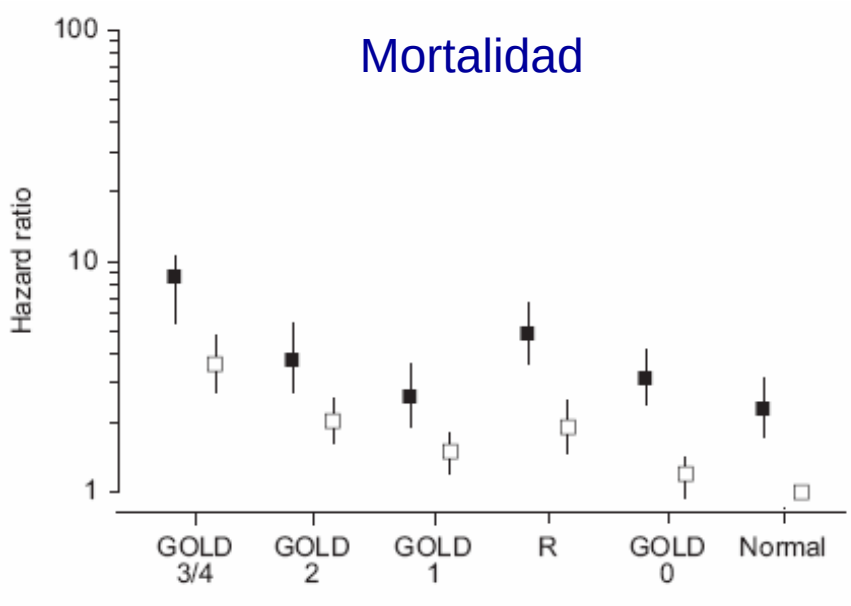
Table 3—*HRs and 95% CI for the association between each pulmonary condition and diabetes status among KPNC survey responders*

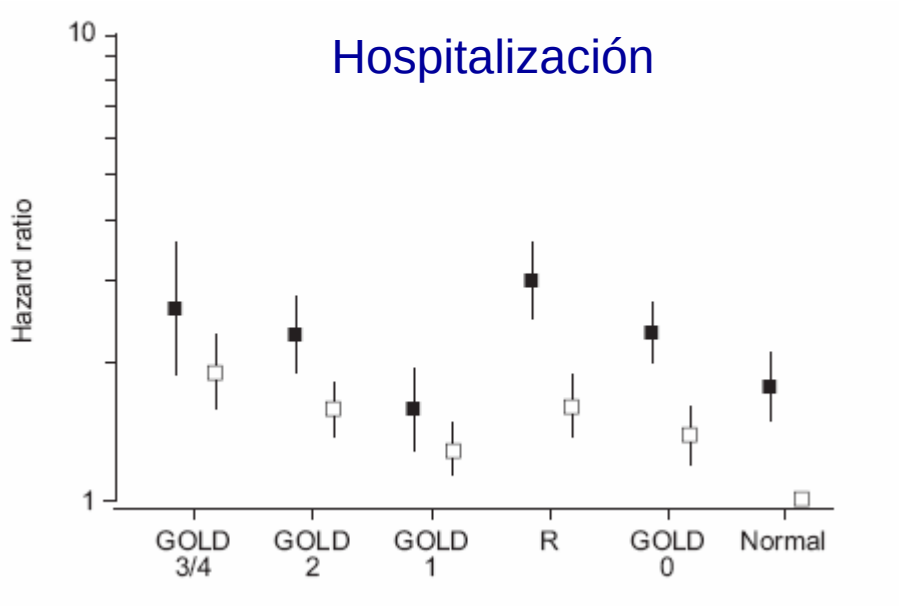
	Model 1*	Model 2†
Asthma‡	2.21 (1.72–2.85)	1.08 (1.03–1.12)
COPD‡	1.57 (1.40–1.77)	1.22 (1.15–1.28)
Fibrosis‡	1.64 (1.23–2.18)	1.54 (1.31–1.81)
Pneumonia‡	2.47 (2.32–2.62)	1.92 (1.84–1.99)
Lung cancer§	1.05 (0.94–1.17)	1.10 (0.96–1.26)

*Adjusted for age, sex, and race/ethnicity. †Adjusted for age, sex, race/ethnicity, smoking, BMI, education, alcohol consumption, and number of outpatient visits. ‡Primary discharge diagnosis or underlying cause of death in the Kaiser Permanente databases. §Identified through the KPNC Cancer Registry.

Erhlich SF et al. Diabetes Care 2010;33:55-60

EPOC, diabetes y morbimortalidad





Mannino DM et al. Eur Respir J 2008; 32: 962-969.

EPOC, diabetes y antibióticos

TABLE 4 *Comparison between exacerbations of COPD treated without—and with antibiotics (n = 1465)*

Characteristic	No antibiotics prescribed, 688 (47%)	Antibiotics prescribed, 777 (53%)	Univariate, OR (95% CI)	Multivariate, OR (95% CI)	*P* value
Mean age (SD)	74.7 (6.5)	74.9 (6.8)	1.0 (1.0–1.0)	–	NS
Male gender	329 (48)	414 (53)	1.2 (1.0–1.5)	1.3 (1.0–1.5)	0.03
Use of oral glucocorticoids[a]	47 (6.8)	56 (7.2)	1.1 (0.7–1.6)	–	NS
Previous use of antibiotics[b]	45 (6.5)	45 (5.8)	0.9 (0.6–1.3)	–	NS
Diabetes mellitus type 1 or 2	45 (6.5)	83 (11)	1.7 (1.2–2.5)	1.7 (1.1–2.4)	0.01
Malignancy[c]	88 (13)	110 (14)	1.1 (0.8–1.5)	–	NS
Heart failure	166 (24)	235 (30)	1.4 (1.1–1.7)	1.3 (1.0–1.7)	0.02
Cardiovascular disease	149 (22)	202 (26)	1.3 (1.0–1.6)	–	NS
Stroke	41 (6.0)	49 (6.3)	1.1 (0.7–1.6)	–	NS
Dementia	11 (1.6)	16 (2.1)	1.3 (0.6–2.8)	–	NS
Kidney disease	14 (2.0)	25 (3.2)	1.6 (0.8–3.1)	–	NS

Bont J et al. Family Practice 2007; 24: 317-322.

Pulmón y diabetes

- ¿Existe una neumopatía diabética?

- ¿Influye la diabetes en la enfermedad pulmonar crónica?

  Sí, aumentando la morbimortalidad y el uso de antibióticos

EPOC y riesgo de diabetes

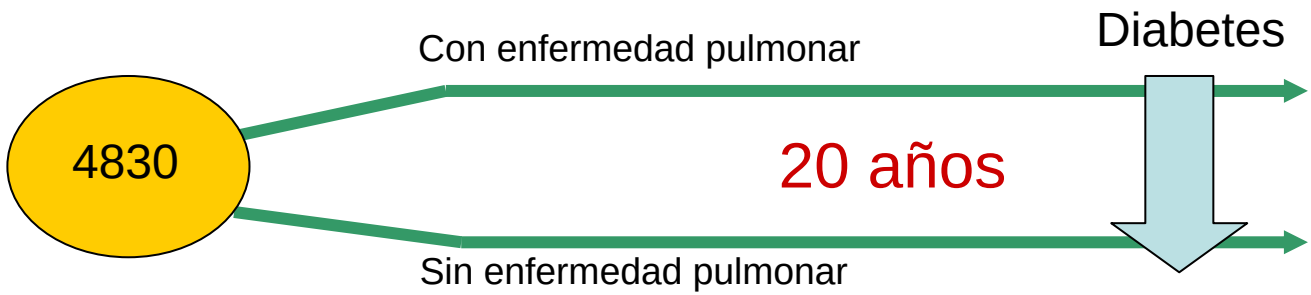


Table 3—*Incidence rates and HRs for diabetes by pulmonary conditions among participants aged 25–74 years, NHEFS, 1971–1975 to 1992–1993*

Pulmonary conditions	No. of cases	Person-years	Unadjusted incidence per 100,000 person-years*	Age-adjusted incidence per 100,000 person-years*	HR (95% CI) Unadjusted	Age-adjusted	Multiple-adjusted†
COPD (moderate or severe)	46	5,647	711	604	1.54 (1.03–2.30)	1.23 (0.84–1.81)	1.02 (0.68–1.53)
COPD (mild)	29	5,929	388	330	0.83 (0.51–1.35)	0.66 (0.40–1.10)	0.66 (0.39–1.12)
Symptoms	78	12,221	616	679	1.31 (0.98–1.76)	1.34 (1.00–1.81)	1.06 (0.76–1.48)
RLD	68	6,076	1,106	1047	2.38 (1.74–3.27)	2.04 (1.47–2.81)	1.45 (1.04–2.03)
Normal	222	47,466	475	516	1.00	1.00	1.00
P for overall test‡					<0.001	<0.001	0.032

Of 4,830 in the total sample, 443 people developed diabetes. *Estimate calculated using sampling weights. †Adjusted for age, sex, race or ethnicity, education, smoking status, systolic blood pressure, use of antihypertensive medication, cholesterol concentration, BMI, alcohol use, recreational exercise, and nonrecreational activity. ‡Wald χ^2 test.

Ford ES, Mannino DM. Diabetes Care 2004; 27: 2966-2970.

EPOC y riesgo de diabetes

Table 2—*Risk of type 2 diabetes from 1988 to 1996 according to COPD or asthma status*

	Person-years	Incident diabetes	Age-adjusted RR (95% CI)	Age- and BMI-adjusted RR (95% CI)	Multivariate RR (95% CI)*
COPD cohort (n = 97,245)					
No COPD	726,840	2,940	1.0 (reference)	1.0 (reference)	1.0 (reference)
COPD	2,505	19	1.8 (1.1–2.8)	1.9 (1.2–3.0)	1.8 (1.1–2.8)
Asthma cohort (n = 94,511)					
No asthma	693,066	2,758	1.0 (reference)	1.0 (reference)	1.0 (reference)
Asthma	15,389	69	1.1 (0.9–1.5)	0.9 (0.7–1.2)	1.0 (0.8–1.2)

*Adjusted for age, BMI (in four categories), sedentary (weekly frequency of moderate-to-vigorous exercise <0.5 h), smoking status (never smoked, former smoker, current smoker [<25 cigarettes/day], or current smoker [≥25 cigarettes/day]), daily alcohol intake, and a dietary score variable.

Nurses´ Health Study

Rana JS et al.
Diabetes Care 2004; 27: 2478-2484

Table 3—*Risk of type 2 diabetes associated with COPD or asthma stratified by smoking status*

	COPD		Asthma	
	n (%)	RR (95% CI)	n (%)	RR (95% CI)
All patients	1,342 (100)	1.8 (1.1–2.8)	2,879 (100)	1.0 (0.8–1.2)
Never smokers	215 (16)	1.4 (0.46–4.5)	1,382 (48)	0.98 (0.69–1.4)
Past smokers	416 (31)	2.2 (1.1–4.4)	1,180 (41)	1.05 (0.73–1.5)
Current smokers	711 (53)	1.7 (0.84–3.4)	317 (11)	0.79 (0.32–1.9)
All smokers	1,127 (84)	2.0 (1.2–3.2)	1,497 (52)	1.01 (0.72–1.4)

*Adjusted for age, BMI (in four categories), sedentary (weekly frequency of moderate-to-vigorous exercise <0.5 h), smoking status (never smoked, former smoker, current smoker [<25 cigarettes/day], or current smoker [≥25 cigarettes/day]), daily alcohol intake, and a dietary score variable.

EPOC y riesgo de diabetes

Table 2 Crude and adjusted† ORs from multivariable analysis of having COPD and a previous diagnoses of CVD, stroke or DM in different strata of smoking status and age in years

Comorbid diseases		Crude OR (95% CI)	Adjusted OR (95% CI) Age (years) 35–44	45–54	55–64	65–74	≥75
CVD	Summary	4.98 (4.85 to 5.81)					
	Never smokers		7.7 (1.9 to 31.5)	3.8 (1.9 to 7.4)	3.4 (2.5 to 4.5)	2.2 (1.9 to 2.5)	2.3 (2.1 to 2.5)
	Ex-smokers		†	3.4 (1.9 to 6.2)	2.1 (1.8 to 2.6)	1.7 (1.6 to 1.9)	1.4 (1.3 to 1.5)
	Current smokers		6.8 (4.1 to 11.3)	2.8 (2.4 to 3.4)	2.2 (2.1 to 2.4)	1.6 (1.5 to 1.7)	1.6 (1.5 to 1.7)
	Unknown		*	34.6 (4.4 to 268.6)	4.3 (1.1 to 17.9)	6.3 (3.3 to 12.0)	4.0 (3.0 to 5.3)
Stroke	Summary	3.34 (3.21 to 3.48)					
	Never smokers		3.7 (0.5 to 26.5)	2.4 (0.8 to 7.6)	1.4 (0.8 to 2.5)	1.6 (1.2 to 2.0)	1.0 (0.9 to 1.2)
DM	Summary	2.04 (1.97 to 2.12)					
	Never smokers		2.1 (0.8 to 5.7)	2.4 (1.5 to 4.0)	1.7 (1.2 to 2.3)	1.3 (1.0 to 1.5)	0.9 (0.8 to 1.1)
	Ex-smokers		*	1.1 (0.5 to 2.3)	1.0 (0.8 to 1.3)	0.9 (0.8 to 1.0)	0.8 (0.7 to 0.9)
	Current smokers		2.4 (1.6 to 3.6)	1.4 (1.2 to 1.7)	1.1 (1.0 to 1.2)	0.8 (0.8 to 0.9)	0.7 (0.7 to 0.8)
	Unknown		*	*	6.0 (2.1 to 16.8)	2.4 (1.0 to 5.7)	1.8 (1.1 to 2.8)

*Unable to calculate as too few observations.
†CVD adjusted for sex; stroke and DM adjusted for sex and previous CVD.
COPD, chronic obstructive pulmonary disease; CVD, cardiovascular disease; DM, diabetes mellitus.

Feary JR et al. Thorax 2010;65:956-962.

Diabetes mellitus

COPD was associated with a small increase in the odds of DM in the younger age groups and was generally slightly higher in never smokers. The greatest effect was seen in the youngest current smokers (OR 2.4, 95% CI 1.6 to 3.6) and 45–55-year-old never smokers (OR 2.4, 95% CI 1.5 to 4.0). In older age groups, COPD was associated with a reduction in DM regardless of smoking status (OR 0.7, 95% CI 0.7 to 0.8 for current smokers; table 2).

Riesgo de diabetes y corticoides inhalados

Table 2 Crude and Adjusted Rate Ratios of Newly Treated Diabetes Associated with Current Use of Inhaled Corticosteroids among Patients Initially Free of Diabetes

	Cases	Controls	Crude Rate Ratio	Adjusted*	
				Rate Ratio	95% CI
Number of subjects	30,167	301,096			
Inhaled corticosteroid use					
No current use (%)	84.5	89.0	1.00	1.00	Reference
Current use† (%)	15.5	11.0	1.51	1.34	1.29-1.39
Low dose (%)	1.4	1.2	1.24	1.18	1.06-1.31
Medium dose (%)	10.8	8.0	1.44	1.30	1.25-1.35
High dose (%)	3.3	1.8	1.97	1.64	1.52-1.76

CI = confidence interval.
*Adjusted for all of the factors listed in Table 1.
†Current use refers to a prescription in the 30 days before the index date.

Table 3 Crude and Adjusted Rate Ratios of Progression to Insulin Use Associated with Current Use of Inhaled Corticosteroids among Patients on Oral Hypoglycemic Agents

	Cases	Controls	Crude Rate Ratio	Adjusted*	
				Rate Ratio	95% CI
Number of subjects	2,099	20,763			
Inhaled corticosteroid use					
No current use (%)	84.1	89.8	1.00	1.00	Reference
Current use† (%)	15.9	10.2	1.68	1.34	1.17-1.53
Low dose (%)	0.8	0.6	1.33	1.08	0.63-1.87
Medium dose (%)	11.4	7.6	1.61	1.30	1.12-1.52
High dose (%)	3.8	2.0	2.11	1.54	1.18-2.02

CI = confidence interval.
*Adjusted for all of the factors listed in Table 1.
†Current use refers to a prescription in the 30 days before the index date.

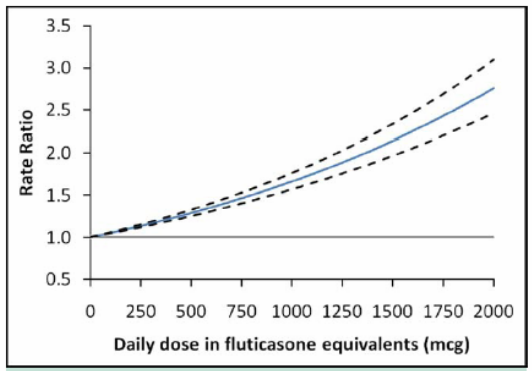


Figure Adjusted rate ratio of diabetes incidence associated with inhaled corticosteroid use, as a function of the current dose converted to fluticasone equivalents (in μg), along with the corresponding 95% confidence limits for the fitted dose-response curve.

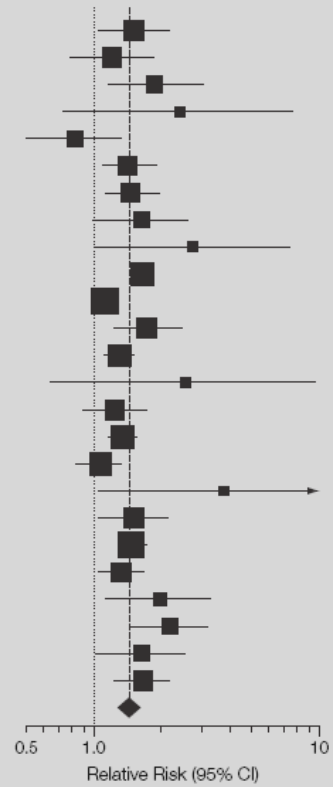
- Mayor incidencia de diabetes
- Mayor progresión de diabetes
- Efecto dosis-dependiente

Suissa S et al. Am J Med 2010; 123: 1001-1006.

Tabaco y riesgo de diabetes

Figure 2. Adjusted Relative Risks of Diabetes for Current Smokers Compared With Nonsmokers

Source	Weight, % (Random Effects Model)	Relative Risk (95% CI)
Cassano et al,[31] 1992	3.88	1.50 (1.07-2.10)
Perry et al,[32] 1995	3.16	1.20 (0.80-1.80)
Rimm et al,[33] 1995	2.59	1.88 (1.17-3.02)
Kawakami et al,[34] 1997	0.62	2.38 (0.77-7.40)
Njølstad et al,[35] 1998	2.69	0.82 (0.52-1.30)
Sugimori et al,[36] 1998	4.97	1.42 (1.10-1.83)
Uchimoto et al,[37] 1999	4.78	1.47 (1.13-1.92)
Strandberg et al,[38] 2000	2.62	1.62 (1.01-2.59)
Nakanishi et al,[39] 2000	0.84	2.74 (1.05-7.13)
Manson et al,[40] 2000	7.42	1.63 (1.50-1.77)
Will et al,[41] 2001	7.69	1.13 (1.07-1.19)
Wannamethee et al,[42] 2001	3.91	1.74 (1.25-2.43)
Hu et al,[27] 2001	6.92	1.30 (1.15-1.47)
Montgomery and Ekbom,[43] 2002	0.46	2.47 (0.66-9.30)
Sawada et al,[44] 2003	4.44	1.24 (0.93-1.66)
Sairenchi et al,[45] 2004	6.80	1.35 (1.18-1.54)
Carlsson et al,[46] 2004	5.71	1.06 (0.86-1.30)
Eliasson et al,[47] 2004	0.53	3.74 (1.08-12.91)
Lyssenko et al,[48] 2005	3.88	1.50 (1.07-2.10)
Patja et al,[49] 2005	6.85	1.46 (1.28-1.66)
Waki et al,[50] 2005	5.58	1.31 (1.06-1.62)
Tenenbaum et al,[51] 2005	2.30	1.94 (1.16-3.25)
Foy et al,[52] 2005	3.52	2.15 (1.49-3.11)
Meisinger et al,[29] 2006	2.90	1.62 (1.05-2.50)
Houston et al,[53] 2006	4.94	1.65 (1.28-2.13)
Overall (I^2=75.5%; P<.001 for Q statistic)	100.00	1.44 (1.31-1.58)



CI indicates confidence interval. Size of data markers indicates the weight of the study.

Willi C et al. JAMA 2007;298:2654-2664

Diabetes, EPOC e inercia terapéutica

	Addition of an antidiabetic medicine or switch to insulin		
	SHR	**95% CI**	**P value**
Number of unrelated comorbidities	0.872	0.839–0.905	<0.001
Cancer	0.703	0.590–0.836	<0.001
Chronic obstructive pulmonary disease	0.866	0.778–0.963	0.008
Dementia	0.682	0.519–0.895	0.006
Depression	0.803	0.742–0.868	<0.001
Urinary incontinence	0.794	0.542–1.164	0.237
Parkinson's disease	0.565	0.457–0.698	<0.001
Age	0.975	0.972–0.977	<0.001
Number of hospitalisations	0.776	0.744–0.809	<0.001
Adherence to antidiabetic medicines	0.599	0.556–0.644	<0.001
Residency (aged care versus community)	0.892	0.853–0.934	<0.001
Endocrinology service	1.196	1.145–1.250	<0.001

Vitry AI et al. PLoS ONE 2010;5(11):e14024.

Pulmón y diabetes

- ¿Existe una neumopatía diabética?
- ¿Influye la diabetes en la enfermedad pulmonar crónica?
- ¿Influye la enfermedad pulmonar crónica en la diabetes?

  Sí, aumentando la inercia terapéutica.

Respiratory Research

Commentary

Chronic Obstructive Pulmonary Disease, inflammation and co-morbidity – a common inflammatory phenotype?

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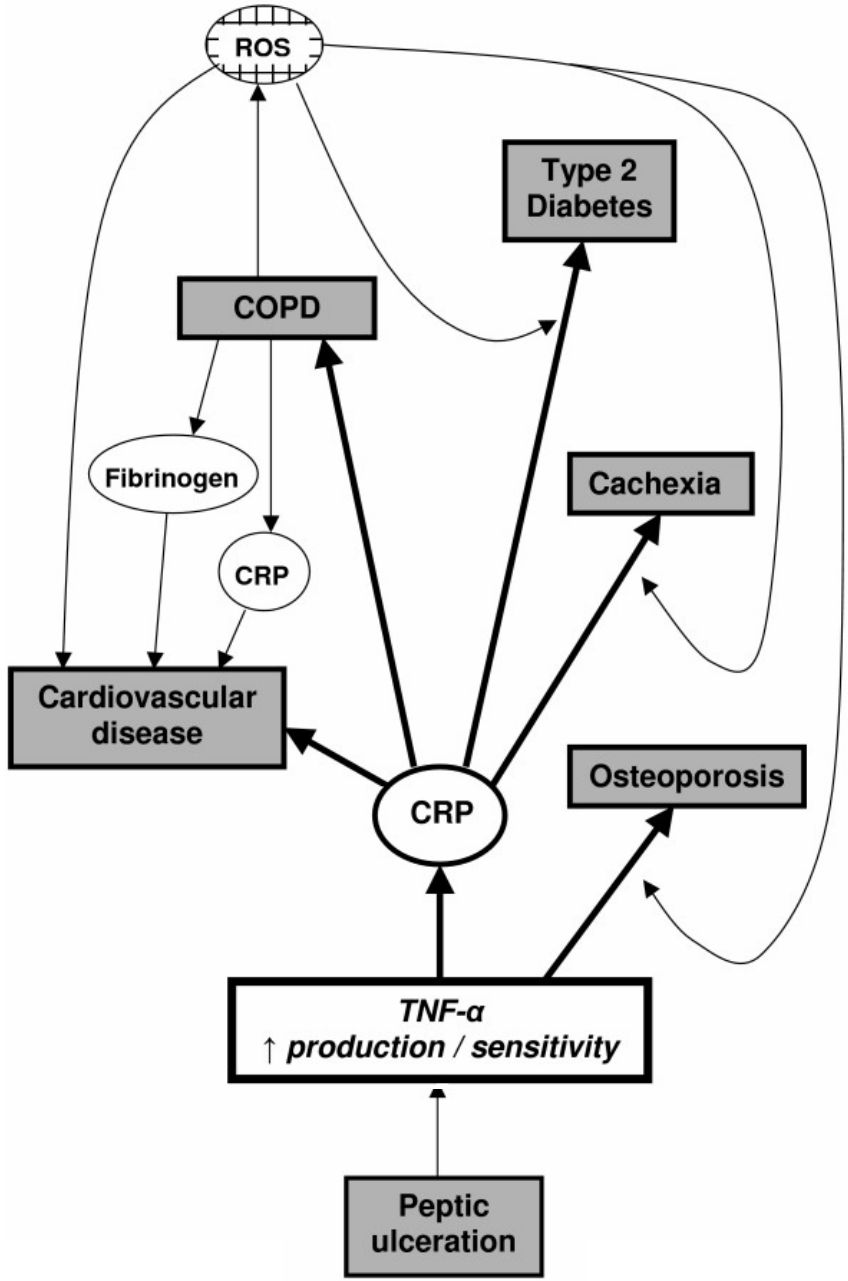
Published: 02 May 2006

Respiratory Research 2006, **7**:70 doi:10.1186/1465-9921-7-70

Received: 06 December 2005

Accepted: 02 May 2006



¡Muchas gracias!