

dice un proverbio chino...



SSc mortality, supervivencia, causas de muerte...

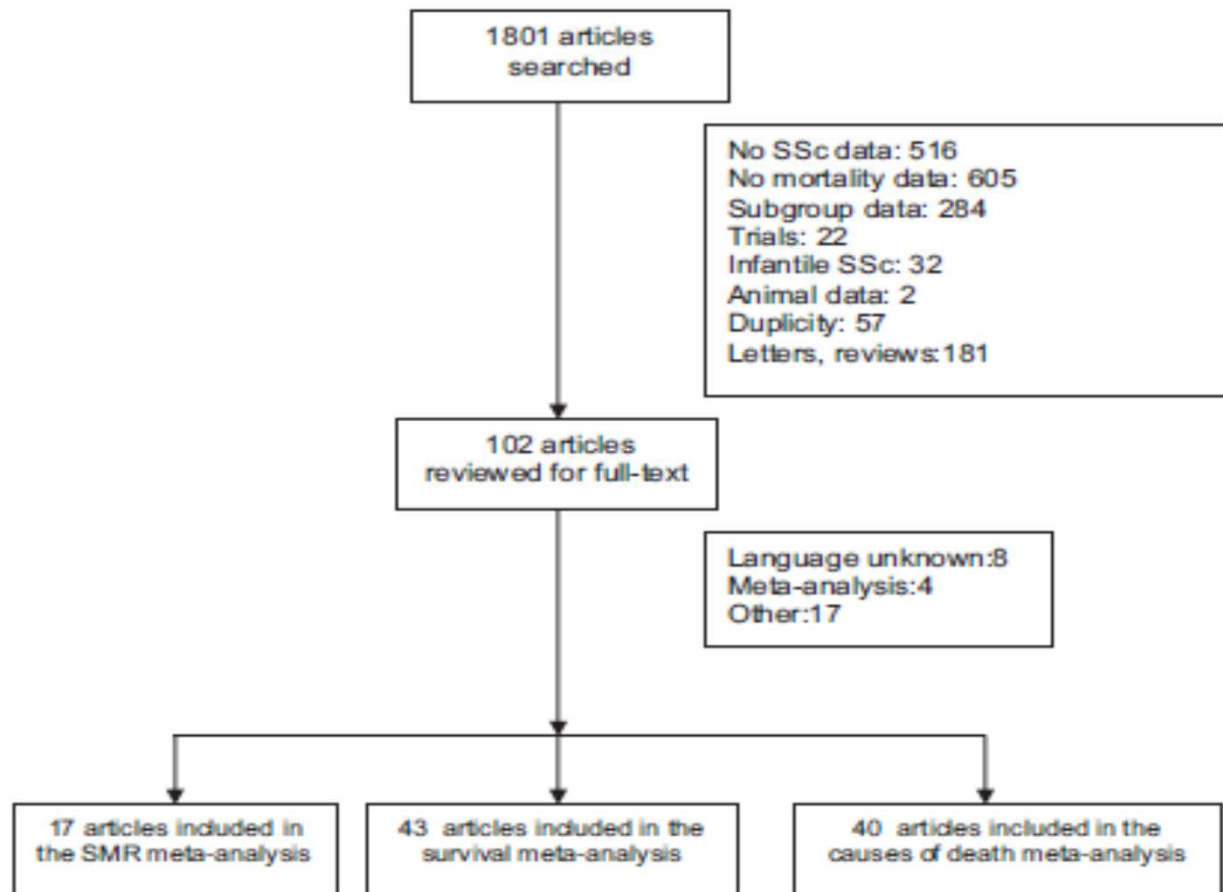


Fig. 1. Flow-chart.

SSc y mortalidad: SMR...

SMR= standardized mortality ratio

Muertes observadas/muertes esperadas

(ajustado por edad y sexo)

SSc y mortalidad: SMR...

Study	Country	Years	Mid-cohort year	Lost to follow-up	QA	No. of deaths	Overall SMR (95% CI)
Zarafonitis [15]	US	1948-1980	1964	40/390 (10%)	7	142	5.40 (4.51-6.29)
Jacobsen [30]	DEN	1960-1996	1978	0	8	160	2.90 (2.50-3.40)
Abu-Shakra [36]	CAN	1976-1990	1983	17/237 (7%)	7	61	4.69 (3.73-5.65)
Walsh and Fenster [1]	US	1981-1990	1985	0	7	2123	1.05 (1.01-1.1)
Bryan [45]	UK	1982-1992	1987	0	7	55	4.05 (3.03-5.22)
Hesselstrand [49]	SWE	1983-1995	1989	0	7	49	4.59 (3.48-6.07)
Hashimoto [55]	JAP	1973-2008	1990	9/405 (2.2%)	8	86	2.76 (2.18-3.35)
Alamanos [58]	GRE	1981-2002	1991	2/109 (2%)	7	36	2.0 (1.2-2.8)
Scussel-Lonzetti [56]	CAN	1984-1999	1991	0	8	66	2.69 (2.10-3.40)
Pérez-Bocanegra [57]	SPA	1976-2007	1991	NA	7	73	1.90 (1.50-2.30)
Joven [60]	SPA	1980-2006	1993	10/204 (4.9%)	9	44	3.10 (1.60-6.10)
Alba [66]	SPA	1986-2010	1998	0	8	151	3.80 (3.18-4.43)
Hissaria [69]	AUS	1993-2007	2000	24/786 (3%)	7	331	1.46 (1.28-1.69)
Mok [73]	CHI	1999-2008	2003	0	8	110	3.94 (3.20-4.68)
Hoffmann-Vold [74]	NOR	1999-2009	2004	0	8	43	2.03 (1.40-2.60)
Strickland [77]	UK	1999-2010	2004	19/223 (8.5%)	7	53	1.34 (0.95-1.74)
Kuo [78]	TAIW	2002-2007	2005	0	8	204	3.24 (2.82-3.71)

SSc y mortalidad...

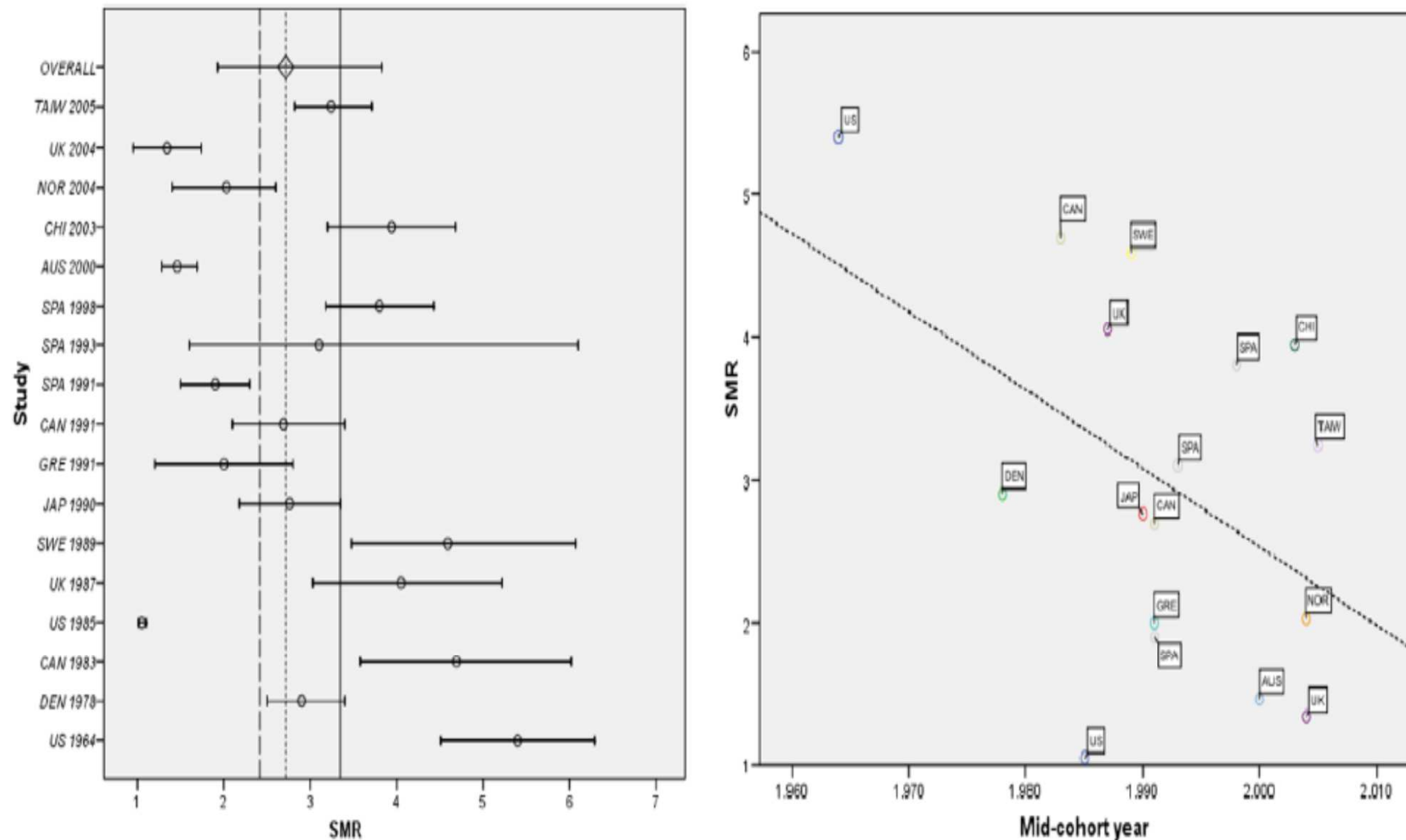


Fig. 2. SMR meta-analysis the Forest plot: overall SMR (discontinuous points) = 2.72 (1.93–3.83), SMR before 1990 (continuous line) = 3.35 (1.57–7.11), and SMR after 1990 (discontinuous lines) = 2.42 (1.89–3.11). Meta-regression between SMR (lnSMR) with mid-cohort year (coefficient $b = 0.055$, $p = 0.064$) and excluding the outlier study (US 1985 by Walsh et al.) (coefficient $b = 0.064$, $p = 0.02$).

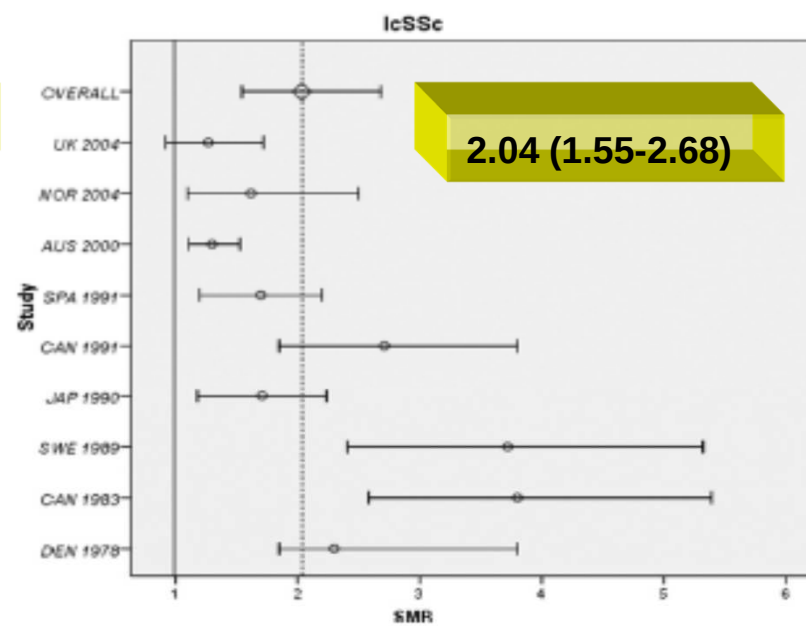
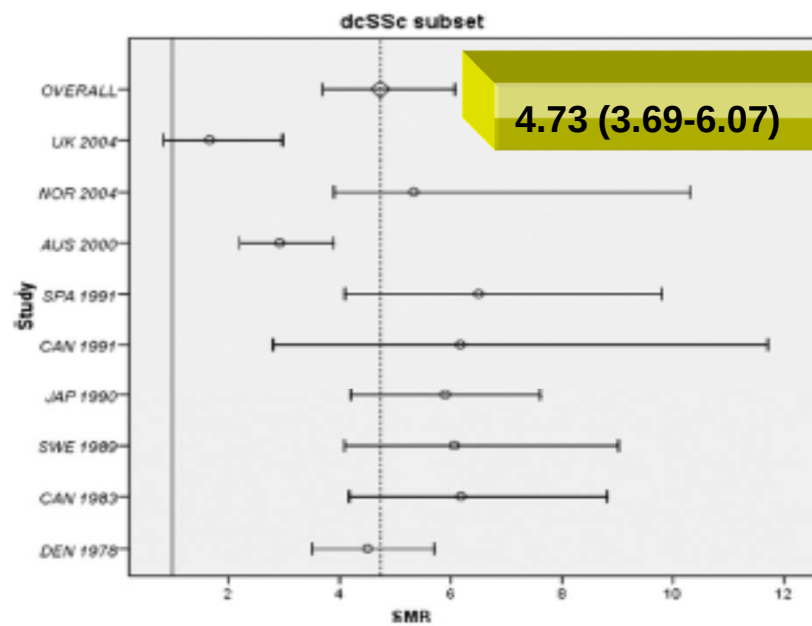
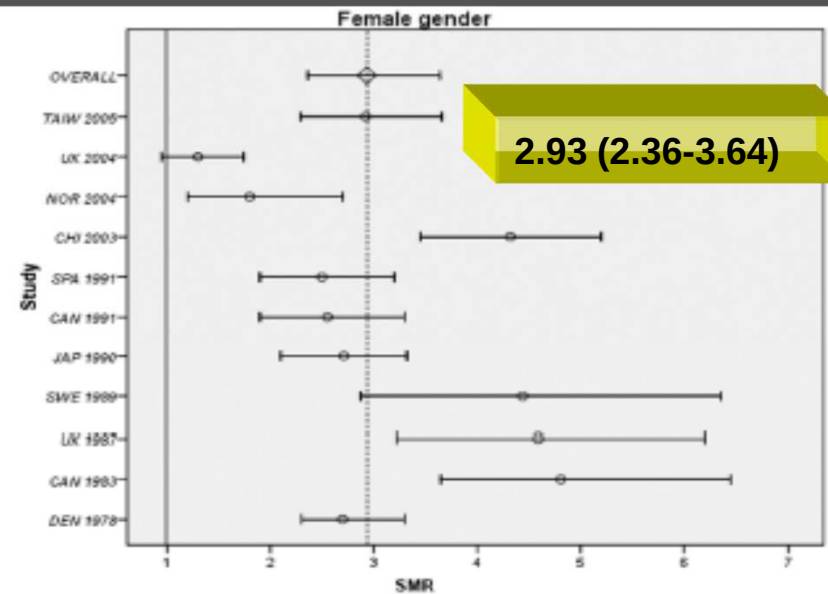
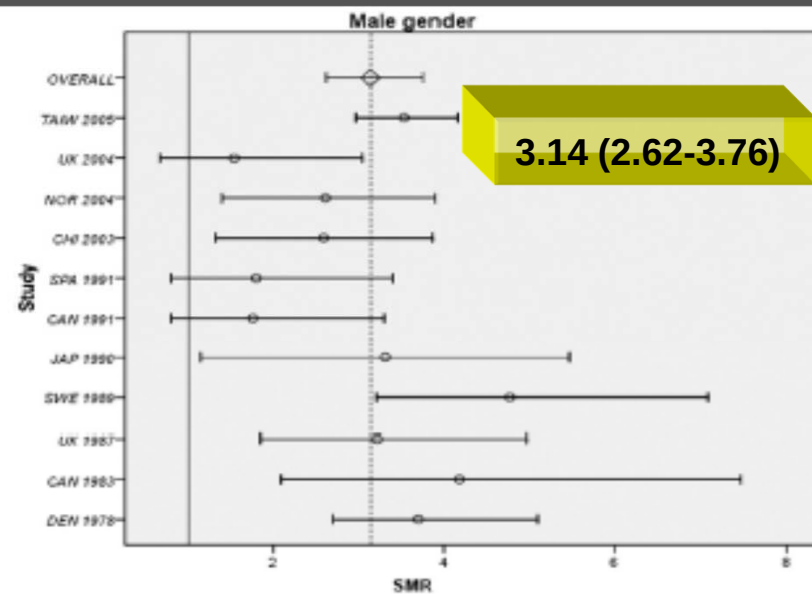


Fig. 3. SMR meta-analysis for different subsets.

SSc y supervivencia...

“No hay que mezclar churras con merinas...”



from dx?

from onset Raynaud?

from onset non-Raynaud?

SSc y supervivencia...

Table 2
Cumulative survival from studies

Study	Country	Years (mid-cohort)	QA (stars)	1-Year survival (%)	5-Year survival (%)	10-Year survival (%)	20-Year survival (%)	From onset/diagnosis
Tuffanelli and Winkelmann [8]	US	1935–1968 (46)	7	NA	70.3	69	NA	Diagnosis
Farmer et al. [9]	US	1945–1952 (48)	7	NA	53	NA	NA	Diagnosis
Bennet et al. [12]	UK	1947–1970 (58)	6	94	73	50	NA	Diagnosis
Medsgers and Masi [13]	US	1955–1970 (62)	7	78	48	NA	NA	Diagnosis
Zarafonitis et al. [15]	US							Diagnosis
Medsgers and Masi [17]	US							Diagnosis
Rowell [18]	US							Diagnosis
Barnett et al. [19]	US							Diagnosis
Goulet et al. [20]	FR							Diagnosis
Giordano et al. [21]	FR							Diagnosis
Altman et al. [22]	US							Diagnosis
Eason et al. [23]	US							Diagnosis
Wynn et al. [24]	US							Diagnosis
Peters-Golden et al. [26]	US							Diagnosis
Ferri et al. [27]	US							Diagnosis
Lally et al. [28]	US							Diagnosis
Jacobsen et al. [30]	US							Diagnosis
Kuwana et al. [32]	JA							Diagnosis
Geirsson et al. [34]	IS							Diagnosis
Kaburaki et al. [37]	JA							Diagnosis
Nishioka et al. [39]	JA							Diagnosis
Simeón [40]	ES							Diagnosis
Bulpiatt [43]	US							Diagnosis
Bryan [45]	US							Diagnosis
Nagy [46]	HU							Diagnosis
Hesselstrand [49]	SE							Diagnosis
Kim [53]	KR							Diagnosis
Mayes [54]	US							Diagnosis
Hashimoto [55]	JA							Diagnosis
Pérez-Bocanegra [57]	ES							Diagnosis
Alamanos [58]	GR							Diagnosis
Nihtyanova [59]	US							Diagnosis
Joven [60]	SPA	1980–2006 (93)	9	95	85	75	55	Onset (non-Raynaud's first symptom)
Ruangjutipopan [61]	THAI	1987–2001 (94)	6	NA	73	67.4	NA	Onset (no definition)
Czirják [62]	HUN	1983–2005 (94)	7	NA	84	72.6	NA	Diagnosis
Arias-Núñez [65]	SPA	1988–2006 (97)	7	NA	83.9	64.9	NA	Diagnosis
Alba [66]	SPA	1986–2010 (98)	8	NA	90.7	NA	NA	Diagnosis
Al-Dhaher [67]	CAN	1994–2004 (99)	7	NA	90	82	NA	Diagnosis
Sampaio-Barros [68]	BRA	1991–2010 (100)	7	NA	90	84	NA	Onset (no definition)
Hoffmann-Vold [74]	NOR	1999–2009 (104)	8	NA	95	86	NA	Onset (non-Raynaud's first symptom)
Vettori [75]	ITA	2000–2008 (104)	6	NA	94.8	NA	NA	Onset (first Raynaud)
Kuo [78]	TAIW	2002–2007 (105)	8	94.9	83.2	NA	NA	Diagnosis

SSc y supervivencia...

	Survival from onset (first Raynaud)			Survival from onset (non-Raynaud's first symptom)			Survival from diagnosis		
	Before 1990 (5 studies)	After 1990 (3 studies)	<i>p</i>	Before 1990 (4 studies)	After 1990 (3 studies)	<i>p</i>	Before 1990 (18 studies)	After 1990 (8 studies)	<i>p</i>
Number of patients	840	1693		846	802		4365	3476	
1-Year survival (% mean) (SD)	–	–	–	92 (NA)	95 (NA)	–	85.3 (9.5)	94.9 (NA)	0.384
5-Year survival (% mean) (SD)	85.1 (10.4)	92.8 (2.9)	0.385	79.7 (8.2)	90 (5.0)	0.118	70.6 (14.3)	84.4 (3.8)	0.001
10-Year survival (% mean) (SD)	71.5 (9.5)	88 (NA)	0.189	72.1 (2.5)	80.5 (7.8)	0.358	58.8 (14.8)	70.9 (10.1)	0.086
20-Year survival (% mean) (SD)	48.6 (18.8)	77.4 (NA)	0.316	42 (NA)	55 (NA)	–	38.6 (9.8)	44.9 (25.6)	0.790

SSc y causas de muerte...

Study	Country	Years (mid-cohort)	dcsc/lcsc/lcSSc/other	Deaths/n	SSc-related death	Lung-related death	Heart-related death	Kidney-related death	GI-related death
Farmer [9]	US	1945–1952 (48)	3%/48.7%/7%/41.3%	115/271 (49%)	17 (14.8%)	5 (29.4%)	6 (35.3%)	1 (5.9%)	1 (5.9%)
Bennet [12]	UK	1947–1970 (58)	NA	263/117 (69.2%)	1 (0.1%)	0 (0%)	1 (9.1%)	0 (0%)	0 (0%)
Rowell [18]	UK						NA	NA	NA
Barnett [19]	AUS						10 (11.6%)	16 (38.1%)	8 (9.3%)
Altman [22]	US						19 (21.3%)	35 (39.3%)	13 (14.6%)
Eason [23]	NZ						4 (22.2%)	5 (27.8%)	2 (11.1%)
Wynn [24]	US						6 (35.3%)	4 (23.5%)	0 (0%)
Ferri [27]	ITA						NA	NA	NA
Lally [28]	US						8 (57.1%)	6 (42.9%)	0 (0%)
Jacobsen [30]	DEN						1 (2.4%)	17 (41.5%)	9 (22%)
Kuwana [32]	JAP						4 (12.5%)	5 (15.6%)	0 (0%)
Geirsson [34]	ICE						1 (50%)	1 (50%)	0 (0%)
Abu-Shakra [36]	CAN						5 (11.4%)	5 (11.4%)	0 (0%)
Nishioka [39]	JAP						31 (48.4%)	12 (18.8%)	13 (20.3%)
Steen [3]	US						NA	NA	NA
Simeón [42]	SPA						0 (0%)	7 (63.6%)	0 (0%)
Bullpitt [43]	US						1 (11.1%)	4 (44.4%)	0 (0%)
Bryan [45]	UK						5 (14.7%)	5 (14.7%)	3 (8.8%)
Geirsson [47]	SWE						4 (40%)	1 (10%)	0 (0%)
Hesselstrand [49]	SWE						1 (6.7%)	1 (6.7%)	3 (20%)
Bond [50]	AUS						14 (32.6%)	6 (14%)	NA
Vlachoyiannopoulos [51]	GRE						2 (33.3%)	2 (33.3%)	0 (0%)
Hashimoto [55]	JAP						NA	NA	NA
Scusell-Lonzetti [56]	CAN						4 (11.4%)	7 (20%)	3 (8.6%)
Alamanos [58]	GRE						21 (58.3%)	2 (5.6%)	0 (0%)
Joven [60]	SPA						8 (22.2%)	1 (2.8%)	3 (8.3%)
Ruangjietpopan [61]	THAI						NA	NA	0 (0%)
Czirják [62]	HUN						29 (33.7%)	16 (18.6%)	8 (9.3%)
Derk [63]	US	1985–2007 (96)	71.3%/21.8%/0%/6.9%	87/87 (100%)	67 (77%)	65 (97%)	55 (82.1%)	2 (3%)	0 (0%)
Arias-Núñez [64]	SPA	1988–2006 (97)	29.5%/70.5%/0%/0%	20/78 (25.6%)	11 (55%)	10 (90.9%)	1 (9.1%)	0 (0%)	0 (0%)
Alba [66]	SPA	1986–2010 (98)	26%/60.1%/0%/13.9%	151/1037 (14.6%)	61 (78.2%)	NA	13 (16.7%)	0 (0%)	5 (4.1%)
Al-Dhalser [67]	CAN	1994–2004 (99)	37%/63%/0%/0%	42/185 (23%)	NA	15 (45.5%)	9 (27.3%)	9 (27.3%)	0 (0%)
Sampaio-Barros [68]	BRA	1991–2010 (90)	31%/56.4%/0%/12.6%	168/947 (17.7%)	110 (65.5%)	53 (48.2%)	27 (24.5%)	12 (10.9%)	5 (4.5%)
Assassi [72]	US	1998–2008 (93)	57.4%/42.6%/0%/0%	52/250 (20.8%)	29 (55.8%)	10 (34.5%)	4 (13.8%)	NA	2 (6.9%)
Mok [73]	CHI	1999–2008 (93)	NA	110/449 (24.5%)	26 (24%)	11 (42.3%)	NA	5 (19.2%)	2 (7.7%)
Hoffmann-Vold [74]	NOR	1999–2009 (94)	22%/67%/0%/11%	43/312 (13.8%)	13 (54.2%)	0 (0%)	5 (20.8%)	6 (25%)	2 (4.7%)
Vettrici [75]	ITA	2000–2008 (94)	20.3%/79.7%/0%/0%	20/251 (8%)	12 (60%)	5 (41.7%)	4 (33.3%)	1 (8.3%)	2 (16.7%)
Hachulla [76]	FR	2002–2006 (94)	27.5%/NA	47/546 (8.6%)	24 (51.1%)	19 (79.2%)	0 (0%)	3 (12.5%)	2 (8.3%)
Strickland [77]	UK	1999–2010 (94)	19.6%/80.4%/0%/0%	53/204 (26%)	19 (35.9%)	9 (47.4%)	4 (21.1%)	0 (0%)	1 (5.3%)
Kuo [78]	TAIW	2002–2007 (95)	NA	204/1479 (13.8%)	57 (27.9%)	9 (4.4%)	29 (0.1%)	14 (6.9%)	10 (5%)

SSc y causas de muerte...

Table 5

SSc-related causes of death. Student's *t* test for independent groups among studies before and after 1990 (mid-cohort year)

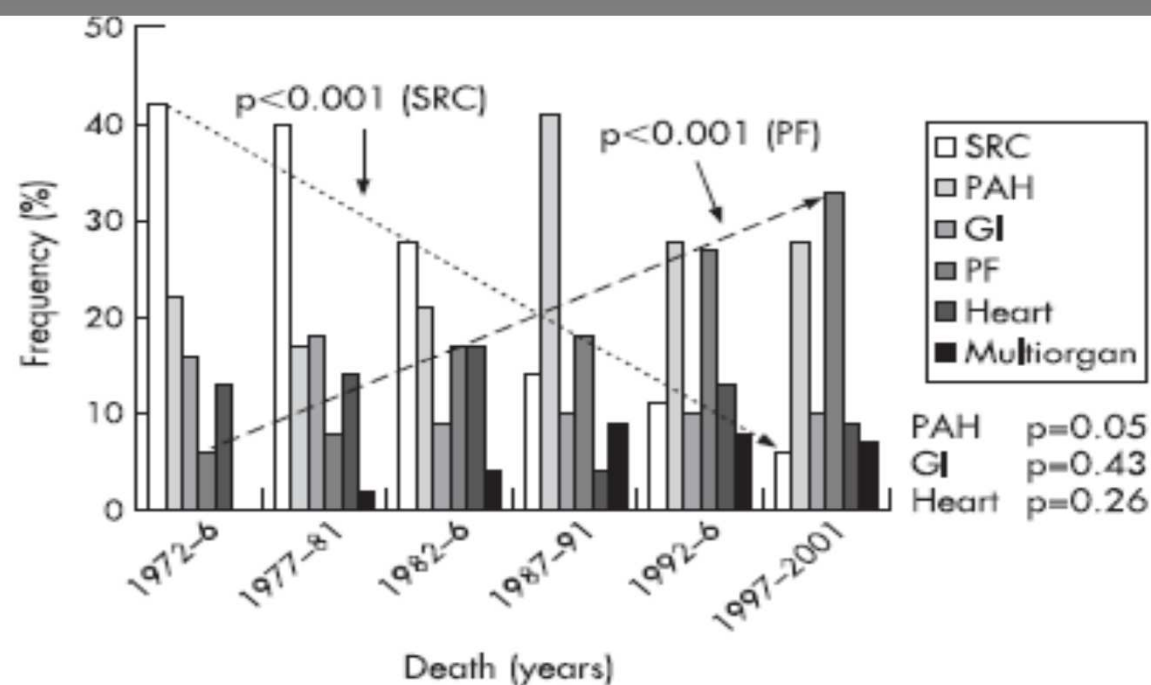
	Before 1990 (22 studies)	After 1990 (18 studies)	<i>p</i>
SSc-related deaths (%) (mean and SD)	52.5 (24.7)	56.7 (17.4)	0.544
Lung (%) (mean and SD)	34.5 (21.3)	57.0 (24.7)	0.008
Heart (%) (mean and SD)	29.3 (23.8)	28.2 (28.1)	0.905
Kidney (%) (mean and SD)	26.4 (17.6)	11.7 (7.9)	0.003
GI (%) (mean and SD)	6.8 (8.7)	6.4 (7.0)	0.881

EXTENDED REPORT

Changes in causes of death in systemic sclerosis, 1972–2002

Virginia D Steen, Thomas A Medsger

Ann Rheum Dis 2007;66:940–944. doi: 10.1136/ard.2006.066068



SSc and poor outcome risk factors...



Risk factor	HR
ILD	2.89 (95%CI:2.24–3.72)
HTAP	2.62 (95%CI:1.64–4.17)
Heart involvement	3.43 (95%CI:1.35–8.70)
Renal involvement	4.22 (95%CI:3.42–5.19)
Age/year	1.05 (95%CI:1.04–1.06)
dcSSc	2.28 (95%CI:1.69–3.08)
High ESR	2.77 (95%CI:2.06–3.71)
Male	1.88 (95% CI:1.48–2.38)

Quien quiera saber más...



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Mortality and survival in systemic sclerosis: Systematic review and meta-analysis

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y en España qué?...

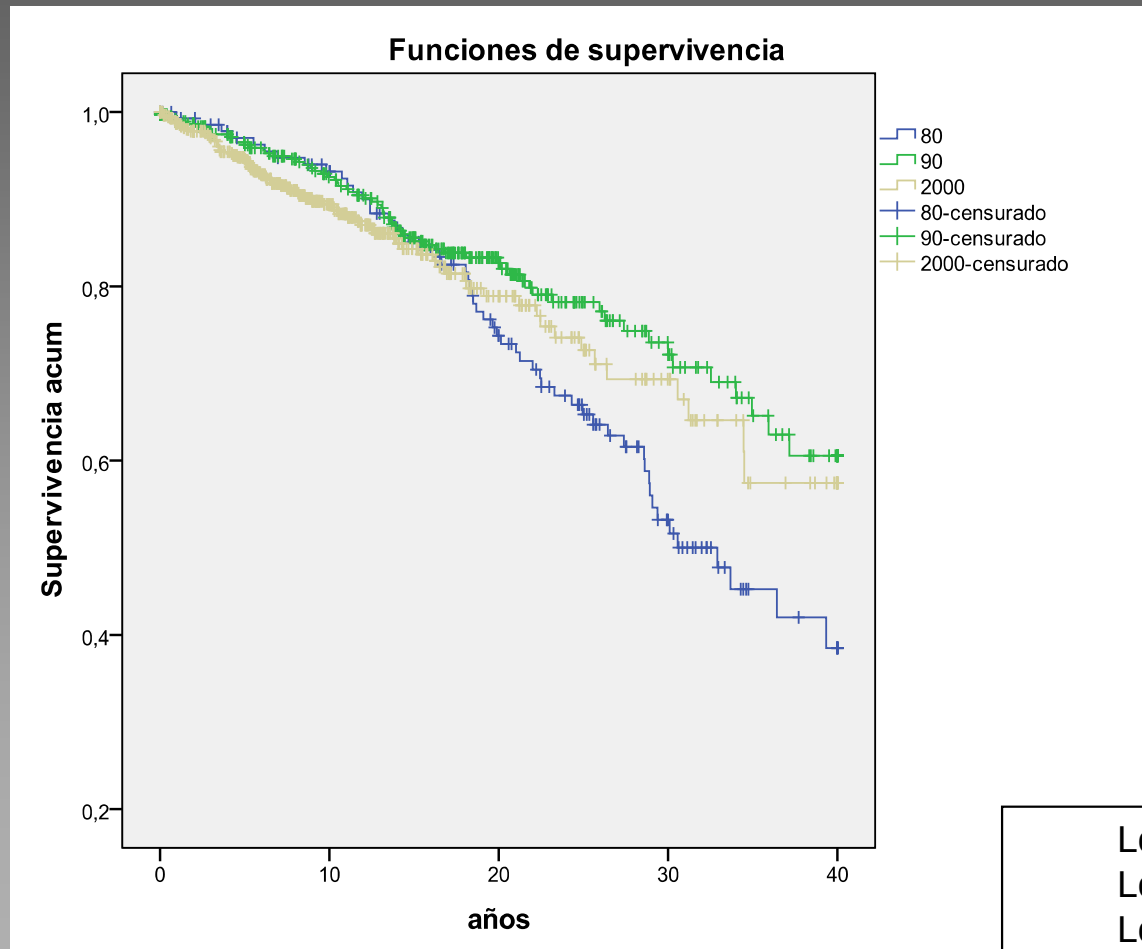


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SSc y mortalidad: SMR...

	PERÍODO	SMR (IC95%)
<i>GLOBAL</i>	1990-2009	2,34(2,24-2,44)
<i>HOMBRES</i>	1990-2009	3,62(3,50-3,74)
<i>MUJERES</i>	1990-2009	2,29(2,18-2,39)
<i>dcSSc</i>	1990-2009	2,13(2,04-2,23)
<i>lcSSc/sine</i>	1990-2009	2,06(1,96-2,15)
<i>≥65 años</i>	1990-2009	1,29(1,26-1,33)
<i><65 años</i>	1990-2009	7,06(6,71-7,41)

Supervivencia desde inicio síntomas...



Log-rank ratio global: p 0,024
Log-rank ratio 80-90: p 0,009
Log-rank ratio 80-2000: p 0,225
Log-rank ratio 90-2000: p 0,209

SSc y supervivencia desde inicio síntomas...

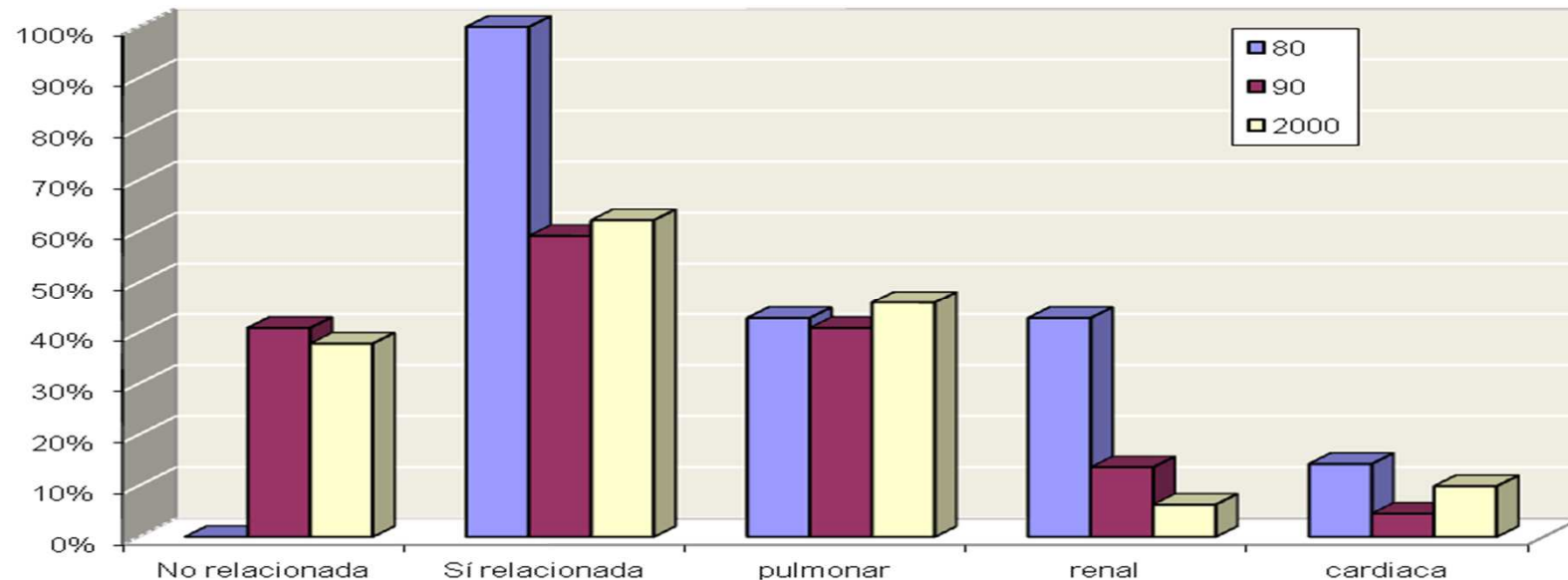


Años seguimiento	Global	lcSSc/sine	dcSSc	EPID	HTAP	CRE	Afectación cardíaca
5	0,956	0,965	0,918	0,940	0,919	0,755	0,908
10	0,910	0,935	0,827	0,864	0,794	0,580	0,833
15	0,848	0,882	0,720	0,781	0,697	0,420	0,751
20	0,795	0,843	0,612	0,705	0,587	0,312	0,685

desde diagnóstico...

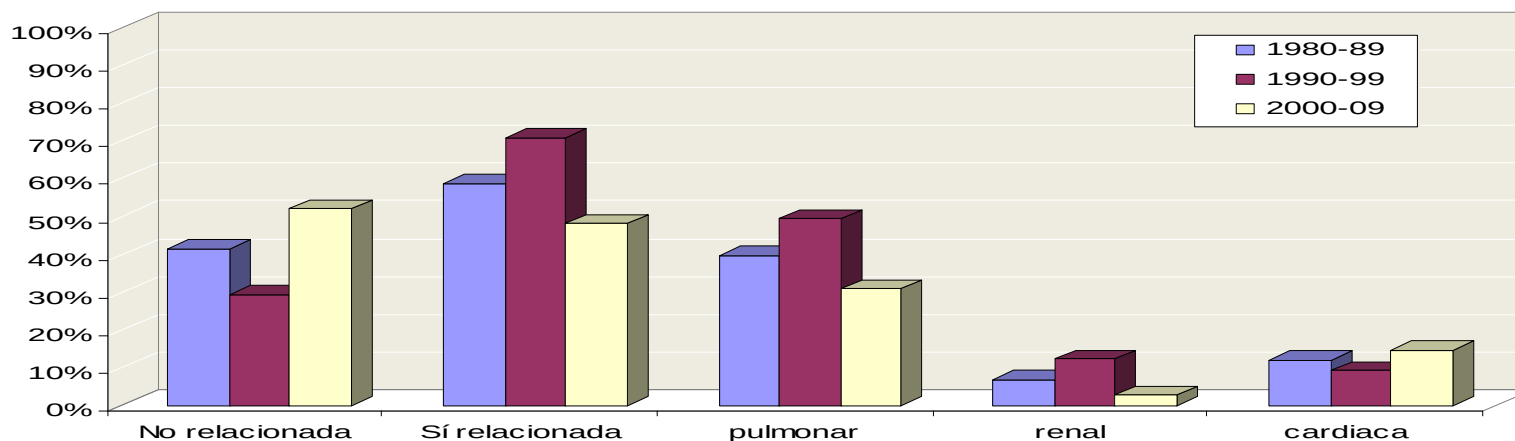
Años seguimiento	Global	lcSSc/sine	dcSSc	EPID	HTAP	CRE	Afectación cardíaca
5	0.889	0.910	0.860	0.889	0.969	0.652	0.856
10	0.771	0.807	0.722	0.771	0.905	0.503	0.748
15	0.664	0.688	0.633	0.664	0.740	0.300	0.626
20	0.593	0.634	0.564	0.593	0.639	0.219	0.584

SSc y causas de muerte según década en que murieron...



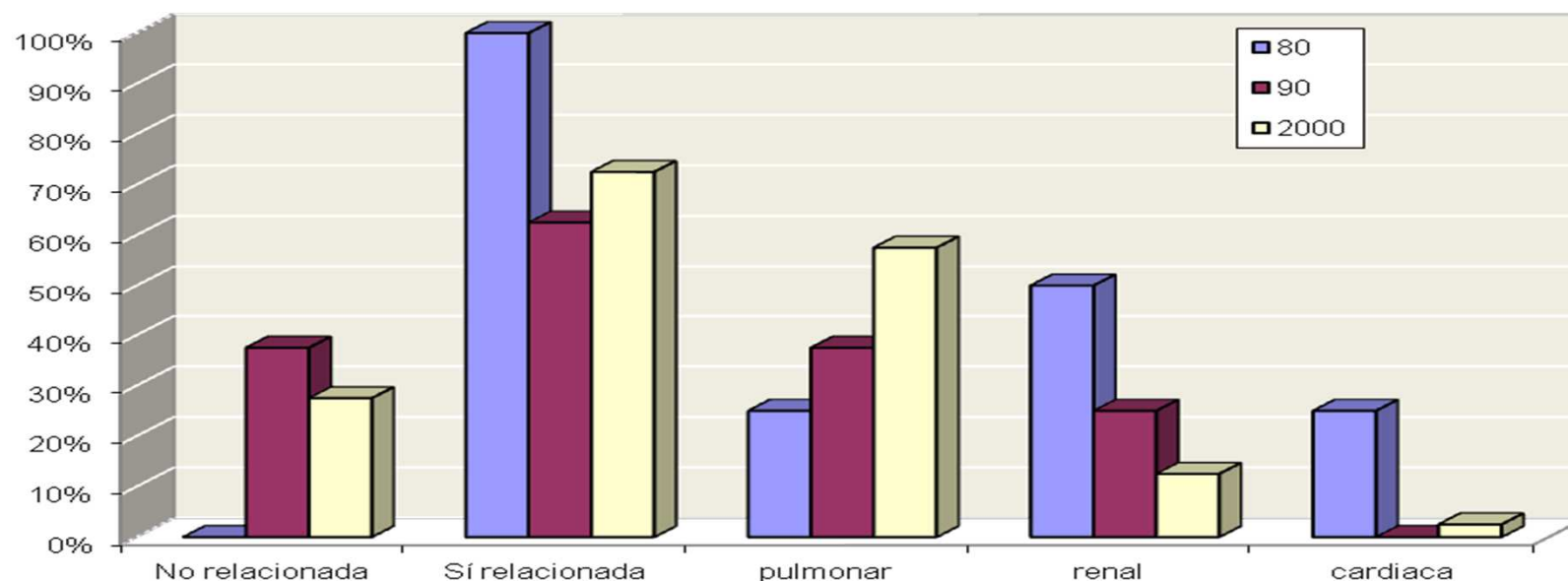
	80´	90´	2000´	p-valor
Muerte no relacionada con SSc	0 (0%)	18 (41%)	42 (38%)	0,109
Muerte relacionada con SSc	7 (100%)	26 (59%)	69 (62%)	
PULMONAR	3 (43%)	18(41%)	51(46%)	0.847
CRE	3 (43%)	6 (23%)	7 (10%)	0,004
CARDIACA	1 (14%)	2 (5%)	11 (10%)	0,486

SSc y causas de muerte según década diagnóstico...



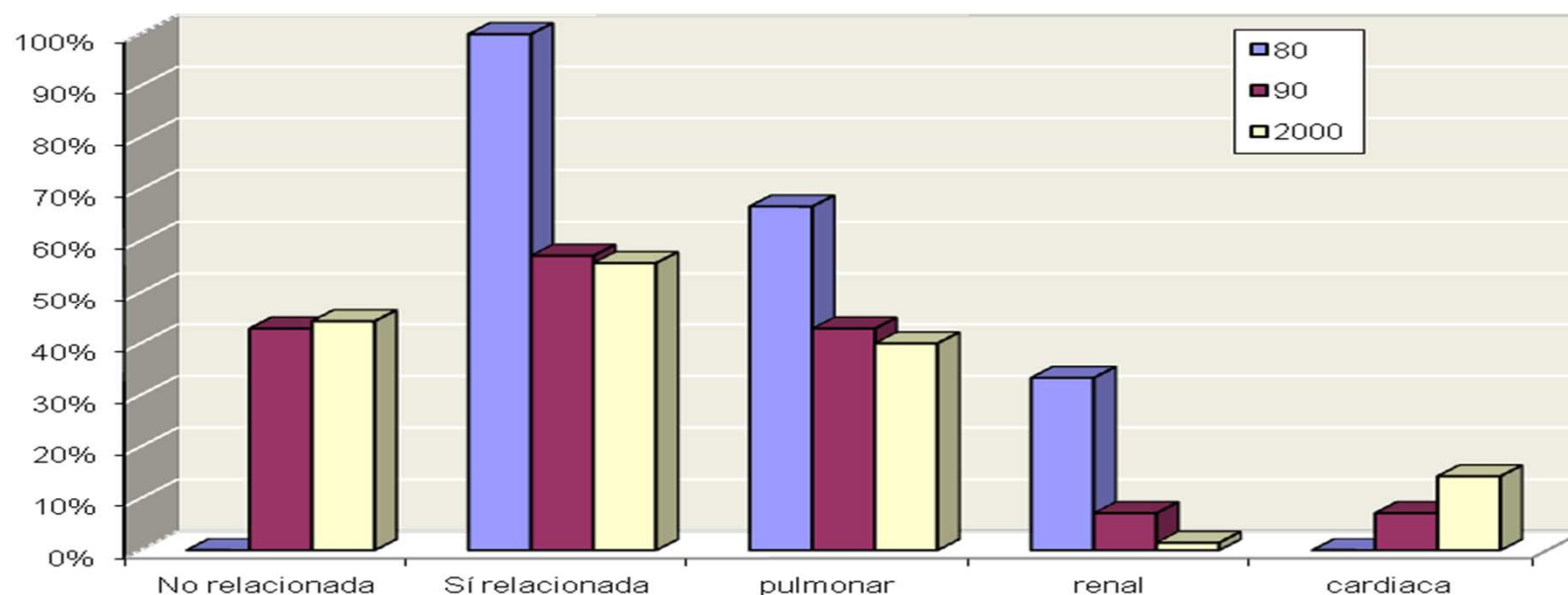
	80´	90´	2000´	p-valor
Muerte no relacionada con SSc	24(41%)	19(29%)	39(52%)	0,024
Muerte relacionada con SSc	34 (59%)	46 (71%)	36 (48%)	
PULMONAR	23 (40%)	32(49%)	23(31%)	0.358
CRE	4 (7%)	8 (12%)	2 (3%)	0,403
CARDIACA	7 (12%)	6 (9%)	11 (15%)	NS

Causas de muerte en dcSSc...



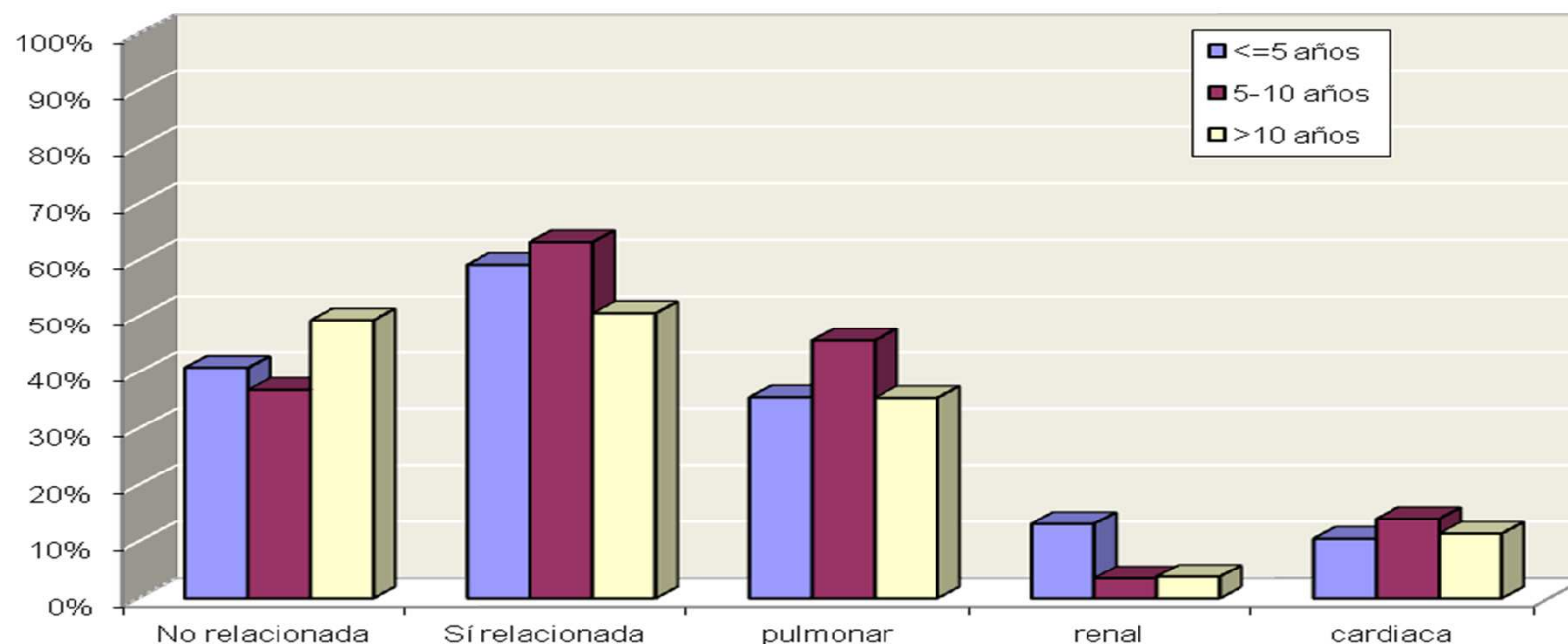
	80'	90'	2000'	p-valor
Muerte no relacionada con SSc	0 (0,0%)	6 (37,5%)	11 (27,5%)	0,323
Muerte relacionada con SSc	4 (100,0%)	10 (62,5%)	29 (72,5%)	
PULMONAR	1 (25,0%)	6 (38%)	23 (58%)	0,235
CRE	2 (50,0%)	4 (25%)	5 (13%)	0,131
CARDIACA	1 (25,0%)	0 (0,0%)	1 (3,4%)	0,039

Causas de muerte en lcSSc/sine...



	80´	90´	2000´	p-valor
Muerte no relacionada con SSc	0 (0,0%)	12 (42,9%)	31 (44,3%)	0,315
Muerte relacionada con SSc	3 (100,0%)	16 (57,1%)	39 (55,7%)	
PULMONAR	2 (66,7%)	12 (43%)	28 (40%)	0,648
CRE	1 (33,3%)	2 (7%)	1 (1%)	0,013
CARDIACA	0 (0%)	2 (7%)	10 (14%)	0,499

Mortalidad precoz, intermedia, tardía...



	≤5años	5-10 años	>10 años	p-valor
<i>Muerte no relacionada con SSc</i>	31 (41%)	21 (37%)	39 (49%)	0,310
<i>Muerte relacionada con SSc</i>	45 (59%)	36 (63%)	40 (51%)	
PULMONAR	27 (36%)	26 (46%)	28 (35%)	0,404
CRE	10 (13%)	2 (4%)	3 (4%)	0,036
CARDIACA	8 (11%)	8 (14%)	9 (11%)	0,817

Mortalidad precoz <5 años

	1980-89	1990-99	2000-09	p-valor
Muerte no relacionada con SSc	1 (17%)	3 (18%)	23 (49%)	0,039
Muerte relacionada con SSc	5 (83%)	14 (82%)	24 (51%)	
PULMONAR	2 (40%)	8 (57%)	16 (67%)	0,005
CRE	3 (60%)	6 (43%)	1 (4%)	
CARDIACA	0 (0%)	0 (0%)	7 (29%)	

Mortalidad tardía >10 años

	1980-89	1990-99	2000-09	p-valor
Muerte no relacionada con SSc	18 (49%)	11 (41%)	5 (83%)	0,168
Muerte relacionada con SSc	19 (51%)	16 (59%)	1 (17%)	
PULMONAR	13 (68%)	11 (69%)	1 (100%)	0,976
CRE	1 (6%)	1 (6%)	0 (0%)	
CARDIACA	5 (26%)	4 (25%)	0 (0%)	

Take home messages...

- SMR mundial global..... 2,72 (1,93-3,83)
 mundial post 1990.....2,42 (1,89-3,11)
 RESCLE 1990-2009.....2,34 (2,24-2,44)
- Supervivencia desde dx
 5 años.....84,4% (RESCLE 88,9%)
 10 años.....70,9% (RESCLE 77,1%)
 20 años.....44,9% (RESCLE 59,3%)
- Factores riesgo
 - Edad al dx
 - Afectación visceral (HTAP, EPID, CRE, cardíaca)
 - dcSSc
 - Sexo masculino
 - VSG elevada

Take home messages...

- La mortalidad por causas no relacionadas con SSc está aumentando en los últimos años, sobretodo tardía.
- La patología pulmonar (EPID e HTAP) ha sido en las 3 décadas estudiadas (1980, 1990, 2000) la principal causa de muerte relacionada con SSc, y su frecuencia relativa va en aumento.
- La patología renal (CRE) ha pasado de ser la segunda causa de muerte de estos pacientes en la década de 1980 (e incluso la primera en el subtipo difuso) a representar la 3er causa de muerte.

Take home messages...

- Causa de muerte en dcSSc
 - 68% patología pulmonar
 - 21% patología renal
 - 11% patología cardíaca
- Causa de muerte en lcSSc/sine
 - 67% patología pulmonar
 - 27% patología cardíaca
 - 6% patología renal

Fortalezas del estudio...

- N° de pacientes incluidos en el RESCLE
 - Registro a nivel nacional
 - Amplio período de estudio

Limitaciones del estudio y retos futuros...

- Pacientes no incluidos en el RESCLE
 - Definición de las causas de muerte
- Diagnóstico de la cardiopatía asociada a SSc



...la vida es una caja de sorpresas