

PROGRAMA PRELIMINAR

37 DIADA INTERNACIONAL

Societat Catalana d'Hematologia i Hemoteràpia

Actualitzacions en
síndromes
mielodisplàsiques



Divendres, 7 de juny de 2013

Auditori de l'Acadèmia, Barcelona



Societat
Catalana
d'Hematologia
i Hemoteràpia



11.30 **CO-MORBILIDAD Y CALIDAD DE VIDA EN SÍNDROMES
MIELODISPLÁSICOS**
Santiago Bonanad. Servicio de Hematología, Hospital de la
Ribera, Alzira, València



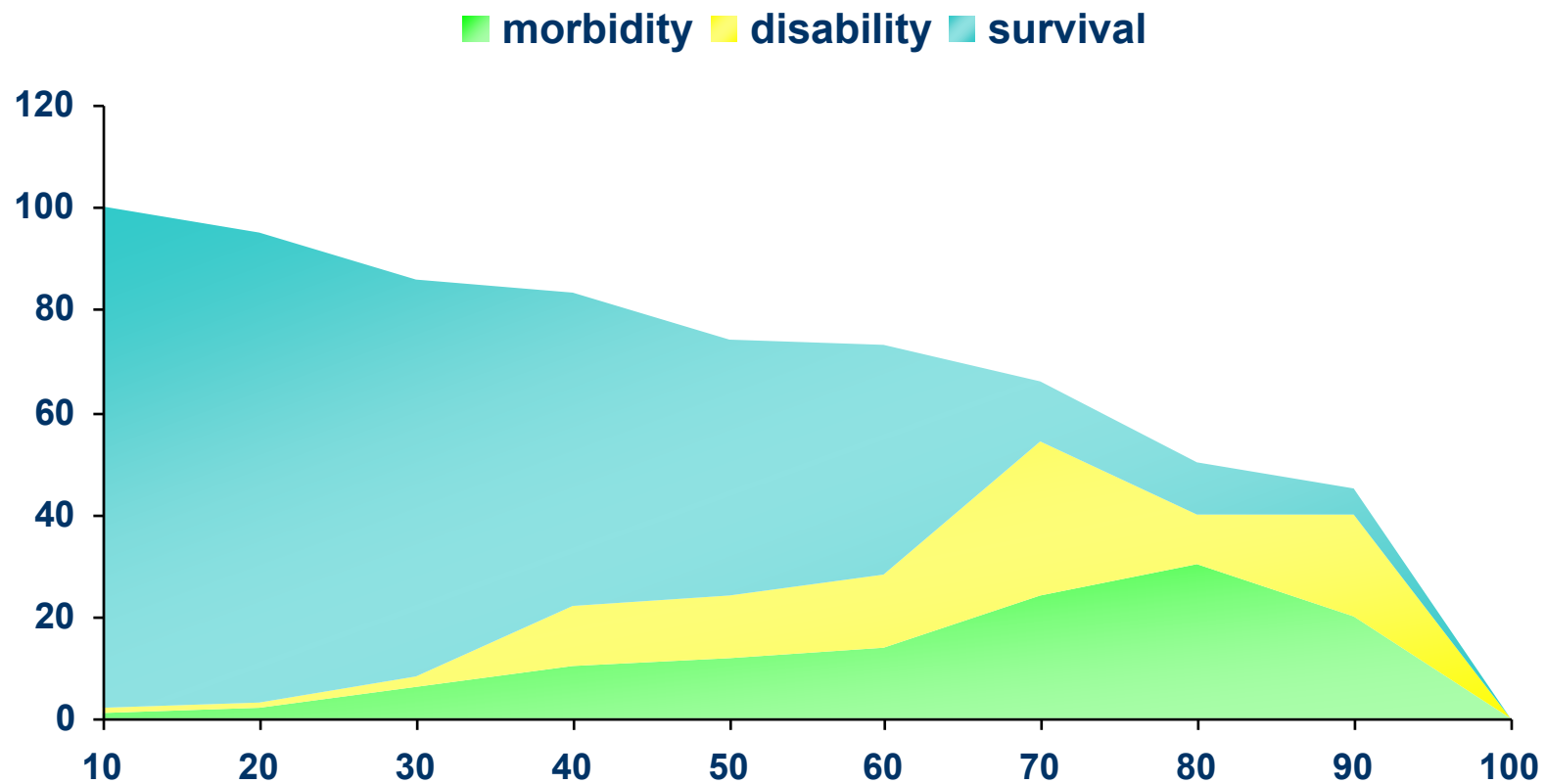
45 min

Comorbilidad y calidad de vida en síndromes mielodisplásicos

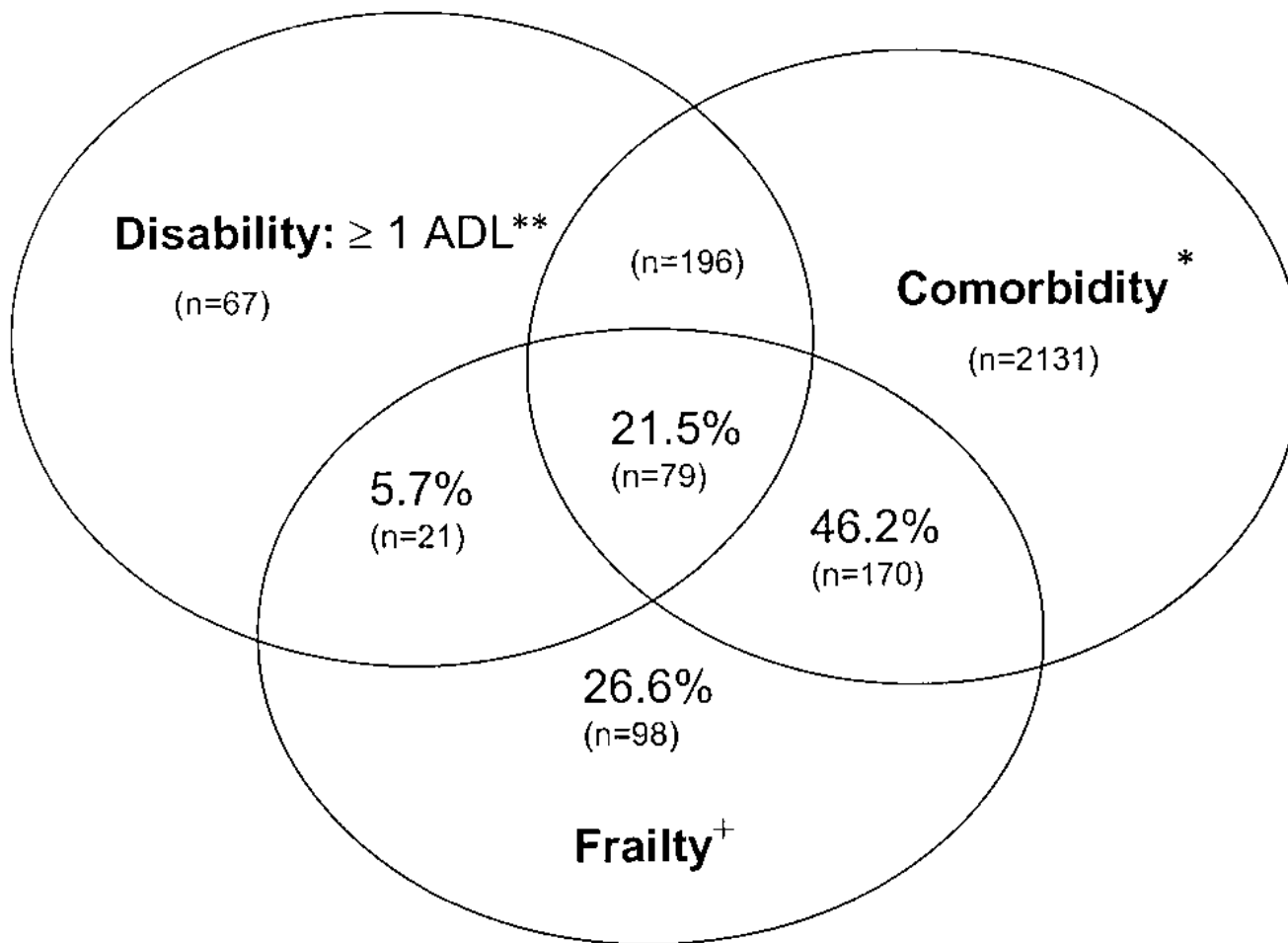


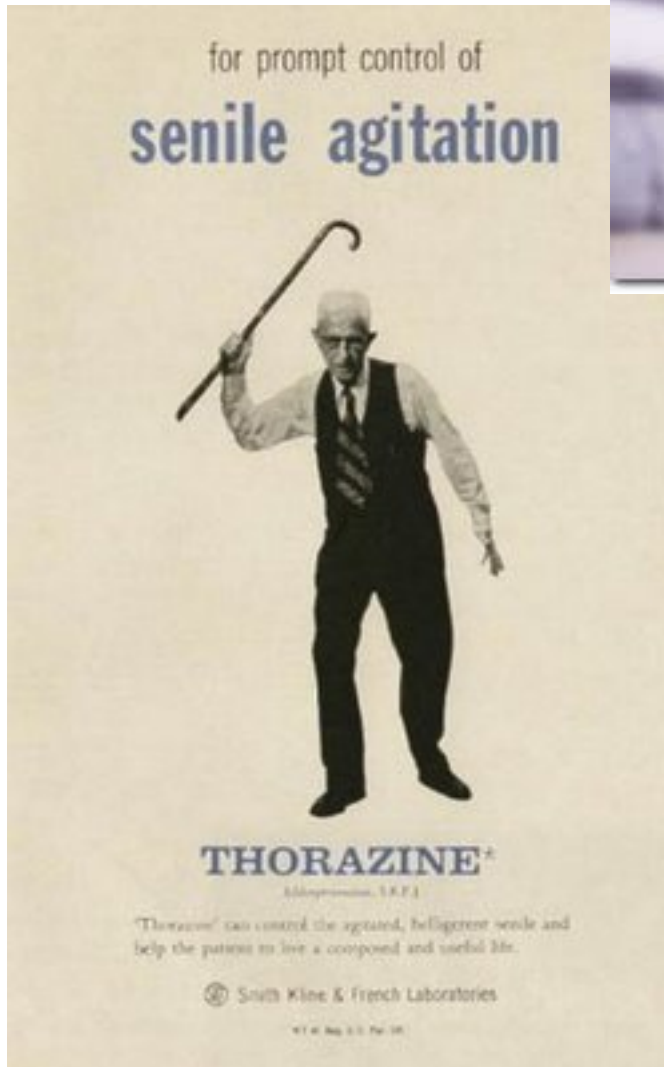
Edad y comorbilidad

Compresión de la morbilidad



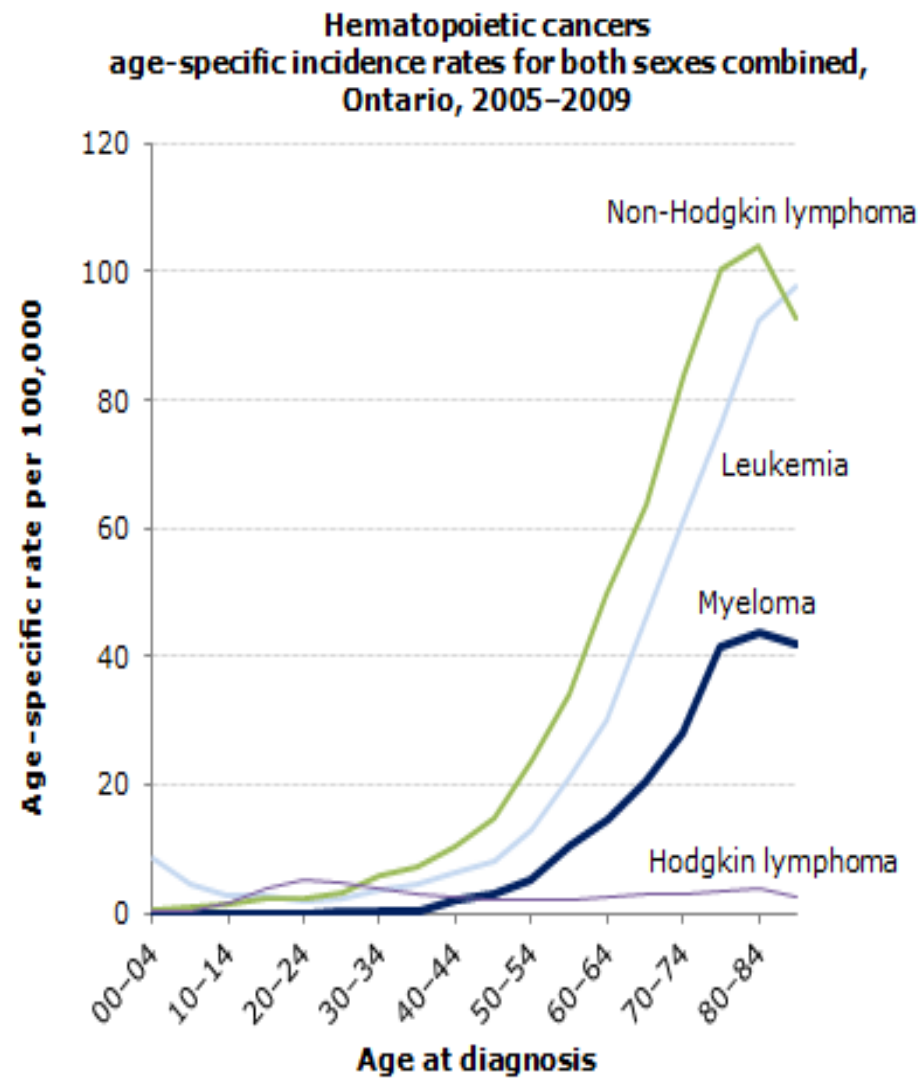
Frailty in Older Adults: Evidence for a Phenotype





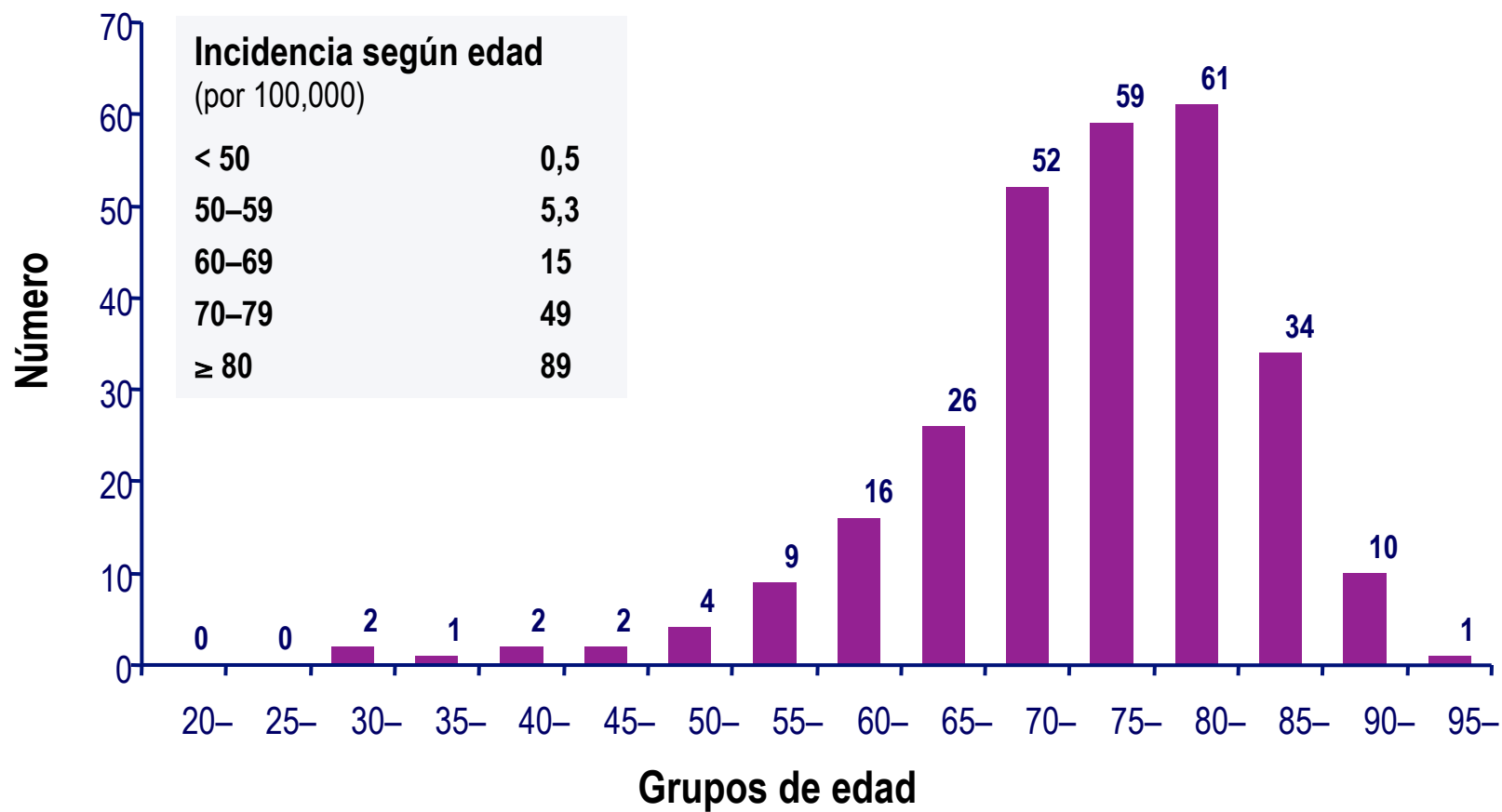
- Edad
- Comorbilidad
- Capacidad funcional
- Fragilidad
- Estudios integrales
- Estudio GAH

Edad en las enfermedades hematológicas



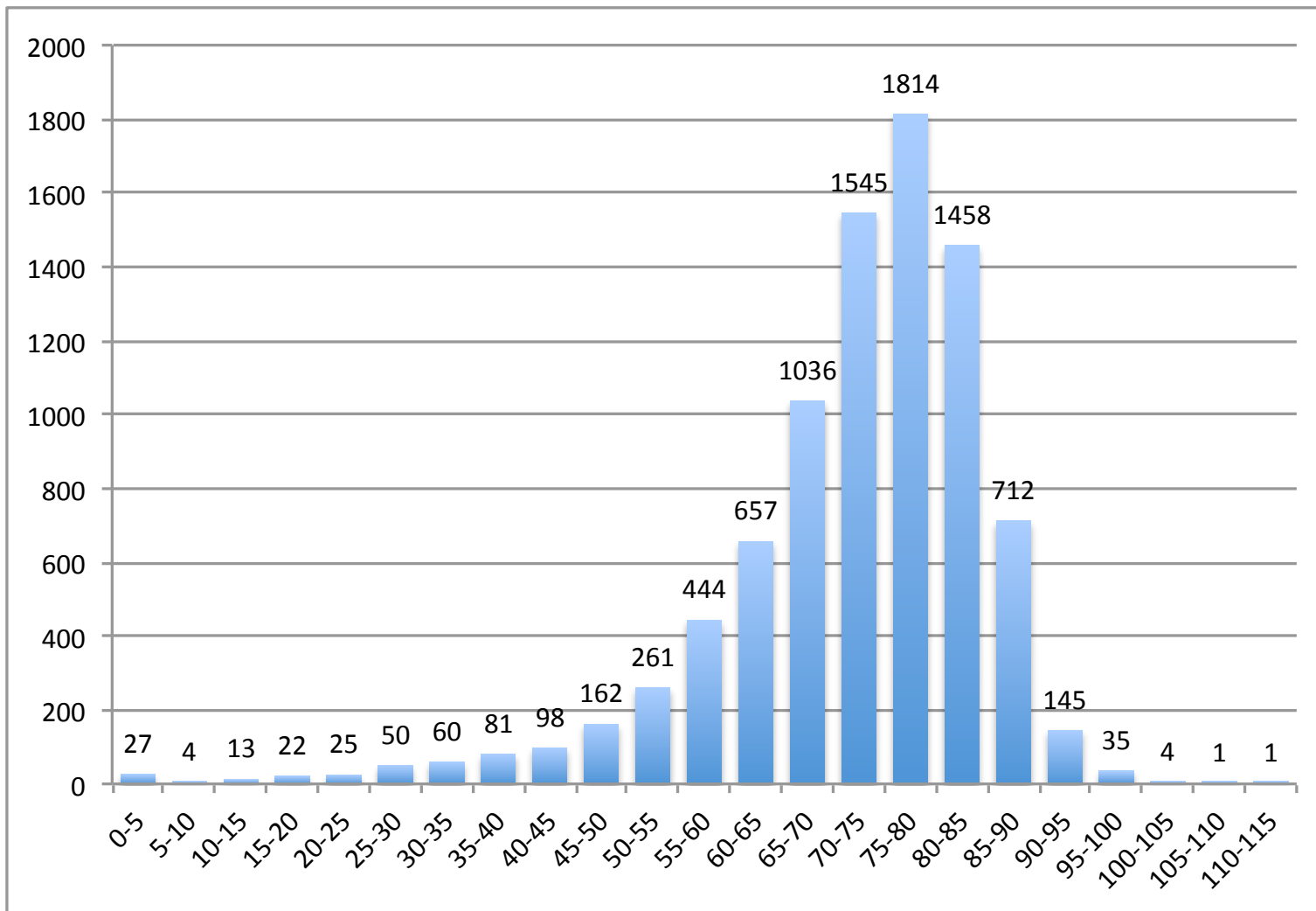
Source: Cancer Care Ontario (Ontario Cancer Registry, 2012)

Incidencia por edad de los SMD

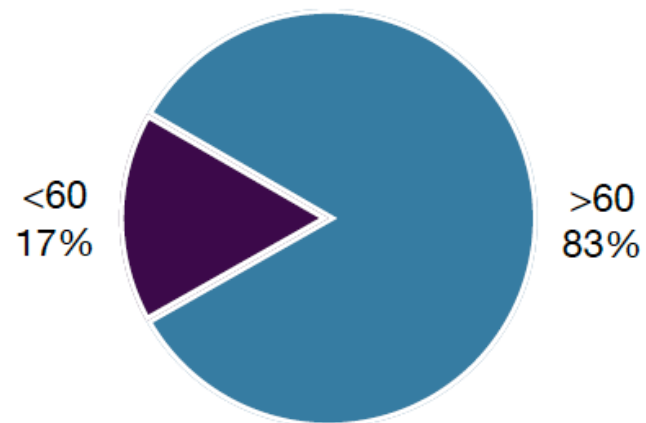
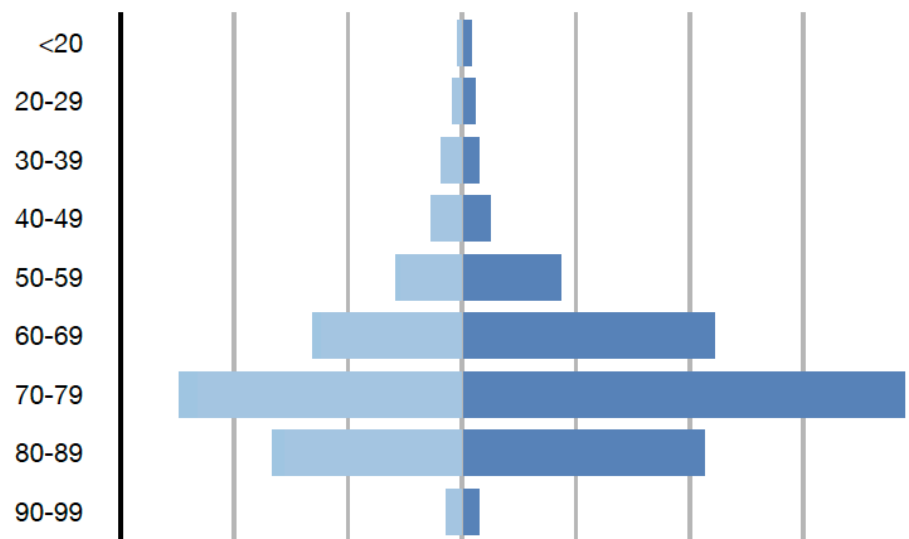


Edad al diagnóstico en el RESMD

N=9395



Ancianos en RESMD



Centros incluidos en el RESMD	140
Total de pacientes registrados	9395
Total de pacientes validados	6680



Notas de prensa

28 de enero de 2010

Proyección de la Población de España a Largo Plazo, 2009-2049

Las tendencias demográficas actuales llevarían a una reducción progresiva del crecimiento poblacional en las próximas décadas

El crecimiento natural de la población se haría negativo desde 2020

La población mayor de 64 años se duplicaría en 40 años y pasaría a representar más del 30% del total debido al envejecimiento de la pirámide poblacional

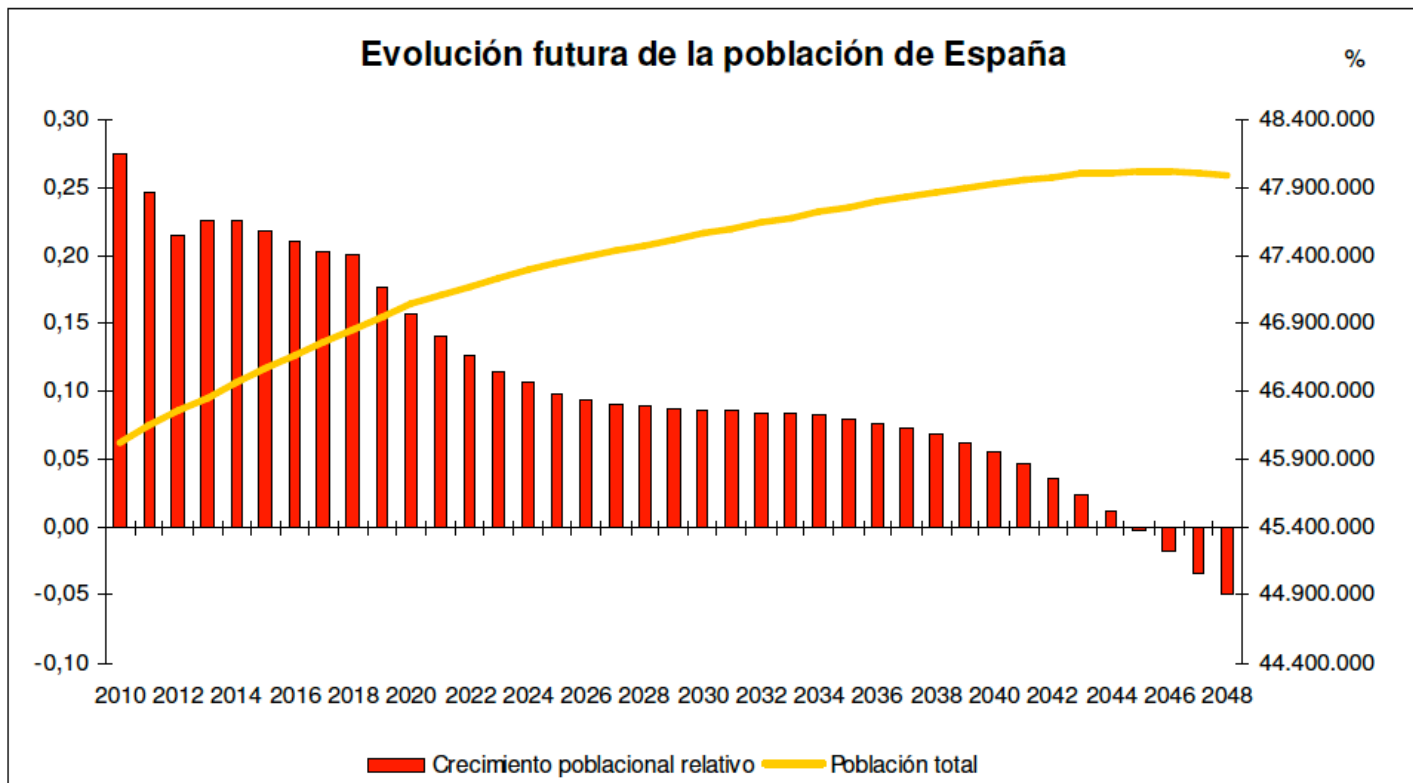
reducción de natalidad
aumento esperanza de vida



envejecimiento poblacional



compresión de la mortalidad
rectangularización de la supervivencia
“squaring of the pyramid”



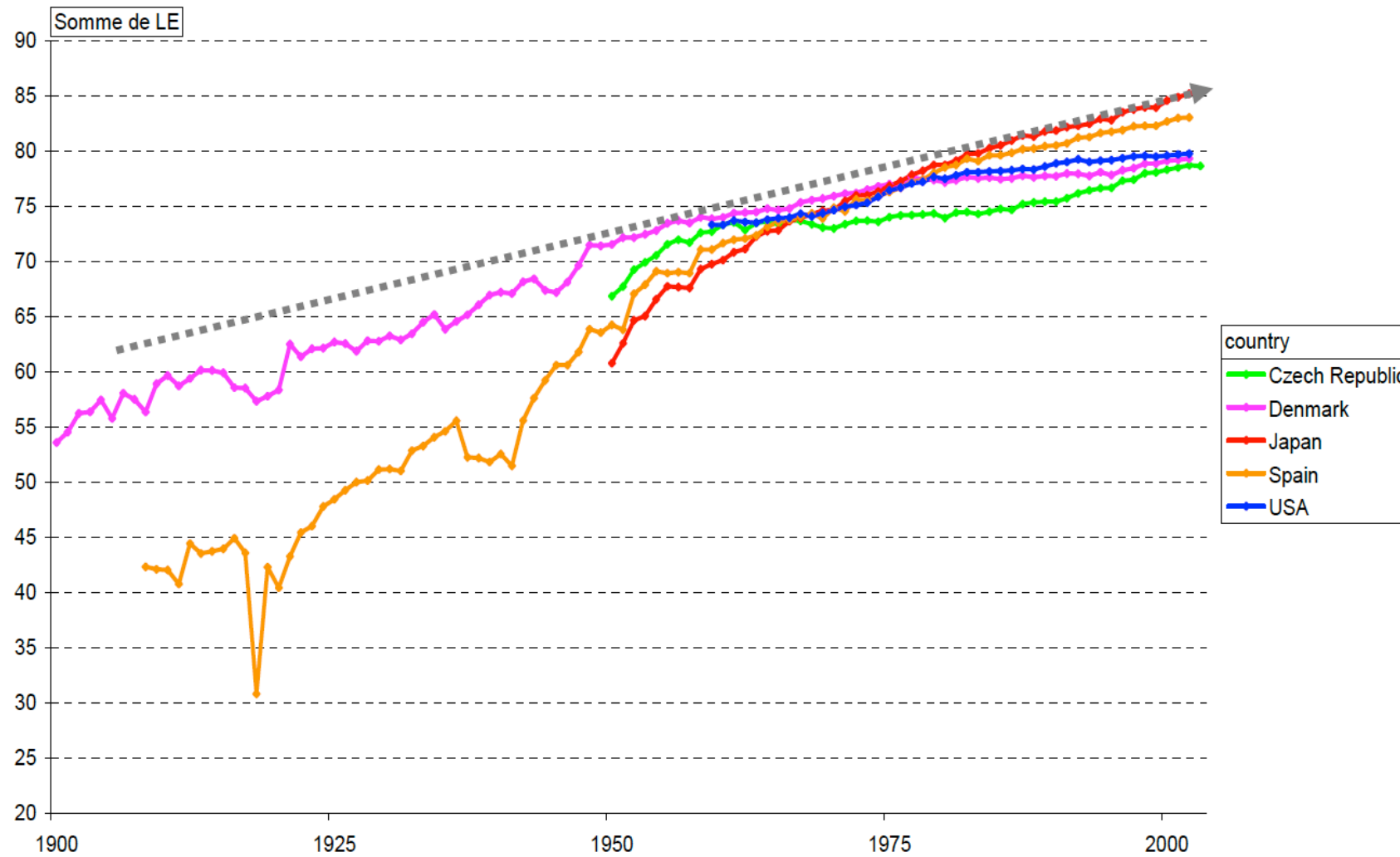
Indicadores de fecundidad

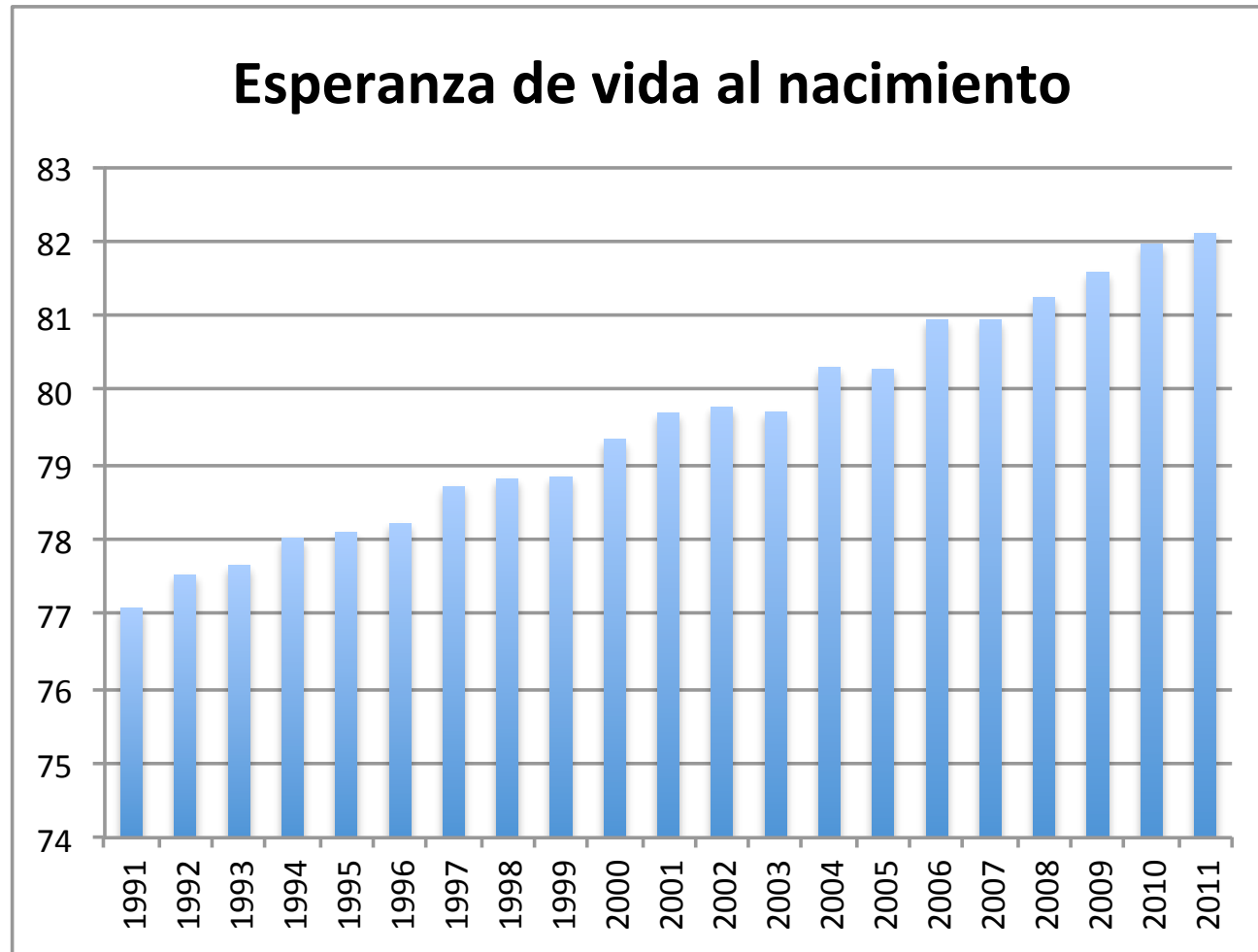
Años	Número medio de hijos por mujer	Edad Media a la Maternidad
2007	1,40	30,83
2008	1,46	30,82
2009	1,44	30,87
2018	1,54	30,92
2028	1,61	30,98
2038	1,67	31,00
2048	1,71	31,02

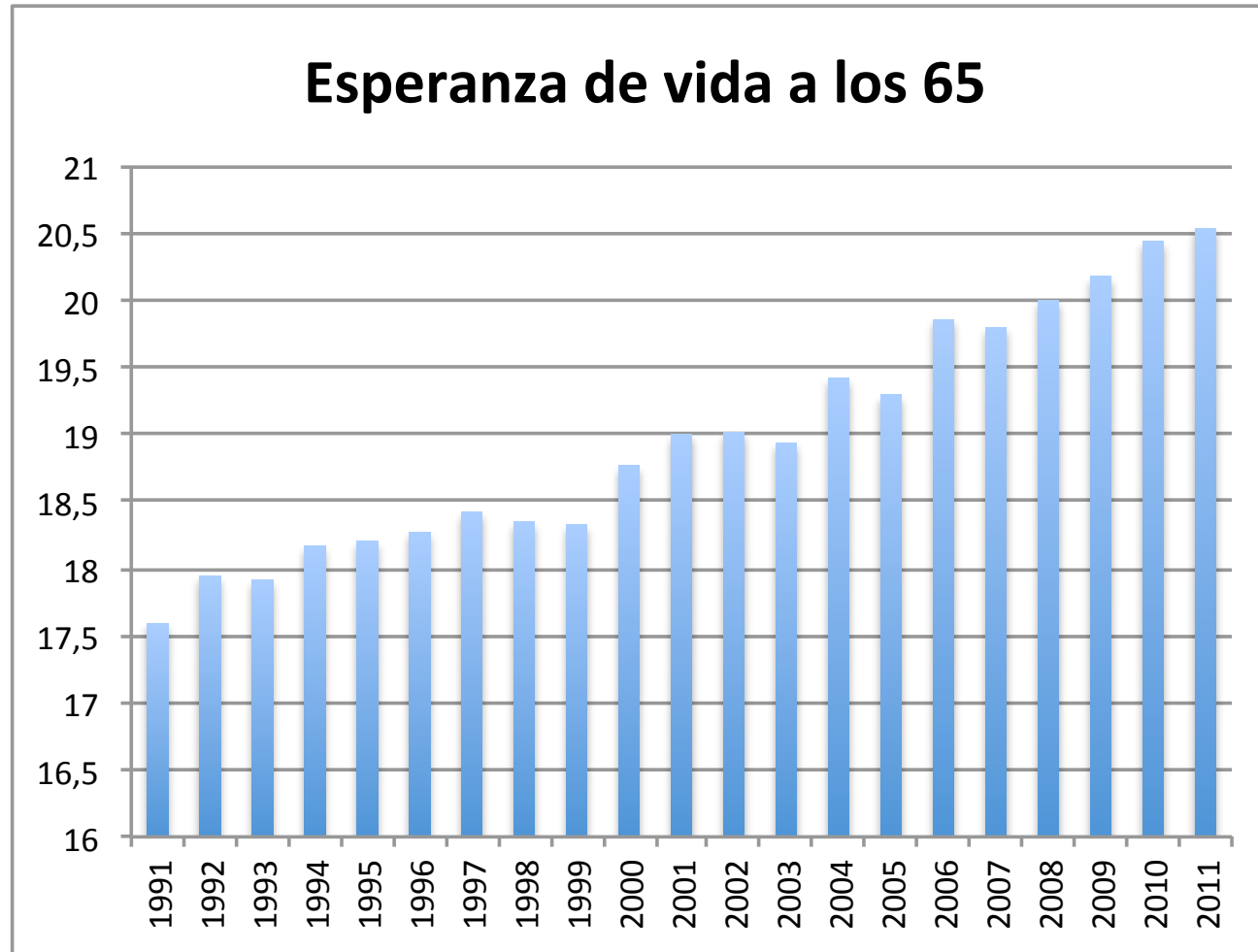
Fuente: Número medio de hijos por mujer 2007- 2008, Indicadores Demográficos Básicos (2008 provisional); Número medio de hijos por mujer 2009-2049, Proyección de Población a Largo Plazo; Edad Media a la Maternidad 2007, Indicadores Demográficos Básicos; Edad Media a la Maternidad 2008-2049, Proyecciones de Población a Largo Plazo;

Esperanza de vida al nacimiento

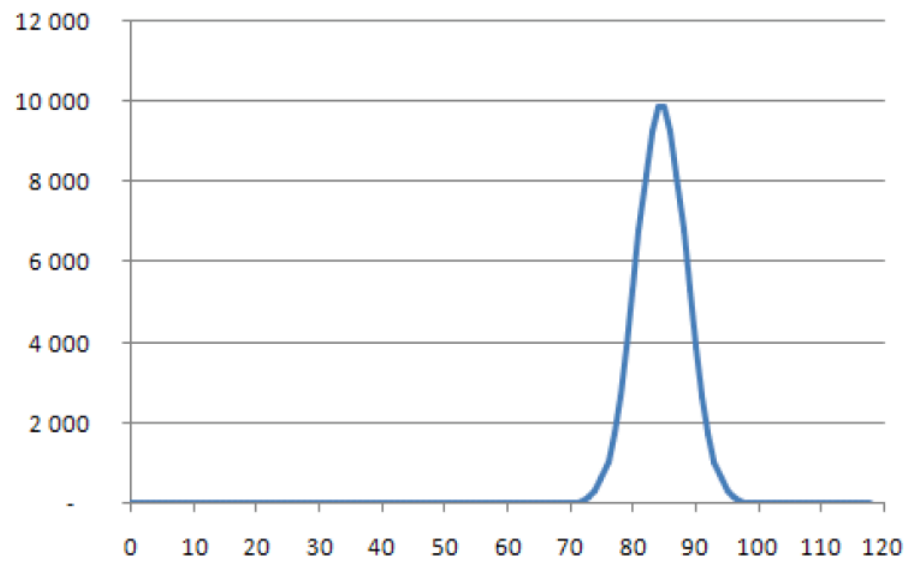
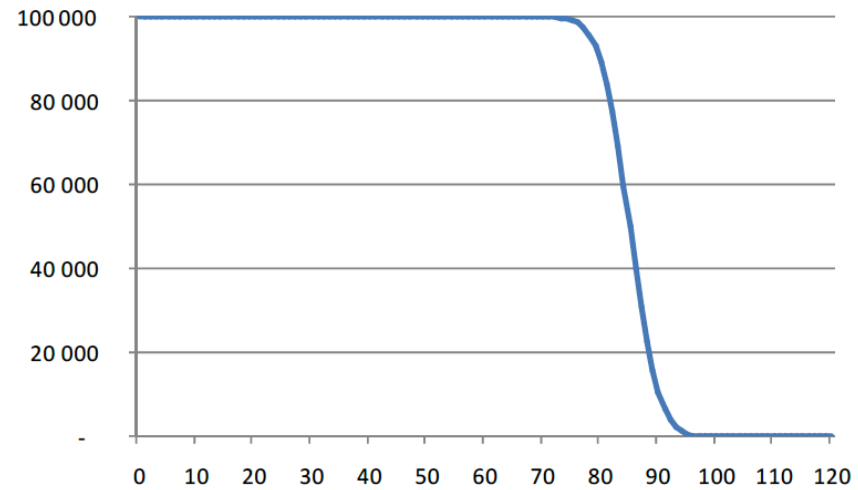
age 0 sex femme



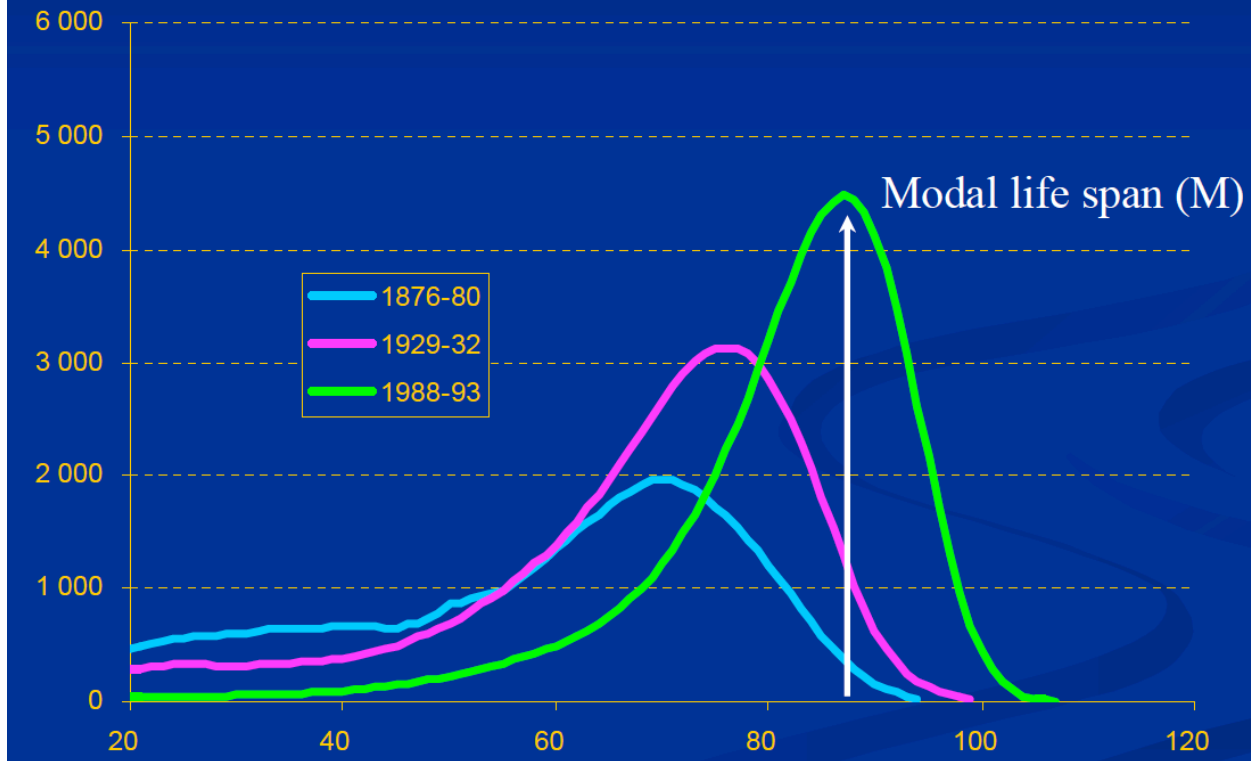




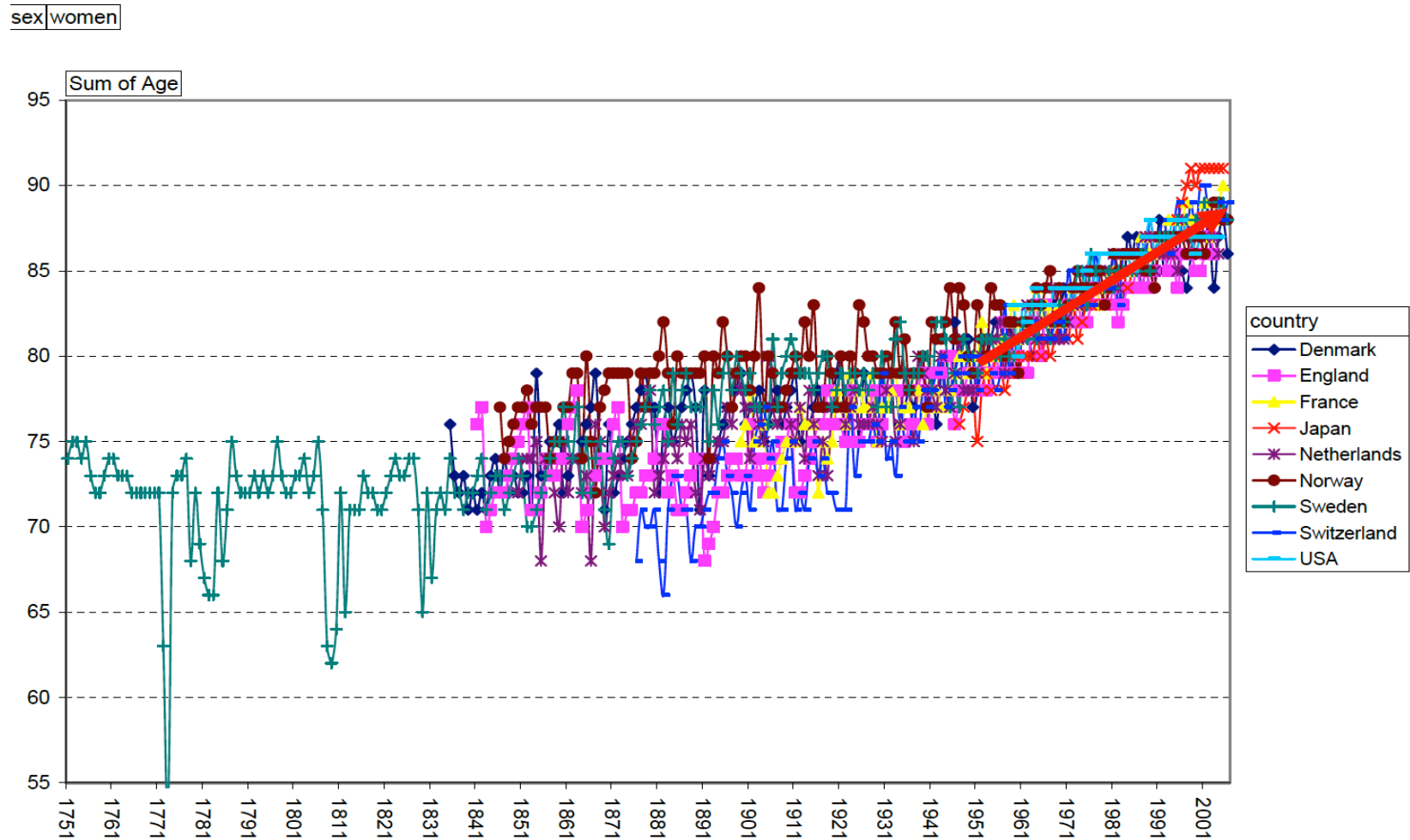
- “Curva ideal” de supervivencia
- Muertes naturales



Longevity revolution Switzerland, 1878, 1930 and 1990

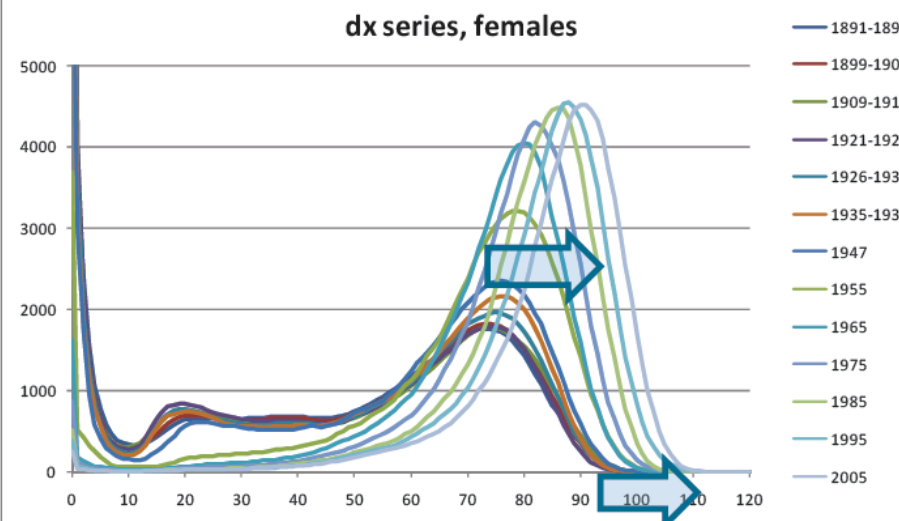
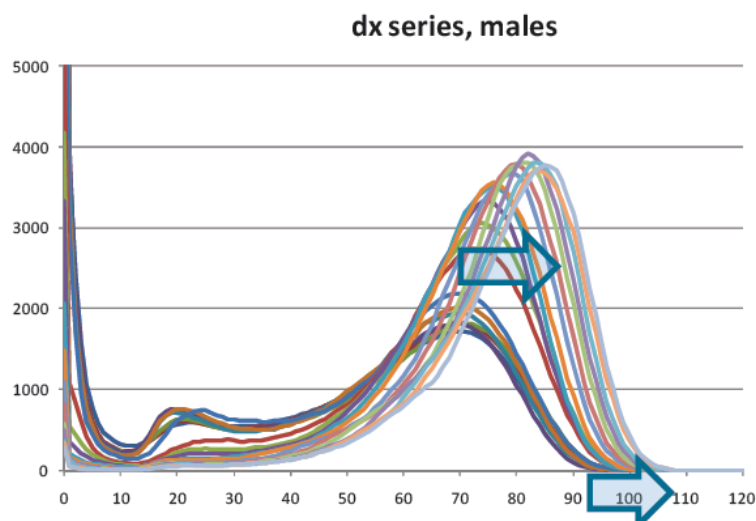
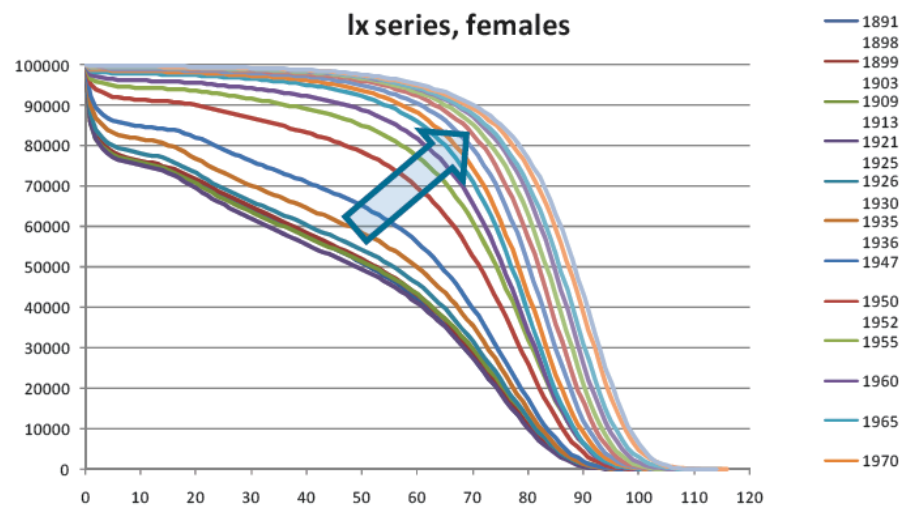
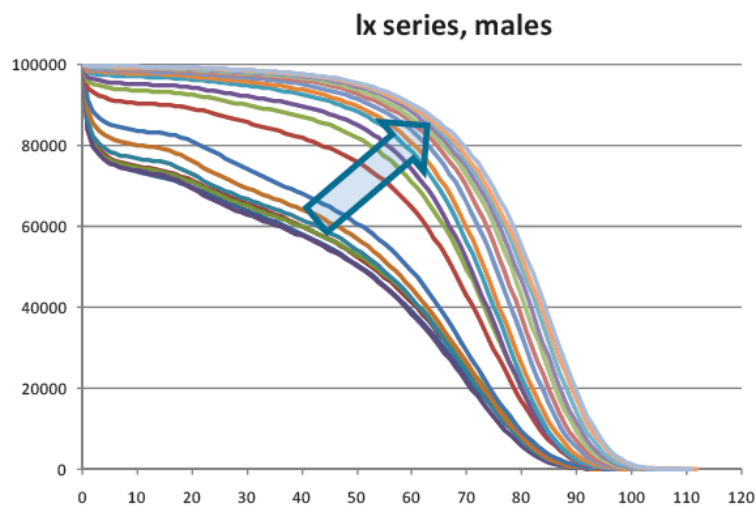


- Aumento de la duración modal de vida (M) desde 1751

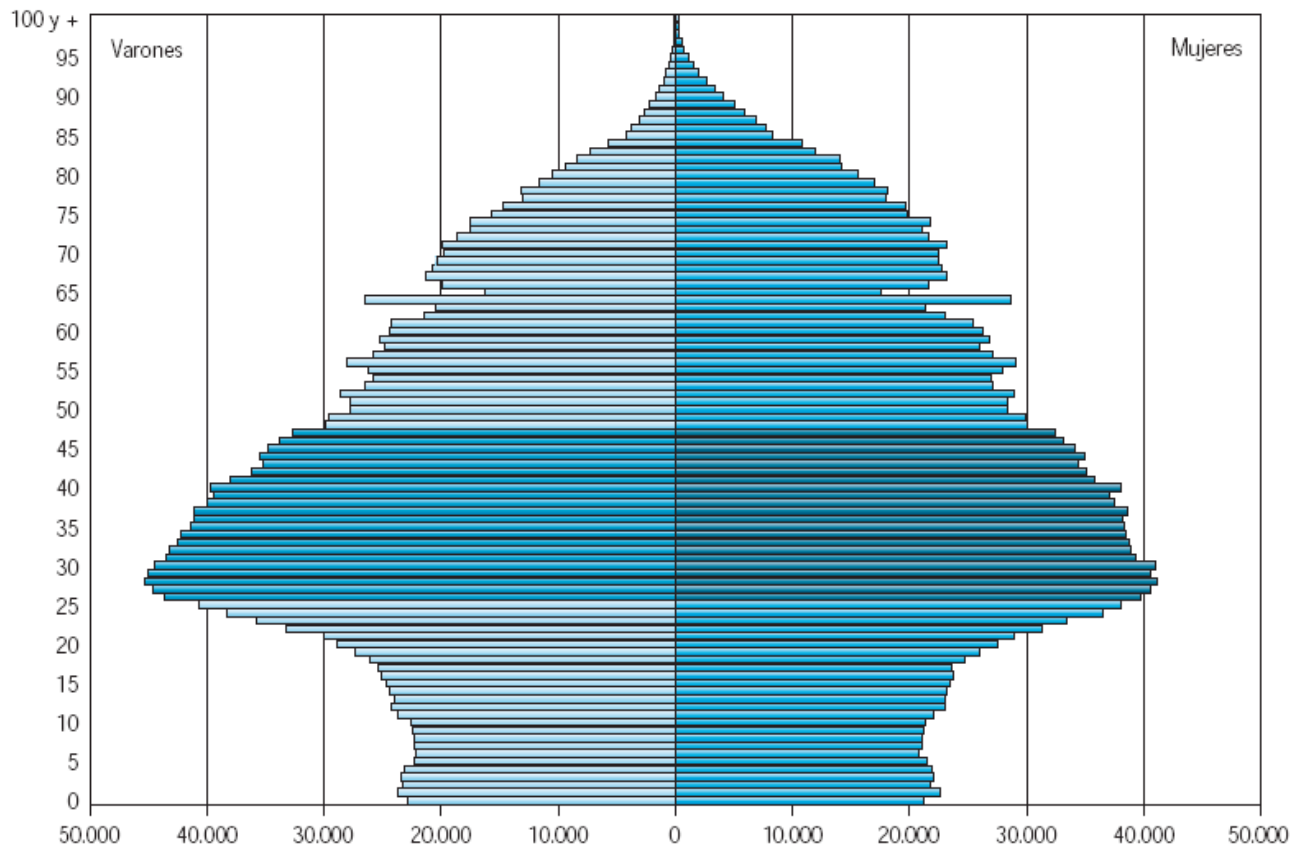


Rectangularización de las curvas de supervivencia

Compresión de la mortalidad



Población según sexo y edad, 2005

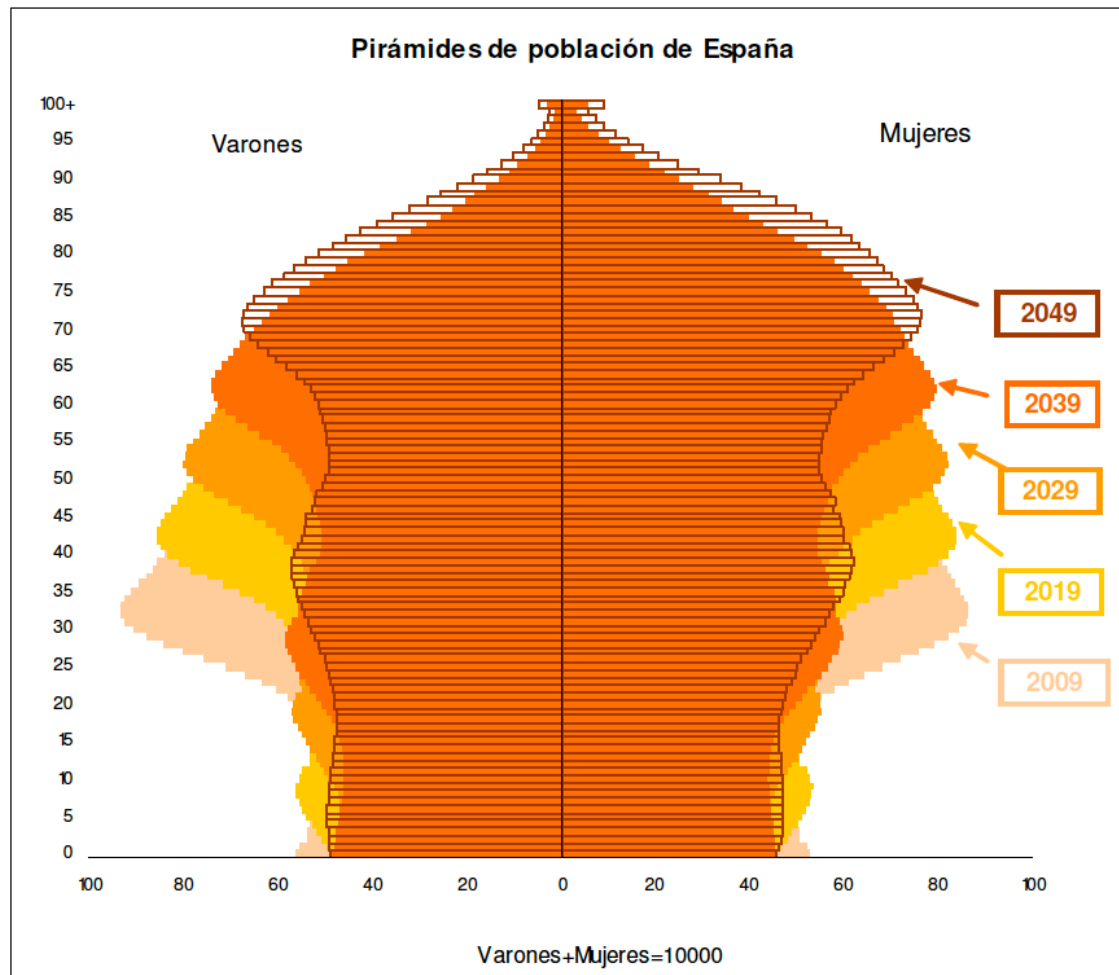


Nota: Posición de la generación del «baby-boom».

De 85 a 100 y más años. Datos absolutos de población ponderados año por año por la población de cada edad a nivel nacional.

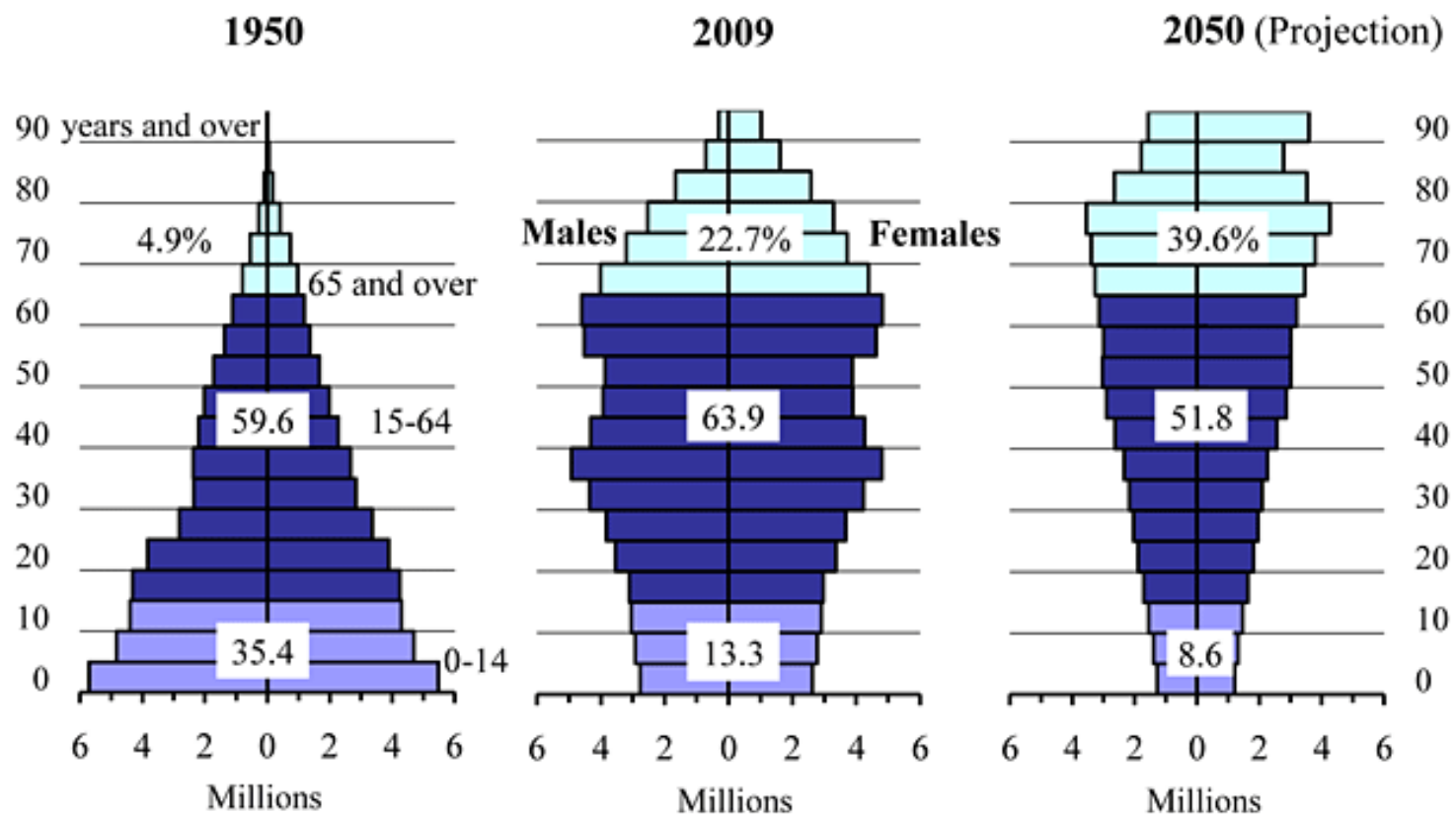
Fuente: INE, INEBASE: *Revisión del Padrón Municipal de Habitantes a 1 de enero de 2005*. INE, 17/01/2006.

Pirámide poblacional



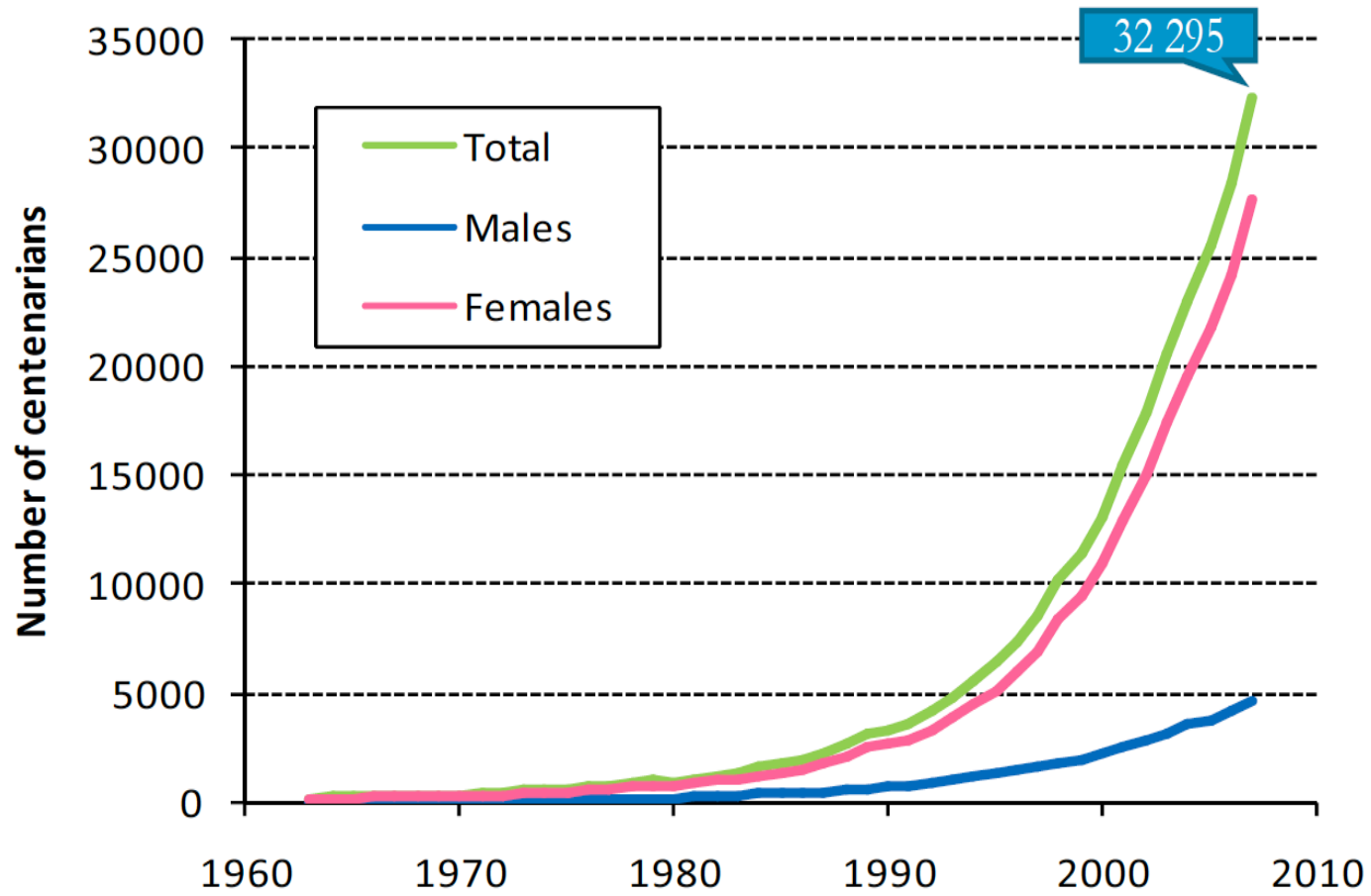
Fuente: Proyección de Población a Largo Plazo

Figure 2.3
Changes in the Population Pyramid



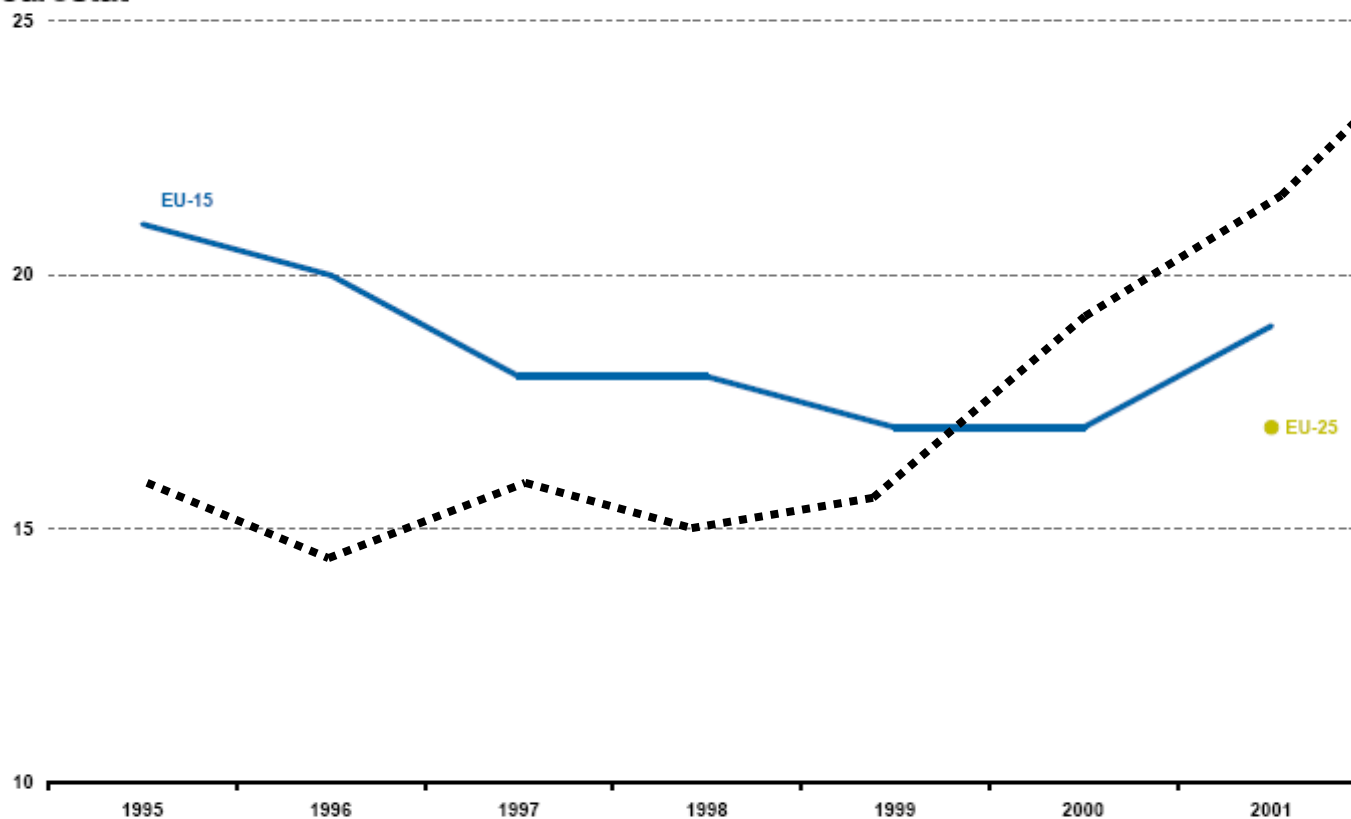
Source: Statistics Bureau, MIC; Ministry of Health, Labour and Welfare.

Centenarian list from 1963 to 2007





AGEING SOCIETY
At-risk-of poverty rate for persons aged 65 and over
%



Source: Eurostat.

Year	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004
Spain	16	14	16	15	16	19	22	28 (bi)	28 (i)	30 (b)
								2002	2003	2004

Last update: 14.03.2006

Oldest data: 1995

Most recent data: 2004

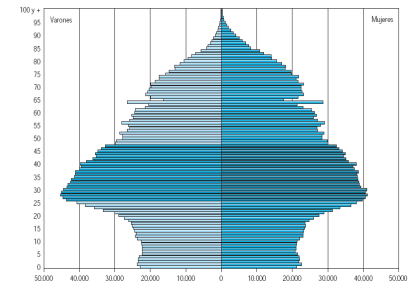
Pirámide poblacional

Dpto. de La Ribera, 2004

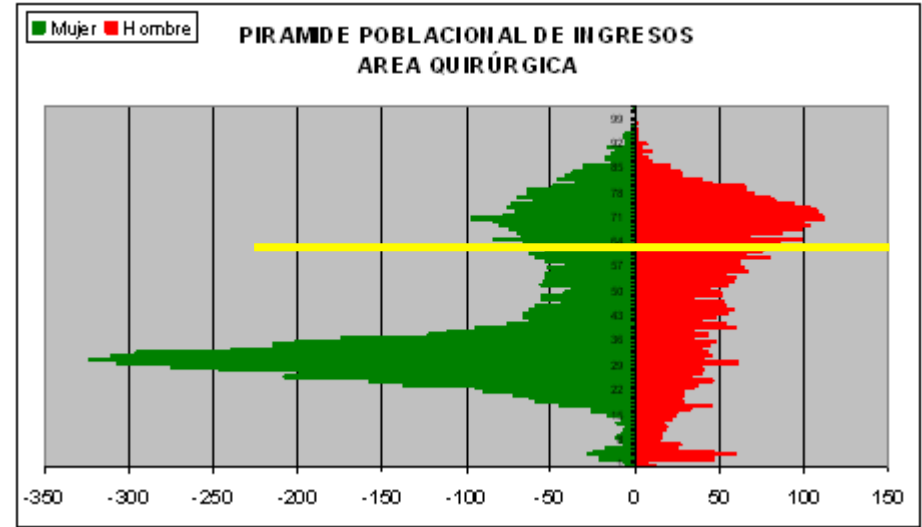
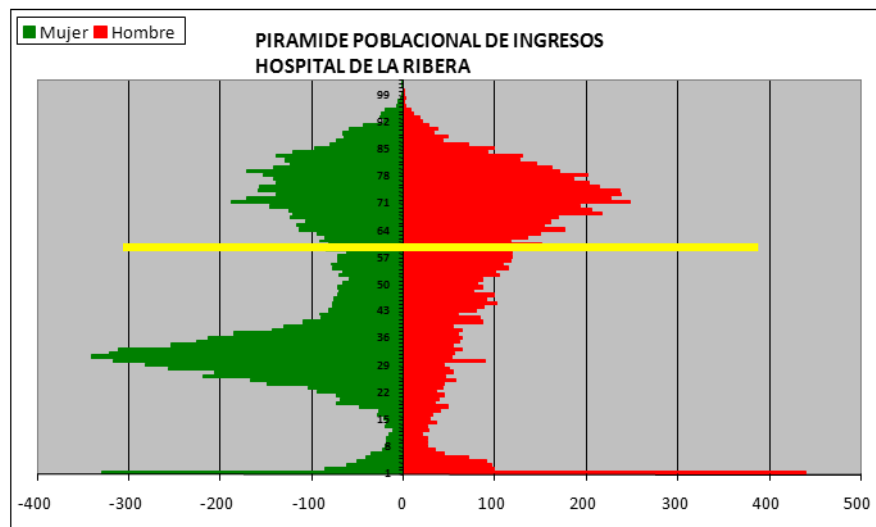
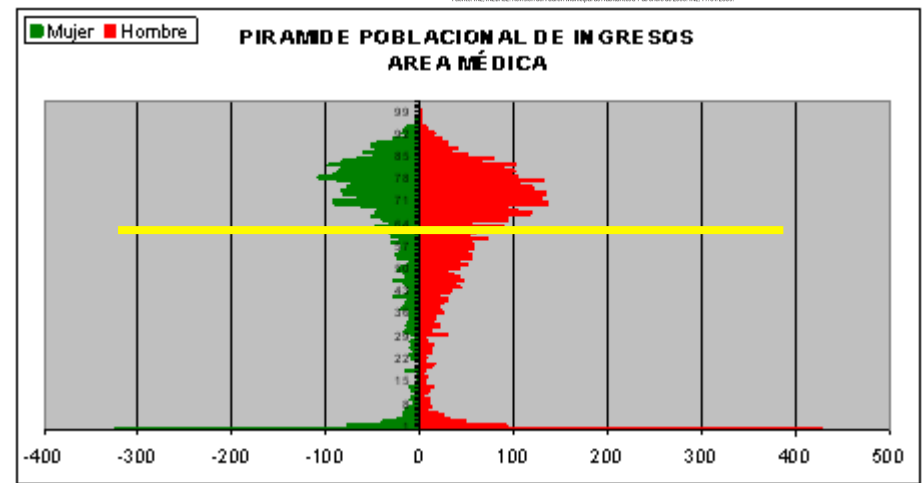
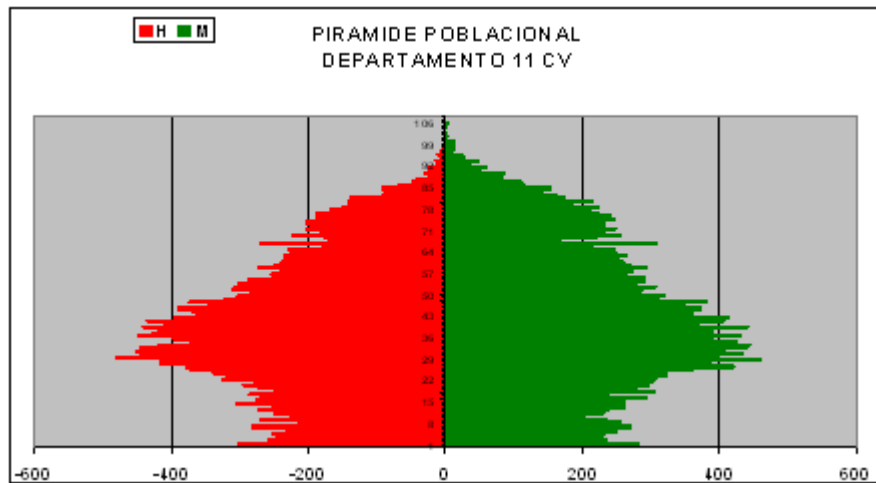
37 DIADA INTERNACIONAL

Población según sexo y edad, 2005

ues
05

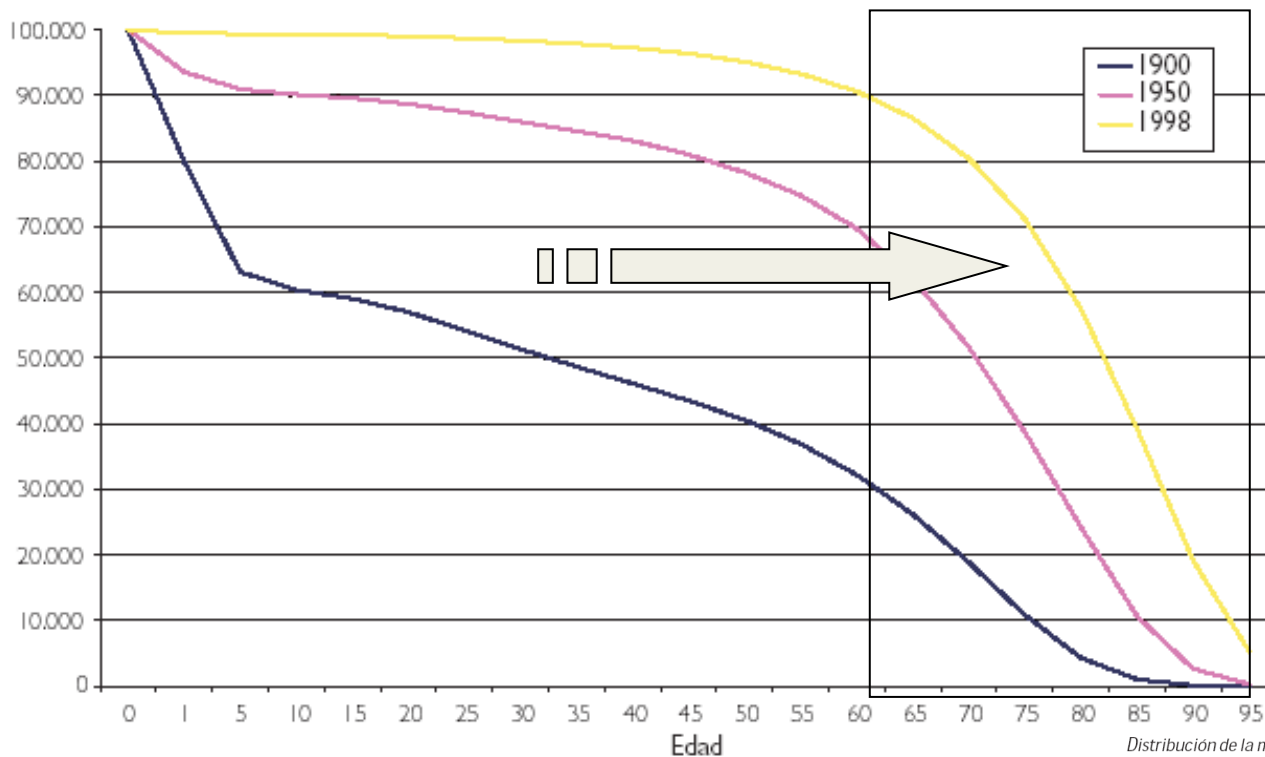


Nota: Posición de la generación del baby boom.
De 85 a 100 y más años. Datos distribuidos de población ponderada año por año por la población de cada edad a nivel nacional.
Fuente: INE, INEBAE. Revision del Padrón Municipal de Habitantes a 1 de enero de 2005. INE, 17/03/2006.



Compresión Morbi-Mortalidad

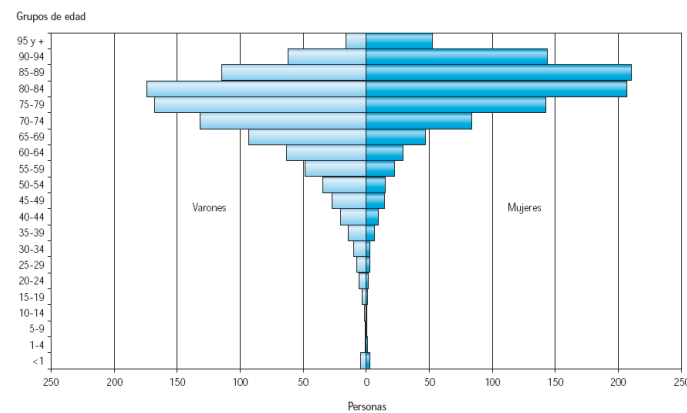
EVOLUCIÓN DE LA SUPERVIVENCIA SEGÚN EDADES, 1900-1998



Fuente: INE: Anuario Estadístico de España, 2004. Edición en CD-Rom. INE, 2004.

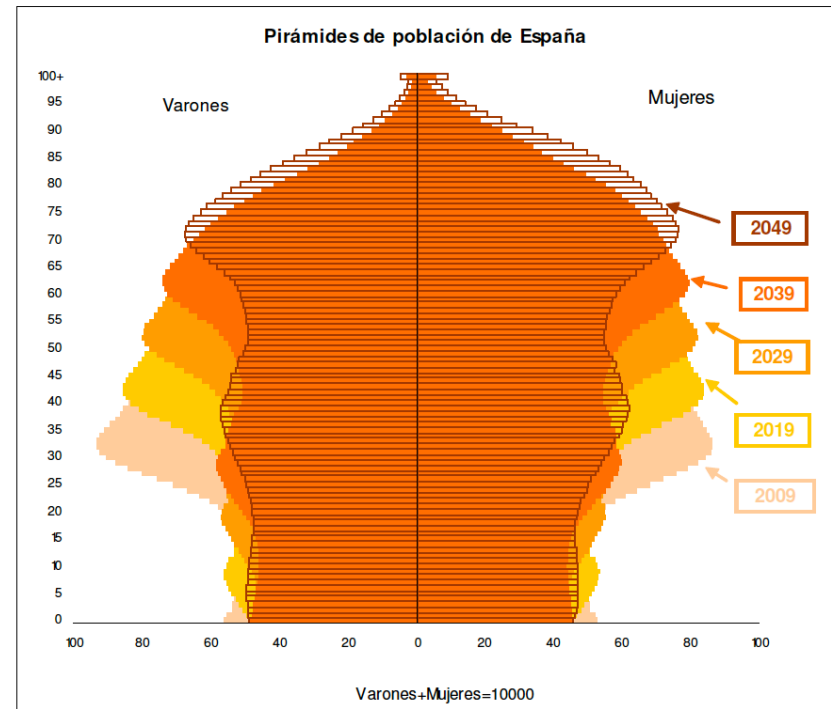
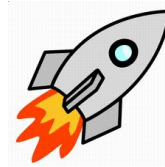
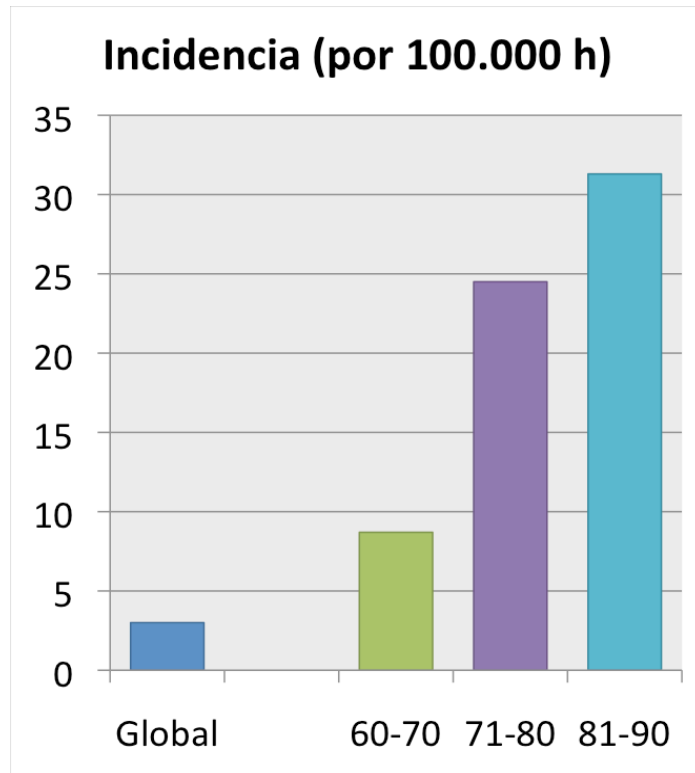
**Hemos retrasado la enfermedad
No la hemos evitado**

Distribución de la mortalidad (todas las causas) por sexo y edad por 1.000 fallecidos, 2004



Fuente: INE, INEBASE: Defunciones según la Causa de Muerte 2001. Distribución de la mortalidad por causas (lista reducida), sexo y edad. INE, 10/04/2006.

SMD y edad



Fuente: Proyección de Población a Largo Plazo

TABLE 1. Median Age and Proportion of Patients Aged 80 Years or Older at Diagnosis of Multiple Myeloma, per Calendar Period

Calendar period	Men		Women		Combined		≥80 y (%)
	No. of cases	Age (y), median (range)	No. of cases	Age (y), median (range)	No. of cases	Age (y), median (range)	
1950-1959	32	65 (45-87)	38	70 (47-85)	70	70 (45-87)	15.7
1960-1969	50	68 (46-96)	69	72 (44-93)	119	69 (44-96)	16.0
1970-1979	81	68 (46-94)	60	73 (40-94)	141	70 (40-94)	22.0
1980-1989	76	71 (49-89)	88	74 (41-90)	164	72 (41-90)	23.8
1990-1999	88	73 (37-94)	85	73 (44-91)	173	73 (37-94)	28.3
2000-2005 ^a	46	73 (31-86)	60	76 (45-94)	106	74 (31-94)	31.1
Total	373	71 (31-96)	400	73 (40-94)	773	72 (31-96)	25.3

^a Six-year period.

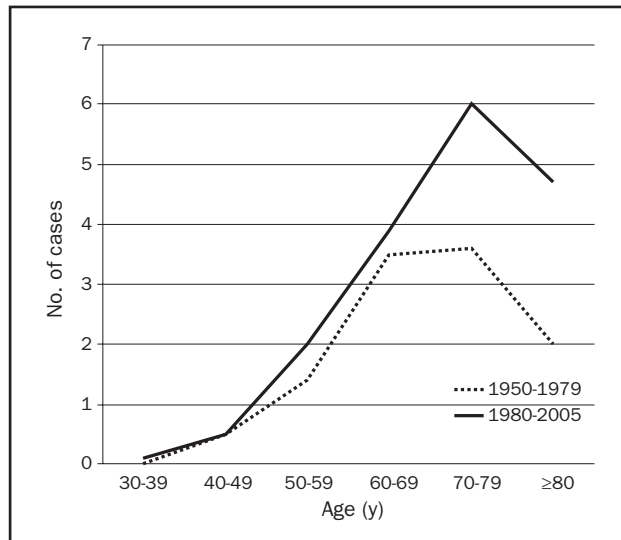
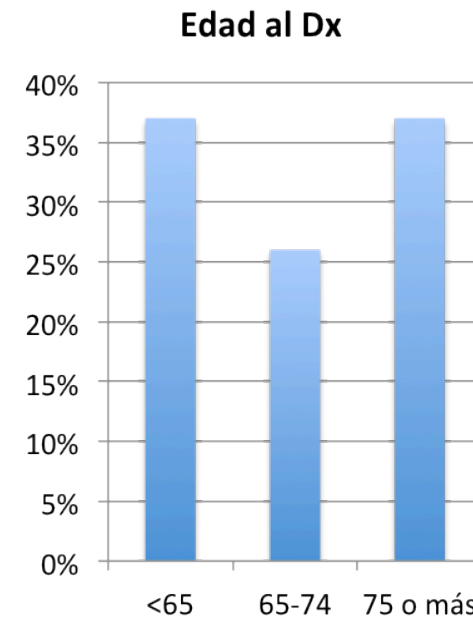


FIGURE 1. Average number of cases of multiple myeloma diagnosed per year, by age at diagnosis and calendar period (1950-1979 vs 1980-2005).

**Patterns of Multiple Myeloma During the Past 5 Decades:
Stable Incidence Rates for All Age Groups in the Population
but Rapidly Changing Age Distribution in the Clinic**

INGEMAR TURESSON, MD, PHD; RAMON VELEZ, MSc, PHD; SIGURDUR Y. KRISTINSSON, MD, PHD;
AND OLA LANDGREN, MD, PHD

Mayo Clin Proc. 2010;85(3):225-230



Palumbo, NEJM 2011

TABLE 2. Average Annual Crude and Age-Adjusted Incidence Rates of Multiple Myeloma in Malmö, Sweden, 1950-2005, by Sex

Calendar period	Men		Women		Combined	
	No. of cases	Rate ^a	No. of cases	Rate ^a	No. of cases	Rate ^a
1950-1959	32	3.2 (3.8)	38	3.5 (3.5)	70	3.3 (3.6)
1960-1969	50	4.2 (4.6)	69	5.4 (4.5)	119	4.8 (4.6)
1970-1979	81	6.9 (6.1)	60	4.7 (3.0)	141	5.9 (4.6)
1980-1989	76	7.0 (5.2)	88	7.3 (4.1)	164	7.1 (4.6)
1990-1999	88	7.5 (5.7)	85	6.6 (3.2)	173	7.0 (4.4)
2000-2005 ^b	46 (77) ^c	5.9 (4.8)	60 (100) ^c	7.3 (4.6)	106 (177) ^c	6.8 (4.8)
Total	373		400		773	

Poisson distribution		
Estimate of change in incidence per 10 y	Men	Women
Significance (2-tailed)	0.0599	-0.0138
	.07	.67

^a Per 100,000 person-years. Rates in parentheses are age-adjusted to European standard population.

^b Six-year period.

^c Number in parentheses is calculated for 10 years for comparison, assuming an unchanged incidence rate during the following 4 years.

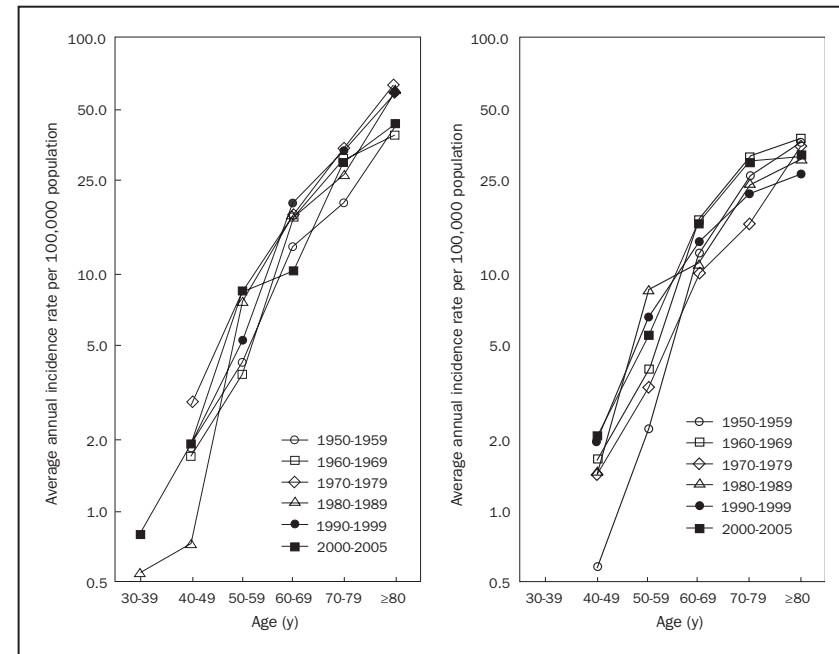
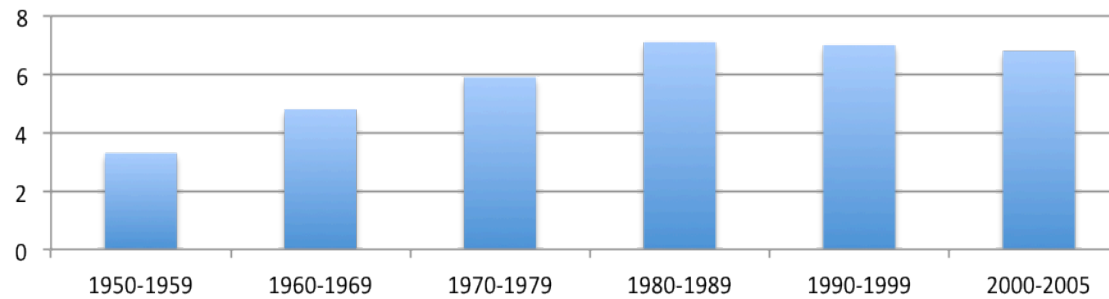


FIGURE 2. Annual incidence rates of multiple myeloma per 100,000 population in Malmö, Sweden, 1950-2005, by age and sex (left, men; right, women).

Incidencia



Trends in Leukemia Incidence and Survival in the United States (1973–1998)

Yang Xie, M.D., M.P.H.^{1,2} **CANCER** May 1, 2003 / Volume 97 / Number 9
 Stella M. Davies, M.D., Ph.D.^{1,2}
 Ying Xiang, M.D.^{1,2}
 Leslie L. Robison, Ph.D.^{1,2}
 Julie A. Ross, Ph.D.^{1,2}

¹ Department of Pediatrics, University of Minnesota, Minneapolis, Minnesota.

² University of Minnesota Cancer Center, Minneapolis, Minnesota.

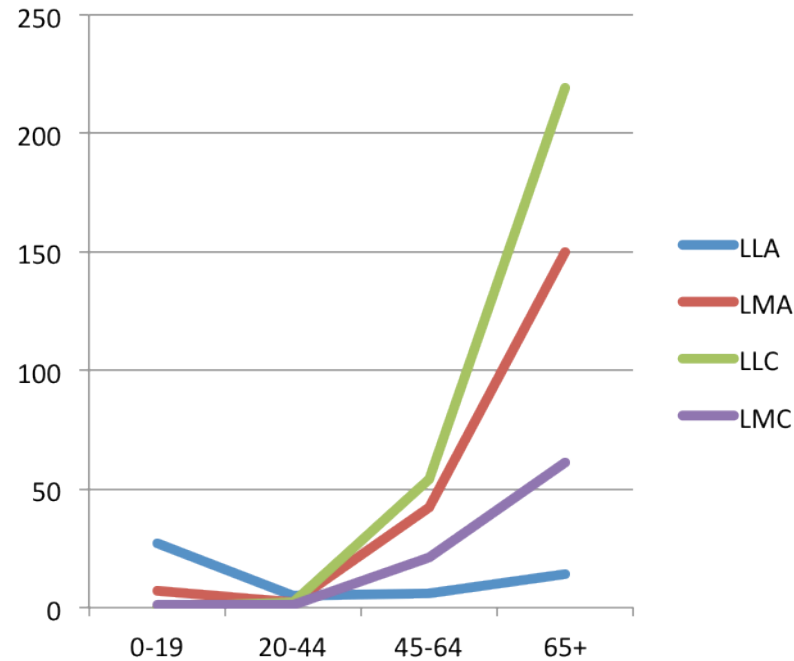


TABLE 2
Trends and Subtype Leukemia Incidence (Rate per Million Persons)
SEER 1973–1998

	No.	Rate ^a	Change (%) ^b	95% CI
ALL (yrs)^c				
Birth–19	4848	27	1.1 ^d	0.6, 1.6
20–44	1111	5	2.6 ^d	1.7, 3.6
45–64	698	6	2.9 ^d	1.7, 4.1
65+	941	14	0.9	–0.2, 2.0
AML (yrs)				
Birth–19	1187	7	0.5	–0.4, 1.4
20–44	2774	12	0.2	–0.6, 0.9
45–64	4756	42	0.3	–0.3, 0.9
65+	10,000	150	0.4 ^d	0.0, 0.8
CLL (yrs)				
Birth–19	3	0	— ^e	— ^e
20–44	503	2	–0.8	–1.7, 0.2
45–64	6128	54	–0.5 ^d	–1.0, –0.1
65+	14,657	219	–0.6 ^d	–1.1, –0.1
CML (yrs)				
Birth–19	206	1	0.1	–2.0, 2.2
20–44	1586	7	–0.6	–1.3, 0.2
45–64	2323	21	–1.2 ^d	–1.7, –0.6
65+	4114	61	–2.2 ^d	–2.7, –1.6

SEER: Surveillance, Epidemiology, and End Results program; CI: confidence interval; ALL: acute lymphoblastic leukemia; AML: acute myeloid leukemia; CLL: chronic lymphoblastic leukemia; CML: chronic myeloid leukemia.

^a Incidence rates are per million persons and are age adjusted to the 1970 U.S. standard million population.

^b Estimated annual percent change (EAPC) was calculated using the weighted least squares method.

^c Median age were 11, 66, 71, and 64 years for ALL, AML, CLL, and CML, respectively.

^d The EAPC is significantly different from zero ($P < 0.05$).

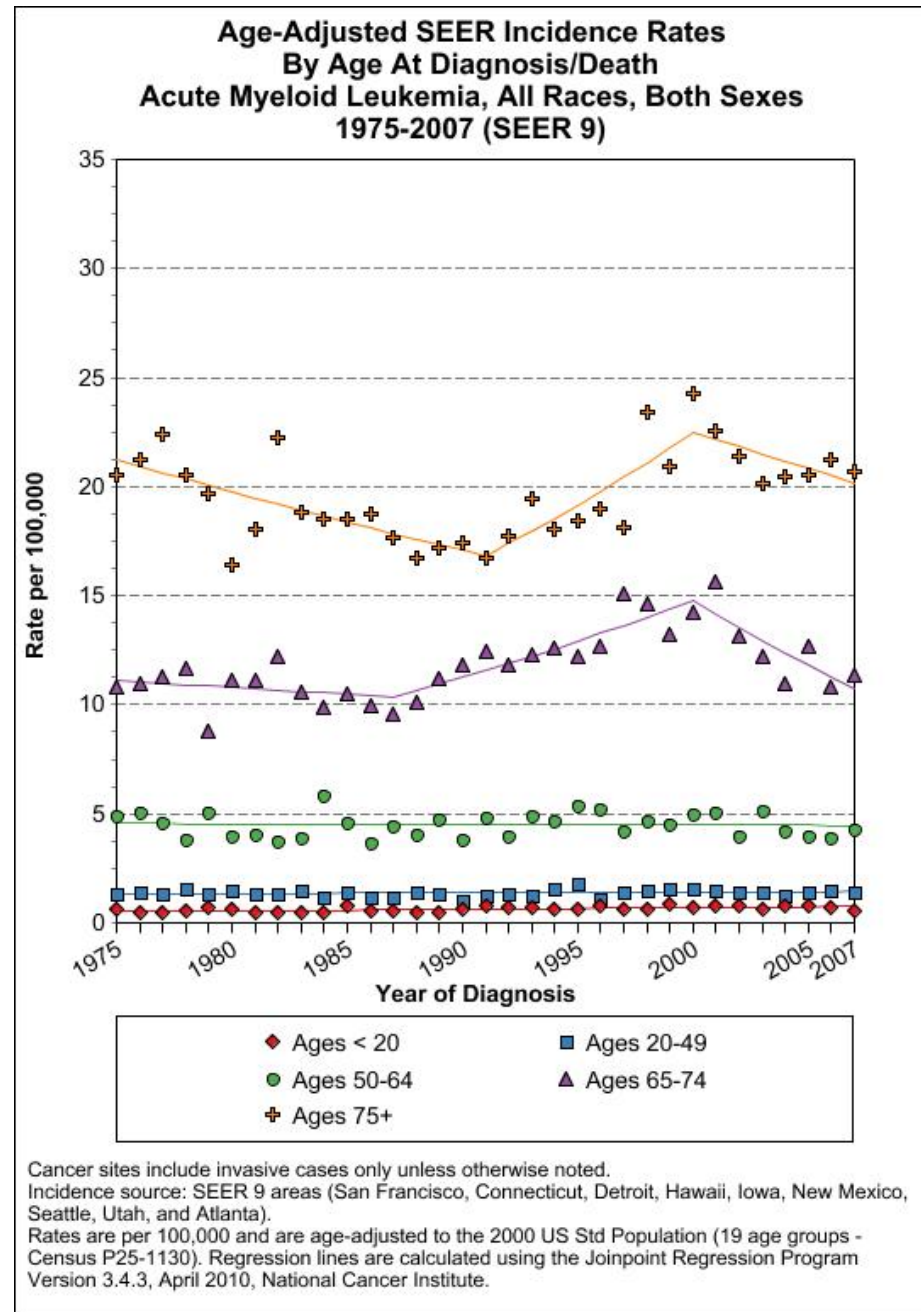
^e Statistic could not be calculated due to small numbers.

Leucemia aguda

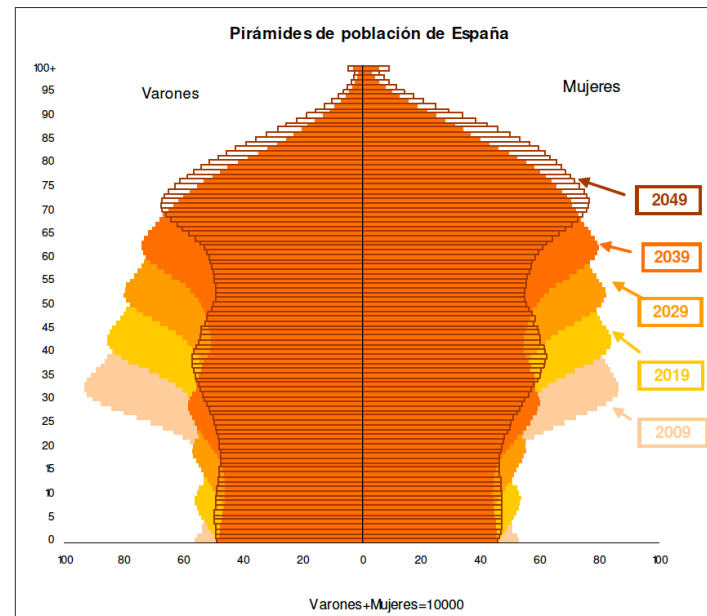
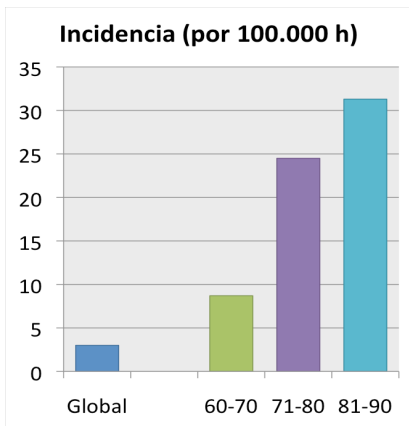


Surveillance Epidemiology and End Results

providing information on cancer statistics to help reduce the burden of this disease on the U.S. population



Neoplasia y edad



Fuente: Proyección de Población a Largo Plazo

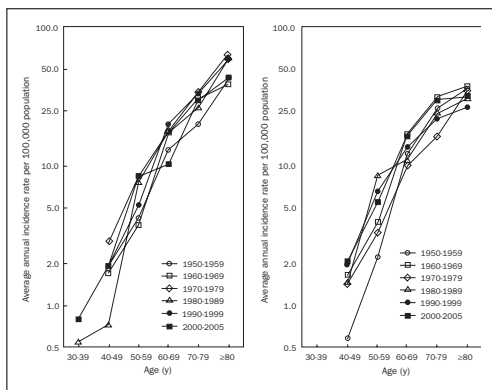
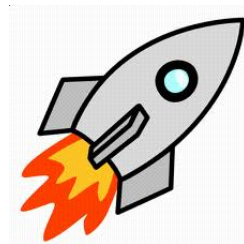
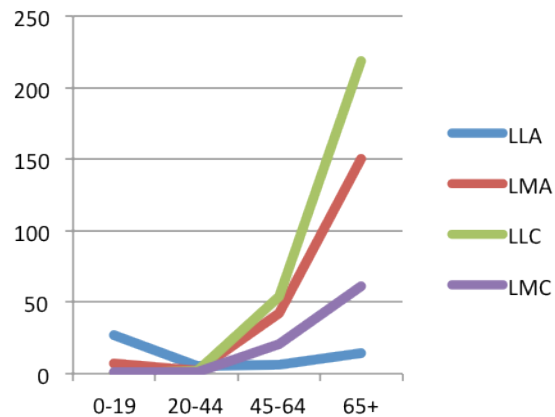


FIGURE 2. Annual incidence rates of multiple myeloma per 100,000 population in Malmö, Sweden, 1950-2005, by age and sex (left, men; right, women).



La edad como factor pronóstico en SMD

- IPE
- Düsseldorf-German Austrian MDS study group
- Lille
- IPSS-WPSS
- MDACC

Table 1 Age as a Risk Factor for Survival and Leukemia Transformation in MDS				
Score	Clinical Outcome			
	Survival		Leukemia Transformation	
	Univariate Analysis (Risk Factor; P Value)	Multivariate Analysis (Risk Factor; P Value)	Univariate Analysis (Risk Factor; P Value)	Multivariate Analysis (Risk Factor; P Value)
Spanish Sanz Score ¹⁴	≥ 60 y; .018	≥ 60 y; .0001	< 60 y; .0004	NS
Düsseldorf Score ⁹	≥ 70 y; .002	≥ 70 y; .008	NS	NR
French Lille Score ¹⁵	≤ 50, 50–60, > 60 y; .003	Age; .0001	NS	NS
IPSS ³	> 60 y; .0001	> 60 y; < .0001	NS	> 60 y; < .0001 25% AML
IPSS-LDH ⁴	≥ 70 y; < .00005	≥ 70 y; < .00005	NS	NS
WPSS ^{5,7}	Advanced age; < .001	NR	NS	NR

- MDACC

Simplified Myelodysplastic Syndrome Risk Score (0-15 Points)*

Prognostic Factor	Coefficient	Points
Performance status		
≥ 2	0.267	2
Age, y		
60-64	0.179	1
≥ 65	0.336	2
Platelets, $\times 10^9/L$		
< 30	0.418	3
30-49	0.270	2
50-199	0.184	1
Hemoglobin < 12 g/dL	0.274	2
Bone marrow blasts, %		
5-10	0.222	1
11-29	0.260	2
WBC $> 20 \times 10^9/L$	0.258	2
Karyotype: Chromosome 7 abnormality or complex ≥ 3 abnormalities	0.479	3
Prior transfusion, yes	0.107	1

- Impacto pronóstico en bajo riesgo, pero no en alto riesgo
- Impacto de la comorbilidad en todos los grupos

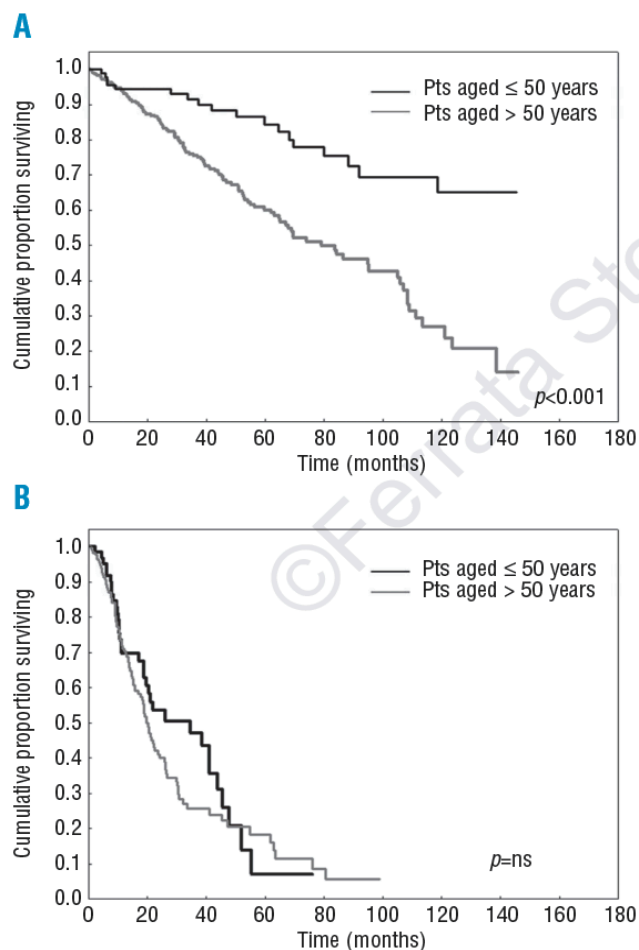


Figure 1. Cumulative probability of survival among 840 patients given a diagnosis of myelodysplastic syndrome at the Department of Hematology and Oncology, Policlinico San Matteo, Pavia Italy, 1992–2007 who are younger than 50 vs. >50 years of age. (A) Patients with refractory anemia or refractory cytopenia with multilineage dysplasia according to WHO criteria. (B) Patients with refractory anemia with excess blasts (types 1 and 2).

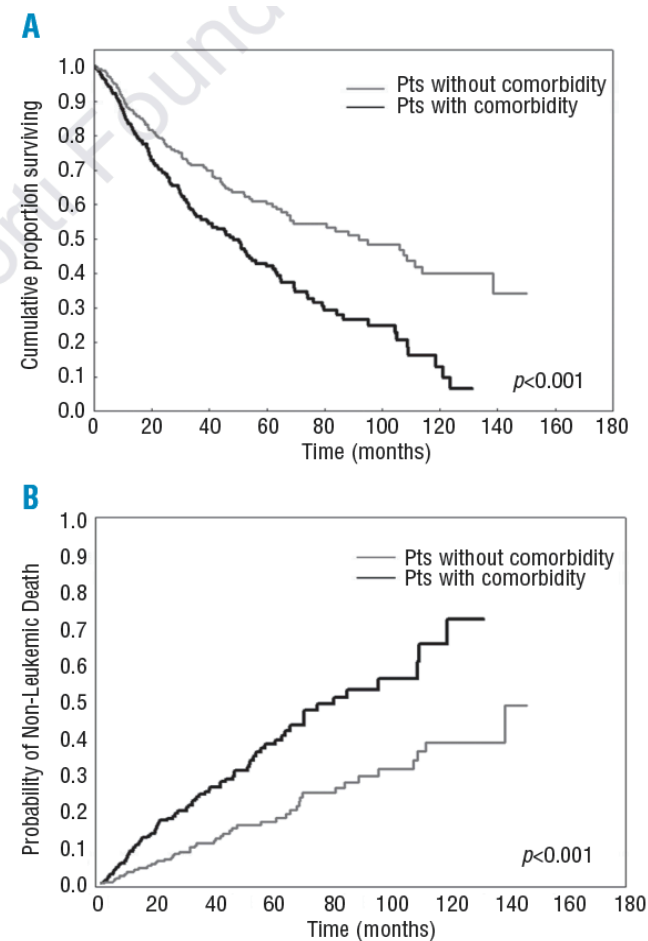


Figure 2. Cumulative probability of survival (A) and risk of non-leukemic death (B) among 840 patients given a diagnosis of myelodysplastic syndrome at the Department of Hematology and Oncology, Policlinico San Matteo, Pavia Italy, 1992–2007 according to the presence of extra-hematologic comorbidity at the time of diagnosis.

Edad como Factor de Respuesta al tratamiento

- Terapia inmunosupresora
- AEE y soporte
- Quimioterapia intensiva
- Nuevas terapias: Hipometilantes

Respuesta a inmunosupresores

- Terapia inmunosupresora
 - La edad influye negativamente en la probabilidad de respuesta

Table 2. Coefficients Obtained From the Multivariate Stepwise Logistic Regression Models of Response Versus Study Medicine,* Age, Sex, and DR15 Allele

Risk Factor	Coefficient (β)	95% CI for β	<i>P</i> for $\beta = 0$
Study medicine			
ATG + CsA	—	—	—
ATG	−1.042	−2.075 to −0.009	.048
Age	−0.097	−0.144 to −0.050	< .001
Sex			
Female	—	—	—
Male	0.443	−0.686 to 1.572	.442
DR15 allele	1.690	0.643 to 2.737	.002

Abbreviations: ATG, antithymocyte globulin; CsA, cyclosporine.
*ATG plus CsA versus ATG.

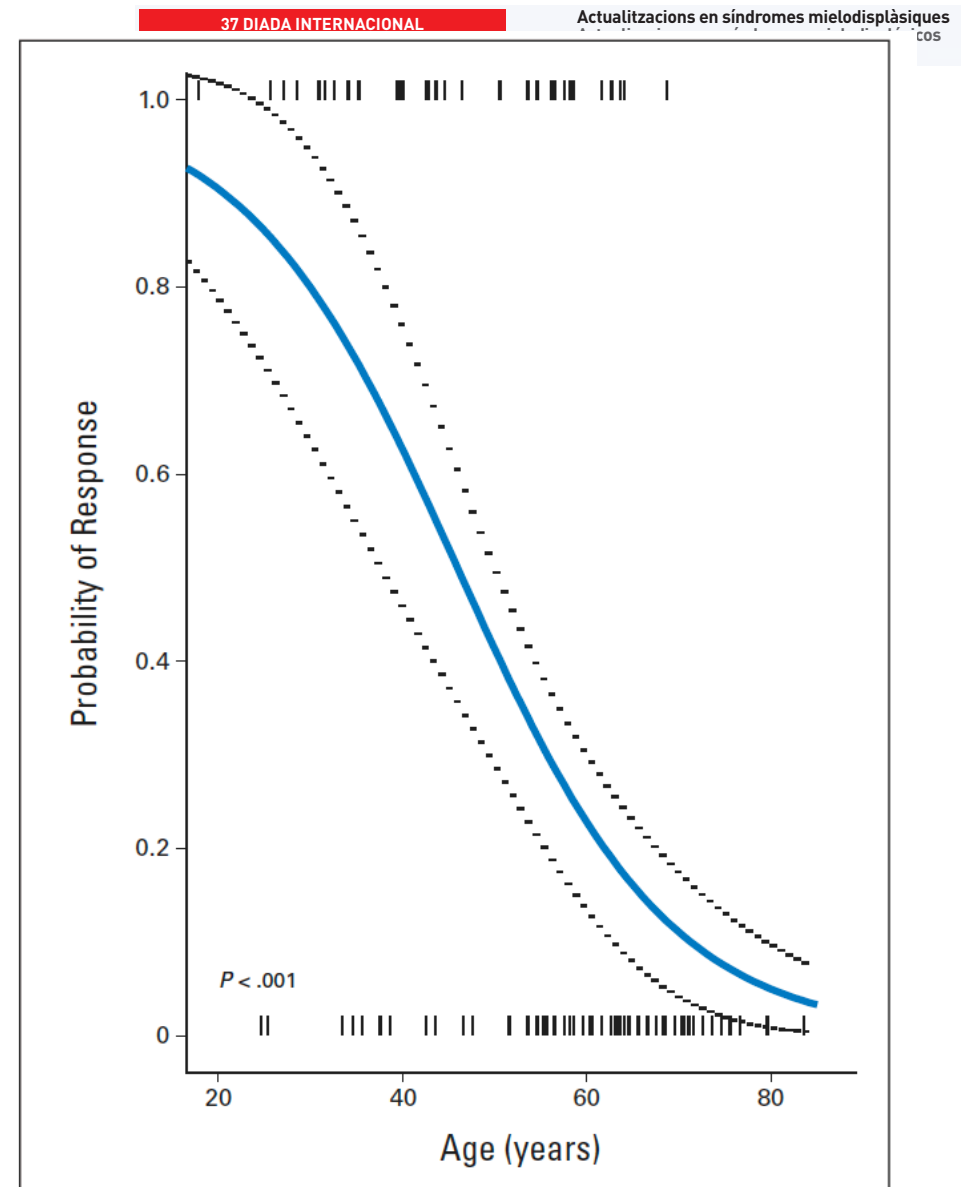


Fig 2. Role of age in predicting response to immunosuppressive therapy. Estimated probability of response versus age was determined using logistic regression analysis. Each “|” symbol represents a patient with his or her corresponding age. The vertical lines at the bottom represent nonresponders, whereas those at the top represent responders. As indicated, older patients are more likely to be nonresponders, and younger patients are more likely to be responders ($P < .001$).

Table 3. Characteristics of patients and prognostic factors of response to rEPO at week 12 according to IWG 2006 criteria (n= 403)

	Overall response, %	Overall response versus nonresponse*					
		Univariate analysis			Multivariate analysis†		
		OR	95% CI	P	OR	95% CI	P
Age, y							
Younger than 70	44	1	—	—	1	—	—
70 or older	54	1.5	1.0-2.2	.06	1.3	0.8-2.2	.22
Sex							
Male	46	1	—	—	1	—	—
Female	55	1.4	1.0-2.1	.08	1.5	0.9-2.3	.08

Table 2. Duration of response to rEPO according to IWG 2000 response criteria

	Patients, no.	Median response duration, mo	Univariate analysis			Multivariate analysis*		
			HR	95% CI	<i>P</i>	HR	95% CI	<i>P</i>
Type of response								
Major	168	24.4	1	—	—	1.00	—	—
Minor	83	13.8	1.8	1.3-2.6	.003	1.63	1.1-2.5	.02
Age, y								
Younger than 70	83	16.8	1	—	—	—	—	—
70 or older	168	20	0.9	0.7-1.4	.73	—	—	—

- SMD alto riesgo y LMA → MDACC, 998 pts, >65, 1980-2006

Regimen	No. patients (%)
Idarubicin + HD ara-C	240 (24)
Idarubicin + HD ara-C + fludarabine	164 (16)
Fludarabine + HD ara-C	95 (10)
Topotecan + HD ara-C	45 (5)
Topotecan + HD ara-C + cyclophosphamide	84 (8)
Clofarabine + HD ara-C	27 (3)
Miscellaneous + standard or HD ara-C	215 (22)
Miscellaneous (no ara-C)	128 (13)

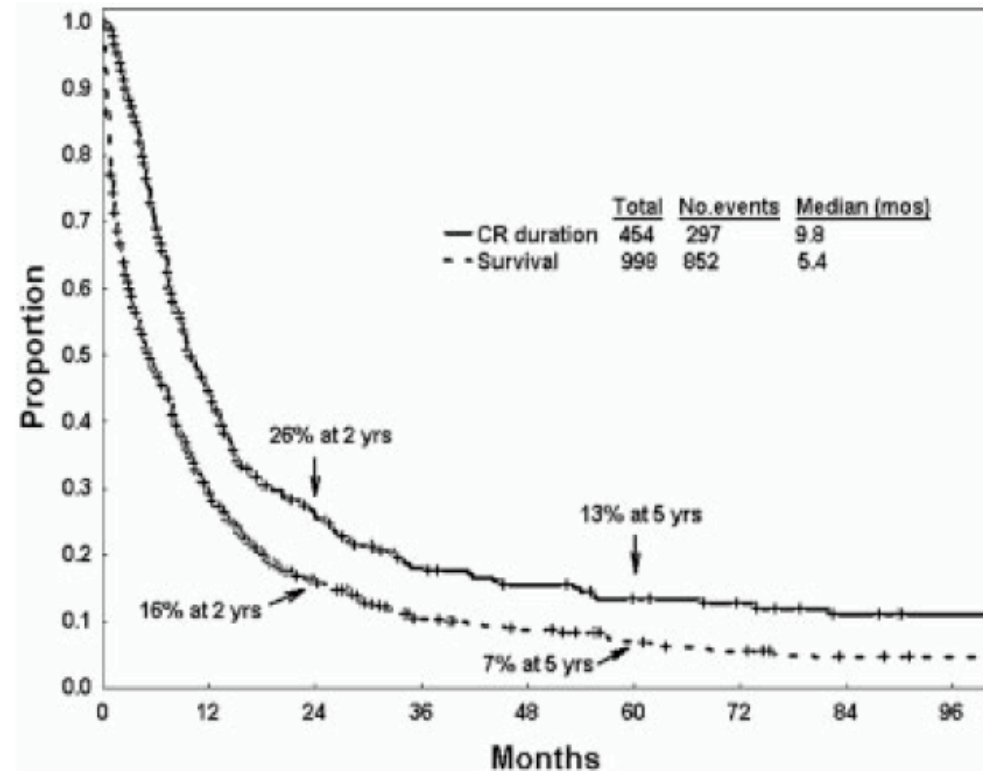


FIGURE 1. Survival and duration of complete response is shown.

- SMD alto riesgo y LMA
 - MDACC, 998 pts, >65, 1980-2006

TABLE 4
Factors Associated with Complete Response, 8-Week Mortality, and Survival

Parameter	Category	No.	No. CR (%)	P	No. (%) 8-wk mortality	P	Survival		
							Median (wks)	1-yr %	P
Total age (years)	65-69	372	183 (49)	0.04	101 (27)	< 0.001	29	31	< 0.001
	70-74	347	164 (47)		111 (32)		34	29	
	75-79	197	77 (39)		76 (39)		18	21	
	≥ 80	82	30 (37)		44 (54)		6	16	
Diagnosis	AML	798	356 (45)	0.50	281 (35)	0.03	20	27	0.10
	MDS ≥ 20% blasts	91	46 (51)		24 (26)		34	35	
	MDS < 20% blasts	109	52 (48)		27 (25)		35	38	
Performance, ECOG	0 - 1	633	322 (51)	< 0.001	148 (23)	< 0.001	34	35	< 0.001
	2	246	104 (42)		98 (40)		17	25	
	3-4	119	28 (24)		86 (72)		3	7	

- SMD alto riesgo y LMA
 - MDACC, 998 pts, >65, 1980-2006

Multivariate Analysis of Prognostic Factors Associated with Complete Response

Adverse factors for CR	<i>P</i>	Hazard risk
Age ≥ 75 yrs	0.002	0.78
Prior therapy for other cancer	0.001	0.46
AHD ≥ 6 mos	< 0.001	0.59
Treatment outside LAFR	< 0.001	0.42
Unfavorable karyotype	< 0.001	0.40
WBC ≥ 25 x 10 ⁹ /L	0.001	0.74
Hemoglobin ≤ 8 g/dL	0.006	0.82
Creatinine > 1.3 mg/dL	0.003	0.77
Performance status > 2 (ECOG)	0.046	0.60

No. adverse factors	No. patients	No. CR (%)	No. (%) 8-wk mortality	Survival	
				Median (mos)	1-yr %
0-1	218	160 (73)	29 (13)	12	49
2-3	527	247 (47)	150 (28)	6	31
≥ 4	252	46 (18)	153 (61)	1	9

- SMD alto riesgo y LMA
 - MDACC, 998 pts, >65, 1980-2006

Multivariate Analysis of Prognostic Factors Associated with 8-Week Induction Mortality

Adverse factors for 8-week mortality	<i>P</i>	Hazard risk
Age ≥ 75 years	0.001	1.3
Performance status ≥ 2, ECOG	< 0.001	1.5
Complex karyotype	< 0.001	1.4
Treatment outside LAFR	< 0.001	3.1
AHD duration ≥ 12 mos	< 0.001	1.4
Creatinine > 1.3 mg/dL	< 0.001	1.4

Risk group	No. adverse factors	No. patients	No. (%) 8-wk mortality	No. (%) CR	Survival	
					Median (mos)	1-yr %
Low	0	195	20 (10)	134 (69)	16	58
Intermediate	1	292	56 (19)	166 (57)	9	35
	2	269	98 (36)	108 (40)	4	22
High	≥ 3	242	158 (65)	46 (19)	1	8

- SMD alto riesgo y LMA
 - MDACC, 998 pts, >65, 1980-2006

Results of Multivariate Analysis of Prognostic Factors for Survival

Adverse factors	<i>P</i>	Hazard risk
Age ≥ 75 yrs	< 0.001	1.2
Unfavorable karyotype	< 0.001	1.7
Treatment outside LAFR	< 0.001	1.6
AHD ≥ 12 months	< 0.001	1.3
Performance status > 2, ECO)	< 0.001	2.1
Lactic dehydrogenase > 600 u/L	< 0.001	1.4
Creatinine > 1.3 mg/dl	0.001	1.2

No. adverse factors	No. patients	Survival			No. (%) CR	No. (%) 8-wk mortality
		Median (mos)	1-yr %	2-yr %		
0	121	18	63	35	87 (72)	12 (10)
1-2	568	7	33	19	292 (51)	146 (26)
≥ 3	301	1	9	3	71 (24)	171 (57)

- Hipometilantes: AZA-001

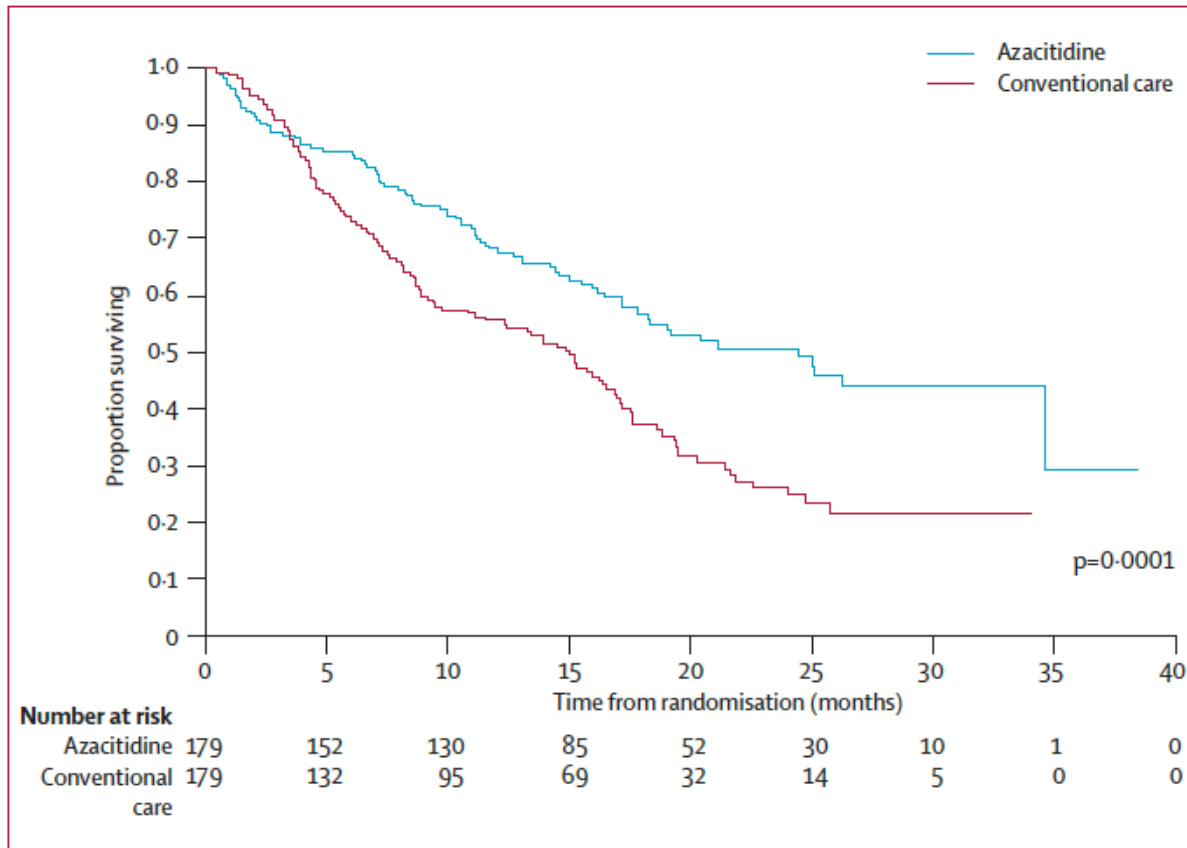


Figure 3: Overall survival

- Hipometilantes: AZA-001

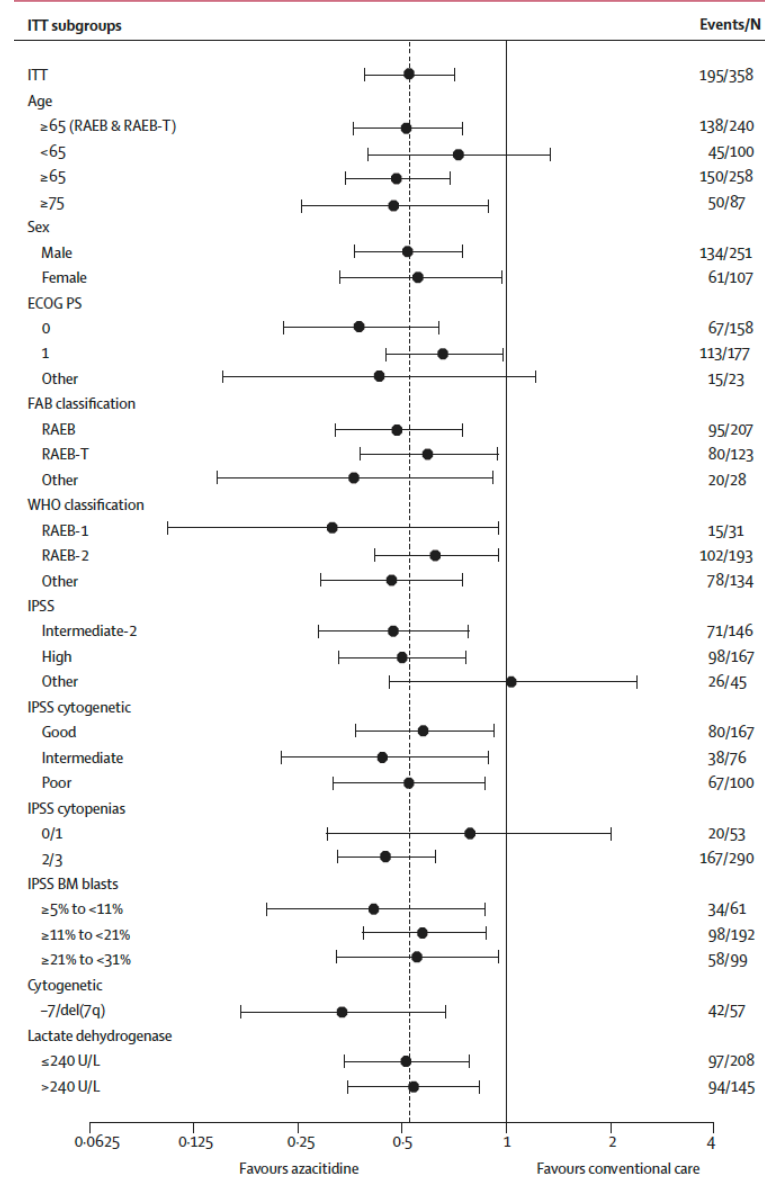


Figure 4: Hazard ratio and 95% CI for overall survival in the intention-to-treat analysis
Hazard ratios and CIs determined with stratified Cox proportional hazards model adjusted for treatment, subgroup, Eastern Cooperative Oncology Group performance status (ECOG PS), lactate dehydrogenase, haemoglobin, number of previous red-blood-cell transfusions, and presence or absence of the cytogenetic -7/del(7q) abnormality. No subgroup-by-treatment interactions were significant (p>0.20). The horizontal axis uses a logarithmic scale. The dotted line is the hazard ratio in the primary intention to treat (ITT) analysis; the hazard ratio and CI are from the stratified Cox regression model with treatment as the only term. FAB=French-American-British. RAEB=refractory anaemia with excess blasts. RAEB-T=RAEB in transformation. IPSS=international prognostic scoring system. BM=bone marrow.

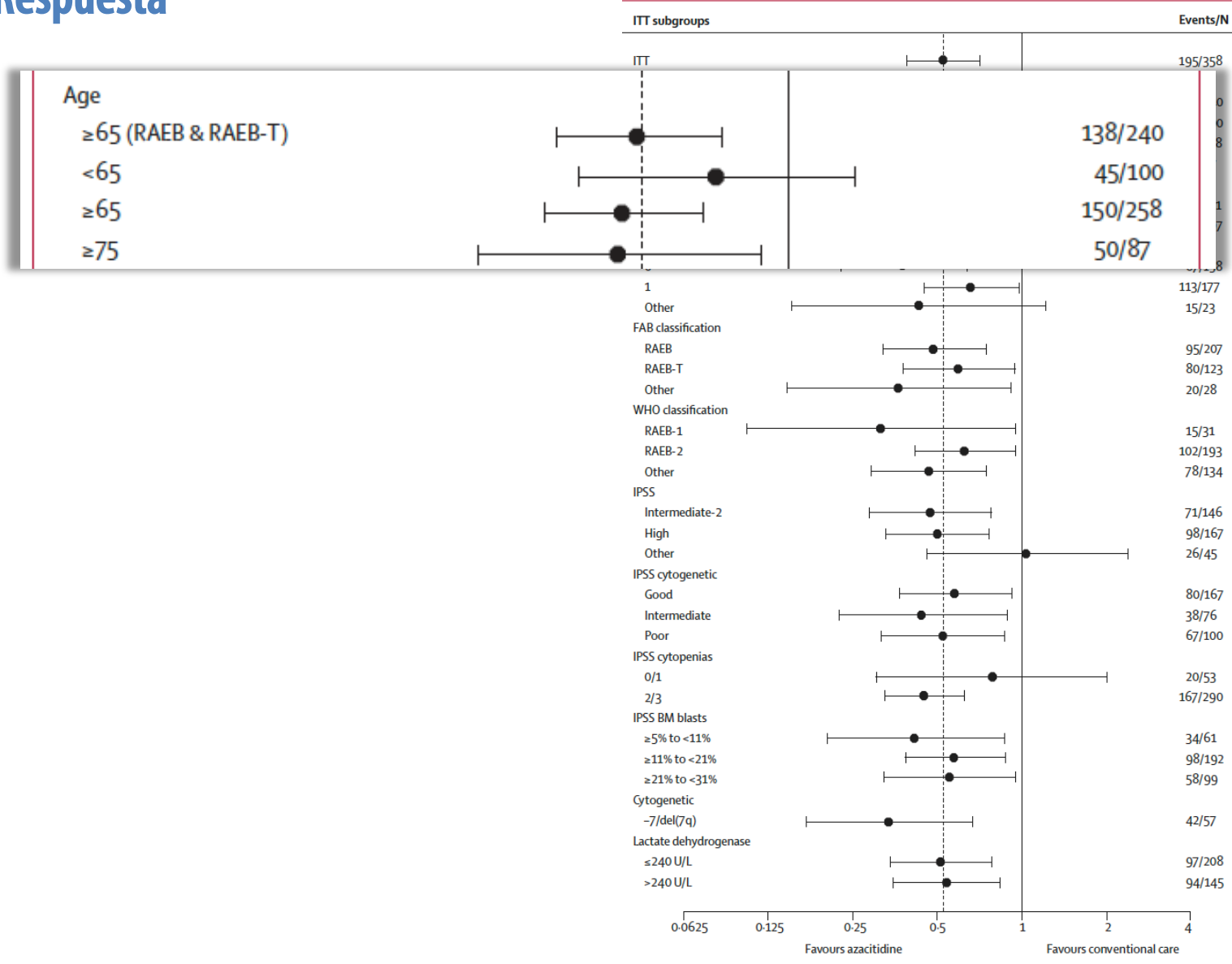


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- AZA-001 ≥ 75

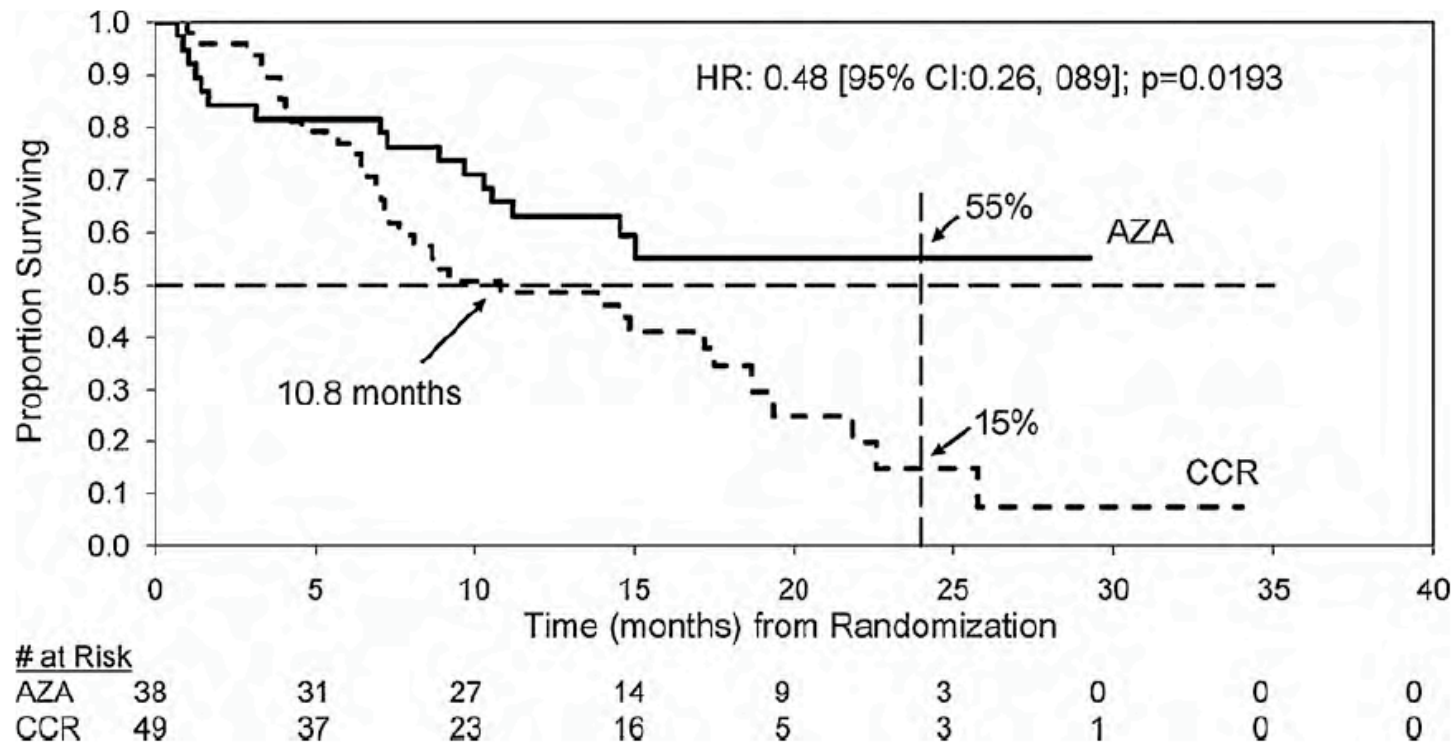
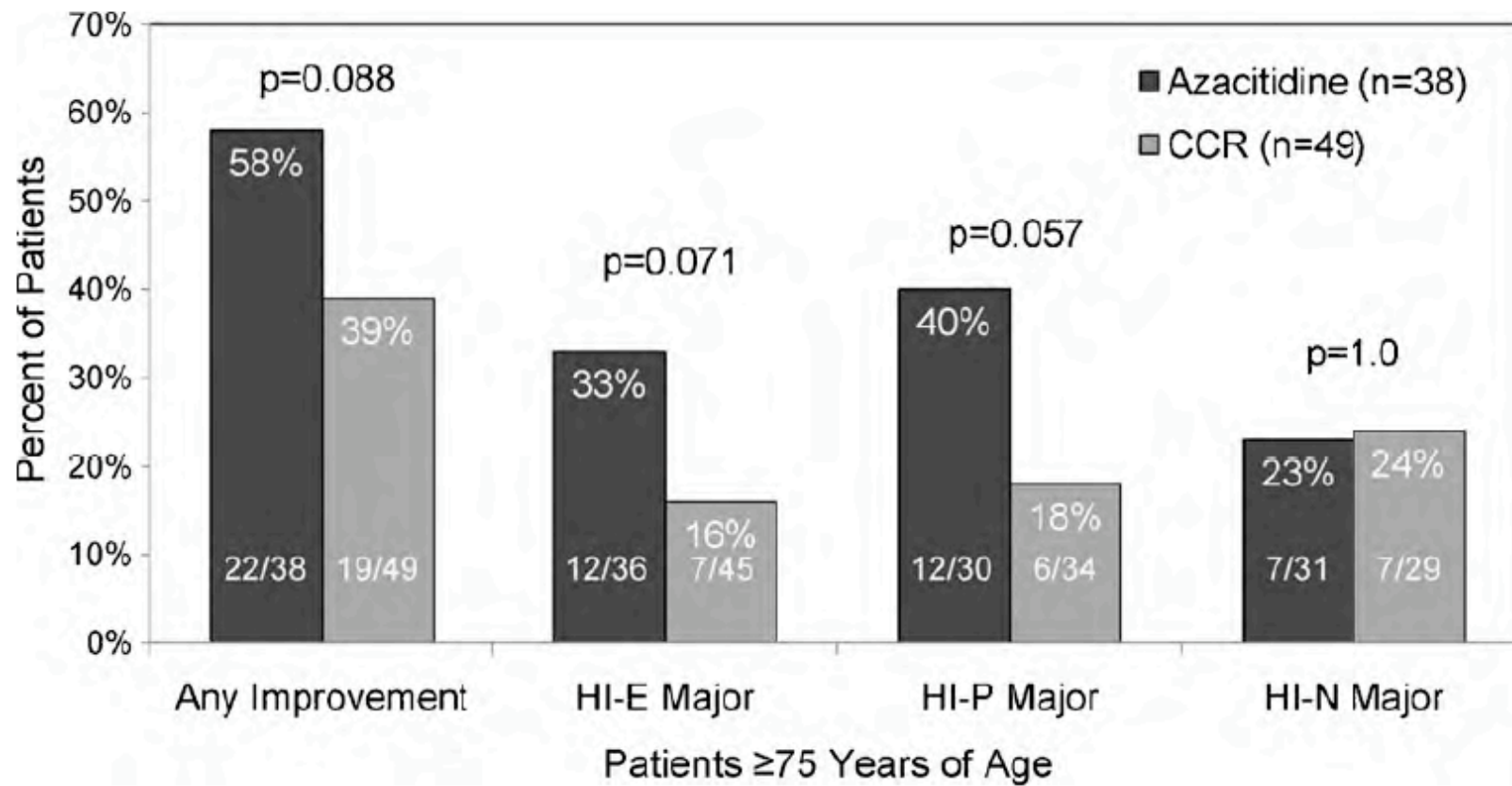


Fig. 2. Overall survival azacitidine (AZA) vs CCR.

- AZA-001 ≥ 75



Prognostic factors of response and overall survival in 282 higher-risk myelodysplastic syndromes treated with azacitidine

Raphael Itzykson, Sylvain Thépot, Bruno Quesnel, Francois Dreyfus, Odile Beyne-Rauzy, Pascal Turlure, Norbert Vey, Christian Recher, Caroline Dartigeas, Laurence Legros, Jacques Delaunay, Célia Salanoubat, Sorin Visanica, Aspasia Stamatoullas, Françoise Isnard, Anne Marfaing-Koka, Stéphane de Botton, Youcef Chelghoum, Anne-Laure Taksin, Isabelle Plantier, Shanti Ame, Simone Boehrer, Claude Gardin, C L Beach, Lionel Adès and Pierre Fenaux

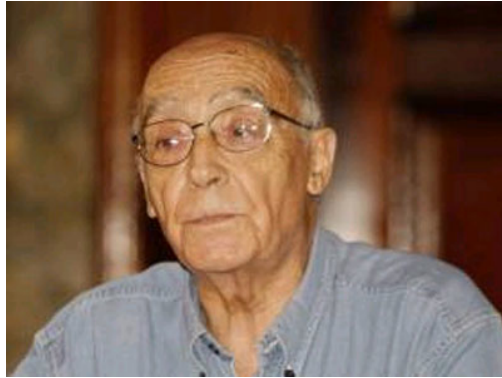
- Hipometilantes

Table 3: Prognostic factors of response achievement and response duration

	Response achievement (n=282)					Response duration (months, n=122)				
	univariate analysis			multivariate analysis		median	univariate		multivariate analysis	
	response rate	%	p	OR [95% CI]	p		range	p	HR [95% CI]	p
Age			0.99					0.94		
> 70 years	67/156	43%				9.2	2-28+			
≤ 70 years	55/126	44%				9.5	2-38+			
ECOG PS			0.02					0.73		
0-1	104/217	48%				9.5	1-38+			
≥2	17/56	30%				9.5	2-24			

Table 4: Prognostic factors of overall survival

	univariate analysis		multivariate analysis	
	median OS	p	HR [95% CI]	p
age		0.38		
> 70 years	12.7			
≤ 70 years	15.0			
ECOG PS		<0.0001		<0.0001
0-1	15.7		1	
≥ 2	7.1		2.0 [1.4-2.9]	



Definición	¿Cronológica ó funcional?. No comparables. ¿Sirve para medir?. ¿Es un elemento útil de medida?
Edad como variable	Todos los estudios hacen referencia a edad cronológica; los análisis estadísticos NO contemplan la edad funcional.
Edad: ¿variable no independiente?	¿ <i>Surrogate marker</i> de otros parámetros? (comorbilidad, capacidades funcionales, tolerancia a la QT, capacidad de cumplimentación de tratamientos y visitas, necesidad de <i>caregiver</i> , ...)
Ensayos Clínicos	Sesgo por escasa representación de los ancianos
Ensayos de Supervivencia	Sesgo por selección de tratamientos favorables en jóvenes
Objetivo / Expectativas del tratamiento	Atender a proyecciones vitales Prolongar “active life expectancy”
Esperanza de vida	Diferente entre jóvenes y ancianos

La edad cronológica no mide adecuadamente



Evaluación integral → EDAD FISIOLÓGICA

SITUACIÓN FÍSICA → Comorbilidad

FUNCIONALIDAD → Capacidad instrumental o de interacción

VULNERABILIDAD → Resistencia al stress por la enfermedad o los tratamientos

- **Medición de la comorbilidad:**
 - Variable multidimensional, que incluye condiciones clínicas distintas a la alteración estudiada, y que influyen en la funcionalidad, supervivencia o tolerancia al tratamiento

- **Evaluación de la funcionalidad:**
 - CGA (*comprehensive geriatric assessment*):
 - Nutricional - Funcional – Mental – Anímica - Social
 - VES-13 (*vulnerable elders survey*)
 - CGA abreviados
 - Test de la marcha (*gait speed*)

- Concepto de **fragilidad**

- **Medición de la comorbilidad:**
 - Variable multidimensional, que incluye condiciones clínicas distintas a la alteración estudiada, y que influyen en la funcionalidad, supervivencia o tolerancia al tratamiento
- Aproximación gero-oncológica

Index	Items	End Point	Comment
Charlson Comorbidity Index (CCI) ³¹	19 conditions, weighted 1–6	1-y mortality in hospitalized internal medicine patients	Simple, most widely used in oncology; underdetects significant ailments, such as anemia and decreased lung function
CCI age ³²	Each decade after 50 years of age, add 1 point	5-y mortality in surgery patients	Composite index
Cumulative Illness Rating Scale (CIRS) ³³	13 organ systems, weighted 0–4		Detailed and comprehensive list of diseases
Cumulative Illness Rating Scale-Geriatric (CIRS-G) ³⁴	14 organ systems, rated 0–4 (weighted)	Geriatric outpatients	Adapted for elderly
Satariano and Ragland ²⁴	Myocardial infarction, types of heart disease, diabetes, other forms of cancer, and respiratory, gallbladder, liver conditions	3-y survival in 936 breast cancer patients based on SEER registry	Simple, qualitative valuation
Kaplan and Feinstein ³⁶	12 ailments weighted, including functional activity (locomotive impairment), alcohol, and miscellaneous	5-y survival in diabetes mellitus	Composite index
Index Of Coexisting Disease ³⁷	Includes 14 diseases (0–4) and a functional index of 12 conditions (0–2)	2-y survival in breast cancer patients	Composite index
Prognostic Index ²³	Composite index based on 12 items (e.g., age, sex, self-reported comorbidity, functional measures)	4-y mortality established in community-dwelling U.S. adults	Not yet validated in oncology patients

- Factores de la enfermedad → Blastos, citopenias y citogenética
 - IPSS, WPSS (IPSS-R)
- Factores del paciente → comorbilidades, bajo PS, disfunción de órganos
 - Scores de comorbilidad (CCI, HCT-CI)
- N=200; *follow-up* 18 m; 66% fallecidos; OS 25m; LFS 24m
 - Progresión de IPSS y WPSS → descenso de OS y LFS
 - Progresión de CCI y HCT-CI → descenso de OS y LFS
 - Valor predictivo de CCI y HCT-CI al diagnóstico, independiente de IPSS/WPSS

Table 1. Cox regression analysis

	OS (HR,CI,p)	LFS (HR,CI,p)
CCI (a)	1.32 (1.09–1.59) 0.005	1.39 (1.15–1.68) 0.001
CCI (b)	1.28 (1.03–1.58) 0.024	1.37 (1.11–1.69) 0.004
HCT-CI (a)	1.32 (1.04–1.69) 0.025	1.33 (1.05–1.70) 0.020
HCT-CI (b)	1.33 (1.01–1.76) 0.041	1.34 (1.03–1.75) 0.033

(a) Adjusted with IPSS; (b) Adjusted with WPSS.

Clinical evaluation of extra-hematologic comorbidity in myelodysplastic syndromes: ready-to-wear versus made-to-measure tool

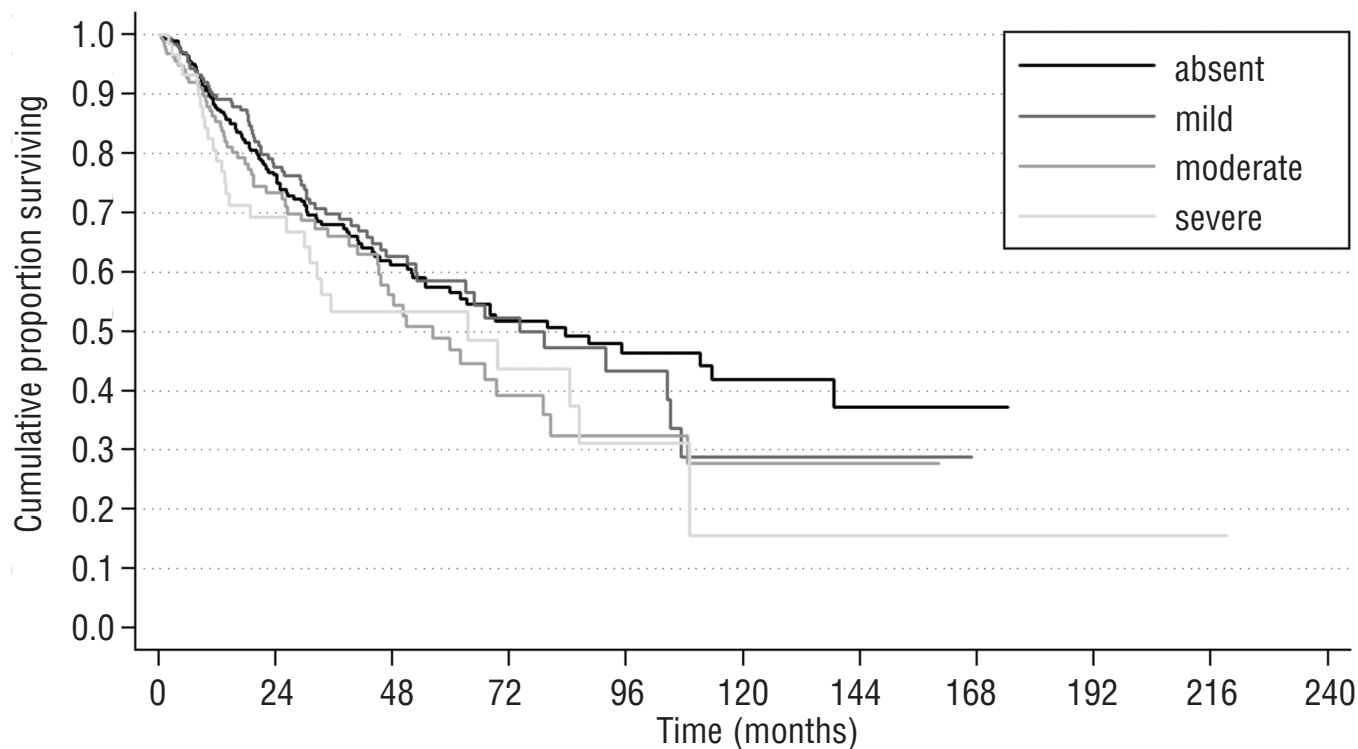


Figure 1. Probability of overall survival according to ACE-27 risk at diagnosis in all 840 MDS patients ($P=0.11$). There was no significant difference in cumulative probability of survival between patients with no comorbidity and those with ACE-27 mild risk ($P=0.68$), or between patients with moderate and severe risk ($P=0.11$), whereas OS was significantly lower in patients with both moderate and severe risk compared to those without comorbidity ($P=0.044$ and $P=0.019$, respectively).

Tabla 11. Índice de comorbilidad de Sorrer (HCT-CI)

Comorbilidad	Definición	Puntos
Arritmia	Fibrilación auricular*, <i>flutter</i> *, enfermedad del seno* o arritmia ventricular*	1
Cardiovascular	Enfermedad coronaria*, infarto de miocardio*, insuficiencia cardiaca congestiva* o fracción de eyección ≤ 50%	1
Valvulopatía	Excepto prolapso de válvula mitral asintomático	3
Cerebrovascular	Accidente isquémico transitorio y/o accidente cerebrovascular isquémico o hemorrágico	1
Pulmonar leve o moderada	DLCO y/o FEV1 66-80% o disnea con actividad ligera o moderada	2
Pulmonar severa	DLCO y/o FEV1 ≤ 65% o disnea de reposo o si requiere oxígeno	3
Hepática leve	Hepatitis crónica o bilirrubina persistente entre VSN hasta 1,5 × VSN o AST/ALT entre VSN hasta 2,5 × VSN	1
Hepática de moderada a grave	Cirrosis, fibrosis, bilirrubina > 1,5 × VSN o AST/ALT > 2,5 × VSN	3
Renal	Creatinina persistente > 2 mg/dL, diálisis o trasplante renal	2
Tumor sólido	Tumores malignos en cualquier momento de la historia del paciente, excluyendo neoplasias cutáneas diferentes del melanoma	3
Reumatológica	Enfermedad reumatológica que requiera tratamiento	2
Enfermedad inflamatoria intestinal	Enfermedad de Crohn o colitis ulcerosa	1
Úlcera péptica	Úlcera péptica que requiera tratamiento	2
Diabetes	Diabetes que requiera tratamiento con insulina o hipoglucemiantes orales	1
Depresión/ansiedad	Depresión o ansiedad que requieran tratamiento o consulta profesional	1
Obesidad	Índice de masa corporal > 35 en adultos	1
Infección	Infección que requiera tratamiento (específico de trasplante)	1

ALT: alanina aminotransferasa; AST: aspartato aminotransferasa; DLCO: capacidad de difusión de CO pulmonar; FEV1: volumen espiratorio forzado en 1 segundo; VSN: valor superior de la normalidad

* Detectada en cualquier momento de la historia del paciente

Fuente: modificado de M.L. Sorrer et al.⁽⁶⁹⁾

- Limitados en general a pacientes en TPH
- HCT-CI: Correlación con supervivencia independiente de IPSS (Zipperer et al. Haematologica 2009)

Table 3 Application of Comorbidity Scores in MDS

Test	Items	End point	Comment	Study
Charlson Comorbidity Index (CCI)	Score based on CCI	Different end points, such as toxicity, survival, and mortality	Adapted CCI applied in HCT. High pretransplantation comorbidity scores predict higher NRM	Sorrer et al. ⁴¹ Diaconescu et al. ⁴²
	CCI	Overall survival	Prognostic factor independent from IPSS in MDS	Pelz et al. ⁴⁰
HCT-Specific Comorbidity Index (HCT-CI)	Modified, weighted score based on CCI <ul style="list-style-type: none"> • New items obesitas, psychiatric, or infectious problems • Refined definitions in several items like cardiac, pulmonary, or hepatic function 	2-y NRM and survival in training set of 708 and validation set of 347 HCT patients	Median age 44.8 y More sensitive and better predictor of survival than CCI	Sorrer et al. ⁴³ Sorrer et al. ⁴⁴
		Overall survival Early death rate	Was used for risk stratification in induction therapy in elderly AML patients	Giles et al. ⁴⁵
Pretransplantation Assessment of Mortality Score (PAM)	8 weighted items, including age, donor type, disease risk, conditioning regimen, renal, hepatic, pulmonary function	2-y all-cause mortality for allogeneic HCT	Age is an item Pulmonary function must be tracked	Parimon et al. ⁴⁶
CCI Kaplan-Feinstein Scale (KFS) ECOG Performance Status (PS)	Parallel evaluation of 2 comorbidity and 1 function scales	TRM in 105 RIC-HCT patients	Combination scale of KFS and PS	Artz et al. ⁴⁷
MDS-specific comorbidity index (MDS-CI)	Adapted from HCT-CI	NLD Overall survival	Retrospective analysis of 840 consecutive MDS patients	Della Porta et al. ⁴⁸

Abbreviations: AML, acute myeloid leukemia; HCT, hematopoietic cell transplantation; IPSS, International Prognostic Scoring System; MDS, myelodysplastic syndromes; NLD, nonleukemic death; NRM, nonrelapse mortality; RIC-HCT, reduced-intensity conditioning hematopoietic cell transplantation; TRM, treatment-related mortality.

MDS-CI

Table 3. Calculation of the MDS-specific comorbidity index (MDS-CI). The five comorbidities listed were found to be independently associated with the risk of NLD in multivariable analysis, and each of them was assigned a score proportional to the regression coefficient of the multivariable Cox's proportional hazards model. This score is taken into account if the specific comorbidity is present, and the MDS-CI is obtained as the sum of individual variable scores.

Comorbidity	HR obtained through a multivariable Cox's survival analysis with NLD as an outcome	Variable weighted score (to be taken into account if the specific comorbidity is present)
Cardiac disease	3.57 ($P<0.001$)	2
Moderate-to-severe hepatic disease	2.55 ($P=0.01$)	1
Severe pulmonary disease	2.44 ($P=0.005$)	1
Renal disease	1.97 ($P=0.04$)	1
Solid tumor	2.61 ($P<0.001$)	1

MDS-CI risk	Sum of individual variable scores	Proportion of patients in the learning cohort belonging to the risk group (%)
Low risk	0	546/840 (65%)
Intermediate risk	1-2	244/840 (29%)
High risk	>2	50/840 (6%)

NLD: non-leukemic death.

- 840 pacientes en Pavia y 504 en Düsseldorf
- Refina el pronóstico en SMD-BR
- Permite definir estrategias de tratamiento en combinación con WPSS

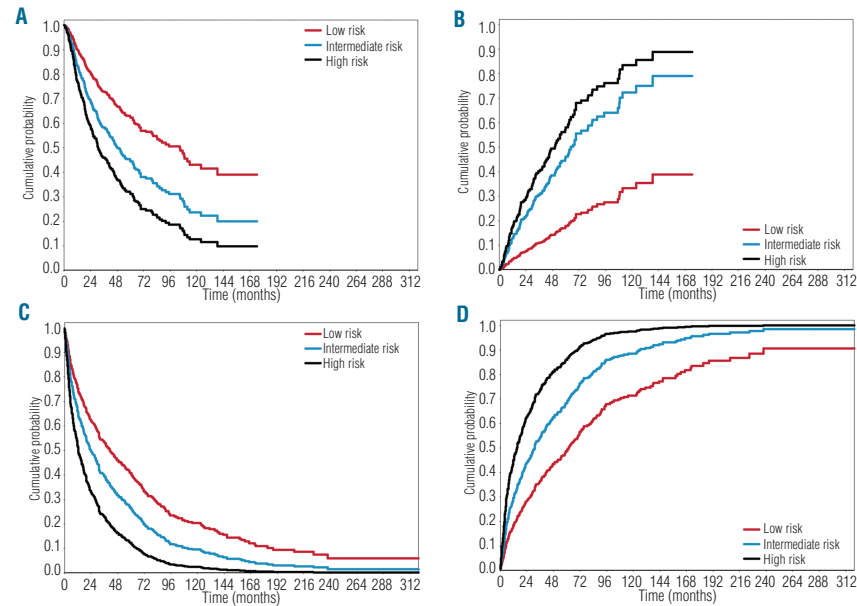


Figure 1. Relationship between MDS-CI category, risk of non-leukemic death and overall survival in the learning and validation cohorts of MDS patients. (A-B) Italian learning cohort; (A) Probability of overall survival according to time-dependent MDS-CI risk. (B) Probability of non-leukemic death according to time-dependent MDS-CI risk. (C-D); German validation cohort. (C) Probability of overall survival according to time-dependent MDS-CI risk. (D) Probability of non-leukemic death according to time-dependent MDS-CI risk.

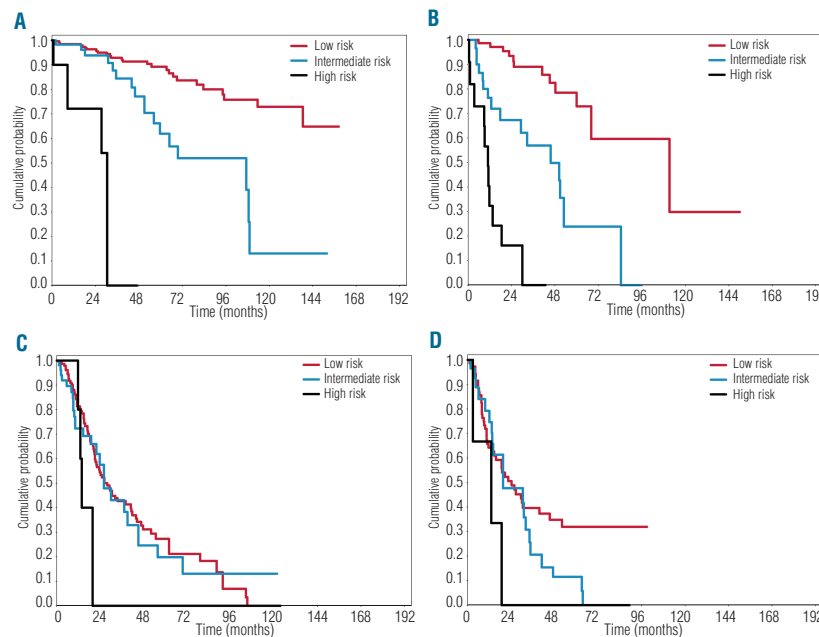


Figure 3. Impact of the MDS-CI category with the WPSS risk groups. (A-D) Probability of overall survival of MDS patients stratified into time-dependent WPSS categories according to time-dependent MDS-CI. (A) Very low and low WPSS risk patients were plotted together in a single group. (B) Intermediate WPSS risk group. (C) High WPSS risk group. (D) Very high WPSS risk group.

Comorbilidad y funcionalidad (Lee)

Tabla 12. Índice de comorbilidad y funcionalidad

Variables	Puntuación
Datos demográficos:	
Edad (60-64 = 1; 65-69 = 2; 70-74 = 3; 75-79 = 4; 80-84 = 5; ≥ 85 = 7)	1-7
Sexo masculino	2
Peso y talla	
Comorbilidad y estilos de vida:	
IMC < 25 kg/m ²	1
Diabetes mellitus	1
Melanoma o cáncer no cutáneo	2
Enfermedad pulmonar crónica (limitante o con O ₂)	2
Insuficiencia cardiaca	2
Ha fumado cigarrillos en la última semana	2
Funcionalidad:	
Dificultades para bañarse o ducharse	2
Dificultad para manejar dinero o contabilidad diaria	2
Dificultad para caminar varias manzanas	2
Dificultad para mover objetos (p. ej.: un sillón)	1

Fuente: modificado de S.J. Lee et al.⁽⁷¹⁾

Development and Validation of a Prognostic Index for 4-Year Mortality in Older Adults

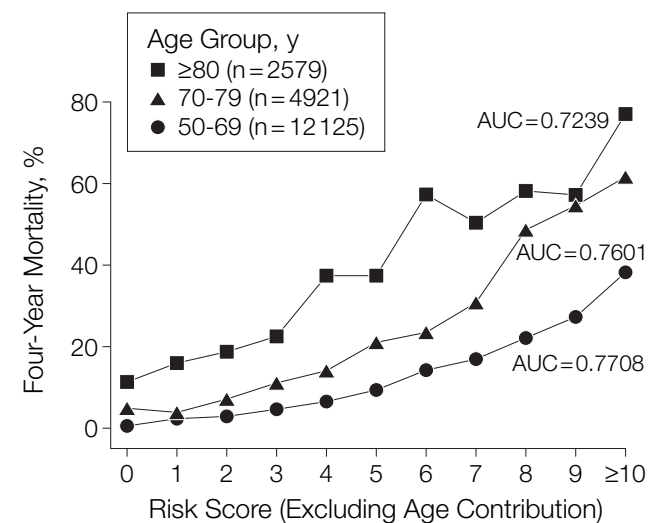
Sei J. Lee, MD

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Mark R. Segal, PhD

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Figure. Four-year Mortality by Risk Score in Differing Age Groups



AUC indicates area under the curve.

- *Comprehensive geriatric assessment (CGA)*
- Pretende la realización de una **valoración geriátrica integral**, que incluye la de la **funcionalidad**
- Definición:
 - *Proceso diagnóstico multidimensional e interdisciplinario, para determinar las capacidades médicas, psicológicas y funcionales de personas ancianas y frágiles, para poder desarrollar planes coordinados e integrados de tratamiento a largo plazo.*
- Valoración de diversos componentes con diferentes instrumentos
- Compleja y laboriosa y muchas veces con necesidad de personal entrenado

■ 1 **Nutricional**

- Sarcopenia / desnutrición
- Historia nutricional, Exploración física, Antropometría (Peso, Talla, SCE, IMC)
- Laboratorio: Albúmina, Transferrina, Prealbúmina
- Valoración multidimensional (antropométrica, psicosocial, dietética) → MNA-SF (Mini Nutritional Assessment -Short Form)

- Clasifica en: Bien nutridos / Riesgo nutricional / Desnutridos



Mini Nutritional Assessment MNA[®]

No Nombre:	Apellidos:	Sexo:	
Fecha:	Edad:	Peso en kg:	Talla en cm:

Responda al cuestionario eligiendo la opción adecuada para cada pregunta. Sume los puntos para el resultado final.

Cribaje	
A Ha comido menos por falta de apetito, problemas digestivos, dificultades de masticación o deglución en los últimos 3 meses? 0 = ha comido mucho menos 1 = ha comido menos 2 = ha comido igual	<input type="checkbox"/>
B Pérdida reciente de peso (<3 meses) 0 = pérdida de peso > 3 kg 1 = no lo sabe 2 = pérdida de peso entre 1 y 3 kg 3 = no ha habido pérdida de peso	<input type="checkbox"/>
C Movilidad 0 = de la cama al sillón 1 = autonomía en el interior 2 = sale del domicilio	<input type="checkbox"/>
D Ha tenido una enfermedad aguda o situación de estrés psicológico en los últimos 3 meses? 0 = sí 2 = no	<input type="checkbox"/>
E Problemas neuropsicológicos 0 = demencia o depresión grave 1 = demencia moderada 2 = sin problemas psicológicos	<input type="checkbox"/>
F1 Índice de masa corporal (IMC = peso / (talla)² en kg/m²) 0 = IMC <19 1 = 19 ≤ IMC < 21 2 = 21 ≤ IMC < 23 3 = IMC ≥ 23	<input type="checkbox"/>
SI EL ÍNDICE DE MASA CORPORAL NO ESTÁ DISPONIBLE, POR FAVOR SUSTITUYA LA PREGUNTA F1 CON LA F2. NO CONTESTE LA PREGUNTA F2 SI HA PODIDO CONTESTAR A LA F1.	
F2 Circunferencia de la pantorrilla (CP en cm) 0 = CP <31 3 = CP ≥ 31	<input type="checkbox"/>
Evaluación del cribaje (máx. 14 puntos)	<input type="checkbox"/> <input type="checkbox"/>
12-14 puntos: estado nutricional normal 8-11 puntos: riesgo de malnutrición 0-7 puntos: malnutrición	

■ 2 Funcional

- Debe evitarse términos vagos (“adecuado a su edad”) e intentar usar escalas
- Tres niveles
 - **ABVD** (básicas = elementales): Indices de KATZ o BARTHEL
 - Cuestionario con 10 ítems (comer, lavarse, vestirse, arreglarse, continencia fecal, continencia urinaria, uso de retrete, trasladarse,, deambular, subir escalones).
 - **AIVD** (instrumentales = independencia): Escala de LAWTON-BRODY
 - 8 ítems (capacidad para usar el teléfono, hacer compras, preparación de la comida, cuidado de la casa, lavado de la ropa, uso de medios de transporte, responsabilidad respecto a su medicación, y manejo de sus asuntos económicos).
 - **AAVD** (avanzadas = socialización y ocio)
 - capacidad de actividades deportivas, de ocio, de transporte, culturales, religiosas

■ 3 Mental

- El diagnóstico de demencia aumenta el riesgo de mortalidad.
- Valoración cognitiva con cuestionarios como MMSE (Mini Mental Status Examination) o el Miniexamen cognoscitivo (MEC) de Lobo.

■ 4 Anímica

- Explora la existencia de depresión, con cuestionarios como GDS (Geriatric Depression Scale de Yesavage), validada en castellano, y con 15 ítems autocumplimentables.
- Existen escalas simples, incluso binarias.

Recommendations from the task force on CGA of the International Society of Geriatric Oncology (SIOG)

- *Question 1: Is there clinically usable biological or other evidence for “degrees of aging”?*
 - Clinical recommendations:
 - The best biological and clinical markers to use in the evaluation of older cancer patients remains to be determined.
 - Biochemical markers such as albumin, hemoglobin, and creatinine clearance can provide prognostic information and clues as to tolerance to treatment.
 - As for clinical markers, functional status assessment should be more extensive than the ECOG performance status evaluation and may include ADL/IADL, and/or a performance test such as the timed get up and go.

Recommendations from the task force on CGA of the International Society of Geriatric Oncology (SIOG)

- *Question 2: What does a CGA detect in addition to oncological/medical assessments?*
 - Based on several randomized clinical trials, CGA-based approach is strongly recommended in elderly patients to improve the detection of problems.
 - As these results were obtained in patients in a wide range of health statuses, there are no substantial reasons not to apply the same approach in elderly “cancer” patient despite the lack of specifically designed randomized trials.
 - Oncologists should be informed that significant clinical information may be missed if a CGA-based approach is not pursued in the older cancer patients.
 - The best form of geriatric assessment pertaining to cancer patients remains to be defined.
 - In addition to the biological and functional assessment elements mentioned under Point 1, screening for depression and cognitive impairment should be conducted.
 - As a practical example, a combination of tools frequently used in geriatric oncology comprises ADL/IADL, the Geriatric Depression Scale, and Folstein’s Mini-Mental Status.

Recommendations from the task force on CGA of the International Society of Geriatric Oncology (SIOG)

- *Question 3: What is the evidence for the effectiveness of CGA?*
 - Published data demonstrated that CGA is effective:
 - in community-dwelling elderly
 - in the context of integrated social and medical home care coordinated by a case manager
 - as the basis for the design of discharge planning
 - for hospitalized patients, both before and after discharge
 - Some evidence points to the fact that patients seen in the oncology setting tend to be healthier and less disabled than traditional geriatric patients.
 - Frail and vulnerable patients appear the ideal candidates for CGA-based approach. Therefore, a two-step approach including a screening step could be used.
 - Even if the best form of CGA for cancer patients remains to be defined, some form of geriatric assessment and intervention can be expected to improve independence, quality of life, and rate of hospitalization of cancer patients, and be cost-effective.
 - Any type of CGA intervention should include a follow-up, since this appears key to the effectiveness of CGA.

Recommendations from the task force on CGA of the International Society of Geriatric Oncology (SIOG)

- *Question 4: Screening tools and alternative assessments*
 - *Screening tools:*
 - Moore's tool is the best tested.
 - Vulnerable elderly: VES 13
 - Michigan Choice
 - EASY Care instrument
 - *Alternative assessments:*
 - Minimum Data Set (MDS), a comprehensive shortened geriatric assessment instrument, The incidence of geriatric problems increases sharply after 70 in cancer patients, we recommend screening for them beyond that age. This should be considered a soft limit.
- One of the screening tools mentioned above can be used. If the screening is positive, it should be followed by a more complete geriatric evaluation (Minimum Data Set or more).
- As older patients, especially the frail, vulnerable, and disabled patients, require more assistance and support, oncologists must be aware of the available resources and activate the process.

- **Fragilidad**
- Sin definición única
 - Situación de especial **vulnerabilidad** asociada a la edad, que se caracteriza por la disminución de la capacidad de respuesta a distintas situaciones de estrés.
- Tres grupos de pacientes:
 - 1) pacientes **aptos** (fit patients),
 - aparentemente más jóvenes que pacientes de su misma edad biológica, asimilables de algún modo a los pacientes jóvenes con ausencia de comorbilidades o muy leves en todo caso, sin limitaciones en las actividades diarias ni dependencia funcional, y candidatos a formas estándar de tratamiento;
 - 2) pacientes en situación **intermedia** (vulnerable patients),
 - comprometidos biológica o médicamente, con presencia significativa de comorbilidades, y limitaciones reversibles para las actividades de la vida diaria o con dependencias funcionales, incapaces de tolerar formas agresivas de tratamiento, y candidatos a tratamientos personalizados;
 - 3) pacientes frágiles (**frail** patients),
 - más viejos biológicamente, con comorbilidades severas, restricciones irreversibles para las actividades de la vida diaria, y en los que únicamente son posibles las medidas de soporte y paliación, ya que cualquier otro tipo de tratamiento conduciría a un mayor deterioro.

- Definición de Fragilidad:
 - Síndrome clínico en el que tres o más de los siguientes criterios estaban presentes:
 - Pérdida de peso no intencional (10 lbs en el año previo)
 - Cansancio
 - Debilidad (test de fuerza)
 - Lentitud en test de marcha
 - Baja actividad física

- El síndrome de fragilidad es predictivo de:
 - caídas
 - deterioro de la movilidad
 - pérdida de independencia de AVD
 - hospitalización
 - muerte

Criteria Used to Define Frailty

- **Weight loss:** “In the last year, have you lost more than 10 pounds unintentionally (i.e., not due to dieting or exercise)?” If yes, then frail for weight loss criterion. At follow-up, weight loss was calculated as: $(\text{Weight in previous year} - \text{current measured weight}) / (\text{weight in previous year}) = K$. If $K \geq 0.05$ and the subject does not report that he/she was trying to lose weight (i.e., unintentional weight loss of at least 5% of previous year’s body weight), then frail for weight loss = Yes.
- **Exhaustion:** Using the CES–D Depression Scale, the following two statements are read. (a) I felt that everything I did was an effort; (b) I could not get going. The question is asked “How often in the last week did you feel this way?” 0 = rarely or none of the time (<1 day), 1 = some or a little of the time (1–2 days), 2 = a moderate amount of the time (3–4 days), or 3 = most of the time. Subjects answering “2” or “3” to either of these questions are categorized as frail by the exhaustion criterion.
- **Physical Activity:** Based on the short version of the Minnesota Leisure Time Activity questionnaire, asking about walking, chores (moderately strenuous), mowing the lawn, raking, gardening, hiking, jogging, biking, exercise cycling, dancing, aerobics, bowling, golf, singles tennis, doubles tennis, racquetball, calisthenics, swimming. Kcals per week expended are calculated using standardized algorithm. This variable is stratified by gender.
Men: Those with Kcals of physical activity per week <383 are frail.
Women: Those with Kcals per week <270 are frail.

- **Walk Time**, stratified by gender and height (gender-specific cutoff a medium height).

Men

Height \leq 173 cm

Height > 173 cm

Women

Height \leq 159 cm

Height > 159 cm

Cutoff for Time to Walk 15 feet criterion for frailty

\geq 7 seconds

\geq 6 seconds

\geq 7 seconds

\geq 6 seconds

- **Grip Strength**, stratified by gender and body mass index (BMI) quartiles:

Men

BMI \leq 24

BMI 24.1–26

BMI 26.1–28

BMI > 28

Women

BMI \leq 23

BMI 23.1–26

BMI 26.1–29

BMI > 29

Cutoff for grip strength (Kg) criterion for frailty

\leq 29

\leq 30

\leq 30

\leq 32

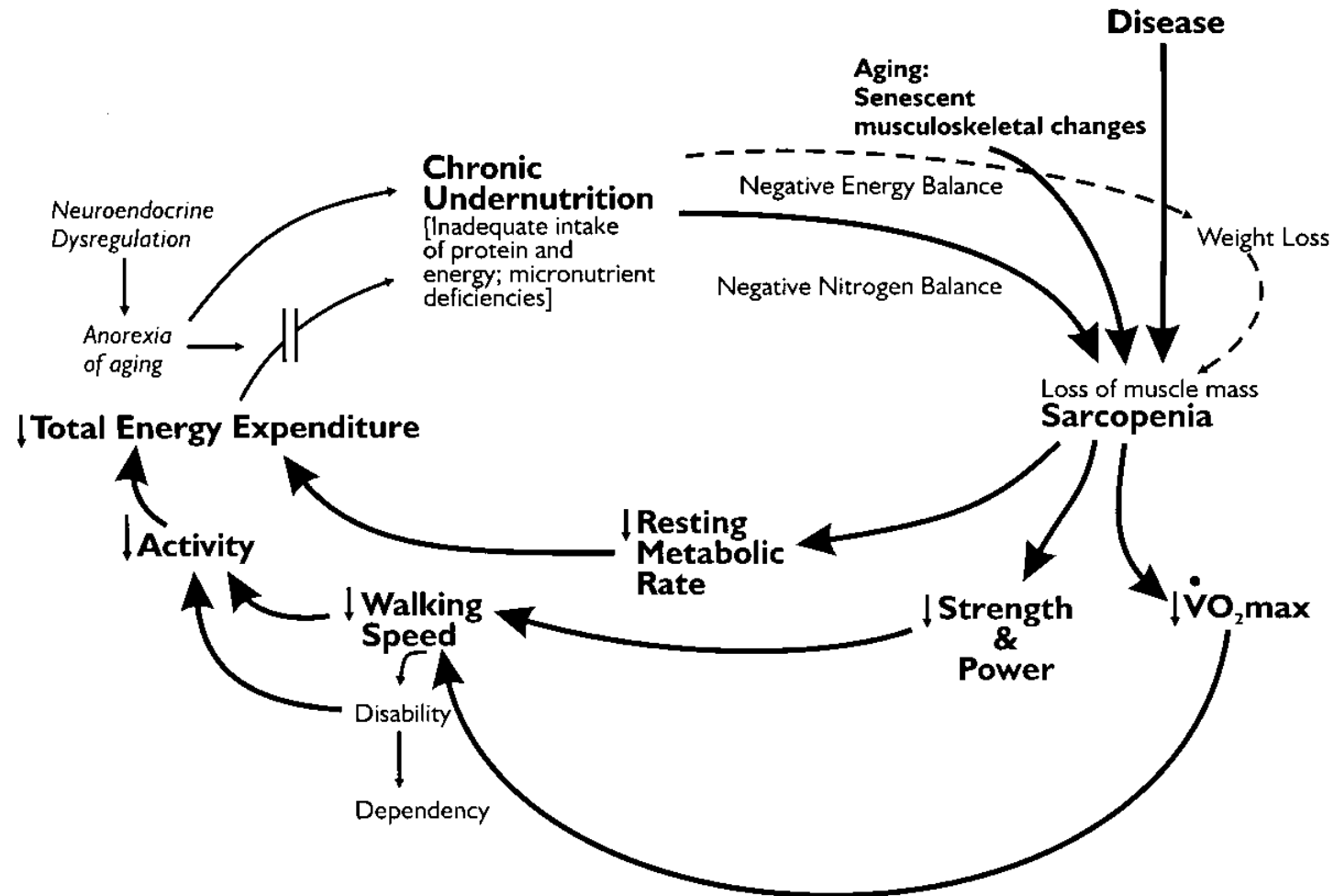
\leq 17

\leq 17.3

\leq 18

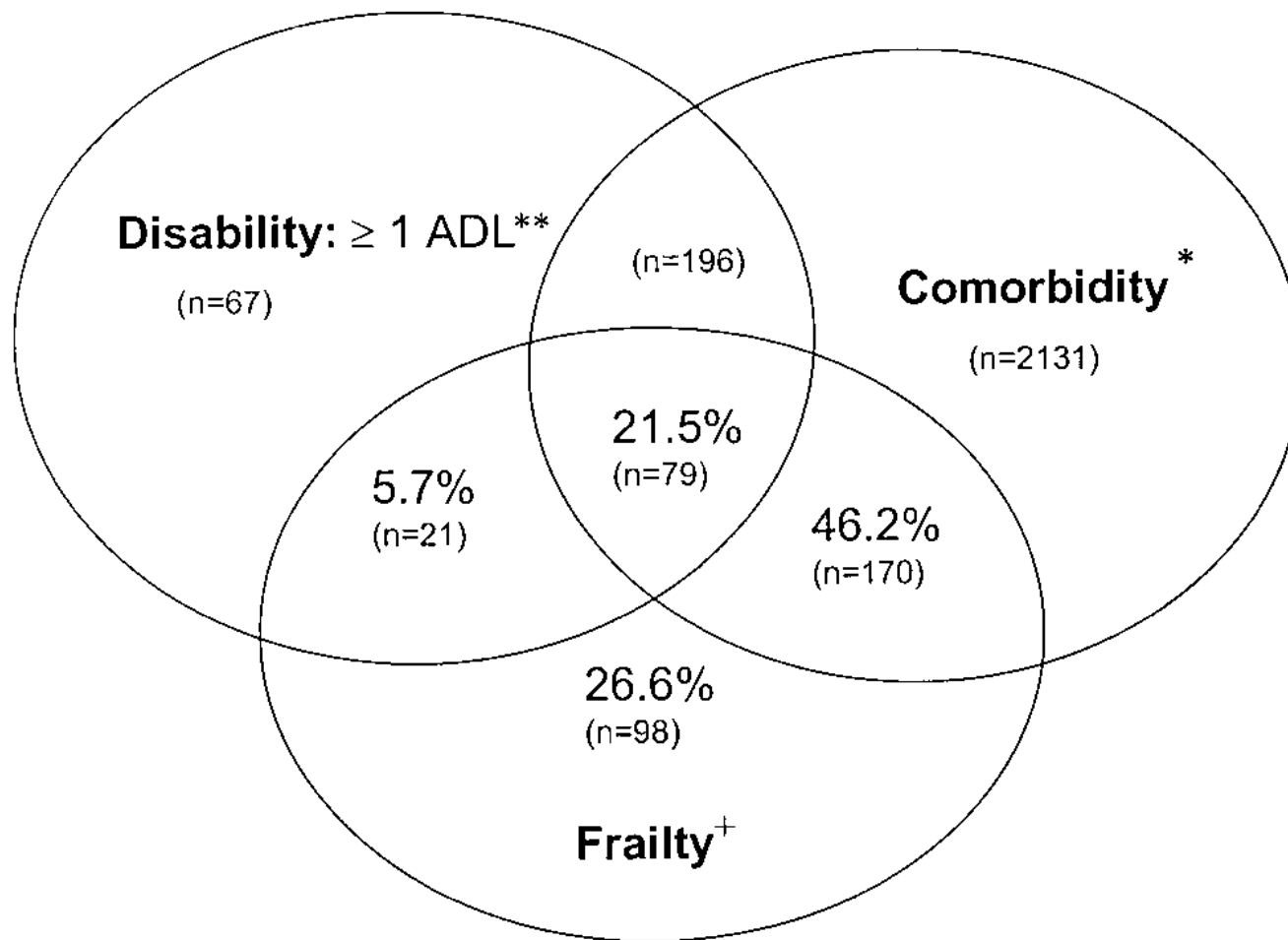
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Frailty in Older Adults: Evidence for a Phenotype

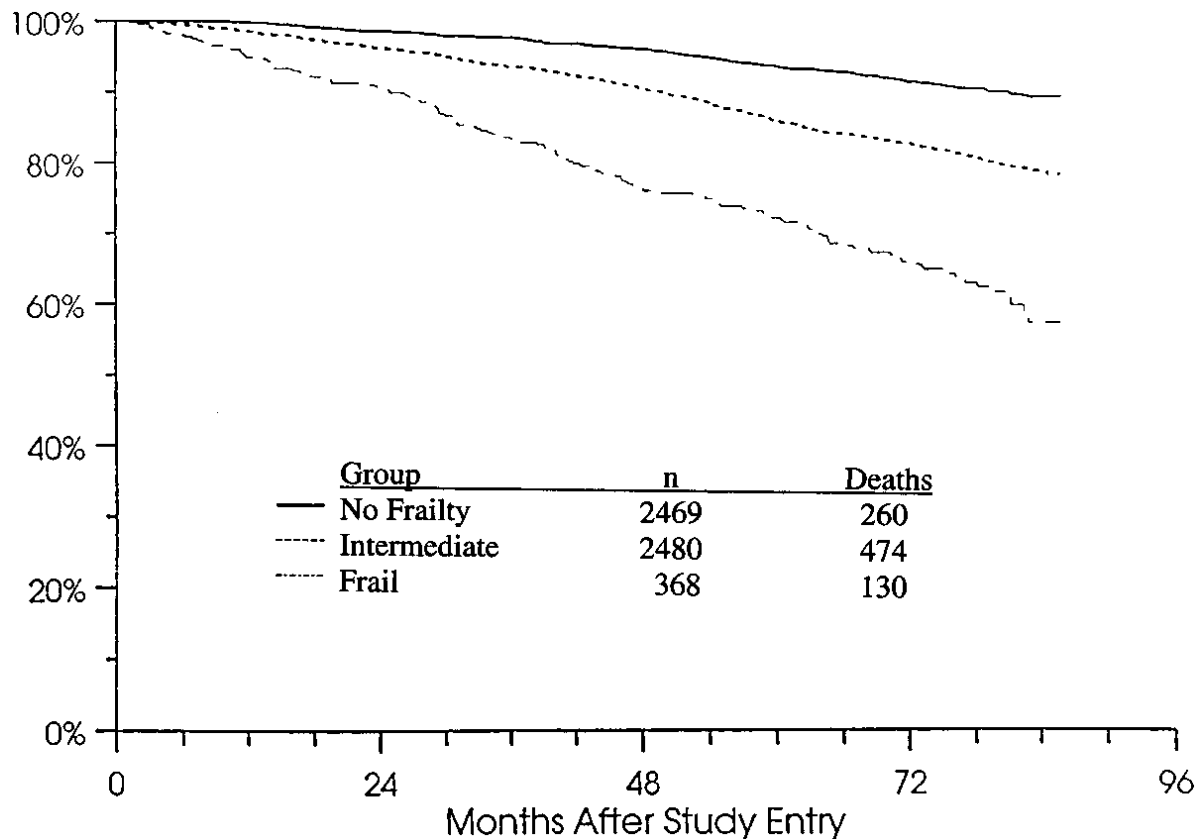


Cycle of frailty hypothesized as consistent with demonstrated pairwise associations and clinical signs and symptoms of frailty.

Frailty in Older Adults: Evidence for a Phenotype



Frailty in Older Adults: Evidence for a Phenotype



Survival curve estimates (unadjusted) over 72 months of follow-up by frailty status at baseline: **Frail** (3 or more criteria present); **Intermediate** (1 or 2 criteria present); **Not frail** (0 criteria present).

- La realización de una valoración por CGA es muy laboriosa
- ¿Es posible comprimir los tests con similar valor predictivo?
 - Escalas abreviadas de *screening*
 - Instrumentos mixtos y simplificados
 - Pruebas surrogadas

VES-13

1. Age _____

SCORE: 1 POINT FOR AGE 75-84
3 POINTS FOR AGE ≥ 85

2. In general, compared to other people your age, would you say that your health is:

- Poor,* (1 POINT)
- Fair,* (1 POINT)
- Good,
- Very good, or
- Excellent

SCORE: 1 POINT FOR FAIR or POOR

3. How much difficulty, on average, do you have with the following physical activities:

	No Difficulty	A little Difficulty	Some Difficulty	A Lot of Difficulty	Unable to do
a. stooping, crouching or kneeling?.....	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/> *	<input type="checkbox"/> *
b. lifting, or carrying objects as heavy as 10 pounds?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/> *	<input type="checkbox"/> *
c. reaching or extending arms above shoulder level?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/> *	<input type="checkbox"/> *
d. writing, or handling and grasping small objects?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/> *	<input type="checkbox"/> *
e. walking a quarter of a mile?.....	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/> *	<input type="checkbox"/> *
f. heavy housework such as scrubbing floors or washing windows?.....	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/> *	<input type="checkbox"/> *

SCORE: 1 POINT FOR EACH * RESPONSE
IN Q3a THROUGH f. MAXIMUM OF 2
POINTS.

4. Because of your health or a physical condition, do you have any difficulty:

- a. shopping for personal items (like toilet items or medicines)?
 - YES → Do you get help with shopping? YES * NO
 - NO
 - DON'T DO → Is that because of your health? YES * NO
- b. managing money (like keeping track of expenses or paying bills)?
 - YES → Do you get help with managing money? YES * NO
 - NO
 - DON'T DO → Is that because of your health? YES * NO

Continued

c. walking across the room? USE OF CANE OR WALKER IS OK.

- YES → Do you get help with walking? YES * NO
- NO
- DON'T DO → Is that because of your health? YES * NO

d. doing light housework (like washing dishes, straightening up, or light cleaning)?

- YES → Do you get help with light housework? YES * NO
- NO
- DON'T DO → Is that because of your health? YES * NO

e. bathing or showering?

- YES → Do you get help with bathing or showering? YES * NO
- NO
- DON'T DO → Is that because of your health? YES * NO

SCORE: 4 POINTS FOR ONE OR MORE *
RESPONSES IN Q4a THROUGH Q4e

Table 4. Sensitivity and Specificity of All Items Versus CGA

Scale	Sensitivity			Specificity			Accuracy		
	No. (n = 134)	%	95% CI (%)	No. (n = 285)	%	95% CI (%)	No. (N = 419)	%	95% CI (%)
VES-13	117	87.3	80.5 to 92.4	177	62.1	56.2 to 67.8	294	70.2	65.5 to 74.5
ADLs	60	44.8	36.2 to 53.6	277	97.2	94.5 to 98.8	337	80.4	76.3 to 84.1
IADLs	61	45.5	36.9 to 54.3	279	97.9	95.5 to 99.2	340	81.1	77.1 to 84.8
ADLs/IADLs	85	63.4	54.7 to 71.6	276	96.8	94.1 to 98.5	361	86.2	82.5 to 89.3
ADLs/IADLs*	102	76.1	68.0 to 83.1	283	99.3	97.5 to 99.9	385	91.9	88.8 to 94.3

Abbreviations: CGA, comprehensive geriatric assessment; VES-13, Vulnerable Elders Survey-13; ADLs, activities of daily living; IADLs, instrumental activities of daily living.
*Corrected for age > 85 years.

Table 5. Correlations Between VES-13 and CGA Items

Scale	Correlation (r)		
	VES-13	ADLs/IADLs	CGA
MMSE	-0.3	-0.2	-0.4
MNA	-0.1	-0.1	-0.1
CIRS-G score	0.2	0.1	0.1
CIRS-G index	0.1	0.1	0.1
DRUGS	0.3	0.2	0.2
VES-13	—	0.6	0.4
ADLs/IADLs	0.5*	—	0.5
CGA	0.4	0.8	—

Abbreviations: VES-13, Vulnerable Elders Survey-13; CGA, comprehensive geriatric assessment; ADLs, activities of daily living; IADLs, instrumental activities of daily living; MMSE, Mini-Mental State Evaluation; MNA, Mini-Nutritional Assessment; CIRS-G, Cumulative Illness Rating Scale for Geriatrics; DRUGS, No. of medications.

*Coefficient is 0.6 for ADLs/IADLs corrected for age.

In conclusion, on the basis of our data, VES-13 is highly sensitive and highly predictive in identifying impaired functional status but has a weak correlation with comorbidity scales. Although it may not be considered a full substitute for CGA, it can be seen as a useful preliminary means of assessing older patients with cancer and selecting those requiring a full geriatric evaluation.

Mini geriatric assessment, 8 simplified modules.

Module	Yes	No
1. Demential syndrom screening Says to the patient the 3 following words: cigar, flower, door. Ask to repeat immediately and few minutes later. Forgetting:	<input type="checkbox"/>	<input type="checkbox"/>
2. Depression screening Ask to the patient: « Do you feel sad or depressed? ».	<input type="checkbox"/>	<input type="checkbox"/>
3. Screening of dependence Is patient able to realise himself following actions? Drive or use public transports Cooking Shopping Make up one's accounts Phone calling Self treatment administration	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>
4. Malnutrition screening (1) Weightkg Weight 3 months agokg Measure heightcm BMI (Weight / size ²)	<input type="checkbox"/>	<input type="checkbox"/>
5. Co-morbidities screening Presence of following pathologies: Congestive heart failure Coronary artery disease Valvular heart disease Chronic lung disease Cerebrovascular disease Peripheral neuropathy Chronic renal insufficiency Hypertension Diabetes Coexisting malignancy Collagen vascular disease Incapacitating arthritis	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>
6. Polymedication screening (2) 1 _____ 2 _____ 3 _____ 4 _____ 5 _____ 6 _____ 7 _____ 8 _____ 9 _____ 10 _____ Review number and type of medication: Total number by therapeutic class: Psychotrope: ____ Cardiovascular (included antiagregant): ____ Anticoagulant: ____ Other: ____	<input type="checkbox"/>	<input type="checkbox"/>
7. Evaluation of the environment Do the patient have following trouble: Trouble with stairs inside and outside the house Stumble often Is there anybody able to help the patient in case of emergency Identification of the caregiver (name, phone):	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>
8. Biology (3) Hemoglobin:g / 100 ml Creatinine:µmol / l Creatinin clearance:ml / min	<input type="checkbox"/> <input type="checkbox"/>	<input type="checkbox"/> <input type="checkbox"/>

Threshold used: (1) loss of more than 5% of weight and/or BMI < 23; (2) 7 medications or more; (3) Hb < 10 g/dl, clearance < 50 ml/min.

Threshold of the comprehensive geriatric assessment.

Screening	Test	Threshold
Mental status	MMSE	≤24
Depression	GDS simplified	≥1
Dependence	ADL	<6
	IADL	<100% of total applicable
Nutrition	MNA	≤23.5
Co-morbidities	CIRS-G	System ≥ 3
Polymedication	Collected	1 anticoagulant or 2 cardiovascular or 2 psychotropic medication or ≥ 10 medications
Environment	Monopodal support Story of fall Social service advice	Social intervention
Biology	Hemoglobin Creatinin clearance	(<10 g/dl) (<50 ml/min)

A mini geriatric assessment helps treatment decision in elderly patients with digestive cancer. A pilot study

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^c Service de Gastroentérologie, Hôpital Avicenne, APHP, 125 rue de Stalingrad, 93000 Bobigny, France

Results: 21 patients over 75 years treated for different digestive cancers were enrolled. The treatments recommended by the cancer multi-disciplinary team meeting after the GMA were: standard treatments in 9 (41%); modified in 10 (47%) and best supportive care in 2 (12%) patients. CGA led to an adaptation of the non-oncological treatment in 15 (72%) and of the social care in 8 (38%) patients, but never modified the oncological strategy.

- Batería de **8 instrumentos** de medida geriátricos
 - QoL, fragilidad, AVD, depresión,
 - Estado mental, movilidad, comorbilidad, PS
- Impacto pronóstico en OS en pacientes >60 años con SMD/LMA
 - BSC
 - Decitabina
 - QT
- 30 minutos
- Mejorías medibles con tratamiento:
 - Fatiga
 - Disnea
 - Déficits funcionales

P.11

Multidimensional geriatric assessment in elderly patients with MDS/AML

B. Deschler*, G. Ihorst, C. Perinchery, J. Hummel, B. Rüter, R. Claus, M. Lübbert. *University of Freiburg, Medical Center, Dept. of Hematology-Oncology, Freiburg, Germany*

blood

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Geriatric assessment predicts survival for older adults receiving induction chemotherapy for acute myelogenous leukemia

Heidi D. Klepin, Ann M. Geiger, Janet A. Tooze, Stephen B. Kritchevsky, Jeff D. Williamson, Timothy S. Pardee, Leslie R. Ellis and Bayard L. Powell

- Elementos procedentes de escalas e instrumentos conocidos
- Función cognitiva
 - Modified Mini Mental State (3MS)
- Depresión
 - 20 items-Center for Epidemiologic Studies Depression Scale (CES-D)
 - Distress Thermometer (VAS)
- Función Física
 - *Self-reported*: Pepper Assessment Tool for Disability (PAT-D)
 - Subescalas para movilidad, AIVD, ABVD
 - Medidas objetivas:
 - Hand Grip strenght
 - Short Physical Performance Battery (SPPB)
- Comorbilidad
 - HTC-CI

Table 2. Baseline GA measure scores among older adults initiating induction chemotherapy for AML (N = 74)

GA scores	Median (25th, 75th)	% Impaired
Cognition		
3MS (range 0-100, impairment < 77)	85.0 (75.0, 91.0)	28.8
Psychological function		
CES-D (range 0-60, impairment > 16)	11.0 (4.0, 21.0)	39.7
DT (range 0-10, impairment ≥ 4)	5.0 (2.0, 8.0)	58.9
PF		
PAT-D* (range 1-5, impairment > 1) at the time of treatment	1.4 (1.0, 1.8)	72.4
ADL subscale	1.0 (1.0, 1.4)	50.0
IADL subscale	1.0 (1.0, 1.7)	40.5
Mobility subscale	2.0 (1.0, 3.0)	68.9
PAT-D* 6-mo recall	1.1 (1.0, 1.3)	
ADL subscale	1.0 (1.0, 1.0)	23.3
IADL subscale	1.0 (1.0, 1.0)	20.6
Mobility subscale	1.0 (1.0, 1.7)	41.1
SPPB (range 0-12, impairment < 9)	8.5 (3.0, 10.0)	50.0
Grip strength (kg)†		
Male	38.0 (32.0, 44.0)	
Female	24.0 (22.0, 28.0)	
Comorbidity		
HCT-CI (impairment > 1)	1.0 (0.0, 3.0)	41.9

For 3MS, SPPB, and grip strength, a higher score reflects better function. For CES-D, DT, PAT-D, and HCT-CI, a higher score reflects worse function.

ADL, Activities of Daily Living; DT, Distress Thermometer; HCT-CI, Hematopoietic Stem Cell Transplantation Comorbidity Index; IADL, Instrumental Activities of Daily Living; PAT-D, Pepper Assessment Tool for Disability.

*Results based on subjects with calculable survey scores (reported in Results section).

†Scores are based on 67 subjects who performed grip strength.

CGA predictivo de OS en LMA

Table 3. Association between clinical characteristics, baseline GA measures, and OS among older adults with AML (N = 73)

Baseline characteristics	Hazard ratio for mortality (95% CI)	
	Unadjusted	Adjusted*
Clinical and demographic characteristics		
Age (per 10-y change)	1.1 (0.7-1.7)	1.3 (0.8-2.0)
Education (reference < high school)		
High school	0.9 (0.4-2.0)	0.9 (0.3-2.6)
College	0.8 (0.4-1.5)	0.8 (0.3-1.8)
ECOG score (continuous)	1.5 (0.9-2.4)	1.2 (0.7-1.9)
Hemoglobin (continuous)	0.8 (0.7-1.0)	0.7 (0.6-0.9)
LDH (≥ 600)	0.5 (0.2-1.4)	0.6 (0.2-1.5)
White blood cell count ($\geq 25,000$)	0.8 (0.4-1.6)	1.3 (0.6-3.0)
Cytogenetic risk group (favorable/intermediate)	0.5 (0.3-0.8)	0.3 (0.2-0.7)
Prior MDS (not present)	0.5 (0.3-0.8)	0.4 (0.2-0.7)
GA measures		
Cognitive impairment (3MS < 77)	2.4 (1.3-4.4)	2.5 (1.2-5.5)
Depressive symptoms (CES-D score ≥ 16)	1.4 (0.8-2.5)	1.0 (0.5-2.0)
Distress (score < 4)	1.2 (0.6-2.1)	1.0 (0.5-1.8)
IADL impairment (any at the time of treatment)	1.3 (0.7-2.2)	0.8 (0.4-1.6)
ADL impairment (any at the time of treatment)	1.3 (0.7-2.1)	1.1 (0.5-2.1)
Mobility impairment (any at the time of treatment)	1.4 (0.7-2.6)	1.0 (0.5-2.1)
Impaired physical performance (SPPB < 9)	1.9 (1.1-3.4)	2.2 (1.1-4.6)
Comorbidity burden (HCT-CI > 1)	1.5 (0.9-2.7)	1.2 (0.7-2.2)

One subject with missing cytogenetic risk group data was excluded.
 ADL, activities of daily living; IADL, instrumental activities of daily living; LDH, lactate dehydrogenase.
 *Adjusted model includes age, gender, ECOG performance status, cytogenetic risk group, prior MDS, and hemoglobin.

- Limitaciones por sesgo de selección, pacientes *aptos* para QT, tamaño muestral y unicentricidad
- Duración: 30 minutos, no práctica
- La comorbilidad NO predijo OS de forma independiente
- F Pronósticos identificados: Deterioro **cognitivo** y Deterioro de **función física**

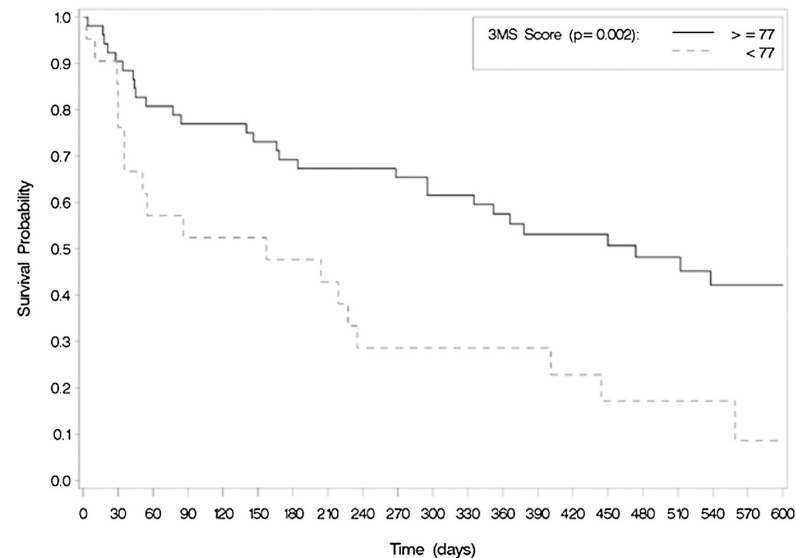


Figure 2. Baseline cognitive function is associated with worse OS among older adults treated for AML (N = 73). Median survival differed using log-rank testing.

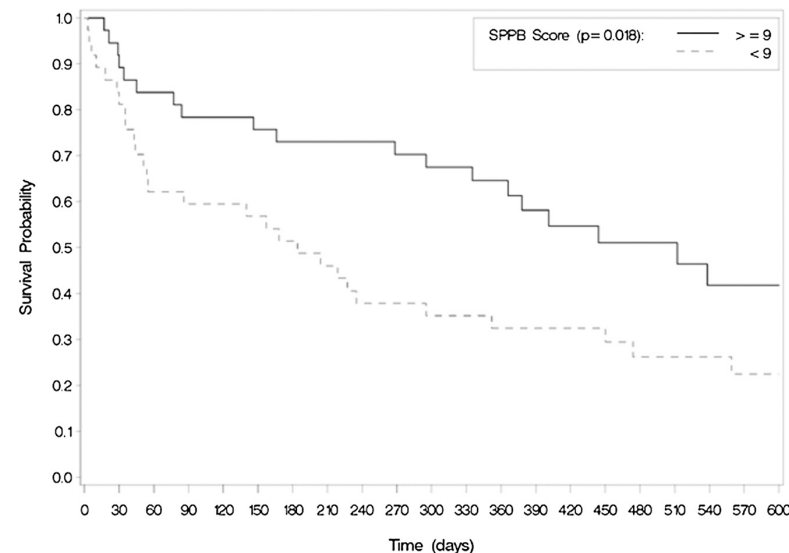
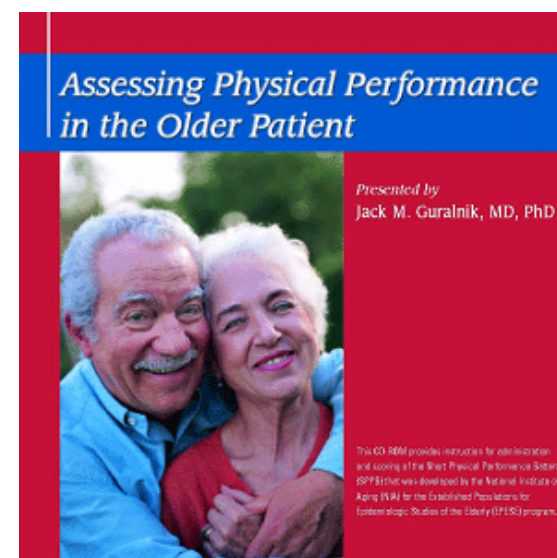


Figure 3. Impaired physical performance is associated with worse OS among older adults treated for AML (N = 74). Median survival differed using log-rank testing.

- *Hand grip strenght*¹:
 - Dinamómetro manual (Kg); medición en ambas manos
 - Predictor en población geriátrica de:
 - Mortalidad
 - Limitaciones funcionales
 - Discapacidad

- SPPB (*short physical performance battery*)²:
 - Función física de miembros inferiores
 - Test de Marcha
 - Levantamiento de silla repetidos
 - Test de equilibrio
 - Predictor en población geriátrica de:
 - Discapacidad futura
 - Hospitalización
 - Mortalidad



1. Rantanen T, J Am Geriatr Soc, 2003
2. Guralnik JM, J Gerontol, 1994

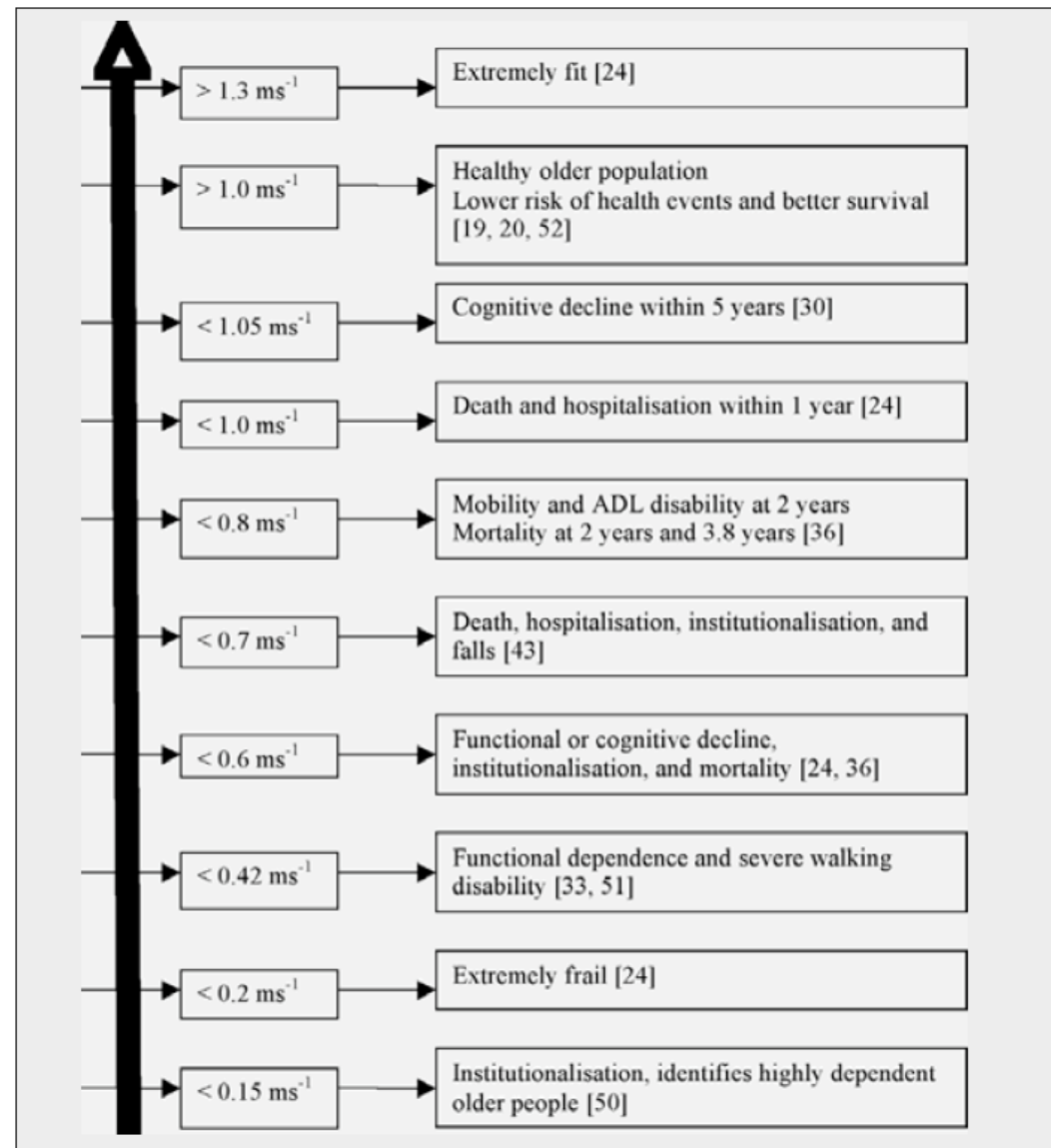
- Herramienta **simple**, unidimensional
 - Sustitutiva de evaluaciones multidimensionales laboriosas
- **Condiciones**
 - Velocidad de marcha normal
 - Cortas distancias
 - Los participantes deben ser autónomos
- Traduce/integra **alteraciones subclínicas** del estado de salud

Prueba de la marcha (*Gait speed*)

- Predictor de:
 - Disfunción motora
 - ABVD
 - Deterioro cognitivo
 - MMSE
 - Mortalidad
 - “cut speed” $<1\text{ms}^{-1}$
 - Riesgo de caídas
 - Institucionalización

Figure 2

Cut-points of gait speed at usual pace and risk of adverse outcomes found in literature



Geriatric Assessment in Hematology



Validation of a comprehensive health status assessment scale in older patients (≥ 65 years) with hematological malignances.



- **Background:**
- Cancer affects mainly older people.
- The National Comprehensive Cancer Network and the International Society of Geriatric Oncology have recommended that some form of geriatric assessment should be conducted to help oncologists to:
 - determine the best treatment for older patients,
 - to identify current health problems
 - to guide interventions to reduce adverse outcomes
 - and to optimize the functional status.
- Currently, the main tool for assessing older patients is a comprehensive geriatric assessment (CGA), although its complexity and duration may hinder its regular use in daily practice as a tool for clinical decision making.
- Several attempts have been made to assess comorbidities in the specific field of mielodysplasia, but they focused mainly on organic damage rather than global assessment.

Validation of a comprehensive health status assessment scale in older patients (≥ 65 years) with hematological malignancies.



- **Aims:**
- To develop and validate an assessment scale (called *Geriatric Assessment in Haematology*, GAH) for use in older patients with hematological malignancies (MDS, AML, MM & CLL).
- GAH integrates the essential dimensions of geriatric assessment
- But is easier to apply, accessible, does not interfere with daily clinical practice and could be useful in clinical decision making.

Validation of a comprehensive health status assessment scale in older patients (≥ 65 years) with hematological malignances.



- **Methods:**
- After item-pool generation, stakeholder consultation and content validation, a brief scale with selected items of several domains has been created.
- Feasibility was confirmed in 83 hematological patients in a previous exploratory experience.
- A multicenter, observational, prospective study has been followed in 18 hospitals in Spain, expecting to enroll 360 treatment-naïve, newly diagnosed patients with MDS or AML, MM and CLL.
- The scale validation process integrates:
 - analysis of criterion validity, concept validity, internal reliability, test-retest reliability, and evaluation of intraclass correlation coefficient (ICC) and factor analysis.
- After psychometric validation phase, further studies will be carried out in order to evaluate its clinical use for prognosis and clinical decision making.

Validation of a comprehensive health status assessment scale in older patients (≥ 65 years) with hematological malignances.



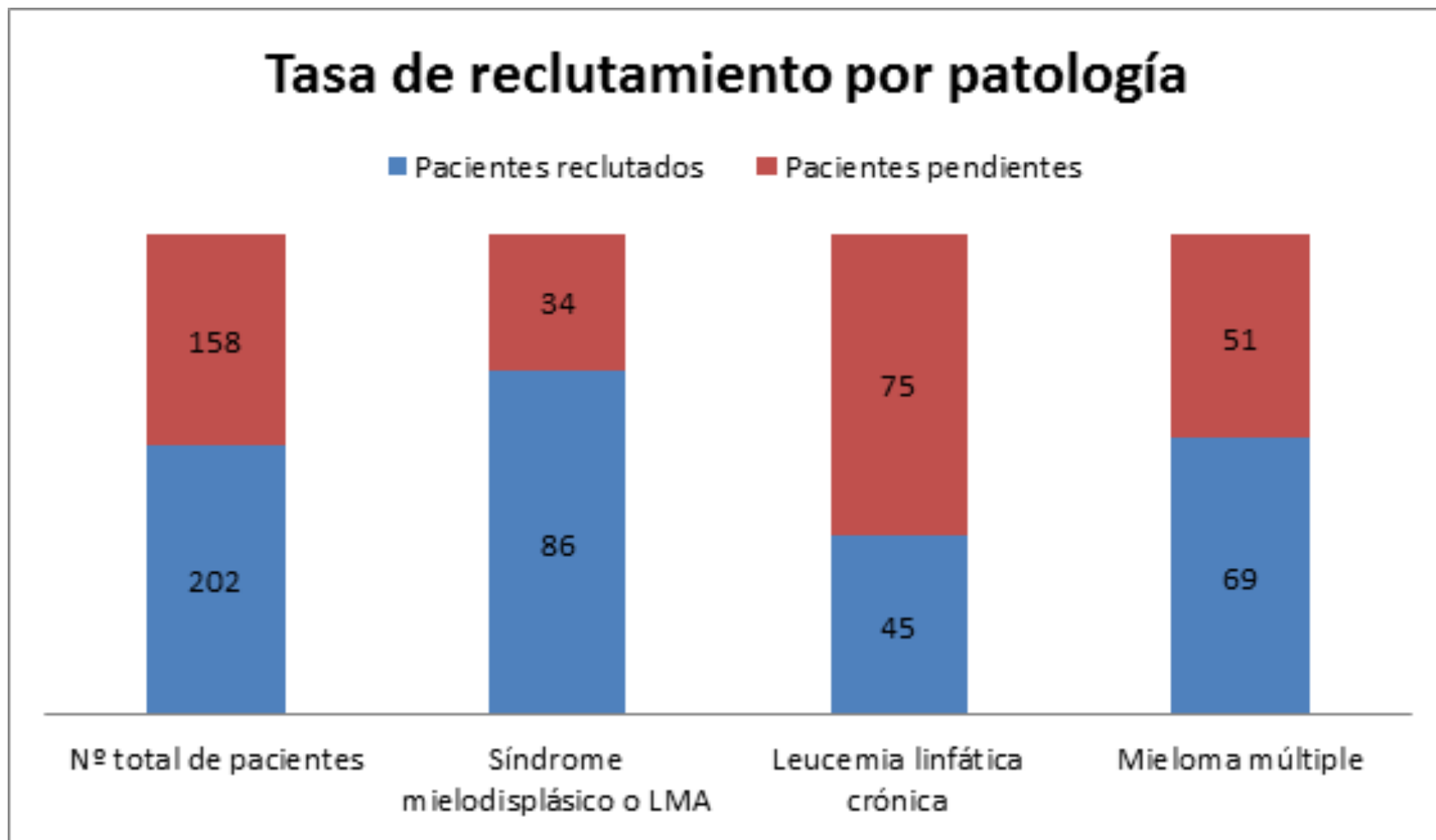
- **Results:**
- 75 patients fulfilling inclusion criteria have been enrolled in the study, 51.5% men, median age at diagnosis 76 years (70-80). According to diagnosis, 44% of patients had MDS or AML, 36% had MM and 20% had CLL.
- Median time for filling in the questionnaire was 12 (10-15) min.
- In the initial testing, GAH showed satisfactory test-retest reliability.
- ICC was statistically significant for each dimension, being greater than 0.66 for 6 of the 8 dimensions ($p < 0.05$).
- Factor analysis will be conducted when recruitment is completed.
- Some differences have been found in subjects with different diseases, although no statistical analysis has been made yet. Based on rough proportions, GAH shows a great potential in terms of sensitivity, specificity and reproducibility between trained observers.

Validation of a comprehensive health status assessment scale in older patients (≥ 65 years) with hematological malignances.

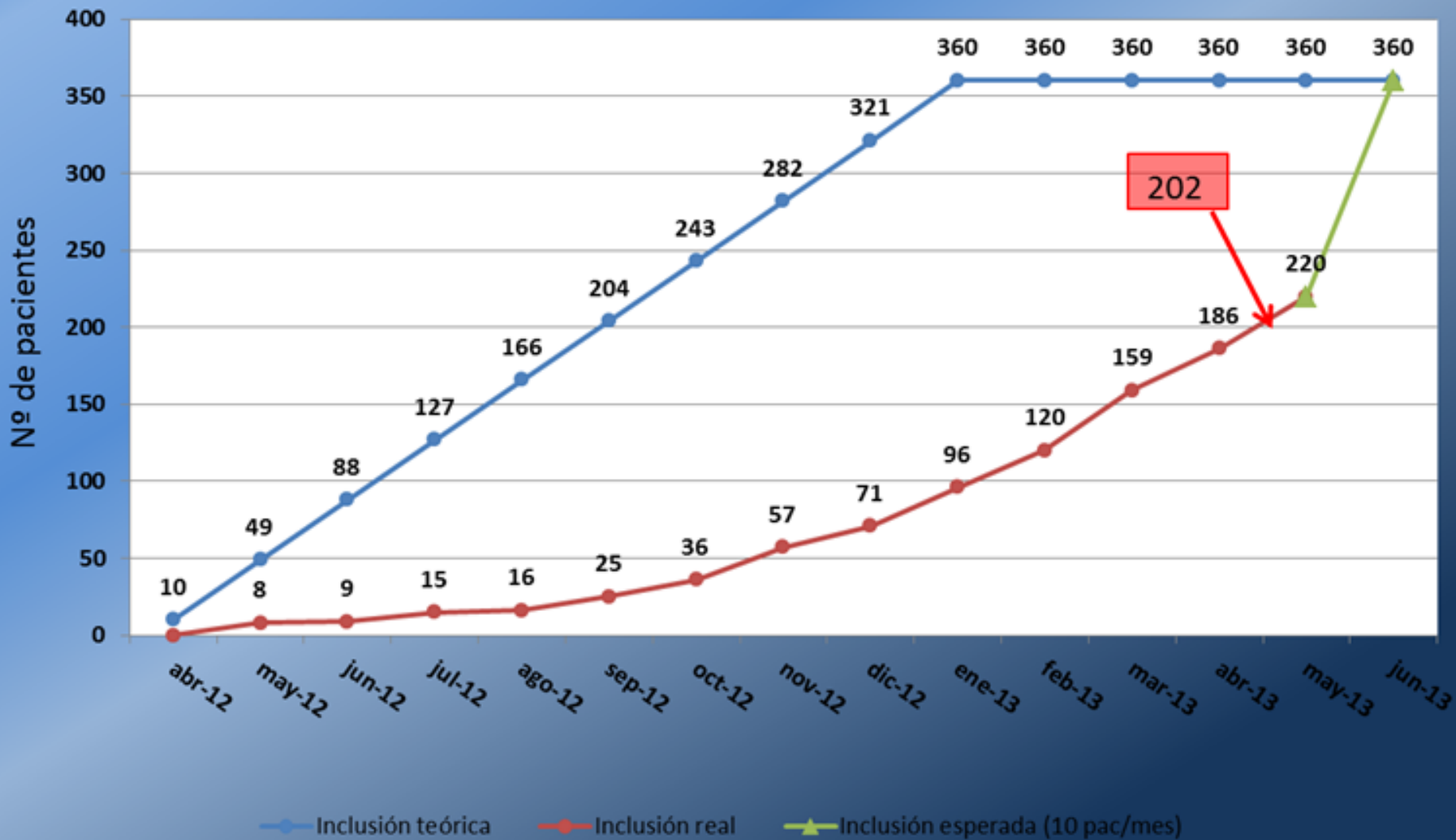


- **Summary / Conclusion:**
- To our knowledge, this is one the first study performed to develop and validate a comprehensive health status assessment in older patients with hematological malignances, which could be used in clinical practice to help haematologists to improve decision making processes in older patients

Validation of a comprehensive health status assessment scale in older patients (≥ 65 years) with hematological malignances.



Reclutamiento





Critical Reviews in Oncology/Hematology 46 (2003) 127–137

 Critical Reviews in
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The frailty syndrome: a critical issue in geriatric oncology

 Luigi Ferrucci^{a,b,*}, Jack M. Guralnik^c, Chiara Cavazzini^b, Stefania Bandinelli^b,
 Fulvio Lauretani^b, Benedetta Bartali^b, Lazzaro Repetto^d, Dan L. Longo^a
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Critical Reviews in Oncology/Hematology 48 (2003) 227–237

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The effectiveness and costs of comprehensive geriatric evaluation and management

Darryl Wieland^{a,b,*}^a Division of Geriatric Medicine, University of South Carolina School of Medicine, 9 Medical Park, #630, Columbia, SC 29204, USA^b Division of Geriatrics Services, Palmetto Health Richland, Columbia, SC, USA

Critical Reviews in Oncology/Hematology 77 (2011) 63–69

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A mini geriatric assessment helps treatment decision in elderly patients with digestive cancer. A pilot study

 Thomas Aparicio^{a,c,*}, Laurence Girard^b, Nadia Bouarioua^a, Claire Patry^b,
 Sylvie Legrain^b, Jean Claude Soulié^a
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Critical Reviews in Oncology/Hematology 59 (2006) 205–210

 Critical Reviews in
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The abbreviated comprehensive geriatric assessment (aCGA) for use in the older cancer patient as a prescreen: Scoring and interpretation

 Janine A. Overcash^{a,*}, Jason Beckstead^{a,1}, Linda Moody^{a,b}, Martine Extermann^{b,2}, Sara Cobb^a
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Critical Reviews in Oncology/Hematology 74 (2010) 97–105

 CRITICAL REVIEWS IN
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Six independent domains are defined by geriatric assessment in elderly cancer patients[☆]

 R. Stauder^{a,*}, K. Moser^a, B. Holzner^b, B. Sperner-Unterwieser^b, G. Kemmler^b
^a Department of Internal Medicine V (Haematology and Oncology), Innsbruck Medical University, Anichstrasse 35, 6020 Innsbruck, Austria^b Department of Biological Psychiatry, Innsbruck Medical University, Austria

Critical Reviews in Oncology/Hematology 55 (2005) 241–252

 Critical Reviews in
**Oncology
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Use of comprehensive geriatric assessment in older cancer patients: Recommendations from the task force on CGA of the International Society of Geriatric Oncology (SIOG)

 Martine Extermann^{a,*}, Matti Aapro^b, Roberto Bernabei^c, Harvey Jay Cohen^d,
 Jean-Pierre Droz^e, Stuart Lichtman^f, Vincent Mor^g, Silvio Monfardini^h,
 Lazzaro Repettoⁱ, Liv Sørbye^j, Eva Topinkova^k

- Situación demográfica particular en las enfermedades hematológicas y concretamente en los SMD
- Valor pronóstico de la edad, pero gran heterogeneidad de fenotipos
- Es necesaria la discriminación basada en parámetros de comorbilidad, funcionalidad y discapacidad
 - Expectativa de vida y tolerancia a tratamientos
- Evaluación de pacientes ancianos basada en:
 - Necesidad de medir la fragilidad → Metodología cuantitativa
 - Perspectivas vitales y recursos disponibles
 - Decisión personalizada
- Instrumentos validados y utilizables en clínica y en investigación

CGA estándar

Minucioso

Lento

Especializado

Escalas abreviadas

GAH

otras

Surrogados

Test de marcha

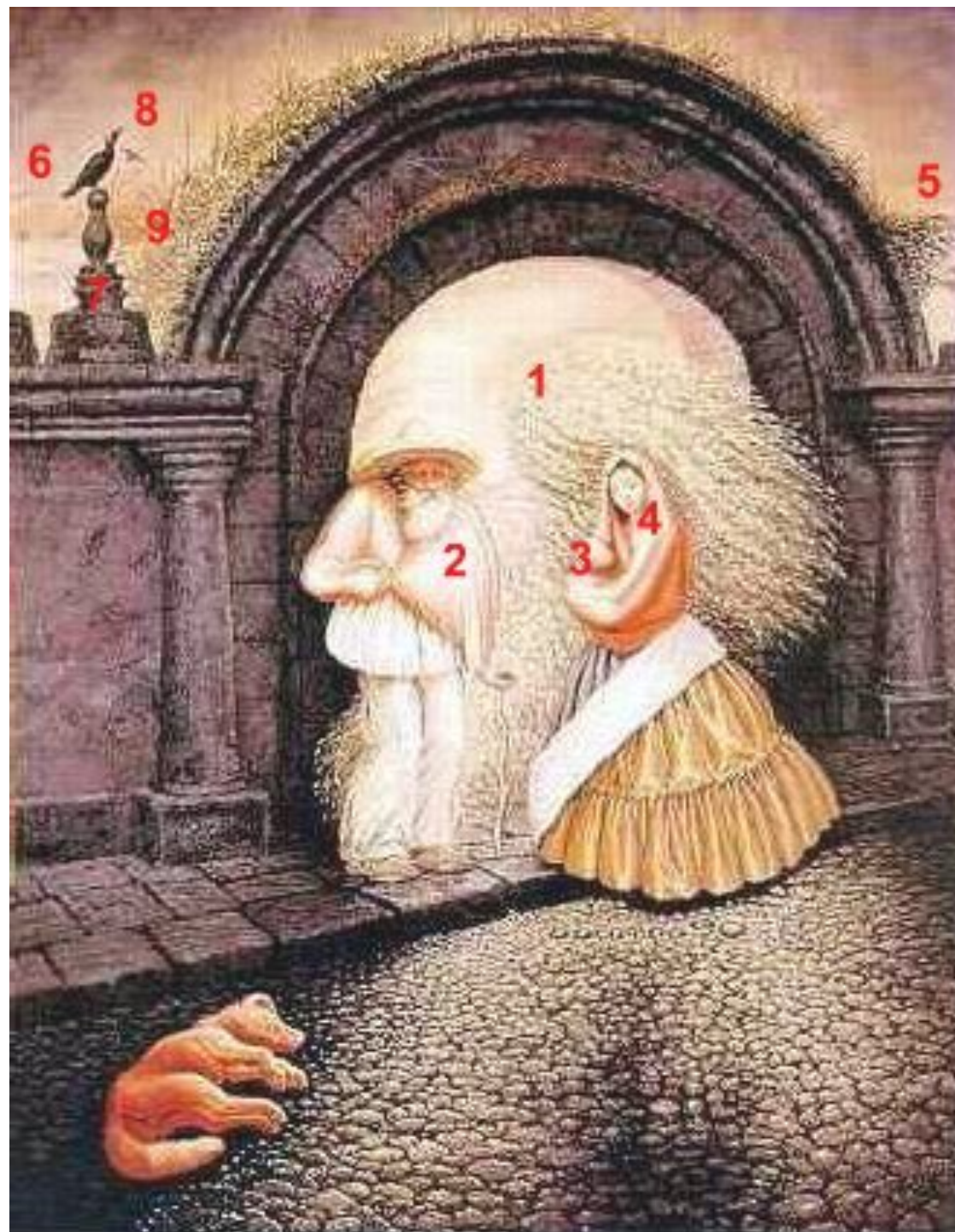
índices clásicos



El síndrome de Aeneas

Aeneas flees burning Troy with Anchises and his son, Federico Barocci, 1598

... las apariencias engañan



When I'm Sixty-Four

The Beatles

When I get older losing my hair,
Many years from now,
Will you still be sending me a valentine
Birthday greetings bottle of wine?

If I'd been out till quarter to three
Would you lock the door,
**Will you still need me, will you still feed me,
When I'm sixty-four?**

oo oo oo oo oo oo oo oooo
You'll be older too, (ah ah ah ah ah)
And if you say the word,
I could stay with you.

I could be handy mending a fuse
When your lights have gone.
You can knit a sweater by the fireside
Sunday mornings go for a ride.

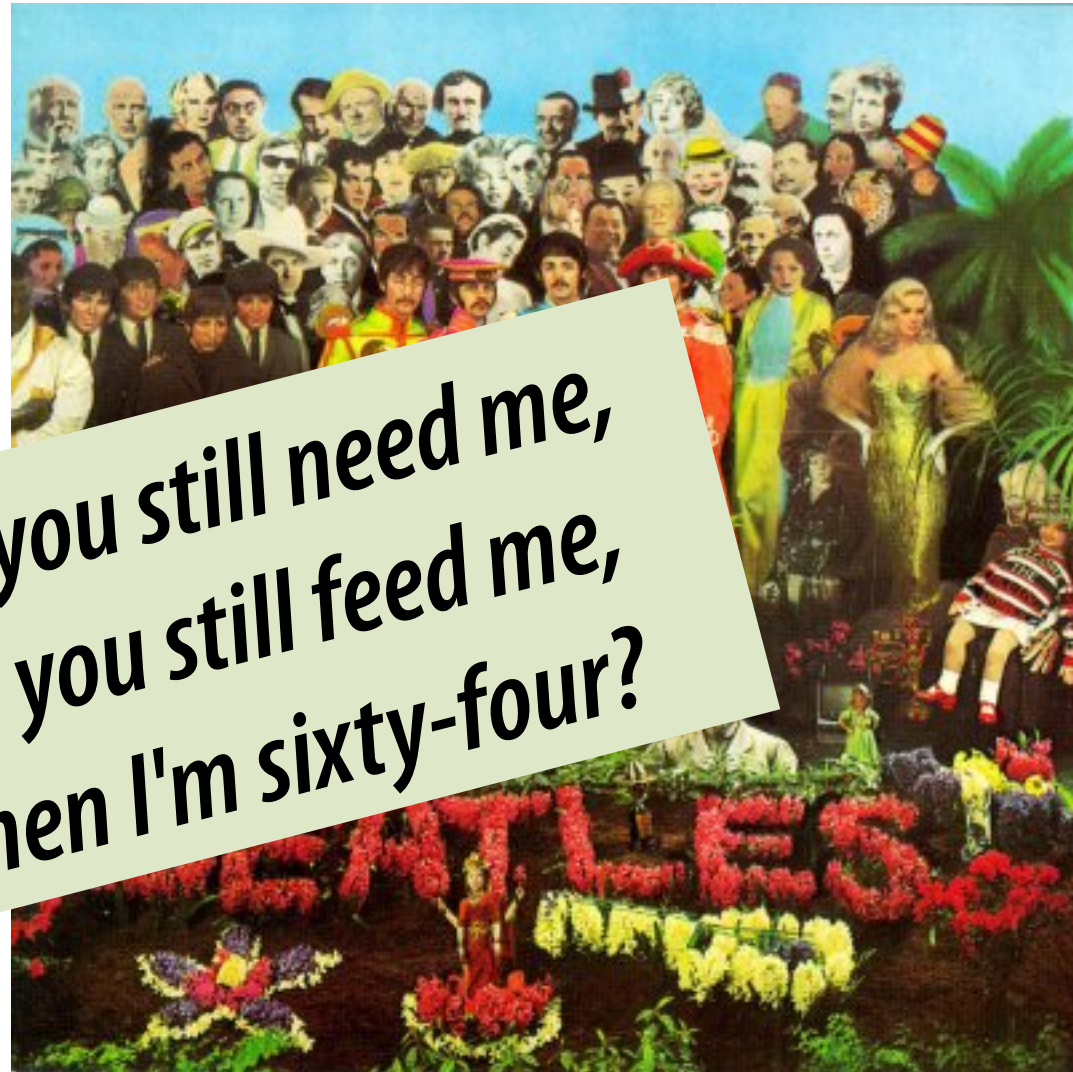
Doing the garden, digging the weeds,
Who could ask for more?
Will you still need me, will you still feed me,
When I'm sixty-four?

Every summer we can rent a cottage
In the Isle of Wight, if it's not too dear
We shall scrimp and save
Grandchildren on your knee
Vera, Chuck, and Dave

Send me a postcard, drop me a line,
Stating point of view.
Indicate precisely what you mean to say
Yours sincerely, Wasting Away.

Give me your answer, fill in a form
Mine for evermore
Will you still need me, will you still feed me,
When I'm sixty-four?

Whooh!



**Will you still need me,
will you still feed me,
When I'm sixty-four?**

"When I'm Sixty-Four" is a love song by The Beatles, written by Paul McCartney (credited to Lennon/McCartney) and released in 1967 on their album **Sgt. Pepper's Lonely Hearts Club Band**.

Gracias