

¿Cuándo no tratar una infección?

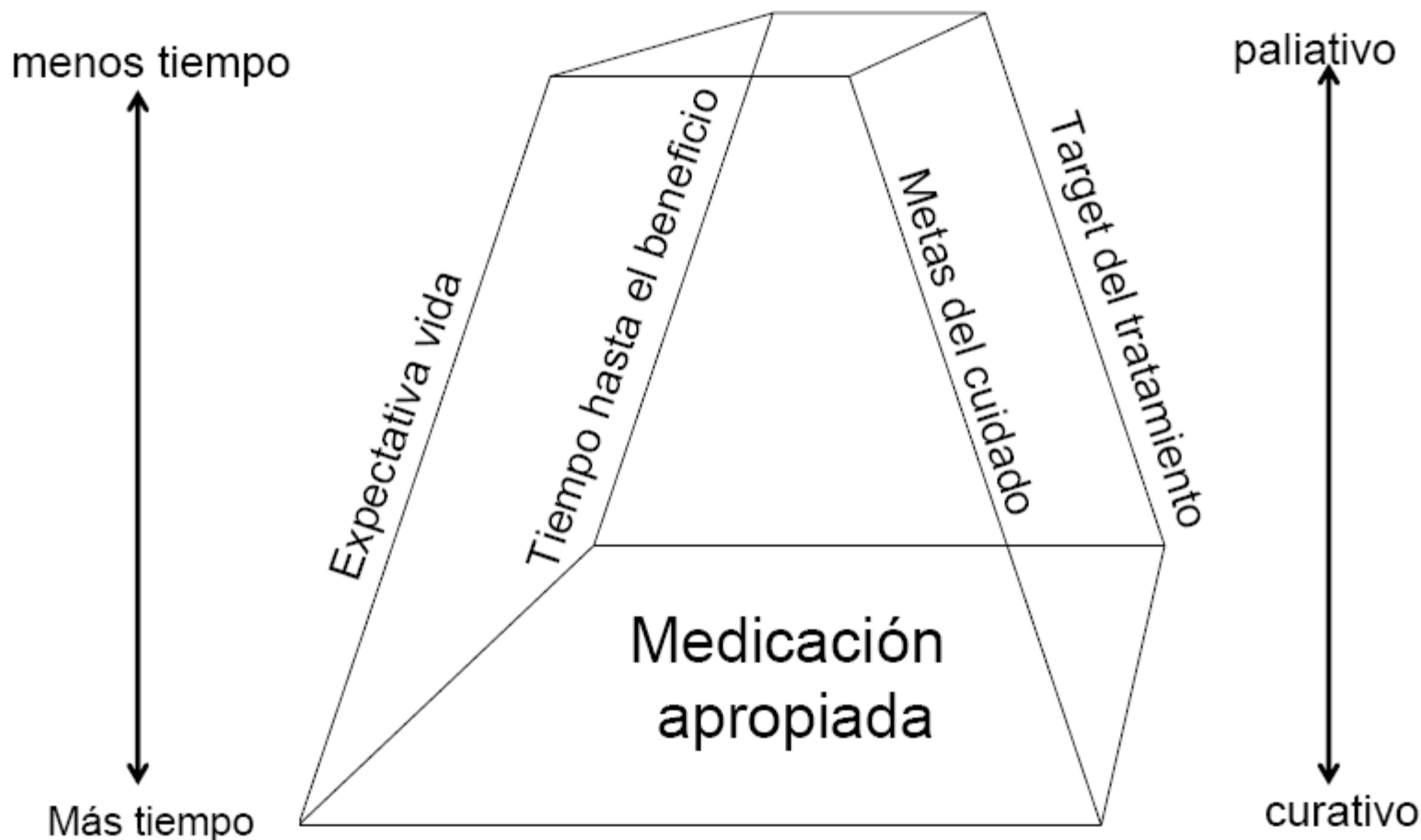
Intentando recomendaciones
basadas en evidencias

El dilema de tratar



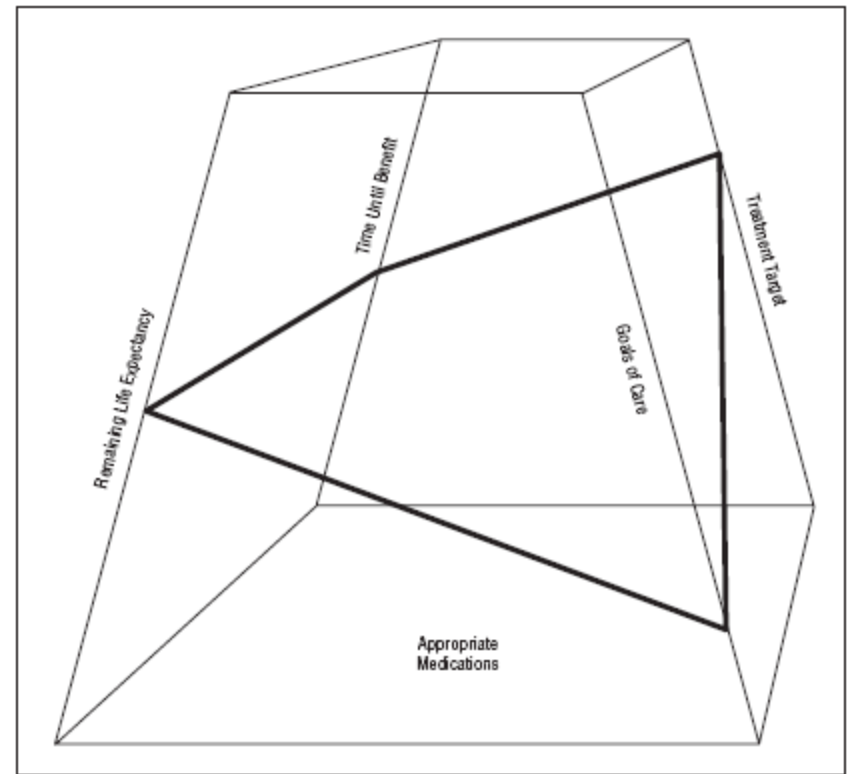
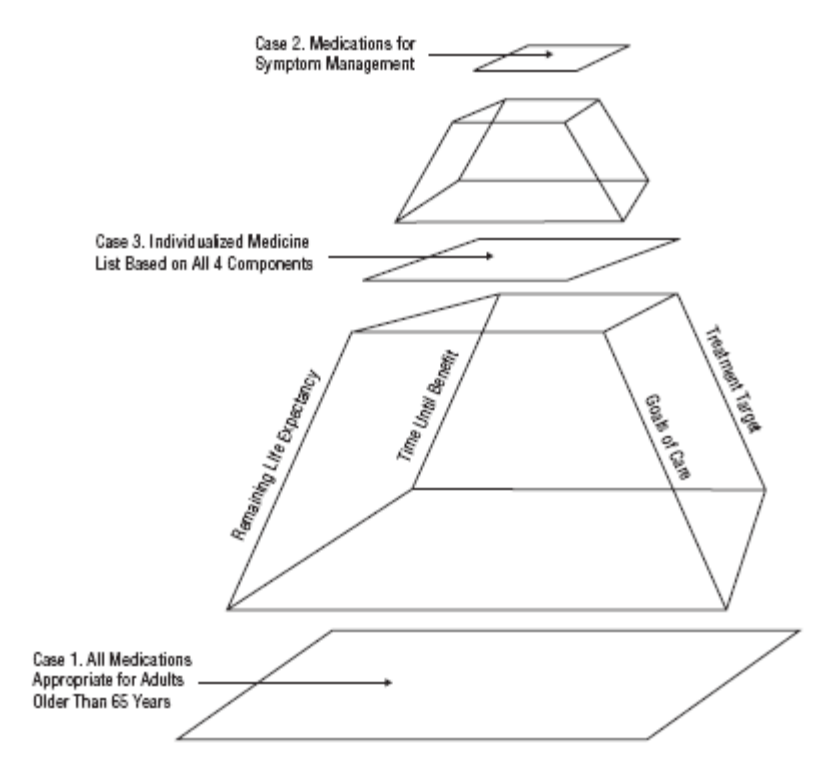
- El peso de la comorbilidad
- La toxicidad de los tratamientos
- El tiempo hasta el beneficio
- La agresividad de la infección
- La fragilidad y el status funcional
- El análisis de las herramientas para la decisión(NNT/NNB/NND)
- Los costos
- Las preferencias de los pacientes

El enfoque del tratamiento en los ancianos frente al final de la vida



Holmes HM, Cox Hayley D, Alexander C, Sachs GA. Reconsidering medication appropriateness for patients late in life, *Arch Int Med* 2006; 166: 605-9.

El enfoque de los tratamientos en los ancianos frente al final de la vida



Holmes Reconsidering medication appropriateness for patients late in the life

Arch Intern Med 2006, 166: 605-9

El peso de la comorbilidad en la decisión de tratar

Table 1. Life Expectancy at Age 65 Without and With Diseases at Baseline, Extra Years of Life Expectancy Without Disease and 95% Confidence Interval (95% CI), by Sex

Disease	Life Expectancy (Years) in Participants		Extra Years of Life Expectancy in Participants Without Disease (95% CI)
	Without Disease	With Disease	
Men			
Coronary heart disease	16.1	12.7	3.4 (2.7 to 4.1)
Stroke	15.6	10.9	4.8 (3.8 to 5.8)
Cognitive impairment	15.4	12.0	3.4 (2.3 to 4.6)
Diabetes	15.4	11.1	4.4 (3.2 to 5.6)
Peripheral vascular disease	15.4	12.6	2.8 (1.6 to 4.0)
Chronic airway obstruction	15.8	13.1	2.7 (1.9 to 3.4)
Arthritis	15.3	15.1	0.2 (-0.5 to 0.8)
Visual impairment	15.3	14.4	0.9 (0.0 to 1.9)
Hearing impairment	15.3	15.0	0.3 (-0.5 to 1.0)
Women			
Coronary heart disease	19.8	17.0	2.8 (2.0 to 3.5)
Stroke	19.6	15.0	4.6 (3.5 to 5.7)
Cognitive impairment	19.7	16.1	3.6 (2.7 to 4.6)
Diabetes	19.5	14.0	5.6 (4.3 to 6.9)
Peripheral vascular disease	19.5	16.1	3.4 (2.0 to 4.8)
Chronic airway obstruction	19.7	17.5	2.2 (1.5 to 2.9)
Arthritis	19.3	19.4	-0.2 (-0.7 to 0.4)
Visual impairment	19.5	18.0	1.5 (0.7 to 2.3)
Hearing impairment	19.3	19.2	0.2 (-0.6 to 0.9)

Table 2. Expected Years Free of Any Disability and Free of Moderate or Severe Disability at Age 65 in Participants With and Without Diseases at Baseline and 95% Confidence Interval (95% CI), by Sex

Disease	Expected Years Free of Any Disability in Participants		Extra Years Free of Any Disability in Participants Without Disease (95% CI)	Expected Years Free of Moderate or Severe Disability in Participants		Extra Years Free of Moderate or Severe Disability in Participants Without Disease (95% CI)
	Without Disease	With Disease		Without Disease	With Disease	
Men						
Coronary heart disease	12.6	9.5	3.0 (2.3 to 3.8)	14.2	11.2	3.0 (2.3 to 3.6)
Stroke	12.3	5.8	6.5 (5.4 to 7.7)	13.9	8.5	5.3 (4.3 to 6.4)
Cognitive impairment	12.0	7.8	4.2 (2.6 to 5.8)	13.6	9.2	4.4 (3.1 to 5.8)
Diabetes	12.0	7.8	4.1 (2.8 to 5.4)	13.6	9.5	4.1 (2.9 to 5.3)
Peripheral vascular disease	12.0	9.2	2.8 (1.4 to 4.1)	13.6	10.9	2.7 (1.5 to 3.8)
Chronic airway obstruction	12.2	10.0	2.3 (1.4 to 3.1)	13.9	11.5	2.4 (1.6 to 3.1)
Arthritis	12.2	11.2	1.0 (0.3 to 1.7)	13.6	13.2	0.5 (-0.2 to 1.1)
Visual impairment	12.0	10.0	2.0 (0.9 to 3.1)	13.6	11.9	1.6 (0.7 to 2.6)
Hearing impairment	11.9	11.4	0.5 (-0.3 to 1.3)	13.5	13.0	0.5 (-0.2 to 1.3)
Women						
Coronary heart disease	11.6	8.3	3.3 (2.5 to 4.1)	15.9	13.5	2.4 (1.7 to 3.2)
Stroke	11.4	5.5	5.8 (4.5 to 7.1)	15.8	10.6	5.2 (4.1 to 6.4)
Cognitive impairment	11.3	6.9	4.4 (2.9 to 5.8)	15.8	11.5	4.3 (3.2 to 5.4)
Diabetes	11.2	6.1	5.1 (3.4 to 6.8)	15.7	10.6	5.1 (3.9 to 6.3)
Peripheral vascular disease	11.2	8.3	2.9 (1.5 to 4.3)	15.6	12.4	3.3 (1.8 to 4.7)
Chronic airway obstruction	11.6	8.9	2.8 (2.0 to 3.6)	15.9	13.7	2.2 (1.5 to 2.9)
Arthritis	12.5	9.9	2.6 (1.9 to 3.3)	16.1	15.0	1.1 (0.5 to 1.7)
Visual impairment	11.4	8.3	3.1 (2.1 to 4.0)	15.7	13.8	1.9 (1.1 to 2.7)
Hearing impairment	11.2	10.0	1.2 (0.3 to 2.1)	15.6	15.0	0.5 (-0.2 to 1.3)

El peso de la comorbilidad en la decisión de tratar

Table 4. Expected Years of Life in Total, Free of Any Disability, and Free of Moderate or Severe Disability at Age 65 by Comorbidity at Baseline and Sex

Number of Diseases at Baseline	N*	Total	Expected Years of Life	
			Free of Any Disability	Free of Moderate or Severe Disability
Men				
None	1140	17.5	14.5	15.7
1	1667	16.0	12.4	14.4
2	1225	14.2	10.5	12.1
3	602	12.8	9.2	10.8
4 or more	292	11.1	6.9	9.1
Women				
None	1447	21.4	15.0	18.3
1	2525	20.1	11.8	16.5
2	1850	18.5	9.2	14.1
3	925	17.0	7.1	12.9
4 or more	524	16.5	6.5	12.0

Note: *Unweighted.

Comorbilidad e infección

Table 2. Prevalence of comorbidity by HIV status and disease cluster.

Variable	Overall			Medical disease			Substance use disorder			Psychiatric disorder		
	HIV-uninfected veterans	HIV-infected veterans	<i>P</i>	HIV-uninfected veterans	HIV-infected veterans	<i>P</i>	HIV-uninfected veterans	HIV-infected veterans	<i>P</i>	HIV-uninfected veterans	HIV-infected veterans	<i>P</i>
No. (%) of veterans	66,840 (66)	33,420 (33)		29,665 (69)	13,137 (31)		14,469 (62)	8947 (38)		14,824 (71)	5966 (29)	
Medical disease												
Any	44	39	<.001	NA	NA	NA	45	51	<.001	46	49	<.001
Hypertension	31	20	<.001	69	51	<.001	28	23	<.001	31	23	<.001
Diabetes	13	8	<.001	28	20	<.001	9	7	<.001	12	10	<.001
Vascular disease	10	6	<.001	23	17	<.001	8	6	<.001	9	7	<.001
Pulmonary disease	9	8	.006	20	21	.004	10	11	.01	11	12	.01
Liver disease	3	13	<.001	8	32	<.001	9	24	<.001	6	20	<.001
Renal disease	1	3	<.001	3	7	<.001	1	2	<.001	1	2	<.001
Substance use disorder												
Any	22	27	<.001	22	35	<.001	NA	NA	NA	42	56	<.001
Alcohol abuse and/or dependence	18	19	<.001	19	26	<.001	82	72	<.001	36	44	<.001
Drug abuse and/or dependence	15	21	<.001	13	26	<.001	67	78	<.001	31	48	<.001
Psychiatric disorder												
Any	22	18	<.001	23	22	.04	43	37	<.001	NA	NA	NA
Major depression and/or bipolar	11	12	.05	12	14	<.001	26	25	.07	52	67	<.001
Schizophrenia	9	5	<.001	8	7	<.001	17	12	<.001	39	28	<.001
PTSD	9	5	<.001	10	8	<.001	17	12	<.001	39	31	<.001
Any comorbid disease	63	60	<.001	NA	NA		NA	NA		NA	NA	
Multimorbidity ^a	4	5	<.001	10	14	<.001	21	20	.3	20	30	<.001

Frente a la infección

- ¿Hemos aprendido lo viejo?
- Bacteriuria asintomática e infecciones relacionadas a cateteres.
- Candiduria
- Micosis superficiales
- La infección respiratoria
- ¿Que sabemos de lo nuevo?
- Hepatitis virales
- Periodontitis
- H Pylori y envejecimiento
- HIV en ancianos



Uso inapropiado de antibióticos en el tracto genitourinario

- Bacteriuria asintomática
- Infección relacionada a catéteres
- Dolor pelviano o prostatitis crónica

Bacteriuria asintomática

- En el 2005 de Infectious Diseases Society of América definió BA como la presencia dos muestras consecutivas de urocultivo positivo para un germen con recuento mayor de 10^5 cfu/mL en pacientes asintomáticos.
- La prevalencia aumenta con la edad. Desde de 1% en edad escolar, hasta >20% en mujeres mayores de 80 años.
- Su prevalencia es mayor pacientes institucionalizados (40%).
- El rastreo de BA está recomendado solo en mujeres en edad embarazadas y pacientes que van a ser sometidos a procedimientos urológicos.
- El rastreo en hombres/mujeres no embarazadas es una recomendación tipo D.

¿Cuan beneficioso es el tratamiento?

- No mejora la sobrevida
- No previene episodios sintomáticos
- No previene el deterioro de la funcion renal

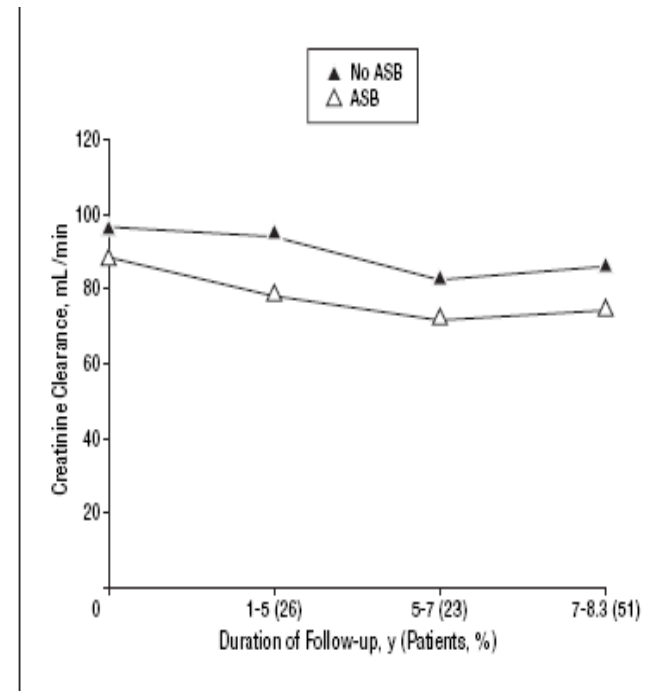


Figure. Change in renal function of women with diabetes mellitus with and without asymptomatic bacteriuria (ASB). To convert creatinine clearance to milliliters per second, multiply by 0.01667.

Asymptomatic Bacteriuria in Women
With Diabetes Mellitus
Effect on Renal Function After 6 Years of Follow-up
Arch Intern Med. 2006;166:2222-2227

El dolor pelviano crónico

Prostatitis refers to several clinical syndromes and has been categorized in four types: 1) acute bacterial infection, 2) chronic bacterial infection, 3) poorly defined chronic pelvic pain syndrome and 4) asymptomatic prostate inflammation.¹ Acute and chronic bacterial prostatitis account for approximately 5% to 10% of all cases of prostatitis.² Both are clearly associated with bacterial infection (often recurrent) and a urine culture that grows uropathogens. However, most men diagnosed with prostatitis have pelvic pain without evidence of infection.

Because antibiotics are not effective for treatment of abacterial chronic prostatitis, their use should be limited to individuals with confirmed positive cultures on expressed prostatic fluid or associated urinary tract infection.³ Recent efforts have been made to disseminate this information and implement appropriate antibiotic prescribing for several common conditions including prostatitis.

El dolor pelviano crónico

Association between Chronic Pelvic Pain Syndrome and Antibiotic Prescriptions among VA Users Excluding Men with a Diagnosis of Infectious/Acute Prostatitis or Urinary Tract Infection and Excluding Men with a Fluoroquinolone Prescription

FY	Prevalence of Chronic Pelvic Pain Syndrome	Adjusted [*] Prevalence Ratio (95% CI)	Adjusted [*] PAR	Men with a Prescription(s)	Attributable Men with Prescription(s)
2003	0.27%	3.57 (3.51, 3.63)	0.68%	412,693	2,814
2002	0.28%	3.50 (3.45, 3.56)	0.69%	417,411	2,896
2001	0.31%	3.28 (3.23, 3.33)	0.71%	426,074	3,004
2000	0.31%	3.10 (3.06, 3.14)	0.66%	427,677	2,802
1999	0.34%	2.76 (2.73, 2.79)	0.59%	448,646	2,636
					Total=14,153

Taylor et al.

* Adjusted for age, race/ethnicity and number of comorbidities

Association between Chronic Pelvic Pain Syndrome and Fluoroquinolone Use among VA Users Excluding Men with a Diagnosis of Infectious/Acute Prostatitis or Urinary Tract Infection

FY	Prevalence of Chronic Pelvic Pain Syndrome	Adjusted [*] Prevalence Ratio (95% CI)	Adjusted [*] PAR	Men with a Prescription(s)	Attributable Men with Prescription(s)
2003	0.50%	7.86 (7.76, 7.95)	3.30%	231,113	7,635
2002	0.51%	7.72 (7.62, 7.82)	3.30%	218,276	7,214
2001	0.55%	7.29 (7.20, 7.39)	3.36%	206,861	6,948
2000	0.54%	7.21 (7.11, 7.32)	3.24%	174,899	5,674
1999	0.56%	7.54 (7.42, 7.66)	3.54%	143,945	5,091
					Total=32,562

Taylor et al.

* Adjusted for age, race/ethnicity and number of comorbidities

Infección por Virus de la hepatitis C

- Prevalencia: 1-3% de la población general, 5-10% de la población anciana.
- 85% de los casos cursan como infección asintomática
- 85% evolucionan a infección crónica hepática
- Riesgo: 15-20% desarrollará cirrosis en 15 años
- HCC: 13% a los 5 años, 29% en 10 años, 45% en 15 años y 55% en mas de 20 años
- Otras complicaciones extrahepáticas

- Solo el 14% recibió tratamiento para el VHC



El dilema del tratamiento frente a la infección por el VHC

CLINICAL SIGNIFICANCE

- Significant differences in hepatocarcinogenesis and survival exist among patients with HCV, according to initial platelet count.
- IFN for a subgroup with intermediate and low platelet counts had significant advantages in regard to hepatocarcinogenesis and survival of elderly patients with chronic HCV.
- Asymptomatic elderly patients with HCV should be observed carefully as to hepatocarcinogenesis by using ultrasonography when the platelet count is $150 \times 1000/\text{mm}^3$ or less.
- IFN therapy should be considered in elderly patients when they have intermediate and low platelet counts.
- In view of the side effects in elderly patients, treatment should be initiated as soon as possible after diagnosis of chronic HCV.

- Síntomas tipo influenza
- Astenia
- Supresión de Medula osea y alteraciones hematológicas
- Trastornos del humor y enfermedades psiquiátricas
- Reacciones dermatológicas y alopecia

Contraindicaciones

- Manifestaciones extrahepaticas
- Enfermedad hepática descompensada
- Enfermedad Autoinmune descompensada
- Mala Adherencia al tratamiento médico
- Imposibilidad de auto administración
- Enfermedad psiquiátrica descompensada o alto riesgo de suicidio

Cuando no tratar

- Paciente con daño histológico mínimo, con bajas chances de progresión
- Baja expectativa de vida por carga de sus comorbilidades
- Abuso de sustancias
- Potencial exacerbaciones de sus comorbilidades por el tratamiento
- Enfermedades psiquiátricas

Porque son excluidos los AM en los ECR en hepatitis C

Table 2. Reasons for Excluding Patients From Antiviral Therapy in VA Clinics

	Muir <i>et al.</i> 2002 (27)	Cawthorne <i>et al.</i> 2002 (28)	Rowan <i>et al.</i> 2004 (29)	Butt <i>et al.</i> 2005 (30)	Tavakoli-Tabasi <i>et al.</i> 2005 (31)	Bini <i>et al.</i> 2005 (32)	Chueng <i>et al.</i> 2006 (33)	Chainuvati <i>et al.</i> 2006 (34)
Patient population	Consecutive HCV Ab+ patients seen in clinic in 1999	All HCV Ab+ patients with ≥1 clinic visit from 1997 to June 2000	All HCV Ab+ patients seen in clinic from September 2000 to May 2002	Consecutive HCV Ab+ patients attending a referral clinic from December 1998 to April 2001	Consecutive viremic HCV patients from September 2000 to May 2002	Prospectively enrolled viremic HCV patients from December 1999 to December 2000 (N = 24; VA centers)	Consecutive viremic HCV patients with ≥1 clinic visit from 2000 to 2001 and 2-yr follow-up	Consecutive viremic HCV patients with ≥1 clinic visit from October 1999 to June 2002
Exclusions from therapy, N (%)	68/100 (68.0)	165/242 (68.2)	406/580 (70.0)	248/354 (70.0)	296/424 (70.0)	2769/4084 (67.8) ^a	175/209 (83.7)	485/647 (75.0) ^b
	Reasons for exclusion (% patients)							
Psychiatric disease	46 ^g	21	27	7	35	18	27 ^g	3
Alcohol and/or substance use	77	18	36	9	18	20	36	11
Advanced liver disease	10	NA	8	13	5	6	1.0	13
Comorbid medical disease	14	7	20	11	19	25 ^c	19 ^d	22
Patient preference	NA	27	5	12	14	NA	4	13
Noncompliance	1	5	4	24	6	4	1	23
Mild disease or normal LFT results	NA	5	NA	14	3 ^e	NA	36	15
Other	NA	17 ^f	NA	5 (HCV RNA), 5 (unknown)	NA	27 (lab abnormalities)	11.5 (poor support)	NA
	Receipt of antiviral therapy, N (%)							
	NA	77/242 (31.8)	174/580 (30.0)	104/354 (29.4)	128/424 (30.0)	722/4084 (17.7)	NA	162/647 (25.0)

^aNoncandidates for treatment according to standardized criteria.

^bIncludes patients considered not eligible for treatment, N = 296/647 (46%), and patients considered eligible but excluded from treatment due to refusal, loss to follow-up, or noncompliance and mild disease, N = 189/647 (29%). Patients with mental illness were excluded only if "unstable," and patients with substance use disorders were excluded if active use within 1 month prior to evaluation.

^cIncludes comorbid medical condition, cardiac ischemia, hemoglobinopathies, and organ transplant.

^dIncludes medical comorbidity and age >65 yr.

^eIncludes 3 patients with normal LFT results and 7 patients with no fibrosis on liver biopsy.

^fIncludes multiple reasons (10%), treatment outside the VA (3.5%), and HCV RNA negative (3.5%)

^gMay be >100% due to overlapping categories.

Ab = antibody; HCV = hepatitis C virus; LFT = liver function test; NA = not available.



Por que son excluidos los AM en los estudios epidemiológicos

Table 3. Reasons for Excluding Patients From Antiviral Therapy in Community-Based Clinics

	Falck-Ytter <i>et al.</i> 2002 (99)	Yawn <i>et al.</i> 2002 (36)	Rocca <i>et al.</i> 2004 (37)	Morrill <i>et al.</i> 2005 (38)	Evon <i>et al.</i> 2007 (39)
Setting	County teaching hospital	Community health clinic	Community health clinic	Community health clinic	University medical practice
Patient population	Consecutive viremic patients from January 1998 to November 1999 attending a referral clinic	HCV Ab+ residents of Olmsted Co. from January 1990 to December 1999	All patients diagnosed with HCV in Olmsted Co. from January 1990 to December 2000 who had a discussion about treatment	Consecutive viremic patients from December 2001 to April 2004 attending a referral clinic	Viremic patients sampled from 2001 to 2003 attending a referral clinic
Number of patients excluded from antiviral therapy (%)	211/293 (72.0)	306/355 (86.0)	179/234 (76.5)	151/208 (72.6)	324/433 (75.0)
	Reasons for exclusion (% patients)				
Psychiatric disease	NA	9	14	15.2	34.3 ^d
Alcohol and/or substance abuse	13	17	19	22.5	33.6
Advanced liver disease	NA	12	6	NA	23.5
Comorbid medical disease	34 ^a	17	27 ^b	7.9	23.8
Patient preference	11	NA	13	16.1	13.3
Noncompliance	37	14	NA	7.9	NA
Normal liver function tests (LFTs)	5	NA	11	NA	4.9
Other	NA	27 (unknown), 3 (no insurance)	8 (no insurance), 2 (language barrier)	18.5 (unknown or other), 11.9 (care delay)	4.9 (financial concerns)
	Receipt of antiviral therapy, N (%)				
	83/293 (28.0)	49/355 (14.0)	55/234 (23.5)	57/208 (27.4)	109/433 (25.0) ^e

^aThe most frequent comorbid disease was psychiatric disease, including depression, bipolar disease, and previous suicidal ideation or attempt.

^bIncludes severe comorbidity, severe HIV infection, old age, pregnancy, and acute hepatitis.

^cForty-two patients out of 324 (13%) of those initially deferred were eventually treated, with a final treatment rate of 151 per 433 (35%).

^dMay be >100% due to overlapping categories.



Tasa de éxito en los AM frente al tratamiento del virus C

Table 4. SVR Rates in Veterans Undergoing Antiviral Therapy

	Year	Treated, N	HCV Patient Population	Regimen	Overall SVR
Cawthorne <i>et al.</i> (28)	2002	41	Retrospective single-center analysis of treatment-naïve outpatients	IFN + RBV	13.8%
Morelli <i>et al.</i> (41)	2002	93	Retrospective single-center analysis of consecutive patients	IFN + RBV	White: 10/55 (17.9%) African American: 0/38 (0%)
Nguyen <i>et al.</i> (42)	2002	145	Retrospective single-center analysis of consecutive patients attending a multidisciplinary hepatitis clinic	IFN alone	16%
Bini <i>et al.</i> (32)	2005	722	Prospective, multicenter study in 24 VA facilities	IFN + RBV	28%
Knott <i>et al.</i> (43)	2006	65	Retrospective single-center analysis of consecutive patients attending an integrated medical/psychiatric HCV clinic	Peg-IFN + RBV	18.4–20.3%
Chainuvati <i>et al.</i> (34)	2006	162	Retrospective single-center analysis of consecutive patients attending a multidisciplinary clinic from October 1999 to June 2002	IFN + RBV or peg-IFN + RBV	34.5%
Groom <i>et al.</i> (100)	2007	103	Retrospective single-center analysis of consecutive patients attending a multidisciplinary clinic	IFN + RBV	24/162 (14.8%)
Backus <i>et al.</i> (44)	2007	5,944	Retrospective database analysis of patients treated at 121 VA facilities as of September 2003	Peg-IFN + RBV Peg-IFN + RBV	12/38 (31.6%) 28/65 (43.1%) 1,551/5,944 (26%)—genotype 1 (20%); genotype 2 (52%); genotype 3 (43%)

HCV = hepatitis C virus; IFN = interferon alpha; peg-IFN = pegylated interferon alpha; RBV = ribavirin; SVR = sustained virologic response; VA = veterans affairs.

Utilizando las evidencias para la decisión

Carcinogénesis

Poblacion general

	Sin T	INF	NNT
5 años	13	7	20
10 años	29	13	8
15 años	45	33	9

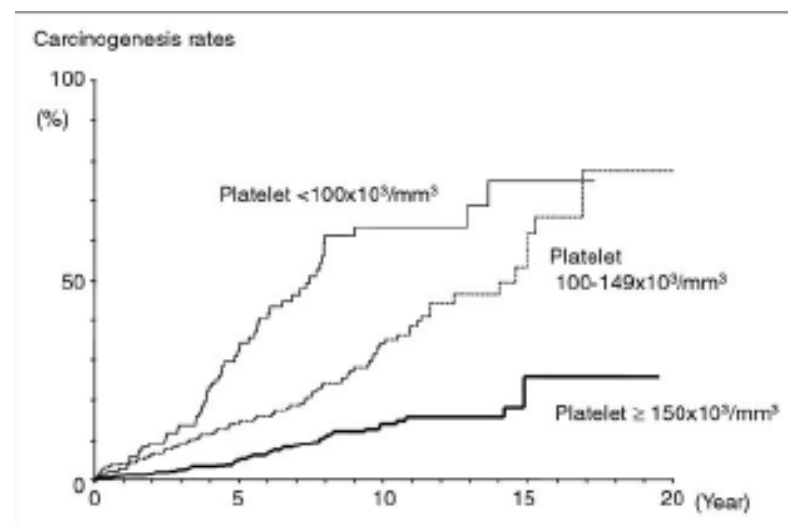
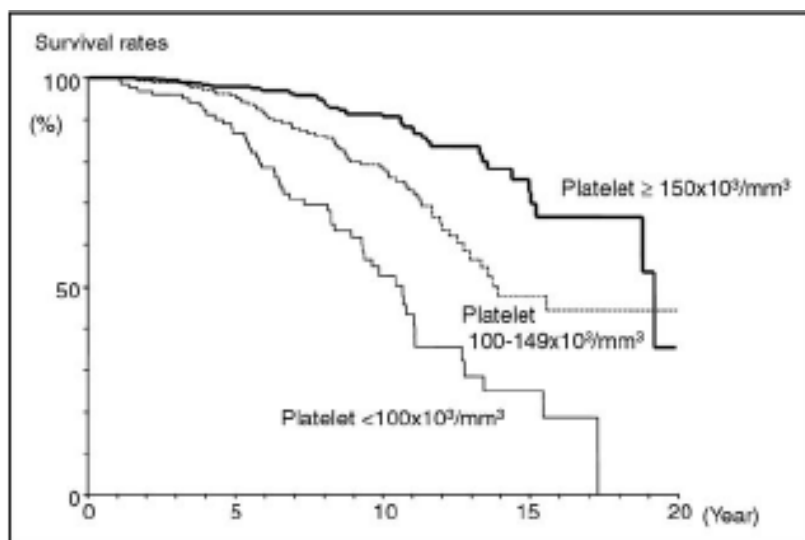
Bajo riesgo

	Sin T	INF	NNT
5 años	5	3,7	76
10 años	14	13	90
15 años	26	25	180

Alto riesgo

	Sin T	INF	NNT
5 años	19	10	10
10 años	43	21	5
15 años	65	39	4

Tasas de sobrevivida y riesgo de cancer Tratamiento vs no tratamiento



Periodontitis

- Niveles bajo y persistentes de inflamación guardan relación con desenlaces cardiovasculares desfavorables
- Relación entre bajo nivel cognitivo, enfermedad coronaria y periodontitis y pérdida de piezas dentarias
- Incremento de cánceres de partes blandas del macizo facial

- ¿Cuan beneficioso es el tratamiento?
- ¿Que queremos prevenir?

El dilema de tratar



- El peso de la comorbilidad
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COMO HACER UNA RECOMENDACIÓN DE TRATAMIENTO

La Bibliografía

Calidad metodológica

Importancia del efecto

Magnitud del efecto

El Médico

Riesgos de la enfermedad

Costos

Riesgos del tratamiento

El Paciente

Valores del paciente

Molestias para el paciente

Máximo y mínimo efecto

Muchas Gracias



GOBIERNO DE LA PROVINCIA DE SALTA

MINISTERIO DE SALUD PUBLICA

SEGURO PROVINCIAL DE SALUD

