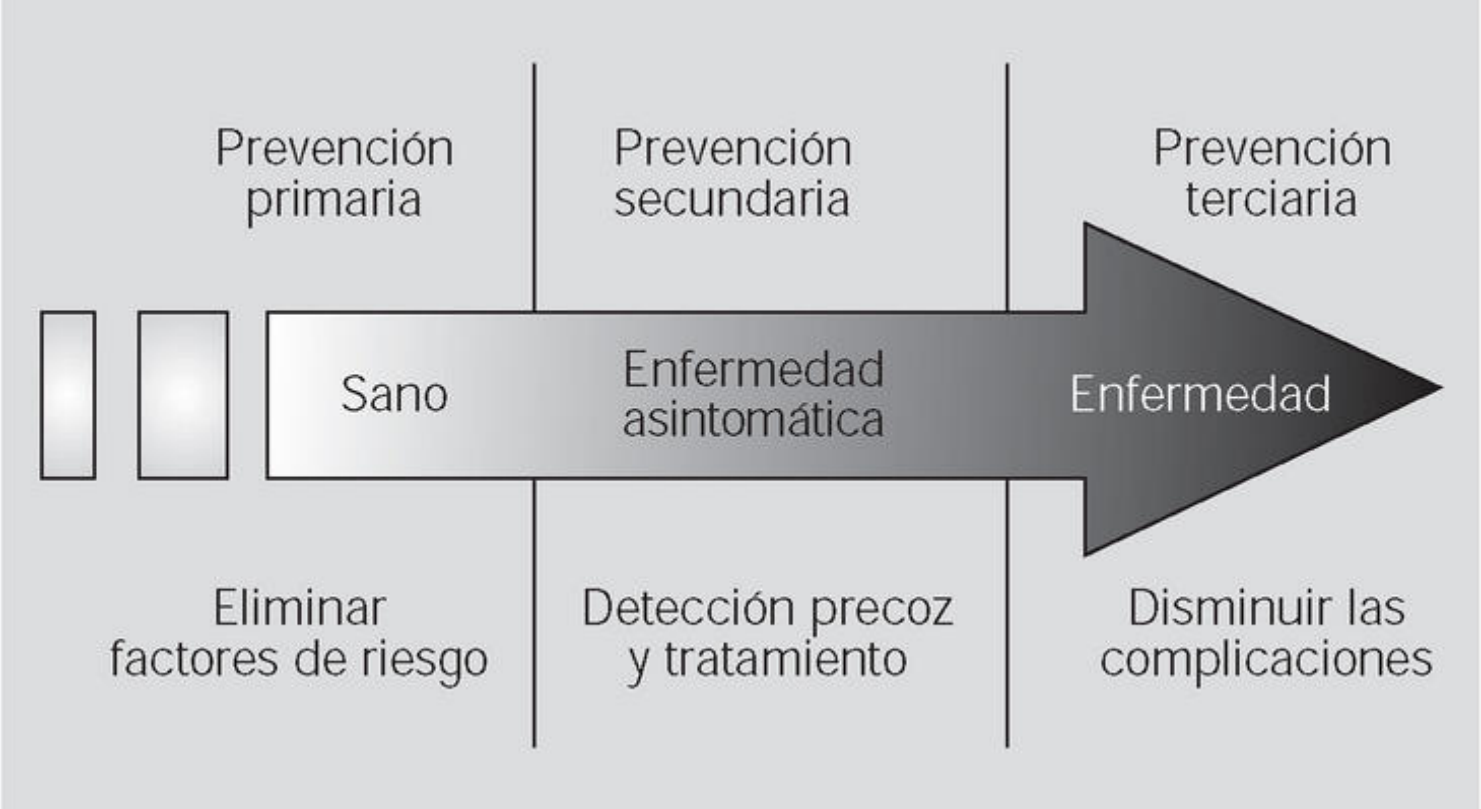
Psicosi.
És millor prevenir.

Dra.Inmaculada Baeza
Servei de Psiquiatria i Psicologia infanto-juvenil,
Coordinadora del Programa de Psicosi incipient,
Hospital Clínic de Barcelona

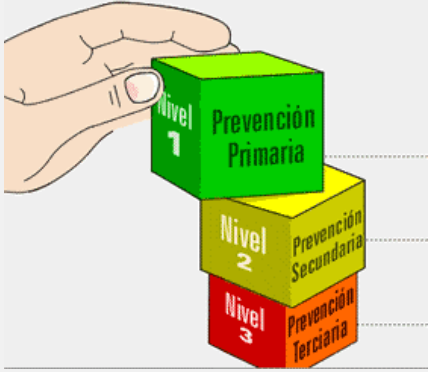
Índice

- Prevención
- Riesgo genético de psicosis
- Riesgo clínico de psicosis
- Estrategias de tratamiento
- Conclusiones

PREVENCIÓN



"Medidas destinadas no solamente a evitar la aparición de la enfermedad, tales como la reducción de factores de riesgo, sino también a detener su avance y atenuar sus consecuencias una vez establecida"



OMS, 1998

Primaria:

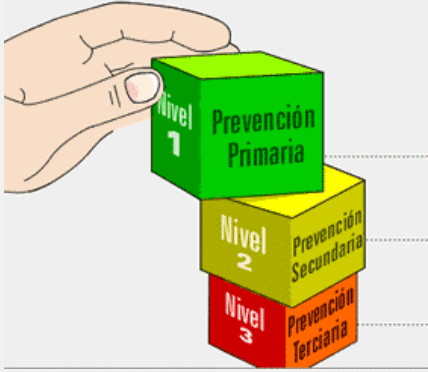
“Medidas orientadas a evitar la aparición de una enfermedad o problema de salud mediante el control de los factores causales y los factores predisponentes o condicionantes”

Objetivo:

Disminuir la incidencia de la enfermedad

Ejemplo:

Disminuir el consumo de tabaco



OMS, 1998

Secundaria:

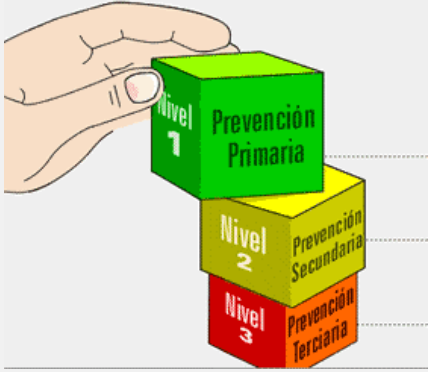
“Diagnostico precoz de la enfermedad incipiente (sin manifestaciones clínicas). Significa la búsqueda en sujetos “aparentemente sanos” de enfermedades lo más precozmente posible. ”

Objetivo:

Disminuir la prevalencia de la enfermedad

Ejemplo:

Mamografía cada dos años a partir de los 50 años



OMS, 1998

Terciaria:

“Acciones relativas a la recuperación ad integrum de la enfermedad clínicamente manifiesta, mediante un correcto diagnostico y tratamiento y la rehabilitación física, psicológica y social en caso de invalidez o secuelas buscando reducir de este modo las mismas. ”

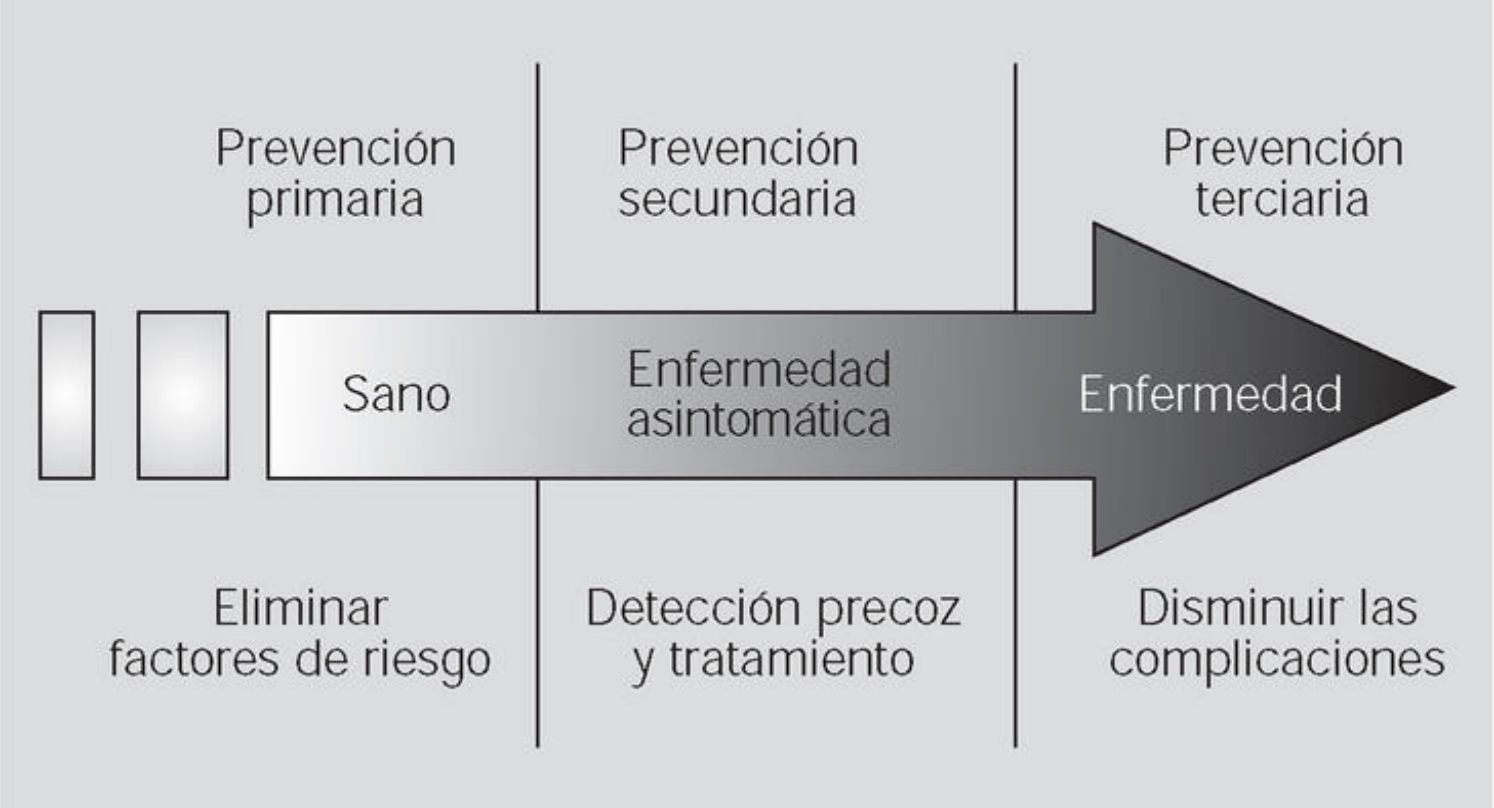
Objetivos:

Disminuir el sufrimiento producido por la enfermedad

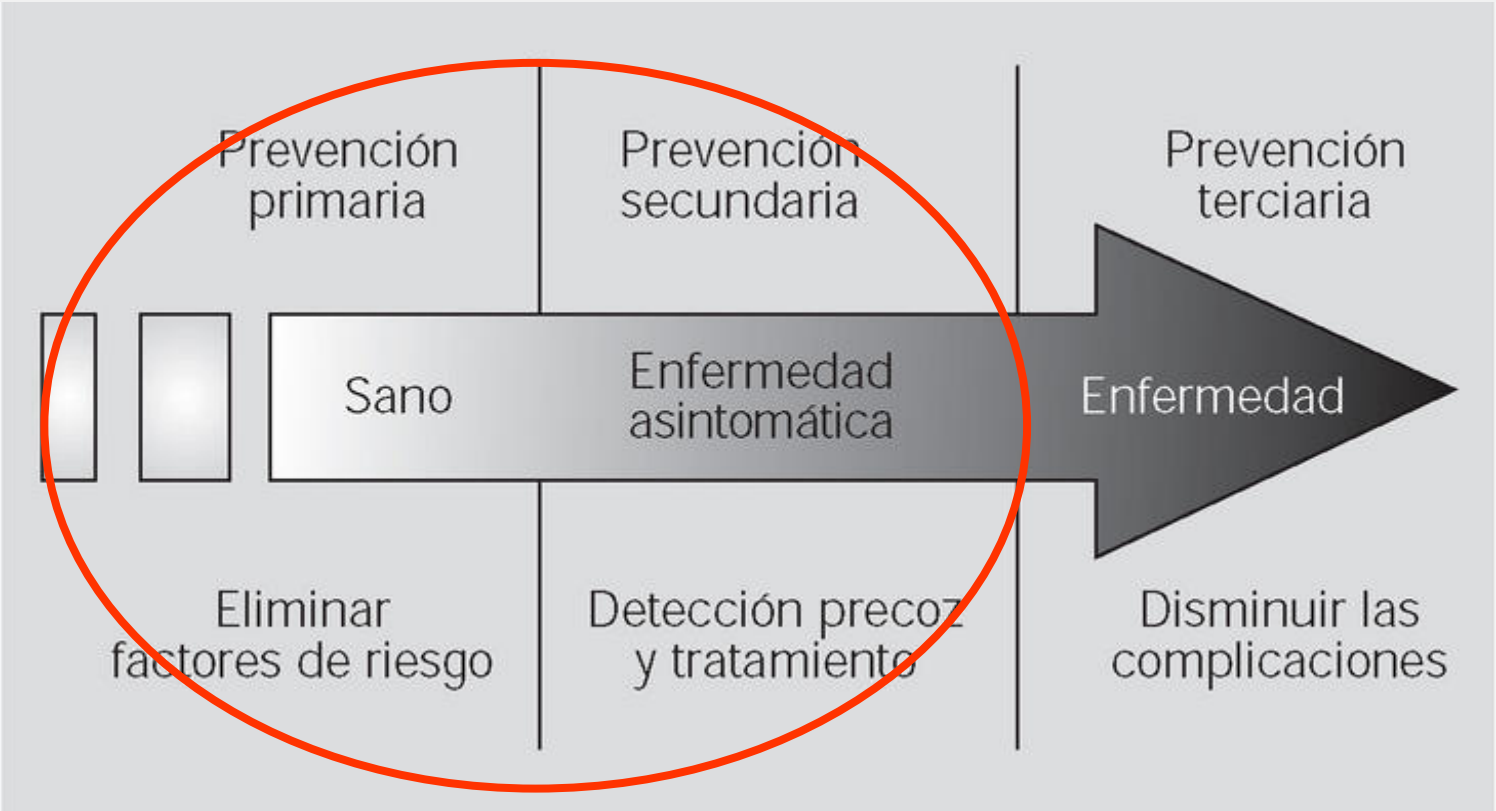
Reducir las recaídas

Ejemplo:

Rehabilitación y fisioterapia después de retirar un yeso por fractura



"La prevención se basa en el control de las enfermedades poniendo énfasis en los factores de riesgo y las poblaciones de riesgo"



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European Psychiatry xxx (2015) xxx–xxx

Contents lists available at ScienceDirect

European Psychiatry

journal homepage: http://www.europsy-journal.com

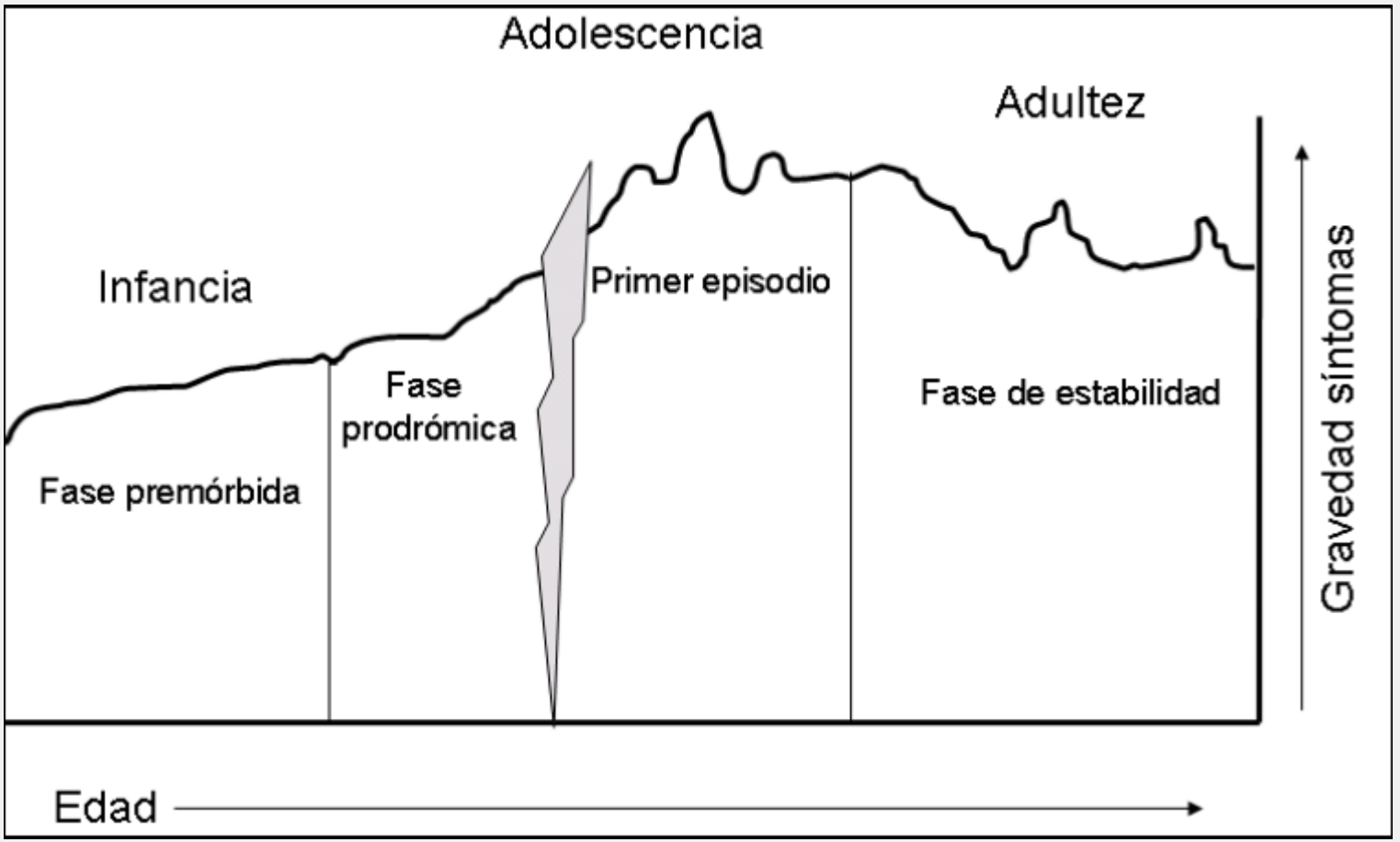
Original article

EPA guidance on the early detection of clinical high risk states of psychoses

F. Schultze-Lutter [a], C. Michel [a], S.J. Schmidt [a], B.G. Schimmelmann [a], N.P. Maric [c], R.K.R. Salokangas [d], A. Riecher-Rössler [e], M. van der Gaag [f,g], M. Nordentoft [h], A. Raballo [i,j], A. Meneghelli [k], M. Marshall [l,m], A. Morrison [n,o], S. Ruhrmann [b], J. Klosterkötter [b,*]

- La prevención en la población general (primaria universal) no está indicada en la actualidad por:
  - Relativa baja incidencia de psicosis
  - Faltan suficientes conocimientos sobre su etiología
  - Faltan factores de riesgo con tamaño del efecto epidemiológico grande

Curso evolutivo



Clinical staging: a heuristic model for psychiatry and youth mental health

Patrick D McGorry, Rosemary Purcell, Ian B Hickie, Alison R Yung, Christos Pantelis and Henry J Jackson

Table 1 Proposed staging model for psychotic and severe mood disorders

Stage	Definition of stage (psychosis or severe mood disorder)
0	Increased risk of psychotic or severe mood disorder. No symptoms currently.
Ia	Mild or non-specific symptoms (including subtle neurocognitive deficits) of psychosis or severe mood disorder. Mild functional change or decline.
Ib	Ultra-high risk: moderate but subthreshold symptoms, with neurocognitive changes and functional decline to caseness (GAF <70)
II	First episode of psychotic or severe mood disorder. Full threshold disorder with moderate to severe symptoms, neurocognitive deficits and functional decline (GAF 30–50).
IIIa	Incomplete remission from first episode of care. (Patient's management could be linked or fast-tracked to Stage IV.)
IIIb	Recurrence or relapse of psychotic or mood disorder which stabilises with treatment at a GAF level ⩽30, or with residual symptoms or neurocognition below the best level achieved after remission from the first episode.
IIIc	Multiple relapses with worsening in clinical extent and impact of illness objectively present.
IV	Severe, persistent or unremitting illness as judged by symptoms, neurocognition and disability criteria.

GAF, Global Assessment of Functioning.
Adapted from McGorry *et al*.[1]

Prevención primaria específica

Prevención secundaria

Prevención terciaria

Clinical staging model framework for psychotic and severe mood disorders[*†]

Stage	Definition	Target populations and referral sources	Potential interventions
0	Increased risk of psychotic or severe mood disorder No symptoms currently	• First-degree teenage relatives of probands	• Improved mental health literacy • Family education, drug education • Brief cognitive skills training
1a	Mild or non-specific symptoms (including neurocognitive deficits) of psychosis or severe mood disorder. Mild functional change or decline	• Screening of teenage populations • *Referral by:* primary care physicians; school counsellors	• Formal mental health literacy • Family psychoeducation, formal CBT • Active substance misuse reduction
1b	Ultra high risk: moderate but subthreshold symptoms, with moderate neurocognitive changes and functional decline to caseness (GAF, < 70)	• *Referral by:* educational agencies; primary care physicians; emergency departments; welfare agencies	• Family psychoeducation, formal CBT • Active substance misuse reduction • Omega-3 fatty acids • Atypical antipsychotic agents • Antidepressant agents or mood stabilisers
2	First episode of psychotic or severe mood disorder Full threshold disorder with moderate to severe symptoms, neurocognitive deficits and functional decline (GAF, 30–50)	• *Referral by:* primary care physicians; emergency departments; welfare agencies; specialist care agencies; drug and alcohol services	• Family psychoeducation, formal CBT • Active substance misuse reduction • Atypical antipsychotic agents • Antidepressant agents or mood stabilisers • Vocational rehabilitation
3a	Incomplete remission from first episode of care Patient's management could be linked or fast-tracked to Stage 4	• Primary and specialist care services	• As for Stage 2, but with additional emphasis on medical and psychosocial strategies to achieve full remission
3b	Recurrence or relapse of psychotic or mood disorder, which stabilises with treatment at a GAF level, or with residual symptoms or neurocognition below the best level achieved after remission from the first episode	• Primary and specialist care services	• As for Stage 3a, but with additional emphasis on relapse prevention and strategies to detect "early warning signs"
3c	Multiple relapses, provided worsening in clinical extent and impact of illness is objectively present	• Specialist care services	• As for Stage 3b, but with emphasis on long-term stabilisation
4	Severe, persistent or unremitting illness, as judged by symptoms, neurocognition, and disability criteria Patient's management could be fast-tracked to this stage at first presentation, based on specific clinical and functional criteria (from Stage 2), or because of failure to respond to treatment (from Stage 3a)	• Specialised care services	• As for Stage 3c, but with emphasis on clozapine, other tertiary treatments, and social participation despite ongoing disability

MJA 2007; 187: S40–S42

Clinical staging model framework for psychotic and severe mood disorders[*†]

Stage	Definition	Target populations and referral sources	Potential interventions
0	Increased risk of psychotic or severe mood disorder No symptoms currently	• First-degree teenage relatives of probands	• Improved mental health literacy • Family education, drug education • Brief cognitive skills training
1a	Mild or non-specific symptoms (including neurocognitive deficits) of psychosis or severe mood disorder. Mild functional change or decline	• Screening of teenage populations • *Referral by:* primary care physicians; school counsellors	• Formal mental health literacy • Family psychoeducation, formal CBT • Active substance misuse reduction
1b	Ultr sym cha (GA		BT n tabilisers
2	Firs disc Full sym dec		BT n tabilisers
3a	Inc Pat fast		l emphasis egies to
3b	Rec whi residual symptoms or neurocognition below the best level achieved after remission from the first episode		al emphasis es to detect "early warning signs"
3c	Multiple relapses, provided worsening in clinical extent and impact of illness is objectively present	• Specialist care services	• As for Stage 3b, but with emphasis on long-term stabilisation
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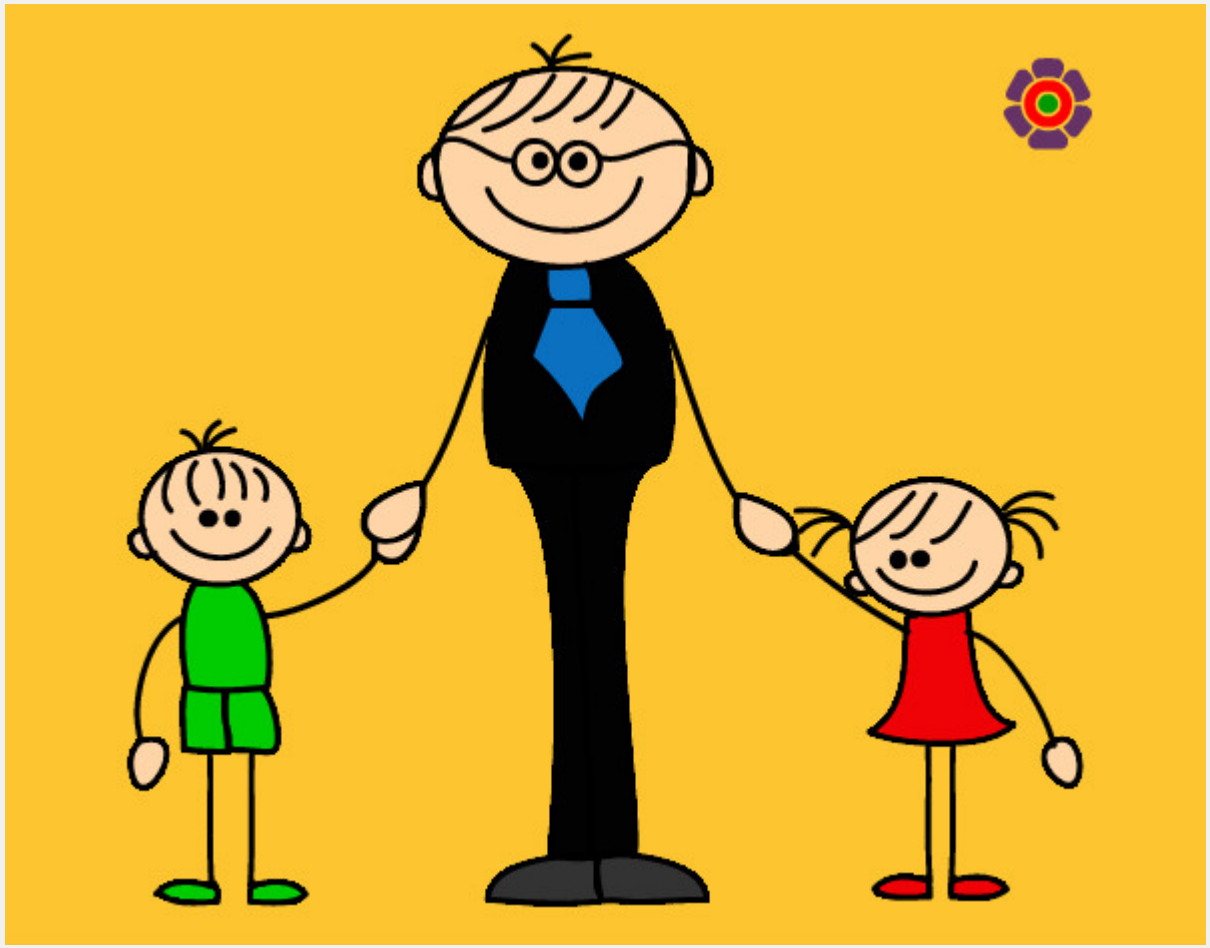
El riesgo genético es el MAYOR factor de riesgo de psicosis

MJA 2007; 187: S40–S42



RIESGO GENÉTICO DE PSICOSIS

La heredabilidad del trastorno se ha estimado aprox. en el 80%

(Sullivan et al, 2003; Cardno et al 1999; Cannon et al. 1998).

Estudios de alto riesgo

Objectivos

- **Detección precoz psicopatología**
- **Detección precoz de la enfermedad**

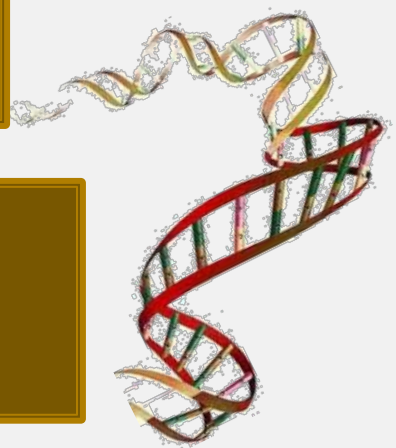
El riesgo de presentar esquizofrenia a lo largo de la vida es 1% y tr.psicótico 3%

(Saha et al, 2005; McGrath et al, 2004)

Base

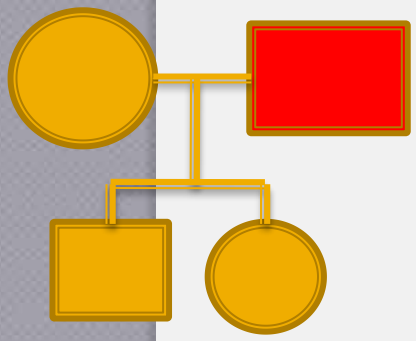
Componente genético

Teoría del neurodesarrollo



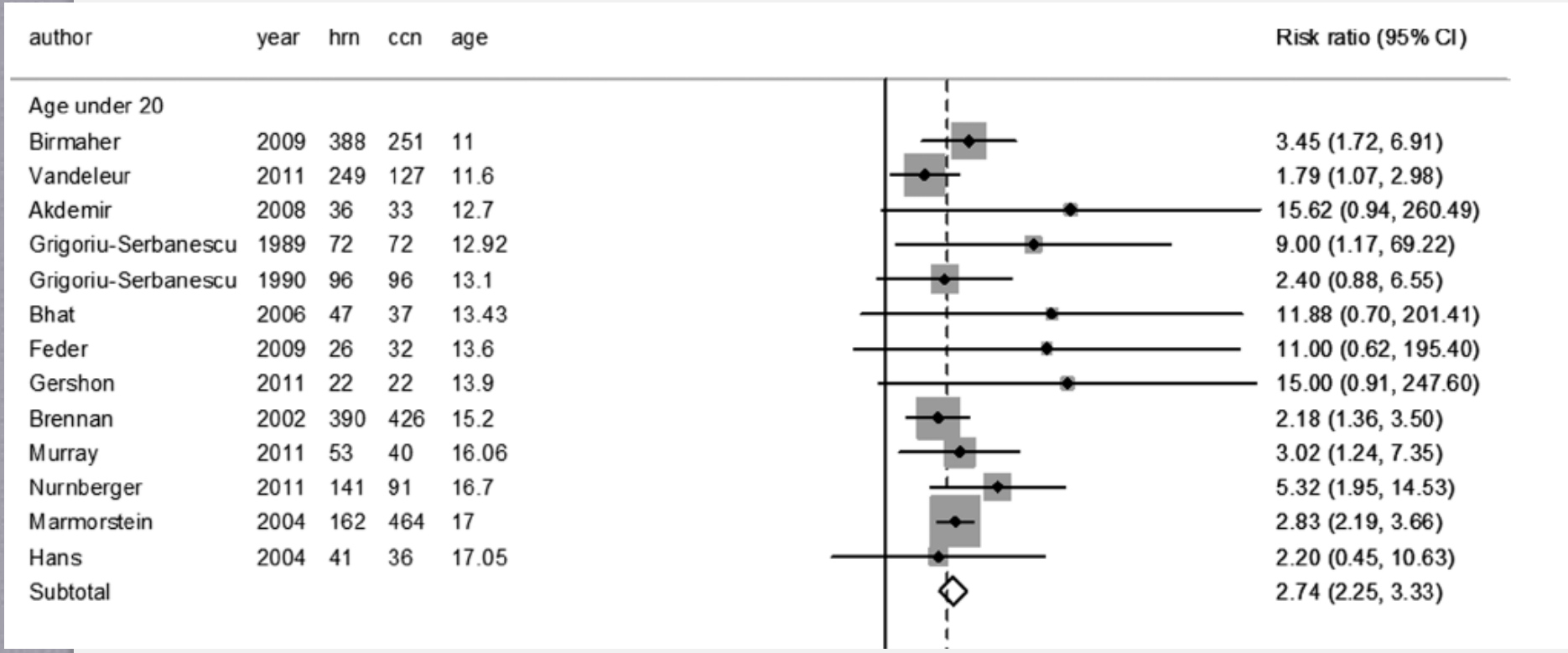
Características clínicas alto riesgo genético

El riesgo se incrementa con la proximidad familiar y el número de familiares afectados por la enfermedad.



Grado de familiaridad	Riesgo esquizofrenia
Dos padres afectados	40-60%
Gemelos monozigóticos	**50-70%**
Hermanos o gemelos dizigóticos	9-18%
Hijos	9-10%
Familiares de segundo grado	3-6%
Familiares de tercer grado	1-3%

Características clínicas alto riesgo genético



1/3 de los hijos de un padre con un trastorno mental grave tendrán un trastorno mental grave

(Rasic et al, 2014)

Características clínicas alto riesgo genético

Psicopatología en la población general

Trastorno	Prevalencias mínimas y máximas observadas en %
Tr. De ansiedad	2,4-14,9%
Tr. depresivo	0,92-7,2%
Tr. conducta	2,7-5,9%
TDAH	0,9-4%

(Costello et al, 2003)

Características clínicas alto riesgo genético

Diagnósticos DSM IV/DSM III-R

Maziade (2008)	Hans (2004)	Keshavan (2003)	Ross (2001)
T.com/apren 21,4% Ansiedad 17,8% TDAH 10,7% Afectivos 10,7%	Ansiedad 39% TDAH/disrup 31,7% Personalidad 31,7% Esquizofrenia 17,1% Afectivos 14,6%	TDAH/disrup 38,6% Afectivos 17,33% Ansiedad 13,33%	TDAH 40% Ansiedad 28% Depresión 12% Psicosis 9%

PSYCHIATRIC DISORDERS IN CHILD AND ADOLESCENT OFFSPRING OF SCHIZOPHRENIA AND BIPOLAR DISORDER PATIENTS: A CONTROLLED STUDY

	SZ-offspring *N=41 N (%)*	*BP-offspring* *N=90 N (%)*	*CC-offspring* *N=107 N(%)*	*χ2/* *F*	*p-* *value*	*post-hoc paired analysis*
Any lifetime Axis I disorder	24(58.5)	33(36.7)	19(17.8)	24.17	.000	SzO>BpO [a] SzO>CcO [c] BpO>CcO [c]
Mood Disorders	2 (4.9)	14(15.6)	5(4.7)	8.15	.02	BpO>CcO [a]
MDD	0	6(6.7)	0	10.16	.006	BpO>CcO [b]
Dysthymia	0	1(1.1)	1(0.9)	.43	.80	
Adjustment depressive disorder	2(4.9)	6(6.7)	4(3.7)	.87	.64	
Depression NOS	0	1(1.1)	0	1.66	.44	
Hypomania/ mania	0	0	0			
Anxiety Disorders	7 (17.1)	11(12.2)	6 (5.6)	5.02	.08	SzO>CcO [a]
SAD	0	2(2.2)	2(1.9)	.87	.65	
GAD	3(7.3)	4 (4.5)	3(2.8)	1.52	.46	
Adjustment anxious disorder	0	1(1.1)	1(0.9)	.43	.80	
PTSD	1(2.4)	1(1.1)	0	2.24	.31	
OCD	0	0	0			
Panic-agoraphobia	0	1(1.1)	0	1.67	.43	
Simple phobia	3 (7.3)	4(4.4)	0	6.70	.03	SzO>CcO [a] BpO>CcO [a]
ADHD	19 (46.3)	16(17.6)	8 (7.5)	30.25	.000	SzO>BpO [b] SzO>CcO [c] BpO>CcO [a]
Disruptive disorders	6 (14.6)	3(3.3)	2 (1.9)	11.50	.003	SzO>BpO [a] SzO>CcO [b]
Others	2(4.9)	2(2.2)	4(3.7)	.69	.70	
Axis I comorbidity	11(26.8)	12(13.3)	6(5.6)	12.65	.02	SzO>CcO [a]
N of AXIS I disorders	0.93(0.97)	0.5(0.82)	0.23(0.54)	13.46	.000	SzO>BpO [a] SzO>CcO [c] BpO>CcO [a]

Bipolar And Schizophrenia
Young offspring Study

Sánchez-Gistau y cols, submitted

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In Review

Bipolar And Schizophrenia Young offspring Study

Sánchez-Gistau y cols, submitted

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N of AXIS I disorders	0.93(0.97)	0.5(0.82)	0.23(0.54)	13.46	.000	SzO>BpO [a] SzO>CcO [c] BpO>CcO [a]

Under review

Bipolar And Schizophrenia Young offspring Study

Sánchez-Gistau y cols, submitted

Curr Psychiatry Rep (2014) 16:439
DOI 10.1007/s11920-014-0439-y

SCHIZOPHRENIA AND OTHER PSYCHOTIC DISORDERS (S SIEGEL, SECTION EDITOR)

Is Prevention a Realistic Goal for Schizophrenia?

Christian Kohler · Karin E. Borgmann-Winter · Irene Hurford · Eli Neustadter · James Yi · Monica E. Calkins

- La estrategia del alto riesgo genético detecta tasas de transición a psicosis más altas que la población general 6-15% en 25-30 años

- Sólo se puede aplicar a la esquizofrenia con historia familiar, no se generaliza a los casos "esporádicos"

RIESGO CLÍNICO DE PSICOSIS

Clinical staging model framework for psychotic and severe mood disorders*†

Stage	Definition	Target populations and referral sources	Potential interventions
0	Increased risk of psychotic or severe mood disorder No symptoms currently	• First-degree teenage relatives of probands	• Improved mental health literacy • Family education, drug education • Brief cognitive skills training
1a	Mild or non-specific symptoms (including neurocognitive deficits) of psychosis or severe mood disorder. Mild functional change or decline	• Screening of teenage populations • *Referral by:* primary care physicians; school counsellors	• Formal mental health literacy • Family psychoeducation, formal CBT • Active substance misuse reduction
1b	Ultra high risk: moderate but subthreshold symptoms, with moderate neurocognitive changes and functional decline to caseness (GAF, <70)	• *Referral by:* educational agencies; primary care physicians; emergency departments; welfare agencies	• Family psychoeducation, formal CBT • Active substance misuse reduction • Omega-3 fatty acids • Atypical antipsychotic agents • Antidepressant agents or mood stabilisers
2	First episode of psychotic or severe mood disorder Full threshold disorder with moderate to severe symptoms, neurocognitive deficits and functional decline (GAF, 30–50)	• *Referral by:* primary care physicians; emergency departments; welfare agencies; specialist care agencies; drug and alcohol services	• Family psychoeducation, formal CBT • Active substance misuse reduction • Atypical antipsychotic agents • Antidepressant agents or mood stabilisers • Vocational rehabilitation
3a	Incomplete remission from first episode of care Patient's management could be linked or fast-tracked to Stage 4	• Primary and specialist care services	• As for Stage 2, but with additional emphasis on medical and psychosocial strategies to achieve full remission
3b	Recurrence or relapse of psychotic or mood disorder, which stabilises with treatment at a GAF level, or with residual symptoms or neurocognition below the best level achieved after remission from the first episode	• Primary and specialist care services	• As for Stage 3a, but with additional emphasis on relapse prevention and strategies to detect "early warning signs"
3c	Multiple relapses, provided worsening in clinical extent and impact of illness is objectively present	• Specialist care services	• As for Stage 3b, but with emphasis on long-term stabilisation
4	Severe, persistent or unremitting illness, as judged by symptoms, neurocognition, and disability criteria Patient's management could be fast-tracked to this stage at first presentation, based on specific clinical and functional criteria (from Stage 2), or because of failure to respond to treatment (from Stage 3a)	• Specialised care services	• As for Stage 3c, but with emphasis on clozapine, other tertiary treatments, and social participation despite ongoing disability

Clinical staging:
a heuristic model for psychiatry and youth mental health

Patrick D McGorry, Rosemary Purcell, Ian B Hickie, Alison R Yung, Christos Pantelis and Henry J Jackson

MJA 2007; 187: S40–S42

Pródromo es el periodo entre el primer cambio apreciable en el comportamiento y la aparición del primer síntoma psicótico.

McGorry y cols., 1997

Modelo de McGorry/McGlashan:

- **Categoría 1-** **(Attenuated Positive Symptoms-APS)**
- **Categoría 2-** **(Brief Limited Intermittent Positive Symmptoms-BLIPS).**
- **Categoría 3- Alto riesgo genético o Trastorno esquizotípico + disminución en funcionamiento (30% escala GAF)**

Modelo Cornblatt/ Simon / Klosterkotter

- **Síntomas negativos atenuados (aplanamiento afectivo, anhedonia, abúlia, aislamiento social)**

(Miller y cols, 2002; Lencz y cols, 2004)

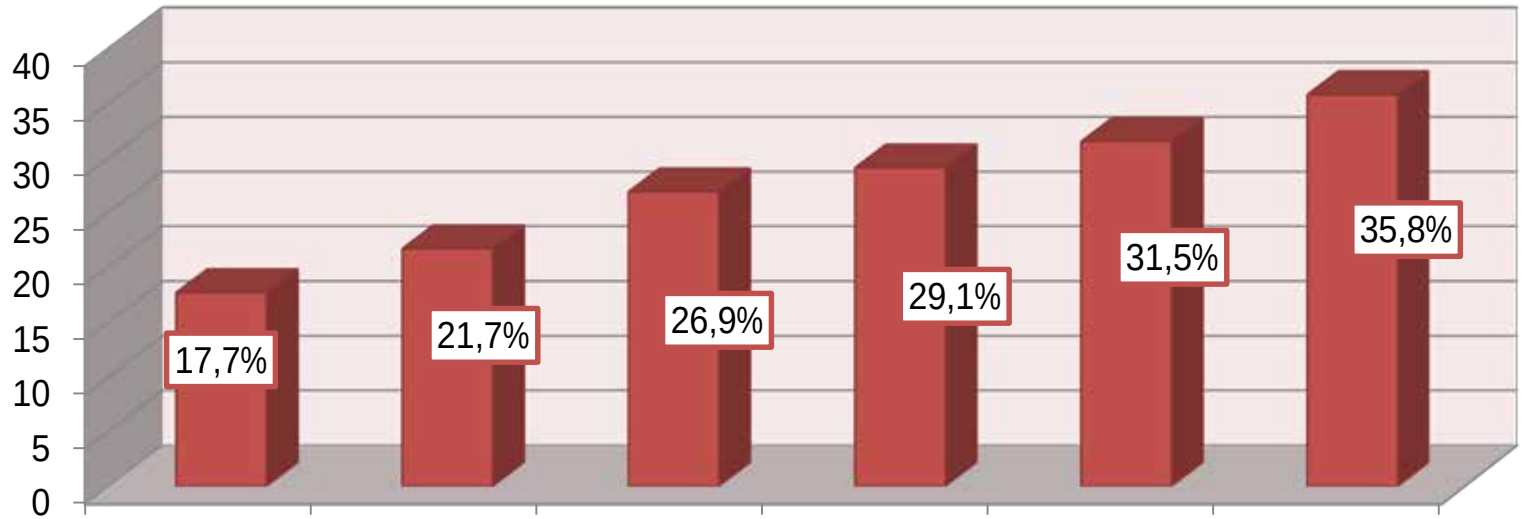
Arch Gen Psychiatry. 2012;69(3):220-229

META-ANALYSIS

Predicting Psychosis

Meta-analysis of Transition Outcomes in Individuals at High Clinical Risk

Paolo Fusar-Poli, MD, PhD; Ilaria Bonoldi, MD; Alison R. Yung, PhD; Stefan Borgwardt, PhD; Matthew J. Kempton, PhD; Lucia Valmaggia, PhD; Francesco Barale, PhD; Edgardo Caverzasi, PhD; Philip McGuire, PhD



Transición a psicosis en los seis primeros meses de seguimiento en una muestra de niños y adolescentes con síndrome de riesgo de psicosis:

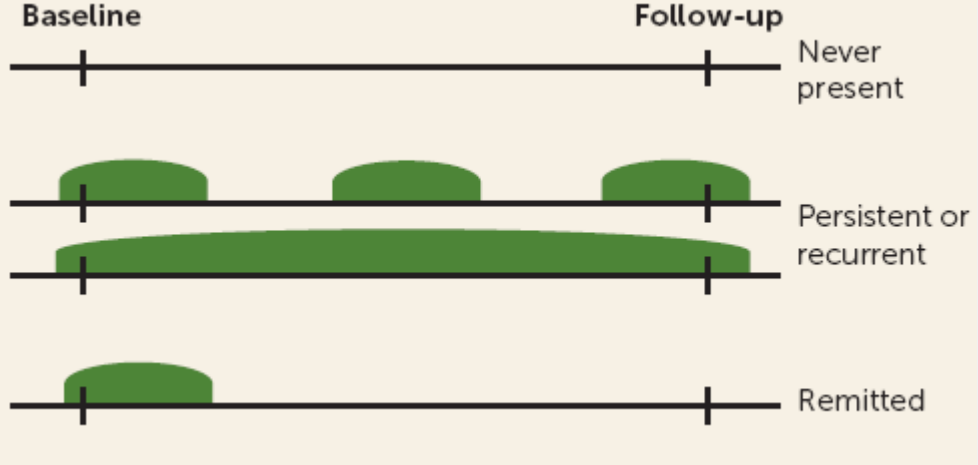
características clínicas y terapéuticas

- 52 sujetos, 15,2±1,7 años, 59% chicas
- 5/52: 9,6% transición a psicosis: 3 T.psicótico, 2 T.bipolar
- Todos los que transitaron con antec.familiares

Tabla 1. Características clínicas basales de los sujetos SRP que transitan a psicosis o no.

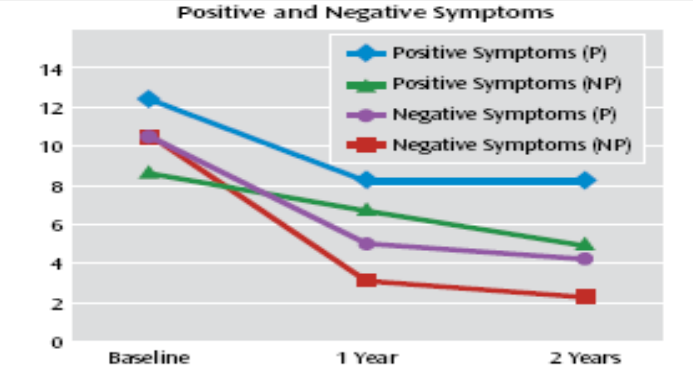
SOPS subscalas	Sujetos SRP que transitan (N=5)	Sujetos SRP que no transitan (N=47)	t	p
Positiva	7,8±1,9	9,8±4,6	-0,904	0,371
Negativa	13±4.8	13±5,4	-0,009	0,993
Desorganizada	6,5±1,7	5,2±3,2	0,813	0,421
General	12,5±1,3	8,3±3,6	2,308	**0,026**
SOPS total	40.8±7,7	36,1±12,0	0,765	0,449
GAF	40,8±17,2	50,1±11,8	-1,445	0,156
GAF social	6,6±1,1	6,1±1,4	-0,728	0,471
GAF rol	4,6±0,5	5,4±1,2	-1,446	0,157

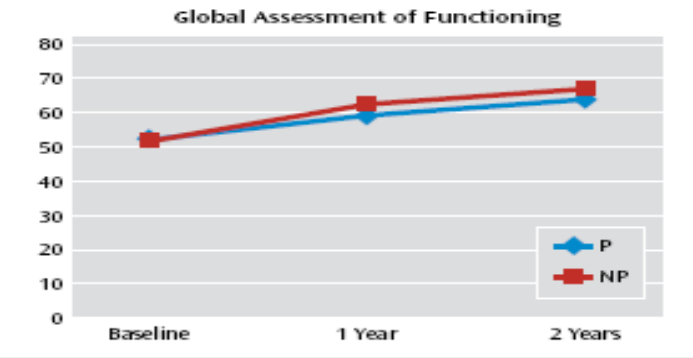
¿Y los que no presentan psicosis?



A los dos años:

- **32% Tr. Ansiedad**
- **14% Tr.depresivo**
- **4% Tr.uso de sustancias**
- **1.4% manía**





(Addington y cols, 2011)

¿Y los que no presentan psicosis?

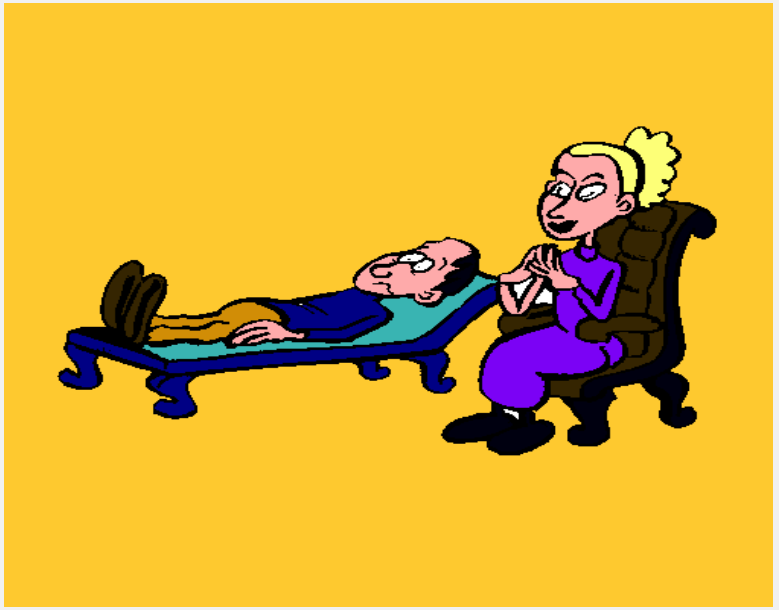
A los 7 años de media (2-14) de la evaluación basal:

- **28% síntomas atenuados**

- **49% Tr.estado de ánimo**
- **35% Tr. Ansiedad**
- **29% Tr.uso de sustancias**

- **7% nunca han cumplido criterios de ningún trastorno**

(Lin y cols, 2015)



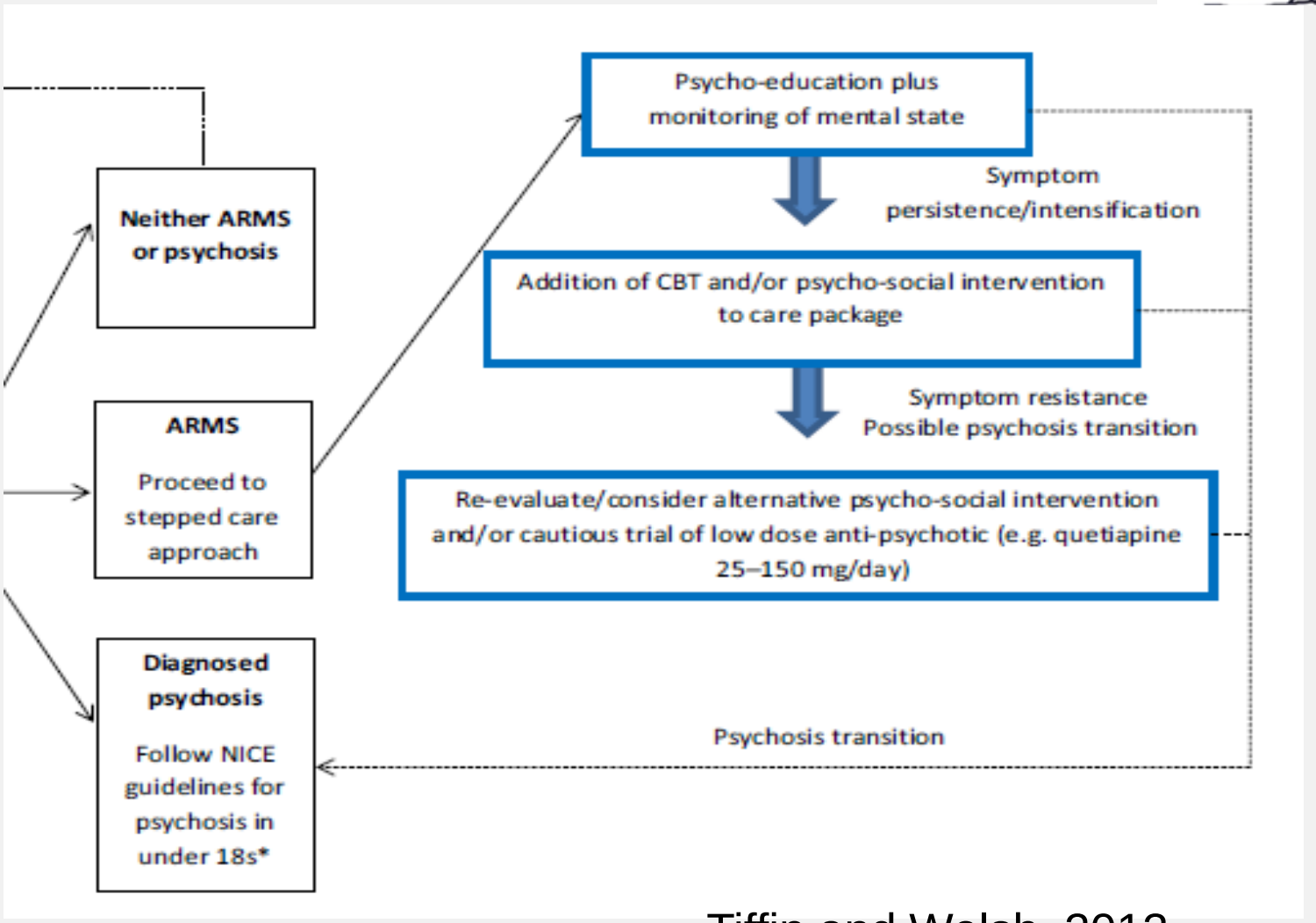
ESTRATEGIAS DE TRATAMIENTO

Pacientes con alto riesgo genético

No existe un tratamiento preventivo:
el tratamiento es sintomático

- En el TDAH, evitar los estimulantes (Kraemer et al, 2010)
  - Primero, tratamiento psicológico/reeducación
  - Si no funciona: atomoxetina de primera opción

Pacientes con alto riesgo clínico



Tiffin and Welsh, 2013

Pacientes con alto riesgo clínico

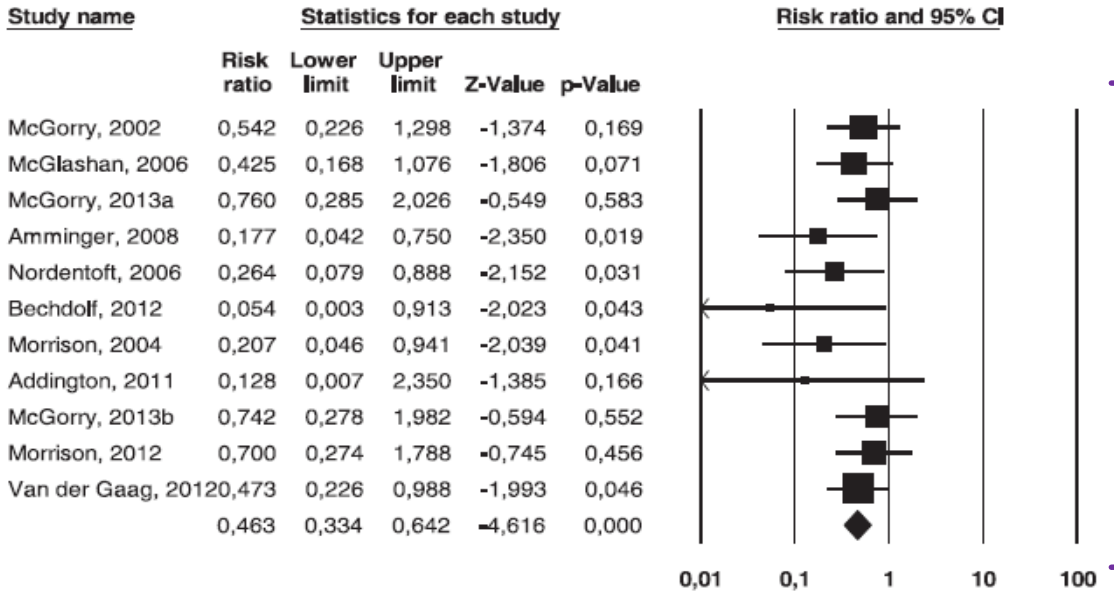
El tratamiento es sintomático

- Antidepresivos: si síntomas depresivos
- Benzodiacepinas: si síntomas de ansiedad
- Antipsicóticos atípicos, si síntomas positivos atenuados.
- Lamotrigina o quetiapina en depresión y antecedentes familiares de trastorno bipolar (Delbello et al, 2007)

Preventing a first episode of psychosis: Meta-analysis of randomized controlled prevention trials of 12 month and longer-term follow-ups

Mark van der Gaag [a,b,*], Filip Smit [a,c,d], Andreas Bechdolf [e], Paul French [f], Don H. Linszen [g], Alison R. Yung [f,h], Patrick McGorry [h], Pim Cuijpers [a]

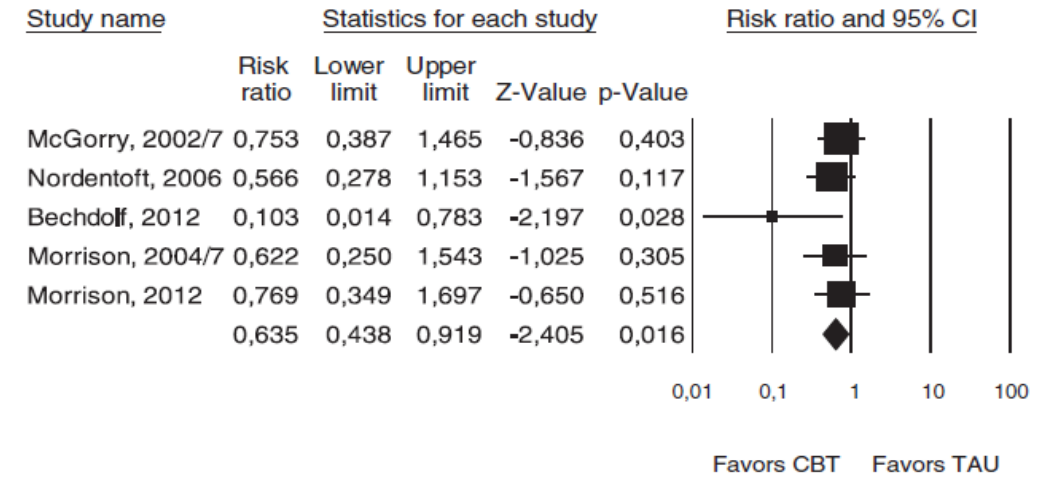
Schizophrenia Research 149 (2013) 56–62



Study name	Risk ratio	Lower limit	Upper limit	Z-Value	p-Value
McGorry, 2002	0,542	0,226	1,298	-1,374	0,169
McGlashan, 2006	0,425	0,168	1,076	-1,806	0,071
McGorry, 2013a	0,760	0,285	2,026	-0,549	0,583
Amminger, 2008	0,177	0,042	0,750	-2,350	0,019
Nordentoft, 2006	0,264	0,079	0,888	-2,152	0,031
Bechdolf, 2012	0,054	0,003	0,913	-2,023	0,043
Morrison, 2004	0,207	0,046	0,941	-2,039	0,041
Addington, 2011	0,128	0,007	2,350	-1,385	0,166
McGorry, 2013b	0,742	0,278	1,982	-0,594	0,552
Morrison, 2012	0,700	0,274	1,788	-0,745	0,456
Van der Gaag, 2012	0,473	0,226	0,988	-1,993	0,046
	0,463	0,334	0,642	-4,616	0,000

↓ Riesgo transición 12m: 54%

RR(0.46; 95CI=0.33-0.64)



Study name	Risk ratio	Lower limit	Upper limit	Z-Value	p-Value
McGorry, 2002/7	0,753	0,387	1,465	-0,836	0,403
Nordentoft, 2006	0,566	0,278	1,153	-1,567	0,117
Bechdolf, 2012	0,103	0,014	0,783	-2,197	0,028
Morrison, 2004/7	0,622	0,250	1,543	-1,025	0,305
Morrison, 2012	0,769	0,349	1,697	-0,650	0,516
	0,635	0,438	0,919	-2,405	0,016

↓ Riesgo transición 24-36m: 37%

RR(0.63 ;95CI=0.44-0.62)

European Psychiatry 30 (2015) 388–404

Contents lists available at ScienceDirect

European Psychiatry

journal homepage: http://www.europsy-journal.com

Original article

EPA guidance on the early intervention in clinical high risk states of psychoses

S.J. Schmidt [a], F. Schultze-Lutter [a], B.G. Schimmelmann [a], N.P. Maric [b], R.K.R. Salokangas [c], A. Riecher-Rössler [d], M. van der Gaag [e,f], A. Meneghelli [g], M. Nordentoft [h], M. Marshall [i,j], A. Morrison [k,l], A. Raballo [m,n], J. Klosterkötter [o,*], S. Ruhrmann [o]

- La intervención temprana ayuda tanto a prevenir un primer episodio psicótico o afectivo como a mejorar el funcionamiento

- La TCC y el tratamiento farmacológico puede ayudar a prevenir o posponer el inicio de una psicosis en adultos

Conclusiones

- Las estrategias de prevención pueden aplicarse a la psicosis, centradas en la prevención primaria específica y secundaria

- El seguimiento de pacientes con alto riesgo genético y clínico puede detectar más casos de psicosis que en la población general

- El tratamiento es sintomático. Puede ayudar a retrasar o disminuir la transición a psicosis

Habría que promover una
CULTURA sanitaria
basada en la PREVENCIÓN en la psicosis.

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