THE RESULTS OF A SPECIFIC CBT INTERVENTION IN YOUNG HELP-SEEKING PATIENTS WITH SOCIAL DECLINE AND AN ULTRA-HIGH RISK FOR DEVELOPING A FIRST EPISODE OF PSYCHOSIS

Zwartsluis
March 14th 2013
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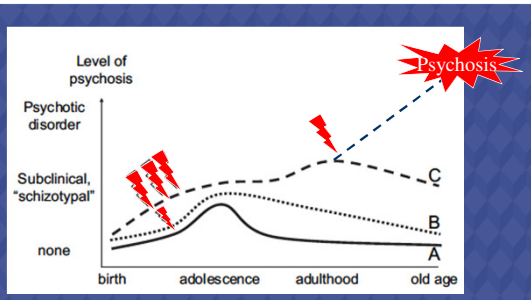
RISK FACTORS

The natural course of dopamine sensitisation



Collip et al, 2008

Baseline PLEs and exposure to trauma, cannabis and urbanisation and transition

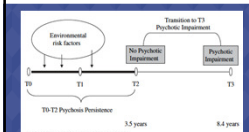
Table 2. *Interaction between baseline psychotic experiences and environmental load on the additive scale (risk difference), the Netherlands Mental Health survey and Incidence Study (NEMESIS)*

Environmental load[a]	Baseline psychotic experiences[b]	With follow-up psychotic experiences[c] (n)	Without follow-up psychotic experiences (n)	Risk of having follow-up psychotic experiences (%)	Risk difference (%)	95% CI	p
Zero	No	43	2161	1·9	18·2	13·4–22·9	0·000
	Yes	56	222	20·1			
One	No	52	1432	3·5	23·1	18·2–28·1	0·000
	Yes	83	228	26·7			
Two	No	14	285	4·7	26·4	18·6–34·2	0·000
	Yes	47	104	31·1			
Three	No	5	26	16·1	33·9	11·3–56·5	0·003
	Yes	14	14	50·0			
Additive interaction[d]				χ^2=6·9	df=1		0·004

CI, Confidence interval; df, degrees of freedom.
[a] Zero = no exposure; one = subjects exposed to only one of the three exposures; two = subjects exposed to two of the three exposures; three = subjects exposed to all exposures.
[b] Any Composite International Diagnostic Interview (CIDI) rating of 2, 3, 4, 5 or 6 on any of the T0 17 CIDI core psychosis items.
[c] Any CIDI rating of 2, 3, 4, 5 or 6 on any of the 17 CIDI psychosis items at T1 or T2.
[d] Test for significant difference in increase in risk with one unit change in exposure rating between group with and without psychotic experiences.

Cougnard et al, 2007

Persistence of PLEs and transition into psychosis



Dominguez et al, 2011

T0–T2 Psychosis Persistence			Transition to T3 Psychotic Impairment[a]					Transition to T3 Psychotic Impairment with additional exclusion[b]				
				Absolute Rates	Relative Risk (Logistic Regression)		Posttest Probability		Absolute Rates	Relative Risk (Logistic Regression)		Posttest Probability
Levels of Psychosis Persistence	*n*	%	*n*	%	OR (CI)	*p*	PP (%) (CI)	*n*	%	OR (CI)	*p*	PP (%) (CI)
Level 0; never	666	78.9	23	3.7	1[c]	—	0[c]	2	3.5	1[c]	—	0[c]
Level 1; once (sporadic)	132	15.6	6	5.3	1.5 (0.6–3.7)	0.414	5.3 (3.7–6.9)	4	3.8	1.1 (0.4–3.2)	0.893	3.8 (2.4–5.2)
Level 2; twice (recurrence)	33	3.9	4	16.0	5.0 (1.6–15.9)	0.006	16.0 (13.2–18.8)	3	10	3.1 (0.7–14.0)	0.151	10.0 (7.6–12.4)
Level 3; thrice (persistence)	14	1.7	3	27.3	9.9 (2.5–39.8)	0.001	27.3 (23.8–30.7)	3	37.5	16.5 (3.7–73.6)	0.000	37.5 (33.7–41.4)
Total subjects	845	100	36	4.3	—	—	—	30	3.5	—	—	—

MAAR....

UHR status is a pluripotent risk factor

	(95% CI)
Psychotic disorder	8% (6.8, 8.4)
Depressive disorder	13% (11.6, 13.9)
Anxiety disorder	4% (3.7, 5.0)
Alcohol/drug misuse disorder	6% (5.4, 7.1)
Any nonpsychotic disorder	7% (5.5, 7.4)
Combined depressive disorder and psychotic disorder	15% (13.8, 16.0)
Combined anxiety disorder and psychotic disorder	9% (7.6, 9.4)
Alcohol/drug misuse disorder and psychotic disorder	10% (8.7, 10.5)
Any disorder	7% (5.5, 7.4)

Table 2. *The effect of different forms of child sexual abuse (CSA) on adult psychiatric disorder (ORs and 95% confidence intervals)*

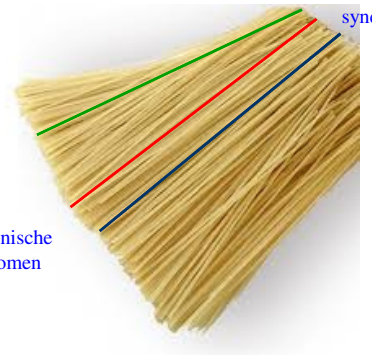
	Overall effect of sexual abuse	Talk most severe	Touch most severe	Non-consensual sexual intercourse
Common mental disorders (CMDs)				
Depressive disorder	1.74 (1.5–2.0)	1.82 (0.9–3.8) $p=0.112$	3.08 (2.0–4.8)	5.07 (2.7–9.6)
Mixed anxiety/depression	1.46 (1.3–1.6)	1.49 (0.97–2.3) $p=0.071$	1.88 (1.4–2.5)	3.72 (2.5–5.6)
GAD	1.64 (1.4–1.9)	1.98 (1.2–3.2) $p=0.005$	2.56 (1.8–3.6)	4.51 (2.6–7.9)
Panic	1.60 (1.3–2.0)	1.30 (0.4–4.0) $p=0.642$	2.78 (1.3–5.8) $p=0.007$	3.8 (1.6–8.7) $p=0.002$
Phobia	2.07 (1.7–2.5)	5.93 (3.4–10.2)	2.29 (1.3–4.2) $p=0.007$	12.12 (6.4–23.0)
OCD	1.84 (1.5–2.3)	4.53 (2.1–9.7)	2.57 (1.3–5.1) $p=0.008$	7.01 (2.9–17.2)
Dependence disorders				
Drug dependence	1.51 (1.3–1.8)	2.37 (1.4–4.0)	1.26 (0.7–2.3) $p=0.446$	5.49 (3.0–10.0)
Alcohol dependence	1.38 (1.2–1.6)	1.71 (1.0–2.9) $p=0.042$	1.41 (0.94–2.1) $p=0.093$	3.71 (2.2–6.4)
Disorders established from screening				
PTSD	1.93 (1.7–2.3)	3.98 (2.4–6.5)	2.95 (1.9–4.6)	8.23 (4.5–15.0)
Eating disorder	1.87 (1.7–2.1)	4.07 (2.9–5.8)	3.03 (2.2–4.2)	6.53 (4.1–10.4)

Table 3 Logistic regression showing association of psychosis with different levels of childhood sexual abuse

	Odds ratio (95% CI)	Adjusted odds ratio (95% CI)[a]	P
Uncomfortable sexual talk	1.25 (0.3–5.9)	1.16 (0.1–9.1)	0.776
Sexual touching	1.61 (0.5–4.8)	2.06 (0.6–7.2)	0.393
Non-consensual sexual intercourse	10.66 (5.0–22.9)	14.95 (5.2–43.1)	<0.0001

a. Adjusted for age, social class, educational level, household income, ethnicity and whether the participant had been brought up by both biological parents until the age of 16.

Etiologie ideaaltypisch

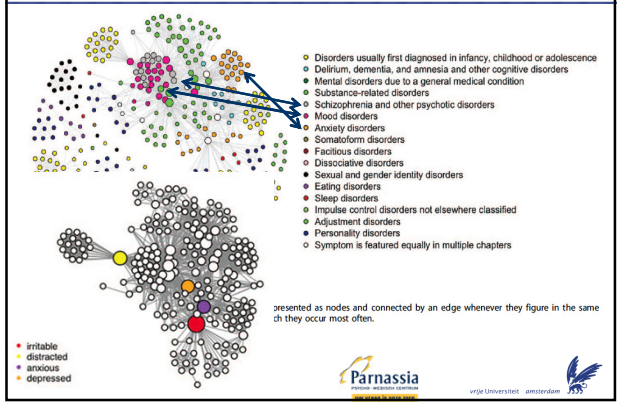


Etiologie in werkelijkheid

Table 1. Properties of the DSM-IV giant component.

Global properties		
Number of symptoms		208
Number of explicitly represented disorders		69
Number of edges		1949
Average shortest path length		2.60
Average number of shortest paths between two symptoms		3.01
Small-worldness index (SWI), based on transitivity		6.20
Clustering coefficient, based on transitivity		0.68
Average degree		18.74
Symptoms with highest degrees		
Symptom name	**Degree**	**ted symptoms**
1. Insomnia	71	34.1%
2. Psychomotor agitation	68	32.7%
3. Psychomotor retardation	61	29.3%
4. Depressed	60	28.8%
Symptoms with highest random walk betweenness		
Symptom name	**Betweenness**	**ted symptoms**
1. Irritable	0.24	23.6%
2. Distracted	0.17	24.0%
3. Anxious	0.16	23.1%
4. Depressed	0.16	28.8%

Symptoom associaties [Borsboom, 2011]



Symptomen zonder onderliggende syndromen

Etiologie ideaaltypisch

Klinisch syndroom

Subklinische symptomen

STATISTICAL POWER IS THE ISSUE IN PREVENTION RESEARCH

PLAYING TRICKS WITH EPIDEMIOLOGY

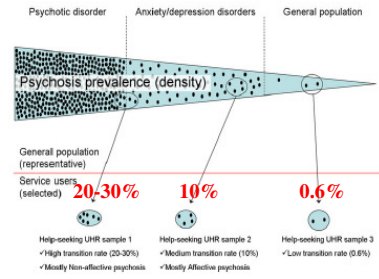
Introduction: The Extended Psychosis Phenotype—Relationship With Schizophrenia and With Ultrahigh Risk Status for Psychosis

Jim van Os[1,2,*] and Richard J. Linscott[1,3]

Extended Psychosis Phenotype: 61 cohorts

Prevalence	7.2%
Incidence	2.5%
Transition rate	7.4%

Linscott, R. J., & van Os, J. (2012). *Psychological Medicine*, 1-17.



Transition rate, success rate, and Number Needed to Treat

Van Os, J., & Delespaul, P. (2005). Toward a world consensus on prevention of schizophrenia. *Dialogues Clin Neurosci*, *7*(1), 53-67.

Predictive value (%)	Treatment success rate (%)	Number needed to treat	Number needed to inconvenience
5	25	80	79
5	50	40	39
[illegible]	[illegible]	[illegible]	19
20	50	10	9
[illegible]	[illegible]	[illegible]	7
50	50	4	3

Table II. The number of people screening positive for subclinical psychotic experiences who needed to be treated to prevent one case of full-blown psychotic disorder, as a function of the predictive value of the test and the success rate of the prodromal treatment in preventing transition to full-blown psychotic disorder.

IT IS ALL ABOUT SAMPLE ENRICHMENT

'Closing in' strategy

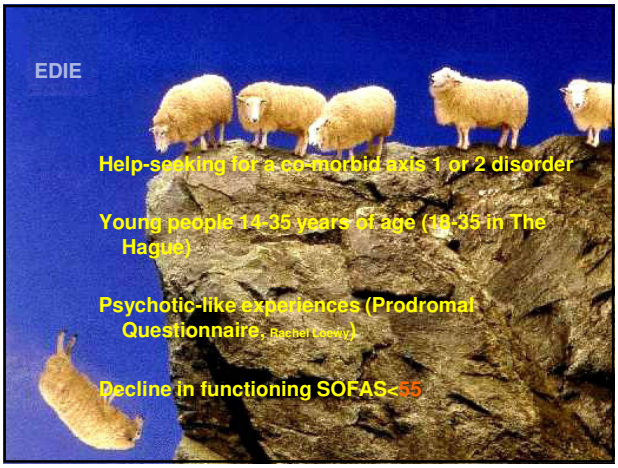
Van Os, J., & Delespaul, P. (2005). Toward a world consensus on prevention of schizophrenia. *Dialogues Clin Neurosci*, 7(1), 53-67.

Predictor A: subclinical psychotic experience	Predictor B: family history schizophrenia	Predictor C: A and B combined
1-year predictive value: 4%	1-year predictive value: 0.5%	2-year predictive value: 25%
Proportion of all schizophrenia predictable by this criterion: 90%	Proportion of all schizophrenia predictable by this criterion: 20%	Proportion of all schizophrenia predictable by this criterion: 18%

The combination of risk factors

Van Os, J., & Delespaul, P. (2005). Toward a world consensus on prevention of schizophrenia. *Dialogues Clin Neurosci*, 7(1), 53-67.

Group	Percentage Psychosis per 2 year
School children	0,04%
Children of psychiatric patients	1 %
1 attenuated psychotic symptom	8 %
1 attenuated psychotic symptom + high neuroticism	12 %
1 attenuated psychotic symptom + cannabis use	13 %
1 attenuated psychotic symptom + help-seeking	14 %
1 attenuated psychotic symptom + depressed mood	15 %
1 attenuated psychotic symptom + decline in social function.	16 %
More than 1 attenuated psychotic symptom	18 %
1 attenuated psychotic symptom + genetic risk	25 %
More than 1 attenuated psychotic symptom +depression	40 %



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ZonMW grant

Goals of CBT in UHR

'Manage' external risk factors

Prevent catastrophising and delusional interpretations to PLEs

→ Education on the effects of dopamine sensitisation on perception and reasoning
→ Metacognitive awareness training of risky thinking styles and ways to handle and cope with cognitive biases and PLEs

Risk management
- No cannabis or other drugs
- Keep attending school and work
- Share thoughts and convictions with others and discuss these

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Cognitive Behavioral Therapy for Subjects at Ultrahigh Risk for Developing Psychosis: A Randomized Controlled Clinical Trial

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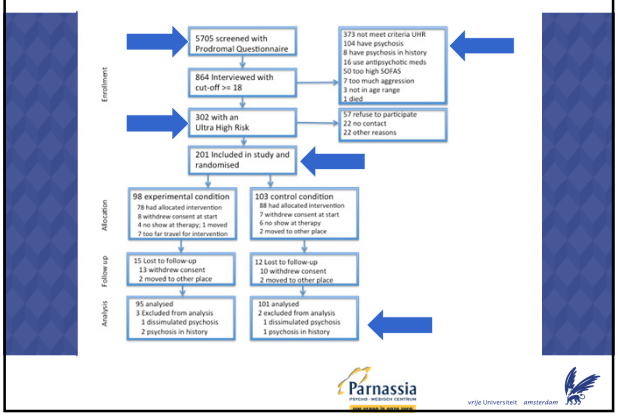
Academic Medical Centre & PsyQ Amsterdam
MHS Friesland, Leeuwarden and province

Flowchart of patients



Baseline characteristics

Table 1. Demographic Characteristics of the Experimental and Control Group

	Experimental (n = 98)	Control (n = 103)	Test Statistic	P value
Age (y), M (SD)	22.9 (5.6)	22.6 (5.5)	$t(199) = 0.365$	.715
Education in years, M (SD)	13.7 (2.5)	14.0 (2.8)	$t(193) = -0.926$	.355
Sex ratio, M/F	49/49	50/53	χ^2 (1) = 0.043	.836
Marital and living conditions			χ^2 (2) = 0.705	.703
Single	71	78		
With partner	22	22		
Employment/school			χ^2 (4) = 4.86	.303
Paid job	45	37		
Unpaid job	5	9		
School	28	29		
Unemployed	12	19		
Otherwise	8	4		
BDI depression, M (SD)	21.0 (11.8)	22.4 (12.8)	$t(197) = -0.779$	.437
CDS depression	6.0 (4.9)	6.3 (4.7)	$t(193) = -0.430$	.667
SIAS anxiety	31.1 (16.5)	32.3 (17.4)	$t(197) = -0.490$	.625
PBIQ-R dysfunctional beliefs	73.2 (15.1)	75.2 (17.5)	$t(196) = -0.886$	.377
CAARMS positive symptoms	10.2 (3.0)	10.3 (2.5)	$t(199) = 0.112$	.911
CAARMS negative symptoms	7.0 (3.3)	7.3 (3.6)	$t(198) = -0.561$	.575
CAARMS distress	173.1 (74.6)	171.0 (75.2)	$t(199) = 0.354$	.724
SOFAS social functioning	46.4 (4.8)	45.6 (5.1)	$t(199) = 0.994$	.321
MANSA quality of life	51.9 (12.4)	51.6 (12.7)	$t(192) = 0.274$	.785

Notes: BDI, Beck Depression Inventory; CDS, Calgary Depression Scales; SIAS, Social Interaction Anxiety Scale; PBIQ, Personal Beliefs about Illness Questionnaire; CAARMS, Comprehensive Assessment of At-Risk Mental States; SOFAS, Social and Occupational Assessment Scale; MANSA, Manchester Short assessment of Quality of Life.

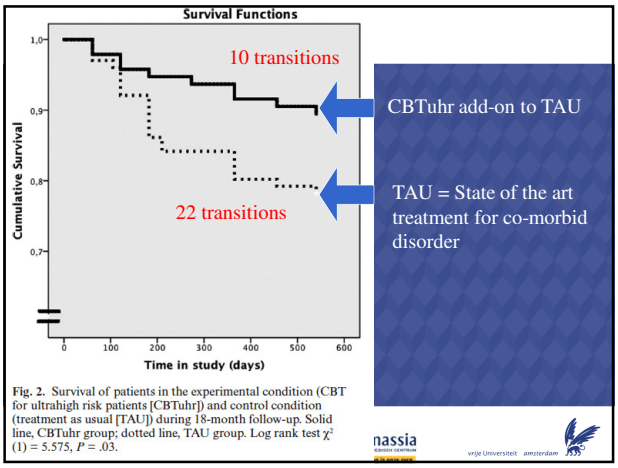


Fig. 2. Survival of patients in the experimental condition (CBT for ultrahigh risk patients [CBTuhr]) and control condition (treatment as usual [TAU]) during 18-month follow-up. Solid line, CBTuhr group; dotted line, TAU group. Log rank test χ^2 (1) = 5.575, P = .03.

Patient status at 18-month follow-up

	Remission	At risk mental state	Psychosis
CBTuhr (n=81)	57 (71%)	14 (17%)	10 (12%)
TAU (n=93)	53 (57%)	18 (19%)	22 (24%)

The Chi-square linear-by-linear association is significant: Chi2 (df=1)=4,266, p=.039

The NNT to prevent a transition was 9

The NNT to bring a patient into remission was 7

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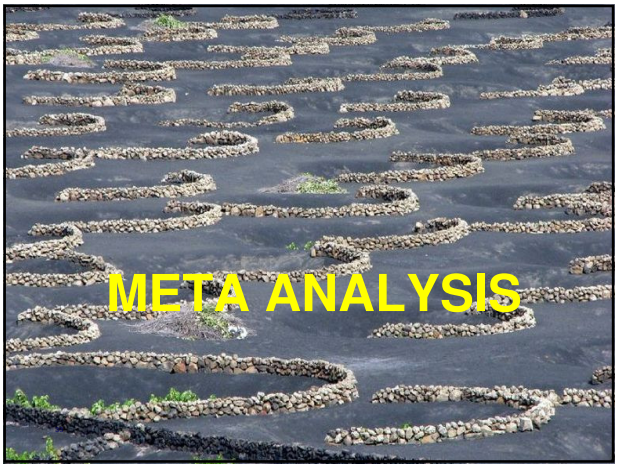

Preventing a first episode of psychosis: meta-analysis of randomized controlled prevention trials of 12 month and longer-term follow-ups

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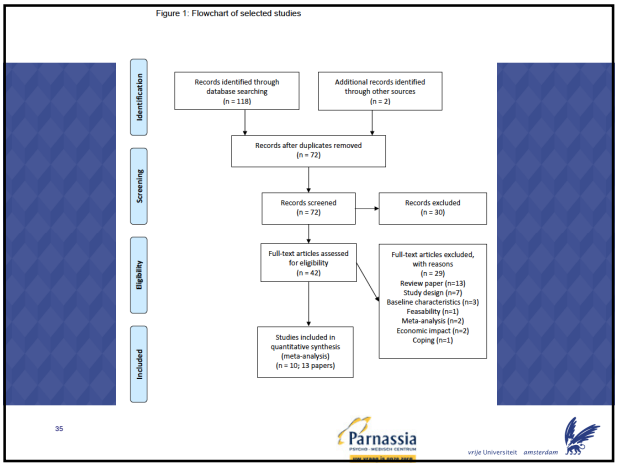

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Table 1: Description of the interventions, patient characteristics, location, transition criteria, and quality of the studies

Intervention	Author	Year	Duration Interv	Experimental Condition: Intervention	Drop-out %	Age Mean (SD)	Male Sex %	Control Condition: Intervention	Drop-out %	Age Mean (SD)	Male Sex (%)	Country	Transit. criterion	CTAM
Anti-psychotic Medication	McGorry et al.	2002	6 m.	1-2 mg /day Risperidone + CBT + NBI	54%	20 (3.6)	58%	NBI	0%	20 (3.6)	58%	AU	CAARMS	80
	McGlashan et al.	2006	12 m.	5-15 mg/day Olanzapine	55%	17 (4.0)	62%	Placebo	35%	18 (5.5)	68%	USA	SIPS	53*
	McGorry et al.	2012	12 m.	0.5-2 mg/day Risperidone + CBT	37%	18 (3.0)	35%	Placebo + ST	32%	19 (3.7)	46%	AU	CAARMS	81
Omega-3 fatty acid	Amminger et al.	2010	2 m.	1.2 gr/day Omega-3 fatty acid	7%	17 (2.4)	34%	Placebo	5%	16 (1.7)	33%	AUS	CAARMS	81
Integrated Psychological Intervention	Nordentoft et al.	2006	24 m.	ACT + SST+ MFP	12%	25 (5.6)	74%	CMHT	19%	25 (3.9)	59%	DK	ICD-10 F2 spectrum	62*
	Bechdolf et al.	2012	12 m.	CBT + SST + CR+ MFP	19%	25 (5.4)	62%	ST	12%	27 (6.2)	65%	GER	EIPS	53*
Cognitive Behavioral Therapy	Morrison et al.	2004	6 m.	CBT	30%	21 (4.9)	60%	Monitoring	30%	22 (5.2)	83%	UK	CAARMS	67
	Addington et al.	2011	6 m.	CBT	41%	21 (4.5)	62%	ST	38%	21 (4.5)	75%	CAN	SIPS	76
	McGorry et al.	2012	12 m.	Placebo + CBT	34%	18 (2.7)	39%	Placebo + ST	32%	19 (3.7)	46%	AU	CAARMS	81
	Morrison et al.	2012	6 m.	CBT	34%	21 (4.2)	62%	Monitoring	35%	21 (4.5)	63%	UK	CAARMS	87
	van der Gaag et al.	2012	6 m.	CBT + TAU	15%	23 (5.6)	50%	TAU	12%	23 (5.5)	49%	NL	CAARMS	87

CTAM = Clinical Trial Assessment Measure; CBT = Cognitive behavioral Therapy; NBI=Needs Based Intervention; ST=Supportive Therapy; ACT=Assertive Community Treatment ; SST= Social skills training; MFP= Multi-family psycho-education; CMHT=Community Mental Health Team; CR=Cognitive remediation; TAU= standard treatment for non-psychotic disorder; AU=Australia; USA=United States of America; AUS=Austria; DK=Denmark; Ger=Germany; UK=United Kingdom; Can=Canada; NL=Netherlands; CAARMS=Comprehensive Assessment of At Risk Mental State; SIPS=Structured Interview for Prodromal Symptoms; ICD-10=International Classification of Diseases, version 10; EIPS=early Initial Prodromal State; *=inferior study quality.

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Table 2: Primary studies included in the meta-analysis: risk by condition, relative risk (RR), 95% confidence interval of RR, and p-value (Intention-to-Treat)

Studies included in the meta-analysis: risk by condition (12 months follow-up)

Intervention	Author	Year	Follow-up period	Experimental Condition		Control Condition		RR	95% CI	p-value
				Event rate	Event %	Event rate	Event %			
Anti-psychotic Medication	McGorry et al.	2002	12 months	6/31	19%	10/28	36%	.542	0.22-1.30	p=.169
	McGlashan et al.	2006	12 months	5/31	16%	11/29	38%	.425	0.16-1.08	p=.071
	McGorry et al.	2012	12 months	7/43	16%	6/28	21%	.760	0.28-2.03	p=.583
Omega-3 fatty acid	Amminger et al.	2010	12 months	2/41	5%	11/40	28%	.177	0.04-0.75	p=.019
Integrated Psychological Interv.	Nordentoft et al.	2006	12 months	3/42	7%	10/37	27%	.264	0.08-0.89	p=.031
	Bechdolf et al.	2012	12 months	0/63	0%	9/65	14%	.054	0.00-0.91	p=.043
Cognitive Behavioral Therapy	Morrison et al.	2004	12 months	2/37	2%	6/23	26%	.207	0.05-0.94	p=.041
	Addington et al.	2011	12 months	0/27	0%	3/24	13%	.128	0.01-2.40	p=.166
	McGorry et al.	2012	12 months	7/44	16%	6/28	21%	.742	0.26-1.98	p=.552
	Morrison et al.	2012	12 months	7/144	5%	10/144	7%	.700	0.27-1.79	p=.456
	Van der Gaag et al.	2012	12 months	9/98	9%	20/103	19%	.473	0.23-1.00	p=.046

Studies included in the meta-analysis: risk by condition (medium-term follow-up: 24-48 months)

	Author	Year	Follow-up period	Experimental Condition		Control Condition		RR	95% CI	p-value
				Event rate	Event %	Event rate	Event %			
	McGorry et al.	2002/2007	36-48 months	10/31	32%	12/28	43%	.753	0.39-1.47	p=.403
	Nordentoft et al.	2006	24 months	9/42	21%	14/37	38%	.566	0.28-1.15	p=.117
	Bechdolf et al.	2012	24 months	1/63	2%	10/65	15%	.103	0.01-0.78	p=.028
	Morrison et al.	2004/2007	36 months	7/37	19%	7/23	30%	.622	0.25-1.54	p=.305
	Morrison et al.	2012	24 months	10/144	7%	13/144	9%	.769	0.35-1.70	p=.516

RR=Risk Ratio; 95% CI=95 % confidence interval

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Figure 2: Forest plot of risk ratio's for the transition to psychosis within 12 months

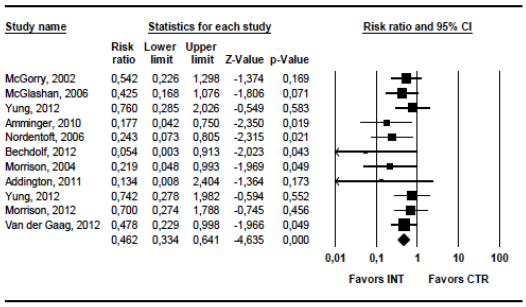

Figure 3: Forst plot: 24 to 48 month follow-up

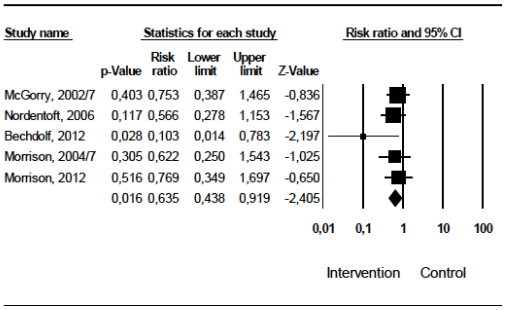

Table 3: Meta-analytic results by follow-up at 12months and 24-48 months and type of intervention

	K	N	RR	95% CI	z-value	p-value	I^2	95% CI	NNT	95% CI	τ^2
12-month Follow-up	11	1140	0.463	0.33-0.64	4.589	0.000	0%	0-60	9	6-15	0.00
* Antipsychotic medication (plus CBT in 2 studies)	3	180	0.553	0.32-0.94	2.177	0.029	0%	0-90	7	4-77	0.00
* Omega-3	1	81	0.177	0.04-0.75	2.350	0.019	0%	*	4	4-14	0.00
* Integrated Psychological Interventions	2	267	0.204	0.07-0.64	2.720	0.007	2%	*	7	4-13	0.16
* Cognitive Behavioral Therapy	5	672	0.516	0.32-0.82	2.771	0.006	0%	0-79	13	7-71	0.00
Medium-term Follow-up (24 to48-months)	5	614	0.635	0.44-0.92	2.405	0.016	0%	0-79	12	6-50	0.00

K= Number of studies; N=Number of participants; RR = Risk ratio; 95%CI = 95 percent confidence interval; I^2 = Heterogeneity; NNT = number needed to treat; τ^2=Tau-square; *=95%CI of I^2 cannot be calculated with df=K-1<3.

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Results

Early detection and indicated prevention are about to become an evidence-based intervention

CBT that showed a transition reduction of 48% and a NNT of 13 in five RCTs with 672 subjects

CBT uhr is cost-effective: increased health for reduced costs

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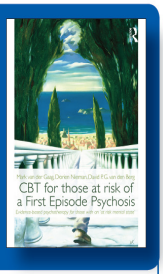
From Routledge

CBT for Those at Risk of a First Episode Psychosis

Evidence-based psychotherapy for those with an 'At Risk Mental State'



By **Mark van der Gaag**, VU University and Parnassia Psychiatric Institute, The Netherlands, **Dorien Nieman**, Academic Medical Centre, The Netherlands and **David P. G. van den Berg**, Parnassia Psychiatric Institute, The Netherlands

"This book is an important contribution to the treatment of people with a high risk for developing psychosis. The authors succeeded in integrating recent research findings on cognitive biases and the psychology of salience into a cognitive behavioural therapy framework. The authors are excellent researchers and therapists and this effective therapy is described stepwise, making this handbook transparent and easy to read." - **Aaron T. Beck, M.D., Professor of Psychiatry, University of Pennsylvania, USA**

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