EBRO MODULE VROEGE PSYCHOSE

Bijlagen

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Netwerk Kwaliteitsontwikkeling GGz
Helling 12
3523 CC UTRECHT
030 737 04 70
secretariaat@kwaliteitsontwikkelingggz.nl

www.kwaliteitsontwikkelingggz.nl

Kwaliteits-
ontwikkeling
GGz

Netwerk voor goede zorg

Inhoudsopgave

Hoofdstuk 3 Organisatie van zorg

Bijlage 3.A Reviewprotocollen Organisatie van zorg

Onderwerp	**H. Organisatie van zorg**
Uitgangsvragen	1. In welke mate beïnvloedt de match tussen patiënt en behandelaar de aard en mate van respons op behandeling en hoe kan een optimale match worden gewaarborgd?
Criteria voor inclusie van studies in de review	
• *Populatie*	• Personen van 12 jaar of ouder met een eerste psychose behandeling • Percentage personen met FEP per studie dient minimaal 75% te zijn. • Co-morbiditeit mag aanwezig zijn (middelenafhankelijkheid bijvoorbeeld) • Exclusie: prodromal states, persons at risk, Prevention of first episode
• *Interventie*	• Therapeutische relatie van goede kwaliteit
• *Vergelijking*	• Therapeutische relatie van onvoldoende kwaliteit
• *Kritische Uitkomstmaten*	• Symptomen • Functioneren (sociaal of psychosociaal) • Kwaliteit van leven • Remissie/relapse • (Her)opnames
• *Belangrijke uitkomstmaten*	• Mentaal welbevinden (, depressie, angst, manie) • Mortaliteit (inclusief suïcide), • Globaal welbevinden, • Bijwerkingen, • Zorgconsumptie (op langere termijn), • Participatie werk of school / Maatschappelijk functioneren,
• *Studiedesign*	• RCT • Observationele studies
• *Minimum omvang steekproef*	-
Search strategie	Narratief
Databases searched	
Data searched	-
De review strategie	Naratief review

Onderwerp	**H. Organisatie van zorg**
Uitgangsvragen	2. Hoe is het effect van inzet van gespecialiseerde intensieve VIP teams op toeleiding naar zorg, ketenafspraken en uitkomsten van zorg bij mensen met een vroege psychose ten opzichte van inzet van andere ambulante teams?
Criteria voor inclusie van studies in de review	
• *Populatie*	• Personen van 12 jaar of ouder met een eerste psychose behandeling • Percentage personen met FEP per studie dient minimaal 75% te zijn. • Co-morbiditeit mag aanwezig zijn (middelenafhankelijkheid bijvoorbeeld) • Exclusie: prodromal states, persons at risk, Prevention of first episode
• *Interventie*	• Gespecialiseerde intensieve multidisciplinaire zorg
• *Vergelijking*	• Care as usual (CAU) (niet gespecialiseerde zorg)
• *Kritische Uitkomstmaten*	• Aantal nieuwe patiënten per 100.000 inwoners/jaar • DUP • Verlaten van de studie om welke reden dan ook (met of zonder aansluitende behandeling elders) • Toe- en afname van symptomen

	• Remissie/relapse als dichotome uitkomstmaat voor symptomatisch herstel dan wel terugval • Functioneren (sociaal of psychosociaal)
• *Belangrijke uitkomstmaten*	• Mentaal welbevinden (, depressie, angst, manie) • Mortaliteit (inclusief suïcide), • Globaal welbevinden, • Bijwerkingen, • Heropnames, • Zorgconsumptie (op langere termijn), • Participatie werk of school / Maatschappelijk functioneren, • Binding school met zorg (???)
• *Studiedesign*	• Meta-analyses en systematic reviews
• *Minimum omvang steekproef*	-
Search strategie	Narratief
Databases searched	MA's en SR's aangeleverd door de werkgroep. + update MA van NICE schizophrenia?
Data searched	-
De review strategie	Naratief review van MA's en SR's

Bijlage 3.B Literatuursearch

Search history organisatie van zorg bij vroege psychose uitgeschreven

Voor de organisatie van zorg bij vroege psychose is gezocht in vier databases: PsycInfo, PubMed, CINAHL en de Cochrane database. Er is gezocht vanaf 2000 en er is niet gelimiteerd op taal. Er is specifiek naar systematic reviews en meta-analyses gezocht.
De searches zijn uitgevoerd op 7 mei 2015.

PsycInfo
In PsycInfo is gezocht op de volgende thesaurustermen voor schizofrenie en psychose:
DE "Schizophrenia" OR DE "Acute Schizophrenia" OR DE "Schizophreniform Disorder" OR DE "Schizoaffective Disorder" OR DE "Delusions" OR DE "Hallucinations" OR DE "Psychosis" OR DE "Acute Psychosis". Aangevuld met de volgende woorden in titel en keyword: "delusional disorder*" OR severe mental ill* OR severe mental disorder* OR psychotic OR psychosis OR psychoses OR schizo*.

Om aan te geven dat het om een 'vroege' psychose moet gaan, zijn al deze zoektermen gecombineerd met de woorden "early symptom*" OR onset OR "early signs" OR first-episode OR "acute phase" in het titel- en keywordveld.

Voor organisatie van zorg is gezocht op de thesaurustermen: DE "Continuum of Care" OR DE "Evidence Based Practice" OR DE "Health Care Utilization" OR DE "Mental Health Program Evaluation" OR DE "Disease Management" OR DE "Interdisciplinary Treatment Approach".
Deze termen zijn aangevuld met de volgende woorden in titel, keyword en abstract: "assertive treatment" OR "assertive community treatment" OR "assertive case management" OR "assertive early intervention" OR "early intervention service*" OR "early intervention program*" OR "early interventions" OR "collaborative care" OR "chronic care model" OR "managed care" OR "collaborative chronic care" OR "integrated care" OR "disease management" OR "multidisciplinary team*" OR "multidisciplinary approach*" OR "multidisciplinary care".

PubMed
In PubMed is gezocht op de volgende thesaurustermen voor schizofrenie/psychose: "Psychotic Disorders"[Mesh:NoExp] OR "Schizophrenia"[Mesh] OR "Hallucinations"[Mesh] OR "Delusions"[Mesh].

Deze termen zijn aangevuld met "severe mental ill" OR "severe mental disorder" OR "severe mentally ill" OR "severe mental disorders" OR "severe mental illness" OR "severe mental illnesses" OR psychotic OR psychosis OR psychoses OR schizophrenia OR schizophrenic OR "delusional disorder" in de velden titel, abstract en other term.

Om aan te geven dat het om een ‘vroege’ psychose moet gaan, is er een combinatie gemaakt met dezelfde woorden die gebruikt zijn in PsycInfo. In PubMed zijn ze gezocht in het titel, abstract en other term veld.

Verder is gezocht op de thesaurusterm "Schizophrenia, Childhood"[Mesh] en "childhood onset schizophrenia" in titel, abstract en other term veld. Ook is specifiek gezocht op de zoektermen "early psychosis" OR "first episode psychosis" OR "early psychoses" OR "first episode psychoses" in het titel, abstract en other term veld.

Voor organisatie van zorg is gezocht op de thesaurustermen: "Disease Management"[Mesh:NoExp] OR "Delivery of Health Care, Integrated"[Mesh:NoExp] OR "Early Medical Intervention"[Mesh] OR "Community Mental Health Services"[Mesh] OR "Evidence-Based Practice"[Mesh].
Deze termen zijn aangevuld met dezelfde woorden in titel en abstract als bij PsycInfo gebruikt zijn.

CINAHL
In CINAHL is gezocht op de thesaurustermen MH "Schizophrenia, Childhood" en "childhood onset schizophrenia" OR "acute schizophrenia" OR "acute phase" AND schizophrenia in het titelveld.
De algemene thesaurustermen voor schizofrenie/psychose: MH "Schizoaffective Disorder" OR MH "Schizophrenia" OR MH "Delusions" OR MH "Hallucinations" OR MH "Psychotic Disorders" zijn gecombineerd met "delusional disorder*" OR severe mental ill* OR severe mental disorder* OR psychotic OR psychosis OR psychoses OR schizo* in het titelveld.

Al deze zoektermen zijn vervolgens gecombineerd met "early symptom*" OR onset OR "early signs" OR first-episode OR "acute phase" in het titelveld, om aan te geven dat het om een ‘vroege’ psychose moet gaan.

Ook is specifiek gezocht op de zoektermen "early psychosis" OR "first episode psychosis" OR "early psychoses" OR "first episode psychoses" in het titelveld.

Voor organisatie van zorg is gezocht op de thesaurusterm MH "Professional Practice, Evidence-Based+" aangevuld met dezelfde woorden in titel en abstract als zijn gebruikt in PsycInfo.

Cochrane
Er is gezocht op de volgende woorden in titel, abstract en keyword: "assertive treatment" OR "assertive community treatment" OR "assertive case management" OR "assertive early intervention" OR "early intervention service" OR "early intervention program" OR "early interventions" OR "collaborative care" OR "chronic care model" OR "managed care" OR "collaborative chronic care" OR "integrated care" OR "disease management" OR "multidisciplinary team" OR "multidisciplinary approach" OR "multidisciplinary teams" OR "multidisciplinary approaches" OR "multidisciplinary care" OR "early intervention services" OR "early intervention programs".

Deze titels zijn handmatig gecheckt op ‘psychose’.

Totalen:
In totaal zijn in PubMed 57 systematic reviews en meta-analyses gevonden, in
PsycInfo 4, in CINAHL 1 en 5 Cochrane reviews. Dit zijn er in totaal: 67. Deze titels zijn ontdubbeld en er zijn 4 dubbele titels verwijderd. Er blijven dan 63 titels over.

Search history therapeutische alliantie bij schizofrenie en psychose
(niet beperkt tot *vroege* psychose)

PsycInfo

#	Query	Limiters/Expanders	Last Run Via	Results
S14	S6 AND S11	Limiters - Publication Type: All Journals; Language: Dutch, English, German Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	206
S13	S6 AND S11	Limiters - Publication Type: All Journals Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	234
S12	S6 AND S11	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	284
S11	S7 OR S8 OR S9 OR S10	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	8,738
S10	TI ("therapeutic relation*" OR "Psychotherapy relation*" OR "psychotherapeutic relation*" OR "therapy relation*") OR KW ("therapeutic relation*" OR "Psychotherapy relation*" OR "psychotherapeutic relation*" OR "therapy relation*")	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	3,324
S9	TI "therapeutic relation*" OR "Psychotherapy relation*" OR "psychotherapeutic relation*" OR "therapy relation*"	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	1,079
S8	DE "Therapeutic Alliance"	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	3,303
S7	TI alliance* OR KW alliance*	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	5,128
S6	S1 OR S2 OR S3 OR S4 OR S5	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	116,496
S5	DE "Psychosis" OR DE "Acute Psychosis"	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	21,808
S4	TI ("early psychosis" OR "first episode psychosis" OR "early psychoses" OR "first episode psychoses") OR KW ("early psychosis" OR "first episode	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	1,643

	psychosis" OR "early psychoses" OR "first episode psychoses")			
S3	TI ("delusional disorder*" OR severe mental ill* OR severe mental disorder* OR psychotic OR psychosis OR psychoses OR schizo*) OR KW ("delusional disorder*" OR severe mental ill* OR severe mental disorder* OR psychotic OR psychosis OR psychoses OR schizo*)	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	109,933
S2	DE "Schizophrenia" OR DE "Acute Schizophrenia" OR DE "Schizophreniform Disorder" OR DE "Schizoaffective Disorder" OR DE "Delusions" OR DE "Hallucinations"	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	78,905
S1	DE "Childhood Schizophrenia" OR TI "childhood onset schizophrenia" OR KW "childhood onset schizophrenia"	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	992

PubMed

Recent queries

Search	Add to builder	Query	Items found	Time
#17	Add	Search (#7 AND #13)	1280	04:08:58
#29	Add	Search (#7 AND #28)	134	04:07:18
#28	Add	Search (#18 OR #25)	3318	04:07:04
#26	Add	Search (#7 AND #25)	42	04:04:56
#25	Add	Search (“therapeutic relations" [TI] OR "Psychotherapy relations" [TI] OR "psychotherapeutic relations" [TI] OR "therapy relations" [TI] OR "therapeutic relationship" [TI] OR "Psychotherapy relationship" [TI] OR "psychotherapeutic relationship" [TI] OR "therapy relationship" [TI] OR "therapeutic relationships" [TI] OR "Psychotherapy relationships" [TI] OR "psychotherapeutic relationships" [TI] OR "therapy relationships" [ti] OR "therapeutic relation" [TI] OR "Psychotherapy relation" [TI] OR "psychotherapeutic relation" [TI] OR "therapy relation" [TI])	486	04:03:33
#19	Add	Search (#7 AND #18)	93	03:53:13
#18	Add	Search (alliance [ti] OR alliances [ti])	2836	03:52:46
#16	Add	Search (#7 AND #15)	1302	03:51:23
#15	Add	Search (#13 OR #14)	53458	03:50:52
#14	Add	Search ("therapeutic alliance"[ti] OR "therapeutic alliances"[ti])	431	03:50:40
#13	Add	Search ("Professional-Patient Relations"[Mesh:NoExp]) OR "Nurse-Patient Relations"[Mesh]	53227	03:50:07
#7	Add	Search (#1 OR #2 OR #3 OR #4 OR #5 OR #6)	168846	03:48:12
#6	Add	Search "Schizophrenia, Childhood"[Mesh] OR "childhood onset schizophrenia" [tiab] OR "childhood onset schizophrenia" [ot]	1624	03:47:52

Recent queries

Search	Add to builder	Query	Items found	Time
#5	Add	Search (("delusional disorder" [tiab] OR "delusional disorders" [tiab] OR "delusional disorder" [ot] OR "delusional disorders" [ot]))	713	03:47:28
#4	Add	Search (psychotic [tiab] OR psychosis [tiab] OR psychoses [tiab] OR schizophrenia [tiab] OR schizophrenic [tiab] OR psychotic [ot] OR psychosis [ot] OR psychoses [ot] OR schizophrenia [ot] OR schizophrenic [ot])	132374	03:47:13
#3	Add	Search ("severe mental ill" [tiab] OR "severe mental disorder" [tiab] OR "severe mentally ill" [tiab] OR "severe mental disorders" [tiab] OR "severe mental illness" [tiab] OR "severe mental illnesses" [tiab] OR "severe mental ill"[ot] OR "severe mental disorder"[ot] OR "severe mentally ill"[ot] OR "severe mental disorders"[ot] OR "severe mental illness"[ot] OR "severe mental illnesses"[ot])	3517	03:46:57
#2	Add	Search "Psychotic Disorders"[Mesh:NoExp] OR "Schizophrenia"[Mesh] OR "Hallucinations"[Mesh] OR "Delusions"[Mesh]	119777	03:45:28
#1	Add	Search ("first episode psychosis" [tiab] OR "first episode psychosis" [ot] OR "acute psychosis" [tiab] OR "acute psychosis" [ot] OR "acute psychoses"[tiab] OR "acute psychoses" [ot] OR "early psychosis" [tiab] OR "early psychoses"[tiab] OR "first episode psychoses" [tiab] OR "early psychosis" [ot] OR "first episode psychoses" [ot] OR "early psychoses" [ot] OR "first episode psychoses" [ot])	3156	03:45:11

#13 professional-patient relations was te algemeen. Leverde teveel ruis op. Niet gebruikt. Breed gezocht op ‘alliance*”.

CINAHL

#	Query	Limiters/Expanders	Last Run Via	Results
S10	S7 OR S9	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL	41
S9	S4 AND S8	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL	11
S8	TI "therapeutic relation*" OR "Psychotherapy relation*" OR "psychotherapeutic relation*" OR "therapy relation*"	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL	249
S7	S4 AND S6	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL	31
S6	TI "alliance*"	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL	1,779
S5	"therapeutic alliance*"	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL	464
S4	S1 OR S2 OR S3	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL	15,607

S3	TI "delusional disorder*" OR severe mental ill* OR severe mental disorder* OR psychotic OR psychosis OR psychoses OR schizo*	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL	8,999
S2	(MH "Schizoaffective Disorder") OR (MH "Schizophrenia") OR (MH "Delusions") OR (MH "Hallucinations") OR MH "Psychotic Disorders"	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL	14,144
S1	MH "Schizophrenia, Childhood"	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL	28

Totalen:

PsycInfo: 206
PubMed: 134
CINAHL: 41
Totaal: 381 Ontdubbeld en 103 dubbele verwijderd. Blijft over: 2

Hoofdstuk 4 Mensen met een ultrahoog risico op het ontwikkelen van een psychose

Bijlage 4.A Review protocol

Onderwerp	**A. Mensen met een Ultrahoog Risico op het ontwikkelen van een psychose**
Uitgangsvragen	1. Welke methoden zijn geschikt voor screening van milde psychotische verschijnselen? 2. Welke methoden zijn geschikt voor diagnostiek van milde psychotische verschijnselen? 3. Welke interventies (psychologisch, psychosociaal en farmacologisch) kunnen het ontstaan van een psychose uitstellen of anderszins tot een betere uitkomst leiden bij mensen met een Ultrahoog Risico op het ontwikkelen van een psychose?
Criteria voor inclusie van studies in de review	
• *Populatie*	Personen van 12 of ouder (die ultrahoog risico hebben op het ontwikkelen van een eerste psychose) (UHR heeft alleen symptomen op subklinisch niveau. Het gaat dan om bizarre opvattingen, achterdocht, perceptuele aberraties en desorganisatie. Bij fep gaat het om pos en neg symptomen.)
• *Interventie (A4)*	• *Farmacologische interventies:* alle antipsychotica welke in Nederland geregistreerd zijn voor de behandeling van psychosen bij jongeren. Off-label gebruik kan overwogen worden indien duidelijk onderbouwd door bewijs. • *Psychologische interventies:* CGT, CRT, Counseling en steunende therapie, Familie interventies, Psychodynamische therapie, Psycho-educatie, Sociale vaardigheidstraining, Vaktherapie
• *Vergelijking*	• Placebo • Care as usual (CAU) • Wachtlijst • Een van de bovengenoemde interventies als alternatieve behandeling
• *Kritische Uitkomstmaten*	• Transitie naar psychose • Duur tot transitie naar psychose • Toe- en afname van symptomen • Functioneren (sociaal of psychosociaal)
• *Belangrijke Uitkomstmaten*	• Mentaal welbevinden (depressie, angst, manie) • Mortaliteit (inclusief suïcide) • Globaal welbevinden • Verlaten van de studie om welke reden dan ook • Bijwerkingen
• *Studiedesign*	• RCT's en systematic reviews • Systematic reviews met check of RCT's na verschijnen systematic review de conclusies kunnen veranderen; indien ja - update van systematic review, indien nee – bestaande review gebruiken om aanbevelingen op te baseren

• *Minimum omvang steekproef*	• RCT: > 10 per arm • Exclusie van studies met >50% attrition uit een arm de trial (tenzij adequatie statistiek is toegepast om te corrigeren voor missende data)
Search strategie	[termen populatie criteria] AND [termen risicogroep] AND [RCT, systematic review]
Databases searched	• Core databases: Embase, CINAHL, Medline, PreMedline, PsycINFO • Topic specific databases: CDSR, CENTRAL, DARE, HTA
Data searched	• Mei 2012 (einde search NICE richtlijn) tot voor commentaarfase huidige richtlijn (maart 2015) • Indien afbakening populatie afwijkt van NICE: 1995 tot maart 2015
De review strategie	• Bestaande systematic reviews worden geselecteerd, beoordeeld en verwerkt in een beschrijvende review. De meta-analyse van NICE wordt als één van de bestaande systematic reviews meegenomen. • If the reviewer identifies a systematic review appropriate to the review question, we will search for studies (with the best available design) conducted or published since the review was conducted, and the reviewer will assess if any additional studies could affect the conclusions of the previous review. If new studies could change the conclusions, we will update the review and conduct a new analysis. If new studies could not change the conclusions of an existing review, the Guideline Development Group will use the existing review to inform their recommendations.
Voetnoot.	

Bijlage 4.B Literatuursearch – Interventies UHR

Uitgangsvraag A4
Alleen hoog-risico-groep
Beperken tot SR's en MA's

PubMed

Recent queries

Search	Add to builder	Query	Items found	Time
#50	Add	Search (#46 AND #47) Filters: Meta-Analysis; Systematic Reviews	59	06:20:52
#48	Add	Search (#46 AND #47)	1465	06:20:52
#47	Add	Search (#20 OR #28 OR #44)	4273899	06:09:59
#46	Add	Search (#15 AND #45)	7174	06:08:48
#45	Add	Search (#16 OR #17 OR #19 OR #22)	618841	06:08:30
#44	Add	Search "Psychotherapy"[Mesh]	148734	06:07:29
#28	Add	Search ((therapy [ti] OR therapies[ti] OR therapeutic[ti] OR treating[ti] OR treatment*[ti] OR psychotherap*[ti]))	1463704	03:35:03

Recent queries

Search	Add to builder	Query	Items found	Time
#22	Add	Search ((“ultra-high risk” [ti] OR “ultra high risk” [ti] OR“high clinical risk” [ti] OR “clinical high risk” [ti] OR “at risk mental state” [ti] OR “risk of progression” [ti] OR “progression to first-episode psychosis” [ti] OR prodromally [ti] OR prodromal* [ti] OR prodrome* [ti] OR transition [ti] OR "mild psychotic symptom" [ti] OR "mild psychotic symptoms" [ti]))	40887	03:32:41
#20	Add	Search "Therapeutics"[Mesh]	3298216	03:31:16
#19	Add	Search "Prodromal Symptoms"[Mesh]	254	03:31:00
#17	Add	Search "at risk"[ti] OR "high risk"[ti] OR "increase risk" [ti] OR "increased risk"[ti] OR "increased risks" [ti] OR "risk group" [ti] OR "risk groups"[ti] OR "risk population"[ti] OR "ultra-high risk"[ti] OR "ultra-high risks"[ti]	41944	03:30:39
#16	Add	Search "Risk Factors"[Mesh]	554163	03:30:28
#15	Add	Search (#11 OR #12 OR #13 OR #14)	138712	03:30:15
#14	Add	Search "delusional disorder" [ti] OR "delusional disorders" [ti]	221	03:22:03
#13	Add	Search psychotic [ti] OR psychosis [ti] OR psychoses [ti] OR schizo*[ti]	88662	03:21:51
#12	Add	Search "severe mental ill"[ti] OR "severe mental disorder"[ti] OR "severe mentally ill"[ti] OR "severe mental disorders"[ti] OR "severe mental illness"[ti] OR "severe mental illnesses"[ti]	1323	03:21:33
#11	Add	Search ("Psychotic Disorders"[Mesh:NoExp] OR "Schizophrenia"[Mesh] OR "Hallucinations"[Mesh] OR "Delusions"[Mesh] OR "Schizophrenia, Childhood"[Mesh])	117413	03:21:10

PsycInfo

0	

#	Query	Limiters/Expanders	Last Run Via	Results
S17	S13 OR S15	Limiters - Methodology: -Systematic Review, -Meta Analysis Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	31
S16	S13 OR S15	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	1,915
S15	S11 AND S14	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	1,038

S14	TI (therapy OR therapies OR therapeutic* OR treating OR treatment* OR psychotherap*) OR KW (therapy OR therapies OR therapeutic* OR treating OR treatment* OR psychotherap*)	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	368,213
S13	S11 AND S12	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	1,609
S12	CC 33*	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	731,068
S11	S4 AND S10	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	7,947
S10	S5 OR S6 OR S7 OR S8 OR S9	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	134,033
S9	DE "Prodrome" OR DE "Onset (Disorders)"	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	10,058
S8	TI ("risk group*" OR “ultra-high risk” OR “ultra high risk” OR“high clinical risk” OR “clinical high risk” OR “at risk mental state” OR “risk of progression” OR “progression to first-episode psychosis” OR "prodromally symptomatic” OR prodromal* OR prodrome OR transition OR “mild psychotic symptom*”) OR KW ("risk group*" OR “ultra-high risk” OR “ultra high risk” OR“high clinical risk” OR “clinical high risk” OR “at risk mental state” OR “risk of progression” OR “progression	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	15,155

	to first-episode psychosis” OR "prodromally symptomatic” OR prodromal* OR prodrome OR transition OR “mild psychotic symptom*”)			
S7	DE "Risk Factors"	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	47,216
S6	TI ("at risk" OR "high risk" OR "increase* risk") OR KW ("at risk" OR "high risk" OR "increase* risk")	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	100,845
S5	DE "At Risk Populations"	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	29,905
S4	S1 OR S2 OR S3	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	110,862
S3	TI ("delusional disorder*" OR severe mental ill* OR severe mental disorder* OR psychotic OR psychosis OR psychoses OR schizo*) OR KW ("delusional disorder*" OR severe mental ill* OR severe mental disorder* OR psychotic OR psychosis OR psychoses OR schizo*)	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	105,673
S2	(DE "Schizophrenia" OR DE "Acute Schizophrenia" OR DE "Schizophreniform Disorder" OR DE "Schizoaffective Disorder" OR DE "Delusions" OR DE "Hallucinations")	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	75,678
S1	DE "Childhood Schizophrenia" OR TI "childhood onset schizophrenia" OR KW "childhood onset schizophrenia"	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	979

enabled

Resultaat:
PubMed: 59
PsycInfo: 31
Samen: 90
Ontdubbeld en 8 dubbele referenties verwijderd. Blijft over: 82 titels.

Bijlage 4.C Summary of findings for systematic reviews – Screening UHR

Reference: Kline, E. & Schiffman, J. Psychosis risk screening: A systematic review. Schizophrenia Research 2014 in press	
Methods	Study aim: Psychosis risk screening efforts to date, with the goal of consolidating available information about screening measures and strategies used in the field. Study design: Systematic review until 8 June 2014 Analysis: Narrative Setting: Mental health services, High school, College and prison.
Patients	Number of studies: K=35 Number of patients: N= - Age:- Sex:- Inclusion: Available in English; reported original research; reported the name of the screener used by investigators; and provided data on either the proportion of the screened sample scoring above reported measure cutoffs, or the proportion of the screened sample meeting interview-based CHR criteria. Exclusion: Studies that reported only the covariance of screener scores with other self-report measures were not included in the review. Baseline characteristics:-
Interventions	Index test: Prodromal Questionnaire (PQ; 92, 21 and 16 items), Prime Screen — Revised (PS-R; 12 items), Youth Psychosis At-Risk Questionnaire Brief Version (YPARQ-B; 28 items), PROD-screen (21 items), Eppendorf Schizophrenia Inventory (ESI; 40 items), BASC Atypicality Scale (9 items within a 176-item survey), Early Detection Primary Care Checklist (PCCL; 20 item and 6 item versions), Community Assessment of Psychic Experiences (CAPE; 42 items) Reference test: Structured Interview for Psychosis Risk Syndromes (SIPS), Comprehensive Assessment of At-Risk Mental States (CAARMS), modified Schedule for Affective Disorders and Schizophrenia for School Aged Children (K-SADS), PROD and Bonn Scale for the Assessment of Basic Symptoms (BSABS)

Outcome	Specificity (Sp), Sensitivity (Se) en Positive Predictive value (PPV)
Results	See table (Bijlage E)
Quality Assessment	Study question:+/- No explicitly reported clinical question (PICO) Search strategy: + Electronic databases: PubMed and psycinfo (Medline minimum) Restrictions: Only English articles Selection process: + Explicit in- and exclusion criteria (e.g. patient group, design, intervention)? YES By two reviewers independently made final selection? YES Flow diagram? NO Quality assessment: - Data extraction: + By two reviewers independently? Yes Process clearly described? Yes Characteristics original studies: + (At least design, population, primary outcomes, follow up length) Handling heterogeneity: - (no meta-analysis) Statistical pooling: - (no meta-analysis) Funding / conflicts of interest: + The funders were not involved in study design, analyses, manuscript preparation, or decision to submit for publication. Overall quality of evidence: ? General conclusion:+

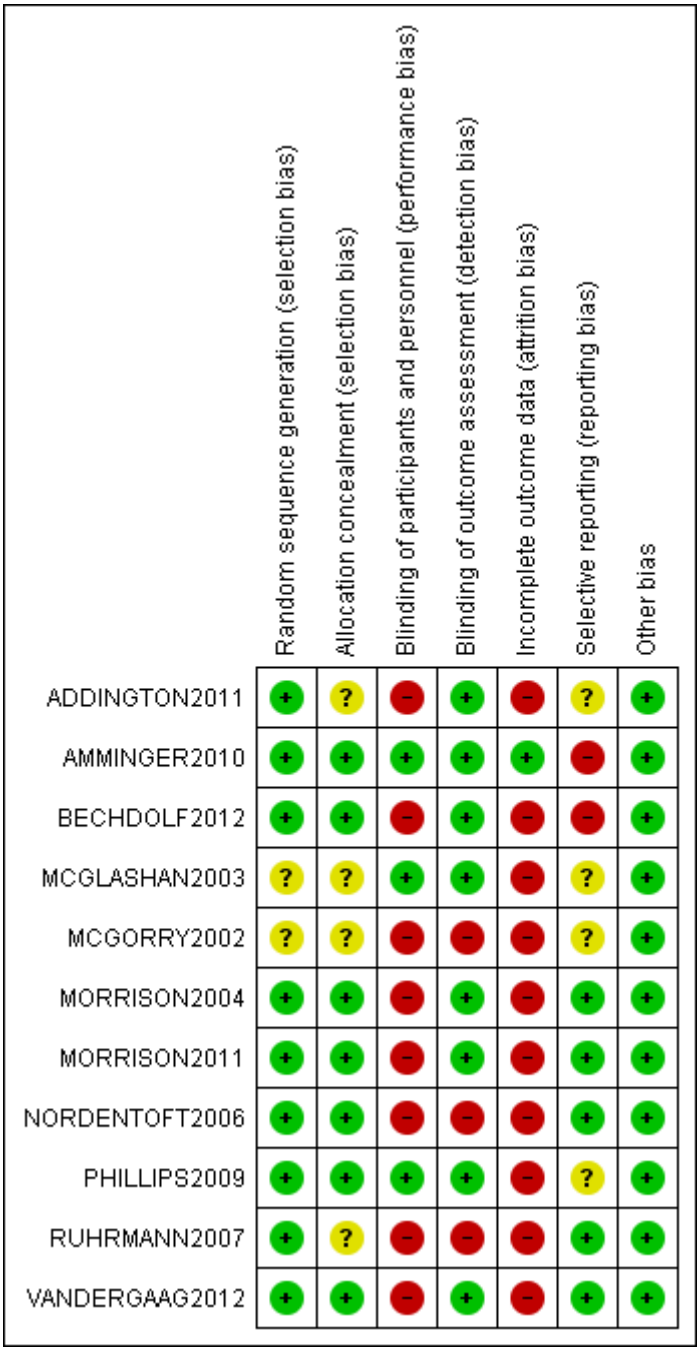
Bijlage 4.D Karakteristieken van de screeningsinstrumenten

*seeking mental health services; **receiving mental health services; "Referred for CHR evaluation
†Incarcerated men; †† College students; ††† High school students
+symp = positive symptoms

Study	Country	Age	N (analysed)	Cut-off (more or equal to)	Sensitivity	Specificity	PPV	Reference test
Prodromal Questionnaire (PQ; 92 items)								
Loewy2005	US	12-35”	113	8 +symp	0.90	0.49	0.78	SIPS, CHR or psychosis diagnoses
Ising2012	NL	18-35*	3733	18 +symp	0.90	0.90	0.52	CAARMS CHR or psychosis diagnoses
Loewy2012	FI	15-18*	408	18 +symp	0.82	0.49	0.51	SIPS CHR diagnoses
VanderGaag2012	NL	14-35*	5705	18 +symp	-	-	0.48	CAARMS
Prodromal Questionnaire — Brief (PQ-B; 21 items)								
Loewy2011	US	12-35”	141	3 endorsment	0.89	0.58	0.93	SIPS, CHR or psychosis diagnoses
				6 distress	0.88	0.68	0.95	SIPS CHR or psychosis diagnoses
Kline2012	US	12-22**	49	6	0.95	0.28	0.48	SIPS CHR or psychosis diagnoses
				38	0.70	0.82	0.74	SIPS CHR or psychosis diagnoses
Kline2014	US	12-22**	66	18 distress	0.77	0.68	0.61	SIPS CHR or psychosis diagnoses
				4 endorsment	0.73	0.83	0.73	SIPS CHR or psychosis diagnoses
Prodromal Questionnaire-16 (16 items) (focusses on +symp)								
Ising2012	NL	18-35*	420	6	0.87	0.87	0.44	CAARMS CHR or psychosis diagnoses
Chen2014	CN	16-22††	579 (99)		1	0.63	0.41	SIPS CHR criteria
Prime Screen — Revised (PS-R; 12 items)								
Kline2012	US	12-22**	49	2 ??	0.80	0.48	0.52	SIPS CHR/psychosis diagnoses
				3 endorsment	0.75	0.66	0.60	SIPS CHR/psychosis diagnoses
Kline2013	US	Adolescent”	52	??	0.81	0.60	0.69	SIPS CHR/psychosis diagnoses
		PS-R and a Caregiver version		??	0.74	0.76	0.77	SIPS CHR/psychosis diagnoses
Youth Psychosis At-Risk Questionnaire Brief Version (YPARQ-B; 28 items) (focusses on +symp)								

Study	Country	Age	N (analysed)	Cut-off (more or equal to)	Sensitivity	Specificity	PPV	Reference test
Ord2004	Palau (strongly oriented with the US)	†††	648 (130)	11 endorsment	0.98	0.81	0.82	Modified K-SADS
Kline2012	US	12-22**	49	11	0.65	0.76	0.65	SIPS CHR/psychosis
				13	0.65	0.90	0.81	SIPS CHR/psychosis
PROD-screen (21 items)								
Heinimaa2003	FI	18+	132	2	0.80	0.76	0.57	CHR status as determined by SIPS interview
Granö2011	FI	12-20”	87	2	1	0.50	0.70	Interview-based PROD diagnoses of CHR/psychosis
Eppendorf Schizophrenia Inventory (ESI; 40 items) (focusses on +symp)								
Niessen2010	NL	16-35”		various	0.50-0.81	0.52-0.94		SIPS or BSABS
BASC Atypicality Scale (9 items within a 176-item survey)								
Thompson2013	US	12-22†††	70	60	0.65	0.87	0.80	SIPS CHR/psychosis
Thompson2014	US	12-22†††	63	60	0.68	0.79	0.79	SIPS CHR/psychosis
	BASC Atypicality scale and parent report			60	0.82	0.79	0.82	SIPS CHR/psychosis
Early Detection Primary Care Checklist (PCCL; 20 item and 6 item versions)								
French2012	UK	14-34”	136	?	0.96	0.10	-	PCCL 20 items vs CAARMS CHR/psychosis
				?	0.89	0.60	-	PCCL 20 items optimized vs CAARMS CHR/psychosis
				?	0.88	0.47	-	PCCL 6 items optimized vs CAARMS CHR/psychosis
Community Assessment of Psychic Experiences (CAPE; 42 items)								
Mossaheb2012	AT	13-24”	165	3.20 +symp	0.67	0.73	0.72	CAARMS CHR diagnoses (15 participants found to have psychosis were excluded from analyses)
				2.80 +symp	0.83	0.49	0.63	

Bijlage 4.E Risk of Bias (RoB) table – Interventies bij mensen met een UHR



Bijlage 4.F GRADE profielen – Interventies bij mensen met een UHR

Date: 2014-08-05
Question: Should Olanzapine vs placebo be used in people with ultra-high risk of developing a first psychosis?
Settings:
Bibliography: . Interventies bij (ultra) hoog risico groepen voor een eerste psychose. Cochrane Database of Systematic Reviews [Year], Issue [Issue].

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Olanzapine	Placebo	Relative (95% CI)	Absolute		
Transition to psychosis at 52 weeks PT												
1[1]	randomised trials	serious[2,3]	no serious inconsistency	no serious indirectness	serious[4]	reporting bias[5]	5/31 (16.1%)	11/29 (37.9%)	RR 0.43 (0.17 to 1.08)	216 fewer per 1000 (from 315 fewer to 30 more)	⨁⨁⨁◯ VERY LOW	
								37.9%		216 fewer per 1000 (from 315 fewer to 30 more)		
Change in mean total symptoms at 52 weeks PT (measured with: [PANSS] ; Better indicated by lower values)												
1[1]	randomised trials	serious[2,3]	no serious inconsistency	no serious indirectness	serious[6]	reporting bias[5]	30	29	-	SMD 0.12 lower (0.63 lower to 0.39 higher)	⨁⨁⨁◯ VERY LOW	
Change in psychosocial functioning at 52 weeks PT (measured with: [GAF]; Better indicated by lower values)												
1[1]	randomised trials	serious[2,3]	no serious inconsistency	no serious indirectness	serious[6]	reporting bias[5]	30	29	-	SMD 0.16 lower (0.67 lower to 0.35 higher)	⨁⨁⨁◯ VERY LOW	
Discontinuation at 52 weeks PT												
1[1]	randomised trials	serious[2,3]	no serious inconsistency	no serious indirectness	serious[4]	reporting bias[5]	17/31 (54.8%)	10/29 (34.5%)	RR 1.59 (0.88 to 2.88)	203 more per 1000 (from 41 fewer to 648 more)	⨁⨁⨁◯ VERY LOW	
								34.5%		204 more per 1000 (from 41 fewer to 649 more)		

[1] MCGLASHAN2003

[2] Unclear sequence generation and allocation concealment (selection bias)

[3] High risk of attrition bias (incomplete outcome data)

[4] Optimal information size was not met (<300 events)

[5] High risk of reporting bias

[6] Optimal information size was not met (<400 participants)

Author(s):
Date: 2014-08-05
Question: Should Amisulpride and needs based intervention (NBI) vs NBI be used in people with ultra-high risk of developing a first psychosis?
Settings:
Bibliography: . Interventies bij (ultra) hoog risico groepen voor een eerste psychose. Cochrane Database of Systematic Reviews [Year], Issue [Issue].

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Amisulpride and needs based intervention (NBI)**	**NBI**	**Relative (95% CI)**	**Absolute**		
Mean endpoint in psychosocial functioning at 26 weeks PT (measured with: [GAF]; Better indicated by lower values)												
1[1]	randomised trials	serious[2,3]	no serious inconsistency	no serious indirectness	serious[4]	none	58	44	-	0.42 lower (0.82 to 0.03 lower)	⨁⨁⨁◯ LOW	
Mean endpoint positive symptoms at 26 weeks PT (measured with: (PANNS); Better indicated by lower values)												
1[1]	randomised trials	serious[2,3]	no serious inconsistency	no serious indirectness[5]	serious[4]	none	58	44	-	SMD 0.53 lower (0.93 to 0.13 lower)	⨁⨁⨁◯ LOW	
Mean endpoint negative symptoms at 26 weeks PT (measured with: (PANNS); Better indicated by lower values)												
1[1]	randomised trials	serious[2,3]	no serious inconsistency	no serious indirectness[5]	serious[4]	none	58	44	-	SMD 0.26 lower (0.65 lower to 0.14 higher)	⨁⨁⨁◯ LOW	

[1] RUHRMANN2007

[2] Unclear allocation concealment (selection bias)

[3] High risk of performance (unblinded participants/personnell), detection (unblinded outcome assessment), and attrition bias (incomplete outcome data)

[4] Optimal information size was not met (<400 participants)

Author(s):
Date: 2014-08-05
Question: Should Risperidone + CBT vs placebo + CBT be used in people with ultra-high risk of developing a first psychosis?
Settings:
Bibliography: . Interventies bij (ultra) hoog risico groepen voor een eerste psychose. Cochrane Database of Systematic Reviews [Year], Issue [Issue].

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Risperidone + CBT	Placebo + CBT	Relative (95% CI)	Absolute		
Transition to psychosis at 52 weeks PT (assessed with: [CAARMS])												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	reporting bias[4]	7/43 (16.3%)	7/44 (15.9%)	RR 1.02 (0.39 to 2.67)	3 more per 1000 (from 97 fewer to 266 more)	⨁⨁⨁◯ VERY LOW	
								15.9%		3 more per 1000 (from 97 fewer to 266 more)		
Mean endpoint total symptoms at 52 weeks PT (measured with: [BPRS]; Better indicated by lower values)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	serious[5]	reporting bias[4]	24	27	-	SMD 0.24 lower (0.79 lower to 0.31 higher)	⨁⨁⨁◯ VERY LOW	
Mean endpoint in psychosocial functioning at 52 weeks PT (measured with: [GAF]; Better indicated by lower values)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	serious[5]	reporting bias[4]	25	26	-	SMD 0.24 higher (0.32 lower to 0.79 higher)	⨁⨁⨁◯ VERY LOW	
Discontinuation at 52 weeks at 52 weeks PT												
1[1]	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[3]	reporting bias[4]	16/43 (37.2%)	15/44 (34.1%)	RR 1.09 (0.62 to 1.92)	31 more per 1000 (from 130 fewer to 314 more)	⨁⨁⨁◯ LOW	
								34.1%		31 more per 1000 (from 130 fewer to 314 more)		

[1] PHILLIPS2009

[2] High risk of attrition bias (incomplete outcome data)

[3] Optimal information size was not met (<300 events)

[4] High risk of reporting bias

[5] Optimal information size was not met (<400 participants)

Author(s):
Date: 2014-08-05
Question: Should Risperidone + CBT vs Supportive counselling (SC be used in people with ultra-high risk of developing a first psychosis?
Settings:
Bibliography: . Interventies bij (ultra) hoog risico groepen voor een eerste psychose. Cochrane Database of Systematic Reviews [Year], Issue [Issue].

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Risperidone + CBT**	**Supportive counselling (SC**	**Relative (95% CI)**	**Absolute**		
Transition to psychosis at 26 weeks PT (assessed with: [CAARMS])												
2[1,2]	randomised trials	serious[3,4]	no serious inconsistency	no serious indirectness	serious[5]	reporting bias[6]	5/74 (6.8%)	12/56 (21.4%)	RR 0.35 (0.13 to 0.95)	139 fewer per 1000 (from 11 fewer to 186 fewer)	⨁◯◯◯ VERY LOW	
								21.4%		139 fewer per 1000 (from 11 fewer to 186 fewer)		
Mean endpoint total symptoms at 26 weeks PT (measured with: [BPRS]; Better indicated by lower values)												
2[1,2]	randomised trials	serious[3,4]	no serious inconsistency	no serious indirectness	serious[7]	reporting bias[6]	74	56	-	SMD 0.15 higher (0.39 lower to 0.7 higher)	⨁◯◯◯ VERY LOW	
Mean endpoint in psychosocial functioning at 26 weeks PT (measured with: [GAF]; Better indicated by lower values)												
1[1]	randomised trials	serious[8]	no serious inconsistency	no serious indirectness	serious[7]	reporting bias[6]	25	18	-	SMD 0.12 lower (0.73 lower to 0.49 higher)	⨁◯◯◯ VERY LOW	
Discontinuation at 26 weeks PT												

2[1,2]	randomised trials	serious[4]	no serious inconsistency	no serious indirectness	serious[5]	reporting bias[6]	7/74 (9.5%)	6/56 (10.7%)	RR 0.76 (0.28 to 2.03)	26 fewer per 1000 (from 77 fewer to 110 more)	⨁◯◯◯ VERY LOW	
								10.7%		26 fewer per 1000 (from 77 fewer to 110 more)		
Transition to psychosis at 52 weeks PT												
2[1,2]	randomised trials	serious[3,4]	no serious inconsistency	no serious indirectness	serious[5]	reporting bias[6]	13/74 (17.6%)	16/56 (28.6%)	RR 0.63 (0.33 to 1.21)	106 fewer per 1000 (from 191 fewer to 60 more)	⨁◯◯◯ VERY LOW	
								28.6%		106 fewer per 1000 (from 192 fewer to 60 more)		
Mean endpoint total symptoms at 52 weeks PT (measured with: [BPRS] ; Better indicated by lower values)												
2[1,2]	randomised trials	serious[3,4]	no serious inconsistency	no serious indirectness	serious[7]	reporting bias[6]	55	46	-	SMD 0.07 higher (0.32 lower to 0.46 higher)	⨁◯◯◯ VERY LOW	
Mean endpoint in psychosocial functioning at 52 weeks PT (measured with: [GAF]; Better indicated by lower values)												
1[2]	randomised trials	serious[4,8]	no serious inconsistency	no serious indirectness	serious[7]	reporting bias[6]	31	28	-	SMD 0 higher (0.51 lower to 0.51 higher)	⨁◯◯◯ VERY LOW	
Discontinuation at FU 52 weeks												
2[1,2]	randomised trials	serious[4]	no serious inconsistency	no serious indirectness	serious[5]	reporting bias[6]	23/74 (31.1%)	20/56 (35.7%)	RR 0.85 (0.43 to 1.67)	54 fewer per 1000 (from 204 fewer to 239 more)	⨁◯◯◯ VERY LOW	
								35.7%		54 fewer per 1000 (from 203 fewer to 239 more)		
Transition to psychosis at FU 156 to 208 weeks COMPLETER												
1[2]	randomised trials	serious[4,8]	no serious inconsistency	no serious indirectness	serious[5]	reporting bias[6]	10/24 (41.7%)	12/17 (70.6%)	RR 0.59 (0.34 to 1.04)	289 fewer per 1000 (from 466 fewer to 28 more)	⨁◯◯◯ VERY LOW	

								70.6%		289 fewer per 1000 (from 466 fewer to 28 more)		
Transition to psychosis at FU 156 to 208 weeks SENSITIVITY												
1[2]	randomised trials					none	17/31 (54.8%)	23/28 (82.1%)	RR 0.67 (0.46 to 0.96)	271 fewer per 1000 (from 33 fewer to 444 fewer)		
								82.1%		271 fewer per 1000 (from 33 fewer to 443 fewer)		
Mean endpoint total symptoms at FU 156 to 208 weeks (measured with: [BPRS]; Better indicated by lower values)												
1[2]	randomised trials	serious[4,8]	no serious inconsistency	no serious indirectness	serious[7]	reporting bias[6]	17	24	-	SMD 0.33 lower (0.96 lower to 0.29 higher)	⨁◯◯◯ VERY LOW	
Mean endpoint in psychosocial functioning at FU 156 to 208 weeks (measured with: [GAF]; Better indicated by lower values)												
1[2]	randomised trials	serious[4,8]	no serious inconsistency	no serious indirectness	serious[7]	reporting bias[6]	17	24	-	SMD 0.15 lower (0.77 lower to 0.47 higher)	⨁◯◯◯ VERY LOW	
Discontinuation at FU 156 to 208 weeks												
1[2]	randomised trials	serious[4]	no serious inconsistency	no serious indirectness	serious[5]	reporting bias[6]	7/31 (22.6%)	11/28 (39.3%)	RR 0.57 (0.26 to 1.28)	169 fewer per 1000 (from 291 fewer to 110 more)	⨁◯◯◯ VERY LOW	
								39.3%		169 fewer per 1000 (from 291 fewer to 110 more)		

[1] PHILLIPS2009

[2] MCGORRY2002

[3] High risk of attrition bias (incomplete outcome data) (k=2)

[4] Unclear sequence generation, allocation concealment, raters unblind to psychological intervention. (k=1)

[5] Optimal information size was not met (<300 events)

[6] High risk of reporting bias

[7] Optimal information size was not met (<400 participants)

[8] High risk of attrition bias (incomplete outcome data)

Author(s):
Date: 2014-08-05
Question: Should CBT vs Supportive counselling (SC) be used in people with ultra-high risk of developing a first psychosis?
Settings:
Bibliography: . Interventies bij (ultra) hoog risico groepen voor een eerste psychose. Cochrane Database of Systematic Reviews [Year], Issue [Issue].

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	CBT	Supportive counselling (SC)	Relative (95% CI)	Absolute		
Transition to psychosis at PT (within/at 26 weeks) COMPLETERS (assessed with: (DSM-IV, PANSS, CAARMS,PANSS))												
4[1,2,3,4]	randomised trials	serious[5,6]	no serious inconsistency	no serious indirectness	serious[7]	none	15/301 (5%)	25/290 (8.6%)	RR 0.62 (0.29 to 1.31)	33 fewer per 1000 (from 61 fewer to 27 more)	⨁⨁⨁◯ LOW	
								10.4%		40 fewer per 1000 (from 74 fewer to 32 more)		
Transition to psychosis at PT (within/at 26 weeks) SENSITIVITY (assessed with: (DSM-IV, PANSS, CAARMS,PANSS))												
4[1,2,3,4]	randomised trials					none	23/312 (7.4%)	33/300 (11%)	RR 0.66 (0.4 to 1.08)	37 fewer per 1000 (from 66 fewer to 9 more)		
								10.3%		35 fewer per 1000 (from 62 fewer to 8 more)		
Mean endpoint total symptoms at PT (within/at 26 weeks) (measured with: [BPRS, SOPS, PANSS, CAARMS-severity] ; Better indicated by lower values)												
2[1,3]	randomised trials	serious[5,8]	no serious inconsistency	no serious indirectness	serious[9]	none	71	52	-	SMD 0.04 higher (0.32 lower to 0.4 higher)	⨁⨁⨁◯ LOW	
Mean endpoint in psychosocial functioning at PT (within/at 26 weeks) (measured with: [GAF]; Better indicated by lower values)												

3[1,2,3]	randomised trials	serious[5,10]				none	150	141	-	SMD 0.02 higher (0.22 lower to 0.26 higher)		
Discontinuation at PT (within/at 26 weeks)												
3[1,2,3,8]	randomised trials	serious[5]	no serious inconsistency	no serious indirectness	serious[7]	none	64/215 (29.8%)	59/196 (30.1%)	RR 1.01 (0.75 to 1.36)	3 more per 1000 (from 75 fewer to 108 more)	⨁⨁⨁◯ LOW	
								31.3%		3 more per 1000 (from 78 fewer to 113 more)		
Transition to psychosis at 52 weeks FU COMPLETERS (assessed with: (DSM-IV, PANSS))												
5[1,2,3,4,11]	randomised trials	no serious risk of bias[12]	no serious inconsistency	no serious indirectness	serious[7]	none	25/333 (7.5%)	44/312 (14.1%)	RR 0.54 (0.34 to 0.86)	65 fewer per 1000 (from 20 fewer to 93 fewer)	⨁⨁⨁◯ MODERATE	
								20%		92 fewer per 1000 (from 28 fewer to 132 fewer)		
Transition to psychosis at 52 weeks FU SENSITIVITY (assessed with: (DSM-IV, PANSS))												
5[1,2,3,4,11]	randomised trials					none	36/349 (10.3%)	53/323 (16.4%)	RR 0.64 (0.44 to 0.93)	59 fewer per 1000 (from 11 fewer to 92 fewer)		
								21.4%		77 fewer per 1000 (from 15 fewer to 120 fewer)		
Mean endpoint total symptoms at 52 weeks FU (measured with: (SOPS, CAARMS severity); Better indicated by lower values)												
3[1,3,11]	randomised trials	serious[5,10]	no serious inconsistency	no serious indirectness	serious[7]	none	89	65	-	SMD 0.05 higher (0.27 lower to 0.37 higher)	⨁⨁⨁◯ LOW	
Mean endpoint in psychosocial functioning 52 weeks FU (measured with: [GAF]; Better indicated by lower values)												
2[1,2]	randomised trials	serious[8,13]	no serious inconsistency	no serious indirectness	serious[9]	none	122	118	-	SMD 0.1 lower (0.36 lower to 0.15 higher)	⨁⨁⨁◯ LOW	
Discontinuation at 52 weeks FU												

5[1,2,3,4,11]	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[7]	none	104/345 (30.1%)	91/320 (28.4%)	RR 1.03 (0.82 to 1.31)	9 more per 1000 (from 51 fewer to 88 more)	⨁⨁⨁◯ MODERATE	
								32.1%		10 more per 1000 (from 58 fewer to 100 more)		
Transition to psychosis at 78 weeks or more FU COMPLETERS (assessed with: (DSM-IV, PANSS))												
4[1,2,4,11]	randomised trials	serious[6,13]	no serious inconsistency	no serious indirectness	serious[7]	none	27/288 (9.4%)	43/282 (15.2%)	RR 0.63 (0.4 to 0.99)	56 fewer per 1000 (from 2 fewer to 91 fewer)	⨁⨁◯◯ LOW	
								21.7%		80 fewer per 1000 (from 2 fewer to 130 fewer)		
Transition to psychosis at 78 weeks or more FU SENSITIVITY (assessed with: (DSM-IV, PANSS))												
4[1,2,4,11]	randomised trials					none	39/302 (12.9%)	87/293 (29.7%)	RR 0.55 (0.25 to 1.19)	134 fewer per 1000 (from 223 fewer to 56 more)		
								37.8%		170 fewer per 1000 (from 283 fewer to 72 more)		
Mean endpoint total symptoms at 78 weeks or mores FU (measured with: (SOPS, CAARMS-severity); Better indicated by lower values)												
1[1]	randomised trials	serious[13,14]	no serious inconsistency	no serious indirectness	serious[9]	none	27	24	-	SMD 0.04 lower (0.59 lower to 0.51 higher)	⨁⨁◯◯ LOW	
Mean endpoint in psychosocial functioning 78 weeks or more FU (measured with: [GAF]; Better indicated by lower values)												
2[1,11]	randomised trials	serious[8,13]	no serious inconsistency	no serious indirectness	serious[9]	none	61	55	-	SMD 0.03 lower (0.45 lower to 0.4 higher)	⨁⨁◯◯ LOW	
Discontinuation at 78 weeks or more FU												
4[1,2,4,11]	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[7]	none	116/301 (38.5%)	99/292 (33.9%)	RR 1.09 (0.88 to 1.35)	31 more per 1000 (from 41 fewer to 119 more)	⨁⨁⨁◯ MODERATE	

								39.6%		36 more per 1000 (from 48 fewer to 139 more)		

[1] ADDINGTON2011

[2] MORRISON2011

[3] PHILLIPS2009

[4] VANDERGAAG2012

[5] Unclear sequence generation k=1, trail registration could not be found k=2

[6] High risk of attrition bias (incomplete outcome data) k=4

[7] Optimal information size was not met (<300 events)

[8] High risk of attrition bias (incomplete outcome data) k=2

[9] Optimal information size was not met (<400 participants)

[10] High risk of attrition bias (incomplete outcome data) k=3

[11] MORRISON2004

[12] Because of the outocome of sensitivity analysis there probably is no attrition bias due to the studies only using completers. Other RoB is minor.

[13] Unclear sequence generation k=1, trail registration could not be found k=1

[14] High risk of attrition bias (incomplete outcome data) k=1

Author(s):
Date: 2014-08-05
Question: Should Integrated therapies vs TAU be used in people with ultra-high risk of developing a first psychosis?
Settings:
Bibliography: . Interventies bij (ultra) hoog risico groepen voor een eerste psychose. Cochrane Database of Systematic Reviews [Year], Issue [Issue].

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Integrated therapies**	**TAU**	**Relative (95% CI)**	**Absolute**		
Transition to psychosis 52 weeks COMPLETERS												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	3/37 (8.1%)	10/30 (33.3%)	RR 0.24 (0.07 to 0.81)	253 fewer per 1000 (from 63 fewer to 310 fewer)	⍰⍰⍰ LOW	

								33.3%		253 fewer per 1000 (from 63 fewer to 310 fewer)		
Transition to psychosis 52 weeks SENSITIVITY												
1[1]	randomised trials					none	8/42 (19%)	17/37 (45.9%)	RR 0.41 (0.2 to 0.85)	271 fewer per 1000 (from 69 fewer to 368 fewer)		
								46%		271 fewer per 1000 (from 69 fewer to 368 fewer)		
Transition to psychosis 104 weeks COMPLETERS												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	9/36 (25%)	14/29 (48.3%)	RR 0.52 (0.26 to 1.02)	232 fewer per 1000 (from 357 fewer to 10 more)	⍰⍰⍰ LOW	
								48.3%		232 fewer per 1000 (from 357 fewer to 10 more)		
Transition to psychosis 104 weeks SENSITIVITY												
1[1]	randomised trials					none	15/42 (35.7%)	22/37 (59.5%)	RR 0.6 (0.37 to 0.98)	238 fewer per 1000 (from 12 fewer to 375 fewer)		
								59.5%		238 fewer per 1000 (from 12 fewer to 375 fewer)		
Discontinuation at 52 weeks												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	5/42 (11.9%)	7/37 (18.9%)	RR 0.63 (0.22 to 1.81)	70 fewer per 1000 (from 148 fewer to 153 more)	⍰⍰⍰ LOW	
								18.9%		70 fewer per 1000 (from 147 fewer to 153 more)		
Discontinuation at 104 weeks												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	6/42 (14.3%)	8/37 (21.6%)	RR 0.66 (0.25 to 1.73)	74 fewer per 1000 (from 162 fewer to 158 more)	⍰⍰⍰ LOW	
								21.6%		73 fewer per 1000 (from 162 fewer to 158 more)		

[1] NORDENTOFT2006

[2] High risk of performance (unblinded participants/personnell), detection (unblinded outcome assessment), and attrition bias (incomplete outcome data)

[3] Optimal information size was not met (<300 events)

Author(s):
Date: 2014-08-05
Question: Should Integrated psychological therapy (IPT) vs Supportive counselling (SC) be used in people with ultra-high risk of developing a first psychosis?
Settings:
Bibliography: . Interventies bij (ultra) hoog risico groepen voor een eerste psychose. Cochrane Database of Systematic Reviews [Year], Issue [Issue].

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Integrated psychological therapy (IPT)	Supportive counselling (SC)	Relative (95% CI)	Absolute		
Transition to psychosis at 52 weeks PT (assessed with: (PANSS))												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	reporting bias[4]	0/63 (0%)	9/65 (13.8%)	RR 0.05 (0 to 0.91)	132 fewer per 1000 (from 12 fewer to 138 fewer)	⨁⨁⨁◯ VERY LOW	
								13.9%		132 fewer per 1000 (from 13 fewer to 139 fewer)		
Transition to psychosis at 104 weeks FU (assessed with: (PANSS))												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	reporting bias[4]	1/63 (1.6%)	10/65 (15.4%)	RR 0.1 (0.01 to 0.78)	138 fewer per 1000 (from 34 fewer to 152 fewer)	⨁⨁⨁◯ VERY LOW	
								15.4%		139 fewer per 1000 (from 34 fewer to 152 fewer)		
Discontinuation at 52 weeks PT												
1[1]	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[3]	reporting bias[4]	12/63 (19%)	8/65 (12.3%)	RR 1.55 (0.68 to 3.53)	68 more per 1000 (from 39 fewer to 311 more)	⨁⨁◯◯ LOW	
								12.3%		68 more per 1000 (from 39 fewer to 311 more)		

Discontinuation at 104 weeks FU												
1[1]	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness[4]	serious[3]	reporting bias[4]	12/63 (19%)	8/65 (12.3%)	RR 1.55 (0.68 to 3.53)	68 more per 1000 (from 39 fewer to 311 more)	⨁⨁⨁◯ LOW	
								12.3%		68 more per 1000 (from 39 fewer to 311 more)		

[1] BECHDOLF2012

[2] High risk of attrition bias

[3] Optimal information size was not met (<300 events)

[4] High risk of reporting bias

Author(s):
Date: 2014-08-05
Question: Should Omega-3 fatty acids vs placebo be used in people with ultra-high risk of developing a first psychosis?
Settings:
Bibliography: . Interventies bij (ultra) hoog risico groepen voor een eerste psychose. Cochrane Database of Systematic Reviews [Year], Issue [Issue].

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Omega-3 fatty acids**	**Placebo**	**Relative (95% CI)**	**Absolute**		
Transition to psychosis at 12 weeks PT COMPLETER												
1[1]	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	reporting bias[3]	1/38 (2.6%)	8/38 (21.1%)	RR 0.12 (0.02 to 0.95)	185 fewer per 1000 (from 11 fewer to 206 fewer)	⨁⨁⨁◯ LOW	
								21.1%		186 fewer per 1000 (from 11 fewer to 207 fewer)		
Transition to psychosis at 12 weeks PT SENSITIVITY												
1[1]	randomised trials					none	4/41 (9.8%)	10/40 (25%)	RR 0.39 (0.13 to 1.14)	153 fewer per 1000 (from 218 fewer to 35 more)		

								25%		153 fewer per 1000 (from 218 fewer to 35 more)		
Transition to psychosis at 52 weeks FU (assessed with: [DSMIV])												
1[1]	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	reporting bias[3]	2/41 (4.9%)	11/40 (27.5%)	RR 0.18 (0.04 to 0.75)	226 fewer per 1000 (from 69 fewer to 264 fewer)	⨁⨁⨁◯ LOW	
								27.5%		226 fewer per 1000 (from 69 fewer to 264 fewer)		
Mean endpoint total symptoms at 52 weeks FU (measured with: [PANSS]; Better indicated by lower values)												
1[1]	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[4]	reporting bias[3]	41	40	-	SMD 1.26 lower (1.74 to 0.78 lower)	⨁⨁⨁◯ LOW	
Mean endpoint psychosocial functioning at 52 weeks FU (measured with: [GAF]; Better indicated by lower values)												
1[1]	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[4]	reporting bias[3]	41	40	-	SMD 1.28 lower (1.76 to 0.8 lower)	⨁⨁⨁◯ LOW	
Discontinuation at 52 weeks FU												
1[1]	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	reporting bias[3]	3/41 (7.3%)	2/40 (5%)	RR 1.46 (0.26 to 8.3)	23 more per 1000 (from 37 fewer to 365 more)	⨁⨁⨁◯ LOW	
								5%		23 more per 1000 (from 37 fewer to 365 more)		

[1] AMMINGER2010

[2] Optimal information size was not met (<300 events)

[3] High risk of reporting bias

[4] Optimal information size was not met (<400 participants)

Bijlage 4.G Forest plots – Interventies UHR

Onderstaand volgen enkele forest plots van vergelijkingen in de meta-analyse passend bij conclusies waarbij:

- Het GRADE niveau hoger ligt dan 'zeer laag'
- Meerdere studies hebben gerapporteerd over de betreffende uitkomstmaat
- Een puntschatting van de effectmaat is vermeld in de conclusie
- Een combinatie van bovenstaande het geval is

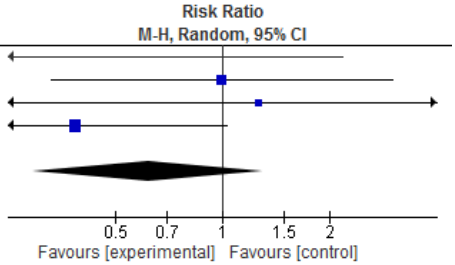
CBT (en Supportive counselling (SC) of placebo) versus SC (en placebo)

Na 26 weken behandeling

Transitie

Study or Subgroup	CBT Events	CBT Total	Supportive counselling (SC) Events	Supportive counselling (SC) Total	Weight	Risk Ratio M-H, Random, 95% CI
ADDINGTON2011	0	19	3	16	6.3%	0.12 [0.01, 2.19]
MORRISON2011	6	144	6	144	34.4%	1.00 [0.33, 3.03]
PHILLIPS2009	4	44	2	28	18.2%	1.27 [0.25, 6.50]
VANDERGAAG2012	5	94	14	102	41.0%	0.39 [0.15, 1.03]
Total (95% CI)		**301**		**290**	**100.0%**	**0.62 [0.29, 1.31]**
Total events	15		25			

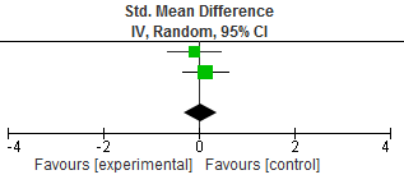
Heterogeneity: Tau² = 0.10; Chi² = 3.60, df = 3 (P = 0.31); I² = 17%
Test for overall effect: Z = 1.26 (P = 0.21)



Totale symptomen

Study or Subgroup	CBT Mean	CBT SD	CBT Total	Supportive counselling (SC) Mean	Supportive counselling (SC) SD	Supportive counselling (SC) Total	Weight	Std. Mean Difference IV, Random, 95% CI
ADDINGTON2011	5.8	5.508176	27	6.3	4.850258	24	42.6%	-0.09 [-0.64, 0.46]
PHILLIPS2009	16.7	6.8	44	15.7	7.4	28	57.4%	0.14 [-0.33, 0.61]
Total (95% CI)			**71**			**52**	**100.0%**	**0.04 [-0.32, 0.40]**

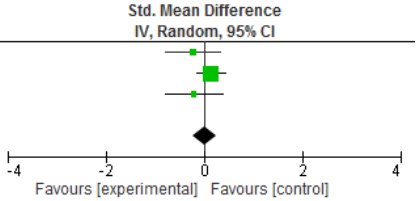
Heterogeneity: Tau² = 0.00; Chi² = 0.40, df = 1 (P = 0.53); I² = 0%
Test for overall effect: Z = 0.22 (P = 0.83)



Psychosociaal functioneren

Study or Subgroup	CBT Mean	CBT SD	CBT Total	Supportive counselling (SC) Mean	Supportive counselling (SC) SD	Supportive counselling (SC) Total	Weight	Std. Mean Difference IV, Random, 95% CI
ADDINGTON2011	-64.2	14.4	27	-61.3	9.9	24	18.7%	-0.23 [-0.78, 0.32]
MORRISON2011	-59.3	16.21	97	-61.61	15.04	98	65.0%	0.15 [-0.13, 0.43]
PHILLIPS2009	-66.8	7.7	26	-64.6	13.6	19	16.3%	-0.20 [-0.80, 0.39]
Total (95% CI)			**150**			**141**	**100.0%**	**0.02 [-0.22, 0.26]**

Heterogeneity: Tau² = 0.00; Chi² = 2.11, df = 2 (P = 0.35); I² = 5%
Test for overall effect: Z = 0.16 (P = 0.87)

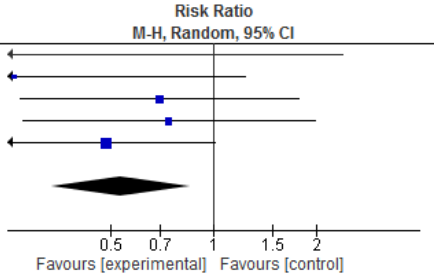


bij 52 weken follow-up

Transitie

Study or Subgroup	CBT Events	CBT Total	Supportive counselling (SC) Events	SC Total	Weight	Risk Ratio M-H, Random, 95% CI
ADDINGTON2011	0	16	3	15	2.6%	0.13 [0.01, 2.40]
MORRISON2004	2	35	5	23	9.1%	0.26 [0.06, 1.24]
MORRISON2011	7	144	10	144	24.9%	0.70 [0.27, 1.79]
PHILLIPS2009	7	44	6	28	22.7%	0.74 [0.28, 1.98]
VANDERGAAG2012	9	94	20	102	40.6%	0.49 [0.23, 1.02]
Total (95% CI)		**333**		**312**	**100.0%**	**0.54 [0.34, 0.86]**
Total events	25		44			

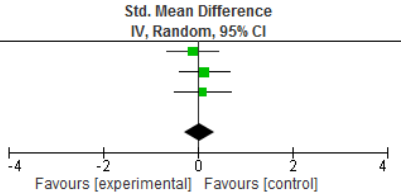
Heterogeneity: Tau² = 0.00; Chi² = 2.51, df = 4 (P = 0.64); I² = 0%
Test for overall effect: Z = 2.60 (P = 0.009)



Totale symptomen

Study or Subgroup	CBT Mean	CBT SD	CBT Total	Supportive counselling (SC) Mean	SC SD	SC Total	Weight	Std. Mean Difference IV, Random, 95% CI
ADDINGTON2011	4.8	5.355838	27	5.35	5.169623	24	34.0%	-0.10 [-0.65, 0.45]
MORRISON2004	49.4667	15.11322	35	47.4	13.12631	23	37.1%	0.14 [-0.38, 0.67]
PHILLIPS2009	16.5	11.1	27	15.3	10.1	18	28.9%	0.11 [-0.49, 0.71]
Total (95% CI)			**89**			**65**	**100.0%**	**0.05 [-0.27, 0.37]**

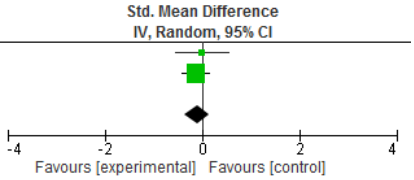
Heterogeneity: Tau² = 0.00; Chi² = 0.45, df = 2 (P = 0.80); I² = 0%
Test for overall effect: Z = 0.30 (P = 0.76)



Psychosociaal functioneren

Study or Subgroup	CBT Mean	CBT SD	CBT Total	Supportive counselling (SC) Mean	SC SD	SC Total	Weight	Std. Mean Difference IV, Random, 95% CI
ADDINGTON2011	-62.7	12.3	27	-62.6	10.2	24	21.2%	-0.01 [-0.56, 0.54]
MORRISON2011	-60.74	16.69	95	-58.59	16.23	94	78.8%	-0.13 [-0.42, 0.16]
Total (95% CI)			**122**			**118**	**100.0%**	**-0.10 [-0.36, 0.15]**

Heterogeneity: Tau² = 0.00; Chi² = 0.15, df = 1 (P = 0.70); I² = 0%
Test for overall effect: Z = 0.81 (P = 0.42)

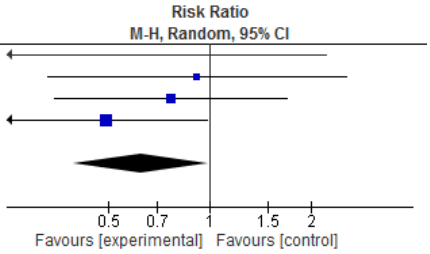


bij 78 weken follow-up

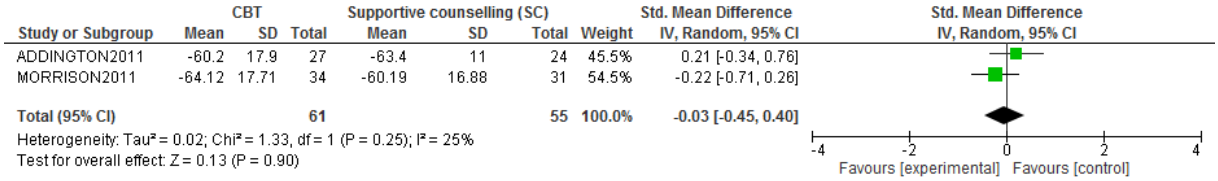
Transitie

Study or Subgroup	CBT Events	CBT Total	Supportive counselling (SC) Events	SC Total	Weight	Risk Ratio M-H, Random, 95% CI
ADDINGTON2011	0	15	3	13	2.5%	0.13 [0.01, 2.22]
MORRISON2004	7	35	5	23	20.2%	0.92 [0.33, 2.55]
MORRISON2011	10	144	13	144	33.5%	0.77 [0.35, 1.70]
VANDERGAAG2012	10	94	22	102	43.7%	0.49 [0.25, 0.99]
Total (95% CI)		**288**		**282**	**100.0%**	**0.63 [0.40, 0.99]**
Total events	27		43			

Heterogeneity: Tau² = 0.00; Chi² = 2.50, df = 3 (P = 0.48); I² = 0%
Test for overall effect: Z = 2.00 (P = 0.05)

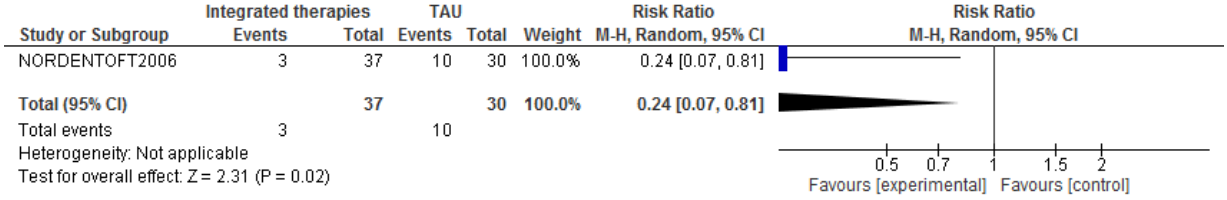


Psychosociaal functioneren



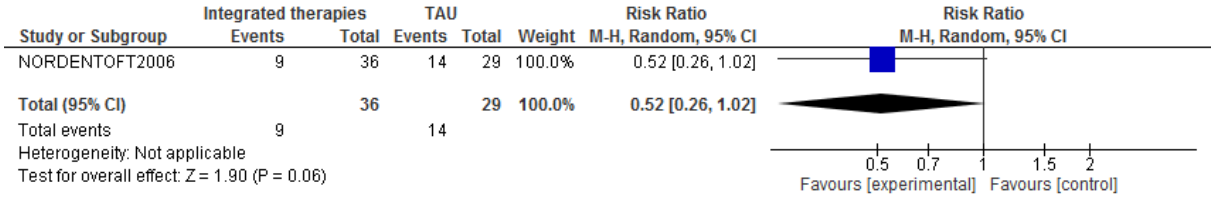
Integrated therapies versus standaard behandeling (TAU)
na 52 weken behandeling

Transitie



na 104 weken behandeling

Transitie



Bijlage 4.H Review protocol – Diagnostiek UHR

Onderwerp	**A. Mensen met een Ultrahoog Risico op het ontwikkelen van een psychose**
Uitgangsvragen	A2. Welke methoden zijn geschikt voor diagnostiek van milde psychotische verschijnselen?
Criteria voor inclusie van studies in de review	
• *Populatie*	• Personen van 12 jaar of ouder een vermoeden op milde psychotische verschijnselen
• *Interventie (A4)*	• Instrumenten voor het diagnosticeren van milde psychotische verschijnselen die in Nederland toepasbaar zijn: de SIPS en de CAARMS

• *Vergelijking*	• Klinisch oordeel • Al dan niet transitie naar psychose
• *Kritische Uitkomstmaten*	• Sensitiviteit • Specificiteit
• *Belangrijke Uitkomstmaten*	• Voorspellende waarde
• *Studiedesign*	• Diagnostische accuratesse studies, bij voorkeur crossectioneel. Terecht en onterecht positief of negatief beoordeelde patiënten.
Search strategie	• Zie bijlage I
Databases searched	• Core databases: Medline, PsycINFO
Data searched	• Januari 1970 tot voor commentaarfase huidige richtlijn (maart 2015)
De review strategie	• If the reviewer identifies a systematic review appropriate to the review question, we will search for studies (with the best available design) conducted or published since the review was conducted, and the reviewer will assess if any additional studies could affect the conclusions of the previous review. If new studies could change the conclusions, we will update the review and conduct a new analysis. If new studies could not change the conclusions of an existing review, the Guideline Development Group will use the existing review to inform their recommendations.

Bijlage 4.I Literatuursearch - Instrumenten diagnostiek UHR

Oorspronkelijke studies

PsycInfo

0	

#	Query	Limiters/Expanders	Last Run Via	Results	Action
S33	S30 OR S32	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	608	
S32	S9 AND S31	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	198	
S31	DE "Psychometrics" OR DE "Testing" OR DE "Classical	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases	117,176	

	Test Theory" OR DE "Computer Assisted Testing" OR DE "Content Analysis (Test)" OR DE "Difficulty Level (Test)" OR DE "Educational Measurement" OR DE "Item Analysis (Test)" OR DE "Item Content (Test)" OR DE "Item Response Theory" OR DE "Rating" OR DE "Repeated Measures" OR DE "Scaling (Testing)" OR DE "Scoring (Testing)" OR DE "Test Administration" OR DE "Test Bias" OR DE "Test Forms" OR DE "Test Interpretation" OR DE "Test Items" OR DE "Test Reliability" OR DE "Test Standardization" OR DE "Test Validity"		Search Screen - Advanced Search Database - PsycINFO	
S30	S9 AND S29	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	444
S29	S20 OR S21 OR S22 OR S23 OR S24 OR S25 OR S26 OR S27 OR S28	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	20,697
S28	"DIGS" OR "Diagnostic Interview for Genetic Studies"	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	178
S27	PSE OR "Present state examination"	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	1,123
S26	"CASH" OR "Comprehensive assessment of Symptoms"	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	2,292
S25	"DIS" OR "Diagnostic Interview Schedule""	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases	3,342

			Search Screen - Advanced Search Database - PsycINFO	
S24	"CIDI" OR "Composite International Diagnostic Interview"	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	2,121
S23	"SCID" OR "Structured clinical interview"	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	5,338
S22	"SIPS" OR SIPS/SOPS OR "structured interview for prodromal symptoms"	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	160
S21	"SCAN" OR "Schedule for clinical assessment in neuropsychiatry"	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	6,430
S20	CAARMS OR "Comprehensive Assessment of At-Risk Mental States"	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	50
S19	S9 AND S18	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	1,918
S18	S10 OR S11 OR S12 OR S17	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	375,428
S17	TI (diagnos* OR psychodiagnos* OR identification OR identifying OR assess* OR reliability OR validity OR prediction OR detection OR sensitivity OR specificity) OR KW (diagnos* OR psychodiagnos* OR identification OR identifying OR assess* OR reliability OR validity OR prediction OR detection OR sensitivity OR specificity)	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	328,671

S16	S9 AND S14	Limiters - Publication Year: 2004-2014 Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	4,137
S15	S9 AND S14	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	6,265
S14	S10 OR S11 OR S12 OR S13	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	1,017,448
S13	TI (diagnos* OR psychodiagnos* OR identification OR identifying OR assess* OR reliability OR validity OR prediction OR detection OR sensitivity OR specificity) OR KW (diagnos* OR psychodiagnos* OR identification OR identifying OR assess* OR reliability OR validity OR prediction OR detection OR sensitivity OR specificity) OR AB (diagnos* OR psychodiagnos* OR identification OR identifying OR assess* OR reliability OR validity OR prediction OR detection OR sensitivity OR specificity)	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	994,456
S12	DE "Diagnostic Interview Schedule" OR DE "Diagnostic and Statistical Manual"	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	6,144
S11	(((((DE "Prognosis") OR (DE "Prediction")) OR (DE "Test Validity" OR DE "Statistical Validity")) OR (DE "Statistical Reliability")) OR (DE "Test Reliability")) OR (DE "Psychological Assessment" OR DE "Behavioral Assessment" OR DE	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	127,515

	"Cognitive Assessment" OR DE "Neuropsychological Assessment")			
S10	(DE "Psychodiagnosis" OR DE "Diagnosis") OR (DE "Dual Diagnosis" OR DE "Psychodiagnostic Typologies" OR DE "Psychodiagnostic Interview" OR DE "Diagnostic Interview Schedule" OR DE "Structured Clinical Interview")	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	62,591
S9	S7 OR S8	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	11,558
S8	TI ("early psychosis" OR "first episode psychosis") OR KW ("early psychosis" OR "first episode psychosis")	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	1,490
S7	S3 AND S6	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	11,303
S6	S4 OR S5	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	152,254
S5	TI ("at risk" OR "high risk" OR "increase* risk" OR "risk group*" OR “ultra-high risk” OR “ultra high risk” OR “high clinical risk” OR “clinical high risk” OR “at risk mental state” OR “risk of progression” OR “first-episode psychosis” OR "prodromally symptomatic” OR prodromal* OR prodrome* OR transition OR “mild psychotic symptom*” OR "early symptom*" OR	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	140,497

	onset OR "early signs" OR first-episode OR "psychosis proneness" OR vulnerability) OR KW ("at risk" OR "high risk" OR "increase* risk" OR "risk group*" OR “ultra-high risk” OR “ultra high risk” OR “high clinical risk” OR “clinical high risk” OR “at risk mental state” OR “risk of progression” OR “first-episode psychosis” OR "prodromally symptomatic” OR prodromal* OR prodrome* OR transition OR “mild psychotic symptom*” OR "early symptom*" OR onset OR "early signs" OR first-episode OR "psychosis proneness" OR vulnerability)			
S4	DE "At Risk Populations" OR DE "Risk Factors" OR DE "Prodrome" OR DE "Onset (Disorders)"	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	85,180
S3	S1 OR S2	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	113,008
S2	TI ("childhood onset schizophrenia" OR "delusional disorder*" OR severe mental ill* OR severe mental disorder* OR psychotic OR psychosis OR psychoses OR schizo*) OR KW ("childhood onset schizophrenia" OR "delusional disorder*" OR severe mental ill* OR severe mental disorder* OR psychotic OR psychosis OR psychoses OR schizo*)	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	106,743
S1	DE "Childhood Schizophrenia" OR DE "Schizophrenia" OR DE	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases	92,371

	"Acute Schizophrenia" OR DE "Schizophreniform Disorder" OR DE "Schizoaffective Disorder" OR DE "Delusions" OR DE "Hallucinations" OR DE "Acute Psychosis" OR DE "Psychosis"		Search Screen - Advanced Search Database - PsycINFO	

enabled

Systematic reviews en Meta-analyses

#	Query	Limiters/Expanders	Last Run Via	Results	Action
S35	S15 OR S33	Limiters - Methodology: - Systematic Review, -Meta Analysis Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	119	
S34	S15 OR S33	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	6,349	
S33	S30 OR S32	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	608	
S32	S9 AND S31	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	198	
S31	DE "Psychometrics" OR DE "Testing" OR DE "Classical Test Theory" OR DE "Computer Assisted Testing" OR DE "Content Analysis (Test)" OR DE "Difficulty Level (Test)" OR DE "Educational Measurement" OR DE "Item Analysis (Test)" OR DE "Item Content (Test)" OR DE "Item Response Theory" OR DE "Rating" OR	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	117,176	

	DE "Repeated Measures" OR DE "Scaling (Testing)" OR DE "Scoring (Testing)" OR DE "Test Administration" OR DE "Test Bias" OR DE "Test Forms" OR DE "Test Interpretation" OR DE "Test Items" OR DE "Test Reliability" OR DE "Test Standardization" OR DE "Test Validity"			
S30	S9 AND S29	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	444
S29	S20 OR S21 OR S22 OR S23 OR S24 OR S25 OR S26 OR S27 OR S28	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	20,697
S28	"DIGS" OR "Diagnostic Interview for Genetic Studies"	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	178
S27	PSE OR "Present state examination"	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	1,123
S26	"CASH" OR "Comprehensive assessment of Symptoms"	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	2,292
S25	"DIS" OR "Diagnostic Interview Schedule"	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	3,342
S24	"CIDI" OR "Composite International Diagnostic Interview"	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	2,121
S23	"SCID" OR "Structured clinical interview"	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases	5,338

			Search Screen - Advanced Search Database - PsycINFO	
S22	"SIPS" OR SIPS/SOPS OR "structured interview for prodromal symptoms"	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	160
S21	"SCAN" OR "Schedule for clinical assessment in neuropsychiatry"	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	6,430
S20	CAARMS OR "Comprehensive Assessment of At-Risk Mental States"	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	50
S19	S9 AND S18	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	1,918
S18	S10 OR S11 OR S12 OR S17	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	375,428
S17	TI (diagnos* OR psychodiagnos* OR identification OR identifying OR assess* OR reliability OR validity OR prediction OR detection OR sensitivity OR specificity) OR KW (diagnos* OR psychodiagnos* OR identification OR identifying OR assess* OR reliability OR validity OR prediction OR detection OR sensitivity OR specificity)	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	328,671
S16	S9 AND S14	Limiters - Publication Year: 2004-2014 Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	4,137
S15	S9 AND S14	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases	6,265

			Search Screen - Advanced Search Database - PsycINFO	
S14	S10 OR S11 OR S12 OR S13	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	1,017,448
S13	TI (diagnos* OR psychodiagnos* OR identification OR identifying OR assess* OR reliability OR validity OR prediction OR detection OR sensitivity OR specificity) OR KW (diagnos* OR psychodiagnos* OR identification OR identifying OR assess* OR reliability OR validity OR prediction OR detection OR sensitivity OR specificity) OR AB (diagnos* OR psychodiagnos* OR identification OR identifying OR assess* OR reliability OR validity OR prediction OR detection OR sensitivity OR specificity)	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	994,456
S12	DE "Diagnostic Interview Schedule" OR DE "Diagnostic and Statistical Manual"	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	6,144
S11	(((((DE "Prognosis") OR (DE "Prediction")) OR (DE "Test Validity" OR DE "Statistical Validity")) OR (DE "Statistical Reliability")) OR (DE "Test Reliability")) OR (DE "Psychological Assessment" OR DE "Behavioral Assessment" OR DE "Cognitive Assessment" OR DE "Neuropsychological Assessment")	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	127,515

S10	DE "Psychodiagnosis" OR DE "Diagnosis" OR (DE "Dual Diagnosis" OR DE "Psychodiagnostic Typologies" OR DE "Psychodiagnostic Interview" OR DE "Diagnostic Interview Schedule" OR DE "Structured Clinical Interview	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	62,591
S9	S7 OR S8	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	11,558
S8	TI ("early psychosis" OR "first episode psychosis") OR KW ("early psychosis" OR "first episode psychosis")	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	1,490
S7	S3 AND S6	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	11,303
S6	S4 OR S5	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	152,254
S5	TI ("at risk" OR "high risk" OR "increase* risk" OR "risk group*" OR “ultra-high risk” OR “ultra high risk” OR “high clinical risk” OR “clinical high risk” OR “at risk mental state” OR “risk of progression” OR “first-episode psychosis” OR "prodromally symptomatic” OR prodromal* OR prodrome* OR transition OR “mild psychotic symptom*” OR "early symptom*" OR onset OR "early signs" OR first-episode OR "psychosis	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	140,497

	proneness" OR vulnerability) OR KW ("at risk" OR "high risk" OR "increase* risk" OR "risk group*" OR “ultra-high risk” OR “ultra high risk” OR “high clinical risk” OR “clinical high risk” OR “at risk mental state” OR “risk of progression” OR “first-episode psychosis” OR "prodromally symptomatic” OR prodromal* OR prodrome* OR transition OR “mild psychotic symptom*” OR "early symptom*" OR onset OR "early signs" OR first-episode OR "psychosis proneness" OR vulnerability)			
S4	DE "At Risk Populations" OR DE "Risk Factors" OR DE "Prodrome" OR DE "Onset (Disorders)"	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	85,180
S3	S1 OR S2	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	113,008
S2	TI ("childhood onset schizophrenia" OR "delusional disorder*" OR severe mental ill* OR severe mental disorder* OR psychotic OR psychosis OR psychoses OR schizo*) OR KW ("childhood onset schizophrenia" OR "delusional disorder*" OR severe mental ill* OR severe mental disorder* OR psychotic OR psychosis OR psychoses OR schizo*)	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	106,743
S1	DE "Childhood Schizophrenia" OR DE "Schizophrenia" OR DE "Acute Schizophrenia" OR	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	92,371

	DE "Schizophreniform Disorder" OR DE "Schizoaffective Disorder" OR DE "Delusions" OR DE "Hallucinations" OR DE "Acute Psychosis" OR DE "Psychosis"				

Bijlage 4.J QUADAS beoordeling voor diagnostische accuratesse studies - Diagnostiek UHR

SIPS

Se= Sensitivity

Sp= Specificity

PV+= Positive Predictive Value

PV-= Negative Predictive Value

LR+, LR-= Likelihood ratio's

AUC= Area under the ROC curve

Methods	Patients	Instruments	Results	Quality Assesment
Reference: Miller 2003 Study aim: To update the predictive validity as described in Miller 2002 Study design: Setting: Patients were drawn from a total of 123 consecutive symptomatic, treatment-seeking individuals who were referred to the PRIME Clinic for a suspected prodromal syndrome, gave written informed consent, and were given the SIPS from January 23, 1998, through September 1, 2002. Location: Yale University, United States Training of assessors: Index test: range). Interviewers were all "certified" SIPS raters. To be certified, each interviewer must have previously participated in sessions with at least five symptomatic prodromal patients where one of the SIPS	Number of patients: n=34 (out of 123 assessed) Age: 12-45 Sex: 68% male (n=23) 32% female (n=11) Ethnicity: not mentioned Inclusion: reporting one or more symptoms that could be prodromal Exclusion: reporting an established diagnosis of psychotic disorder Co-morbidity: not mentioned Other: individuals were treatment-seeking and referred to the PRIME clinic for a suspected prodromal syndrome	Index test: SIPS Reference test: "Criteria for onset of frank psychosis used by our group are the POPS criteria, part of the SIPS interview. The POPS requires that one or more of the positive items from the SOPS be scored at a psychotic level of intensity and also describes psychotic symptom frequency and duration criteria" Time interval and treatment in between both tests: 6, 12, 18 and 24 months	Target condition: Schizophrenia prodrome / converter Prevalence in sample: According to research assessment (considered 'gold standard'): 6 mo: 18% 12 mo: 21% 18 mo: 30% 24 mo: 35% Results: 6 mo Se: 1.00 (1,00 – 1,00) Sp: 0.71 (0,55 – 0,88) Prevalentie: 0,18 PV+: 0.43 PV- : 1.00 LR+: 3,50 LR-: 0,00 Perc correct: 76% 12 mo Se: 1.00 (1,00 – 1,00) Sp: 0.74 (0,58 – 0,91) Prevalentie: 0,21 PV+: 0.50 PV- : 1.00 LR+: 3,86 LR-: 0,00 Perc correct: 79%	DOMAIN 1: PATIENT SELECTION Could the selection of patients have introduced bias (selection bias)?RISK: HIGH/**LOW**/UNCLEAR Is there concern that the included patients do not match the review question (spectrum bias)? CONCERN: HIGH/**LOW**/UNCLEAR DOMAIN 2: INDEX TEST(S) Could the conduct or interpretation of the index test have introduced bias? RISK: HIGH/**LOW**/UNCLEAR Is there concern that the index test, its conduct, or interpretation differ from the review question? CONCERN: HIGH/**LOW**/UNCLEAR DOMAIN 3: REFERENCE STANDARD Could the reference standard, its conduct, or its interpretation have introduced bias? RISK: **HIGH**/LOW/UNCLEAR Is there concern that the target condition as defined by the reference standard does not match the review question? CONCERN: HIGH/**LOW**/UNCLEAR DOMAIN 4: FLOW AND TIMING

Methods	Patients	Instruments	Results	Quality Assesment
developers was the primary rater and must be judged by one of the SIPS developers as competent to administer the SIPS independently (Miller et al. 2002). Reference test:			18 mo Se: 1.00 (1,00 – 1,00) Sp: 0.74 (0,54 – 0,93) Prevalentie: 0,30 PV+: 0.62 PV- : 1.00 LR+: 3,80 LR-: 0,00 Perc correct: 81% 24 mo Se: 1.00 (1,00 – 1,00) Sp: 0.73 (0,51 – 0,96) Prevalentie: 0,35 PV+: 0.67 PV- : 1.00 LR+: 3,75 LR-: 0,00 Perc correct: 83%	Could the patient flow have introduced bias? RISK: HIGH/LOW/**UNCLEAR**

Methods	Patients	Instruments	Results	Quality Assesment
Reference: Woods 2009 Study aim: This study evaluated the diagnostic validity of the prospective ‘‘prodromal risk syndrome’’ construct. Study design: Prospectief cohortonderzoek Setting: multi-site study (8 sites) in US. 860 nonpsychotic subjects enrolled between 1998 en 2005 were categorized into 5 nonoverlapping groups as described in figure 1 Location: United States Training of assessors:	Number of patients: 638/860 subjects followed up at least 6 months T0: 0 days: 638 200 days: 599 400 days: 522 600 days: 412 800 days: 304 1000 days: 201 Age: only reported for the different subgroups separately: mean age between 16.1 and 19.4 in the different subgroups Sex: only reported for the different subgroups separately: % males between 42.5% and 62.1% in the different subgroups	Index test: SIPS: prodromal patients met the criteria for prodromal syndromes outlined in the SIPS after clinical referral. One or more of 3 criteria had to be met: (1) new onset or recent worsening of subsyndromal (‘‘attenuated’’) positive psychotic symptoms, (2) very brief periods of fully psychotic positive symptoms, or (3) deterioration in functioning within the last year and schizotypal personality disorder (SPD) or a having first-degree relative with psychosis. Reference test: Conversion to psychosis was defined according to criteria operationalized in the SIPS. These criteria define frank psychosis as the presence of positive symptoms of sufficient intensity that are either seriously disorganizing or dangerous or that have been present for a	Target condition: Conversion to psychosis Prevalence in sample: According to research assessment (considered ‘gold standard’): 6 mo: 7% 12 mo: 13% 18 mo: 20% 24 mo: 31% 30 mo: 49% Results: 6 mo Se: 1.00 (1,00 – 1,00) Sp: 0.57 (0,53 – 0,61) Prevalentie: 0,07 PV+: 0.15 PV- : 1.00 LR+: 2,34	DOMAIN 1: PATIENT SELECTION Could the selection of patients have introduced bias (selection bias)?RISK: HIGH/LOW/**UNCLEAR** Is there concern that the included patients do not match the review question (spectrum bias)? CONCERN: HIGH/**LOW**/UNCLEAR DOMAIN 2: INDEX TEST(S) Could the conduct or interpretation of the index test have introduced bias? RISK: HIGH/**LOW**/UNCLEAR Is there concern that the index test, its conduct, or interpretation differ from the review question? CONCERN: HIGH/**LOW**/UNCLEAR DOMAIN 3: REFERENCE STANDARD

Methods	Patients	Instruments	Results	Quality Assesment
Index test: Not mentioned Reference test: Not mentioned (same test as index test, but at a later time)	Ethnicity: not mentioned Inclusion: subjects mostly clinically referred because of psychotic like symptoms (excepts for some persons with first-degree relatives) Exclusion: not mentioned Co-morbidity: DSM-IV diagnostic comorbidity with the prodrome at baseline was common: 69% had one or more mood/anxiety diagnoses, 25% had one or more substance abuse or dependence diagnoses, and 44% had one or more Axis II diagnoses Other: subjects zijn op niet geheel consistente manier gerecruiteerd op de 8 verschllende sites.	month, at least half the days, at least an hour per day Time interval and treatment in between both tests: 6, 12, 18, 24 and 30 months	LR-: 0,00 Perc correct: 60% 12 mo Se: 0.96 (0,91 – 1,00) Sp: 0.58 (0,54 – 0,63) Prevalentie: 0,13 PV+: 0.26 PV- : 0.99 LR+: 2,30 LR-: 0,07 Perc correct: 63% 18 mo Se: 0.95 (0,90 – 1,00) Sp: 0.58 (0,53 – 0,63) Prevalentie: 0,20 PV+: 0.36 PV- : 0.98 LR+: 2,26 LR-: 0,09 Perc correct: 65% 24 mo Se: 0.90 (0,84 – 0,96) Sp: 0.58 (0,52 – 0,65) Prevalentie: 0,31 PV+: 0.49 PV- : 0.93 LR+: 2,17 LR-: 0,17 Perc correct: 68% 30 mo Se: 0,89 (0,83 – 0,95) Sp: 0.68 (0,59 – 0,77) Prevalentie: 0,49 PV+: 0.73 PV- : 0.86 LR+: 2,75 LR-: 0,16 Perc correct: 78%	Could the reference standard, its conduct, or its interpretation have introduced bias? RISK: HIGH/LOW/**UNCLEAR** Is there concern that the target condition as defined by the reference standard does not match the review question? CONCERN: HIGH/**LOW**/UNCLEAR DOMAIN 4: FLOW AND TIMING Could the patient flow have introduced bias? RISK: HIGH/LOW/**UNCLEAR**

Se= Sensitivity

Sp= Specificity
PV+= Positive Predictive Value
PV-= Negative Predictive Value
LR+, LR-= Likelihood ratio's
AUC= Area under the ROC curve

CAARMS

Methods	Patients	Instruments	Results	Quality Assesment
Reference: Yung 2005 Study aim: To assess (amongst others) the predictive validity of CAARMS-defined UHR criteria Study design: longitudinal follow-up study (consecutive referrals to the service for non-psychotic young people were invited to participate in a longitudinal follow-up study) Setting: 1 site, 1 country Location: Melbourne, Australia Training of assessors: Index test: Not mentioned Reference test: Not mentioned	Number of patients: n=150 Age: 15-24 Sex: not mentioned Ethnicity: not mentioned Inclusion: (consecutive referrals to the service for non-psychotic young people were invited to participate in a longitudinal follow-up study): Exclusion: not mentioned Co-morbidity: not mentioned Other: subjects were help-seeking	Index test: Clinicians unstructured CAARMS Reference test: CAARMS Time interval and treatment in between both tests: six months follow-up	Target condition: Transition to psychosis Prevalence in sample: 0,04, so very low which might be due to the short follow-up Results: Se: 0.83 (0,54 – 1,13) Sp: 0.74 (0,66 – 0, 81) Prevalentie: 0,04 PV+: 0.12 PV- : 0.99 LR+: 3,16 LR-: 0,23 Perc correct: 74%	DOMAIN 1: PATIENT SELECTION Could the selection of patients have introduced bias (selection bias)?RISK: HIGH/**LOW**/UNCLEAR Is there concern that the included patients do not match the review question (spectrum bias)? CONCERN: **HIGH**/LOW/UNCLEAR DOMAIN 2: INDEX TEST(S) Could the conduct or interpretation of the index test have introduced bias? RISK: HIGH/**LOW**/UNCLEAR Is there concern that the index test, its conduct, or interpretation differ from the review question? CONCERN: HIGH/**LOW**/UNCLEAR DOMAIN 3: REFERENCE STANDARD Could the reference standard, its conduct, or its interpretation have introduced bias? RISK: HIGH/LOW/**UNCLEAR** Is there concern that the target condition as defined by the reference standard does not match the review question? CONCERN: HIGH/**LOW**/UNCLEAR DOMAIN 4: FLOW AND TIMING Could the patient flow have introduced bias? RISK: HIGH/**LOW**/UNCLEAR

Se= Sensitivity
Sp= Specificity
PV+= Positive Predictive Value
PV-= Negative Predictive Value
LR+, LR-= Likelihood ratio's
AUC= Area under the ROC curve

Methods	Patients	Instruments	Results	Quality Assesment
Reference: Yung 2006 Study aim: To investigate the prevalence of UHR status in a sample of help-seeking young people aged 15–24. To determine the predictive validity of the UHR criteria by following the sample up for 6 months. To investigate whether psychosocial functioning is predictive of onset of psychotic disorder in the UHR+ group and the sample as a whole. Study design: cohort study Setting: "…we recruited a cohort who presented to a clinical service for young people with mental health problems…" Location: Melbourne, Australia Training of assessors: Index test: "Research assessments were conducted by graduate psychologists who had been specifically trained in administration of the CAARMS." Reference test:	Number of patients: n=292 (out of 629) Age: 15-24 Mean age 18.13 yrs Sex: 49% male (n=143) 51% female (n=149) Ethnicity: Inclusion: all referrals to ORYGEN Youth Health (OYH) between April and October 2003 who were not already psychotic. Age between 15-24, residing in OYH's catchment area Exclusion: presence of psychotic disorder, known organic cause for presentation, known intellectual disability (IQ<70) and an inability to speak English. Co-morbidity: not mentioned Other: subjects were help-seeking	Index test: CAARMS (to assess APS and BLIPS) FIGS + GAF or CGAS (to assess Trait criteria) (uiteindelijk 106/119 APS only; 8/119 Trait only; 5/119 APS+Trait; 0/119 BLIPS) Reference test: Using the CAARMS cut off criteria for frank psychosis for 195/292 participants Using clinical notes from medical record files for the remaining subjects (97/292) Time interval and treatment in between both tests: Transition to psychosis assessed after 6 months	Target condition: Transition to psychosis Prevalence in sample: 13 young people had become psychotic within 6 months (4.5% 95%CI: 2.5% - 7.7% Results (whole sample): Se: 0.92 (0,78 – 1,07) Sp: 0.62 (0,56 – 0,67) Prevalentie: 0,04 PV+: 0.10 PV- : 0.99 LR+: 2,41 LR-: 0,12 Perc correct: 63% Results (PACE): Se: 1.00 (1.00 – 1,00) Sp: 0.49 (0,41 – 0,58) Prevalentie: 0,05 PV+: 0.09 PV- : 1.00 LR+: 1.97 LR-: 0,00 Perc correct: 52% Results (YouthScope): Se: 0.83 (0,54 – 1,13) Sp: 0.73 (0,66 – 0,81) Prevalentie: 0,04 PV+: 0.12	DOMAIN 1: PATIENT SELECTION Could the selection of patients have introduced bias (selection bias)?RISK: HIGH/**LOW**/UNCLEAR Is there concern that the included patients do not match the review question (spectrum bias)? CONCERN: HIGH/**LOW**/UNCLEAR DOMAIN 2: INDEX TEST(S) Could the conduct or interpretation of the index test have introduced bias? RISK: HIGH/**LOW**/UNCLEAR Is there concern that the index test, its conduct, or interpretation differ from the review question? CONCERN: HIGH/**LOW**/UNCLEAR DOMAIN 3: REFERENCE STANDARD Could the reference standard, its conduct, or its interpretation have introduced bias? RISK: HIGH/LOW/**UNCLEAR** Is there concern that the target condition as defined by the reference standard does not match the review question? CONCERN: HIGH/**LOW**/UNCLEAR DOMAIN 4: FLOW AND TIMING Could the patient flow have introduced bias? RISK: HIGH/LOW/**UNCLEAR**

Methods	Patients	Instruments	Results	Quality Assesment
"Research assessments were conducted by graduate psychologists who had been specifically trained in administration of the CAARMS."			PV- : 0.99 LR+: 3,14 LR-: 0,23 Perc correct: 74%	

Se= Sensitivity

Sp= Specificity

PV+= Positive Predictive Value

PV-= Negative Predictive Value

LR+, LR-= Likelihood ratio's

AUC= Area under the ROC curve

Methods	Patients	Instruments	Results	Quality Assesment
Reference: Yung 2008 Study aim: The primary aim was to determine the medium term (2 year) predictive validity of the ultra high risk (UHR) criteria in a sample of adolescents and young adults seeking help from a youth mental health service. Study design: cohort study Setting: "…we recruited a cohort who presented to a clinical service for young people with mental health problems…" Location: Melbourne, Australia Training of assessors: Index test: "Research assessments were conducted by graduate psychologists who had been specifically trained in administration of the CAARMS." Reference test: "Research assessments were conducted by graduate psychologists	Number of patients: n=292 (out of 629) Age: 15-24 Sex: 49% male (n=143) 51% female (n=149) Ethnicity: Inclusion: all referrals to ORYGEN Youth Health (OYH) between April and October 2003 who were not already psychotic. Age between 15-24, residing in OYH's catchment area Exclusion: presence of psychotic disorder, known organic cause for presentation, known intellectual disability (IQ<70) and an inability to speak English. Co-morbidity: not mentioned Other: subjects were help-seeking	Index test: CAARMS (to assess APS and BLIPS) FIGS + GAF or CGAS (to assess Trait criteria) (uiteindelijk 106/119 APS only; 8/119 Trait only; 5/119 APS+Trait; 0/119 BLIPS) Reference test: Using the CAARMS cut off criteria for frank psychosis for 193/292 participants Using clinical notes from medical record files for the remaining subjects (99/292) Time interval and treatment in between both tests: Transition to psychosis assessed after 2 years	Target condition: Transition to psychosis Prevalence in sample: 21 individuals (7.2%) developed psychotic disorder at 2 year follow up Results: Whole sample Se: 0.90 (0,78 – 1,03) Sp: 0.63 (0,57 – 0,69) Prevalentie: 0,07 PV+: 0.16 PV- : 0.99 LR+: 2,45 LR-: 0,15 Perc correct: 65% PACE subgroup: Se: 1.00 (1,00 – 1,00) Sp: 0.52 (0,43 – 0,60) Prevalentie: 0,09 PV+: 0.17 PV- : 1.00 LR+: 2,06 LR-: 0,00 Perc correct: 56% YouthScope subgroup: Se: 0.75 (0,45 – 1,05)	DOMAIN 1: PATIENT SELECTION Could the selection of patients have introduced bias (selection bias)?RISK: HIGH/**LOW**/UNCLEAR Is there concern that the included patients do not match the review question (spectrum bias)? CONCERN: HIGH/**LOW**/UNCLEAR DOMAIN 2: INDEX TEST(S) Could the conduct or interpretation of the index test have introduced bias? RISK: HIGH/**LOW**/UNCLEAR Is there concern that the index test, its conduct, or interpretation differ from the review question? CONCERN: HIGH/**LOW**/UNCLEAR DOMAIN 3: REFERENCE STANDARD Could the reference standard, its conduct, or its interpretation have introduced bias? RISK: HIGH/LOW/**UNCLEAR** Is there concern that the target condition as defined by the reference standard does not match the review question? CONCERN: HIGH/**LOW**/UNCLEAR DOMAIN 4: FLOW AND TIMING

Methods	Patients	Instruments	Results	Quality Assesment
who had been specifically trained in administration of the CAARMS."			Sp: 0.74 (0,66 – 0,81) Prevalentie: 0,05 PV+: 0.14 PV- : 0.98 LR+: 2,86 LR-: 0,34 Perc correct: 74%	Could the patient flow have introduced bias? RISK: HIGH/LOW/**UNCLEAR**

Se= Sensitivity
Sp= Specificity
PV+= Positive Predictive Value
PV-= Negative Predictive Value
LR+, LR-= Likelihood ratio's
AUC= Area under the ROC curve

Toelichting

Item	Omschrijving
Referentie:	1e auteur (publicatiejaar)
Doel studie:	doel (aim; objectives) van de studie (bijvoorbeeld: accuratesse test, reproduceerbaarheid test, bepaling van afkappunt of vergelijkbaarheid van twee of meer tests)
Studieopzet:	specificeer de onderzoeksopzet (dwarsdoorsnedeonderzoek, prospectief cohort onderzoek, rct)
Setting:	aantal centra, betrokken landen, 1e/2e/3e lijn, stad/platteland/stad-platteland
Locatie:	specificeer naam / plaats instelling
Training onderzoekers:	specificeer het aantal, de training en expertise van degenen die de tests uitvoeren en van degenen die de testuitslagen beoordelen onderzoekers
Aantal:	aantal patiënten betrokken in studie en aantal geanalyseerd, en aantal patiënten niet geanalyseerd met opgaaf van reden (bijv. niet interpreteerbare resultaten)
Leeftijd:	gemiddelde; standaarddeviatie of bereik (minimum – maximum)
Sekseratio:	percentage vrouw
Etniciteit:	Percentage participanten van etnische achtergrond
In- en exclusie:	specificeer met name ook de karakteristieken en de fase van de ziekte
Ziekteprevalentie:	specificeer schatting van de prevalentie in de algehele bevolking

Co-morbiditeit:	Ontwikkelingsachterstand danwel de ontwikkelingsleeftijd, verstandelijke handicap, taalachterstand, ggz problematiek, epilepsie, genetische aandoeningen, eerdere testresultaten.
Overig:	B.v. SES, opleidingsniveau ouders, verwijzing, procedure.
Level:	1, 2a, 2b, of 3.
Indextest:	beschrijf de indextest, afkappunten, wie het instrument afnam en of de onderzoekers geblindeerd waren. Multidisciplinair team of monodiscipinair. Percentage ontbrekende of oninterpreteerbare testresultaten
Referentietest:	beschrijf de referentietest, afkappunten, wie het instrument afnam en of de onderzoekers geblindeerd waren. Multidisciplinair team of monodiscipinair. Percentage ontbrekende of oninterpreteerbare testresultaten
Tijdsinterval en behandeling tussen beide tests:	geef aan of er sprake was van een tijdsinterval of behandeling
Onderzochte stoornissen:	Criteria targetconditie, prevalentie van de onderzochte stoornissen in de steekproef.
Resultaten:	specificeer de accuratesse uitkomsten: Sensitiviteit (Se); Specificiteit (Sp); Positief voorspellende waarde (PPV); Negatief voorspellende waarde (NPV); Likelihood ratio's (LR+, LR-); Area under the ROC curve (AUC) etc. met inbegrip van een betrouwbaarheidsinterval. Vermeld ook de neveneffecten / complicaties van de indextest en referentietest.
Kwaliteitsbeoordeling:	zie literatuurbeoordelingsformulieren; bewijskracht conform EBRO-classificatie; belangenverstrengeling: b.v. financiering (overheidsgeld, farmaceutische industrie, instelling van gezondheidszorg) of andere belangen.

Hoofdstuk 5 Diagnostiek van psychose

Bijlage 5.A Klinische schaal voor de beoordeling van dimensies van psychose.

Naam:

Leeftijd:

Geslacht:
Datum:

I Hallucinaties	Afwezig	Twijfelachtig (Ernst of duur niet voldoende om als psychose te worden beschouwd)	Aanwezig, maar in lichte mate (weinig aandrang om gehoor te geven aan de stemmen,, niet veel hinder van stemmen)	Aanwezig en matig (enige aandrang om gehoor te geven aan de stemmen of heeft enige hinder van de stemmen)	Aanwezig en ernstig (sterke aandrang om gehoor te geven aan de stemmen of heeft veel hinder van de stemmen)
II Wanen	Afwezig	Twijfelachtig (Ernst of duur niet voldoende om als psychose te worden beschouwd)	Aanwezig maar in lichte mate (weinig aandrang om gehoor te geven aan de wanen, niet veel hinder van wanen)	Aanwezig en matig (enige aandrang om gehoor te geven aan de wanen of heeft enige hinder van de wanen)	Aanwezig en ernstig (sterke aandrang om gehoor te geven aan de wanen of heeft veel hinder van de wanen)
III Gedesorganiseerde spraak	Afwezig	Twijfelachtig (Ernst of duur niet voldoende om als desorganisatie te worden beschouwd)	Aanwezig maar licht (enige moeite met volgen van de gesproken taal)	Aanwezig en matig (de gesproken taal is vaak moeilijk te volgen)	Aanwezig en ernstig (de gesproken taal is bijna niet te volgen)
IV Abnormale psychomotoriek	Afwezig	Twijfelachtig (Ernst of duur niet voldoende om als abnormale psychomotoriek te worden beschouwd)	Aanwezig, maar licht (af en toe abnormale of bizarre psychomotoriek of katatonie)	Aanwezig en matig (frequent abnormale of bizarre psychomotoriek of katatonie)	Aanwezig en ernstig (abnormale of bizarre psychomotoriek of katatonie bijna constant aanwezig)
V Negatieve Symptomen (affectieve vervlakking of initiatiefverlies	Afwezig	Twijfelachtige vermindering van mimiek, prosodie, gestiek of eigen initiatief in het gedrag	Aanwezige, maar lichte vermindering van mimiek, prosodie, gestiek of eigen initiatief in het gedrag	Aanwezige en matige vermindering in mimiek, prosodie, gestiek of eigen initiatief in het gedrag	Aanwezige en ernstige vermindering in mimiek, prosodie, gestiek of eigen initiatief in het gedrag
VI Cognitieve beperkingen	Afwezig	Twijfelachtig (cognitief functioneren wijkt niet duidelijk af van wat kan worden verwacht gezien de	Aanwezig maar licht (enige achteruitgang in het cognitieve functioneren; slechter dan verwacht gezien de leeftijd en	Aanwezig en matig (duidelijke achteruitgang in het cognitieve functioneren; slechter dan verwacht gezien	Aanwezig en ernstig (ernstige achteruitgang in het cognitieve functioneren; slechter

		leeftijd en SES; dwz minder dan 0,5 SD van gemiddelde)	SES; 0,5-1 SD onder het gemiddelde)	de leeftijd en SES; 1-2 SD onder het gemiddelde)	dan verwacht gezien de leeftijd en SES; > 2 SD onder het gemiddelde)
VII Depressiviteit	Afwezig	Twijfelachtig (voelt zich soms verdrietig, somber, gedeprimeerd of hopeloos; maakt zich wel zorgen over het idee dat hij/zij iemand in de steek heeft gelaten of gefaald te hebben, maar niet op een gepreoccupeerde manier)	Aanwezig maar licht (frequente perioden waarin hij/zij zich erg verdrietig, somber, matig gedeprimeerd of hopeloos voelt; maakt zich op een enigszins gepreoccupeerde manier zorgen over het idee dat hij/zij iemand in de steek heeft gelaten of gefaald heeft)	Aanwezig, matig ernstig (frequente perioden van diepe depressiviteit of hopeloosheid; gepreoccupeerd bezig met schuld, dingen verkeerd te hebben gedaan)	Aanwezig en ernstig (dagelijks diepe depressiviteit of hopeloosheid; schuldwanen of onredelijke zelfverwijten, die duidelijk niet in verhouding staan tot de omstandigheden)
VIII Manie	Afwezig	Twijfelachtig (af en toe verhoogde, expansieve of prikkelbare stemming of enige rusteloosheid)	Aanwezig, maar licht (frequente perioden met een iets verhoogde, expansieve of prikkelbare stemming of rusteloosheid)	Aanwezig en matig (frequente perioden van een sterk verhoogde, expansieve of prikkelbare stemming, of rusteloosheid)	Aanwezig en ernstig (dagelijks een sterk verhoogde, expansieve of prikkelbare stemming, of rusteloosheid)

Bijlage 5.B Achtergrondinformatie vragenlijsten

Hallucinaties / Wanen / Gedesorganiseerde spraak / Negatieve symptomen (dimensie 1 tm 3 en 5)

In het handboek en het protocol wordt de Positive and Negative Syndrome Scale (PANSS) aangeraden, tevens wordt in het protocol ook de mogelijkheid geboden om voor de Brief Psychiatric Rating Scale (BPRS) te kiezen.

PANSS (Kay, Opler, en Fiszbein, 1986; Vertaling Linszen, de Haan, Kuipers, en Dingemans,
AMC afdeling psychiatrie)
Doel: Gestandaardiseerde techniek ter evaluatie van positieve en negatieve symptoomklassen (samenvoeging van de BPRS en de Psychopathology Rating Scale
(Kay et al., 1987))
Praktijktoepassing: Het interview duurt ongeveer 45 minuten om af te nemen. Wordt in toenemende mate ingezet om de psychopathologie te beoordelen tijdens de jaarlijkse routine outcome monitoring.
Vorm: Semi-gestructureerd interview. 30 items, onderverdeeld in 3 subschalen: positieve-(7 items), negatieve-(7 items), en algemene psychopathologie (16 items).
Psychometrie: Het interview is betrouwbaar en valide (construct en criterium). (Kay et al. 1988)

BPRS (Overall en Gorham, 1962; Vertaling Dingemans, 1986))
Doel: Brengt de ernst van psychotische symptomen in kaart
Praktijktoepassing: Wordt in toenemende mate ingezet om de psychopathologie te beoordelen tijdens de jaarlijkse routine outcome monitoring.
Vorm: Interview en een observatiedeel in 24 items met betrekking op positieve en negatieve symptomen, somatisatie, angst, affect, suicidaliteit, en autisme. De items worden beoordeeld door middel van een zes- tot negenpuntsschaal.
Psychometrie: De 24-itemsversie is gevalideerd bij adolescenten en bleek in tegenstelling tot de 18-item versie affectieve symptomen te herkennen (Dingemans et al., 1995)

Abnormale psychomotoriek (dimensie 4)
In het protocol en het handboek worden geen standaard instrumenten aangeraden. Belangrijke oorzaken van abnormale psychomotoriek zijn katatonie en door antipsychotica geïnduceerde bewegingsstoornissen. De meest gebruikte instrumenten zijn de Bush-Francis Catatonia Rating Scale[2] voor katatonie, en de Simpson Angus Scale [3] en de St Hans Rating Scale[4] voor bewegingsstoornissen.

Cognitieve beperkingen (dimensie 6)
Het GROUP protocol raadt aan om een NPO te doen met behulp van de Behavioural Assessment of the Dysexecutive Syndrome (BADS), 15 Woordentest (15WT) en Wechsler Adult Intelligence Scale (WAISIII).

WAIS-III(-NL)
Doel: Meten algemene intelligentie bij personen van 16 jaar of ouder
Praktijktoepassing: Het is een veelomvattend en tijdrovend instrument. De gehele test duurt bij gezonde subjecten gemiddeld 80 minuten, en gemiddeld 100 minuten in een klinische setting. Deze kan worden afgenomen door een psychodiagnostisch werker. De scoring en interpretatie door een orthopedagoog of psycholoog neemt 120 minuten in beslag. Blyler Gold, Iannone, en Buchanan (2000) verkorte versie van de WASI-III ontwikkeld en is geschikt voor het schatten van algemene intelligentie bij patiënten met schizofrenie en gezonde subjecten.
Vorm: De originele versie bestaat uit 16 subtaken.

Psychometrie: Volgens COTAN-beoordeling 2006 worden de kwaliteit van het testmateriaal, de handleiding en de betrouwbaarheid van instrument als goed beoordeeld. De begripsvaliditeit is voldoende en de criteriumvaliditeit is onvoldoende (deze is niet onderzocht). De WAIS blijkt verder een groter onderscheid te maken tussen patiënten met schizofrenie en gezonde controles in vergelijking met andere intelligentie tests, zoals de National Adult Reading Test (Heinrich en Zakzanis, 1998).

BADS (Wilson, Alderman, Burgess, Emslie, en Evans, 1996; Vertaling Krabbendam en Kalff, 1998)
Doel: Meten van executieve functies (prestatie op taken gebaseerd op situaties uit het dagelijks leven). De test beoogt cognitieve flexibiliteit, temporele schatting en planning van gedrag in nieuwe situaties te onderzoeken.
Praktijktoepassing: De lijst wordt door klinisch psycholoog, neuropsycholoog, andere neuropsychologische diagnostici afgenomen in ongeveer 45 minuten (geen tijdslimiet).
Vorm: Test met 6 subtaken.
Psychometrie: Volgens COTAN-beoordeling 1999 is de kwaliteit van het testmateriaal en de handleiding als goed beoordeeld. De betrouwbaarheid en validiteit is niet onderzocht en daarom als onvoldoende beoordeeld. Verder is uit onderzoek gebleken dat patiënten met schizofrenie met name bij deze tests een disfunctioneren laten zien dan bij andere executieve functietests, zoals bijvoorbeeld de Tower of London (Krabbendam, Vugt, Derix, en Jolles, 1999).

15WT (Kalverboer en Deelman, 1986)
Doel: Meten van het verbaal geheugen bij personen van 14 jaar en ouder
Praktijktoepassing: Onder supervisie van een psycholoog kan deze lijst worden afgenomen in 15 minuten en vervolgens in 10 minuten geïnterpreteerd.
Vorm: In de test wordt het direct reproduceren van de woorden, het reproduceren van de woorden na een interval, en herkenning van de woorden gemeten.
Psychometrie: Volgens COTAN-beoordeling 2000 is de kwaliteit van het testmateriaal en de handleiding voldoende. De betrouwbaarheid en begripsvaliditeit van het instrument zijn voldoende en de criteriumvaliditeit is onvoldoende (deze is niet onderzocht).

<u>Depressiviteit (dimensie 7)</u>
In het handboek wordt de Beck Depression Inventory (BDI) aangeraden, in het protocol ook maar daar kan men ook nog voor de Calgary Depression Scale for Schizophrenia (CDSS) kiezen.

CDS (Addington, Addington, en Matica-Tyndale, 1993; Vertaling; Dingemans, 1995)
Doel: Inventarisatie van depressieve klachten bij personen met schizofrenie.
Praktijktoepassing: Afname moet worden verricht door iemand die veel ervaring heeft met de schaal.
Vorm: Een semigestructureerde 9 item schaal met vier score mogelijkheden per item.
Psychometrie: Het is een Valide en betrouwbaar instrument. Een score van boven de 6 heeft een specificiteit van 0.82 en een sensitiviteit van 0.85 om een ernstige depressieve episode te detecteren. (Addington et al. 1993)

BDI (Beck et al., 1961; Beck et al., 1979; Vertaling BDI-II-NL; van der Does, 2002)
Doel: Het instrument wordt gebruikt voor het beoordelen van symptomen die overeenkomen met de DSM-IV-criteria voor depressieve stoornissen. Met de BDI-II-NL kan geen diagnose gesteld worden, hiervoor is aanvullend onderzoek door een clinicus nodig. (bij personen van 13 jaar en ouder met schizofrenie in acute of reststadia van de stoornis)
Praktijktoepassing: De lijst wordt veel gebruikt in de praktijk en kan door gedragstherapeuten met klinische training en ervaring, psychiaters, psychologen in ongeveer 15 minuten worden afgenomen en geïnterpreteerd.
Vorm: Een instrument bestaand uit 21 items met steeds vier uitspraken. De cliënt moet bij elk item die uitspraak aankruisen die het best beschrijft hoe hij zich de afgelopen twee weken gevoeld heeft. De items betreffen somberheid, pessimisme, mislukkingen, enz. Er zijn vier antwoordmogelijkheden. De BDI-II is onderverdeeld in

drie dimensies: Affectief, Cognitief en Somatisch met resp. 5, 7 en 9 items. De BDI-II kan ook mondeling worden afgenomen.
Psychometrie: Volgens COTAN-beoordeling 2004 worden de kwaliteit van het testmateriaal, de handleiding en de betrouwbaarheid van instrument als goed beoordeeld. De begripsvaliditeit is voldoende en de criteriumvaliditeit is onvoldoende (deze is niet onderzocht). Verder bleek in een studie (Viinamaki et al. 2004) dat bij een cut-off score van 14/15 de beste resultaten worden bereikt om een depressie te herkennen (Se:0.84 , Sp:0.81; AUC: 0.81). Als er nog een diagnostisch interview op volgt, wordt er aangeraden om de cutoff score te verlagen om de sensitiviteit van het instrument te verhogen.

Manie (dimensie 8)

Young Mania Rating Scale (YMRS) (Young et al. 1978)
Doel: In kaart brengen ernst van manische symptomen in de laatste 48 uur.
Praktijktoepassing: Het kost een ervaren hulpverlener 15-30 minuten om de lijst af te nemen.
Vorm: Een instrument bestaand uit 11 items met steeds vijf ernst inschattingen (van afwezig tot ernstig). De volgende items worden behandeld in de Nederlandse versie (Altrecht 1995) van de YMRS: Verhoogde stemming, Verhoogde motorische activiteit – energie, Seksuele interesse, Slaap, Prikkelbaarheid, Spraak, Taal- en denkstoornissen, Inhoud, Verstorende – agressief gedrag, Uiterlijk en Inzicht. Een uitslag van 12 of hoger wordt vaak als manie aangeduid.
Psychometrie: De YMRS is een betrouwbaar en valide instrument (Young et al. 1978)

Functionele beperkingen
In het handboek en het protocol wordt de GAF aangeraden om af te nemen, maar in de DSM-5 wordt dit instrument vervangen door de World Health Organization Disability Assessment Schedule (WHO-DAS). Daarnaast raadt het protocol de Health of the Nation Outcome Scale (HONOS) aan en het handboek de Clinical Global Impression scale (CGI) en Personal and Social Performance scale (PSP).

WHO-DAS2
Doel: De WHODAS2 kan gebruikt worden om bij een diagnose volgens de DSM-5 de mate van ernst van een stoornis te bepalen. Het biedt informatie over de gevolgen van de stoornis voor het dagelijks functioneren.
Praktijktoepassing: Afname van de 36-item interviewversie duurt 20 tot 45 minuten
Vorm: Er zijn drie afnamevarianten: een interviewversie, een zelfinvulversie, en een ‘proxy’-versie die door een derde partij (familie, behandelaar en dergelijke) ingevuld kan worden.
De volledige versie heeft 36 items en resulteert in een totaalscore voor het algemene functioneren en zes schaalscores voor de verschillende domeinen van functioneren. De verkorte versie heeft twaalf items en resulteert in een algemene functioneringsscore. Beide versies zijn beschikbaar voor alle drie de afnamevarianten. Daarnaast is er een getrapte 12+24-item versie die gebruikt kan worden om te screenen voor probleemgebieden van functioneren. De getrapte versie kan als interview worden afgenomen of door computer-adaptive testing (CAT; nog niet beschikbaar in het Nederlands).
Voor patiënten met een ernstige psychiatrische aandoening en/of cognitieve beperkingen wordt aangeraden de interviewversie en/ of de proxy-versie te gebruiken. De zelfinvulversie is dan minder geschikt.
Psychometrie: De WHODAS2 is een betrouwbaar en valide instrument en is getest in verschillende landen en populaties. (Ustun et al. 2009)

HoNOS (Wing, Beevor, Curtis, Park, Hadden en Burns,1998; vertaling Mulder, Wierdsma en Sytema, 2000)
Doel: Routinematig inventariseren van de geestelijke gezondheid
en sociaal functioneren van mensen met een psychische ziekte

Praktijktoepassing: De lijst moet worden ingevuld door de eigen behandelaar. Het instrument is gevoelig voor verandering, of voor stagnatie van het functioneren, en in principe geschikt voor alle GGZ patiënten. Het is een eenvoudig
en in een korte tijdsduur te gebruiken schaal.
Vorm: De HoNOS bestaat uit twaalf items op een vijfpuntsschalen bestaande uit vier subschalen: gedragsproblemen, beperkingen, symptomatologie en sociale problemen. Een analyse naar subschalen geeft een psychotische en een neurotische dimensie. In de vertaling van Mulder et al. (2001) is er nog een addendum toegevoegd met drie extra items (maniforme ontremming, motivatie, compliance met medicatie).
Psychometrie: De lijst blijkt goed te correleren met andere lijsten zoals de CANSAS en de BPRS en heeft een redelijke betrouwbaarheid (Mulder, Staring, Loos, Buwalda, Kuijpers, Sytema, en Wierdsma, 2004).

CGI
Doel: Beoordeling van het globaal functioneren van een patiënt.
Praktijktoepassing: De hulpverlener beoordeelt hoe ernstig de symptomen zijn en of er verbeteringen/verslechteringen zijn opgetreden ten opzichte van de laatste meting.
Vorm: Een instrument bestaand uit twee onderdelen (CGI-S en CGI-I) en bestaat uit 7 items. Een lage score houdt in dat de patiënt niet ziek of erg verbeterd is. Een hoge score betekent dat de patiënt ernstig ziek is of de situatie enorm verslechterd is.
Psychometrie: In 2003 is de Clinical Global Impression – Schizophrenia Scale (CGIS) gepubliceerd (Halo et al., 2003). Deze schaal is volgens dezelfde studie een valide en betrouwbaar instrument. Het instrument is in het Nederlands vertaalde (Nolen, AZG Groningen)

PSP
Doel: Het meten van het psychosociaal functioneren bij patiënten met schizofrenie
Praktijktoepassing: Het kost de hulpverlener 5 minuten om het instrument af te nemen.
Vorm: Het gaat om een 100-punts schaal bestaande uit vier onderdelen: 1.Nuttige sociale activiteiten; 2.Persoonlijke en sociale relaties; 3. Zelfverzorging en 4. Storend en agressief gedrag. Elk gebied heeft als beoordeling in zes niveaus van ernst (van afwezig tot zeer ernstig).
Psychometrie: Volgens de ontwikkelaars van het instrument is in een Duits onderzoek aangetoond dat het een betrouwbaar en valide instrument is (ook tijdens een acutefase van de stoornis). (http://www.medscape.com/viewarticle/582326_7)

<u>Categoriale diagnostiek</u>
Voor de categoriale diagnostiek kunnen semigestructureerde interviews worden afgenomen zoals de: Comprehensive Assessment of Symptoms and History (CASH) (Andreasen et al., 1992), (Gestructureerd Klinisch Interview voor de vaststelling van DSM-IV As-I Stoornissen (SCID) (Wing et al., 1998) en de verkorte Schedule for Clinical Assessment in Neuropsychiatry **(**(mini-)SCAN). Er is weinig gepubliceerd bewijs dat het gebruik van semigestructureerde diagnostische interviews leidt tot een meer betrouwbare en valide diagnostiek. De vroege psychose richtlijn baseert zich daarom op uitspraken van de werkgroep van de MDR Schizofrenie. Deze werkgroep is van mening dat het zinvol is om bij iedere patiënt bij wie men een schizofrene stoornis vermoedt, een semigestructureerd diagnostisch interview af te nemen (cash, scan, scid), omdat deze procedure de kans op missen van belangrijke psychopathologische stoornissen verkleint en soms nog belangrijke aanvullende informatie oplevert.

SCAN 2.1 (vertaling Giel & Nienhuis 2000; origineel: Wing et al., 1998); WHO, 1992, 1999)
Doel: Het vaststellen van de aan- en afwezigheid van psychiatrische symptomen, zoals opgenomen in de DSM-IV
Praktijktoepassing: Individueel afgenomen via de pen-en-papiermethode. De afnameduur is variabel. In praktijk lastig toepasbaar, door zijn lengte.
Vorm: Kenmerkend is dat het interview een veel breder scala aan vragen omvat dan andere diagnostische instrumenten. Vragen gaan over As-1 stoornissen, zoals stemmingsstoornissen, angststoornissen,

eetstoornissen, psychotische stoornissen, afhankelijkheid van middelen, somatoforme stoornissen en cognitieve achteruitgang. Met de SCAN worden geen persoonlijkheidsstoornissen gemeten.
Psychometrie: De concurrente validiteit met de SCAN is goed (Nienhuis e.a. 2010).

Mini-SCAN
Doel: Vaststellen (differentiaal) diagnose.
Praktijktoepassing: Verkorte versie SCAN, waardoor beter toepasbaar in de praktijk. Het neem gemiddeld 30 minuten in beslag. (bij een poliklinische patiënt met depressieve en/of angstklachten)
Vorm: Semigestructureerd. Papier en online/digitaal.
Afname wijze: Screening op alle veelvoorkomende stoornissen om bij een positief gescreende stoornis vervolgvragen te stellen. Scoring is door aan te geven of een symptoom wel of niet aanwezig is.

CASH (Andreasen et al. 1992)
Doel: Vaststellen (differentiaal) diagnose, speciaal ontwikkeld voor onderzoeken waarin personen met schizofrenie of een affectieve stoornis werden geïncludeerd.
Praktijktoepassing: Vanwege de hoeveelheid informatie die wordt verzameld kan het als basis dienen voor verschillende systemen van diagnostiek (bijv. ICD en DSM)
Vorm: De vragen zijn zo opgesteld dat er informatie komt met betrekking tot de huidige en vroegere symptomen, premorbide functioneren, cognitief functioneren, sociodemografische de status, de behandeling, en het verloop van de ziekte
Psychometrie: Tijdens de ontwikkeling zijn er betrouwbaarheid en validatie studies verricht.

SCID
Doel: Gestructureerd Klinisch Interview voor de vaststelling van DSM-IV As-I Stoornissen bij volwassenen
Praktijktoepassing: Afname duur is variabel. De interviewer moet kennis hebben van As-I stoornissen en van persoonlijkheidsstoornissen. Daarnaast moet de interviewer bekend zijn met de verschillende verschijningsvormen van psychopathologie en maar vooral van de diagnostische criteria van de DSM-IV.
Vorm: Er kunnen in totaal 292 vragen worden afgenomen waarbij alle DSM criteria voor de belangrijkste psychiatrische stoornissen worden gescoord als aanwezig, twijfelachtig of afwezig.

Familie
In het GROUP protocol wordt geen instrument aangeraden voor heteroanamnese en het handboek raadt het Interview for the Retrospective Assessment of the Onset and course of schizophrenia (IRAOS) aan.

IRAOS
Doel: Het nagaan van premorbide (sociale) ontwikkeling, en het ontstaan en verloop van ernstige psychische aandoeningen (bijvoorbeeld schizofrenie, affectieve psychosen).
Praktijktoepassing: Gemiddelde duurt de afname 1,5-2 uur, en er is ongeveer dezelfde hoeveelheid tijd nodig om de informatie te coderen.
Vorm: De IRAOS is een semigestructureerd interview oorspronkelijk ontwikkeld voor de beoordeling van het ontstaan en beloop van schizofrenie. De huidige, tweede versie is uitgebreid zodat het van toepassing is op alle psychotische stoornissen (affectieve en niet-affectieve). De IRAOS bestaat uit onderdelen over sociodemografische variabelen (levensgeschiedenis, scholing, beroepsopleiding, inkomen en woonsituatie, informatie over de familiegeschiedenis, pre- en perinatale complicaties, partner), behandeling en symptoom ontwikkeling (ontstaansdatum, remissie, terugval, en verloop van de vroege psychose).
Psychometrie: Het instrument heeft een hoge betrouwbaarheid en is valide.

Bijlage 5.C Search history patiëntkenmerken en beloop bij vroege psychose

NIEUW

PsycInfo

#	Query	Limiters/Expanders	Last Run Via	Results
S31	S26 AND S29	Limiters - Publication Type: All Journals Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	207
S30	S26 AND S29	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	224
S29	S27 OR S28	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	134,104
S28	TI (prospect* OR course OR prognosis OR prognostic OR predict*) OR KW (prospect* OR course OR prognosis OR prognostic OR predict*)	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	117,736
S27	DE "Disease Course" OR DE "Prognosis" OR DE "Recovery (Disorders)" OR DE "Remission (Disorders)" OR DE "Spontaneous Remission" OR DE "Symptom Remission"	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	27,209
S26	S12 AND S25	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	1,548

S25	S15 OR S16 OR S17 OR S18 OR S19 OR S20 OR S21 OR S22 OR S23 OR S24	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	401,131
S24	DE "Side Effects (Drug)"	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	20,470
S23	(((DE "Employment Status" OR DE "Unemployment") OR (DE "Daily Activities")) OR (DE "School Attendance")) OR (DE "Education")	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	43,309
S22	(DE "Aggressive Behavior") OR (DE "Aggressiveness")	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	23,878
S21	TI life-events OR KW life-events	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	6,131
S20	DE "Comorbidity"	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	22,289
S19	DE "Addiction" OR DE "Alcoholism" OR DE "Drug Addiction" OR DE "Alcohol Abuse" OR DE "Pathological Gambling" OR DE "Dual Diagnosis" OR DE "Physical Disorders"	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	65,600
S18	DE "Drug Usage" OR DE "Alcohol Drinking Patterns" OR DE "Drug Abuse" OR DE "Intravenous Drug Usage" OR DE "Marijuana Usage"	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	68,431

S17	DE "Trauma" OR DE "Emotional Trauma"	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	23,284
S16	DE "Self Perception" OR DE "Health Attitudes" OR DE "Attribution" OR DE "Insight" OR DE "Awareness" OR DE "Treatment Compliance"	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	67,367
S15	DE "Family" OR DE "Social Support" OR DE "Family Relations" OR DE "Significant Others" OR DE "Social Networks" OR DE "Family Relations" OR DE "Social Isolation"	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	100,925
S14	S12 OR S13	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	10,971
S13	TI ("early psychosis" OR "first episode psychosis") OR KW ("early psychosis" OR "first episode psychosis")	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	1,489
S12	S4 AND S11	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	10,713
S11	S5 OR S6 OR S7 OR S8 OR S9 OR S10	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	146,348
S10	TI ("early symptom*" OR onset OR "early signs" OR first-episode) OR KW ("early symptom*" OR onset OR "early signs" OR first-episode)	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	19,072

S9	TI ("risk group*" OR “ultra-high risk” OR “ultra high risk” OR “high clinical risk” OR “clinical high risk” OR “at risk mental state” OR “risk of progression” OR “first-episode psychosis” OR "prodromally symptomatic” OR prodromal* OR prodrome* OR transition OR “mild psychotic symptom*”) OR KW ("risk group*" OR “ultra-high risk” OR “ultra high risk” OR “high clinical risk” OR “clinical high risk” OR “at risk mental state” OR “risk of progression” OR “first-episode psychosis” OR "prodromally symptomatic” OR prodromal* OR prodrome* OR transition OR “mild psychotic symptom*”)	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	16,538
S8	DE "Prodrome" OR DE "Onset (Disorders)"	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	10,175
S7	DE "Risk Factors"	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	48,430
S6	TI ("at risk" OR "high risk" OR "increase* risk") OR KW ("at risk" OR "high risk" OR "increase* risk")	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	102,861
S5	DE "At Risk Populations"	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	30,241

S4	S1 OR S2 OR S3	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	111,847
S3	TI ("delusional disorder*" OR severe mental ill* OR severe mental disorder* OR psychotic OR psychosis OR psychoses OR schizo*) OR KW ("delusional disorder*" OR severe mental ill* OR severe mental disorder* OR psychotic OR psychosis OR psychoses OR schizo*)	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	106,625
S2	DE "Schizophrenia" OR DE "Acute Schizophrenia" OR DE "Schizophreniform Disorder" OR DE "Schizoaffective Disorder" OR DE "Delusions" OR DE "Hallucinations"	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	76,314
S1	DE "Childhood Schizophrenia" OR TI "childhood onset schizophrenia" OR KW "childhood onset schizophrenia"	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	982

Recent queries

Search	Add to builder	Query	Items found	Time
#101	Add	Search (#82 AND #91)	182	05:43:00
#99	Add	Search (#91 OR #98)	693514	05:41:28
#98	Add	Search prospect* [ti] OR course[ti] OR prognosis[ti] OR prognostic[ti] OR prediction[ti] OR predictive[ti] OR predicts[ti]	332499	05:41:05
#91	Add	Search ("Disease Progression"[Mesh]) OR "Prognosis"[Mesh:NoExp]	460402	05:38:26
#82	Add	Search (#17 AND #81)	3056	05:35:05
#81	Add	Search (#76 OR #80)	900392	05:34:43
#80	Add	Search "Drug-Related Side Effects and Adverse Reactions"[Mesh]	88201	05:34:26
#76	Add	Search (#27 OR #31 OR #33 OR #47 OR #52 OR #56 OR #59 OR #65 OR #69 OR #72 OR #75)	816500	05:32:42
#75	Add	Search "daily activities" [ti]	522	05:30:58
#72	Add	Search "daytime activities"[ti]	6	05:29:11
#69	Add	Search ("Employment"[Mesh:NoExp]) OR "Unemployment"[Mesh]	40469	05:28:01
#65	Add	Search ((("Substance-Related Disorders"[Mesh]) OR "Gambling"[Mesh]) OR "Comorbidity"[Mesh]) OR "Diagnosis, Dual (Psychiatry)"[Mesh]	286105	05:27:05
#59	Add	Search "Substance-Related Disorders"[Mesh]	222985	05:20:51
#56	Add	Search "Aggression"[Mesh:NoExp]	26460	05:20:21
#52	Add	Search "Life Change Events"[Mesh]	19171	05:18:38
#47	Add	Search (((((("Self Concept"[Mesh]) OR "Attitude to Health"[Mesh:NoExp]) OR "Health Knowledge, Attitudes, Practice"[Mesh]) OR "Awareness"[Mesh]) OR "Patient Compliance"[Mesh]) OR "Patient Acceptance of Health Care"[Mesh]	358823	05:16:53

Recent queries

Search	Add to builder	Query	Items found	Time
#33	Add	Search "Social Isolation"[Mesh]	13789	05:13:21
#31	Add	Search ((("Family"[Mesh:NoExp]) OR "Family Relations"[Mesh:NoExp]) OR "Social Support"[Mesh]) OR "Social Environment"[Mesh]	148314	05:11:28
#27	Add	Search "significant others" [ti]	249	05:09:45
#17	Add	Search (#13 OR #16)	11307	04:42:21
#16	Add	Search ("early psychosis" [ti] OR "first episode psychosis" [ti] OR "early psychoses" [ti] OR "first episode psychoses" [ti])	1291	04:41:41
#13	Add	Search (#5 AND #12)	11051	04:29:21
#12	Add	Search (#6 OR #7 OR #10 OR #11)	703780	04:29:09
#11	Add	Search ("early symptom" [ti] OR "early symptoms"[ti] OR onset [ti] OR "early signs" [ti] OR first-episode [ti])	46753	04:28:25
#10	Add	Search “ultra-high risk” [ti] OR “ultra high risk” [ti] OR“high clinical risk” [ti] OR “clinical high risk” [ti] OR “at risk mental state” [ti] OR “first-episode psychosis” [ti] OR prodromally [ti] OR prodromal* [ti] OR prodrome* [ti] OR transition [ti] OR "mild psychotic symptom" [ti] OR "mild psychotic symptoms" [ti] OR progression [ti]	80295	04:26:37
#7	Add	Search "at risk"[ti] OR "high risk"[ti] OR "increase risk" [ti] OR "increased risk"[ti] OR "increased risks" [ti] OR "risk group" [ti] OR "risk groups"[ti] OR "risk population"[ti] OR "ultra-high risk"[ti] OR "ultra-high risks"[ti]	42604	04:23:54
#6	Add	Search ("Prodromal Symptoms"[Mesh] OR "Risk Factors"[Mesh])	560841	04:23:35
#5	Add	Search (#1 OR #2 OR #3 OR #4)	139836	04:11:46
#4	Add	Search "delusional disorder" [ti] OR "delusional disorders" [ti]	222	04:11:25
#3	Add	Search psychotic [ti] OR psychosis [ti] OR psychoses [ti] OR schizo*[ti]	89506	04:11:12
#2	Add	Search "severe mental ill"[ti] OR "severe mental disorder"[ti] OR "severe mentally ill"[ti] OR "severe mental disorders"[ti] OR "severe mental illness"[ti] OR "severe mental illnesses"[ti]	1345	04:10:40

Recent queries

Search	Add to builder	Query	Items found	Time
#1	Add	Search ("Psychotic Disorders"[Mesh:NoExp] OR "Schizophrenia"[Mesh] OR "Hallucinations"[Mesh] OR "Delusions"[Mesh] OR "Schizophrenia, Childhood"[Mesh])	118195	04:10:22

Bijlage 5.D Evidence tabel Profielkenmerken

Legenda: FEP=first episode psychosis; S =Schizofrenie; SR=Systematic review; MA=meta-analyse; een SR of MA staat in een grijs vak en een losse studies in een wit vak.

Kenmerk *(Overkoepelende uitkomst)*	Studie, Design en diagnose deelnemers	Kenmerk zoals in de studie	Uitkomst zoals in de studie	Resultaat/Conclusie
Trauma/ Levensverhaal				
Toe/afname symptomen	Braehler2013, vergelijkingsstudie met controle groep, FEP, S	Childhood trauma	Dissociative symptoms	Chronic patients reported the highest level of dissociation. More severe childhood trauma was associated with greater dissociative symptoms in all groups although most strongly in chronic patients. Emotional abuse showed the strongest associations with dissociation, with these being strongest for chronic patients, followed by FIRST-EPISODE patients and least for controls. Men showed a stronger association between physical neglect and dissociation than women, irrespective of group.
Mortaliteit (Suïcide)	Hor2010, SR, (S)	Family History of suicide	Suicide	Positively associated
Zorgconsumptie	Lecomte2008, cross-sectional, early psychosis	See **results**	Medication adherence. poor service engagement, symptoms	Forward Wald logistic regression suggested that more positive symptoms, having witnessed violence as a child and high agreeableness as a personality trait predicted poor medication adherence. Forward linear regression revealed that physical abuse as a child, lack of knowledge regarding consumer rights, difficulties in building an alliance, low neuroticism and high agreeableness predicted poor service engagement. Profiles of non-adherers or low service engagement were strongly linked to childhood trauma, and high agreeableness, as well as more severe symptoms and poor alliance.

Middelengebruik				
Toe/afname symptomen	Alvarez Jiminez2012, MA,(FEP)	Persistent substance use disorder (comorbid diagnosis of substance abuse or dependence according to DSM criteria))	Relapse	Increased the risk 3-fold
	Archie2009, SR, (FEP)	Substances abuse	Symptoms and relapse and remission	Increase in positive symptoms (5 out of 7 studies) and risk of relapse (2 out of 2 studies). Less negative symptoms in users (5 out of 6 studies).
Toe/afname symptomen	Hides2006, prospective cohort, recent-onset psychosis	Cannabis use	psychotic symptoms and increase risk of psychotic relapse	A higher frequency of cannabis use was predictive of psychotic relapse, after controlling for medication adherence, other substance use and duration of untreated psychosis. An increase in psychotic symptoms was predictive of relapse to cannabis use, and medication adherence reduced cannabis relapse risk.
Toe/afname symptomen	Stone2014, long. Naturalistic coh, FEP	Cannabis use	Postive and negative symptoms	Level of cannabis use was associated conceptual disorganization, but not with delusions, hallucinations, negative symptoms or daily functioning. Cannabis users who reduced or stopped their use following contact with services had the greatest improvement in symptoms at 1 year compared with continued users and non-users. Continued users remained more symptomatic than non-users at follow-up.
Toe/afname symptomen	Lambert2005, prospective cohort, FEP	Substance use	Remission and symptoms	A Cox regression analysis indicated that a decrease or cessation of substance use significantly increased the probability of remission, whilst persistent SUD substantially reduced the likelihood. In addition, patients who reduced use appeared to have better outcomes at 18 months than those patients who had never used substances. Baseline SUD was not found to have any significant influence on symptom remission.
Toe/afname symptomen	Hui2013, retrospective cohort, FEP	Smoking	Relapse	Multivariate Cox-proportional hazards regression analysis revealed that medication non-adherence, smoking, and shorter baseline hospitalization were associated with an increased risk of relapse in 3 years.
Toe/afname symptomen **En** *Mortaliteit*	Mufi-ç2009, vergelijkend onderzoek, FEP	Substance abuse	Suicidality	The results show a statistically significant difference in the suicidality and aggression in patients with FIRST-EPISODE psychosis.
Toe/afname symptomen **En** (Psycho)Sociaal functioneren	Wade2007, prospective cohort, FEP	Substance abuse	Symptomatic or social functional outcome and quality of life	Multiple linear regression showed that heavy substance use disorder was significantly associated with more severe positive symptoms at 15 months (vs. no substance use disorder, p = .006; vs. mild substance use disorder, p = .023). Heavy substance use disorder was also significantly associated with poorer social functioning at 15 months (vs. no substance use disorder, p = .025; vs. mild substance use disorder, p = .047). Heavy

				substance use disorder was not associated with negative symptoms or quality of life after controlling for the effects of potential confounding variables.
Toe/afname symptomen **En** (Psycho)sociaal functioneren	Faber2014, randomized, open-label, controlled trial, FEP	Continued Cannabis use	Measures for psychopathology and social role functioning	Continued cannabis use was not associated with symptomatic or functional remission or clinical recovery. After 2 years, cannabis use was related to certain aspects of social role functioning (economic and social activities; explained variance 5.6% and 8.4%, respectively) but not to psychopathology (Positive and Negative Syndrome Scale Positive, Negative, or General symptoms). CONCLUSIONS: Our findings support the notion that continued cannabis use after the onset of a FIRST-EPISODE psychosis is correlated with worse social outcome and should be discouraged whenever possible, but its role in outcome is modest in comparison to other factors.
(Psycho)Sociaal functioneren	Archie2009, SR, (FEP)	Substances abuse	Psychosocial	Probably no effect (7 out of 8 studies) Most studies found insignificant differences between patients with and without substance abuse in terms of social functioning, cognition, and employment. However, when the analysis was categorized into mild and severe substance use disorder, an association was found between heavy substance use disorder and poor social functioning, as well as poorer quality of life [25]. These associations did not apply to patients with mild substance use disorder [25].
Mortaliteit (Suïcide)	Hawton2005, MA, (S)	Drug misuse	Suicide	Increased risk (OR=3.21,95% CI1.99-5.17)
	Hor2010, SR, (S)	Substance misuse	Suicide	Positively assosiated
Mortaliteit (Suïcide (attempt))	Gonzalez-Pinto2007, prospective cohort, FEP	Stimulant abuse	Suicide (attempt)	With an 8-fold (95% CI = 1.45 to 44.40) higher risk among patients with baseline stimulant abuse (cocaine and amphetamine).
Zorgconsumptie	Archie2009, SR, (FEP)	Substances abuse	Poor treatment compliance	Increased risk in 3 out of 5 studies.
	Archie2009, SR, (FEP)	Substances abuse	(Re-)Hospitalization	Unclear, increased risk in 2 out of 4 studies.
Zorgconsumptie	Tarricone2014, cohort, FEP	Substance abuse	Hospitalization	Substance users had a significantly higher rate of hospitalizations during the follow-up after adjusting for age, gender and other potential confounders (OR 5.84, 95% CI 2.44-13.97, $p \leq 0.001$)
Zorgconsumptie	Stowkowy2012, cohort, FEP	Cannabis use	Disengagement to treatment program	An examination of those who dropped out at different times revealed that those who dropped out prior to 6 months had significantly greater cannabis ($p < 0.05$) and other drug use ($p < 0.01$).
Zorgconsumptie	Lambert2010, cohort, FEP	Comorbid substance use	Long-term refusal or nonadherence of antipsychotic treatment	Comorbid substance use predicted both medication refusal and nonadherence;

Zorgconsumptie	Le Quach2009, prospective cohort, FEP	Substance abuse	Poor adherence to medication	After 1 year of treatment substance abuse, predict poor adherence to medication.
Zorgconsumptie	Miller2009, prospective cohort, FEP	Cannabis use	Non-adherence and treatment dropout	Cannabis use significantly increased hazard of non-adherence by a factor of 2.4 (p < .001) and hazard of dropout by a factor of 6.4 (p = .034). Conclusion: Results indicate that cannabis use is a risk factor for non-adherence to medication and dropout from treatment.
Zorgconsumptie	Perkins2008, RCT, FEP/S	Substance abuse	Treatment discontinuation and medication nonadherence	Ongoing substance abuse significantly predicted poor medication adherence (p < .01).
Zorgconsumptie	Kamali2006, prospective cohort, FEP	Alcohol and drug misuse	Adherence antipsychotic medication	Alcohol misuse at baseline and previous drug misuse predict non-adherence.
Zorgconsumptie	Schimmelmann2006, cohort, FEP	Substance abuse and first use	Service disengagement	Persistent substance use during treatment (HR = 2.6; 95% CI 1.1 -5.9) contributed significantly to predicting service disengagement. Initial substance use was related to service disengagement.
Ziekte inzicht				
Toe/afname symptomen	Alvarez Jiminez2012, MA,(FEP)	Lower insight	Relapse	Increased the risk 1.9-fold, when one study causing heterogeneity is excluded from the analysis
Toe/afname symptomen	Capdevielle2013, naturalistic study, FEP	The different dimensions of insight (having a mental disorder, response to medication, social consequences of the mental disorder)	Symptomatic remission	Our results show that concerning the current episode, only awareness of the social consequences and of the positive symptoms significantly improved during follow-up. Insight into the past episode improved for awareness of having a mental disorder, the social consequences and the positive symptoms of mental illness. Cross-sectional associations between insight and PANSS show weak to moderate, albeit significant, associations. Most of the dimensions of insight are positively and significantly associated with remission.
Toe/afname symptomen	Saeedi2007, prospective cohort, Early psychosis	Insight	Psychotic symptoms, depression	A comparison of those with good to those with poor insight revealed that at each assessment point those with poor insight had significantly higher ratings on positive, negative and general psychopathology symptoms (all at p<0.001). Additionally those with good insight had significantly higher levels of depression at baseline (p=0.001).

Toe/afname symptomen	Buchy2010, prospective cohort, FEP	Insight (good, increasing, decreasing, moderate poor and very poor)	Positive and negative symptoms, and depressive and anxious symptoms	Very poor and moderate poor insight groups displayed greater overall negative symptoms than patients with good and increasing insight trajectories. The good insight group showed significantly greater overall depressive symptoms than the diminished and very poor insight groups.
Toe/afname symptomen **En** *Mortaliteit (Suïcide)*	Crumlish2005, prospective cohort, FEP	Insight	Depression symptoms,	Insight improved with time. Recognition of mental illness at 6 months predicted depression and attempted suicide at 4 years.
Toe/afname symptomen **En** *(Psycho)sociaal functioneren*	O'Connor2013, prospective cohort, FEP	Insight (clinical and cognitive)	Symptom severity and psychosocial function	Cognitive insight (a measure of self-reflectiveness and self-certainty) was the best baseline predictor of overall psychopathology at 12 months. Other neuropsychological and insight measures were poor predictors of psychosocial function at 1 year.
Toe/afname symptomen **En** *(Psycho)sociaal functioneren* **En** *Zorgconsumptie*	Drake2007, prospective cohort, FEP	Insight	Time to relapse and readmission and on social function and symptoms	The hazard ratio for relapse, per unit increase in the insight score, was estimated in a Cox proportional hazards model to be 0.943 (95% CI = 0.892 to 0.996; p = .035). Those with the best insight scores had an estimated rate of relapse that was 39% of that of those with the worst scores (95% CI = 16% to 93%). Readmission was highly correlated with relapse, so poor insight also predicted readmission (hazard ratio 0.934; 95% CI = 0.876 to 0.996; p = .036). However, insight did not independently predict symptoms or social function after adjustment for other predictors of outcome. CONCLUSION: Insight predicted both relapse and readmission. The details of the beliefs and assumptions determining outcome remain unclear
Mortaliteit (Suïcide)	Hawton2005, MA, (S)	Fear of mental disintegration	Suicide	Increased risk (OR=12.1,95% CI1.89- 81.3)
	Hor2010, (S)	Presence of insight	Suicide	Strong evidential basis as risk factor
	Lopez-Morinigo2012,SR, (FEP, S)	Awareness of having a mental illness	Suicide	Ten of the fifteen studies failed to demonstrate a positive association. If there is an association, it appears to be mediated by other variables such as depression and, above all, hopelessness.
Zorgconsumptie	Czobor2013, cohort, FEP	Insight/ hostility	Adhere to their pharmacologic treatment	Hostility of a patient predicts non-adherence and lack of insight is even a greater risk of non-adherence.
Zorgconsumptie	Lambert2010, cohort, FEP	Insight	Long-term refusal or nonadherence of antipsychotic treatment	Poor insight predicted both medication refusal and nonadherence;
Zorgconsumptie	Le Quach2009, prospective cohort, FEP	Attitude	Poor adherence to medication	Negative attitudes towards medication (and lack of consistent family support) are the strongest predictors for poor adherence to medication for FIRST-EPISODE psychotic patients in the first 2 years. After 1 year of treatment, unawareness of the effect of

				medication and lack of positive attitudes towards medication also predict poor adherence to medication.
Zorgconsumptie	Perkins2008, RCT, FEP/S	Ilness insight	Treatment discontinuation and medication nonadherence	An association between poor medication adherence and illness insight at study entry was found at trend level (p = .059)
Zorgconsumptie	Kamali2006, prospective cohort, FEP	Insight	Adherence antipsychotic medication	Lack of insight at baseline predict non-adherence.
Zorgconsumptie	Schimmelmann2006, cohort, FEP	Insight	Service disengagement	Insight at baseline was not related to service disengagement.
Agressie				
Mortaliteit (Suïcide)	Hawton2005, MA, (S)	Agitation or motor restlessness	Suicide	Increased risk (OR=2.61, 95% CI1.54-4.41)
Zorgconsumptie	Czobor2013, cohort, FEP	Insight/ hostility	Adhere to their pharmacologic treatment	Hostility of a patient predicts non-adherence and lack of insight is even a greater risk of non-adherence.
Zorgconsumptie	De Haan2007, prospective cohort, FEP	Hostility	Medication non-adherence	Standard multiple regression analysis revealed that hostility and uncooperativeness (p = 0.007) and involuntary admission (p = 0.02) were associated with the level of adherence during 5 year follow-up after admission.
Mortaliteit (Suïcide)	Hawton2005, MA, (S)	Previous suicide attempts	Suicide	Increased risk,), previous suicide attempts (OR=4.09,95% CI 2.79-6.01)
	Hor2010, SR, (S)	Number of prior suicide attempts	Suicide	Strong evidential basis as risk factor
Sociale rollen				
Toe/afname symptomen	Alvarez Jiminez2012, MA, (FEP)	Poorer premorbid adjustment	Relapse	Increased the risk 2.2-fold
Steun				
Toe/afname symptomen	Alvarez Jiminez2012, MA, (FEP)	Carers' critical comments (but not overall expressed emotion)	Relapse	Increased the risk 2.3-fold

Toe/afname symptomen	Hui2013, retrospectief cohort, FEP	Shorter baseline hospitalization	Relapse	Multivariate Cox-proportional hazards regression analysis revealed that medication non-adherence, smoking, and shorter baseline hospitalization were associated with an increased risk of relapse in 3 years.
Toe/afname symptomen	Gearing2009, retrospective cohort, FEP children/ adolescent	Decline in social support	Relapse	Cox proportional hazards regression identified 4 key risk factors for relapse, including receiving clinical treatment, and a decline in social support before first admission
Mortaliteit (Suïcide)	Hawton2005, MA, (S)	Recent loss	Suicide	Increased risk (OR=4.03,95%CI1.37-11.8)
Zorgconsumptie	Stowkowy2012, cohort, FEP	Family member support,	Disengagement to treatmentprogram	Predictors of disengagement were examined via Cox proportional hazards models which revealed that not having a family member involved in the program (HR = 0.310; CI = 0.196 0.490) contributed significantly to predicting disengagement from treatment.
Zorgconsumptie	Le Quach2009, prospective cohort, FEP	Family support	Poor adherence to medication	(Negative attitudes towards medication and) lack of consistent family support are the strongest predictors for poor adherence to medication for FIRST-EPISODE psychotic patients in the first 2 years.
Zorgconsumptie	Rabinovitch2009, FEP	social and family support	Nonadherence to antipsychotic therapy	Nonadherent patients were less likely to have received a good level of social support, as rated by their respective case manager, and more likely to be and to have refused medication at the first offer of treatment. Using logistic regression, both the level of social support (OR = 3.552, P = 0.03) (and early medication acceptance (OR = 11.092, P < 0.001)) were significant as predictors of adherence.
Zorgconsumptie	Schimmelmann2006, cohort, FEP	Family support	Service disengagement	Living without family during treatment (HR = 4.8; 95% CI 2.1 -11.2), contributed significantly to predicting service disengagement.
Juridisch of Onvrijwillige behandeling in de voorgeschiedenis (VG)				
Zorgconsumptie	Lambert2010, cohort, FEP	Forensic history	Long-term refusal or nonadherence of antipsychotic treatment	A forensic history was specifically predictive of medication refusal.
Zorgconsumptie	Lecomte2008, cross-sectional, early psychosis	History of legal problems	Medication adherence and poor service engagement	Profiles of non-adherers or low service engagement were strongly linked to childhood trauma, and high agreeableness, as well as more severe symptoms and poor alliance. Males with histories of legal problems were also more prevalent in both groups.
Zorgconsumptie	De Haan2007, prospective cohort, FEP	Involuntary admission	Medication non-adherence	Standard multiple regression analysis revealed that hostility and uncooperativeness (p = 0.007) and involuntary admission (p = 0.02) were associated with the level of adherence during 5 year follow-up after admission.

Samenwerking (Therapietrouw)				
Toe/afname symptomen	Alvarez Jiminez2012, MA, (FEP)	Medication non-adherence	Relapse	Increased the risk 4-fold
Toe/afname symptomen	Hui2013, retrospectief cohort, FEP	Medication non-adherence	Relapse	Multivariate Cox-proportional hazards regression analysis revealed that medication non-adherence, smoking, and shorter baseline hospitalization were associated with an increased risk of relapse in 3 years.
Toe/afname symptomen	Lambert2010, cohort, FEP	Long-term refusal or nonadherence of antipsychotic treatment	Illness outcome	With respect to illness outcome, nonadherent patients were worse off when compared with fully adherent patients, and medication refusers were even worse off compared with nonadherent patients.
Toe/afname symptomen	Gearing2009, retrospective cohort, FEP children/adolescent	Medication nonadherence	Relapse	Cox proportional hazards regression identified 4 key risk factors for relapse, including medication nonadherence.
Mortaliteit (Suïcide)	Hawton2005, MA, (S)	Poor adherence to treatment	Suicide	Increased risk (OR=3.75,95% CI 2.20-6.37)
	Hor2010, SR, (S)	Delivery of and adherence to effective treatment	Suicide	Protective factor
Zorgconsumptie	Chan2014, long. cohort, FEP	Poor medication compliance	Disengagement to service treatment	Poorer medication compliance in the first month of treatment were significant predictors of disengagement from service
Zorgconsumptie	Rabinovitch2009, FEP	Early medication acceptance	Nonadherence to antipsychotic therapy	Using logistic regression, (both the level of social support (OR = 3.552, P = 0.03) and) early medication acceptance (OR = 11.092, P < 0.001) were significant as predictors of adherence.
Zorgconsumptie	Lecomte2008, cross-sectional, early psychosis	Building an alliance	Poor service engagement	Forward Wald logistic regression suggested that more positive symptoms, having witnessed violence as a child and high agreeableness as a personality trait predicted poor medication adherence. Forward linear regression revealed that physical abuse as a child, lack of knowledge regarding consumer rights, difficulties in building an alliance, low neuroticism and high agreeableness predicted poor service engagement.
Zorgconsumptie	Perkins2008, RCT, FEP/S	Low medication adherence	Treatment discontinuation and medication nonadherence	Low medication adherence (p = .02) were independent predictors of discontinuation against medical advice.
Zorgconsumptie	De Haan2007, prospective cohort, FEP	Uncooperativeness	Medication non-adherence	Standard multiple regression analysis revealed that hostility and uncooperativeness (p = 0.007) and involuntary admission (p = 0.02) were associated with the level of adherence during 5 year follow-up after admission.

Bijlage 5.E Review protocol – diagnostiek psychose

Onderwerp	**B. Diagnostiek van psychose**
Uitgangsvragen	B1. Hoe voer je (categoriale en dimensionele) diagnostiek van niet-affectieve psychose uit (met welk classificatiesysteem en welke instrumenten)? Subvraag: B2. Op welke manier neem je patiëntprofiel en stadium van de aandoening mee in de diagnostiek?
Criteria voor inclusie van studies in de review	
• *Populatie*	• Personen van 12 of ouder met een niet-affectieve (eerste) psychose
• *Interventie*	Categoriale diagnoses van niet-affectieve (eerste) psychose • Semi-structured diagnostic interviews, bijv: CASH, SCAN, SCID, CIDI Dimensionele diagnoses van niet-affectieve (eerste) psychose • Specifiek Model, bijv: GROUP protocol
• *Vergelijking*	• Gouden standaard: Diagnostic Statistical Manual (DSM) or International Classification of Diseases (ICD) diagnosis of personality disorders.
• *Kritische Uitkomstmaten*	• Sensitiviteit: de kans dat het instrument een positieve uitslag geeft bij mensen die een niet-affectieve (eerste) psychose hebben (correct geïdentificeerde positieven) • Specificiteit: de kans dat bij mensen die geen niet-affectieve (eerste) psychose hebben het resultaat van de test negatief is (correct geïdentificeerde negatieven).
• *Belangrijke uitkomstmaten*	• Positief Voorspellende Waarde: gaat over welke proportie van alle personen met een positieve uitslag een correcte diagnose heeft door het instrument • Negatief Voorspellende Waarde: gaat over welke proportie van alle personen met een negatieve uitslag een correcte diagnose heeft door het instrument • Area under the Curve (AUC): is een maat waarbij voor elk afkappunt de correct geïdentificeerde positieven als functie wordt genomen van de niet-correct geïdentificeerde positieven. Het is een algemene uitkomstmaat, die aangeeft of een test goed kan discrimineren tussen mensen met of zonder niet-affectieve (eerste) psychose. Een AUC score is voor de klinische praktijk weinig bruikbaar omdat deze niet gebaseerd is op een specifiek afkappunt.
• *Studiedesign*	• Cross-sectioneel
Databases searched	• CINAHL, Medline en PsycINFO
Data searched	• 1970 tot heden
De review strategie	• De informatiespecialist voert de zoek strategie uit. De reviewer selecteert de studies in twee fases. Een eerste selectie op titel en abstract. Met een tweede full tekst selectie van twijfel artikelen. • De reviewer verwerkt de resultaten in evidence tabellen en beoordeeld de individuele studies op kwaliteit met de QUADAS II. • Mocht er een systematische review van voldoende kwaliteit worden gevonden over dit onderwerp, dan wordt deze ge-update. • Literatuurlijsten van gevonden studies worden gecontroleerd op gemiste studies en experts wordt gevraagd of er mogelijk studies zijn gemist.

Bijlage 5.F Search history – Profielkenmerken en beloop

Profielkenmerken: Psychinfo en medline
Oorspronkelijke studies (zelfde voor reviews gedaan)

PsycInfo

0

#	Query	Limiters/Expanders	Last Run Via	Results
S31	S26 AND S29	Limiters - Publication Type: All Journals Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	207
S30	S26 AND S29	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	224
S29	S27 OR S28	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	134,104
S28	TI (prospect* OR course OR prognosis OR prognostic OR predict*) OR KW (prospect* OR course OR prognosis OR prognostic OR predict*)	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	117,736
S27	DE "Disease Course" OR DE "Prognosis" OR DE "Recovery (Disorders)" OR DE "Remission (Disorders)" OR DE "Spontaneous Remission" OR DE "Symptom Remission"	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	27,209
S26	S12 AND S25	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	1,548
S25	S15 OR S16 OR S17 OR S18 OR S19 OR S20 OR S21 OR S22 OR S23 OR S24	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	401,131
S24	DE "Side Effects (Drug)"	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases	20,470

			Search Screen - Advanced Search Database - PsycINFO	
S23	(((DE "Employment Status" OR DE "Unemployment") OR (DE "Daily Activities")) OR (DE "School Attendance")) OR (DE "Education")	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	43,309
S22	(DE "Aggressive Behavior") OR (DE "Aggressiveness")	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	23,878
S21	TI life-events OR KW life-events	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	6,131
S20	DE "Comorbidity"	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	22,289
S19	DE "Addiction" OR DE "Alcoholism" OR DE "Drug Addiction" OR DE "Alcohol Abuse" OR DE "Pathological Gambling" OR DE "Dual Diagnosis" OR DE "Physical Disorders"	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	65,600
S18	DE "Drug Usage" OR DE "Alcohol Drinking Patterns" OR DE "Drug Abuse" OR DE "Intravenous Drug Usage" OR DE "Marijuana Usage"	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	68,431
S17	DE "Trauma" OR DE "Emotional Trauma"	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	23,284
S16	DE "Self Perception" OR DE "Health Attitudes" OR DE "Attribution" OR DE "Insight" OR DE "Awareness" OR DE "Treatment Compliance"	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	67,367
S15	DE "Family" OR DE "Social Support" OR DE "Family	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases	100,925

	Relations" OR DE "Significant Others" OR DE "Social Networks" OR DE "Family Relations" OR DE "Social Isolation"		Search Screen - Advanced Search Database - PsycINFO	
S14	S12 OR S13	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	10,971
S13	TI ("early psychosis" OR "first episode psychosis") OR KW ("early psychosis" OR "first episode psychosis")	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	1,489
S12	S4 AND S11	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	10,713
S11	S5 OR S6 OR S7 OR S8 OR S9 OR S10	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	146,348
S10	TI ("early symptom*" OR onset OR "early signs" OR first-episode) OR KW ("early symptom*" OR onset OR "early signs" OR first-episode)	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	19,072
S9	TI ("risk group*" OR “ultra-high risk” OR “ultra high risk” OR “high clinical risk” OR “clinical high risk” OR “at risk mental state” OR “risk of progression” OR “first-episode psychosis” OR "prodromally symptomatic” OR prodromal* OR prodrome* OR transition OR “mild psychotic symptom*”) OR KW ("risk group*" OR “ultra-high risk” OR “ultra high risk” OR “high clinical risk” OR “clinical high risk” OR “at risk mental state” OR “risk of progression” OR “first-episode psychosis” OR "prodromally symptomatic”	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	16,538

	OR prodromal* OR prodrome* OR transition OR “mild psychotic symptom*”)			
S8	DE "Prodrome" OR DE "Onset (Disorders)"	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	10,175
S7	DE "Risk Factors"	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	48,430
S6	TI ("at risk" OR "high risk" OR "increase* risk") OR KW ("at risk" OR "high risk" OR "increase* risk")	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	102,861
S5	DE "At Risk Populations"	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	30,241
S4	S1 OR S2 OR S3	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	111,847
S3	TI ("delusional disorder*" OR severe mental ill* OR severe mental disorder* OR psychotic OR psychosis OR psychoses OR schizo*) OR KW ("delusional disorder*" OR severe mental ill* OR severe mental disorder* OR psychotic OR psychosis OR psychoses OR schizo*)	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	106,625
S2	DE "Schizophrenia" OR DE "Acute Schizophrenia" OR DE "Schizophreniform Disorder" OR DE "Schizoaffective Disorder" OR DE "Delusions" OR DE "Hallucinations"	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	76,314
S1	DE "Childhood Schizophrenia" OR TI "childhood onset schizophrenia" OR KW	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	982

	"childhood onset schizophrenia"			

enabled

PubMed

Recent queries

Search	Add to builder	Query	Items found	Time
#101	Add	Search (#82 AND #91)	182	05:43:00
#99	Add	Search (#91 OR #98)	693514	05:41:28
#98	Add	Search prospect* [ti] OR course[ti] OR prognosis[ti] OR prognostic[ti] OR prediction[ti] OR predictive[ti] OR predicts[ti]	332499	05:41:05
#91	Add	Search ("Disease Progression"[Mesh]) OR "Prognosis"[Mesh:NoExp]	460402	05:38:26
#82	Add	Search (#17 AND #81)	3056	05:35:05
#81	Add	Search (#76 OR #80)	900392	05:34:43
#80	Add	Search "Drug-Related Side Effects and Adverse Reactions"[Mesh]	88201	05:34:26
#76	Add	Search (#27 OR #31 OR #33 OR #47 OR #52 OR #56 OR #59 OR #65 OR #69 OR #72 OR #75)	816500	05:32:42
#75	Add	Search "daily activities" [ti]	522	05:30:58
#72	Add	Search "daytime activities"[ti]	6	05:29:11
#69	Add	Search ("Employment"[Mesh:NoExp]) OR "Unemployment"[Mesh]	40469	05:28:01
#65	Add	Search ((("Substance-Related Disorders"[Mesh]) OR "Gambling"[Mesh]) OR "Comorbidity"[Mesh]) OR "Diagnosis, Dual (Psychiatry)"[Mesh]	286105	05:27:05
#59	Add	Search "Substance-Related Disorders"[Mesh]	222985	05:20:51
#56	Add	Search "Aggression"[Mesh:NoExp]	26460	05:20:21
#52	Add	Search "Life Change Events"[Mesh]	19171	05:18:38
#47	Add	Search (((((("Self Concept"[Mesh]) OR "Attitude to Health"[Mesh:NoExp]) OR "Health Knowledge, Attitudes, Practice"[Mesh]) OR "Awareness"[Mesh]) OR "Patient Compliance"[Mesh]) OR "Patient Acceptance of Health Care"[Mesh]	358823	05:16:53
#33	Add	Search "Social Isolation"[Mesh]	13789	05:13:21
#31	Add	Search ((("Family"[Mesh:NoExp]) OR "Family Relations"[Mesh:NoExp]) OR "Social Support"[Mesh]) OR "Social Environment"[Mesh]	148314	05:11:28
#27	Add	Search "significant others" [ti]	249	05:09:45
#17	Add	Search (#13 OR #16)	11307	04:42:21
#16	Add	Search ("early psychosis" [ti] OR "first episode psychosis" [ti] OR "early psychoses" [ti] OR "first episode psychoses" [ti])	1291	04:41:41

Recent queries

Search	Add to builder	Query	Items found	Time
#13	Add	Search (#5 AND #12)	11051	04:29:21
#12	Add	Search (#6 OR #7 OR #10 OR #11)	703780	04:29:09
#11	Add	Search ("early symptom" [ti] OR "early symptoms"[ti] OR onset [ti] OR "early signs" [ti] OR first-episode [ti])	46753	04:28:25
#10	Add	Search “ultra-high risk” [ti] OR “ultra high risk” [ti] OR“high clinical risk” [ti] OR “clinical high risk” [ti] OR “at risk mental state” [ti] OR “first-episode psychosis” [ti] OR prodromally [ti] OR prodromal* [ti] OR prodrome* [ti] OR transition [ti] OR "mild psychotic symptom" [ti] OR "mild psychotic symptoms" [ti] OR progression [ti]	80295	04:26:37
#7	Add	Search "at risk"[ti] OR "high risk"[ti] OR "increase risk" [ti] OR "increased risk"[ti] OR "increased risks" [ti] OR "risk group" [ti] OR "risk groups"[ti] OR "risk population"[ti] OR "ultra-high risk"[ti] OR "ultra-high risks"[ti]	42604	04:23:54
#6	Add	Search ("Prodromal Symptoms"[Mesh] OR "Risk Factors"[Mesh])	560841	04:23:35
#5	Add	Search (#1 OR #2 OR #3 OR #4)	139836	04:11:46
#4	Add	Search "delusional disorder" [ti] OR "delusional disorders" [ti]	222	04:11:25
#3	Add	Search psychotic [ti] OR psychosis [ti] OR psychoses [ti] OR schizo*[ti]	89506	04:11:12
#2	Add	Search "severe mental ill"[ti] OR "severe mental disorder"[ti] OR "severe mentally ill"[ti] OR "severe mental disorders"[ti] OR "severe mental illness"[ti] OR "severe mental illnesses"[ti]	1345	04:10:40
#1	Add	Search ("Psychotic Disorders"[Mesh:NoExp] OR "Schizophrenia"[Mesh] OR "Hallucinations"[Mesh] OR "Delusions"[Mesh] OR "Schizophrenia, Childhood"[Mesh])	118195	04:10:22

Bijlage 5.G Studiekenmerken Review diagnostiek – patiëntprofiel

Subvraag 3.
Op welke manier neem je patiëntprofiel (en stadium van de aandoening) mee in de diagnostiek?

Overzicht Studiekenmerken Diagnostiek - Profielkenmerken

Profielkenmerk (studies zoveel mogelijk op geordend)	**Referentie** MA – Meta-analyse SR – Systematic review P – type 'illness' of the participants (FEP = First episode of psychosis; FHR = Fmailial High Risk; CHR = Clinicla High Risk; UHR= Ultra High Risk BLIPS = brief limited intermittent psychotic symptoms; APS = attenuated psychotic symptoms;	**Aim + Uitkomstmaat*** *1. toe-/afname symptomen* *2. sociaal functioneren* *3. mortaliteit* *4. zorgconsumptie* *5. (kwaliteit van leven)* *O = Outcome* *FU = Follow-up*	**Samenvatting** R – Results L – Beperkingen van de studies Ref – Referentie (zwart is uniek, rood is dubbel)
Combinatie van kenmerken	Alvarez Jiminez, 2012 MA – 29 studies P – FEP	Aim: Identify *risk factors* for and rates of relapse in the early course of psychosis O:relapse (FU 1, 1,5, 2, 3 en 7,5 jaar)	R: Medication non-adherence (OR=4.09, 95% CI 2.55–6.56), persistent substance use disorder (OR=2.27, 95% CI 1.37–3.76), carers' critical comments (but not overall expressed emotion) ((OR=2.35, 95% CI 1.16–4.77) and poorer premorbid adjustment (OR=2.25, 95% CI 1.37–3.69), increased the risk for relapse 4-fold, 3-fold, 2.3-fold and 2.2-fold, respectively. Clinical variables and general demographic variables have little impact on relapse rates. L: Future studies need to address the methodological limitations of the extant research (e.g. definition of relapse), focus on the identification of protective factors and evaluate theoretically derived models of relapse. Ref: Alvarez-Jimenez2011, Apiquian-Guitart2006, Chen2005, Coldham2002, Cougnard2006, Craig2000, Drake2007, Geddes1994, Gleeson2005, Holthausen2007, Leff1990, MacMillan1986, Malla2008, Norman2005, Novak-Grubic2002, Owens2010, Rabiner1986, Rajkumar1989, Robinson1999, Rund2007, Saravanan2010, Sorbara2003, Stirling1991, Turkington2009, Ucok2006, Verdoux2000, Wade2006, Wolwer2008, Wood2006
	Strobl, 2012 SR – 18 studies P – FHR, CHR (BLIPS/APS)	Aim: Review of the methods and performance characteristics of models developed for *predicting the onset of psychosis* O: psychosis or schizophrenia onset	R: Quality of life and life functioning as well as structural brain imaging emerged as the most promising predictors of psychosis onset. Other predictors were, Personality, Substance Abuse and Medications, Neurocognition, Genetic Predictors The authors also discuss the standard for predicting psychosis onset. Common predictors are age, gender, family history, positive and negative symptoms, social anhedonia for negative symptoms, unusual thought content for positive symptoms, disorganization symptoms, specifically bizarre thinking sleep disturbances and attention deficits. Indeed, measures of positive, negative and

			disorganized symptoms in addition to their sub-scores have consistently been able to predict psychosis onset and thus have become a standard. L: Ref: FHR - Eack2008 Carter2002 Job2006 Gothelf2011 CHR - Cannon2008, Ramirez2010, Amminger2006, Richer-Rossler2009, Ruhrmann2010, Yung2003, Yung2004, Dragt2011, Lencz2006, Seidman2010, Koutsouleris2009, Bodatsch2011, Koutsouleris2011
	Hawton, 2005 MA – 29 studies P - Schizophrenia	Aim: To identify *risk factors* for suicide in schizophrenia O: suicide	O: Factors with robust evidence of increased risk of suicide were previous depressive disorders (OR=3.03, 95% CI 2.06-4.46), previous suicide attempts (OR=4.09,95% CI 2.79-6.01), drugmisuse (OR=3.21,95% CI1.99-5.17), agitation or motor restlessness (OR=2.61, 95% CI1.54-4.41), fear of mental disintegration (OR=12.1,95% CI1.89- 81.3), poor adherence to treatment (OR=3.75,95% CI 2.20-6.37) and recent loss (OR=4.03,95%CI1.37-11.8). *Reduced risk* was associated with hallucinations (OR=0.50,95% CI 0.35-0.71). (Prevention of suicide in schizophrenia is likely to result from treatment of affective symptoms, improving adherence to treatment, and maintaining special vigilance in patients with risk factors, especially after losses.) L: Publication bias, examination of few potential risk factor and a disbalance between the amout of studies, variation in definition of risk factors between studies, some studies included participants with schizoaffective disorder. Ref:Allebeck1987, Casadebaig1999a+b, Cheng1990, Cohen1964, Coehn1990, DeHert1995, Digman1986, Drake1984, Funahashi2000, Havaki1994, Hu1991, Law1986, Lim1991, Modestin1992, Roos1992, Rossau1997, Roy1982, Roy1995, Shaffer1974, Shah1999, Stebla199, Stephens1999, Taiminen1994, Taiminen2001, Warnes1968, Wilkinson1984, Wolfersdorf2003, Woldersdorf1989
1. Trauma / levensverhaal	Karanikas, 2014 SR – 22 studies P – FEP	Aim: review the evidence on cortisol abnormalities and its psychopathological correlates in FEP.	O: The evidence suggests a role for cortisol in psychosis, although the association of cortisol with psychopathological symptoms is currently non-specific. Higher cortisol levels in blood samples have been consistently replicated, whereas saliva studies (few studies) measuring baseline cortisol levels have exhibited divergent results. Moreover, longitudinal studies have revealed a cortisol upregulation in FEP with a subsequent decrease induced by antipsychotic treatment. For these mechanisms to be further elucidated, research should further focus on more pure diagnostic entities, clearly defined stages of the disorder and refined methods (multiple as opposed to single sampling, estimation of cortisol reactivity rather than basal secretion). L: Ref: Cesková2006, Belvederi2012, Garcia-Rizo2012, Mizrahi2012, Spelman2007, Garner2011, Venkatasubramanian2010, Ryan2004, Kale2010, Guest2011, Abel1996, Ryan2003, Strous2004, Walsh2005, Venkatasubramanian2007, Ryabn2004, Phassouliotis2013, Mondelli2010, Hempel2010, Pruessner2013, VanVenrooij2012, Walker2001
	Matheson, 2013b MA – 25 studies P - Schizophrenia	Aim: review evidence on the possible *risk factor childhood adversity* (harmful experiences, including emotional or psychological abuse, physical abuse, sexual abuse,	R: Moderate to high quality evidence suggests increased rates of childhood adversity in schizophrenia compared to controls [odds ratio (OR) 3.60, p<0.00001]. L: Retrospective measures (recall bias), no included studies presented data on other potentially causal variables. Other limitations of this review are that causation and specificity for schizophrenia have not been established. Without sufficient data that could be pooled or

		neglect and other negative life events) in people with schizophrenia. O: Schizophrenia	categorized regarding the severity of trauma and the severity of symptoms experienced, we were unable to investigate dose dependence. Ref: Friedman & Harrison, 1984; Craine et al. 1988; Stein et al. 1988; Ross et al. 1989; Byrne et al. 1990; Fink & Golinkoff, 1990; Goff et al. 1991; Darves-Bornoz et al. 1995; Nettelbladt et al. 1996; Nurcombe et al. 1996; Wurr & Partridge, 1996; Wexler et al. 1997; Honig et al. 1998; Friedman et al. 2002; Hlastala & McClellan, 2005; Spence et al. 2006; Choi et al. 2009; Rubino et al. 2009; Conus et al. 2010; Husted et al. 2010; Kingdon et al. 2010; McCabe et al. 2012; Aas et al. 2011; Alvarez et al. 2011; Vogel et al. 2011
	Beards, 2013 MA – 16 studies P – FEP or subclinical psychotic experiences (16 years or older)	Aim: review of the *relationship* between *life events and onset of psychotic disorder/experiences* is timely. O: onset of psychotic disorder/experiences	R: There was a positive associations between exposure to adult life events and subsequent onset of psychotic disorder/experiences. The meta-analysis yielded an overall weighted OR of 3.19 (95% CI 2.15–4.75). Most studies suggest the number of events prior to onset is higher (compared with a comparison group) in those with psychosis or psychotic experiences, with our meta-analysis suggesting around a 3-fold increased odds of life events in the period prior to psychosis onset; and (c) more tentatively, there are some indications that intrusive events may be particularly relevant to the development of psychosis. L: The methodological quality of the majority of studies was low, any studies were limited by small sample sizes and the use of checklist measures of life events, with no consideration of contextual influences on the meaning and interpretation of events. Ref:Day1987, Gureje1988, Chakraborty2007, Faravelli2007, Raune2009, Mondelli2010, Brown1968, Canton1985, AlKhani1986, Dohrenwend1987, Bebbington1993, Vinokur1975, John2004, Jenkins2010, VanNierop2012, Lataster2012
2. Middelengebruik	Archie, 2009 SR – 12 studies P – FEP (with vs without substances abuse), schizophrenia spectrum and affective spectrum patients	Aim: whether first episode psychosis (FEP) patients who meet criteria for substance abuse have worse outcomes than FEP patients who do not abuse substances O: symptoms, relapse, hospitalization, treatment compliance, psychosocial functioning	R: patients with substance abuse experienced increased -positive symptoms in five out of seven studies; -risk of relapse in two out of two studies; -risk of poor treatment compliance in three out of five studies. Only one of six studies examining negative symptoms found a significant association with substance abuse and only one out of eight studies found any associations between psychosocial outcomes and substance abuse. With respect to re-hospitalization, two out of four studies suggested that the risk was significantly higher for patients with substance abuse. One study suggested that the risk of re-hospitalization increased with the degree of substance use. Interestingly, significant associations were found between re-hospitalization and abuse of substances, such as cannabis, cocaine, opiates, and ecstasy - but not alcohol. The remaining two studies showed an increase in re-hospitalization among patients with substance abuse, but this association did not reach statistical significance. L: Many studies had methodological problems (small sample sizes, reliance upon self-report of substance use, assessments that were not blinded, and inconsistent definitions of FEP and substance abuse). Publication bias. A number of variables were not controlled that could confound the results, such as diagnosis, rehabilitation, medication,and treatment effects. Ref: Wade2006, Farrelly2007, Linszen1994, Kovasznay1997, Buhler2002, Pencer2003, Addington2007, Miller2007, Green2004, Sorbara2003, Archie2007, Stirling2005
	Addington, 2014 SR – 10 studies P - CHR	Aim: association between substance use and psychosis. O: transition to psychosis.	R: The results of these studies varied. Two out of the ten studies found a significant association between the use of substances and subsequent transition to psychosis. In one of these studies, substance abuse was a predictor of psychosis when included as a variable in a prediction algorithm. In the other study, the abuse of cannabis and nicotine was associated with transition to psychosis. L: Evidence was limited, only 10 studies. the longitudinal use/abuse of substances

			has not been adequately addressed in the studies and the majority of studies lacked details on severity, frequency and quantity of substance use. Ref: Philips2002, Kristensen2007 Corcoran2008 Cannon2008 Ruhrmann2010 Dragt2012 Auther2012 Dragt2012 Korver2010 Thompson2011
	Moore,2007 MA – 35 studies (11 studies about psychosis,) P – Cannabis users	Aim: the evidence pertaining to cannabis use and occurrence of psychotic or affective mental health outcomes. O: Psychosis and psychotic disorder, Depression, suicidal thoughts, and anxiety outcomes	R: Increased risk of any psychotic outcome in individuals who had ever used cannabis (pooled adjusted odds ratio=1·41, 95% CI 1·20–1·65). Findings were consistent with a dose-response effect, with greater risk in people who used cannabis most frequently (2·09, 1·54–2·84). Depression, suicidal thoughts, and anxiety outcomes were examined separately. Findings for these outcomes were less consistent, and fewer attempts were made to address non-causal explanations, than for psychosis. A substantial confounding effect was present for both psychotic and affective outcomes. L: Ref: Tien1990, Henquet2005, VanOs2002, Wiles2006, Andreassons1987, Zammit2002, Zammit2004, Arseneault2002, Caspi2005, Fergusson2003, Fergusson2005
	Wisdom, 2011 – 14 studies (9 studies with substance abuse treatment and 5 without) P – FEB and comorbid substance abuse	Aim: investigate the course of substance use disorders and the response to specialized substance abuse treatments O: Drug and alcohol use, mental health and functional outcome	R:Onvoldoende beschreven voor mental health and functional outcome. Bovendien zijn de 'resultaten' daarover zeer diffuus (onduidelijk, niet gemeten, gemengde resultaten geen verandering en verbetering) L: Ref:
	McGrath, 2010 – studies P -	Aim: To explore the association between cannabis use and psychosis-related outcomes with the use of sibling pair analysis reduces the influence of unmeasured residual confounding. O: nonaffective psychosis, hallucinations, and Peters et al Delusions Inventory score	R: L: Ref:
3. Ziekte-inzicht / opvatting over psychose	Hor, 2012 SR – 51 studies (not all on risk factors) P - Schizophrenia	Aim: Review of all original studies concerning suicide in schizophrenia O: Risk factors were grouped according to type and strength of association with suicide	R: *Risk factors* with a *strong* association with later suicide included being young, male, and with a high level of education. Illness-related risk factors were *important* predictors, with number of prior suicide attempts, depressive symptoms, active hallucinations and delusions, and the presence of insight all having a strong evidential basis. A family history of suicide, and comorbid substance misuse were also *positively associated* with later suicide. The only consistent *protective* factor for suicide was delivery of and adherence to effective treatment. L: MA was not possible because of different designs of the studies. Ref:-

	Lopez-Morinigo, 2012 SR – 15 studies P – schizoaffect. schizophrenia and FEP.	Aim: review the role of insight in the risk of suicide attempts and completed suicide O: suicide	R: Ten of the fifteen studies failed to demonstrate a positive (awareness of having a mental illness) association between insight and risk for suicide. There is little evidence to support the suggestion that insight may represent a risk factor for suicide in patients with schizophrenia. If there is an association between such risk and insight, it appears to be mediated by other variables such as depression and, above all, hopelessness. L: Initially, a MA was attempted with the data available. However, this approach was not feasible owing to the methodological differences between the studies. Recall bias in studies, missings, only 4 studies used a validated instrument for insight. Ref: Hu1991, Harvey2008, Robinson2009, Bakst2009, Kim2003, Bourgeois2004, Crumlish2005, Gonzalez2008, Acosta2009, Robinson2010, Yen2002, Schennach-Wolff2009, Amador1996, Barret2010, Restifo2009
	Kao, 2010 – studies P -	Aim: O: suicide	R: L: Ref:
4. Agressie	Geen	-	-
5. Sociale rollen	Matheson, 2013 MA – 6 studies P – UHR (9-14, losse studie), schizophrenia	Aim: Assess the evidence for childhood *social withdrawal* among adults with schizophrenia (and, comparatively, in UHR children) O: diagnosis of a schizophrenia spectrum disorder	R: A large effect of increased childhood social withdrawal in adults with schizophrenia (SMD score = 1.035, 95% CI = 0.304-1.766, p = 0.006), with no indication of publication bias. L: There was considerable heterogeneity (I2 = 91%). Retrospective reporting by caregivers in 5 studies. Ref:Goethals2008, Miller2002, Mratori2005, Neumann1995, Rossi2000, Welham2009
	Pinikahana, 2003 (narratief uitgevoerd, er wordt een keuze gemaakt in welke risicofactoren er wel/niet worden gepresenteerd) SR – studies P - schizophrenia	Aim: Evidence on risk factors for suicide in patients with schizophrenia O: suicide	R: Young white males diagnosed with schizophrenia who are depressed, unmarried, unemployed, socially isolated and functionally impaired and who lack external support are the most vulnerable in the early stages of schizophrenic illness. L: Variation between studies in sample size, sampling techniques, research design and methodology. Ref:
	Velthorst 2014 SR – 32 studies (waarvan 15 over rol van sociale tekort bij transitie) P - UHR	Aim: Overzicht geven van literatuur over *sociale tekorten* in de uhr-fase en over de rol die deze tekorten spelen bij de voorspelling van een eerste psychose. O: transitie naar eerste psychose	R: Jongeren die voldoen aan één of meer uhr-criteria hebben meer last van sociale beperkingen dan de algemene populatie. Effectgroottes wijzen op middelgrote tot zeer grote verschillen (Cohens d varieerde van 0,63-4,18). Binnen de hulpzoekende populatie met uhr blijken chronische beperkingen in het sociaal functioneren en het rolfunctioneren evenals een achteruitgang in sociaal functioneren in belangrijke mate bij te dragen aan de voorspelling van een eerste psychose. L: Ref: Rol van sociale tekort bij transistie: Yung2003, Yung2004, Mason2004, Cornblatt2007, Cannon2008, Velthorst2009, Lemos-Giraldeze2009, Velthorst2010, Fusar-Poli2010, Thompson2011, Jang2011, Dragt2011, Cornblatt2012, Nieman2013, Velthorst2013, (Sociaal disfunctioneren tijdens UHR fase: Ballon2007, Cornblatt2007, Addington2008, Niendam2007, Willhite2008, Shim2008, VanRijn2011, Fusar-Poli2010, Lin2011, Carrion2011, Corcoran2011, Grano2011, Aston2012, Velthorst2011, Addignton2011, Mittal2011)
	Tarbox, 2008 SR – studies	Aim: to clarify how preschizophrenia	R: Poor social functioning does differentiate preschizophrenia children and adolescents from their peers and can be a sensitive and potentially specific predictor of schizophrenia. Age (but not sex)

	P – Schizophrenia spectrum illness	children/adolescents differ in their social behavior O: (ontwikkeling schizofrenie)	appears to be an important moderator of the strength and specificity of the association between particular social deficits and later schizophrenia. L: Ref:
6. Steun omgeving	(Koutra, 2014) SR – 27 studies P - FEP	Aim: a review of the literature focusing on the family environment of FEP patients. O: illness related characteristics	R: Although relatives EE (expressed emotions) is a robust predictor of relapse in chronic schizophrenia [23], in studies of FEP patients this relationship is unclear L: Ref:
7. Juridische VG	Geen		

Hoofdstuk 6 Farmacotherapie

Bijlage 6.A De zoekstrategie

Onderwerp: Farmacotherapie bij vroege psychose
Door: Angita Peterse, 9 & 10 februari 2015.

PubMed

Recent queries

Search	Add to builder	Query	Items found	Time
#155	Add	Search (#149 OR #137)	38	09:06:25
#149	Add	Search (#141 AND systematic [sb]) Filters: Publication date from 2012/01/01	10	08:55:15
#145	Add	Search (#144 AND (rct OR random*)) Filters: Publication date from 2012/01/01	109	08:50:40
#144	Add	Search (#130 OR #141) Filters: Publication date from 2012/01/01	454	08:49:12
#141	Add	Search (#19 AND #140)	629	08:47:21
#140	Add	Search "Drug Therapy"[Mesh]	1059813	08:47:02
#137	Add	Search (#131 AND systematic [sb])	38	07:52:30
#136	Add	Search (#131 AND systematic [sb]) Filters: Publication date from 2012/01/01	38	07:52:30
#133	Add	Search (#131 AND (rct OR random*))	107	07:49:40
#132	Add	Search (#131 AND (rct OR random*)) Filters: Publication date from 2012/01/01	107	07:49:39
#131	Add	Search (#19 AND #129) Filters: Publication date from 2012/01/01	433	07:49:16
#130	Add	Search (#19 AND #129)	2793	07:49:16
#129	Add	Search (#22 OR #44 OR #48 OR #103 OR #116 OR #126)	362648	07:48:31
#128	Add	Search (#19 AND #22)	2751	07:46:59
#127	Add	Search (#19 AND #126)	1	07:43:50
#126	Add	Search (((((((("Acebutolol"[Mesh]) OR "Atenolol"[Mesh]) OR "Betaxolol"[Mesh]) OR "Bisoprolol"[Mesh]) OR "Celiprolol"[Mesh]) OR "esmolol" [Supplementary Concept]) OR "Metoprolol"[Mesh]) OR "nebivolol" [Supplementary Concept]	12720	07:43:25
#117	Add	Search (#19 AND #116)	8	07:36:33
#116	Add	Search ((((((((((("bucindolol" [Supplementary Concept]) OR "Carteolol"[Mesh]) OR "carvedilol" [Supplementary Concept]) OR	43524	07:36:18

Recent queries

Search	Add to builder	Query	Items found	Time
		"Labetalol"[Mesh]) OR "Nadolol"[Mesh]) OR "Oxprenolol"[Mesh]) OR "Penbutolol"[Mesh]) OR "Pindolol"[Mesh]) OR "Propranolol"[Mesh]) OR "Sotalol"[Mesh]) OR "Timolol"[Mesh]) OR "Eucommiaceae"[Mesh]		
#104	Add	Search (#19 AND #103)	18	06:09:23
#103	Add	Search ((((((((((("Anti-Inflammatory Agents, Non-Steroidal"[Mesh]) OR "Diclofenac"[Mesh]) OR "Naproxen"[Mesh]) OR "Aspirin"[Mesh]) OR "Phenylbutazone"[Mesh]) OR "Indomethacin"[Mesh]) OR "Ketoprofen"[Mesh]) OR "Piroxicam"[Mesh]) OR "Diflunisal"[Mesh]) OR "Fenoprofen"[Mesh]) OR "nabumetone" [Supplementary Concept]) OR "Tolmetin"[Mesh]) OR "Ibuprofen"[Mesh]) OR "Prednisone"[Mesh]	166523	06:09:06
#49	Add	Search (#19 AND #48)	32	05:44:55
#48	Add	Search "Fish Oils"[Mesh]	19674	05:44:41
#45	Add	Search (#19 AND #44)	427	05:43:11
#44	Add	Search "Butyrophenones"[Mesh] OR "Thioxanthenes"[Mesh] OR "Adrenergic beta-Antagonists"[Mesh]	60355	05:42:44
#22	Add	Search "Antipsychotic Agents" [Pharmacological Action]	105456	04:59:34
#19	Add	Search (#1 OR #8 OR #18)	14851	04:40:21
#18	Add	Search "Schizophrenia, Childhood"[Mesh] OR "childhood onset schizophrenia" [tiab] OR "childhood onset schizophrenia" [ot]	1616	04:39:34
#8	Add	Search (#6 AND #7)	12451	05:00:55
#7	Add	Search ("early symptom" [tiab] OR "early symptoms" [tiab] OR onset [tiab] OR "early signs" [tiab] OR first-episode [tiab] OR "acute phase" [tiab] OR "early symptom" [ot] OR "early symptoms" [ot] OR onset [ot] OR "early signs" [ot] OR first-episode [ot] OR "acute phase" [ot]))	397114	05:00:36
#6	Add	Search ((#2 OR #3 OR #4 OR #5))	166349	05:00:08
#5	Add	Search (("delusional disorder" [tiab] OR "delusional disorders" [tiab] OR "delusional disorder" [ot] OR "delusional disorders" [ot]))	700	04:59:42
#4	Add	Search (psychotic [tiab] OR psychosis [tiab] OR psychoses [tiab] OR schizophrenia [tiab] OR schizophrenic [tiab] OR psychotic [ot] OR psychosis [ot] OR psychoses [ot] OR schizophrenia [ot] OR schizophrenic [ot])	130411	04:40:41
#3	Add	Search ("severe mental ill" [tiab] OR "severe mental disorder" [tiab] OR "severe mentally ill" [tiab] OR "severe mental disorders"	3406	04:40:20

Recent queries				
Search	Add to builder	Query	Items found	Time
		[tiab] OR "severe mental illness" [tiab] OR "severe mental illnesses" [tiab] OR "severe mental ill"[ot] OR "severe mental disorder"[ot] OR "severe mentally ill"[ot] OR "severe mental disorders"[ot] OR "severe mental illness"[ot] OR "severe mental illnesses"[ot])		
#2	Add	Search (("Psychotic Disorders"[Mesh:NoExp] OR "Schizophrenia"[Mesh] OR "Hallucinations"[Mesh] OR "Delusions"[Mesh]))	118791	04:40:00
#1	Add	Search "first episode psychosis" [tiab] OR "first episode psychosis" [ot] OR "acute psychosis" [tiab] OR "acute psychosis" [ot] OR "acute psychoses"[tiab] OR "acute psychoses" [ot] OR "early psychosis" [tiab] OR "early psychoses"[tiab] OR "first episode psychoses" [tiab] OR "early psychosis" [ot] OR "first episode psychoses" [ot] OR "early psychoses" [ot] OR "first episode psychoses" [ot]	3056	04:39:40

PsycInfo

#	Query	Limiters/Expanders	Last Run Via	Results
S22	S20 AND (rct OR random*)	Limiters - Publication Year: 2012-; Methodology: -Systematic Review, -Meta Analysis Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	2
S21	S20 AND (rct OR random*)	Limiters - Publication Year: 2012- Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	54
S20	S16 OR S18	Limiters - Publication Year: 2012- Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	226
S19	S16 OR S18	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	1,069
S18	S9 AND S17	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases	919

			Search Screen - Advanced Search Database - PsycINFO	
S17	DE "Drug Therapy"	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	111,636
S16	S9 AND S15	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	798
S15	S10 OR S11 OR S12 OR S13 OR S14	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	34,724
S14	TI "fish oil*" OR AB "fish oil*" OR KW "fish oil*"	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	170
S13	DE "Anti Inflammatory Drugs" OR DE "Aspirin" OR DE "Glucocorticoids"	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	3,458
S12	DE "Neuroleptic Drugs" OR DE "Aripiprazole" OR DE "Clozapine" OR DE "Molindone" OR DE "Nialamide" OR DE "Olanzapine" OR DE "Quetiapine" OR DE "Reserpine" OR DE "Risperidone" OR DE "Spiroperidol" OR DE "Sulpiride" OR DE "Tetrabenazine") OR (DE "Neuroleptic Drugs" OR DE "Aripiprazole" OR DE "Clozapine" OR DE "Molindone" OR DE "Nialamide" OR DE "Olanzapine" OR DE "Quetiapine" OR DE "Reserpine" OR DE "Risperidone" OR DE "Spiroperidol" OR DE	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	25,974

	"Sulpiride" OR DE "Tetrabenazine")			
S11	DE "Fatty Acids"	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	1,975
S10	DE "Adrenergic Blocking Drugs" OR DE "Alpha Methylparatyrosine" OR DE "Dihydroergotamine" OR DE "Hydroxydopamine (6-)" OR DE "Phenoxybenzamine" OR DE "Propranolol" OR DE "Yohimbine"	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	3,523
S9	S1 OR S4 OR S8	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	6,249
S8	S6 AND S7	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	5,231
S7	S2 OR S3 OR S5	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	114,943
S6	TI ("early symptom*" OR onset OR "early signs" OR first-episode OR "acute phase") OR KW ("early symptom*" OR onset OR "early signs" OR first-episode OR "acute phase")	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	19,913
S5	DE "Psychosis" OR DE "Acute Psychosis"	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	21,389
S4	TI ("early psychosis" OR "first episode psychosis" OR "early psychoses" OR "first episode psychoses") OR KW ("early psychosis" OR "first episode psychosis" OR "early	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	1,581

	psychoses" OR "first episode psychoses")			
S3	TI ("delusional disorder*" OR severe mental ill* OR severe mental disorder* OR psychotic OR psychosis OR psychoses OR schizo*) OR KW ("delusional disorder*" OR severe mental ill* OR severe mental disorder* OR psychotic OR psychosis OR psychoses OR schizo*)	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	108,616
S2	DE "Schizophrenia" OR DE "Acute Schizophrenia" OR DE "Schizophreniform Disorder" OR DE "Schizoaffective Disorder" OR DE "Delusions" OR DE "Hallucinations"	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	77,860
S1	DE "Childhood Schizophrenia" OR TI "childhood onset schizophrenia" OR KW "childhood onset schizophrenia"	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	989

CINAHL

#	Query	Limiters/Expanders	Last Run Via	Results
S28	S25	Limiters - Published Date: 20120101- Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL	8
S27	S24	Limiters - Published Date: 20120101-; Publication Type: Meta Analysis, Systematic Review Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL	3
S26	S24	Limiters - Publication Type: Meta Analysis, Systematic Review Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL	10

S25	S24 AND (rct OR random*)	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL	41
S24	S17 OR S23	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL	177
S23	S11 AND S22	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL	148
S22	S19 OR S20 OR S21	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL	3,578
S21	(MH "Hallucinations/DT") OR (MH "Delusions/DT")	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL	114
S20	(MH "Psychotic Disorders/DT") OR (MH "Schizophrenia/DT") OR (MH "Schizophrenia, Childhood/DT")	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL	3,484
S19	S11 AND S18	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL	1
S18	(MH "Drug Therapy")	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL	5,946
S17	S11 AND S16	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL	153
S16	S12 OR S13 OR S14 OR S15	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL	44,231

S15	(MH "Adrenergic Beta-Antagonists+") OR (MH "Nadolol+") OR (MH "Timolol+") OR (MH "Labetalol")	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL	5,733
S14	(MH "Antiinflammatory Agents, Non-Steroidal+") OR (MH "Prednisolone") OR (MH "Prednisone") OR (MH "Triamcinolone") OR (MH "Antiinflammatory Agents, Steroidal+")	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL	25,262
S13	(MH "Fish Oils+") OR (MH "Fatty Acids, Omega-3+")	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL	5,314
S12	(MH "Antipsychotic Agents+") OR (MH "Antipsychotic Agents, Butyrophenone+") OR (MH "Antipsychotic Agents, Phenothiazine+") OR (MH "Olanzapine+")	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL	8,818
S11	S4 OR S9 OR S10	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL	721
S10	TI "early psychosis" OR "first episode psychosis" OR "early psychoses" OR "first episode psychoses" OR "acute psychoses" OR "acute psychosis"	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL	338
S9	S7 AND S8	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL	545
S8	TI "early symptom*" OR onset OR "early signs" OR first-episode OR "acute phase"	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL	6,628
S7	S5 OR S6	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases	15,299

			Search Screen - Advanced Search Database - CINAHL	
S6	TI "delusional disorder*" OR severe mental ill* OR severe mental disorder* OR psychotic OR psychosis OR psychoses OR schizo*	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL	8,802
S5	(MH "Schizoaffective Disorder") OR (MH "Schizophrenia") OR (MH "Delusions") OR (MH "Hallucinations") OR MH "Psychotic Disorders"	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL	13,900
S4	S1 OR S2 OR S3	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL	60
S3	TI "acute phase" AND schizophrenia	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL	6
S2	TI "childhood onset schizophrenia" OR "acute schizophrenia"	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL	28
S1	MH "Schizophrenia, Childhood"	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL	27

Cochrane

ID Search Hits
#1 MeSH descriptor: [Psychotic Disorders] explode all trees 1559
#2 MeSH descriptor: [Schizophrenia] explode all trees 4962
#3 MeSH descriptor: [Hallucinations] explode all trees 227
#4 MeSH descriptor: [Delusions] explode all trees 117
#5 "early symptom*" or onset or "early signs" or first-episode or "acute phase":ti,ab,kw (Word variations have been searched) 24449
#6 "early psychosis" or "first episode psychosis" or "early psychoses" or "first episode psychoses":ti,ab,kw (Word variations have been searched) 282
#7 "delusional disorder*" or severe mental ill* or severe mental disorder* or psychotic or psychosis or psychoses or schizo*:ti,ab,kw (Word variations have been searched) 13446
#8 "childhood onset schizophrenia":ti,ab,kw (Word variations have been searched) 18
#9 #1 or #2 or #3 or #4 or #7 13556

#10 #9 and #5 1156
#11 #6 or #8 or #10 1185
#12 MeSH descriptor: [Drug Therapy] explode all trees 118083
#13 #11 and #12 102
#14 antipsychotic medication for childhood-onset schizophrenia:ti (Word variations have been searched) 1
#15 #13 or #14 103
#16 MeSH descriptor: [Psychotic Disorders] explode all trees and with qualifier(s): [Drug therapy - DT] 810
#17 MeSH descriptor: [Schizophrenia] explode all trees and with qualifier(s): [Drug therapy - DT] 3346
#18 MeSH descriptor: [Delusions] explode all trees and with qualifier(s): [Drug therapy - DT] 41
#19 MeSH descriptor: [Hallucinations] explode all trees and with qualifier(s): [Drug therapy - DT] 56
#20 #16 or #17 or #18 or #19 3811
#21 #20 and #5 359
#22 #13 or #21 387

Cochrane Reviews
There are 16 results from 8715 records for your search on #22 - #13 or #21 in Cochrane Reviews in the strategy currently being edited. Vanaf 2012: 6 results.

Other Reviews (DARE)
There are 6 results from 34181 records for your search on #22 - #13 or #21 in Other Reviews in the strategy currently being edited. Vanaf 2012: 2 results.

Cochrane reviews en Other reviews geïmporteerd in RefMan database FarmacotherapieSRMa.

Health Technology Assessment (HTA): 0 results.

Trials
There are 363 results from 843892 records for your search on #22 - #13 or #21 in Trials in the strategy currently being edited. Vanaf 2012: 47 results.

Trials geïmporteerd in Refman database FarmacotherapieRCT.

Totalen:

RCT's:

PubMed: 109
PsycInfo: 54
CINAHL: 8
Cochrane: 47
Totaal: 218. Ontdubbeld en 85 dubbele titels verwijderd. Blijft over: 133.

Systematic reviews en Meta analyses:

PubMed: 38
PsycInfo: 2
CINAHL: 3
Cochrane: 8
Totaal: 51. Ontdubbeld en 9 dubbele titels verwijderd. Blijft over: 42.

Bijlage 6.B Review protocol

Reviewprotocol – Medicamenteuze behandeling

Onderwerp	**D. Medicamenteuze behandeling voor mensen met een eerste psychose**
Uitgangsvragen	D1. Wanneer kan Shared Decision Making voor keuzes rond medicatie (en psychosociale interventies) worden toegepast en op welke manier kan dit het beste worden ingevuld? NB: deze niet op basis van de wetenschappelijke literatuur. D2. Wat is de effectiviteit van verschillende orale anti-psychotische middelen en add-on medicatie, vergeleken bij alternatieve interventies en strategieën (placebo, wachtlijst)? D3. Wat is het bijwerkingenprofiel van verschillende antipsychotische middelen en andere farmacologische interventies, vergeleken bij alternatieve interventies en strategieën (placebo, wachtlijst, CAU) en wat zijn de verschillen in bijwerkingen voor verschillende subgroepen (ziektestadia, patiëntprofiel)? D4. Dient de dosering en duur van toepassen van medicatie ter preventie van relapse anders te zijn voor mensen met een eerste psychose in vergelijking tot andere ziektestadia?
Criteria voor overwegen inclusie van studies in de review	
• *Populatie*	• Personen van 12 jaar met een eerste psychose (e.g. first episode psychosis, early onset psychosis, recent onset schizofrenia) • Late onset first psychoses (patiënt rond 35 jaar) • Percentage personen met FEP, EOS of late onset per studie dient minimaal 75% te zijn. • Co-mobiditeit mag aanwezig zijn (middelenafhankelijkheid bijvoorbeeld) • Exclusie: personen met een affectieve psychose (depressie, bipolaire stoornis, manie), prodromal states, persons at risk, Prevention of first episode

• *Interventie*	• Alle antipsychotica welke in Nederland geregistreerd zijn voor de behandeling van psychosen
	• Medicatie in aanvulling op antipsychotica, zoals:
	  ○ Bèta-blokkers
	  ○ Visolie
	  ○ Ontstekingsremmers (waaronder aspirine)
	  ○ Andere add-on medicatie

• *Vergelijking*	• Placebo • Care as usual (CAU) • Wachtlijst • Een van de bovengenoemde interventies als alternatieve behandeling
• *Kritische Uitkomstmaten*	• Mentaal welbevinden (continue uitkomstmaten voor symptomen, depressie, angst, manie) • Remissie/relapse als dichotome uitkomstmaat voor symptomatisch herstel dan wel terugval • Bijwerkingen, waaronder suïcide • Verlaten van de studie om welke reden dan ook / drop-out

• *Belangrijke uitkomstmaten*	• Globaal welbevinden (CGI, GAF, SOFAS)
	• Functioneel herstel, gebaseerd op:
	  ○ Psychosociaal functioneren
	  ○ Sociaal functioneren /rolfunctioneren

• *Studiedesign*	• RCT's, meta-analyses en systematic reviews
• *Minimum omvang steekproef*	• RCT: > 10 per arm • Exclusie van studies met >50% attrition uit één arm van de trial (tenzij adequate statistiek is toegepast om te corrigeren voor missende data)

Search strategie	[patiënt] AND [RCT, meta-analyse, systematic review] AND [pharmacological interventions]
Databases searched	In overleg met de informatiespecialist wordt een zoekstrategie uitgezet in internationale wetenschappelijke databases. Opties[#]: • Core databases: Embase, Cochrane database for systematic reviews, CINAHL, Medline, PreMedline, PsycINFO • Topic specific databases: CDSR, CENTRAL, DARE, HTA
Data searched	Twee stappen: • In februari 2015 wordt de zoekstrategie uitgezet. Er wordt gezocht vanaf 2012 (einde search NICE richtlijn kinderen in mei 2012), met een laatste update voor commentaarfase van de huidige richtlijn (verwacht in maart 2015) • Voor de periode tot 2012 worden 2 richtlijnen van NICE gebruikt: die over schizofrenie en psychoses voor kinderen en voor volwassenen. • Optie: Onze patiëntenpopulatie wijkt iets af van de richtlijn van NICE voor kinderen. Search eventueel aanvullen voor periode 1995-2012 met studies voor patiënten van 18 jaar of ouder met FEP of late onset (indien de NICE richtlijn voor volwassenen niet voldoet).
De review strategie	• Indien SRs en MAs beschikbaar zijn per farmacologische behandeling, is dat het uitgangspunt. Indien er geen SR of MA beschikbaar is, wordt gebruik gemaakt van RCTs. • Bestaande systematic reviews en meta-analyses worden geselecteerd, beoordeeld en verwerkt in een beschrijvende review. De meta-analyse in de richtlijnen van NICE worden als één van de bestaande systematic reviews meegenomen. • Optie: Systematic reviews met check of RCT's na verschijnen systematic review de conclusies kunnen veranderen; indien ja - update van systematic review, indien nee – bestaande review gebruiken om aanbevelingen op te baseren*. • Voor meer detail zie bijlage.

Voetnoot.

* Indien er tijd over is kunnen SRs en MAs aangevuld worden met oorspronkelijke studies. If the reviewer identifies a systematic review appropriate to the review question, we will search for studies (with the best available design) conducted or published since the review was conducted, and the reviewer will assess if any additional studies could affect the conclusions of the previous review. If new studies could change the conclusions, we will update the review and conduct a new analysis. If new studies could not change the conclusions of an existing review, the Guideline Development Group will use the existing review to inform their recommendations.

[#] Medline, PreMedline = staan ook in Pubmed

CDSR = Cochrane database of systematic reviews

DARE zit in COCHRANE onder 'other reviews', wordt dus doorzocht als je in de Cochrane zoekt.

CENTRAL = PubMed Central, is database met vrij toegankelijke artikelen, staan ook in PubMed, dus hoeft niet apart doorzocht te worden.

HTA = Health Technology Assessment Database, zit ook in Cochrane.

BIJLAGE - Algemene reviewstrategie voor de totale richtlijn

Stap 1. Zoeken en selecteren

De reviewer zoekt, in samenwerking met de informatiespecialist, per uitgangsvraag naar oorspronkelijke studies (met het best beschikbare design) en systematische reviews voor het beantwoorden van de uitgangsvraag. Voor de selectie van studies wordt gebruik gemaakt van de selectiecriteria in het reviewprotocol.

Stap 2. Reviewen van oorspronkelijke studies: eigen MA of beschrijvend

Wanneer *enkel oorspronkelijke studies* worden gevonden die voldoen aan de inclusiecriteria wordt per uitgangsvraag besloten of er in de analyse een beschrijvende review wordt gemaakt of een kwantitatieve meta-analyse.
Een eigen meta-analyse wordt alleen gemaakt wanneer:

- gevonden studies rapporteren over de 'kritische' / 'belangrijke' patiënt relevante uitkomstmaten (bv. kwaliteit van leven, uitval door bijwerkingen)
- er is geen sprake van (te grote) klinische of statistische heterogeniteit tussen studies
- de effectmaten in de verschillende studies gelijk zijn of er voldoende ruwe data in de publicaties beschikbaar zijn om deze naar dezelfde effectmaat om te rekenen (zonder ruwe data op te vragen bij de onderzoekers)

NB: Wanneer oorspronkelijke studies worden gebruikt die ook in de NICE richtlijn zijn opgenomen kan hiervan de Risk-of-bias assessment van NICE gebruikt worden en kunnen voor de data extractie de gegevens in de evidence tabellen van NICE gebruikt worden – bij hen "sum of finding tables".

Stap 3. Besluiten of bestaande reviews kunnen gebruiken
Wanneer de reviewer een *bestaande systematische review* (meta-analyse of beschrijvende systematische review, *inclusief reviews van NICE*) identificeert welke geschikt is voor het beantwoorden van de uitgangsvraag, gaan we op zoek naar oorspronkelijke studies (met het best beschikbare design) die zijn gepubliceerd *sinds de publicatie van de review*. De reviewer zal beoordelen of meer recente studies de conclusies uit de bestaande review kunnen beïnvloeden.

Stap 4. Updaten (A) of gebruiken (B) bestaande reviews
Indien:

- A. nieuwe studies de conclusies in de bestaande review(s) zouden kunnen veranderen, zullen we de *review updaten* en een nieuwe analyse uitvoeren (beschrijvend of kwantitatief).
- B. nieuwe studies de conclusies van bestaande review(s) *niet* zouden kunnen veranderen, zal de werkgroep de *bestaande review(s) gebruiken* om hun aanbevelingen op te baseren.

Stap 5.
Voor het beoordelen van de kwaliteit van bewijs per uitkomstmaat met het *GRADE systeem* wordt als volgt omgegaan met uitzonderingen:

- wanneer er maar 1 oorspronkelijke studie beschikbaar is voor een uitkomstmaat: wordt 2 stappen ge-down-grade voor *imprecision* / *onnauwkeurigheid* (omdat de n te klein blijft)
- wanneer effectmaten voor een uitkomstmaat niet naar één maat kunnen worden omgerekend: wordt 2 stappen ge-down-grade voor *Study limitations* / *Risk of bias* (in verband met selective outcome reporting; je weet dat de studie bestaat maar je kan 'm niet meenemen). Daarnaast wordt de body of evidence voor de uitkomstmaat 2 keer beoordeeld (voor beide effectmaten).
- wanneer een bestaande review wordt gebruikt waarin de Risk of Bias per studie niet wordt gerapporteerd (vaak bij SR's): worden de oorspronkelijke studies opgevraagd en wordt hierin de Risk of bias bepaald

Verkennende search
In april 2014 is er een brede search verricht in PsycInfo en Pubmed naar bestaande systematic reviews (SR) en meta-analyses (MA) over (Ultra Hoog Risico groepen voor een) vroege psychose. Hierbij is geen limitering gezet op taal of jaar. Na ontdubbelen bleven er in totaal 535 referenties over. De resultaten van de eerste selectie staan per onderwerp in de voetnoot. Belangrijkste exclusie redenen tijdens de eerste selectie waren: onderzoeksgroep waren patiënten met schizofrenie, geen review maar onderzoek, Chinese populatie, onderzoek naar antipsychotica bij kinderen en adolescenten in het algemeen, risico's of afwijkend gedrag bij personen met een eerste psychose of schizofrenie, relatie substance abuse en psychose.

Opvallend is dat er voor 2004 nauwelijks reviews zijn met betrekking tot vroege psychose. Verder is er een review gevonden die 'late onset' heeft bekeken (na het 40ste levensjaar)

Bijlage 6.C Evidence tabel systematische reviews – medicatie

Summary of findings for systematic reviews of intervention studies on adjunct medication to antipsychotics in patiënts with early schizophrenia or FEP

NSAIDs

Reference: NITTA2013 **Nitta M, Kishimoto T, Muller N, Weiser M, Davidson M, Kane JM et al. Adjunctive use of nonsteroidal anti-inflammatory drugs for schizophrenia: a meta-analytic investigation of randomized controlled trials. Schizophr Bull 2013; 39(6):1230-1241.**	
Methods	Study aim: To meta-analytically assess the efficacy, effectiveness, and side effect profile of adjunctive nonsteroidal anti-inflammatory drugs (NSAIDs) vs placebo in schizophrenia. Study design: Meta-analysis. Only double blind placebo controlled RCTs. Search took place December 31, 2012. Analysis: meta-analysis Setting: inpatiënts
Patiënts	Number of studies: K=1 (Müller2010) on first-episode patiënts (<2 years), of 8 studies in total that were included in the review. Number of patiënts: N=49 Age: mean 28.6 years Sex: 40% F Inclusion: Randomized, double-blind, placebo-controlled studies examining the efficacy of adjunctive use of any NSAIDs for schizophrenia spectrum disorders. Studies not containing usable data for effect size calculation were excluded. Exclusion: Baseline characteristics: inpatiënts (setting), German patiënts (country)
Interventions	Intervention: amisulpride (SGA) (200-1000 mg) plus celecoxib (400 mg) Control: amisulpride (SGA)(200-1000 mg) plus placebo Follow-up time: 6 weeks (PT)

Outcome	Primary: PANSS total score Secondary: PANSS positive score and PANSS negative score
Results	PANSS total score: Hedges' g -0.247 (95%CI -0.80 to 0.30, p=0.377 (ns)) PANSS positive score: Hedges' g -0.41 (95%CI -0.96 to 0.14, p=0.146 (ns)) PANSS negative score: Hedges' g -0.11 (95%CI -0.65 to 0.44, p=0.702 (ns))
Quality Assessment	Study question: + Explicit clinical question, PICO: yes Search strategy: + Electronic databases: (Medline minimum: yes, several) Restrictions: no Selection process: ? Explicit in- and exclusion criteria (e.g. patiënt group, design, intervention: yes) By two reviewers independently made final selection: no Flow diagram: yes Quality assessment: - (no mentioning whatsoever of RoB assessment of individual studies) Explicit list of criteria (at least allocation concealment and blinding of assessors): no By two reviewers independently: no How consensus was reached and level of agreement: not Results individual studies reported: no Data extraction:? By two reviewers independently: unclear Process clearly described: no Characteristics original studies: + At least design, population, primary outcomes, follow up length: yes Handling heterogeneity: + Clinical heterogeneity?: subgroups yes Statistical heterogeneity: accounted for (random effects model): yes Or explored (subgroup or meta-analyses), refrain from pooling. Statistical pooling: + Funding / conflicts of interest: no commercial funding. Overall quality of evidence: ?

Toelichting

Item:	Omschrijving
Referentie:	1e auteur (publicatiejaar)
Doel studie:	doel (aim; objectives) van de studie
Studieopzetten:	specificeer de onderzoeksopzet (randomised clinical trials, clinical trials etc.)
Blindering:	specificeer type blindering (dubbelblind; enkelblind etc.)
Analyse:	voor RCTs bijvoorbeeld: intention-to-treat analyse of per-protocol analyse
Studieduur:	verschil tussen start- en einddatum van de studie (follow-up periode inbegrepen)
Setting:	aantal centra, betrokken landen, 1e/2e/3e lijn, stad/platteland/stad-platteland
Locatie:	specificeer naam / plaats instelling
Aantal:	aantal patiënten berekend voor iedere groep en aantal patiënten daadwerkelijk in iedere groep
Leeftijd:	gemiddelde; standaarddeviatie of bereik (minimum – maximum)
Sekseratio:	percentage vrouw
Inclusie / exclusie:	specificeer de in- en exclusiecriteria
Baseline karakteristieken:	Bijvoorbeeld bijzonderheden. Specificeer met name of er verschillen zijn tussen de groepen
Interventie / controle:	specificeer de interventies (bijv. dosering, frequentie, duur, intensiteit, discipline hulpverlener)
Follow-up duur:	Specificeer de duur van de follow-up en het laatste meetmoment
Uitkomstmaat:	Specificeer de primaire en secundaire uitkomstmaten incl. instrumenten. Alleen uitkomstmaten die relevant zijn voor het maken van een aanbeveling over de interventie (bij voorkeur door werkgroep bepaald). Alleen resultaten between groups rapporteren, not within groups.
Resultaten:	Dichotome maten als RR, OR en ARR kunnen uitgerekend worden ('calculated') als er niet gepoold is en de benodigde gegevens aanwezig zijn (aantal pt met gewenste en ongewenste uitkomst, per groep). Conclusie van auteurs eventueel toevoegen.
Beoordeling:	zie literatuurbeoordelingsformulieren; bewijskracht conform CBO-classificatie; financiering: bijv. overheidsgeld, farmaceutische industrie, instelling van gezondheidszorg.

Bijlage 6.D Studiekenmerken, resultaten en beoordeling van de kans op vertekening van de resultaten van randomised controlled trials (RCTs)

Subject: Add-on medication to pharmacotherapy in patiënts with FEB

Fish oil (not add on but instead of AP)

Reference: **Emsley R, Chiliza B, Asmal L, du Plessis S, Phahladira L, van Niekerk E et al. A randomized, controlled trial of omega-3 fatty acids plus an antioxidant for relapse prevention after antipsychotic discontinuation in first-episode schizophrenia. Schizophrenia Research 2014; 158(1-3):230-235.**	
Methods	Study aim: This study investigated whether a combination of omega-3 polyunsaturated fatty acids (ω−3 PUFAs) and a metabolic antioxidant, alpha-lipoic acid (α-LA), is effective in preventing relapse after antipsychotic discontinuation in subjects who were successfully treated for 2–3 years after a first-episode of schizophrenia or related illness. Study design: A randomized, double-blind, placebo controlled study. Blinding: Double blind Analysis: intention-to-treat, and LOCF Study duration: 2 years Setting: South Africa Location: ?
Patiënts	Number of patiënts: N=33 (N=80 was needed to detect a 20% difference). Recruitment was terminated prematurely due to the high relapse rates in both treatment groups and the severity of the relapses. Inclusion: All of the participants were drawn from completers of an earlier study that we conducted in which patiënts with a first psychotic episode were treated for two to three years with flexible doses of flupenthixol decanoate (FGA, injection). Additional criteria: • completion of the initial study without relapse • currently in remission according to the Remission in Schizophrenia Working Group criteria • aged between 18 and 48 years • meeting DSM-IV diagnosis of schizophrenia, schizoaffective or schizophreniform disorder Exclusion: • other DSM-IV axis I diagnosis • current substance dependence • clinically significant general medical condition • mental retardation

	Baseline characteristics: • the group mean (SD) age was 29.7 (6.0) years; • there were 73% men; • ethnicity comprised 76% mixed, 15% black and 9% white; • and DSM IV diagnosis was 79% schizophrenia, 18% schizophreniform and 3% schizoaffective disorder.

Interventions	Intervention (N=21): Antipsychotic treatment was tapered and discontinued over 6 months. Patiënts received a combination of omega-3 polyunsaturated fatty acids (fish oil) and a metabolic antioxidant alpha-lipoic acid (ω−3 PUFAs + α-LA). This was not as an add-on to AP, since no AP treatment took place anymore. Control (N=12): Antipsychotic treatment was tapered and discontinued over 6 months. Patiënts received a placebo treatment (not as an add-on to AP, since no AP treatment took place). Both conditions: Anxiolytic, hypnotic and antidepressant medication was permitted when indicated. Duration of follow-up: 2 years or until relapse
Outcome measures	Primary: 2-year relapse rate. Relapse was defined according to the criteria of Csernansky et al. (2002). These are essentially: a 25% increase in PANSS total score; deliberate self-injury; emergence of clinically significant suicidal or homicidal ideation; or violent behavior resulting in significant injury to another person or significant property damage. Secondary: • time to relapse • changes in psychopathology (PANSS, CGI) was assessed at 4 weekly intervals • social and occupational functioning (SOFAS) was assessed at 6 months intervals • quality of life (WHOQOL-BREF) was assessed at 6 months intervals
Results	Recruitment was terminated prematurely due to the high relapse rates in both treatment groups and the severity of the relapses. Results: No significant group differences were found on primary and secondary outcomes: • Relapse: Of the experimental group 19/21 (90%) relapsed and one (5%) completed two years without relapse (p = 0.6). 9/12 (75%) randomized to placebo relapsed and none completed two years without relapse. • Time to relapse: No significant difference was found in the mean times to relapse; these were 39.8 ± 25.4 and 38.3 ± 26.6 weeks for the intervention and placebo groups, respectively. • Relapse symptom severity: There were no significant differences between the groups in relapse symptom severity. Conclusion:

	The study was underpowered due to premature termination. No evidence was found that omega-3 polyunsaturated fatty acids and a metabolic antioxidant could be a suitable alternative to maintenance antipsychotic treatment in relapse prevention in this small study. Antipsychotic discontinuation after a single episode of schizophrenia carries a very high risk of relapse.
RoB Assessment* (Cochrane template)	*Selection bias:* 1. Random sequence generation ? 2. Allocation concealment ? *Performance bias:* 3. Blinding patiënts and professionals + *Detection bias:* 4. Blinding of outcome assessment ? *Attrition bias:* 5. Incomplete outcome data + *Reporting bias:* 6. Selective reporting + *Other bias:* 7. Comparability of treatment groups at baseline + 8. Group received the same care apart from the interventions studied + 9. Sufficient duration of follow up + Conflicts of interest: + The study was funded with a grant from a non-commercial organization. Some of the authors have received honoraria from pharmaceutical industries. However, it is unlikely that this may have caused bias. RoB: In general, well designed study, but some aspects are not reported. There seems limited risk of bias.

*

+ = judgement of reviewer(s) is that there is a low risk of bias
- = judgement of reviewer(s) is that there is a high risk of bias
? = no information available, no judgement possible of reviewers on risk of bias

Antibiotics

Reference: **Chaudhry IB, Hallak J, Husain N, Minhas F, Stirling J, Richardson P et al. Minocycline benefits negative symptoms in early schizophrenia: a randomised double-blind placebo-controlled clinical trial in patiënts on standard treatment. J Psychopharmacol 2012; 26(9):1185-1193.**	
Methods	Study aim: Whether the addition of minocycline to treatment as usual (TAU) for 1 year in early psychosis would benefit the negative symptoms of schizophrenia, and improve overall outcome in early schizophrenia compared with placebo.

	Study design: Double blind placebo-controlled trial Blinding: double blind (patiënts, clinicians and outcome assessors) Analysis: intention to treat (ITT) Study duration: 12 months Setting: Psychiatric units in Brazil (1) and Pakistan (5) Location: ?
Patiënts	Number of patiënts: N=144 Inclusion: (1) patiënts aged 18–65 years; (2) DSM-IV diagnosis of schizophrenia, schizoaffective disorder, psychosis not otherwise specified or schizophreniform disorder (3) within first 5 years of diagnosis; (4) competent and willing to give informed consent; (5) stable on medication 4 weeks prior to baseline; (6) able to take oral medication; (7) if female, willing to use adequate contraceptive precautions and to have monthly pregnancy tests. Exclusion: (1) relevant medical illness (renal, hepatic, cardiac, serious dermatological disorders such as exfoliative dermatitis, systemic lupus erythematosis); (2) prior history of intolerance to any of the tetracyclines; (3) concomitant penicillin therapy; (4) concomitant anticoagulant therapy; (5) presence of a seizure disorder, not including clozapine-induced seizures; (6) currently taking valproic acid; (7) any change of psychotropic medications within the previous 6 weeks; (8) diagnosis of substance abuse (except nicotine or caffeine) or dependence; (9) pregnant or breast-feeding. Baseline characteristics: • Sex: 40% F • Age: M 26.2 (SD 5.9) • Country: 80% from Pakistan, 20% from Brazil
Interventions	Intervention (N=71): TAU (antipsychotic treatment) and minocycline (200 mg/d) Control (N=73): TAU (antipsychotic treatment) and placebo Duration of follow-up: 12 months PT
Outcome measures	Primary: PANSS negative symptoms subscale Secondary: PANSS total scores an PANSS positive symptoms subscale, CGI, GAF, side effects, drop out
Results	Results 12 months PT. Only negative symptoms for both countries together, other outcomes separate due to non-consistency across countries. PANSS negative symptoms subscale:

	• Pakistan and Brazil together: Significant difference in effect (SMD -0.51, n=94, 95% CI -0.92 to -0.10) in favour of the experimental treatment. PANSS positive symptoms subscale: • Pakistan: SMD -0.22 (n=70, 95% CI -0.69, 0.25, n.s.) • Brazil: significant difference in effect (SMD -1.20, n=24, 95% CI -2.08 to -0.32) in favour of the experimental treatment. PANSS total sore: • PANSS total score Pakistan: SMD -0.26 (n=70, 95% CI -0.73 to 0.21, n.s.) • PANSS total score Brazil: significant difference in effect (SMD -1.40, n=24, 95% CI-2.32 to -0.49) in favour of the experimental treatment. CGI: • Pakistan: SMD -0.10 (n=70, 95% CI -0.57 to 0.37, n.s.) • Brazil: significant difference in effect (SMD -1.11, n=24, 95% CI -1.98 to -0.24) in favour of the experimental treatment. GAF: • Pakistan: SMD -0.24 (n=71, 95% CI -0.71 to 0.23 n.s.) • Brazil: SMD -0.43 (n=24, 95% CI -1.25 to 0.38 n.s.) Dropout: • Discontinuation: n=25 in each group. • Due to side effects: n=3 in experimental, n=2 in control group • Death (incl suicide): n=3 in experimental group, n=1 in control group • Suicide: n=1 in control group Side effects: Side effects could not have compromised masking of treatment. • In the minocycline group: nausea (n=12), headache (n=9), anorexia (n=7), vomiting (n=5), dizziness (n=4), skin discolouration (n=3) and visual disturbances (n=3). • In placebo group: headache (n=17), dizziness (n=14), nausea (n=11), tooth discoloration (n=6), visual disturbances (n=6), anorexia (n=5), vomiting (n=5), rash (n=4), oesophageal irritation (n=4), skin discolouration (n=3), and vertigo (n=3). Drop out: 35% and 34% in experimental and control group respectively. Conclusion: The addition of minocycline to TAU early in the course of schizophrenia seems to improve negative symptoms.
RoB Assessment* (Cochrane template)	*Selection bias:* 1. Random sequence generation + 2. Allociation concealment + *Performance bias:* 3. Blinding patiënts and professionals + *Detection bias:* 4. Blinding of outcome assessment + *Attrition bias:*

	5. Incomplete outcome data – (35% missing outcomes, missings not imputed) *Reporting bias:* 6. Selective reporting + *Other bias:* 7. Comparability of treatment groups at baseline + 8. Group received the same care apart from the interventions studied ? TAU not described 9. Sufficient duration of follow up + 10. Funding + RoB: Well designed study, but TAU was not specified and the handling of missing data was insufficient, both which may cause a risk of bias.

*

+ = judgement of reviewer(s) is that there is a low risk of bias

- = judgement of reviewer(s) is that there is a high risk of bias

? = no information available, no judgement possible of reviewers on risk of bias

Metformine

Reference: **Wu RR, Jin H, Gao K, Twamley EW, Ou JJ, Shao P et al. Metformine for treatment of antipsychotic-induced amenorrhea and weight gain in women with first-episode schizophrenia: a double-blind, randomized, placebo-controlled study. Am J Psychiatry 2012; 169(8):813-821.**	
Methods	Study aim: To assess the efficacy of metformine for antipsychotic-induced amenorrhea and weight gain among female patiënts with first-episode schizophrenia. Study design: randomized, double-blind, placebo-controlled trial Blinding: double-blind (patiënts and assessors) Analysis: intention to treat Study duration: 6-months Setting: China Location: outpatiënt clinic
Patiënts	Number of patiënts: N=84 Inclusion: • Patiënts had to be relatively stable (total score <60 on the PANSS); • had to have initiated treatment for the first episode of schizophrenia within the past year; • patiënts were stable: <60 total score PANSS • had to have experienced amenorrhea within the first year of treatment with one of four antipsychotics— clozapine, olanzapine, risperidone, or sulpiride;

	• had to have been either discharged from inpatiënt units or first seen in the clinic in the 12 months before enrollment; • and had to have taken only one antipsychotic, with no more than a 25% change in dosage, over the past 6 months. Exclusion: • If there was evidence of liver or renal dysfunction, cardiovascular disease, or diabetes mellitus; • if they were pregnant or lactating; • or if they had a psychiatric diagnosis other than schizophrenia or a current history of a substance use disorder. Baseline characteristics: • Sex: 100% F • Age: mean 26.4 years (SD 3.4) • Duration of amenorrhea: mean 3.9 months • Length of antipsychotic medication: 6.35 months • Patiënts with a BMI above normal range: n=18 (21%) • Patiënts that had gained more than 10% of their body weight compared to their weight prior to taking antipsychotics: n=59 (70.2%)
Interventions	Intervention (N=42): Metformine (1000 mg/day) Control (N=42): Placebo Any antipsychotics (clozapine, olanzapine, risperidone, or sulpiride) that patiënts were taking before enrollment in the study remained at the same dosage throughout the course of the study. Duration of follow-up: 6 months PT
Outcome measures	Primary: the proportion of patiënts whose menstruation was restored, as well as changes in body weight and body mass index (BMI). Secondary: PANSS score, frequency of adverse events, discontinuation.
Results	• Restored menstruation: Menstruation was resumed significantly in the metformine group (n=28, 66.7%) compared to the placebo group (n=2, 4.8%) (RR 0.35, n=84, 95% CI 0.23 to 0.54, large significant effect). Patiënts in the control group have 65% less chance to resume menstruation. The mean time to menstruation restoration in the intervention group was 2 months (SD 0.5). • Body weight and BMI: The mean body weight and BMI values decreased significantly in the metformine group, and increased in the placebo group. Patiënts in the metformine group lost on average 2.3 kg, whereas in the placebo group, the mean body weight increased with on average 2.1 kg. Similarly, the mean BMI decreased by 0.93 in the metformine group, while it increased by a mean of 0.85 in the placebo group. • Losing body weight: RR 0.73 (n=84, 95% CI 0.60 to 0.89, moderate significant effect). Patiënts in the control group have 27% less chance to have lost more than 10% of their body weight. • PANSS: No unfavourable effects of metformine on the positive and negative symptoms of schizophrenia were observed (data not presented). • Adverse events: There were no significant differences in the frequency and types of adverse events reported between the two groups. Adverse events that affected more than 5% of the overall sample are nausea, extrapyramidal symptoms, insomnia and agitation, somnolence, headache and dry mouth.

	• Discontinuation: Eight of 84 patiënts discontinued: 3 due to hospitalisation, 5 due to loss-to-follow-up. A total of 76 patiënts (90.5%) completed the 6-month treatments, 39 (92.8%) of whom were in the metformine group and 37 (88.1%) in the placebo group. Conclusion: This study has shown clearly that the addition of metformine to antipsychotics is a potential treatment to restore antipsychotic-induced amenorrhea in female patiënts with schizophrenia.
RoB Assessment* (Cochrane template)	*Selection bias:* 1. Random sequence generation + 2. Allociation concealment + *Performance bias:* 3. Blinding patiënts and professionals + *Detection bias:* 4. Blinding of outcome assessment + *Attrition bias:* 5. Incomplete outcome data + *Reporting bias:* 6. Selective reporting + *Other bias:* 7. Comparability of treatment groups at baseline + 8. Group received the same care apart from the interventions studied + 9. Sufficient duration of follow up + 10. Funding: + RoB: Overall, the risk of bias seems low.

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Reference: **Wang M, Tong JH, Zhu G, Liang GM, Yan HF, Wang XZ. Metformine for treatment of antipsychotic-induced weight gain: a randomized, placebo-controlled study. Schizophr Res 2012; 138(1):54-57.**	
Methods	Study aim: To evaluate the efficacy of metformine for treatment of antipsychotic-induced weight gain in patiënts with first episode schizophrenia. Study design: placebo controlled RCT Blinding: double blind Analysis: completers (n=66) Study duration: 12 weeks

	Setting: China Location: outpatiënt clinic
Patiënts	Number of patiënts: N=72 Inclusion: • Patiënts aged 18-60 years with a first psychotic episode of schizophrenia (DSM-IV) ; • participants gained more than 7% of their predrug body weight (cut-off for clinical significance) within the first year of treatment with a targeted antipsychotic agent – clozapine, olanzapine, risperidone, or sulpiride – ; • patiënts were either discharged from inpatiënt units or first seen in the clinic in the 12 months before enrollment so their weight and antipsychotic treatment were documented; • had to have relatively stable improvement (the total score of PANSS≤60). Exclusion: If patiënts had liver or renal dysfunction, cardiovascular disease, diabetes mellitus, arthritis, pulmonary or neurological disease; were pregnant or lactating. Baseline characteristics: • Age: Mean 26.2 (SD 2.9) • Sex: 48% F • Duration of schizophrenia: 9.5 months
Interventions	Intervention (N=32): Metformine (1000 mg/d) Control (n=34): Placebo Any antipsychotics (clozapine, olanzapine, risperidone, or sulpiride) that patiënts were taking before enrollment in the study remained at the same dosage throughout the course of the study. Duration of follow-up: 12 weeks PT
Outcome measures	Results are from completers analysis (itt using LOCF revealed similar findings, according to authors) Primary: body weight Secondary: BMI, PANSS, adverse effects, discontinuation
Results	Body weight: Over the 12-week study period, patiënts in the placebo group continued to gain weight compared with baseline (mean 2.5 kg), whereas, compared with baseline, weight decreased in the metformine group (mean 3.3 kg). The difference between groups in kg PT (mean metformine group 61.9 (SD 6.0) kg; placebo group 66.9 (SD 5.1)) was large and significant, and in favour for the metformine group (SMD -0.89, n=66, 95%CI -1.40 to -0.38). More patiënts in the metformine group (N=13), compared with the placebo group (N=3), decreased their initial body weight by more than 7%, the cut-off for clinically significance, which was a significant difference (RR 0.65, n=66, 95%CI 0.48 to 0.88). Patiënts in the control group have 35% less chance to have lost more than 7% of their body weight. BMI: Similarly, the mean body mass index decreased by 1.3 in the metformine group and increased by 0.9 in the placebo group. The difference between groups in BMI at PT was significant (mean

	metformine group 23.5 (SD 1.3); placebo group 25.2 (SD 1.2)), and in favour for the metformine group (SMD -1.34, n=66, 95%CI -1.88 to -0.81). PANSS: no significant changes from baseline. Adverse events: There were no significant differences in the frequency and types of adverse effects reported between the two groups. Adverse events that affected more than 5% in the entire sample were nausea, extrapyramidal symptoms, insomnia and agitation, somnolence and dry mouth. Discontinuation: 8.4% discontinued (4 patiënts in the intervention and 2 patiënts in the control group). Conclusion: In this 12-week study, metformine was effective and safe in attenuating antipsychotic-induced weight gain in first-episode schizophrenia patiënts. Patiënts displayed good adherence to metformine.
RoB Assessment* (Cochrane template)	*Selection bias:* 1. Random sequence generation + 2. Allociation concealment + *Performance bias:* 3. Blinding patiënts and professionals + *Detection bias:* 4. Blinding of outcome assessment + *Attrition bias:* 5. Incomplete outcome data - *Reporting bias:* 6. Selective reporting + *Other bias:* 7. Comparability of treatment groups at baseline + 8. Group received the same care apart from the interventions studied + 9. Sufficient duration of follow up +/? 10. Funding: + RoB: low risk of bias overall. However, possible risk of bias due to dropout (4 in intervention and 2 in placebo group within 4 weeks) and handling of incomplete data: completers analysis.

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Melatonin

Reference: **Modabbernia A, Heidari P, Soleimani R, Sobhani A, Roshan ZA, Taslimi S et al. Melatonin for prevention of metabolic side-effects of olanzapine in patiënts with first-episode schizophrenia: randomized double-blind placebo-controlled study. J Psychiatr Res 2014; 53:133-140.**	
Methods	Study aim: To determine the efficacy of melatonin 3 mg/day in preventing olanzapine-induced side-effects in patiënts with FES. Study design: RCT Masking: The patiënts and their family members, the evaluator, the person responsible for administering intervention, and the statistician were blind to allocation. Analysis: Intention-to-treat. Missing data were imputed of patiënts with at least one post-baseline measurement. Study duration: 8 weeks Setting: Iran Location: Academic psychiatric hospital (first weeks in hospital, then outpatiënt clinic).
Patiënts	Number of patiënts: N=48, N=36 in analysis (75%) Inclusion: • Patiënts diagnosed with SCID-I (DSM-IV-TR criteria) • with a First Episode Schizophrenia (FES) • who were eligible for starting olanzapine Exclusion: • married women who were at reproductive age (unless they used a reliable non-hormonal contraception method) • history of significant head trauma (causing loss of consciousness more than 5 min) • need for administration of other antipsychotics, and • addictive disorders Baseline characteristics: • Gender: 31% Female • Age: Mean 32.8 years (SD 5.4) • Weight: 65.3 kg (SD 7.8 kg)
Interventions	All patiënts received Olanzapine (titrated up to 25 mg/d), and clonazepam 2 mg at night for sleep enhancement. Intervention (N=24): addition of melatonine (3 mg/d) Control (N=24): placebo Duration of follow-up: 8 weeks PT
Outcome measures	Primary: • Weight

	Secondary: • BMI • The Positive and Negative Syndrome Scale (PANSS-scores) • Side effects
Results	Weight: By week 8, patiënts in the melatonin group gained significantly less weight (3.3% of the baseline) than the placebo group (8.5% of the baseline). The mean difference in weight was 3.2 kg (MD=3.2 kg, 95% CI 0.5; 6.0, P=0.023). Nine patiënts in the placebo group (50%) compared with four patiënts in the melatonin group (22%) experienced clinically significant weight gain (defined as >7% of the baseline weight) by the end of the study. Waist circumference: By week 8, patiënts in the melatonin group experienced significant less increase in waist circumference (MD=2.83 cm, 95%CI 0.12 to 5.54, t(34)=2.13, P=0.041) than the placebo group. BMI: By week 8, patiënts in the melatonin group experienced significant less increase in BMI (MD=1.07 kg/m2, 95%CI 0.15 to 1.99, t(34)=2.38, P=0.024). PANSS-scores: By week 8, patiënts in the intervention group achieved significantly more reduction in their PANSS total score (MD=12.9, 95% CI 2.8 to 23.0, t(34)= 2.61, P=0.014) than the placebo group. No significant differences in positive or negative symptoms were demonstrated between both groups post treatment. Drop-out: 7 patiënts (29%) in each group dropped out after randomisation; for 6 patiënts in each group no follow-up assessment was available and they were left out of the ITT analysis. Not reported whether it was selective drop-out. Side effects: No serious adverse events or extrapyramidal symptoms were reported. To summarize, in patiënts treated with olanzapine, short-term melatonin treatment attenuates weight gain, abdominal obesity, and BMI. It might also provide additional benefit for treatment of psychosis.
RoB Assessment* (Cochrane template)	*Selection bias:* 1. Random sequence generation + 2. Allociation concealment + *Performance bias:* 3. Blinding patiënts and professionals + *Detection bias:* 4. Blinding of outcome assessment + *Attrition bias:* 5. Incomplete outcome data – (high drop-out % in both groups)

	Reporting bias: 6. Selective reporting + *Other bias:* 7. Comparability of treatment groups at baseline + 8. Group received the same care apart from the interventions studied + 9. Sufficient duration of follow up + RoB: Overall low risk of bias, although high drop-out % in both groups.

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Ranitidine

Reference: **Ranjbar F, Ghanepour A, Sadeghi-Bazargani H, Asadlo M, Alizadeh A. The effect of ranitidine on olanzapine-induced weight gain. Biomed Res Int 2013; 2013:639391.**	
Methods	Study aim: The aim of this study was to assess the efficacy of ranitidine in attenuating or preventing Olanzapine-induced weight gain in first episode schizophrenia (FES). Study design: A (quasi randomized and controlled) parallel two-arm study design Masking: Clinicians, patiënts and researchers were blind to the medication type Analysis: unclear (no handling missing data reported) Study duration: 16 weeks Setting: Iran Location: psychiatric university hospital
Patiënts	Number of patiënts: N=52 Inclusion: • patiënts with a diagnosis of schizophrenia, schizoaffective and schizophreniform (DSM-IV criteria) and were planned to be treated with olanzapine • planned hospitalization for more than 16 weeks • the official informed consent of the patiënts' authorized guardian Exclusion: • presence of comorbid physical illnesses • simultaneous use of drugs that might affect weight Baseline characteristics:

	• Sex: 36.5% female • Age: mean 38.1 (SD 11) years • Weight: mean 62.3 (SD 9.6) kg • BMI: 23.1 (SD 3.3)
Interventions	All patiënts received Olanzapine. Intervention: Ranitidine (starting dose 600 mg/d) Control: Placebo Duration of follow-up: weekly measures, final one at 16 weeks PT
Outcome measures	Primary: Difference between groups in BMI trend scores Secondary: Difference between groups in BMI change scores
Results	Incomplete outcome data: Corresponding author of the study was contacted on May 6th 2015.
RoB Assessment* (Cochrane template)	*Selection bias:* 1. Random sequence generation ? 2. Allociation concealment ? *Performance bias:* 3. Blinding patiënts and professionals + *Detection bias:* 4. Blinding of outcome assessment + *Attrition bias:* 5. Incomplete outcome data - *Reporting bias:* 6. Selective reporting - *Other bias:* 7. Comparability of treatment groups at baseline + 8. Group received the same care apart from the interventions studied + 9. Sufficient duration of follow up + RoB: Several methodological limitations were encountered: • Unclear how the randomisation procedure and allocation concealment was carried out • Unclear whether the patiënts had a first episode of schizophrenia (this is only mentioned in the summary, not in the rest of the article and thus not in the inclusion criteria) • Incomplete outcome data, unclear how missing data were handled, no information on dropout, no other outcomes were presented than BMI

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Pregnenolone

Reference: **Ritsner MS, Bawakny H, Kreinin A. Pregnenolone treatment reduces severity of negative symptoms in recent-onset schizophrenia: an 8-week, double-blind, randomized add-on two-center trial. Psychiatry Clin Neurosci 2014; 68(6):432-440.**	
Methods	Study aim: This report aimed to test the efficacy and safety of the neurosteroid pregnenolone in patiënts with DSM-IV recent onset schizophrenia or schizoaffective disorder in subjects with suboptimal response to antipsychotics. Add-on pregnenolone could diminish persistent clinical symptoms. Study design: RCT Masking: Double blind (patiënts and clinicians, who were also outcome assessors) Analysis: intention-to-treat, imputed missings Study duration: 8 weeks Setting: Israel Location: in- and outpatiënts of two large state referral hospitals: Sha'ar Menashe Mental Health Center and Tirat Carmel Mental Health Center.

Patiënts	Number of patiënts: N=60 (analysis based on all patiënts)
	
	Inclusion:
	• Between 18 and 40 years of age
	• DSM-IV diagnosis of schizophrenia or schizoaffective disorder
	• Recent episode (<5 years)
	• Suboptimal response to antipsychotics (residual symptoms)
	
	Exclusion:
	• An unstable medical or neurological condition
	• any significant medical or neurological illnesses or substance abuse
	• pregnancy
	• treatment with any steroid or hormonal supplement (e.g. estrogen)
	
	Baseline characteristics:
	• Age: Mean 27.2 (SD 5.4)
	• Age of onset: Mean 23.8 (SD 5.0)
	• Sex: 13% female
	• Antipsychotics use at baseline:
	  ○ first generation antipsychotics (n=24, 40%)
	  ○ second generation antipsychotics (n=23, 38%)
	  ○ first and second generation antipsychotics combined (n=13, 22%)
	• Other medication at baseline:
	  ○ patiënts continued to take mood stabilizers (n=14)
	  ○ benzodiazepines (n=19)
	  ○ anti-Parkinson agents (n=33)
	  ○ antidepressants (n=3)

Interventions	Intervention (n=29): antipsychotics (FGA, SGA or combination) and pregnenolone (50 mg/d) Control (n=31): antipsychotics (FGA, SGA or combination) and placebo Duration of follow-up: At 2, 4, 6 weeks and at 8 weeks PT
Outcome measures	Primary: • Total scores, Negative symptoms score, Positive symptoms score (PANSS) Secondary: • Functioning (GAF) • Side effects • Discontinuation

Results	• Negative symptoms: Adjunctive pregnenolone significantly reduced PANSS negative scale scores, in comparison to placebo, with moderate effect size (SMD -0.76, 95% CI -1.29 to -0.24). The effect was especially present among patiënts in the intervention group who were not concomitantly treated with mood stabilisers.
	• Other outcome assessments did not show significant differences between groups:
	  ○ PANSS total scale (SMD -0.51, 95%CI -1.02 to 0.01)
	  ○ PANSS positive scale (SMD 0.04, 95% CI -0.47 to 0.54)
	  ○ GAF scores (SMD 0.22, 95%CI -0.29 to 0.73)
	• Side effects: No differences in extrapyramidal symptom between groups. Pregnenolone was well tolerated.
	• Discontinuation: 8 patiënts (13.3%). No significant difference between groups (4 in each group, not related to adverse effects).
	
	In sum, adjunctive pregnenolone reduces the severity of negative symptoms in recent onset schizophrenia and schizoaffective disorder, especially among patiënts who are not treated with concomitant mood stabilizers.

RoB Assessment* (Cochrane template)	*Selection bias:* 1. Random sequence generation + 2. Allociation concealment + *Performance bias:* 3. Blinding patiënts and professionals + *Detection bias:* 4. Blinding of outcome assessment + *Attrition bias:* 5. Incomplete outcome data + *Reporting bias:* 6. Selective reporting + *Other bias:* 7. Comparability of treatment groups at baseline + 8. Group received the same care apart from the interventions studied + 9. Sufficient duration of follow up +

	RoB: This study has few methodological limitations. However, the study has a modest sample size and short duration.

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Toelichting

Item:	Omschrijving
Referentie:	1e auteur (publicatiejaar)
Doel studie:	doel (aim; objectives) van de studie
Studieopzet:	specificeer de onderzoeksopzet (randomised clinical trial, clinical trial etc.)
Blindering:	specificeer type blindering (dubbelblind; enkelblind etc.)
Analyse:	voor RCTs bijvoorbeeld: intention-to-treat analyse of per-protocol analyse
Studieduur:	verschil tussen start- en einddatum van de studie (follow-up periode inbegrepen)
Setting:	aantal centra, betrokken landen, 1e/2e/3e lijn, stad/platteland/stad-platteland
Locatie:	specificeer naam / plaats instelling
Aantal:	aantal patiënten berekend voor iedere groep en aantal patiënten daadwerkelijk in iedere groep
Inclusie / exclusie:	specificeer de in- en exclusiecriteria.
Baseline karakteristieken:	Sekseratio (percentage vrouw), leeftijd (gemiddelde, SD of bereik), diagnose, comorbiditeit, etc.
Interventie / controle:	specificeer de interventies (bijv. dosering, frequentie, duur, intensiteit, discipline hulpverlener)
Follow-up duur:	Specificeer de duur van de follow-up en het laatste meetmoment
Uitkomstmaat:	Specificeer de primaire en secundaire uitkomstmaten incl. instrumenten. List only outcome measures that are essential for making a recommendation on the intervention.
Resultaten:	Report only between groups differences, not within groups. Specificeer de effectgrootte (incl. betrouwbaarheidsinterval) van de interventie & bijwerkingen / complicaties. Always include associated harms.

Hoofdstuk 7 Psychologische, psychosociale en verpleegkundige interventies

Bijlage 7.A Summary of findings for systematic reviews of intervention studies

Reference: van Dusseldorp,L, Goossens P, van AT. Mental health nursing and first episode psychosis. Issues Ment Health Nurs 2011; 32(1):2-19.	
Methods	Study aim: Identify mental health nursing's contribution to the care and treatment of patients with a first episode of psychosis Study design: All forms of research Analysis: Content Analysis, First, the focus of each article was determined. Second, the categories were identified. And third, the central themes (i.e., domains of nursing) were identified. The content analysis was peer reviewed by the second and third authors. Setting: -
Patients	Number of studies: K= 27 Inclusion: The majority of the 27 articles described the contribution of mental health nurses to the care for patients with schizophrenia or psychosis in general. Given that the population described in these articles also included patients with a FEP, however, it was decided to include these articles as well. Exclusion: articles about first psychosis related to an organic or substance-induced psychotic disorder and articles published before 1989. Baseline characteristics:
Interventions	Intervention: Mental health nursing's contribution to the care and treatment Control:- Follow-up time:-
Outcome	Primary:- Secondary: -
Results	3 qualitative studies, 6 quantitative studies, 5 narrative reviews, 9 practice reports, and 4 opinion reports were included The review suggests that mental health nurses should reflect upon their own daily practices within the following five domains: development of therapeutic relation, relapse prevention, enhancement of social functioning, stimulation of medication adherence, and support of family members. Extraction of results is limited to the 5 quantitative studies (Renwick et al., 2009; Mullen et al., 2002, Waldheter et al., 2008), one narrative reviews (Reed, 2008) and one systematic review (Askey et al., 2007) including FEP-patients <u>Therapeutic Relationship (Discharge planning)</u>

	Early intervention and treatment are critical for the achievement of better clinical outcomes and the alleviation of psychological impact on patients and their families. The therapeutic relationship is the basis of care in mental health nursing and must be built on good rapport, trust, genuineness, and patient-centered goals if it is to be effective (Reed, 2008). The therapeutic relationship can help alleviate not only anxiety but also confusion and thereby enable the patient to feel more in control <u>Relapse prevention (Acknowledge the interaction between symptoms and appraisal of stress, Increase coping abilities)</u> Significant relation (p = .001) between higher levels of depression and higher levels of subjective stress. Significant relation (p = .004) between lower levels of psychotic symptoms and higher levels of perceived stress. (Renwick et al., 2009) <u>Enhancement of Social Functioning</u> Articles showed mental health nurses to play an important role in psychosocial interventions aimed to support the social functioning of the patient. (Renwick et al., 2009; Waldheter et al., 2008) Waldheter and colleagues (2008) report significantly positive results of CBT conducted on an individual basis on symptom improvement, particularly for positive symptoms (i.e., delusions or hallucinations), adaption to illness, and increased quality of life. Given the documented potential of CBT, researchers have called for integration of CBT into the treatment services provided for early psychosis. <u>Stimulation of Medication Adherence (Medication management)</u> Mental health nurses play a critical role in the administration and management of such medication (Reed, 2008) <u>Support of Family Members</u> (Mental health nurses should be at the forefront of Multiple family group education program, Mullen2002) Significant improvements (p =.00) in perceived knowledge and understanding of families. (Integrated treatment involving family, Reed2008) Early intervention and treatment are crucial to achieve better clinical outcomes and alleviate the psychological impact on patients and their families. (Acknowledge relatives', judgments, Psycho-education, Avoid a poor prognosis message, Recognize emotional grief and isolation, Appraise problems faced by families and possible tendency to use avoidant coping strategies, Train the multidisciplinary team to be family-inclusive, Gain access to specialist supervision, Askey2007) There is limited and conflicting evidence regarding efficacy of family intervention for this population. Definitive RCTs are required to establish efficacy. At this point, evidence suggests that family intervention may be an effective intervention for High Expressed Emotion families.
Quality Assessment (AMSTAR)	Study question: + Explicit clinical question, PICO • What is known about the contribution of mental health nursing to the care and treatment of patients with a first episode psychosis? • What level of evidence supports this knowledge? Search strategy: + Electronic databases: (Medline minimum) Medline, PsycINFO, EMBASE, CINAHL, NAZ (Database with Dutch nursing research articles), Cochrane Central Register of Controlled Trials and Cochrane Database of Systematic Reviews. Restrictions: (language, year of publication) January 1989 to May 2009 Articles in Dutch, English, French, and German were considered Selection process: + Explicit in- and exclusion criteria (e.g. patient group, design, intervention)? Articles in which the content of the nursing process is described were included with no special requirements regarding research design of the publication type.

	Exclusion: articles about first psychosis related to an organic or substance-induced psychotic disorder By two reviewers independently made final selection? Yes Flow diagram? Yes Quality assessment: + (Polit, D. F., & Beck, C. T. (2008). Nursing research: Generating and assessing evidence for nursing practice (8th ed.). Philadelphia: Lippincott Williams & Wilkins.) Explicit list of criteria (at least allocation concealment and blinding of assessors)? No By two reviewers independently? No How consensus was reached and level of agreement? Peer reviewed by co-authors Results individual studies reported? Yes Data extraction: - By two reviewers independently? No Process clearly described? Unclear Characteristics original studies: - At least design, population, primary outcomes, follow up length? It is clear that not all included studies included FEP patient, mostly with schizophrenia or psychosis. But it is not clear which studies. Not all studies are reported in the data-extraction table. Handling heterogeneity: - Clinical heterogeneity?: subgroups Statistical heterogeneity: accounted for (random effects model), explored (subgroup or meta-analyses), refrain from pooling. No meta-analysis Statistical pooling: - Funding / conflicts of interest: + Overall quality of evidence: - Low quality because of designs and population included in the review General conclusion:+ / -
Literatuur	Askey, R., Gamble, C.,&Gray, R. (2007). Family work in first-onset psychosis: A literature review. *Journal of Psychiatric and Mental Health Nursing*, *14*, 356–365. Mullen, A., Murray, L., & Happell, B. (2002). Multiple family group interventions in first episode psychosis: Enhancing knowledge and understanding. International Journal of Mental Health Nursing, 11, 225–232. Reed, S. I. (2008). First-episode psychosis: A literature review. International Journal of Mental Health Nursing, 17, 85–91. Renwick, L., Jackson, D., Turner, N., Sutton, M., Foley, S., McWilliams, S., O'Callaghan, E. (2009). Are symptoms associated with increased levels of perceived stress in first episode psychosis? International Journal of Mental Health Nursing, 18, 186–194 Waldheter, E. J., Penn, D. L., Perkins, D. O., Mueser, K. T., Owens, L. W., & Cook, E. (2008). The Graduated Recovery Intervention Program for first episode psychosis: Treatment development and preliminary data. Community Mental Health Journal, 6, 443–455.

Reference: Revell, E.R., et al., A systematic review and meta-analysis of cognitive remediation in early schizophrenia, Schizophr. Res. (2015), http://dx.doi.org/10.1016/j.schres.2015.08.017	
Methods	Study aim: The authors hypothesised that CR would have a positive effect on cognition, symptoms and functioning of those experiencing a first episode of psychosis. We also hypothesised that this effect would be moderated by participant and treatment characteristics. Study design: RCT Analysis: Meta-analysis Setting:
Patients	Number of studies: K=12 Number of patients: N=615 Age: mean age 21,8 Sex: 37% female Inclusion: Exclusion: Baseline characteristics: Most participants were taking antipsychotic medication although eight studies included participants taking no medication (range 3–24%). Participants were first episode of psychosis patients with the exception of the Holzer et al. (2014) studywhich also included a proportion of ultra high risk patients. The effect of this was examined in a sensitivity analysis and, as removing this study had no effect on the global cognition, symptoms and functioning outcomes, the study was included in the analysis.
Interventions	Intervention: Cognitive remediation Control: (specialized) TAU, Social contact, Enriched supportive therapy, Computer game, Occupational therapy Follow-up time: Post treatment
Outcome	Primary: Global cognition was used as the primary Outcome. Secondary: The same procedure was used to determine symptom and functioning effect sizes.
Results	Global cognition (all studies) Overall, CR had a nonsignificant positive effect on global cognition of 0.13 (95% CI −0.04, 0.31; I2= 0% P=0.61) (N=615) MATRICS domain SMD 95% confidence intervals Processing speed 0.19; −0.01, 0.40 (N=487)

	Working memory 0.19; −0.00, 0.38 (N=557) Visual learning and memory 0.09; −0.10, 0.29 (N=516) Verbal learning and memory 0.23; 0.01, 0.46 (N=513) Attention/vigilance 0.06; −0.31, 0.44 (N=107) Reasoning/problem solving 0.21; −0.03, 0.45 (N=473) Social cognition 0.30; −0.00, 0.61 (N=117) Symptoms and functioning (N=615) Significant positive effects of CR were seen on both global symptoms (SMD 0.19; CI 0.02, 0.36; I2=0% p=0.45) and functioning (SMD 0.18; CI 0.01, 0.36; I2=0% p=0.45).
Quality Assessment (AMSTAR)	**+**; **-**; **?**; **NA** (Not applicable) Yes, No, Can't answer (Not applicable) 1. Was an 'a priori' design provided?+ Yes 2. Was there duplicate study selection and data extraction?+ *Databases were searched independently by two authors (ER and ZK)* *and included all abstracts published up to May 2015. Two reviewers (ER and ZK) screened all studies independently. Any disagreements* *were resolved in discussion with another researcher (RD).* 3. Was a comprehensive literature search performed? + Yes all relevant databases and *Reference lists were hand-searched and first authors of included reports and those known to be conducting relevant research were contacted.* 4. Were limitations in the literature search reported?+ The Cochrane Collaboration's 'risk of bias tool' was used. 5. Was a list of studies (included and excluded) provided?+ Yes 6. Were the characteristics of the included studies provided?+ Yes 7. Was the scientific quality of the included studies assessed and documented?+ 8. Was the scientific quality of the included studies used appropriately in formulating conclusions?+ 9. Were the methods used to combine the findings of studies appropriate? - No, although MA with random effect model was used. But they combined active and TAU groups. 10. Was the likelihood of publication bias assessed?+ Funnel plots showed no evidence of publication bias. 11. Was the conflict of interest stated?+ Yes GRADE: No General conclusion: moderately good review. The control conditions were very heterogeneous and not all relevant results were completely reported (eg I2 and N per outcome), otherwise a good review

*We spreken bij het Trimbos af (29-07-2015): Oordeel met name baseren op transparantie, 'Yes' betekent een lage RoB.

Overall

Gedurende de behandeling beveelt de werkgroep, in lijn met de NICE guideline, aan om de voortgang van de verschillende uitkomstmaten routinematig en systematisch te worden bijgehouden inclusief de patiënt tevredenheid en de tevredenheid van familieleden.

Bijlage 7.B Search history

RCT's apart en Systematic reviews en Meta-analyses apart in een Reference Manager databse.

PubMed

Recent queries

Search	Add to builder	Query	Items found	Time
#26	Add	Search #24 AND systematic [sb]	121	06:59:47
#25	Add	Search (#24 AND (rct OR random*))	287	06:58:54
#24	Add	Search (#19 AND #23)	1568	06:58:32
#23	Add	Search (#20 OR #21 OR #22)	593238	06:58:17
#22	Add	Search counseling [tiab] OR counseling [ot] OR psycho-education [tiab] OR psycho-education [ot] OR psychoeducation [tiab] OR psychoeducation [ot] OR "Meta Cognitive Training" [tiab] OR "Meta Cognitive Training" [ot] OR "metacognitive training" [tiab] OR "metacognitive training" [ot] OR "metacognitive therapy" [tiab] OR "metacognitive therapy" [ot] OR mindfullness [tiab] OR mindfullness [ot]	47080	06:57:24
#21	Add	Search (intervention [tiab] OR interventions [tiab] OR intervention [ot] OR interventions [ot])	554028	06:56:00
#20	Add	Search ((therapy [tiab] OR therapies[tiab] OR therapeutic[tiab] OR treating[tiab] OR treatment [tiab] OR treatments [tiab] psychotherapy [tiab] OR psychotherapeutic [tiab] OR psychotherapeutical [tiab] OR psychotherapeutics [tiab]) OR therapy [ot] OR therapies[ot] OR therapeutic[ot] OR treating[ot] OR treatment [ot] OR treatments [ot] psychotherapy [ot] OR psychotherapeutic [ot] OR psychotherapeutical [ot] OR psychotherapeutics [ot])	1970	06:55:43
#19	Add	Search (#1 OR #17 OR #18)	14571	06:51:20
#18	Add	Search (("Schizophrenia, Childhood"[Mesh] OR "childhood onset schizophrenia" [tiab] OR "childhood onset schizophrenia" [ot]))	1609	06:50:46
#17	Add	Search (#15 AND #16)	12199	05:55:55
#16	Add	Search ("early symptom" [tiab] OR "early symptoms" [tiab] OR onset [tiab] OR "early signs" [tiab] OR first-episode [tiab] OR "acute phase"	391418	05:54:10

Recent queries

Search	Add to builder	Query	Items found	Time
		[tiab] OR "early symptom" [ot] OR "early symptoms" [ot] OR onset [ot] OR "early signs" [ot] OR first-episode [ot] OR "acute phase" [ot]))		
#15	Add	Search (#2 OR #12 OR #13 OR #14)	164534	05:46:32
#14	Add	Search ("delusional disorder" [tiab] OR "delusional disorders" [tiab] OR "delusional disorder" [ot] OR "delusional disorders" [ot])	690	05:45:54
#13	Add	Search (psychotic [tiab] OR psychosis [tiab] OR psychoses [tiab] OR schizophrenia [tiab] OR schizophrenic [tiab] OR psychotic [ot] OR psychosis [ot] OR psychoses [ot] OR schizophrenia [ot] OR schizophrenic [ot])	128760	05:45:16
#12	Add	Search ("severe mental ill" [tiab] OR "severe mental disorder" [tiab] OR "severe mentally ill" [tiab] OR "severe mental disorders" [tiab] OR "severe mental illness" [tiab] OR "severe mental illnesses" [tiab] OR "severe mental ill"[ot] OR "severe mental disorder"[ot] OR "severe mentally ill"[ot] OR "severe mental disorders"[ot] OR "severe mental illness"[ot] OR "severe mental illnesses"[ot])	3330	05:43:42
#2	Add	Search ("Psychotic Disorders"[Mesh:NoExp] OR "Schizophrenia"[Mesh] OR "Hallucinations"[Mesh] OR "Delusions"[Mesh])	117800	05:31:35
#1	Add	Search "first episode psychosis" [tiab] OR "first episode psychosis" [ot] OR "acute psychosis" [tiab] OR "acute psychosis" [ot] OR "acute psychoses"[tiab] OR "acute psychoses" [ot] OR "early psychosis" [tiab] OR "early psychoses"[tiab] OR "first episode psychoses" [tiab] OR "early psychosis" [ot] OR "first episode psychoses" [ot] OR "early psychoses" [ot] OR "first episode psychoses" [ot]	2972	05:30:19

PsycInfo

#	Query	Limiters/Expanders	Last Run Via	Results
S24	S22	Limiters - Methodology: -Systematic Review, - Meta Analysis Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	26
S23	S22 AND (rct OR random*)	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	298

S22	S9 AND S21	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	1,823
S21	S10 OR S11 OR S12 OR S13 OR S14 OR S15 OR S16 OR S17 OR S18 OR S19 OR S20	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	780,549
S20	(DE "Psychoeducation") OR TI (psychoeducation OR "psycho education") OR KW (psychoeducation OR "psycho education")	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	3,454
S19	DE "Social Skills Training" OR (DE "Mindfulness") OR (DE "Acceptance and Commitment Therapy")	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	7,916
S18	TI ("family interventions" OR "family therapy") OR KW ("family interventions" OR "family therapy")	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	11,282
S17	DE "Family Therapy" OR DE "Conjoint Therapy" OR DE "Strategic Family Therapy" OR DE "Structural Family Therapy"	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	19,267
S16	((DE "Supportive Psychotherapy" OR) OR (DE "Relapse Prevention")) OR (DE "Suicide Prevention")	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	5,281
S15	TI ("Supportive therapy" OR "integrated therapy" OR "relapse prevention" OR "suicide prevention") OR KW (	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	4,050

	"Supportive therapy" OR "integrated therapy" OR "relapse prevention" OR "suicide prevention")			
S14	DE "Counseling" OR TI counseling OR KW counseling	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	45,506
S13	TI ("metacognitive training" OR "metacognitive therapy" OR "meta cognitive therapy" OR "meta cognitive training") OR KW ("metacognitive training" OR "metacognitive therapy" OR "meta cognitive therapy" OR "meta cognitive training")	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	141
S12	TI ("cognitive behavioural therapy" OR "cognitive behavioral therapy" OR CBT) OR KW ("cognitive behavioural therapy" OR "cognitive behavioral therapy" OR CBT)	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	7,319
S11	CC 33*	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	745,836
S10	DE "Movement Therapy" OR DE "Psychotherapeutic Techniques" OR DE "Active Listening" OR DE "Animal Assisted Therapy" OR DE "Autogenic Training" OR DE "Brief Relational Therapy" OR DE "Cotherapy" OR DE	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	35,656

	"Dream Analysis" OR DE "Empty Chair Technique" OR DE "Ericksonian Psychotherapy" OR DE "Guided Imagery" OR DE "Mirroring" OR DE "Morita Therapy" OR DE "Motivational Interviewing" OR DE "Mutual Storytelling Technique" OR DE "Network Therapy" OR DE "Paradoxical Techniques" OR DE "Psychodrama" OR DE "Creative Arts Therapy" OR DE "Art Therapy" OR DE "Dance Therapy" OR DE "Music Therapy" OR DE "Poetry Therapy" OR DE "Recreation Therapy" OR DE "Improvisation"			
S9	S1 OR S4 OR S8	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	6,157
S8	S6 AND S7	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	5,142
S7	S2 OR S3 OR S5	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	113,621
S6	TI ("early symptom*" OR onset OR "early signs" OR first-episode OR "acute phase") OR KW ("early symptom*" OR onset OR "early signs" OR first-episode OR "acute phase")	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	19,620

S5	DE "Psychosis" OR DE "Acute Psychosis"	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	21,085
S4	TI ("early psychosis" OR "first episode psychosis" OR "early psychoses" OR "first episode psychoses") OR KW ("early psychosis" OR "first episode psychosis" OR "early psychoses" OR "first episode psychoses")	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	1,544
S3	TI ("delusional disorder*" OR severe mental ill* OR severe mental disorder* OR psychotic OR psychosis OR psychoses OR schizo*) OR KW ("delusional disorder*" OR severe mental ill* OR severe mental disorder* OR psychotic OR psychosis OR psychoses OR schizo*)	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	107,411
S2	DE "Schizophrenia" OR DE "Acute Schizophrenia" OR DE "Schizophreniform Disorder" OR DE "Schizoaffective Disorder" OR DE "Delusions" OR DE "Hallucinations"	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	76,897
S1	DE "Childhood Schizophrenia" OR TI "childhood onset schizophrenia" OR KW "childhood onset schizophrenia"	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	986

CINAHL

#	Query	Limiters/Expanders	Last Run Via	Results
S24	S22	Limiters - Publication Type: Meta Analysis, Systematic Review Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL	17
S23	S22 AND (rct OR random*)	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL	64
S22	S13 AND S21	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL	343
S21	S14 OR S15 OR S16 OR S17 OR S18 OR S19 OR S20	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL	511,518
S20	TI ("psycho education" OR psychoeducation) OR AB ("psycho education" OR psychoeducation)	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL	553
S19	TI ("family interventions" OR "family therapy") OR AB ("family interventions" OR "family therapy")	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL	876
S18	TI (counseling OR "Supportive therapy" OR "integrated therapy" OR "relapse prevention" OR "suicide prevention") OR AB (counseling OR "Supportive therapy" OR "integrated therapy" OR "relapse prevention" OR "suicide prevention")	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL	13,785

S17	TI ("metacognitive training" OR "metacognitive therapy" OR "meta cognitive therapy" OR "meta cognitive training") OR AB ("metacognitive training" OR "metacognitive therapy" OR "meta cognitive therapy" OR "meta cognitive training")	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL	21
S16	(MH "Counseling") OR (MH "Suicide Prevention (Iowa NIC)") OR (MH "Family Therapy") OR (MH "Psychoeducation") OR (MH "Social Skills Training") OR (MH "Art Therapy") OR (MH "Acceptance and Commitment Therapy") OR (MH "Mindfulness")	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL	19,571
S15	TI ("cognitive behavioural therapy" OR "cognitive behavioral therapy" OR CBT) OR AB ("cognitive behavioural therapy" OR "cognitive behavioral therapy" OR CBT)	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL	2,608
S14	TI (therapy OR therapies OR therapeutic OR treating OR treatment OR treatments psychotherapy OR psychotherapeutic OR psychotherapeutical OR psychotherapeutics OR intervention*) OR AB (therapy OR therapies OR therapeutic OR treating OR treatment OR treatments psychotherapy OR	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL	494,213

	psychotherapeutic OR psychotherapeutical OR psychotherapeutics OR intervention*)			
S13	S5 OR S11 OR S12	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL	707
S12	TI "early psychosis" OR "first episode psychosis" OR "early psychoses" OR "first episode psychoses" OR "acute psychoses" OR "acute psychosis"	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL	329
S11	S9 AND S10	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL	535
S10	TI "early symptom*" OR onset OR "early signs" OR first-episode OR "acute phase"	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL	6,504
S9	S6 OR S7 OR S8	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL	15,116
S8	TI "delusional disorder*" OR severe mental ill* OR severe mental disorder* OR psychotic OR psychosis OR psychoses OR schizo*	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL	8,695
S7	(MH "Psychotic Disorders")	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL	3,831

S6	(MH "Schizoaffective Disorder") OR (MH "Schizophrenia") OR (MH "Delusions") OR (MH "Hallucinations")	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL	10,789
S5	S1 OR S2 OR S3 OR S4	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL	60
S4	TI "acute phase" AND schizophrenia	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL	6
S3	TI "acute schizophrenia"	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL	16
S2	TI "childhood onset schizophrenia"	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL	12
S1	(MH "Schizophrenia, Childhood")	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL	27

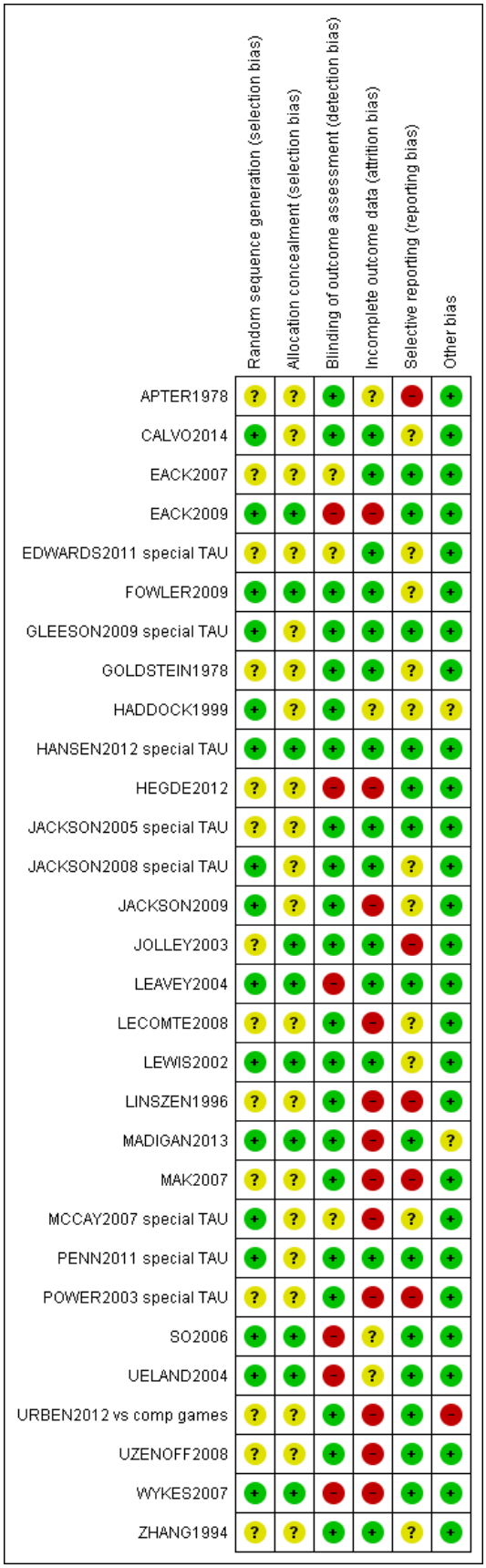
Bijlage 7.C Review protocol

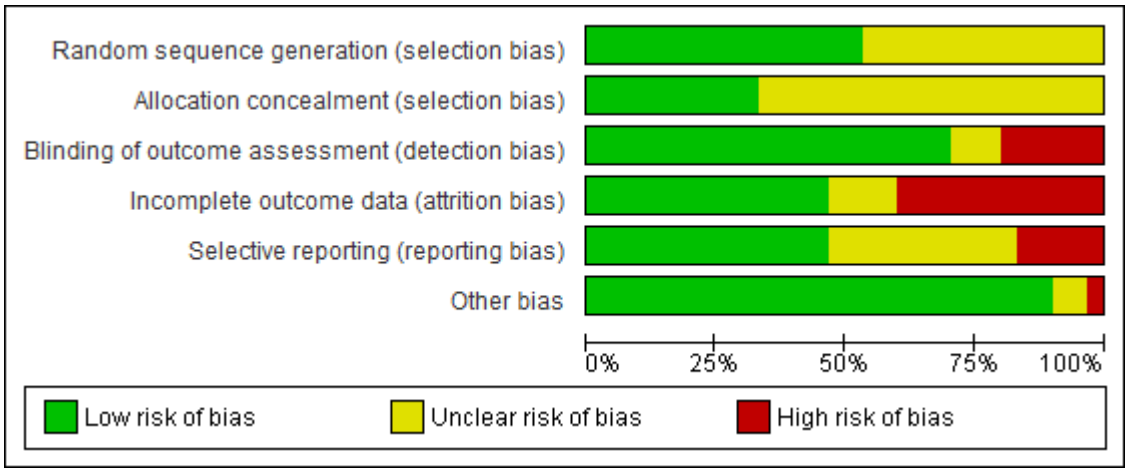
Psychologische en psychosociale interventies voor mensen met een eerste psychose (FEP)

Onderwerp	**C. Psychologische en psychosociale interventies voor mensen met een eerste psychose**
Uitgangsvragen	C1. Wat zijn de voordelen (effectiviteit) en nadelen (bijwerkingen) van verschillende psychologische en psychosociale interventies ten opzichte van de vergelijking? (opm aan werkgroep: inclusief enkele verpleegkundige- en familie interventies) C1a. In welke mate heeft de combinatie van interventies, de duur van interventies en het format van de interventies (bijvoorbeeld groepsgewijs of individueel) invloed op deze voor- en nadelen?
Criteria voor inclusie van studies in de review	
• *Populatie*	• Personen van 12 – gemiddeld 25 jaar met een eerste psychose (e.g. first episode psychosis, early onset psychosis, recent onset schizofrenia) • Late onset first psychoses (pt rond 35 jaar) • Co-mobiditeit mag aanwezig zijn (bv middelenafhankelijkheid) • Exclusie: prodromal states, persons at risk, Prevention of first episode
• *Interventie*	All psychological, psychosocial interventions, e.g.:
	• CBT
	• Psychological or psychosocial interventions for relapse prevention
	• Counseling en steunende therapie
	• Familie interventies
	• Early intervenion*
	• Psycho-educatie
	• Sociale vaardigheidstraining
	• Cognitive remediation therapy
	• Integrated treatment
	• Vaktherapie (drama, muziektherapie, art therapy, beeldende vorming, bewegen)
	• Relevante verpleegkundige interventies: Acceptance and Commitment Therapy (ACT), Psychomotor therapy (PMT), Leefstijl, Mindfullness, meta-cognitive training (MCT)
	Exclusion:
	• Assertive Community Treatment (ACT), Supported Employment (SE), vocational services, individual placement and support (IPS)
• *Vergelijking*	• Care as usual (CAU) • Wachtlijst • Een van de bovengenoemde interventies als alternatieve behandeling
• *Kritische Uitkomstmaten*	Mentaal welbevinden en sociaal functioneren/rolfunctioneren: • Remission / relapse • Mentaal welbevinden (symptomen, depressie, angst, manie) • (Re)hospitalisation / time-to-(re)hospitalisation • Globaal welbevinden (CGI, GAF, GAS) • (Psycho)sociaal functioneren (SOFAS, RFS) • Kwaliteit van leven
• *Belangrijke Uitkomstmaten*	• Mortaliteit (inclusief suïcide) • Dropout, verlaten van de studie om welke reden dan ook
• *Studiedesign*	• Systematic reviews met check of RCT's na verschijnen systematic review de conclusies kunnen veranderen; indien ja - update van systematic review, indien nee – bestaande review gebruiken om aanbevelingen op te baseren
• *Minimum omvang steekproef*	• RCT: > 10 per arm • Exclusie van studies met >50% attrition uit een arm van de trial (tenzij adequate statistiek is toegepast om te corrigeren voor missende data)
Search strategie	[termen populatie criteria] AND [RCT, systematic review]
Databases searched	• Core databases: Embase, CINAHL, Medline, PreMedline, PsycINFO

	• Topic specific databases: CDSR, CENTRAL, DARE, HTA
Data searched	• Mei 2012 (einde search NICE richtlijn) tot voor commentaarfase huidige richtlijn (maart 2015) • Indien afbakening populatie afwijkt van NICE: 1995 tot maart 2015
De review strategie	• Bestaande systematic reviews vanaf 2012 worden geselecteerd, beoordeeld en verwerkt in een beschrijvende review. De meta-analyse van NICE wordt als één van de bestaande systematic reviews meegenomen. • If the reviewer identifies a systematic review appropriate to the review question, we will search for studies (with the best available design) conducted or published since the review was conducted, and the reviewer will assess if any additional studies could affect the conclusions of the previous review. If new studies could change the conclusions, we will update the review and conduct a new analysis. If new studies could not change the conclusions of an existing review, the Guideline Development Group will use the existing review to inform their recommendations.
Voetnoot. * 'Early intervention in schizophrenia has two elements that are distinct from standard care: early detection and phase-specific treatment. Both elements may be offered as supplements to standard care, or may be provided through a specialised early intervention team. Early intervention is now well established as a therapeutic approach in America, Europe and Australasia.' Kan bestaan uit CT, social skills training and family intervention. Bv OPUS onderzoek.	

Bijlage 7.D Risk of Bias

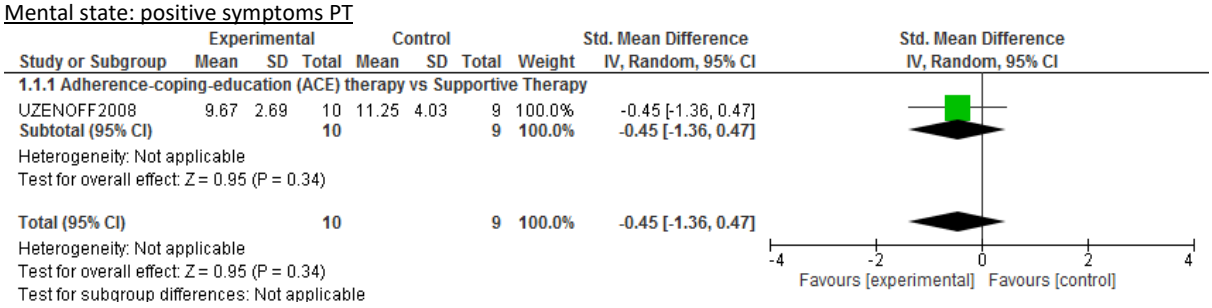



Random sequence generation (selection bias)
Allocation concealment (selection bias)
Blinding of outcome assessment (detection bias)
Incomplete outcome data (attrition bias)
Selective reporting (reporting bias)
Other bias
0%
25%
50%
75%
100%
Low risk of bias
Unclear risk of bias
High risk of bias

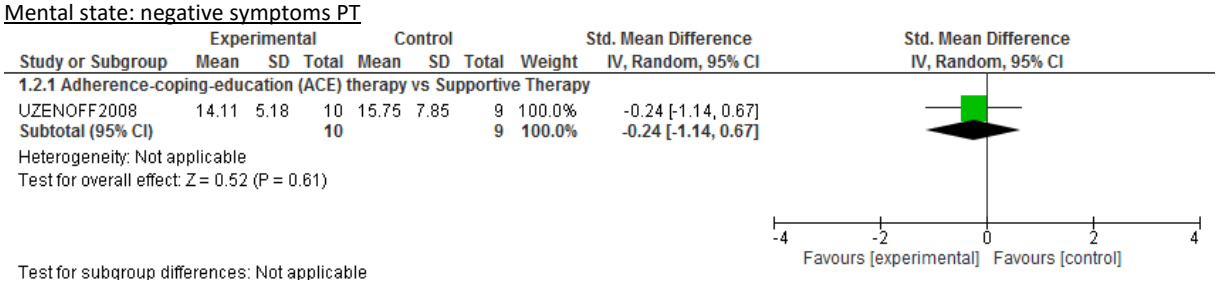
Bijlage 7.E Forest plots – Psychologische interventies

1st comparison Adherence therapy (ACE) vs TAU (Supportive therapy)

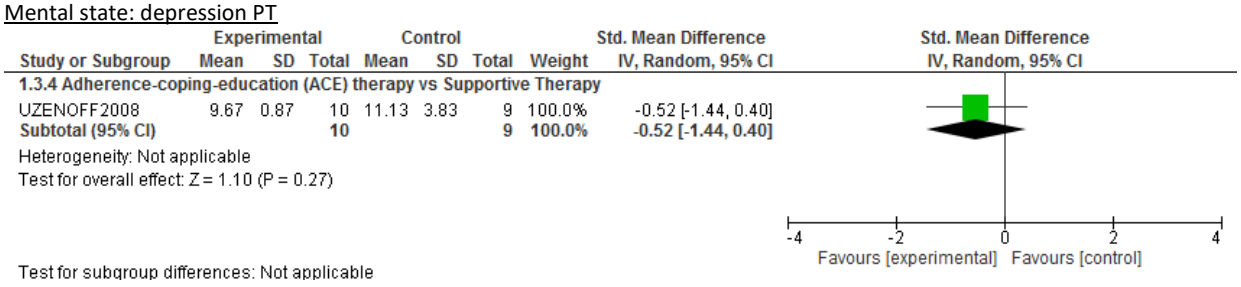
Mental state: positive symptoms PT



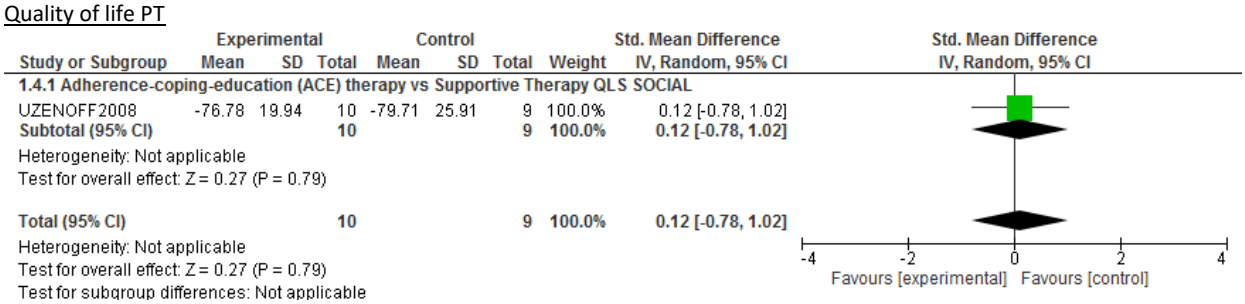
Mental state: negative symptoms PT



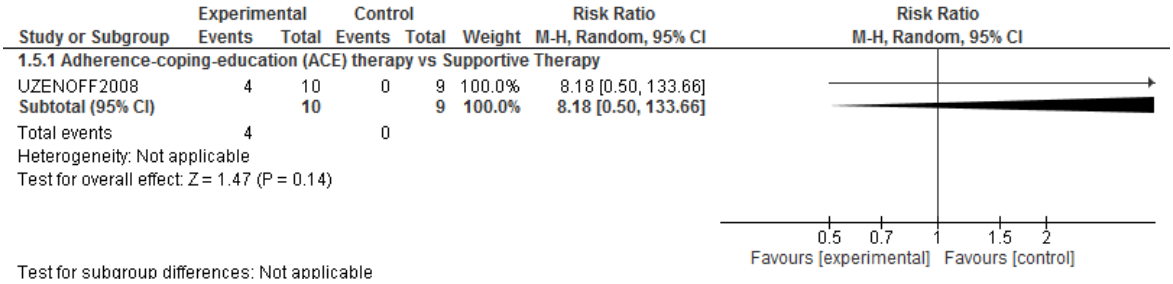
Mental state: depression PT



Quality of life PT



Response, any (number) PT



Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
1.5.1 Adherence-coping-education (ACE) therapy vs Supportive Therapy						
UZENOFF2008	4	10	0	9	100.0%	8.18 [0.50, 133.66]
Subtotal (95% CI)		**10**		**9**	**100.0%**	**8.18 [0.50, 133.66]**
Total events	4		0			

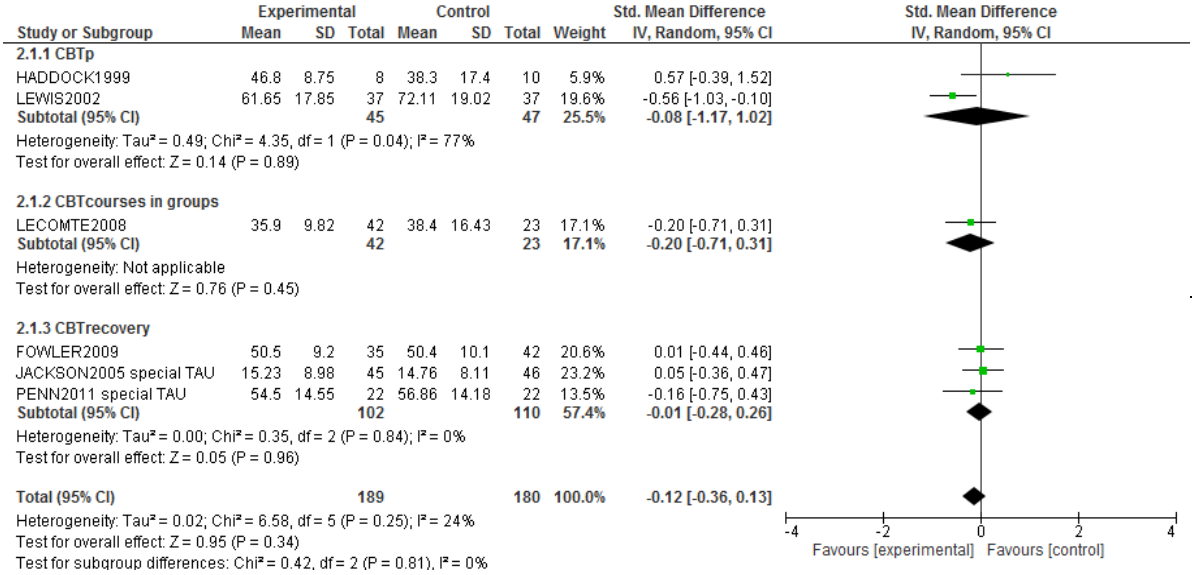
Heterogeneity: Not applicable
Test for overall effect: Z = 1.47 (P = 0.14)

Test for subgroup differences: Not applicable

2nd comparison CBT vs (gespecialiseerde) TAU/WL/Attention Control

POST-TREATMENT

Mental state: total symptoms PT



Study or Subgroup	Experimental Mean	Experimental SD	Experimental Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI
2.1.1 CBTp								
HADDOCK1999	46.8	8.75	8	38.3	17.4	10	5.9%	0.57 [-0.39, 1.52]
LEWIS2002	61.65	17.85	37	72.11	19.02	37	19.6%	-0.56 [-1.03, -0.10]
Subtotal (95% CI)			**45**			**47**	**25.5%**	**-0.08 [-1.17, 1.02]**

Heterogeneity: Tau² = 0.49; Chi² = 4.35, df = 1 (P = 0.04); I² = 77%
Test for overall effect: Z = 0.14 (P = 0.89)

2.1.2 CBTcourses in groups								
LECOMTE2008	35.9	9.82	42	38.4	16.43	23	17.1%	-0.20 [-0.71, 0.31]
Subtotal (95% CI)			**42**			**23**	**17.1%**	**-0.20 [-0.71, 0.31]**

Heterogeneity: Not applicable
Test for overall effect: Z = 0.76 (P = 0.45)

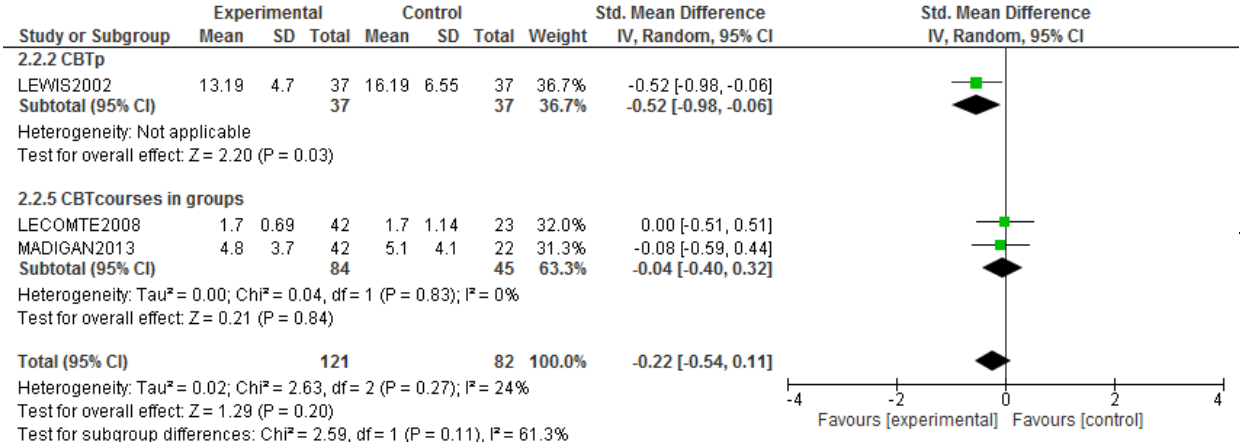
2.1.3 CBTrecovery								
FOWLER2009	50.5	9.2	35	50.4	10.1	42	20.6%	0.01 [-0.44, 0.46]
JACKSON2005 special TAU	15.23	8.98	45	14.76	8.11	46	23.2%	0.05 [-0.36, 0.47]
PENN2011 special TAU	54.5	14.55	22	56.86	14.18	22	13.5%	-0.16 [-0.75, 0.43]
Subtotal (95% CI)			**102**			**110**	**57.4%**	**-0.01 [-0.28, 0.26]**

Heterogeneity: Tau² = 0.00; Chi² = 0.35, df = 2 (P = 0.84); I² = 0%
Test for overall effect: Z = 0.05 (P = 0.96)

Total (95% CI)			**189**			**180**	**100.0%**	**-0.12 [-0.36, 0.13]**

Heterogeneity: Tau² = 0.02; Chi² = 6.58, df = 5 (P = 0.25); I² = 24%
Test for overall effect: Z = 0.95 (P = 0.34)
Test for subgroup differences: Chi² = 0.42, df = 2 (P = 0.81), I² = 0%

Mental state: positive symptoms PT



Study or Subgroup	Experimental Mean	Experimental SD	Experimental Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI
2.2.2 CBTp								
LEWIS2002	13.19	4.7	37	16.19	6.55	37	36.7%	-0.52 [-0.98, -0.06]
Subtotal (95% CI)			**37**			**37**	**36.7%**	**-0.52 [-0.98, -0.06]**

Heterogeneity: Not applicable
Test for overall effect: Z = 2.20 (P = 0.03)

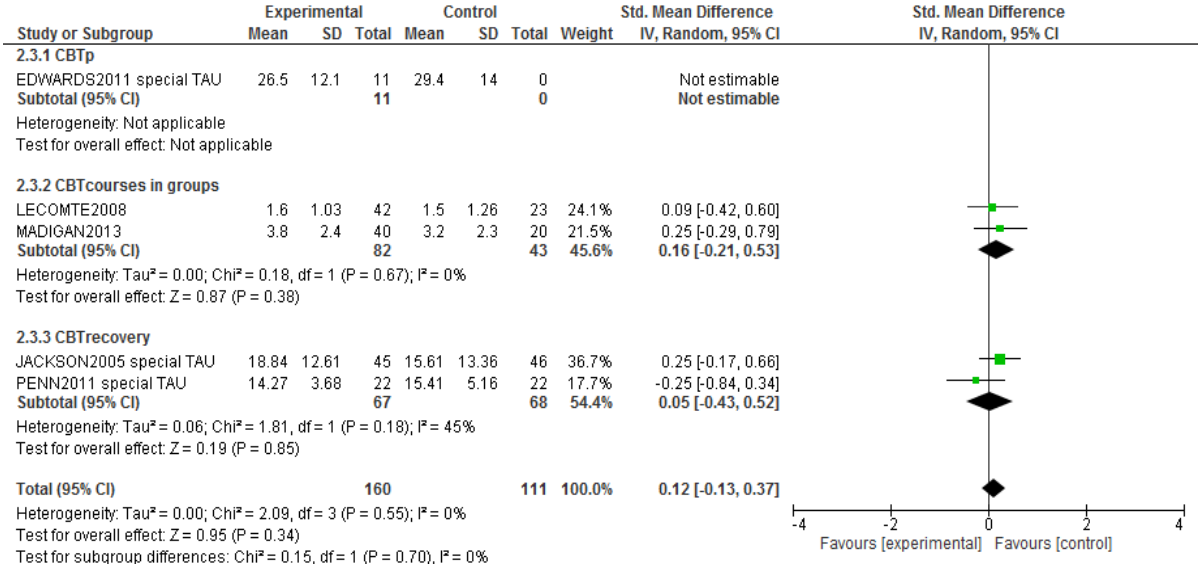
2.2.5 CBTcourses in groups								
LECOMTE2008	1.7	0.69	42	1.7	1.14	23	32.0%	0.00 [-0.51, 0.51]
MADIGAN2013	4.8	3.7	42	5.1	4.1	22	31.3%	-0.08 [-0.59, 0.44]
Subtotal (95% CI)			**84**			**45**	**63.3%**	**-0.04 [-0.40, 0.32]**

Heterogeneity: Tau² = 0.00; Chi² = 0.04, df = 1 (P = 0.83); I² = 0%
Test for overall effect: Z = 0.21 (P = 0.84)

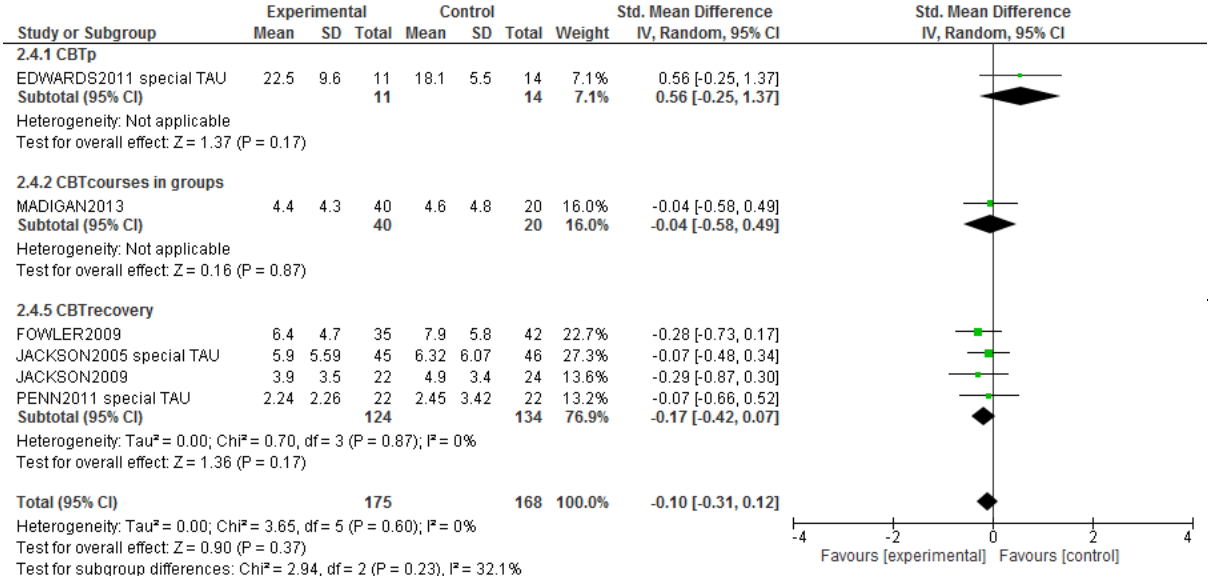
Total (95% CI)			**121**			**82**	**100.0%**	**-0.22 [-0.54, 0.11]**

Heterogeneity: Tau² = 0.02; Chi² = 2.63, df = 2 (P = 0.27); I² = 24%
Test for overall effect: Z = 1.29 (P = 0.20)
Test for subgroup differences: Chi² = 2.59, df = 1 (P = 0.11), I² = 61.3%

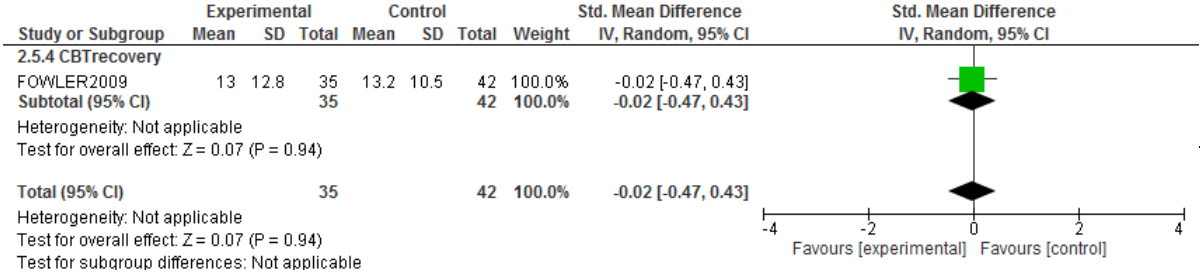
Mental state: negative symptoms PT



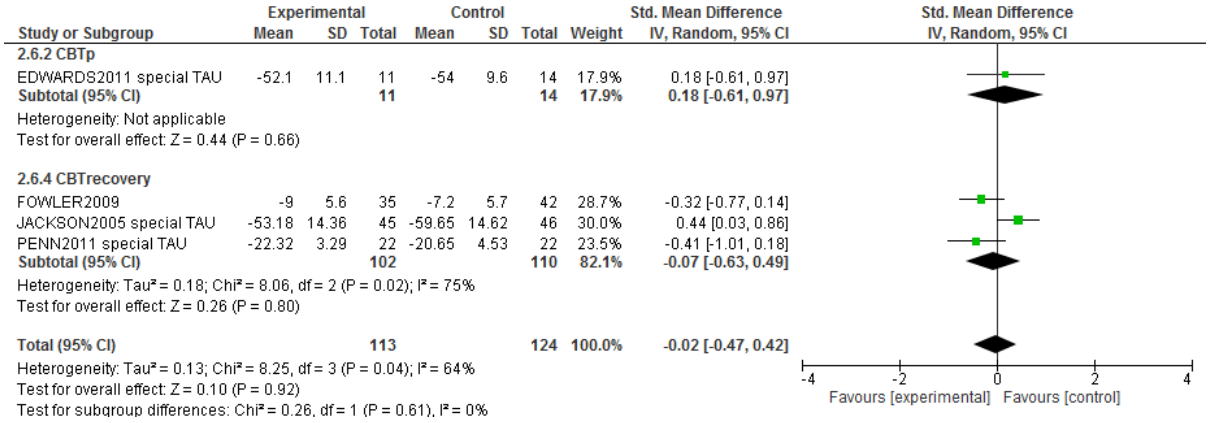
Mental state: depression PT



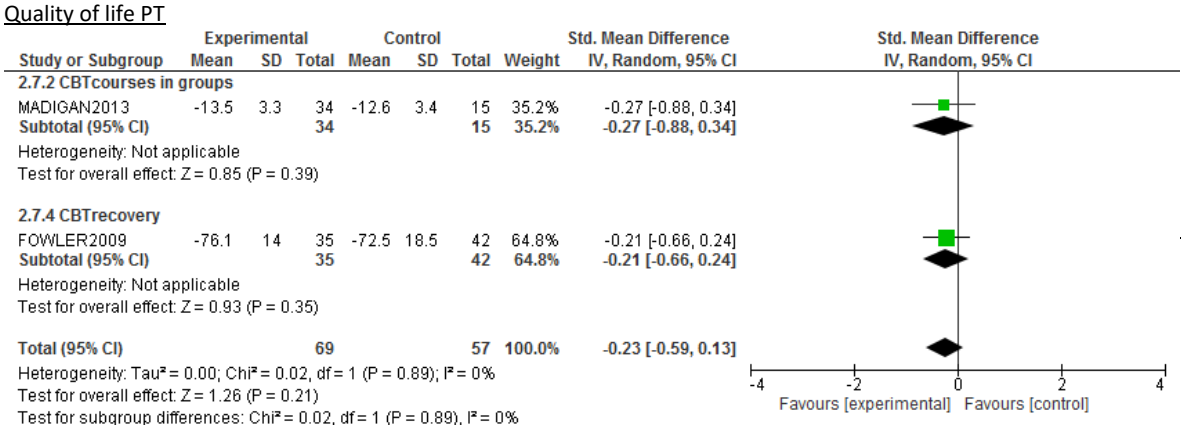
Mental state: anxiety PT



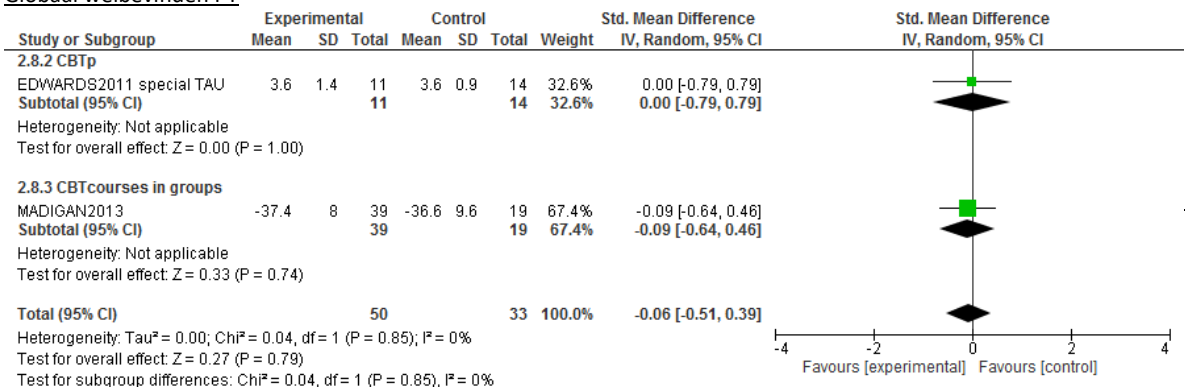
(Psycho)social Functioning PT



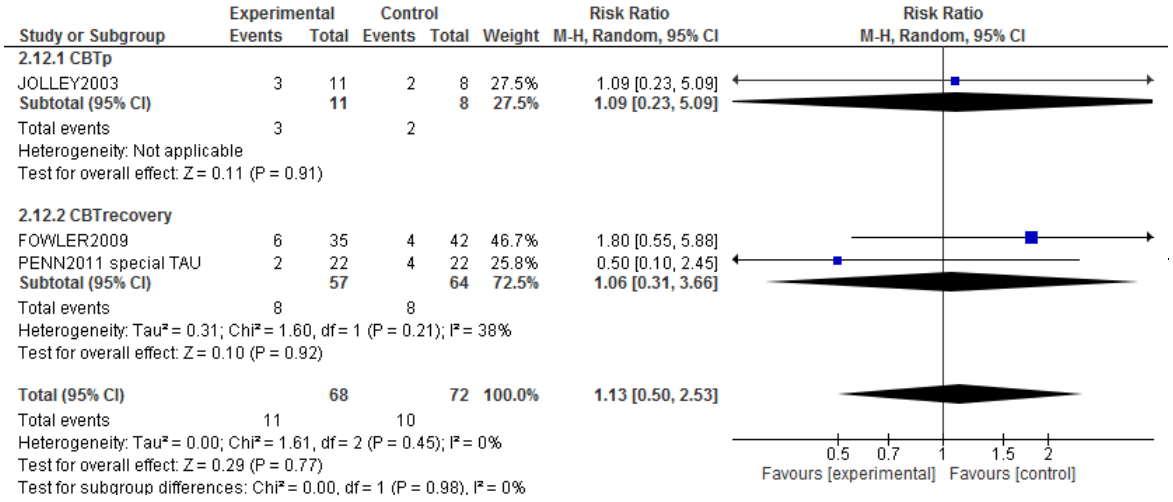
Quality of life PT



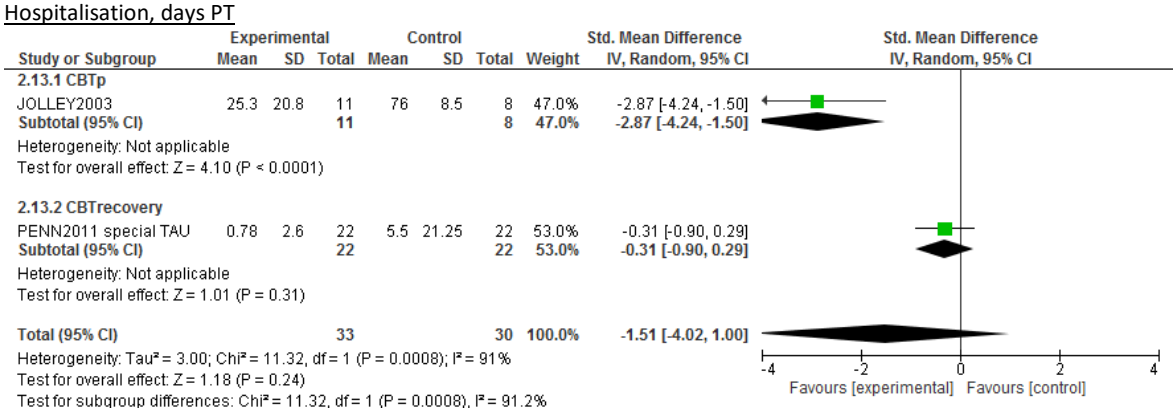
Globaal welbevinden PT



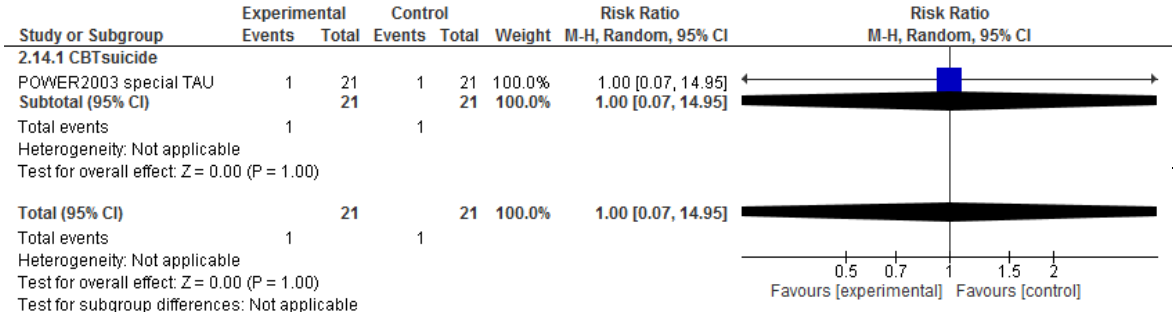
Hospitalisations, number admitted PT



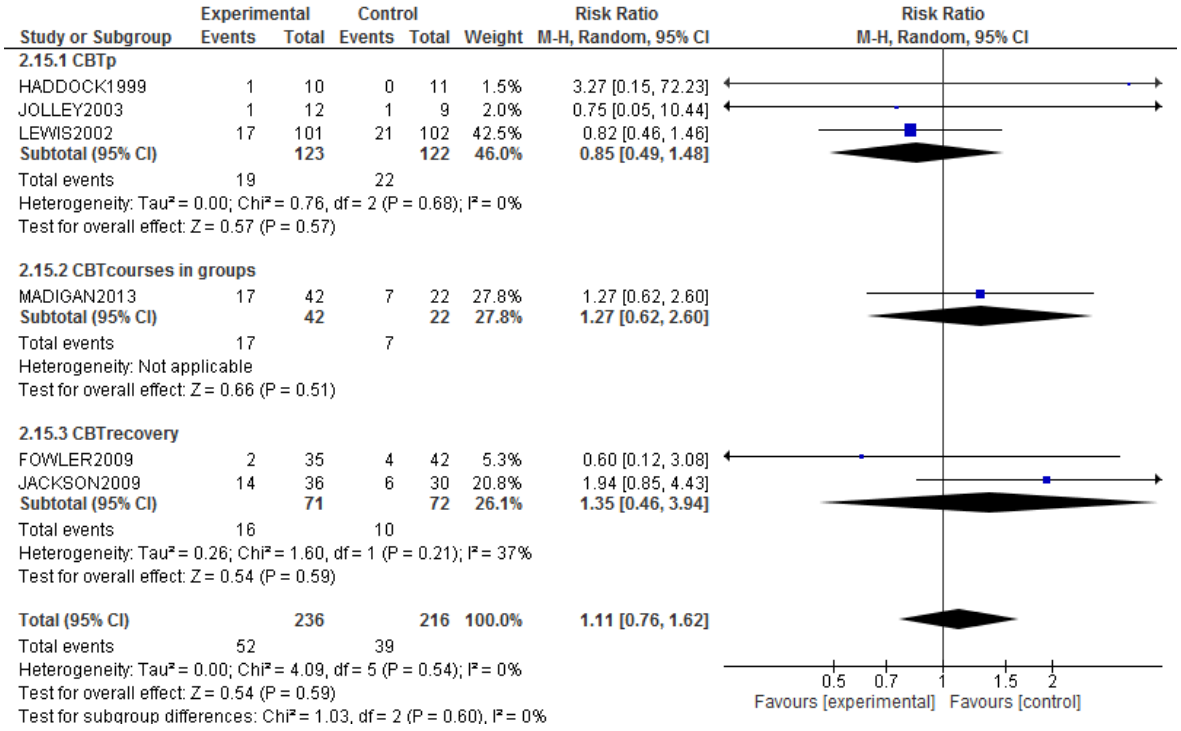
Hospitalisation, days PT



Mortality: number of deaths by suicide (assuming dropout did not die by suicide) PT

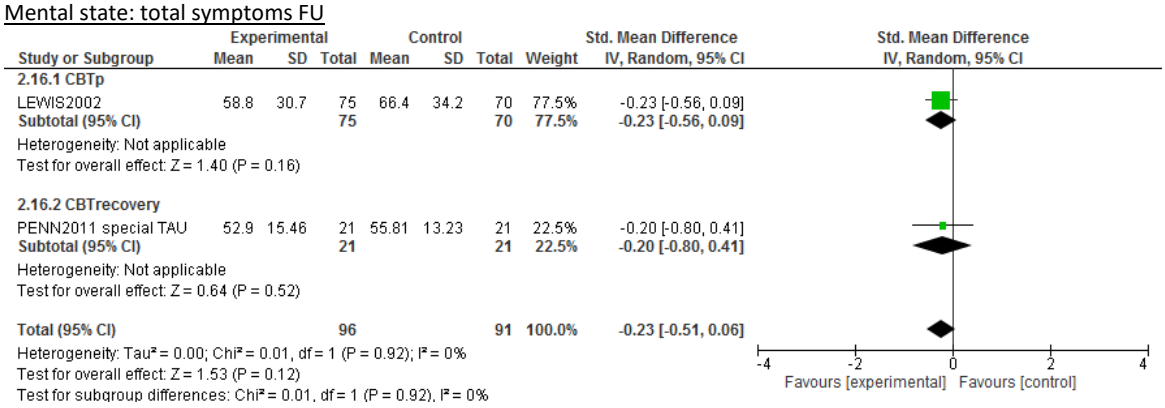


Leaving the study early for any reason PT

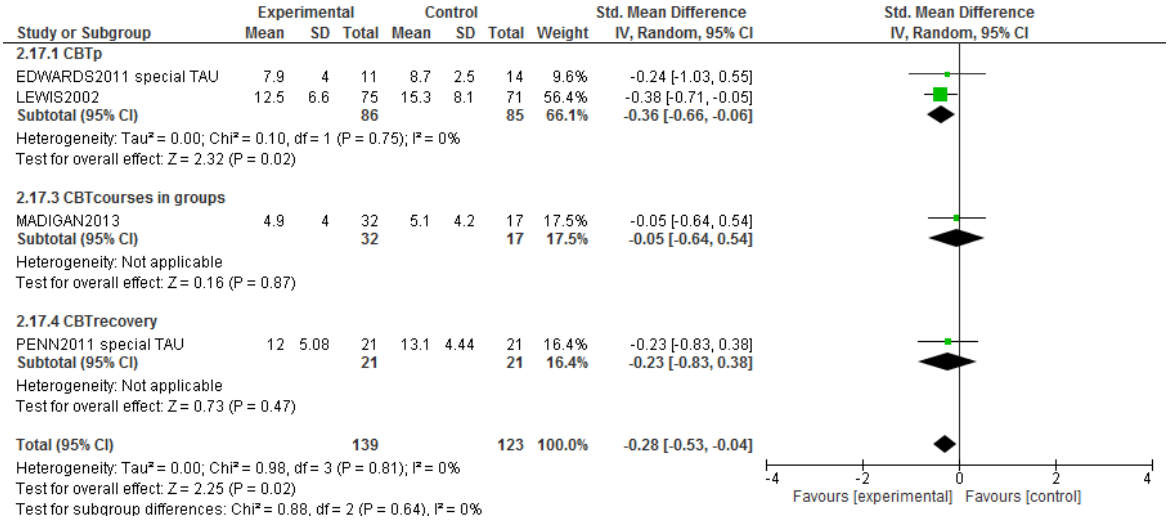


FOLLOW-UP

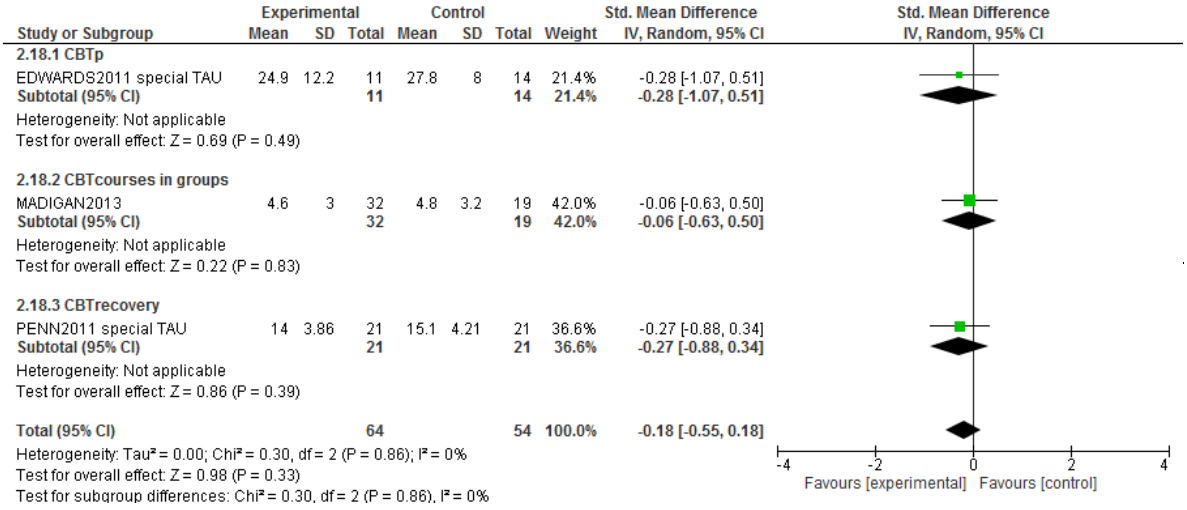
Mental state: total symptoms FU



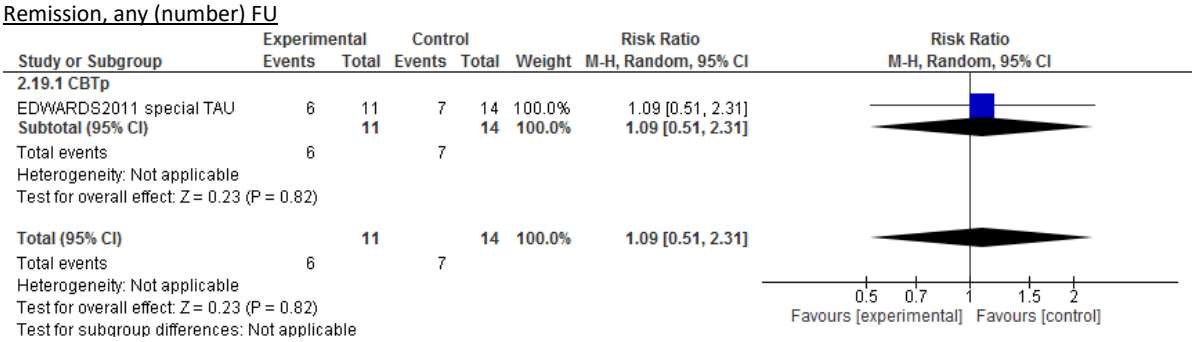
Mental state: positive symptoms FU



Mental state: negative symptoms FU

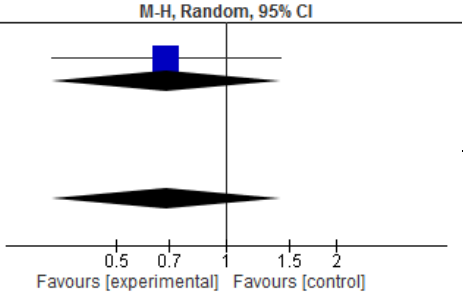


Remission, any (number) FU



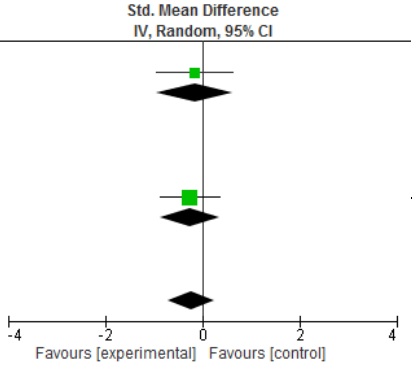
Relapse FU

Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
2.20.1 CBTp vs supportive therapy						
HADDOCK1999	5	10	8	11	100.0%	0.69 [0.34, 1.41]
Subtotal (95% CI)		**10**		**11**	**100.0%**	**0.69 [0.34, 1.41]**
Total events	5		8			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.02 (P = 0.31)						
Total (95% CI)		**10**		**11**	**100.0%**	**0.69 [0.34, 1.41]**
Total events	5		8			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.02 (P = 0.31)						
Test for subgroup differences: Not applicable						



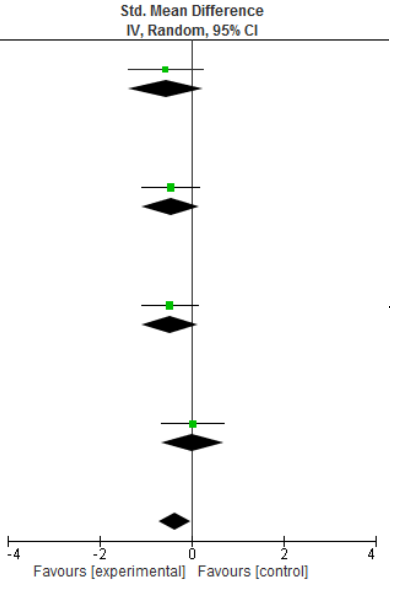
(Psycho)social Functioning FU

Study or Subgroup	Experimental Mean	Experimental SD	Experimental Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI
2.21.3 CBTp								
EDWARDS2011 special TAU	-55.4	10.5	11	-53.8	9.8	14	37.1%	-0.15 [-0.94, 0.64]
Subtotal (95% CI)			**11**			**14**	**37.1%**	**-0.15 [-0.94, 0.64]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.38 (P = 0.70)								
2.21.6 CBTrecovery								
PENN2011 special TAU	-23	2.98	21	-22.09	3.85	21	62.9%	-0.26 [-0.87, 0.35]
Subtotal (95% CI)			**21**			**21**	**62.9%**	**-0.26 [-0.87, 0.35]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.84 (P = 0.40)								
Total (95% CI)			**32**			**35**	**100.0%**	**-0.22 [-0.70, 0.26]**
Heterogeneity: Tau² = 0.00; Chi² = 0.04, df = 1 (P = 0.83); I² = 0%								
Test for overall effect: Z = 0.89 (P = 0.37)								
Test for subgroup differences: Chi² = 0.04, df = 1 (P = 0.83), I² = 0%								

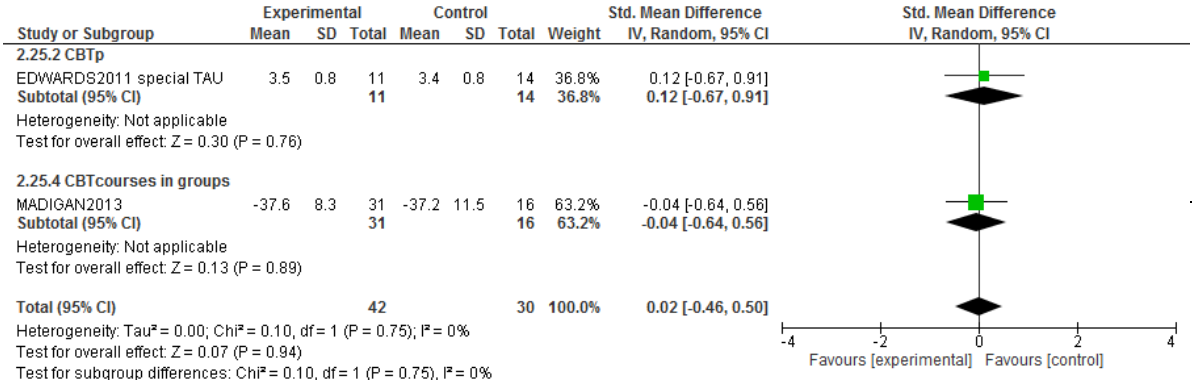


Quality of life FU

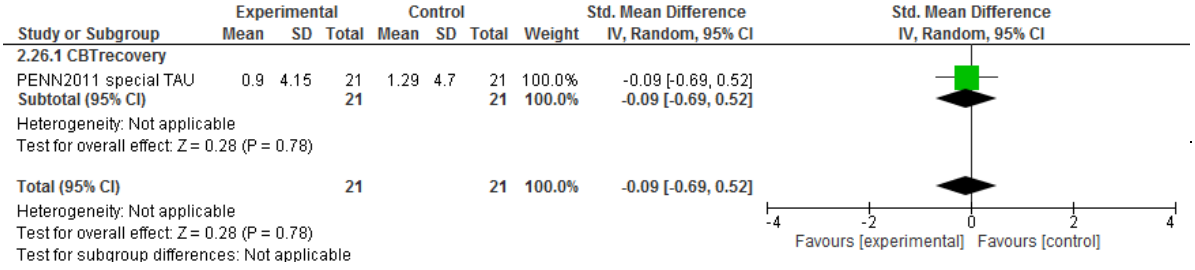
Study or Subgroup	Experimental Mean	Experimental SD	Experimental Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI
2.23.1 CBTp								
EDWARDS2011 special TAU	-63.3	16.1	11	-54.5	14.6	14	17.4%	-0.56 [-1.36, 0.25]
Subtotal (95% CI)			**11**			**14**	**17.4%**	**-0.56 [-1.36, 0.25]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.35 (P = 0.18)								
2.23.2 CBTcourses in groups								
MADIGAN2013	-12.6	3.4	34	-11.1	2.9	14	28.6%	-0.45 [-1.08, 0.18]
Subtotal (95% CI)			**34**			**14**	**28.6%**	**-0.45 [-1.08, 0.18]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.41 (P = 0.16)								
2.23.3 CBTrecovery								
PENN2011 special TAU	-7.73	1.771017	21	-6.93	1.538083	21	30.0%	-0.47 [-1.09, 0.14]
Subtotal (95% CI)			**21**			**21**	**30.0%**	**-0.47 [-1.09, 0.14]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.51 (P = 0.13)								
2.23.4 CBTsuicide								
POWER2003 special TAU	2.3	3.5	15	2.2	3.9	18	24.1%	0.03 [-0.66, 0.71]
Subtotal (95% CI)			**15**			**18**	**24.1%**	**0.03 [-0.66, 0.71]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.07 (P = 0.94)								
Total (95% CI)			**81**			**67**	**100.0%**	**-0.36 [-0.70, -0.02]**
Heterogeneity: Tau² = 0.00; Chi² = 1.66, df = 3 (P = 0.65); I² = 0%								
Test for overall effect: Z = 2.11 (P = 0.04)								
Test for subgroup differences: Chi² = 1.66, df = 3 (P = 0.65), I² = 0%								



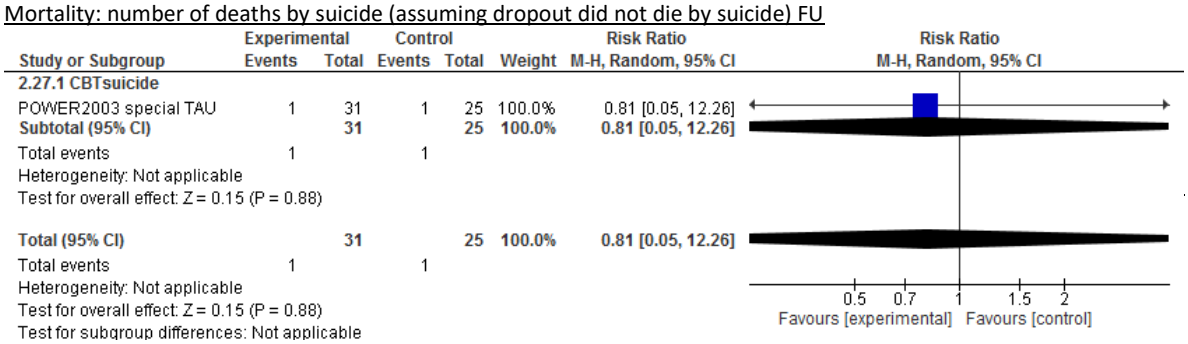
Globaal welbevinden (FU)



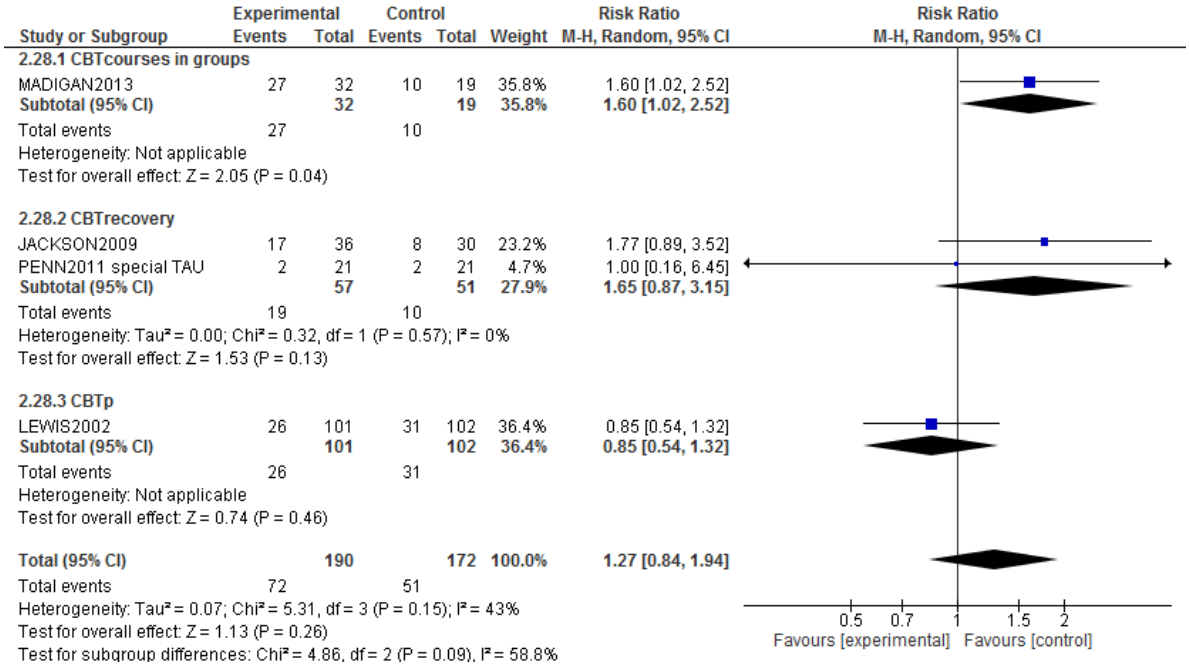
Hospitalisation, days FU



Mortality: number of deaths by suicide (assuming dropout did not die by suicide) FU



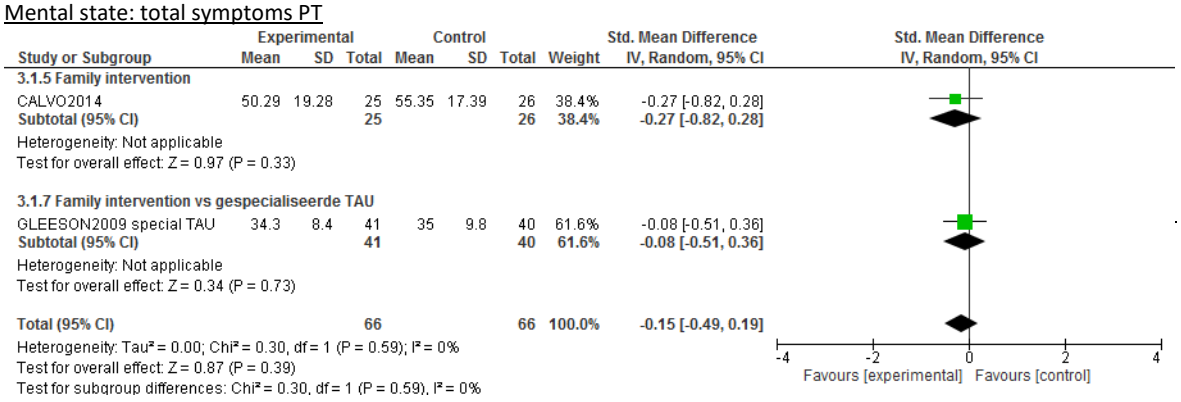
Leaving the study early for any reason FU



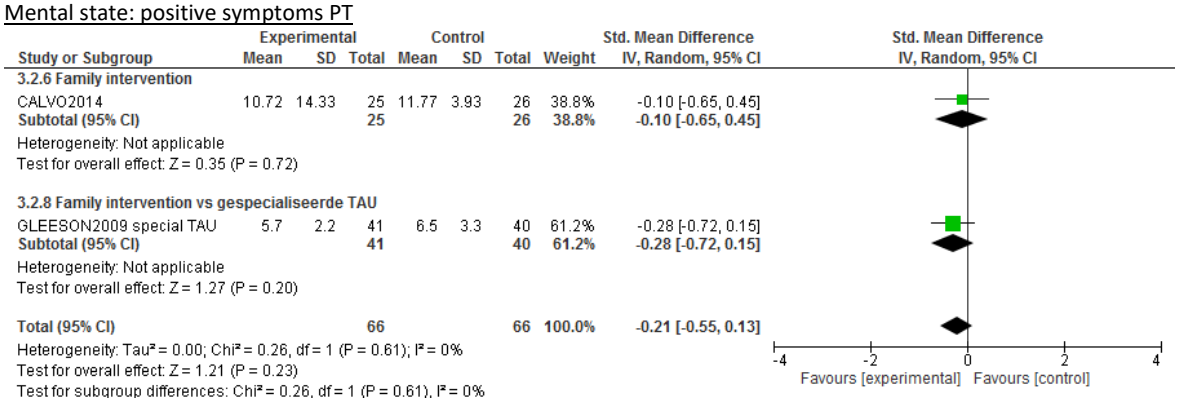
3[d] comparison Family interventie vs (gespecialiseerde) TAU

POST-TREATMENT

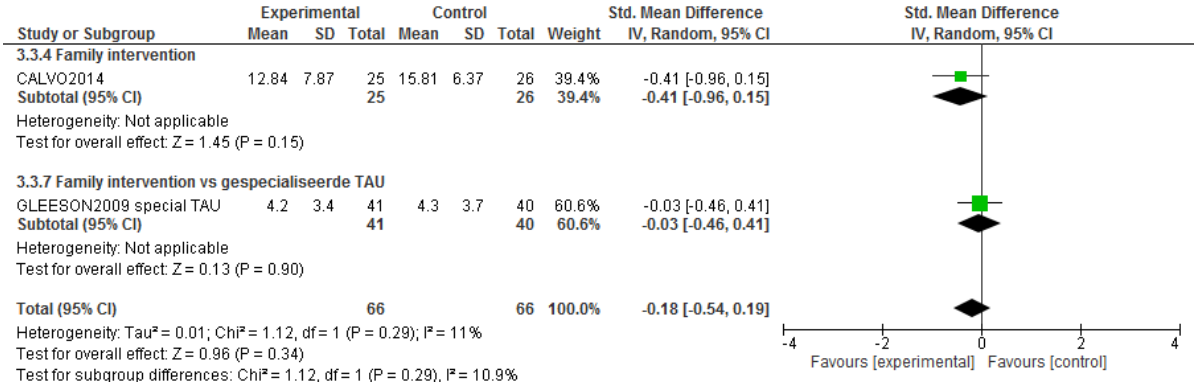
Mental state: total symptoms PT



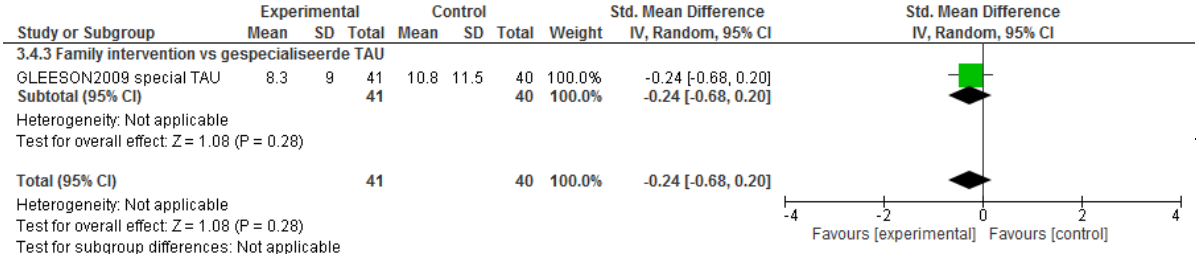
Mental state: positive symptoms PT



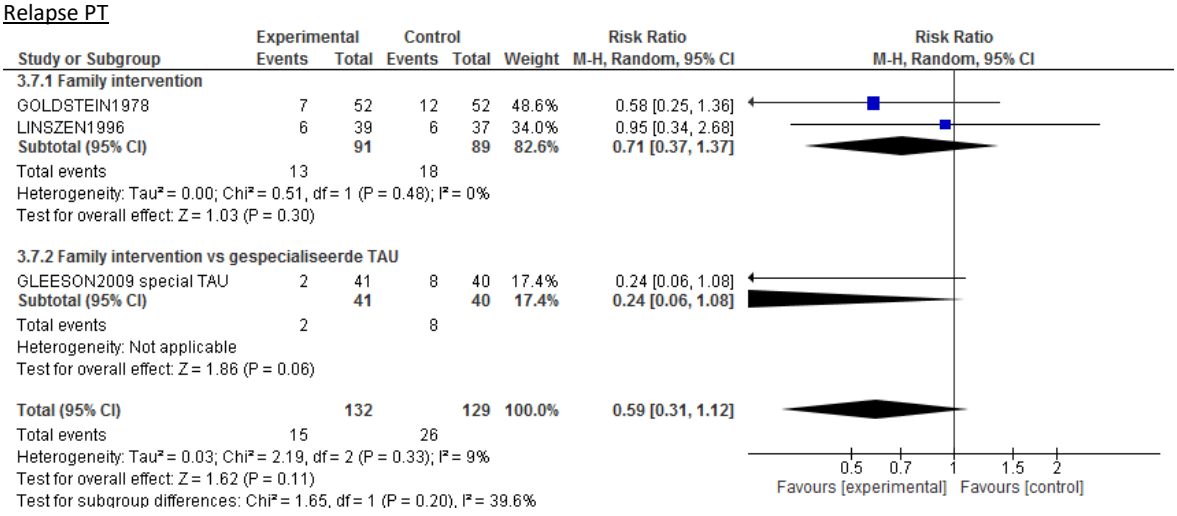
Mental state: negative symptoms PT



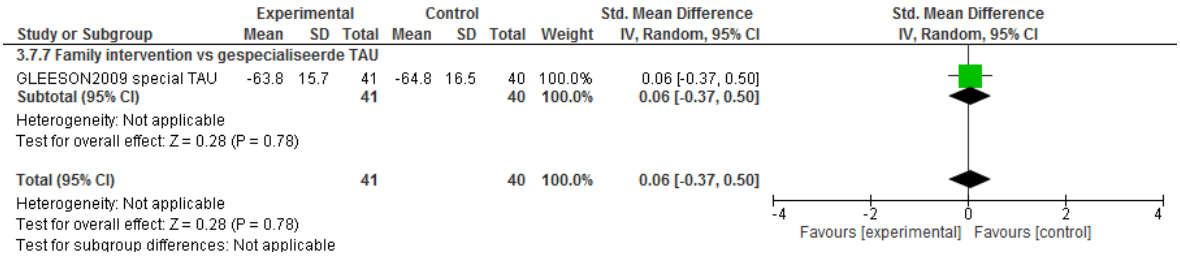
Mental state: depression PT



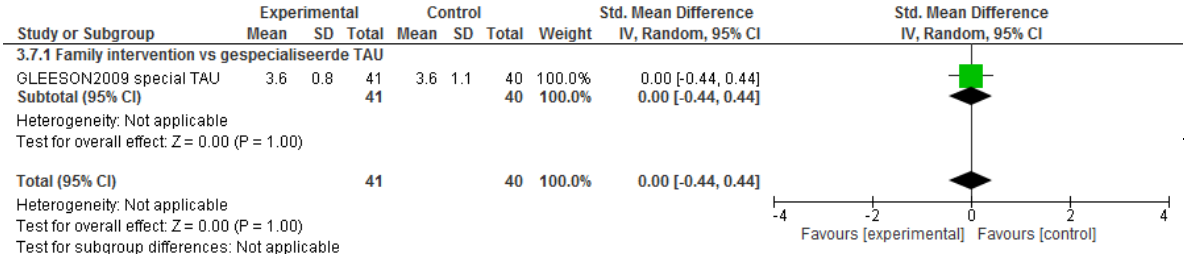
Relapse PT



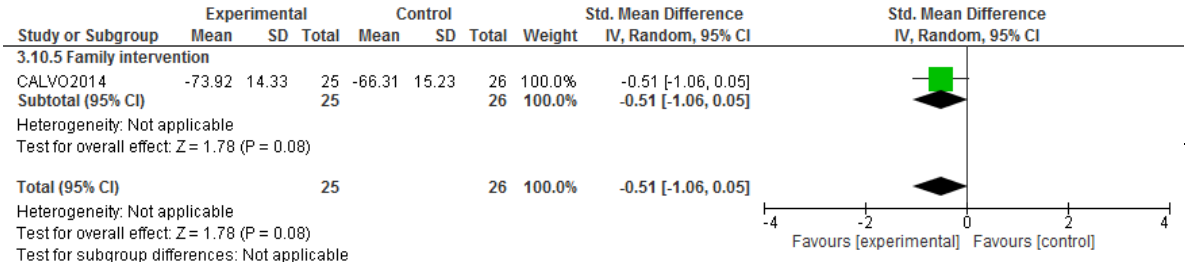
(Psycho)social functioning PT



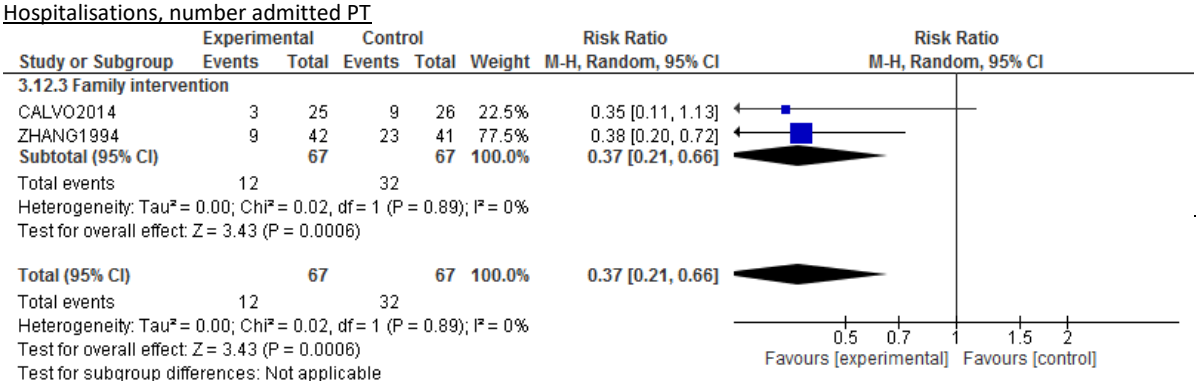
Quality of life PT



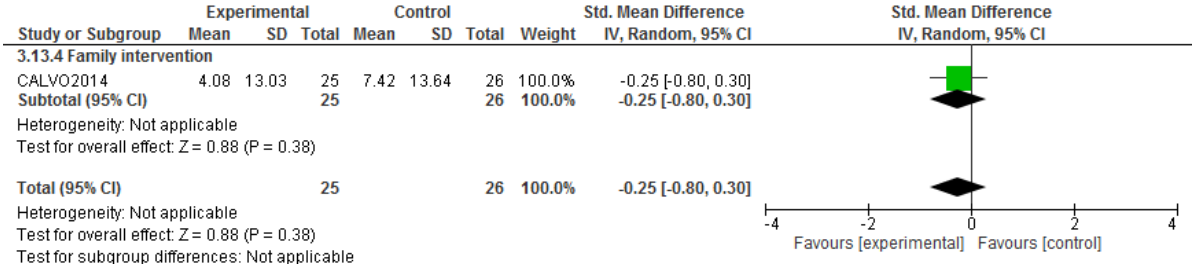
Globaal welbevinden PT



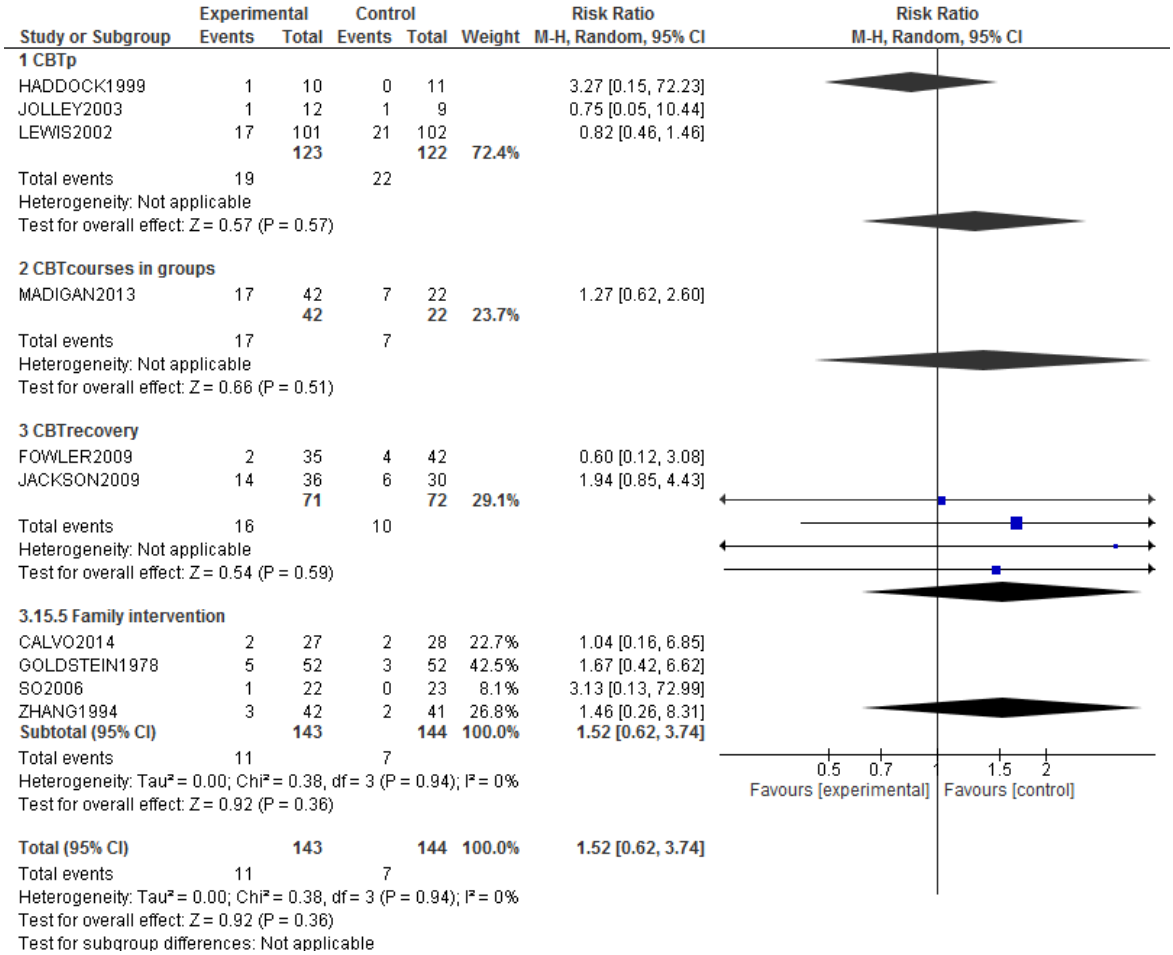
Hospitalisations, number admitted PT



Hospitalisation, days PT

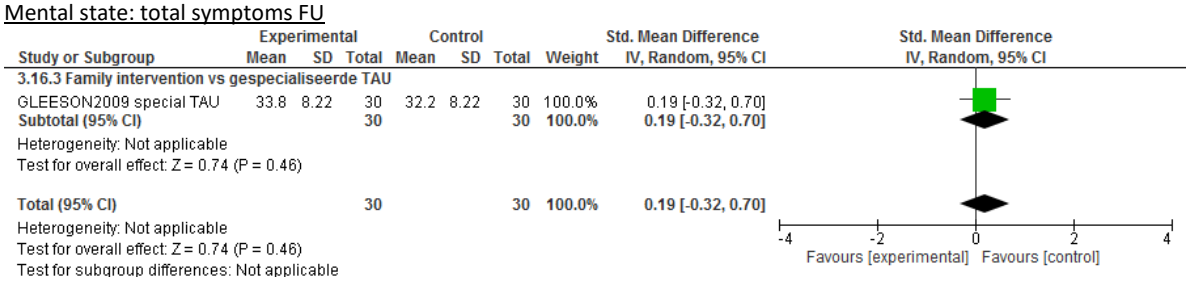


Leaving the study early for any reason PT

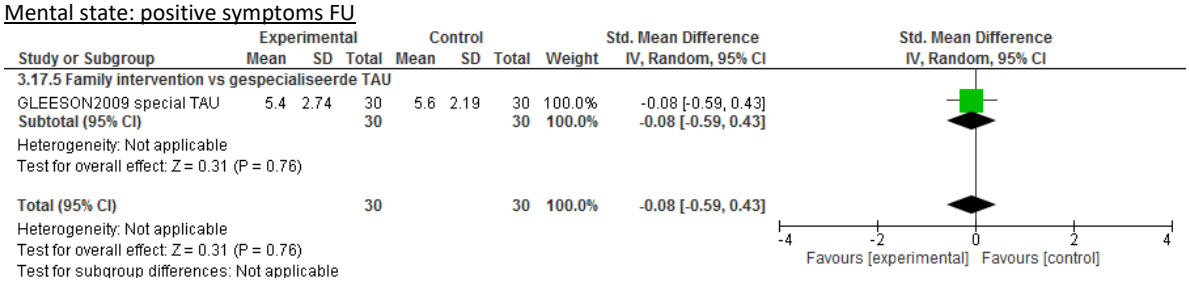


FOLLOW-UP

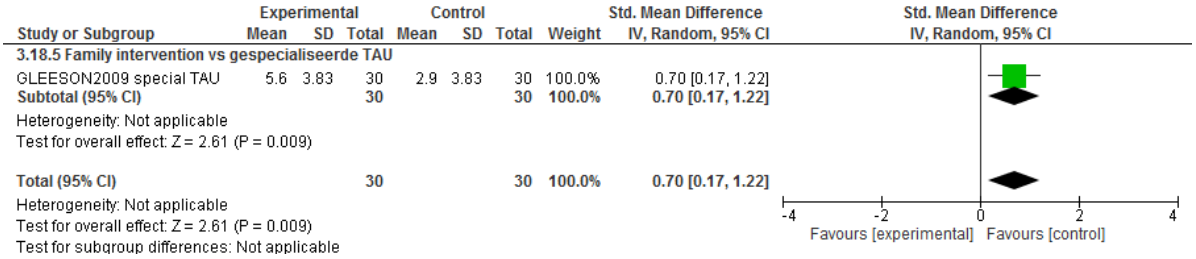
Mental state: total symptoms FU



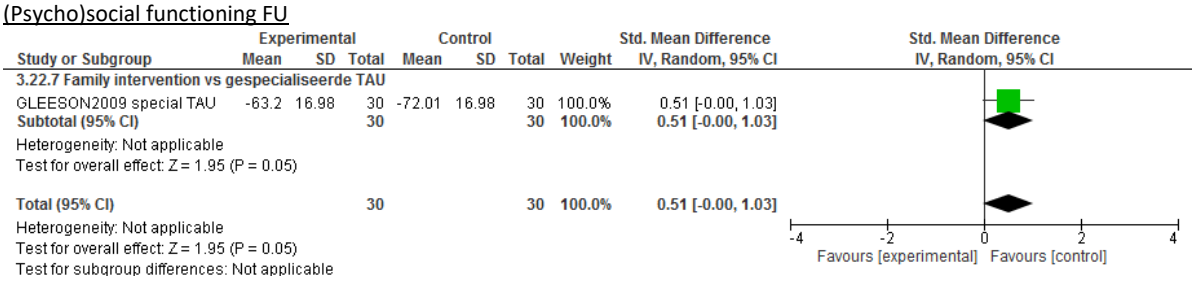
Mental state: positive symptoms FU



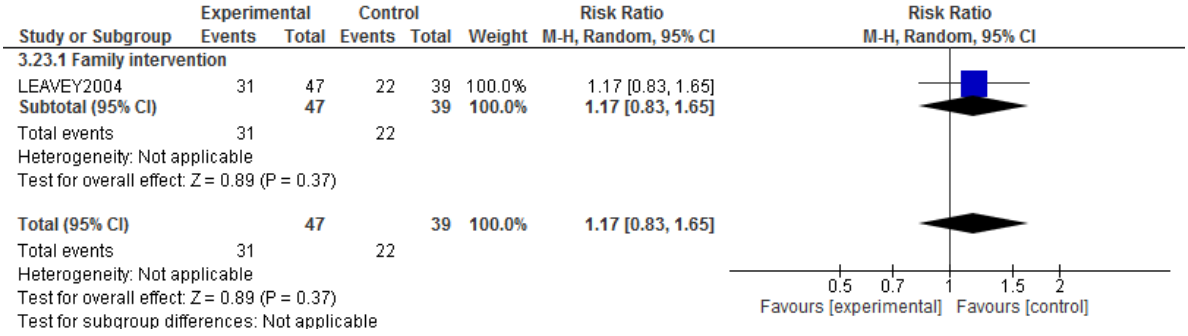
Mental state: negative symptoms FU



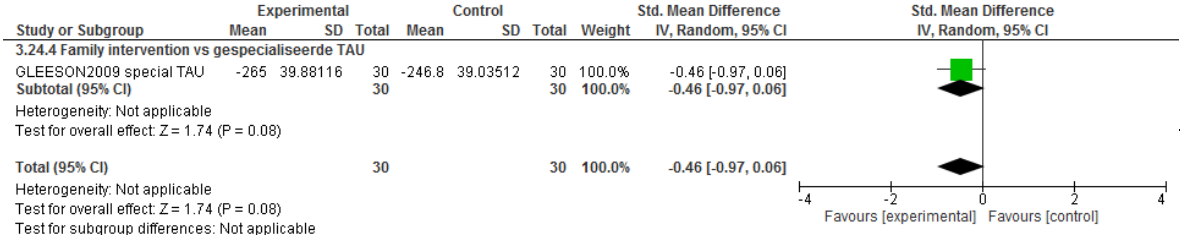
(Psycho)social functioning FU



(Psycho)social functioning FU (Not able to live independently)

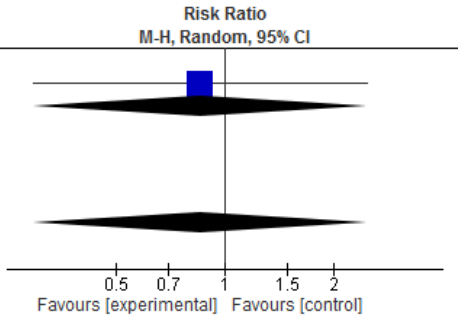


Quality of life FU



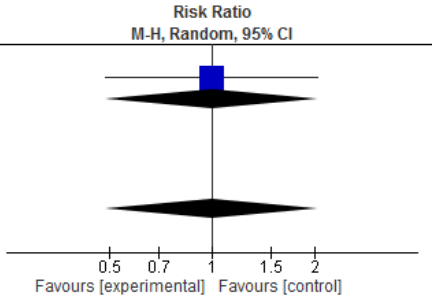
Hospitalisations, number admitted FU

Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
3.26.1 Family intervention						
LEAVEY2004	6	57	6	49	100.0%	0.86 [0.30, 2.49]
Subtotal (95% CI)		**57**		**49**	**100.0%**	**0.86 [0.30, 2.49]**
Total events	6		6			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.28 (P = 0.78)						
Total (95% CI)		**57**		**49**	**100.0%**	**0.86 [0.30, 2.49]**
Total events	6		6			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.28 (P = 0.78)						
Test for subgroup differences: Not applicable						



Leaving the study early for any reason FU

Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
3.28.6 Family intervention vs gespecialiseerde TAU						
GLEESON2009 special TAU	11	41	11	41	100.0%	1.00 [0.49, 2.04]
Subtotal (95% CI)		**41**		**41**	**100.0%**	**1.00 [0.49, 2.04]**
Total events	11		11			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.00 (P = 1.00)						
Total (95% CI)		**41**		**41**	**100.0%**	**1.00 [0.49, 2.04]**
Total events	11		11			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.00 (P = 1.00)						
Test for subgroup differences: Not applicable						

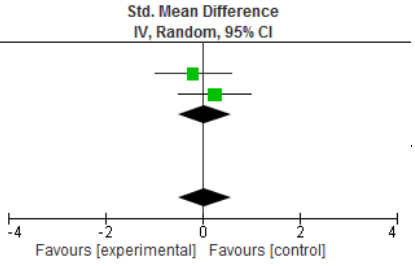


4th comparison CRT vs (gespecialiseerde) TAU

POST-TREATMENT

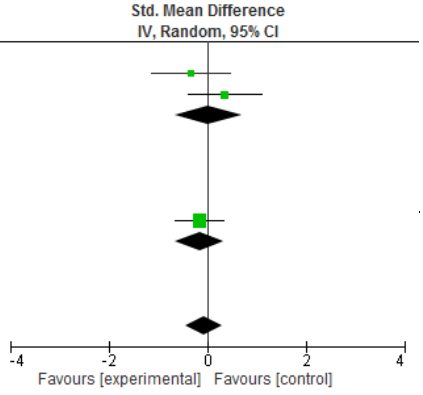
Mental state: total symptoms PT

Study or Subgroup	Experimental Mean	Experimental SD	Experimental Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI
4.1.6 CRT								
UELAND2004	45.1	11.7	14	47.5	13.2	11	47.0%	-0.19 [-0.98, 0.60]
URBEN2012 vs comp games	66.3	17.9	15	60.8	23.6	13	53.0%	0.26 [-0.49, 1.00]
Subtotal (95% CI)			**29**			**24**	**100.0%**	**0.05 [-0.49, 0.59]**
Heterogeneity: Tau² = 0.00; Chi² = 0.64, df = 1 (P = 0.42); I² = 0%								
Test for overall effect: Z = 0.17 (P = 0.86)								
Total (95% CI)			**29**			**24**	**100.0%**	**0.05 [-0.49, 0.59]**
Heterogeneity: Tau² = 0.00; Chi² = 0.64, df = 1 (P = 0.42); I² = 0%								
Test for overall effect: Z = 0.17 (P = 0.86)								
Test for subgroup differences: Not applicable								

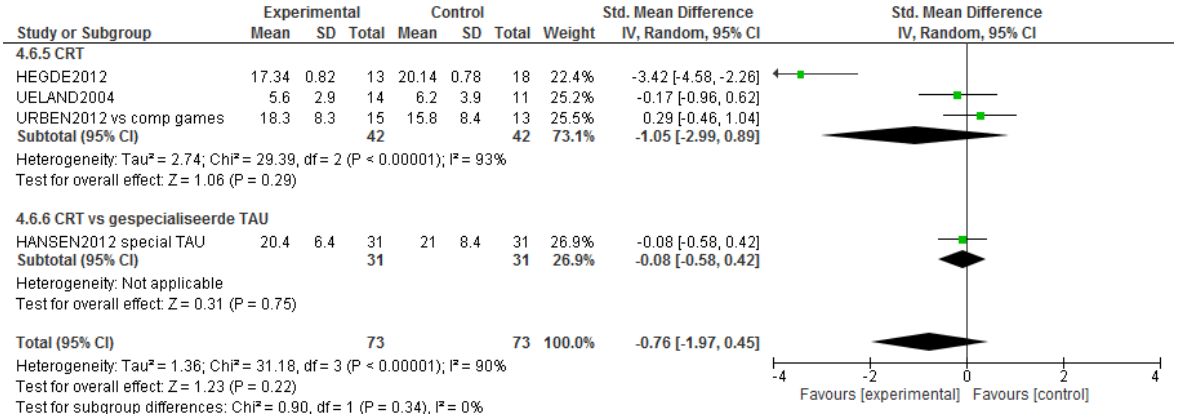


Mental state: positive symptoms PT

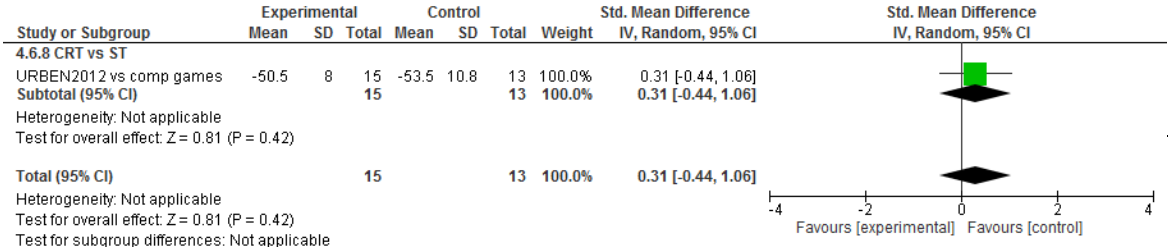
Study or Subgroup	Experimental Mean	Experimental SD	Experimental Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI
4.3.4 CRT								
UELAND2004	12.7	5.5	14	14.4	4.2	11	21.4%	-0.33 [-1.13, 0.47]
URBEN2012 vs comp games	14.3	5.2	15	12.4	5.2	13	24.1%	0.35 [-0.39, 1.10]
Subtotal (95% CI)			**29**			**24**	**45.5%**	**0.03 [-0.64, 0.70]**
Heterogeneity: Tau² = 0.08; Chi² = 1.51, df = 1 (P = 0.22); I² = 34%								
Test for overall effect: Z = 0.08 (P = 0.94)								
4.3.7 CRT vs gespecialiseerde TAU								
HANSEN2012 special TAU	16.7	5.9	31	17.7	6.7	31	54.5%	-0.16 [-0.66, 0.34]
Subtotal (95% CI)			**31**			**31**	**54.5%**	**-0.16 [-0.66, 0.34]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.61 (P = 0.54)								
Total (95% CI)			**60**			**55**	**100.0%**	**-0.07 [-0.44, 0.30]**
Heterogeneity: Tau² = 0.00; Chi² = 1.76, df = 2 (P = 0.41); I² = 0%								
Test for overall effect: Z = 0.37 (P = 0.71)								
Test for subgroup differences: Chi² = 0.18, df = 1 (P = 0.67), I² = 0%								



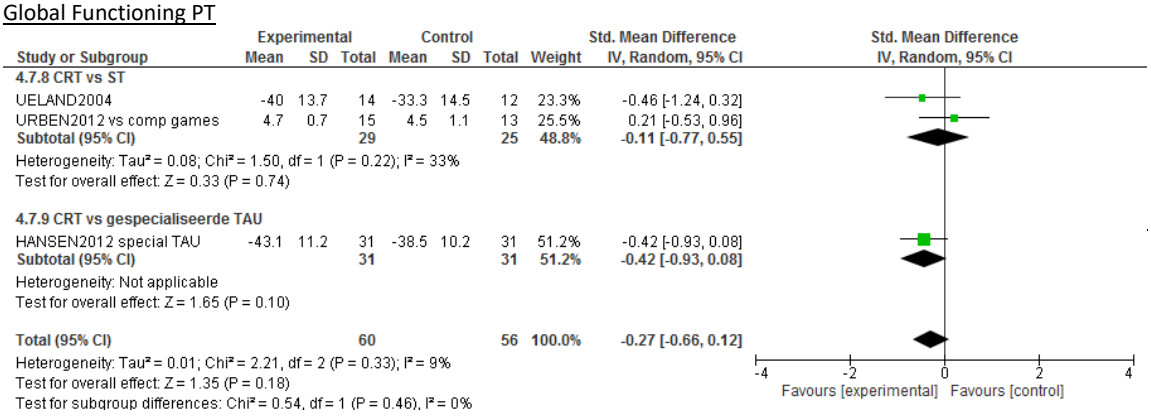
Mental state: negative symptoms PT



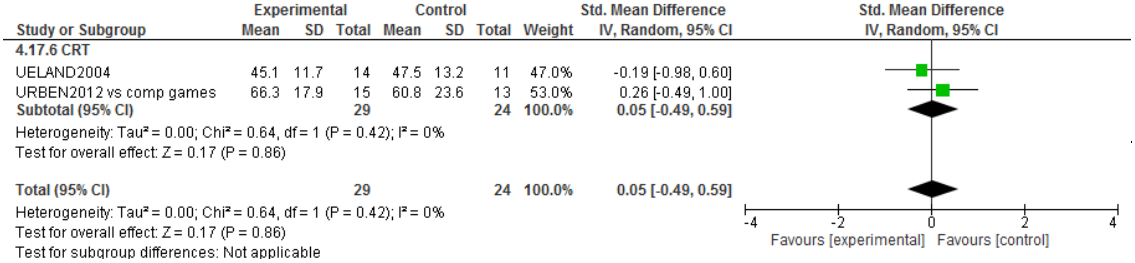
(Psycho)social functioning PT



Global Functioning PT

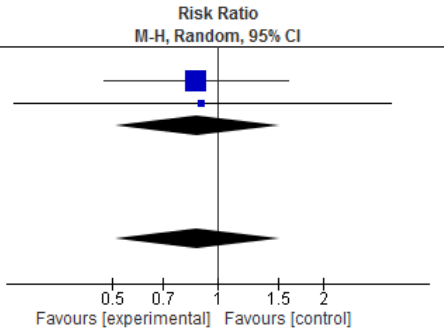


Hospitalisation, days PT



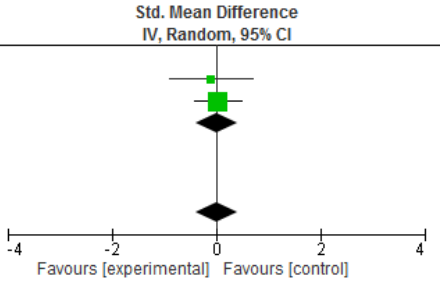
Leaving the study early for any reason PT

Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
4.18.4 CRT						
HEGDE2012	10	22	12	23	80.9%	0.87 [0.48, 1.59]
WYKES2007	4	21	4	19	19.1%	0.90 [0.26, 3.12]
Subtotal (95% CI)		**43**		**42**	**100.0%**	**0.88 [0.51, 1.51]**
Total events	14		16			
Heterogeneity: Tau² = 0.00; Chi² = 0.00, df = 1 (P = 0.96); I² = 0%						
Test for overall effect: Z = 0.47 (P = 0.64)						
Total (95% CI)		**43**		**42**	**100.0%**	**0.88 [0.51, 1.51]**
Total events	14		16			
Heterogeneity: Tau² = 0.00; Chi² = 0.00, df = 1 (P = 0.96); I² = 0%						
Test for overall effect: Z = 0.47 (P = 0.64)						
Test for subgroup differences: Not applicable						



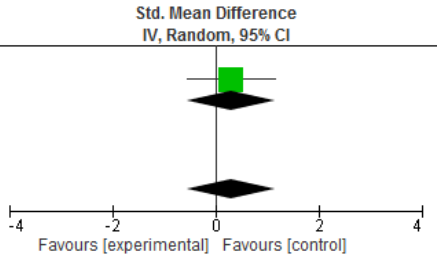
Executief functioneren PT

Study or Subgroup	Experimental Mean	Experimental SD	Experimental Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI
4.6.4 CRT								
UELAND2004	-4.6	2	14	-4.4	2.2	10	24.0%	-0.09 [-0.90, 0.72]
WYKES2007	-2.3	2.4	37	-2.4	2.2	37	76.0%	0.04 [-0.41, 0.50]
Subtotal (95% CI)			**51**			**47**	**100.0%**	**0.01 [-0.39, 0.41]**
Heterogeneity: Tau² = 0.00; Chi² = 0.08, df = 1 (P = 0.78); I² = 0%								
Test for overall effect: Z = 0.05 (P = 0.96)								
Total (95% CI)			**51**			**47**	**100.0%**	**0.01 [-0.39, 0.41]**
Heterogeneity: Tau² = 0.00; Chi² = 0.08, df = 1 (P = 0.78); I² = 0%								
Test for overall effect: Z = 0.05 (P = 0.96)								
Test for subgroup differences: Not applicable								



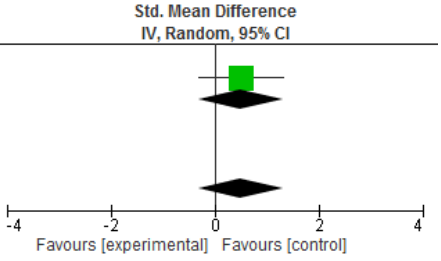
Korte termijn geheugen PT

Study or Subgroup	Experimental Mean	Experimental SD	Experimental Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI
4.7.4 CRT								
UELAND2004	-71.5	12.2	13	-75.4	13.1	9	100.0%	0.30 [-0.56, 1.15]
Subtotal (95% CI)			**13**			**9**	**100.0%**	**0.30 [-0.56, 1.15]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.68 (P = 0.49)								
Total (95% CI)			**13**			**9**	**100.0%**	**0.30 [-0.56, 1.15]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.68 (P = 0.49)								
Test for subgroup differences: Not applicable								



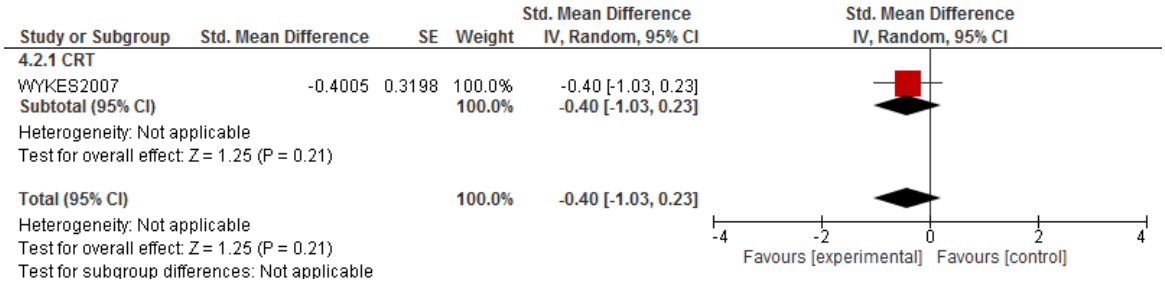
Lange termijn geheugen PT

Study or Subgroup	Experimental Mean	Experimental SD	Experimental Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI
4.8.4 CRT								
UELAND2004	-8.6	2.8	14	-9.9	2	11	100.0%	0.51 [-0.30, 1.31]
Subtotal (95% CI)			**14**			**11**	**100.0%**	**0.51 [-0.30, 1.31]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.23 (P = 0.22)								
Total (95% CI)			**14**			**11**	**100.0%**	**0.51 [-0.30, 1.31]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.23 (P = 0.22)								
Test for subgroup differences: Not applicable								

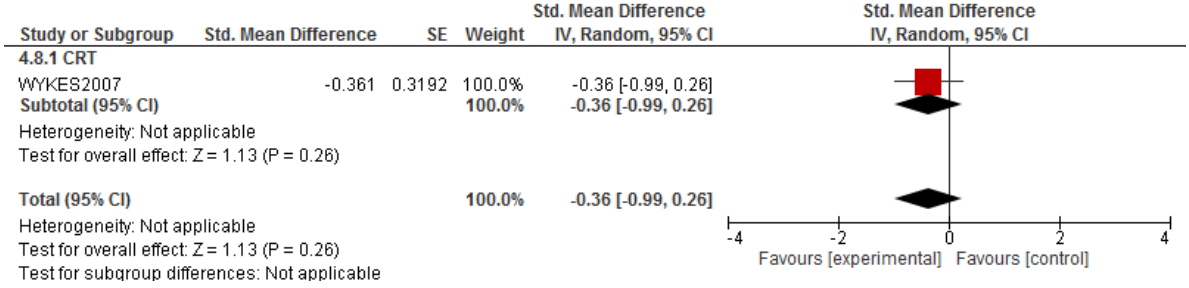


GEMMIDDELDE VAN PT en FU

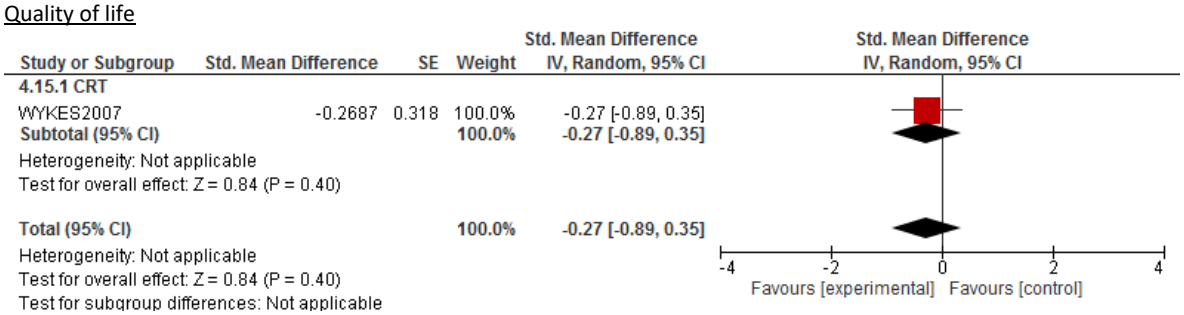
Mental state: total symptoms FU



Functioning: social (social behavior scale)

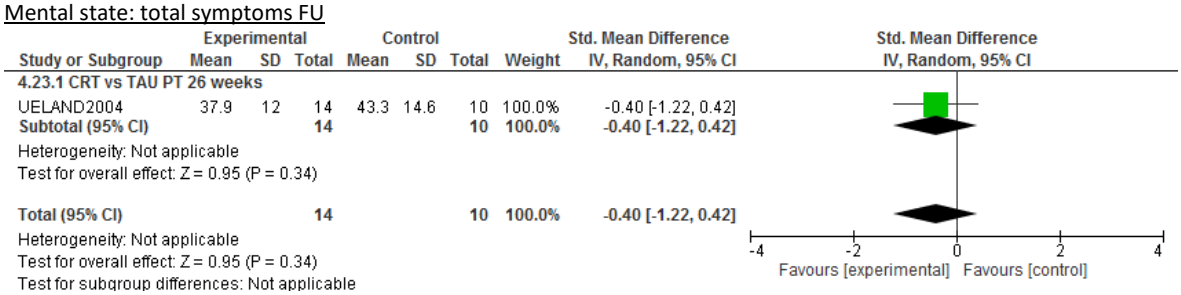


Quality of life

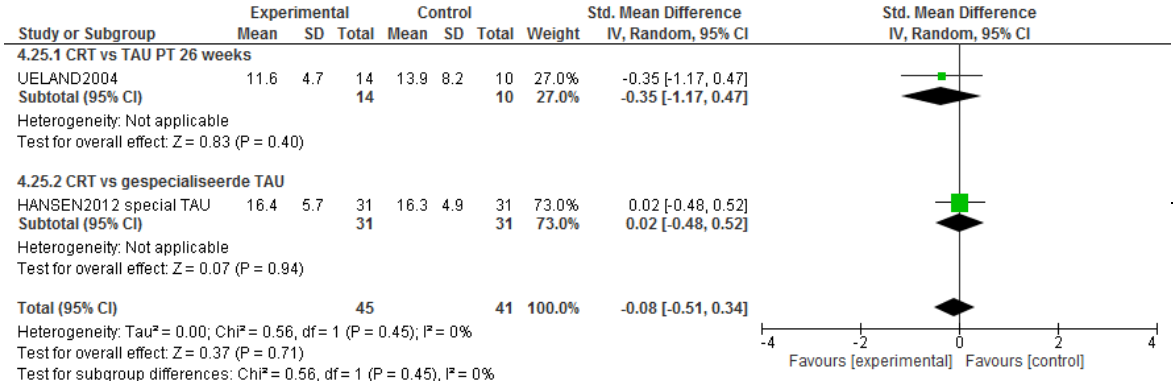


FOLLOW-UP

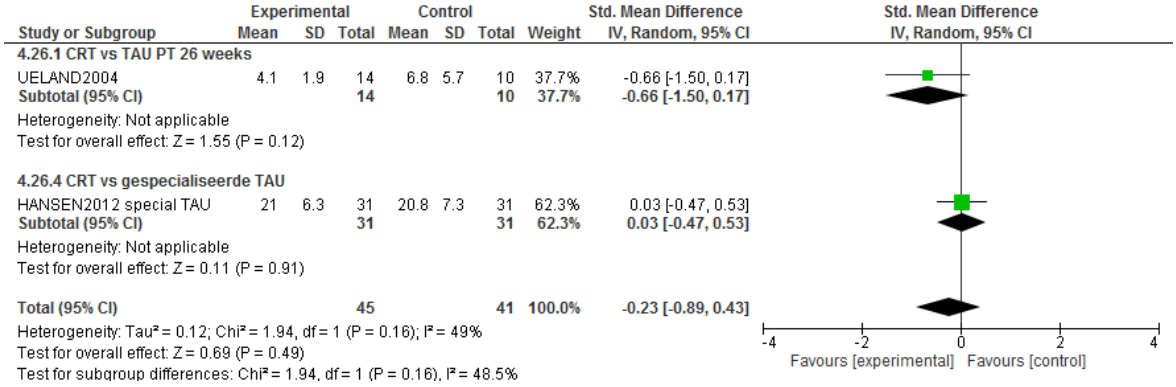
Mental state: total symptoms FU



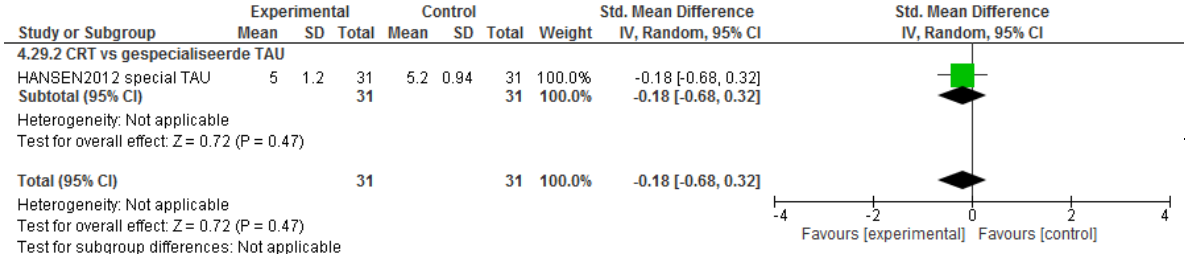
Mental state: positive symptoms FU



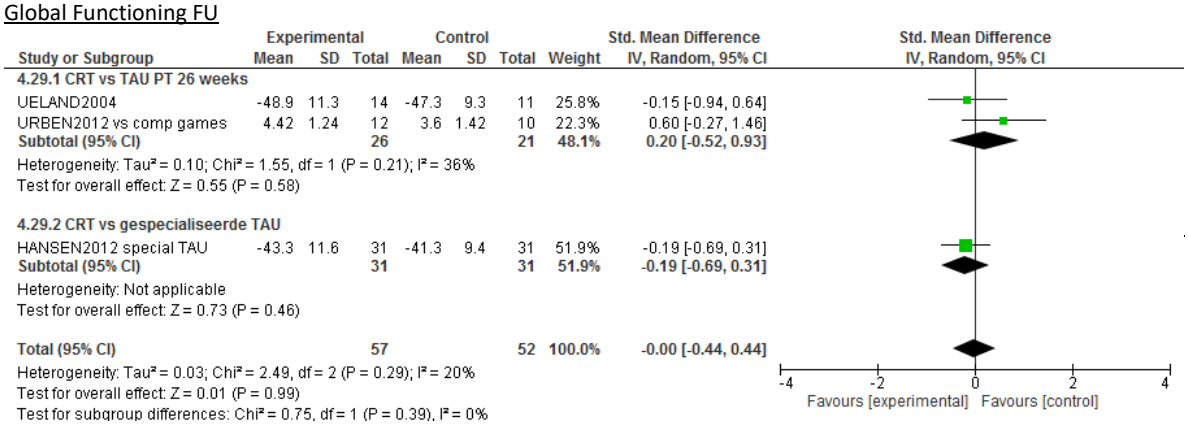
Mental state: negative symptoms FU



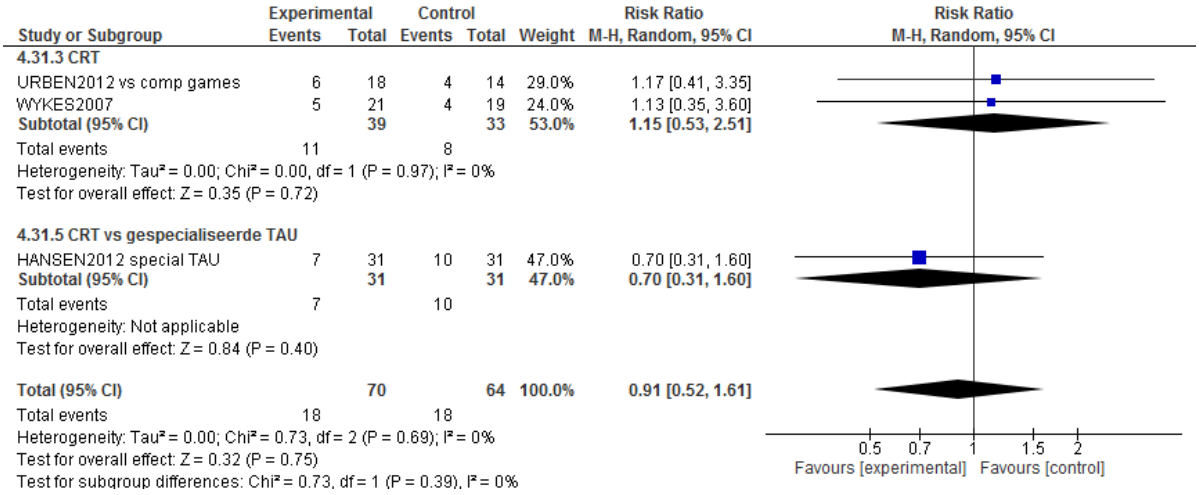
Quality of life FU



Global Functioning FU



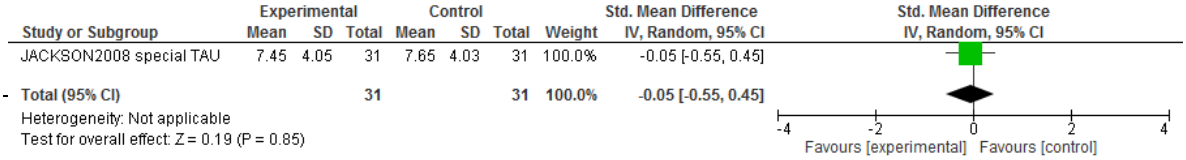
Leaving the study early for any reason FU



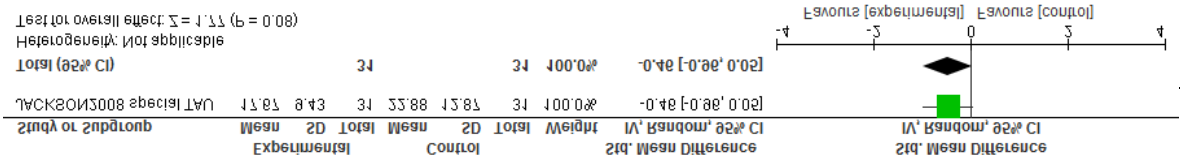
5th comparison CBT vs EPPIC TAU with Befriending (active control)

POST-TREATMENT

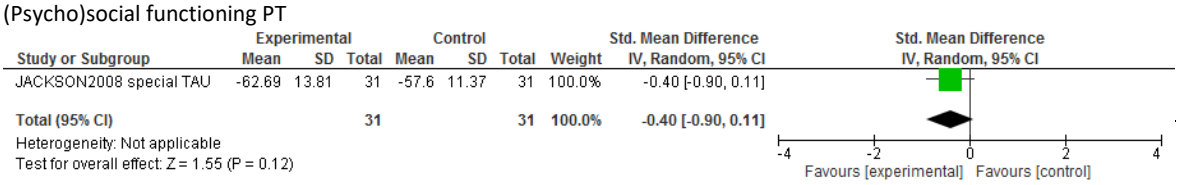
Mental state: positive symptoms PT



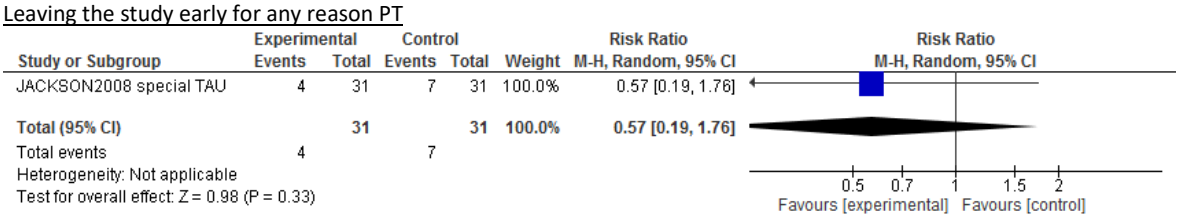
Mental state: negative symptoms PT



(Psycho)social functioning PT



Leaving the study early for any reason PT

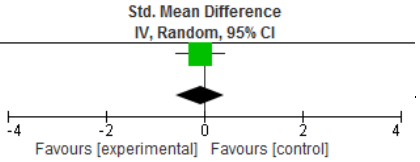


FOLLOW-UP

Mental state: positive symptoms FU

Study or Subgroup	Experimental Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
JACKSON2008 special TAU	7.2	4.08	31	7.55	4.76	31	100.0%	-0.08 [-0.58, 0.42]
Total (95% CI)			**31**			**31**	**100.0%**	**-0.08 [-0.58, 0.42]**

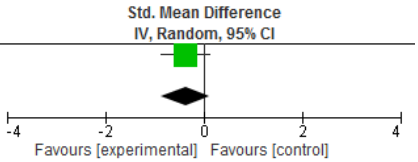
Heterogeneity: Not applicable
Test for overall effect: Z = 0.31 (P = 0.76)



Mental state: negative symptoms FU

Study or Subgroup	Experimental Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
JACKSON2008 special TAU	14.66	10.9	31	19.55	14.79	31	100.0%	-0.37 [-0.87, 0.13]
Total (95% CI)			**31**			**31**	**100.0%**	**-0.37 [-0.87, 0.13]**

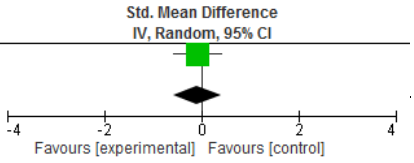
Heterogeneity: Not applicable
Test for overall effect: Z = 1.45 (P = 0.15)



(Psycho)social functioning FU

Study or Subgroup	Experimental Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
JACKSON2008 special TAU	-64.21	15.18	31	-62.91	15.18	31	100.0%	-0.08 [-0.58, 0.41]
Total (95% CI)			**31**			**31**	**100.0%**	**-0.08 [-0.58, 0.41]**

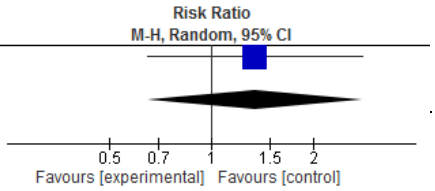
Heterogeneity: Not applicable
Test for overall effect: Z = 0.33 (P = 0.74)



Relapse FU

Study or Subgroup	Experimental Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
JACKSON2008 special TAU	12	30	8	27	100.0%	1.35 [0.65, 2.80]
Total (95% CI)		**30**		**27**	**100.0%**	**1.35 [0.65, 2.80]**
Total events	12		8			

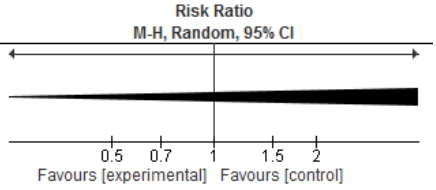
Heterogeneity: Not applicable
Test for overall effect: Z = 0.81 (P = 0.42)



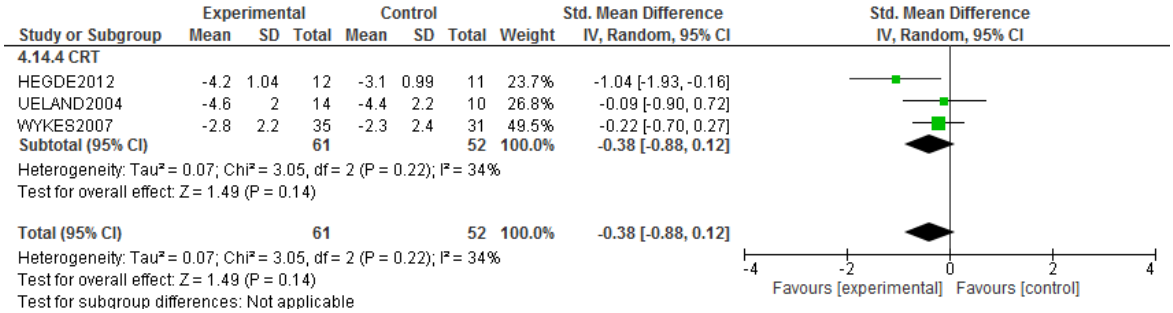
Mortality: number of deaths by suicide (assuming dropout did not die by suicide) FU

Study or Subgroup	Experimental Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
JACKSON2008 special TAU	2	31	0	31	100.0%	5.00 [0.25, 100.08]
Total (95% CI)		**31**		**31**	**100.0%**	**5.00 [0.25, 100.08]**
Total events	2		0			

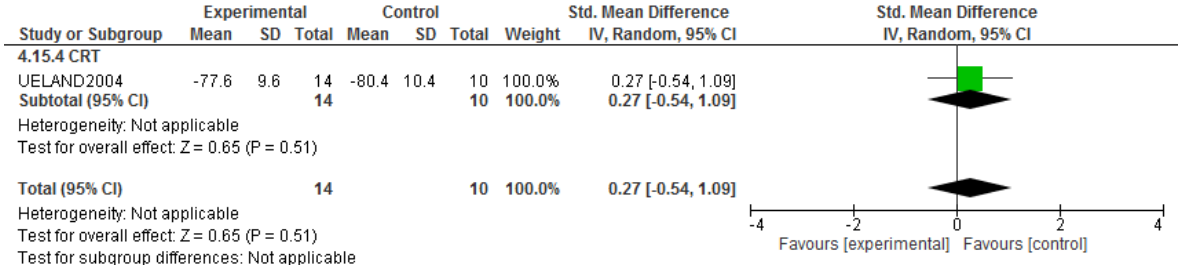
Heterogeneity: Not applicable
Test for overall effect: Z = 1.05 (P = 0.29)



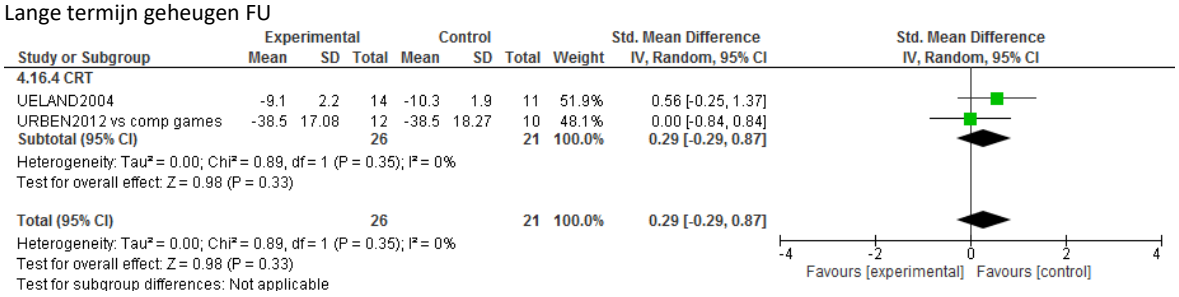
Executief functioneren FU



Korte termijn geheugen FU



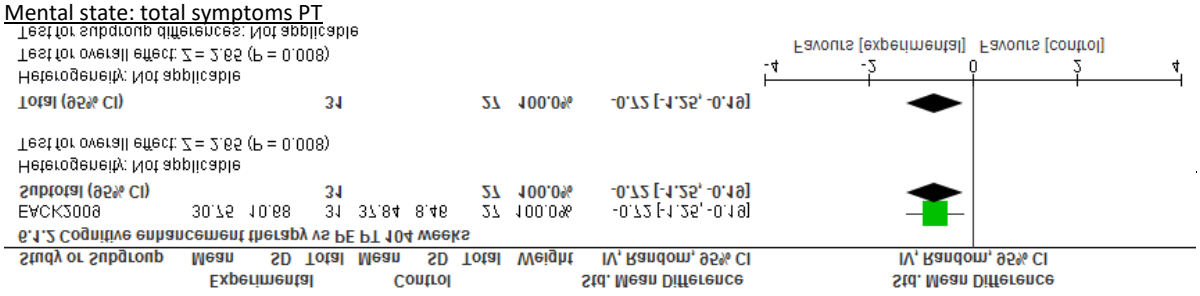
Lange termijn geheugen FU



6th comparison CRT vs PE and illness management

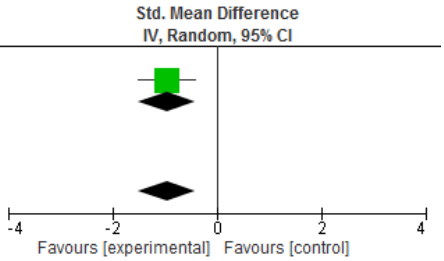
POST-TREATMENT

<u>Mental state: total symptoms PT</u>



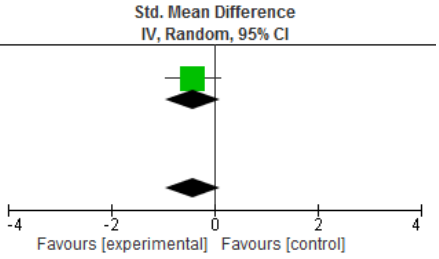
Mental state: negative symptoms PT

Study or Subgroup	Experimental Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
6.2.2 Cognitive enhancement therapy vs PE PT 104 weeks								
EACK2009	1.63	0.6	31	2.3	0.78	27	100.0%	-0.96 [-1.51, -0.41]
Subtotal (95% CI)			**31**			**27**	**100.0%**	**-0.96 [-1.51, -0.41]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 3.44 (P = 0.0006)								
Total (95% CI)			**31**			**27**	**100.0%**	**-0.96 [-1.51, -0.41]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 3.44 (P = 0.0006)								
Test for subgroup differences: Not applicable								



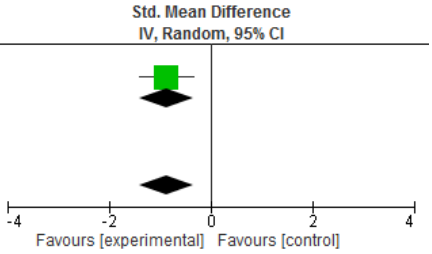
Mental state: depression PT

Study or Subgroup	Experimental Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
6.1.2 Cognitive enhancement therapy vs PE PT 104 weeks								
EACK2009	1.97	0.82	31	2.28	0.64	27	100.0%	-0.41 [-0.93, 0.11]
Subtotal (95% CI)			**31**			**27**	**100.0%**	**-0.41 [-0.93, 0.11]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.55 (P = 0.12)								
Total (95% CI)			**31**			**27**	**100.0%**	**-0.41 [-0.93, 0.11]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.55 (P = 0.12)								
Test for subgroup differences: Not applicable								



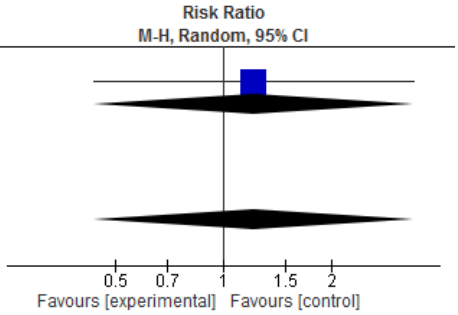
Global Functioning PT

Study or Subgroup	Experimental Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
6.5.2 Cognitive enhancement therapy vs PE PT 104 weeks								
EACK2009	-69.18	8.2	31	-61.39	9.62	27	100.0%	-0.86 [-1.41, -0.32]
Subtotal (95% CI)			**31**			**27**	**100.0%**	**-0.86 [-1.41, -0.32]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 3.13 (P = 0.002)								
Total (95% CI)			**31**			**27**	**100.0%**	**-0.86 [-1.41, -0.32]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 3.13 (P = 0.002)								
Test for subgroup differences: Not applicable								

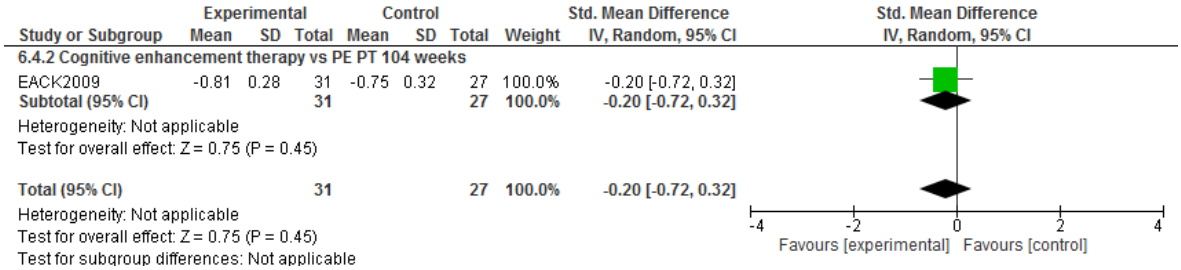


Leaving the study early for any reason PT

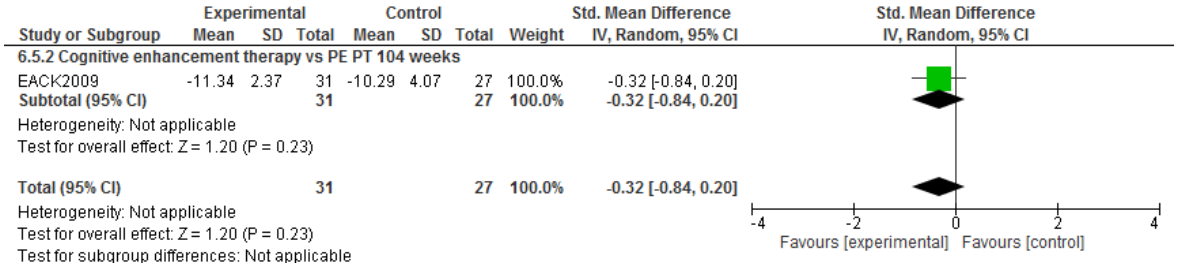
Study or Subgroup	Experimental Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
6.6.1 Cognitive enhancement therapy vs PE PT 104 weeks						
EACK2009	7	31	5	27	100.0%	1.22 [0.44, 3.40]
Subtotal (95% CI)		**31**		**27**	**100.0%**	**1.22 [0.44, 3.40]**
Total events	7		5			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.38 (P = 0.70)						
Total (95% CI)		**31**		**27**	**100.0%**	**1.22 [0.44, 3.40]**
Total events	7		5			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.38 (P = 0.70)						
Test for subgroup differences: Not applicable						



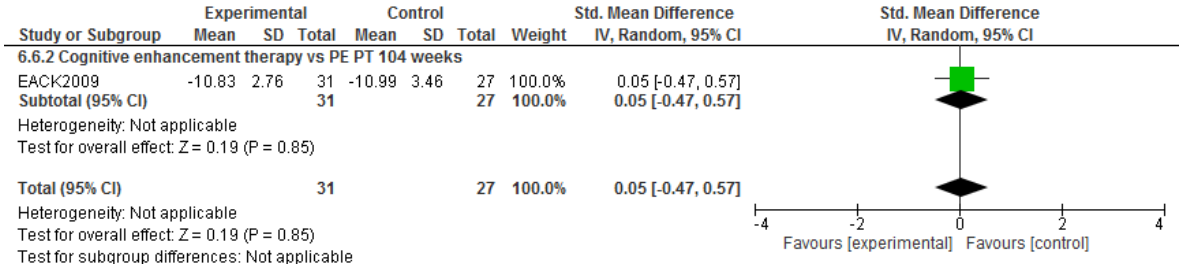
Executief functioneren PT



Korte termijn geheugen PT



Lange termijn geheugen PT



Bijlage 7.F GRADE profielen – Psychologische interventies

PT = Post Treatment; FU= Follow up

Question: Adherence therapy (ACE) vs TAU for First Episode Psychosis (fep)?
Bibliography: Psychological and Psychosocial Interventions for First Episode Psychosis (fep).

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Adherence therapy (ACE)	TAU	Relative (95% CI)	Absolute		
Mental state: positive symptoms PT - Adherence-coping-education (ACE) therapy vs Supportive Therapy (Better indicated by lower values)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	10	9	-	SMD 0.45 lower (1.36 lower to 0.47 higher)	⨁◯◯◯ VERY LOW	
Mental state: negative symptoms PT - Adherence-coping-education (ACE) therapy vs Supportive Therapy (Better indicated by lower values)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	10	9	-	SMD 0.24 lower (1.14 lower to 0.67 higher)	⨁◯◯◯ VERY LOW	
Mental state: depression PT - Adherence-coping-education (ACE) therapy vs Supportive Therapy (Better indicated by lower values)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	10	9	-	SMD 0.52 lower (1.44 lower to 0.4 higher)	⨁◯◯◯ VERY LOW	
Quality of life PT - Adherence-coping-education (ACE) therapy vs Supportive Therapy QLS SOCIAL (Better indicated by lower values)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	10	9	-	SMD 0.12 higher (0.78 lower to 1.02 higher)	⨁◯◯◯ VERY LOW	
Response, any (number) PT - Adherence-coping-education (ACE) therapy vs Supportive Therapy												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[4]	none	4/10 (40%)	0/9 (0%)	RR 8.18 (0.5 to 133.66)	-	⨁◯◯◯ VERY LOW	
								0%		-		

[1] UZENHOFF2008
[2] High risk of attrition bias (incomplete outcome data)
[3] Optimal information size was not met (<100 participants)
[4] Optimal information size was not met (<50 events)

Question: Should CBT be used versus (gespecialiseerde) TAU for First Episode Psychosis (fep)?
Bibliography: Psychological and Psychosocial Interventions for First Episode Psychosis (fep).

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	CBT	Control	Relative (95% CI)	Absolute		
Mental state: total symptoms PT (Better indicated by lower values)												
6[1,2,3,4,5,6]	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[7]	none	189	180	-	SMD 0.12 lower (0.36 lower to 0.13 higher)	⨁⨁⨁◯ MODERATE	
Mental state: positive symptoms PT (Better indicated by lower values)												
3[1,2,8]	randomised trials	serious[9]	no serious inconsistency	no serious indirectness	serious[7]	none	121	82	-	SMD 0.22 lower (0.54 lower to 0.11 higher)	⨁⨁◯◯ LOW	
Mental state: negative symptoms PT (Better indicated by lower values)												
5[1,5,6,8,10]	randomised trials	serious[9]	no serious inconsistency	no serious indirectness	serious[7]	none	160	111	-	SMD 0.12 higher (0.13 lower to 0.37 higher)	⨁⨁◯◯ LOW	
Mental state: depression PT (Better indicated by lower values)												
6[4,5,8,10,11]	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[7]	none	175	168	-	SMD 0.1 lower (0.31 lower to 0.12 higher)	⨁⨁⨁◯ MODERATE	
Mental state: anxiety PT - CBTrecovery (Better indicated by lower values)												
1[4]	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[12]	none	35	42	-	SMD 0.02 lower (0.47 lower to 0.43 higher)	⨁⨁◯◯ LOW	
(Psycho)social Functioning PT (Better indicated by lower values)												
4[4,5,6,10]	randomised trials	no serious risk of bias	serious[13]	no serious indirectness	serious[7]	none	113	124	-	SMD 0.02 lower (0.47 lower to 0.42 higher)	⨁⨁◯◯ LOW	
Quality of life PT (Better indicated by lower values)												
2[4,8]	randomised trials	serious[9]	no serious inconsistency	no serious indirectness	serious[7]	none	69	57	-	SMD 0.23 lower (0.59 lower to 0.13 higher)	⨁⨁◯◯ LOW	
Globaal welbevinden PT (Better indicated by lower values)												
2[8,10]	randomised trials	serious[9]	no serious inconsistency	no serious indirectness	very serious[12]	none	50	33	-	SMD 0.06 lower (0.51 lower to 0.39 higher)	⨁◯◯◯ VERY LOW	
Hospitalisations, number admitted PT												
3[4,6,14]	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[15]	none	11/68 (16.2%)	10/72 (13.9%)	RR 1.13 (0.5 to 2.53)	18 more per 1000 (from 69 fewer to 213 more)	⨁⨁◯◯ LOW	

								18.2%		24 more per 1000 (from 91 fewer to 278 more)		
Hospitalisation, days PT (Better indicated by lower values)												
2[6,14]	randomised trials	no serious risk of bias	very serious[16]	no serious indirectness	very serious[12]	none	33	30	-	SMD 1.51 lower (4.02 lower to 1 higher)	⨁◯◯◯ VERY LOW	
Mortality: number of deaths by suicide (assuming dropout did not die bysuicide) PT - CBTsuicide												
1[17]	randomised trials	serious[9]	no serious inconsistency	no serious indirectness	very serious[15]	none	1/21 (4.8%)	1/21 (4.8%)	RR 1 (0.07 to 14.95)	0 fewer per 1000 (from 44 fewer to 664 more)	⨁◯◯◯ VERY LOW	
								4.8%		0 fewer per 1000 (from 45 fewer to 670 more)		
Leaving the study early for any reason PT												
6[2,3,4,5,8,14]	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[16]	none	52/236 (22%)	39/216 (18.1%)	RR 1.11 (0.76 to 1.62)	20 more per 1000 (from 43 fewer to 112 more)	⨁⨁⨁◯ MODERATE	
								15.6%		17 more per 1000 (from 37 fewer to 97 more)		
Mental state: total symptoms FU - CBTrecovery (Better indicated by lower values)												
2[2,6]	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[7]	none	139	123	-	SMD 0.28 lower (0.53 to 0.04 lower)	⨁⨁⨁◯ MODERATE	
Mental state: positive symptoms FU (Better indicated by lower values)												
3[6,8,10]	randomised trials	serious[9]	no serious inconsistency	no serious indirectness	serious[7]	none	64	52	-	SMD 0.16 lower (0.53 lower to 0.22 higher)	⨁⨁◯◯ LOW	
Mental state: negative symptoms FU (Better indicated by lower values)												
3[6,8,10]	randomised trials	serious[9]	no serious inconsistency	no serious indirectness	serious[7]	none	64	54	-	SMD 0.18 lower (0.55 lower to 0.18 higher)	⨁⨁◯◯ LOW	
Remission (BPRS-P, CGI) 24 weeks FU - CBTp												
1[10]	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[15]	none	6/11 (54.5%)	7/14 (50%)	RR 1.09 (0.51 to 2.31)	45 more per 1000 (from 245 fewer to 655 more)	⨁⨁◯◯ LOW	
								50%		45 more per 1000 (from 245 fewer to 655 more)		
Relapse FU - CBTp vs supportive therapy												
1[3]	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[15]	none	5/10 (50%)	8/11 (72.7%)	RR 0.69 (0.34 to 1.41)	225 fewer per 1000 (from 480 fewer to 298 more)	⨁⨁◯◯ LOW	
								72.7%		225 fewer per 1000 (from 480 fewer to 298 more)		
(Psycho)social Functioning FU (Better indicated by lower values)												

2[6,10]	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[12]	none	32	35	-	SMD 0.22 lower (0.7 lower to 0.26 higher)	⨁⨁⨁◯ LOW	
Quality of life FU (Better indicated by lower values)												
4[6,8,10,17]	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[7]	none	81	67	-	SMD 0.36 lower (0.7 to 0.02 lower)	⨁⨁⨁◯ MODERATE	
Globaal welbevinden (FU) (Better indicated by lower values)												
2[8,10]	randomised trials	serious[9]	no serious inconsistency	no serious indirectness	very serious[12]	none	42	30	-	SMD 0.02 higher (0.46 lower to 0.5 higher)	⨁◯◯◯ VERY LOW	
Hospitalisation, days FU - CBTrecovery (Better indicated by lower values)												
1[6]	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[12]	none	21	21	-	SMD 0.09 lower (0.69 lower to 0.52 higher)	⨁⨁◯◯ LOW	
Mortality: number of deaths by suicide (assuming dropout did not die bysuicide), 36 weeks FU - CBTsuicide												
1[17]	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[15]	none	1/31 (3.2%)	1/25 (4%)	RR 0.81 (0.05 to 12.26)	8 fewer per 1000 (from 38 fewer to 450 more)	⨁⨁◯◯ LOW	
								4%		8 fewer per 1000 (from 38 fewer to 450 more)		
Leaving the study early for any reason FU												
3[5,6,8]	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[16]	none	72/190 (37.9%)	51/172 (29.7%)	RR 1.62 (1.12 to 2.34)	184 more per 1000 (from 36 more to 397 more)	⨁⨁⨁◯ MODERATE	
								26.7%		166 more per 1000 (from 32 more to 358 more)		

[1] LECOMTE2008
[2] LEWIS2002
[3] HADDOCK1999
[4] FOWLER2009
[5] JACKSON2009
[6] PENN2011
[7] Optimal information size was not met (<400 participants)
[8] MADIGAN2013
[9] High risk of attrition (incomplete outcome data)
[10] EDWARDS2011
[11] JACKSON2005
[12] Optimal information size was not met (<100 participants)
[13] Statistical heterogeneity (I2 > 50% and P<0.1)
[14] JOLLEY2003
[15] Optimal information size was not met (<50 events)
[16] Optimal information size was not met (<300 events)
[17] POWER2003

Question: Family interventie vs (gespecialiseerde) TAU for First Episode Psychosis (fep)?
Bibliography: Psychological and Psychosocial Interventions for First Episode Psychosis (fep). Cochrane Database of Systematic Reviews [Year], Issue [Issue].

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Family interventie	(gespecialiseerde) TAU	Relative (95% CI)	Absolute		
Mental state: total symptoms PT (Better indicated by lower values)												
2[1,2]	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[3]	none	66	66	-	SMD 0.15 lower (0.49 lower to 0.19 higher)	⨁⨁⨁◯ MODERATE	
Mental state: positive symptoms PT (Better indicated by lower values)												
2[1,2]	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[3]	none	66	66	-	SMD 0.21 lower (0.55 lower to 0.13 higher)	⨁⨁⨁◯ MODERATE	
Mental state: negative symptoms PT (Better indicated by lower values)												
2[1,2]	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[3]	none	66	66	-	SMD 0.18 lower (0.54 lower to 0.19 higher)	⨁⨁⨁◯ MODERATE	
Mental state: depression PT - Family intervention vs gespecialiseerde TAU (Better indicated by lower values)												
1[2]	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[4]	none	41	40	-	SMD 0.24 lower (0.68 lower to 0.2 higher)	⨁⨁◯◯ LOW	
Relapse PT												
3[2,5,6]	randomised trials	serious[7]	no serious inconsistency	no serious indirectness	very serious[8]	none	15/132 (11.4%)	26/129 (20.2%)	RR 0.59 (0.31 to 1.12)	83 fewer per 1000 (from 139 fewer to 24 more)	⨁◯◯◯ VERY LOW	
								20%		82 fewer per 1000 (from 138 fewer to 24 more)		
(Psycho)social functioning PT - Family intervention vs gespecialiseerde TAU (Better indicated by lower values)												
1[2]	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[4]	none	41	40	-	SMD 0.06 higher (0.37 lower to 0.5 higher)	⨁⨁◯◯ LOW	
Quality of life PT - Family intervention vs gespecialiseerde TAU (Better indicated by lower values)												
1[2]	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[4]	none	41	40	-	SMD 0 higher (0.44 lower to 0.44 higher)	⨁⨁◯◯ LOW	
Globaal welbevinden PT - Family intervention (Better indicated by lower values)												
1[1]	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[4]	none	25	26	-	SMD 0.51 lower (1.06 lower to 0.05 higher)	⨁⨁◯◯ LOW	
Hospitalisations, number admitted PT - Family intervention												
2[1,9]	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[8]	none	12/67 (17.9%)	32/67 (47.8%)	RR 0.37 (0.21 to 0.66)	301 fewer per 1000 (from 162 fewer to 377 fewer)	⨁⨁◯◯ LOW	
								45.4%		286 fewer per 1000 (from 154 fewer to 359 fewer)		
Hospitalisation, days PT - Family intervention (Better indicated by lower values)												

1[1]	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[4]	none	25	26	-	SMD 0.25 lower (0.8 lower to 0.3 higher)	⨁⨁⨁◯ LOW	
Leaving the study early for any reason PT - Family intervention												
4[1,6,9,10]	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[8]	none	11/143 (7.7%)	7/144 (4.9%)	RR 1.52 (0.62 to 3.74)	25 more per 1000 (from 18 fewer to 133 more)	⨁⨁⨁◯ LOW	
								5.3%		28 more per 1000 (from 20 fewer to 145 more)		
Mental state: total symptoms FU - Family intervention vs gespecialiseerde TAU (Better indicated by lower values)												
1[2]	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[4]	none	30	30	-	SMD 0.19 higher (0.32 lower to 0.7 higher)	⨁⨁⨁◯ LOW	
Mental state: positive symptoms FU - Family intervention vs gespecialiseerde TAU (Better indicated by lower values)												
1[2]	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[4]	none	30	30	-	SMD 0.08 lower (0.59 lower to 0.43 higher)	⨁⨁⨁◯ LOW	
Mental state: negative symptoms FU - Family intervention vs gespecialiseerde TAU (Better indicated by lower values)												
1[2]	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[4]	none	30	30	-	SMD 0.7 higher (0.17 to 1.22 higher)	⨁⨁⨁◯ LOW	
(Psycho)social functioning FU - Family intervention vs gespecialiseerde TAU (Better indicated by lower values)												
1[2]	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[4]	none	30	30	-	SMD 0.51 higher (0 to 1.03 higher)	⨁⨁⨁◯ LOW	
(Psycho)social functioning (Not able to live independently) 52 weeksFU - Family intervention												
1[11]	randomised trials	serious[12]	no serious inconsistency	no serious indirectness	very serious[13]	none	31/47 (66%)	22/39 (56.4%)	RR 1.17 (0.83 to 1.65)	96 more per 1000 (from 96 fewer to 367 more)	⨁⨁⨁◯ VERY LOW	
								56.4%		96 more per 1000 (from 96 fewer to 367 more)		
Quality of life FU - Family intervention vs gespecialiseerde TAU (Better indicated by lower values)												
1[2]	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[4]	none	30	30	-	SMD 0.46 lower (0.97 lower to 0.06 higher)	⨁⨁⨁◯ LOW	
Hospitalisation FU - Family intervention												
1[11]	randomised trials	serious[12]	no serious inconsistency	no serious indirectness	very serious[8]	none	6/57 (10.5%)	6/49 (12.2%)	RR 0.86 (0.3 to 2.49)	17 fewer per 1000 (from 86 fewer to 182 more)	⨁⨁⨁◯ VERY LOW	
								12.2%		17 fewer per 1000 (from 85 fewer to 182 more)		
Leaving the study early for any reason FU - Family intervention vs gespecialiseerde TAU												
1[2]	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[8]	none	11/41 (26.8%)	11/41 (26.8%)	RR 1 (0.49 to 2.04)	0 fewer per 1000 (from 137 fewer to 279 more)	⨁⨁⨁◯ LOW	
								26.8%		0 fewer per 1000 (from 137 fewer to 279 more)		

[1] CALVO2014

[2] GLEESON2009

[3] Optimal information size was not met (<400 participants)

[4] Optimal information size was not met (<100 participants)
[5] LINSZEN1996
[6] GOLDSTEIN1978
[7] High risk of attrition bias (incomplete outcome data)
[8] Optimal information size was not met (<50 events)
[9] ZHANG1994
[10] SO2006
[11] LEAVEY2004
[12] High risk of detection bias (raters unblind)
[13] Optimal information size was not met (<55 events)

Question: CRT vs (gespecialiseerde) TAU for First Episode Psychosis (fep)?
Bibliography: . Psychological and Psychosocial Interventions for First Episode Psychosis (fep). Cochrane Database of Systematic Reviews [Year], Issue [Issue].

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	CRT	(gespecialiseerde) TAU	Relative (95% CI)	Absolute		
Mental state: total symptoms PT - CRT (Better indicated by lower values)												
2[1,2]	randomised trials	serious[3]	no serious inconsistency	no serious indirectness	very serious[4]	none	29	24	-	SMD 0.05 higher (0.49 lower to 0.59 higher)	⨁◯◯◯ VERY LOW	
Mental state: total symptoms (PANSS) average over PT and FU - CRT (Better indicated by lower values)												
1[5]	randomised trials	serious[3]	no serious inconsistency	no serious indirectness	very serious[4]	none	21	19	-	SMD 0.4 lower (1.03 lower to 0.23 higher)	⨁◯◯◯ VERY LOW	
Mental state: positive symptoms PT (Better indicated by lower values)												
3[1,2,5]	randomised trials	serious[3]	no serious inconsistency	no serious indirectness	serious[6]	none	60	55	-	SMD 0.07 lower (0.44 lower to 0.3 higher)	⨁⨁◯◯ LOW	
Mental state: negative symptoms PT (Better indicated by lower values)												
4[1,2,7,8]	randomised trials	serious[3]	very serious[9]	no serious indirectness	serious[6]	none	73	73	-	SMD 0.76 lower (1.97 lower to 0.45 higher)	⨁◯◯◯ VERY LOW	
(Psycho)social functioning PT - CRT vs ST (Better indicated by lower values)												
1[2]	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[4]	none	15	13	-	SMD 0.31 higher (0.44 lower to 1.06 higher)	⨁⨁◯◯ LOW	
Global Functioning PT (Better indicated by lower values)												
3[1,2,8]	randomised trials	serious[3]	no serious inconsistency	no serious indirectness	serious[4]	none	60	56	-	SMD 0.27 lower (0.66 lower to 0.12 higher)	⨁⨁◯◯ LOW	

Hospitalisation, days PT - CRT (Better indicated by lower values)												
2[1,2]	randomised trials	serious[3]	no serious inconsistency	no serious indirectness	very serious[4]	none	29	24	-	SMD 0.05 higher (0.49 lower to 0.59 higher)	⨁◯◯◯ VERY LOW	
Leaving the study early for any reason PT - CRT												
2[5,7]	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[10]	none	14/43 (32.6%)	16/42 (38.1%)	RR 0.88 (0.51 to 1.51)	46 fewer per 1000 (from 187 fewer to 194 more)	⨁◯◯◯ LOW	
								36.6%		44 fewer per 1000 (from 179 fewer to 187 more)		
(Psycho)social functioning (social behavior scale) average over PT and FU - CRT (Better indicated by lower values)												
1[5]	randomised trials	serious[3]	no serious inconsistency	no serious indirectness	very serious[6]	none	21	19	-	SMD 0.36 lower (0.99 lower to 0.26 higher)	⨁◯◯◯ VERY LOW	
Quality of life average over PT and FU - CRT (Better indicated by lower values)												
1[5]	randomised trials	serious[3]	no serious inconsistency	no serious indirectness	very serious[4]	none	21	19	-	SMD 0.27 lower (0.89 lower to 0.35 higher)	⨁◯◯◯ VERY LOW	
Mental state: total symptoms FU - CRT vs TAU (Better indicated by lower values)												
1[1]	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[4]	none	14	10	-	SMD 0.4 lower (1.22 lower to 0.42 higher)	⨁◯◯◯ LOW	
Mental state: positive symptoms FU (Better indicated by lower values)												
2[1,8]	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[4]	none	45	41	-	SMD 0.08 lower (0.51 lower to 0.34 higher)	⨁◯◯◯ LOW	
Mental state: negative symptoms FU (Better indicated by lower values)												
2[1,8]	randomised trials	no serious risk of bias	serious[11]	no serious indirectness	very serious[4]	none	45	41	-	SMD 0.23 lower (0.89 lower to 0.43 higher)	⨁◯◯◯ VERY LOW	
Quality of life FU - CRT vs gespecialiseerde TAU (Better indicated by lower values)												
1[8]	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[4]	none	31	31	-	SMD 0.18 lower (0.68 lower to 0.32 higher)	⨁◯◯◯ LOW	
Global Functioning FU (Better indicated by lower values)												
3[1,2,8]	randomised trials	serious[3]	no serious inconsistency	no serious indirectness	serious[6]	none	57	52	-	SMD 0 higher (0.44 lower to 0.44 higher)	⨁◯◯◯ LOW	
Leaving the study early for any reason FU												
3[2,5,8]	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[10]	none	18/70 (25.7%)	18/64 (28.1%)	RR 0.91 (0.52 to 1.61)	25 fewer per 1000 (from 135 fewer to 172 more)	⨁◯◯◯ LOW	
								28.6%		26 fewer per 1000 (from 137 fewer to 174 more)		

[1] UELAND2004

[2] URBEN2012

[3] High risk for attrition and detection bias
[4] Optimal information size was not met (<100 participants)
[5] WYKES2007
[6] Optimal information size was not met (<400 participants)
[7] HEDGE2012
[8] HANSEN2012
[9] Statistical heterogeneity (I2 > 90% and P<0.1)
[10] Optimal information size was not met (<50 events)
[11] Statistical heterogeneity (I2 > 50% and P<0.1)

Question: CBT vs EPPIC TAU with Befriending (active control) for First Episode Psychosis (fep)?
Bibliography: . Psychological and Psychosocial Interventions for First Episode Psychosis (fep). Cochrane Database of Systematic Reviews [Year], Issue [Issue].

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	CBT	EPPIC TAU with Befriending (active control)	Relative (95% CI)	Absolute		
Mental state: positive symptoms (Brief Psychiatric Rating Scale PsychoticSubscale [BPRS-P]) 14 weeks PT (Better indicated by lower values)												
1[1]	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[2]	none	31	31	-	SMD 0.05 lower (0.55 lower to 0.45 higher)	⨁⨁⨁◯ LOW	
Mental state: negative symptoms (Scale for Assessment of Negative Symptoms[SANS]) 14 weeks PT (Better indicated by lower values)												
1[1]	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[2]	none	31	31	-	SMD 0.46 lower (0.96 lower to 0.05 higher)	⨁⨁⨁◯ LOW	
(Psycho)social functioning PT (Better indicated by lower values)												
1[1]	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[2]	none	31	31	-	SMD 0.4 lower (0.9 lower to 0.11 higher)	⨁⨁⨁◯ LOW	
Leaving the study early for any reason, 14 weeks PT												
1[1]	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[3]	none	4/31 (12.9%)	7/31 (22.6%)	RR 0.57 (0.19 to 1.76)	97 fewer per 1000 (from 183 fewer to 172 more)	⨁⨁⨁◯ LOW	
								22.6%		97 fewer per 1000 (from 183 fewer to 172 more)		
Mental state: positive symptoms (BPRS-P) 52 weeks FU (Better indicated by lower values)												

1[1]	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[2]	none	31	31	-	SMD 0.08 lower (0.58 lower to 0.42 higher)	⨁⨁⨁◯ LOW	
Mental state: negative symptoms (SANS) 52 weeks FU (Better indicated by lower values)												
1[1]	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[2]	none	31	31	-	SMD 0.37 lower (0.87 lower to 0.13 higher)	⨁⨁⨁◯ LOW	
(Psycho)social functioning FU (Better indicated by lower values)												
1[1]	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[2]	none	31	31	-	SMD 0.08 lower (0.58 lower to 0.41 higher)	⨁⨁⨁◯ LOW	
Relapse: number of participants hospitalised 52 weeks FU												
1[1]	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[3]	none	12/30 (40%)	8/27 (29.6%)	RR 1.35 (0.65 to 2.8)	104 more per 1000 (from 104 fewer to 533 more)	⨁⨁⨁◯ LOW	
								29.6%		104 more per 1000 (from 104 fewer to 533 more)		
Mortality: number of deaths by suicide, 52 weeks FU												
1[1]	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[3]	none	2/31 (6.5%)	0/31 (0%)	RR 5 (0.25 to 100.08)	-	⨁⨁⨁◯ LOW	
								0%		-		

[1] JACKSON2008

[2] Optimal information size was not met (<100 participants)

[3] Optimal information size was not met (<50 events)

Question: CRT vs PE and illness management for First Episode Psychosis (fep)?
Bibliography: Psychological and Psychosocial Interventions for First Episode Psychosis (fep).

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	CRT	PE and illness management	Relative (95% CI)	Absolute		
Mental state: total symptoms (BPRS) PT (Better indicated by lower values)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	31	27	-	SMD 0.72 lower (1.25 to 0.19 lower)	⨁⨁⨁◯ VERY LOW	
Mental state: negative symptoms (BPRS) PT (Better indicated by lower values)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	31	27	-	SMD 0.96 lower (1.51 to 0.41 lower)	⨁⨁⨁◯ VERY LOW	
Mental state: depression PT (Better indicated by lower values)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	31	27	-	SMD 0.41 lower (0.93 lower to 0.11 higher)	⨁⨁⨁◯ VERY LOW	
Global Functioning PT (Better indicated by lower values)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	31	27	-	SMD 0.86 lower (1.41 to 0.32 lower)	⨁⨁⨁◯ VERY LOW	
Leaving the study early for any reason PT												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	7/31 (22.6%)	5/27 (18.5%)	RR 1.22 (0.44 to 3.4)	41 more per 1000 (from 104 fewer to 444 more)	⨁⨁⨁◯ VERY LOW	
								18.5%		41 more per 1000 (from 104 fewer to 444 more)		

[1] EACK2009
[2] High risk of attrition (incomplete outcome data) and detection bias (raters unblind)
[3] Optimal information size was not met (<100 participants)

Hoofdstuk 8 Maatschappelijke participatie

Bijlage 8.A Review protocol Maatschappelijke participatie

Onderwerp	E. Participatie in de maatschappij: werk, opleiding en cognitie
Uitgangsvragen	E1. Welke interventies zijn effectief in het verhogen van de participatie in de maatschappij op verschillende levensgebieden (werk, leren, sociale contacten, wonen, dagbesteding, antistigma)? E1b. In welke mate kan het trainen van sociale en cognitieve vaardigheden, als add on bij deze interventies, de effectiviteit ervan vergroten?
Criteria voor inclusie van studies in de review	
Populatie	• Personen van 12 of ouder met een (niet-affectieve) eerste psychose (of eerste keer in behandeling voor psychose) • Niet groep Ultra-High-Risc, subklinische psychotische klachten, prodromale klachten
Interventie	1.Interventies voor werk - Supported employment / IPS 2.Interventies voor leren - Supported education / Begeleid leren 3.Interventies voor wonen 4.Interventies voor dagbesteding / vrije tijd 5.Interventies voor sociale contacten 6.Interventies voor anti-stigma: gericht op de patiënt (niet campagnes en programma's voor publiek en professionals) 7.(Sociale) cognitieve vaardigheidstraining als "add-on" (combinatie behandeling) + Sociale vaardigheidstraining als "add-on" 8.Algemene rehabilitatie methoden
Vergelijking	-Care as usual (CAU) -Wachtlijst -Een van de bovengenoemde interventies of overige psychosociale interventies als alternatieve behandeling
Kritische uitkomstmaten	-Deelname aan werk / opleiding / dagbesteding / sociale contacten -Functioneren (sociaal, psychosociaal, cognitief) -Zorgconsumptie -Toe- en afname zelf-stigma
Belangrijke Uitkomstmaten	-Vinden van werk / opleiding / dagbesteding -Duur tot vinden van werk / opleiding / dagbesteding -Kwaliteit van leven -Toe- en afname van symptomen -Relapse / Heropname -Verlaten van de studie om welke reden dan ook -Remissie
Studiedesign	-RCT's en systematic reviews -non-RCT's met vergelijkingsgroep
Minimum omvang steekproef	-RCT: > 10 per arm -Exclusie van studies met >50% attrition uit een arm de trial (tenzij adequatie statistiek is toegepast om te corrigeren voor missende data)

Search strategie	[termen populatie criteria] AND [RCT, systematic review, comparison group] AND [interventie]
Databases searched	Core databases: CINAHL, Medline, PreMedline, PsycINFO
Data searched	-Mei 2012 (einde search NICE richtlijn) tot voor commentaarfase huidige richtlijn (maart 2015) -Indien afbakening populatie afwijkt van NICE: 1995 tot maart 2015

Bijlage 8.B Search history maatschappelijke participatie

Voor de maatschappelijke participatie van vroege psychose is gezocht in drie databases: PsycInfo, PubMed en CINAHL. Er is niet gelimiteerd op taal of jaar. Er is specifiek naar systematic reviews, meta-analyses en rct's gezocht. De searches zijn uitgevoerd op 1 en 3 december 2014.

PsycInfo

De termen voor de doelgroep:
In PsycInfo is gezocht op de volgende thesaurustermen voor schizofrenie en psychose:
DE "Schizophrenia" OR DE "Acute Schizophrenia" OR DE "Schizophreniform Disorder" OR DE "Schizoaffective Disorder" OR DE "Delusions" OR DE "Hallucinations" OR DE "Psychosis" OR DE "Acute Psychosis". Aangevuld met de volgende woorden in titel en keyword: "delusional disorder*" OR severe mental ill* OR severe mental disorder* OR psychotic OR psychosis OR psychoses OR schizo*.

Om aan te geven dat het om een 'vroege' psychose moet gaan, zijn al deze zoektermen gecombineerd met de woorden "early symptom*" OR onset OR "early signs" OR first-episode OR "acute phase" in het titel- en keywordveld.

Verder is gezocht op de thesaurusterm DE "Childhood Schizophrenia" en "childhood onset schizophrenia" in het titel- en keywordveld. Ook is specifiek gezocht op de zoektermen "early psychosis" OR "first episode psychosis" OR "early psychoses" OR "first episode psychoses" in het titel- en keywordveld.

De termen voor de leefgebieden en subthema's:
Voor maatschappelijke participatie zijn termen gezocht die betrekking hebben op 6 leefgebieden: wonen, werk, leren/opleiding, stigma, sociale contacten en dagelijks leven Daarnaast zijn termen gezocht die betrekking hebben op 2 sub thema's: algemene rehabilitatiemethoden en sociale/cognitieve training als "add on".

Voor wonen is gezocht op de thesaurustermen DE "Housing" OR DE "Assisted Living" OR DE "Residential Care Institutions" OR DE "Independent Living Programs" OR DE "Living Arrangements" OR DE "Shelters" OR DE "Halfway Houses".

Voor sociale contacten is gezocht op de thesaurustermen DE "Online Social Networks" OR DE "Social Interaction" OR DE "Social Skills" OR DE "Social Skills Training" OR DE "Social Support" OR DE "Family Relations" OR DE "Significant Others" OR DE "Social Networks" OR DE "Social Isolation" OR DE "Support Groups" OR DE "Twelve Step Programs" OR DE "Peer Relations" OR DE "Social Capital" OR DE "Interpersonal Relationships" OR DE "Marital Relations" OR DE "Therapeutic Social Clubs".

Voor werk is gezocht op de thesaurustermen DE "Quality of Work Life" OR DE "Rehabilitation" or DE "Psychosocial Rehabilitation" OR DE "Vocational Rehabilitation" or DE "Supported Employment" or DE "Vocational Evaluation" or DE "Work Adjustment Training" OR DE "Job Performance".

Voor leren/opleiding is gezocht op de thesaurustermen DE "Education" OR DE "Educational Programs" OR DE "Learning".

Voor stigma is gezocht op de thesaurustermen DE "Social Acceptance" OR DE "Social Deprivation" or DE "Social Isolation" or DE "Social Discrimination" or DE "Stigma" or DE "Stereotyped Attitudes" or DE "Community Involvement" OR DE "Social Integration" OR DE "Prejudice".

Voor dagelijks leven is gezocht op de thesaurustermen DE "Leisure Time" OR DE "Recreation" OR DE "Occupational Therapy" OR DE "Activities of Daily Living".

Voor algemene rehabilitatie benaderingen is gezocht op thesaurustermen DE "Rehabilitation" OR DE "Psychosocial Rehabilitation" OR DE "Social Integration" OR DE "Psychosocial Readjustment".

Voor sociale/cognitieve training als “add on” is gezocht op thesaurustermen DE "Social Skills Training" OR DE "Cognitive Rehabilitation" OR DE "Cognitive Mediation" OR DE "Cognitive Therapy" OR DE "Cognitive Behavior Therapy" OR DE "Cognitive Techniques".

Deze thesaurustermen zijn aangevuld met woorden in titel en keyword: "supported education" OR "supported housing" or "supported living" or "individual placement and support" or leisure or recreation* or "social context" or "social relation*" OR “social interaction*” OR “social network*” OR “social skill*” or befriending or "social capital" or “interpersonal relation*” or "community support" or “social support” OR "skills training" OR "boston university approach" OR “participation” OR “reintegration” OR “integration” OR "strength* model" OR “readjustment” OR “housing first" OR "fountainhouse model" OR “residential care” OR stigma* OR anti-stigma OR self-stigma OR “social integration” OR “social acceptance” OR “social deprivation” OR “social isolation” OR “social discrimination” OR “stereotyp*” OR “community involvement” OR “community integration” OR "supported employment" OR "social support*" OR vocational OR occupational OR "peer support" OR "support group*" OR "twelve step" OR “peer relation*” or housing OR “assisted living” OR “activities of daily living” OR rehabilitation OR “therapeutic social club*” OR “work adjustment” OR “education*” OR “significant other*” OR “family relation*” OR “marital relation*” OR “halfway house*” OR “half way house*” OR “psychosocial deprivation” OR “social environment” OR “selfhelp groups” OR “self help groups” OR “independent living” OR prejudice OR "social enterprise*" OR "social inclusion" OR "social skills training" OR "social skills intervention*" OR "cognitive behavior* therapy" OR "cognitive therapy" OR "cognitive mediation" OR "cognitive remediation" OR "cognitive rehabilitation" OR "cognitive training" OR "cognitive enhancement*" OR "cognitive psychotherapy" OR "cognitive behaviour therapy" OR "cogntive behavioural therapy" OR "cognitive skills interventions" OR "cognitive skills training" OR "cognitive skills program".

PubMed

De termen voor de doelgroep:
In PubMed is gezocht op de volgende thesaurustermen voor schizofrenie/psychose: "Psychotic Disorders"[Mesh:NoExp] OR "Schizophrenia"[Mesh] OR "Hallucinations"[Mesh] OR "Delusions"[Mesh].

Deze termen zijn aangevuld met "severe mental ill" OR "severe mental disorder" OR "severe mentally ill" OR "severe mental disorders" OR "severe mental illness" OR "severe mental illnesses" OR psychotic OR psychosis OR psychoses OR schizophrenia OR schizophrenic OR "delusional disorder" in de velden titel, abstract en other term.

Om aan te geven dat het om een ‘vroege’ psychose moet gaan, is er een combinatie gemaakt met dezelfde woorden die gebruikt zijn in PsycInfo. In PubMed zijn ze gezocht in het titel, abstract en ‘other term’ veld.

Verder is gezocht op de thesaurusterm "Schizophrenia, Childhood"[Mesh] en "childhood onset schizophrenia" in titel, abstract en other term veld. Ook is specifiek gezocht op de zoektermen "early psychosis" OR "first episode psychosis" OR "early psychoses" OR "first episode psychoses" in het titel, abstract en other term veld.

De termen voor de leefgebieden en sub thema's:

Voor wonen is gezocht op de thesaurustermen Assisted Living Facilities"[Mesh] OR "Residential Facilities"[Mesh:NoExp] OR "Halfway Houses"[Mesh] OR "Housing"[Mesh] OR "Independent Living"[Mesh] OR "Residence Characteristics"[Mesh].

Voor sociale contacten is gezocht op de thesaurustermen "Interpersonal Relations"[Mesh:NoExp] OR "Social Support"[Mesh] OR "Social Environment"[Mesh] OR "Community Networks"[Mesh] OR "Family Relations"[Mesh:NoExp] OR "Social Isolation"[Mesh:NoExp] OR "Self-Help Groups"[Mesh:NoExp] OR "Peer Group"[Mesh].

Voor werk is gezocht op de thesaurustermen "Rehabilitation"[Mesh:NoExp] OR "Rehabilitation, Vocational"[Mesh]OR "Employment, Supported"[Mesh].

Voor leren/opleiding is gezocht op de thesaurustermen "Education"[Mesh:NoExp] OR "Learning"[Mesh:NoExp].

Voor stigma is gezocht op de thesaurustermen "Stereotyping"[Mesh] OR "Prejudice"[Mesh] OR "Social Distance"[Mesh] OR "Social Isolation"[Mesh] OR "Social Stigma"[Mesh] OR "Social Discrimination"[Mesh:NoExp] OR "Community Integration"[Mesh] OR "Social Adjustment"[Mesh] OR "Psychosocial Deprivation"[Mesh].

Voor dagelijks leven is gezocht op de thesaurustermen "Occupational Therapy"[Mesh] OR "Leisure Activities"[Mesh:NoExp] OR "Recreation"[Mesh:NoExp] OR "Activities of Daily Living"[Mesh].

Voor algemene rehabilitatiemethoden is gezocht op de thesaurusterm "Rehabilitation"[Mesh:NoExp] OR "Community Integration"[Mesh: NoExp].

Voor sociale/cognitieve training als "add on" is gezocht op thesaurustermen "Cognitive Therapy"[Mesh:NoExp]

Deze thesaurustermen zijn aangevuld met woorden in titel en 'other terms':
"supported education" OR "supported housing" or "supported living" OR "individual placement and support" OR leisure OR recreation* OR "social context" OR "social relation*" OR "social interaction" OR "social interactions" OR "social network" OR social networks OR "social skill" OR "social skills" OR befriending OR "social capital" OR "interpersonal relation" OR "interpersonal relations" OR "interpersonal relationship" OR "interpersonal relationships" OR "community support" OR "social support" OR "skills training" OR "participation" OR "reintegration" OR "integration" OR "strength model" OR "strengths model" OR "Boston University Approach" OR "readjustment" OR "rehabilitation" OR "housing first" OR "fountainhouse model" OR "residential care" OR stigma OR stigmatising OR stigmatization OR stigmatisation OR anti-stigma OR self-stigma OR "social integration" OR "social acceptance" OR "social deprivation" OR "social isolation" OR "social discrimination" OR stereotype OR stereotypes OR stereotyping OR "community involvement" OR "community integration" OR "supported employment" OR "social support" OR vocational OR occupational OR "peer support" OR "support group" OR "support groups" OR "twelve step" OR "peer relation" OR "peer relations" OR "peer relationship" OR "peer relationships" OR housing OR "assisted living" OR "activities of daily living" OR "therapeutic social club" OR "therapeutic social clubs" OR "work adjustment" OR "education" OR educational OR "significant other" OR "significant others" OR "family relation" OR "family relations" OR "marital relation" OR "marital relations" OR "halfway house" OR "halfway houses" OR "half way house" OR

“half way houses” OR “psychosocial deprivation” OR “social environment” OR “selfhelp groups” OR “self help groups” OR “independent living” OR prejudice OR "social enterprise*" OR "social inclusion" OR "social skills training" OR "social skills intervention" OR "social skills training" OR "social skills interventions" OR “cognitive behavioural therapy” OR "cognitive therapy" OR "cognitive mediation" OR "cognitive remediation" OR "cognitive rehabilitation" OR "cognitive training" OR "cognitive enhancement" OR "cognitive enhancements" OR "cognitive skills intervention" OR "cognitive skills interventions" OR "cognitive skills training" OR "cognitive skills program" OR "cognitive skills learning" OR "cognitive psychotherapy" OR “cognitive rehabilitation” OR “cognitive techniques”.

CINAHL

De termen voor de doelgroep:

In CINAHL is gezocht op de thesaurusterm MH "Schizophrenia, Childhood" en "childhood onset schizophrenia" OR "acute schizophrenia" OR "acute phase" AND schizophrenia in het titelveld. De algemene thesaurustermen voor schizofrenie/psychose: MH "Schizoaffective Disorder" OR MH "Schizophrenia" OR MH "Delusions" OR MH "Hallucinations" OR MH "Psychotic Disorders" zijn gecombineerd met "delusional disorder*" OR severe mental ill* OR severe mental disorder* OR psychotic OR psychosis OR psychoses OR schizo* in het titelveld.

Al deze zoektermen zijn vervolgens gecombineerd met "early symptom*" OR onset OR "early signs" OR first-episode OR "acute phase" in het titelveld, om aan te geven dat het om een ‘vroege’ psychose moet gaan.

Ook is specifiek gezocht op de zoektermen "early psychosis" OR "first episode psychosis" OR "early psychoses" OR "first episode psychoses" in het titelveld.

De termen voor de leefgebieden en subthema’s:

Voor wonen is gezocht op de thesaurustermen MH "Assisted Living" OR MH "Residential Facilities" OR MH "Halfway Houses" OR MH "Housing" OR MH "Community Living" OR MH "Residence Characteristics".

Voor sociale contacten is gezocht op de thesaurustermen MH "Interpersonal Relations" OR MH "Social Support Iowa NOC" OR MH "Support, Psychosocial" OR MH "Social Environment" OR MH "Community Networks" OR MH "Family Relations" OR MH "Social Isolation" OR MH "Support Groups" OR MH "Peer Group" OR MH "Social Networks" OR MH "Social Capital" OR MH "Social Skills" OR MH "Social Skills Training" OR MH "Significant Other".

Voor werk is gezocht op de thesaurustermen MH "Rehabilitation" OR MH "Rehabilitation, Vocational" OR MH "Employment, Supported" OR MH "Rehabilitation, Psychosocial" OR MH "Community Reintegration" OR MH "Quality of Working Life" OR MH "Job Re-Entry" OR MH "Job Performance".

Voor leren/opleiding is gezocht op de thesaurustermen MH "Education" OR MH "Learning".

Voor stigma is gezocht op de thesaurustermen MH "Stigma" OR MH "Stereotyping" OR MH "Prejudice" OR MH "Social Isolation" OR MH "Community Reintegration" OR MH "Social Adjustment" OR MH "Psychosocial Deprivation".

Voor dagelijks leven is gezocht op de thesaurustermen MH "Occupational Therapy" OR MH "Leisure Activities" OR MH "Recreation" OR MH "Activities of Daily Living".

Voor algemene rehabilitatiemethoden is gezocht op de thesaurustermen MH "Rehabilitation" OR MH "Rehabilitation, Psychosocial" (zie ook boven).

Voor sociale/cognitieve training als “add on” is gezocht op thesaurustermen MH "Social Skills Training" OR MH "Cognitive Therapy".

Deze thesaurustermen zijn aangevuld met woorden in titel. Hiervoor zijn dezelfde woorden gebruikt als in PubMed.

Totaal resultaat uit de volledige search:

Systematic reviews en meta-analyses
In totaal zijn in PubMed 36 systematic reviews en meta-analyses gevonden, in PsycInfo 5 en in CINAHL 2. Dit zijn er in totaal: 43. Deze titels zijn ontdubbeld en er zijn 2 dubbele titels verwijderd. Er blijven dan 41 titels over.

Randomised Controlled Trials
In totaal zijn in PubMed 177 RCT’s gevonden, in PsycInfo 78 en in CINAHL 11.
Dit zijn er in totaal 266. Deze titels zijn ontdubbeld en er zijn 58 dubbele verwijderd. Er blijven dan 208 titels over.

Overige studietypes
Op de overige geselecteerde studietypes bleven in PubMed 55 titels over, in PsycInfo 436 en in CINAHL 117. In CINAHL is geen verdere limitering op studietype gedaan om zo ook de specifieke verpleegkundige literatuur mee te nemen in de search. In totaal 608 titels. Na ontdubbeling en het verwijderen van 57 dubbele titels blijven er 551 titels over.

Bijlage 8.C Overzicht geëxcludeerde studies (obv full text)

RCT's + non-RCT's met controle groep

(Domein: 1.werk; 2.leren; 3.wonen; 4.dagbesteding/vrije tijd; 5.sociale contacten; 6.zelf-stigma; 7.cogn/sociale skills als add on); 8.rehab algemeen)

	Auteurs	Titel	Commentaar
	Domein werk & leren		
1	Downing, 2006	Downing DT. The impact of early psychosis on learning: supported education for teens and young adults. *OT Practice 2006; 11(12):7-10.*	
2	Lauber, 2009	Individual placement and support improves employment of young people with first episode psychosis.	Is sub-analyse van Killackey, 2008
3	Killackey 2015	Wanneer gaat resultaatartikel van methode beschrijving (2013) volgen?	Gemaild: Wanneer gaat follow up verschijnen?
4	Nuechterlein, submitted (*auteur is gemaild; niet gereageerd)*	Successful return to work or school after a first episode of schizophrenia: the UCLA randomized controlled trial of IPS and workplace fundamentals module training.	Hand search (Bond, 2014) Was submitted toen Bond, 2014 was accepted. Cross-sectional series
5	Baksheev, 2012	Predictors of vocational recovery among young people with first-episode psychosis: Findings from a randomized controlled trial.	Secundaire analyse van Killackey, 2008 Gaat over voorspellers
6	Graig, 2014	Vocational rehabilitation in early psychosis: Cluster randomised trial.	IPS, maar alleen vergelijk met en zonder motivational interviewing "to adress ambivalence" bij professionals.
7	Killackey, 2013	A randomized controlled trial of vocational intervention for young people with first-episode psychosis: Method.	Beschrijving method. Gemaild wanneer follow up resultaten volgen
8	Rinaldi, 2010	The Individual Placement and Support approach to vocational rehabilitation for young people with first episode psychosis in the UK	Geen controle groep
9	Rinaldi, 2004	Rinaldi M, McNeil K, Firn M, Koletsi M, Perkins R, Singh SP. What are the benefits of evidence-based supported employment for patients with first-episode psychosis? *Psychiatric Bulletin 2004; 28(8):281-284.*	Geen controle groep.
10	Linszen, 1996		Doelgroep schizofrenie
	Domein 3. Wonen		

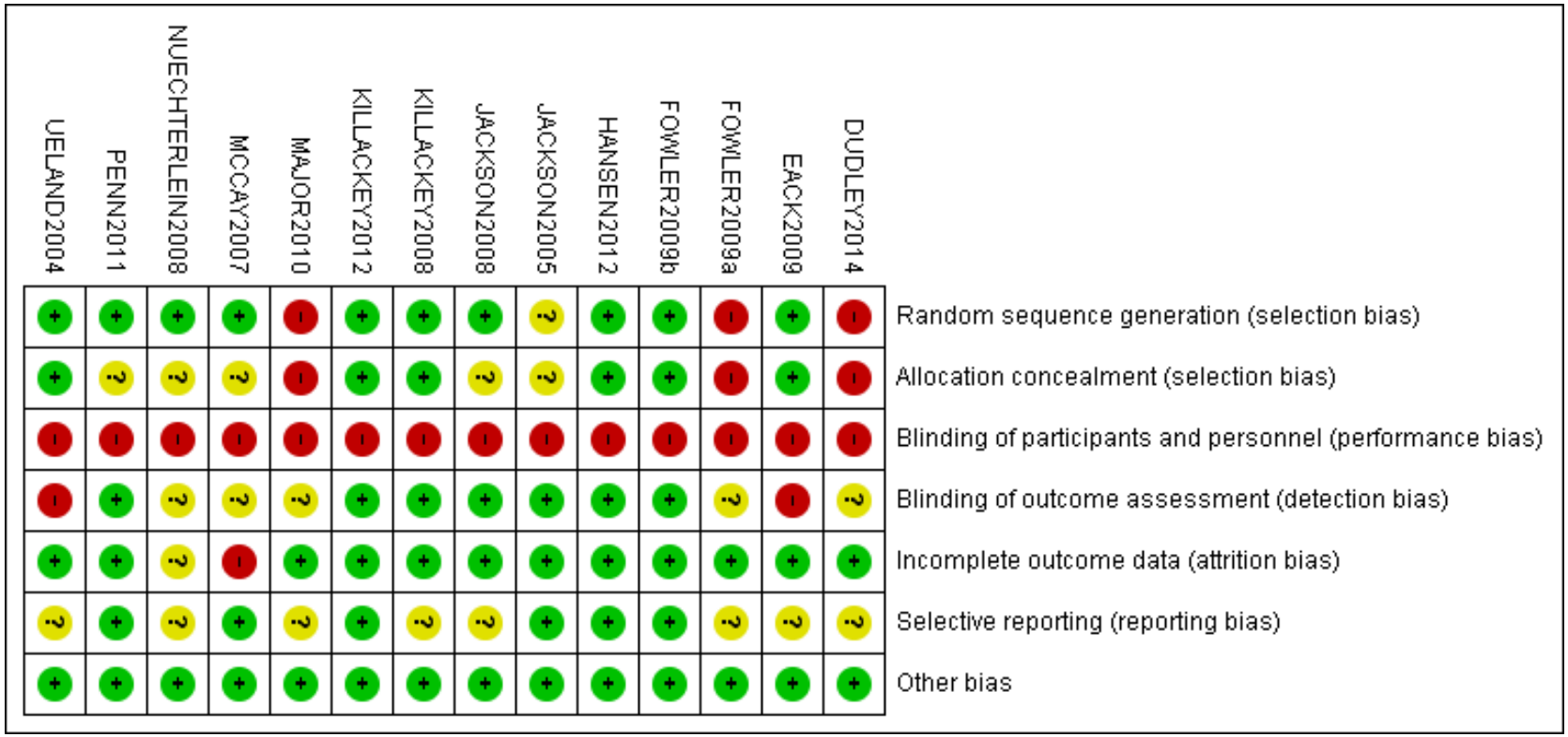
1	Mosher, 1995	The treatment of acute psychosis without neuroleptics: six-week psychopathology outcome data from The Soteria Project.	Wonen? Nee: effect van minimal antipsychotics
	Domein 4. Vrije tijd / dagbesteding		
-	Geen studie geëxcludeerd obv full text		
	Domein 5. Sociale contacten		
1	Thorup, 2006 > (zie ook PETERSEN 2005)	Social network among young adults with first-episode schizophrenia spectrum disorders: results from the Danish OPUS trial. *Soc Psychiatry Psychiatr Epidemiol 2006; 41(10):761-770*	OPUS: org van zorg
2	Kauranen, 2000	Akuutin psykoosipotilaan sosiaalinen verkosto ja sen muutos verkostokeskeisess+ñ hoidossa. = The change of social network of first episode psychotic patients in a network oriented treatment. *Psykologia 2000; 35(5):403-415.*	Design artikel? Artikel zelf is in het Fins
3	Tempier, 2012	Does assertive community outreach improve social support? Results from the Lambeth Study of early-episode psychosis **(LEO).**	LEO: org van zorg
4	Petersen, 2005	A randomised multicentre trial of integrated versus standard treatment for patients with a first episode of psychotic illness. *BMJ 2005; 331(7517):602.*	OPUS: effect op positive and negeative symptoms
5	Robinson, 2010 *(auteur gemaild wanneer resultaten beschikbaar)*	Study protocol: The development of a pilot study employing a randomised controlled design to investigate the feasibility and effects of a peer support program following discharge from a specialist first-episode psychosis treatment centre	Is design artikel
6	Gleeson, 2014	Safety and privacy outcomes from a moderated online social therapy for young people with first-episode psychosis.	Exclusie: geen controlegroep
7	Waghorn, 2014	A multi-site randomised controlled trial of evidence-based supported employment for adults with severe and persistent mental illness.	Exclusie doelgroep: inclusive criterium van studie: not be in an acute phase of illness
8	Robinson, 2010	Study protocol: The development of a pilot study employing a randomised controlled design to investigate the feasibility and effects of a peer support program following discharge from a specialist first-episode psychosis treatment centre.	Is design artikel
	Domein 6. Zelf-stigma		

1	Janssen, 2003	Janssen I, Hanssen M, Bak M, Bijl RV, De Graaf R, Vollebergh W et al. Discrimination and delusional ideation. *The British Journal of Psychiatry 2003; 182(1):71-76.*	Percieved discrimination is vorm van self-stigma? **Maar: geen interventie**
	Domein 7. Cogn en sociale vaardigheden als add on (inclusief CRT)		
1	Lee, 2013	Cognitive remediation improves memory and psychosocial functioning in first-episode psychiatric out-patients. *Psychological Medicine; 2013; 43(6): 1161-1173.*	P: first episode psychose (61,5/63%) en depressie (38,5/37%) Gecorrigeerd voor diagnose) I: CRT + TAU (geen add on) C: TAU O: functioning outcome: SFS **(**one of primary outcomes)
2	Ostergaard, 2014	CRT combined with an early intervention service in FEP.	P: FEP I: CRT + EIS (is hier TAU- geen add on) C: EIS alone O: primary outcome is functional capacity
3	Urben, 2012	Computer-assisted cognitive remediation in adolescents with psychosis or at risk for psychosis: a 6-month follow-up. (+ zie Holzer, submitted): A RCT of effectiveness of a computer-assisted cognitive remediation (CACR) program in adolescents with psychosis or at high risk of psychosis.	P: adolescent psychosis (65%) or UHR I: CRT + TAU (geen "add on") C: computer games + TAU O: SOFAS + employment activities
4	Nahum, 2014	A novel, online social cognitive training program for young adults with schizophrenia: a pilot study. *Schizophrenia Res Cogn; 2014; 1(1); e11-e19.*	P: young adults with schizophrenia I: Social cogn training (SocialVille) no add on C: healthy controls O: maten op social cognition en social functioning (alleen in exp groep)
5	Vesterager, 2011	Cognitive training plus a comprehensive psychosocial programme (OPUS) versus the comprehensive psychosocial programme alone for patients with first-episode schizophrenia (the NEUROCOM trial): a study protocol for a centrally randomised, observer-blinded multi-centre clinical trial.	Study protocol Resultaten al bekend > Is Ostergaard, 2014 (zie boven)
6	Puig, 2014	CRT in adolescents with early onset schizophrenia: a RCT *Journal of the American Academy of Child & Adolescent Psychiatry 2014; 53(8):859-868.*	P: adolescents with EOS I: CRT + TAU (geen add on) C: TAU

			O: Wel functioning outcomes (LSP, VABS, GAS), maar als secondary outcomes
7	Drake, 2013	A naturalistic, randomized, controlled trial combining cognitive remediation with cognitive–behavioural therapy after *first*-episode non-affective psychosis	P: FEP I: CRT als add on bij CBT C: O: duur van CBT sessie, geen functioning outcomes
8	Kidd, 2012	Cognitive Remediation in a Supported Education Setting	Geen controle groep
9	Eack, 2011	Effects of cognitive engancement therapy on employment outcomes in early schizophrenia: results from a 2 year randomized trial.	P: early course schizophrenia (dur ill: 3.19 j) I: CET=CRT + social cogn group sessions C: EST (supportive therapy) O: mechanisms of improvement
10	Bartholomeusz, 2013	Social cognition training as an intervention for improving functional outcome in first Episode psychosis: A feasibility study.	Geen controle groep Kleine n, maar wel ook effect gemeten
11	Wykes, 2007	CRT for young early onset patients with schizophrenia: an exploratory rct	-alleen gericht op improving cognitive functions (geen functioning outcomes)
12	Twamley et al, 2008	Development and pilot testing of a novel compensatory cognitive training intervention for people with psychosis	P: chronically ill (psychosis) I: CRT + pharmacotherapy C: pharmacotherapy alone O: ook functional outcomes
13	Lopez-Luengo, 2005	Effects of a neuropsychological rehabilitation programme on schizophrenic patients' subjective perception of improvement.	P: stable schizophrenia I: CRT C: TAU O: perceived impr, niet gericht op daadw maatschappelijke participatie
	Domein 8. Algemene rehabilitatie		
1	Nordentoft, 2010 (TWIJFEL I en O)	Deinstitutionalization revisited: A 5-year follow-up of a randomized clinical trial of hospital-based rehabilitation versus specialized assertive intervention (OPUS) versus standard treatment for patients with first-episode schizophrenia spectrum disorders.	P: FEP I: hospital-based rehab C1: OPUS / C2: standard care

			O: use of psychiatric bed days + days in supported housing
2	Jackson, 2008	Acute phase and 1-year follow-up results of a randomized controlled trial of CBT versus befriending for first-episode psychosis: **The ACE project.**	Exclusie: CBT voor herstel, maar is geen rehab vorm, toch echt CBT
3	Uzenoff, 2008	Uzenoff SR, Perkins DO, Hamer RM, Wiesen CA, Penn DL. A preliminary trial of adherence-coping-education (**ACE) therapy** for early psychosis. *J Nerv Ment Dis 2008; 196(7):572-575.*	CBT voor herstel ACE includeren; nee, zie Jackson, 2008.
4	Nordentoft, 2006 *(via IBL opgevraagd)*	OPUS: a randomised multicenter trial of integrated versus standard treatment for patients with a first-episode psychosis--secondary publication	OPUS: Social skill training als add on? Nee, is vast onderdeel van integrated treatment.
5	Li x, 2002 *(Via IBL opgevraagd)*	Effects of social rehabilitation on late-onset schizophrenia.	Rehab (doelgroep?) In Chinees; kunnen niet lezen
6	Min Q, 2001 *(via IBL opgevraagd)*	Early rehabilitation of schizophrenics.	Rehab. Design? In Chinees: kunnen niet lezen
7	Zaytseva, 2010	Zaytseva Y, Gurovich IY, Shmukler A. Effectiveness of the integrated long-term program of management of patients after first psychotic episode in 5-year follow-up. *Psychiatr Danub 2010; 22 Suppl 1:S92-S94.*	P: FEP I: EIS (med, psych treatment, case man, MD team) C: routine care O: symptoms, relapse, unemployability, social status
8	Lloyd, 2000	Lloyd C, Bassett J, Samra P. Rehabilitation Programmes for Early Psychosis. *British Journal of Occupational Therapy 2000; 63(2):76-82.*	Paper describes a model of care and best practice in FEP (no effect)

Bijlage 8.D Risk of Bias (RoB) – Maatschappelijke participatie



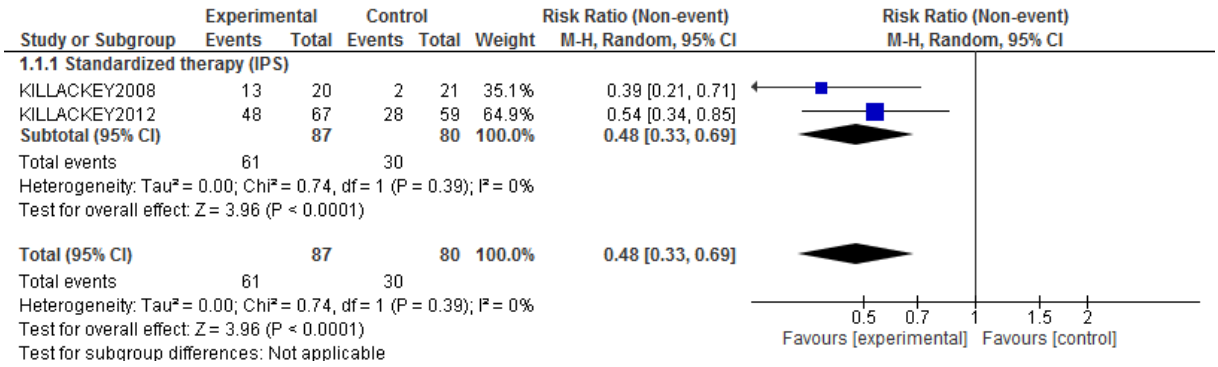
Bijlage 8.E Forest plots Maatschappelijke participatie – nov 2015

Onderstaand volgen Forest plots voor 3 vergelijkingen:

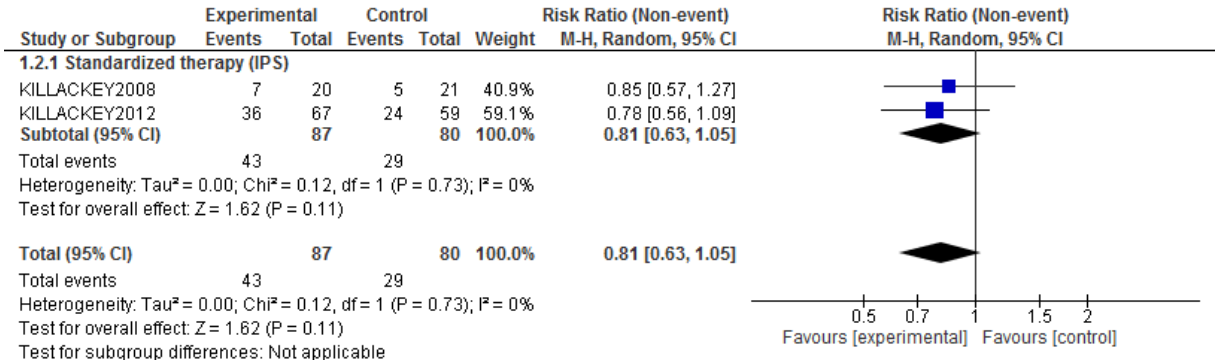
1. *Vocational therapy vs. TAU*
2. *Recovery CBT vs. TAU*
3. *Recovery CBT vs. befriending*

Vergelijking 1. Vocational therapy vs. TAU

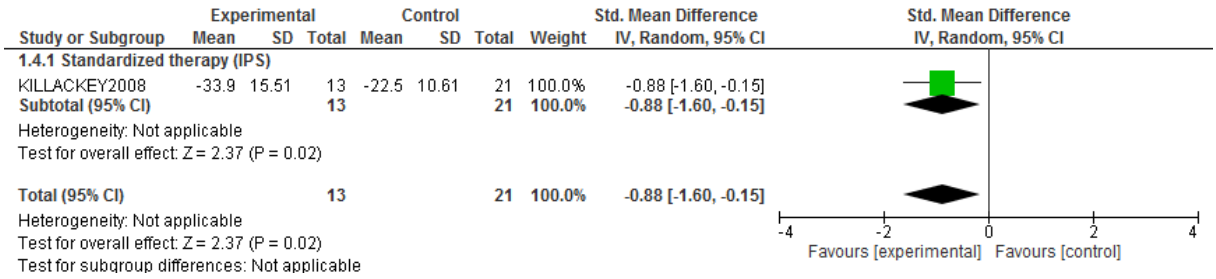
1.1 Employed (number) PT



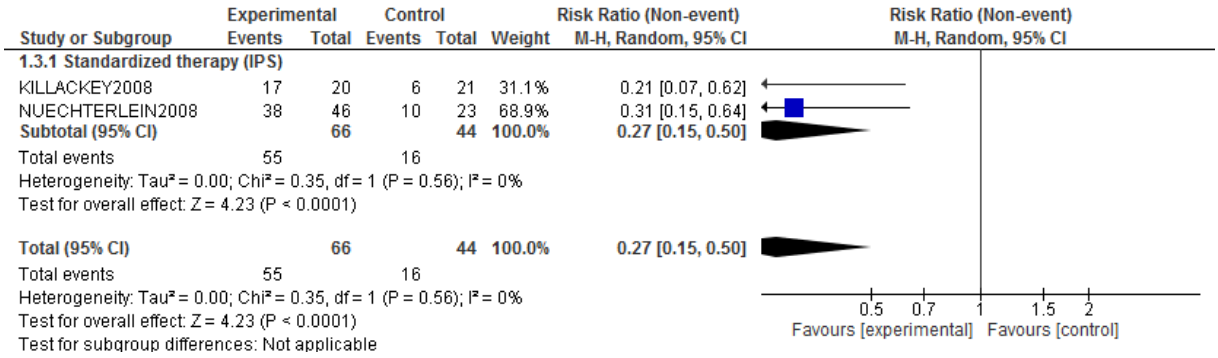
1.2 Enrolled in education (number) PT



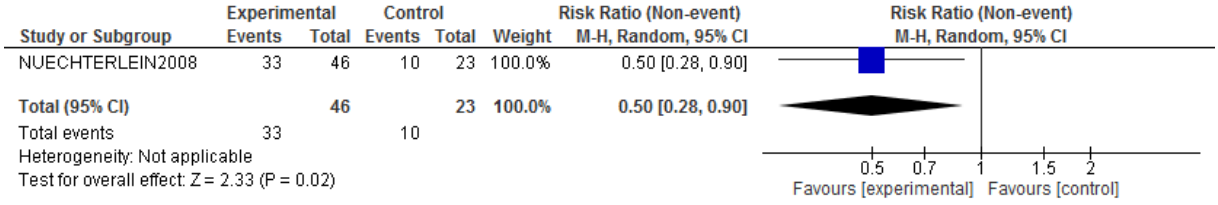
1.3 Employed (hours per week) PT



1.4 Employed or enrolled in education (number) PT – 26 weken

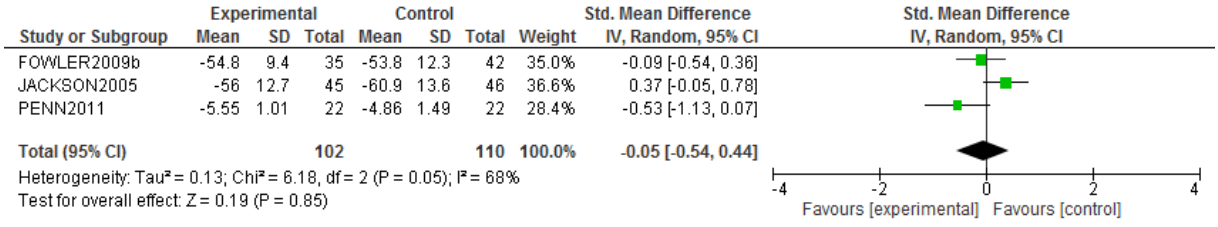


1.5 Employed or enrolled in education (number) FU - 78 weken

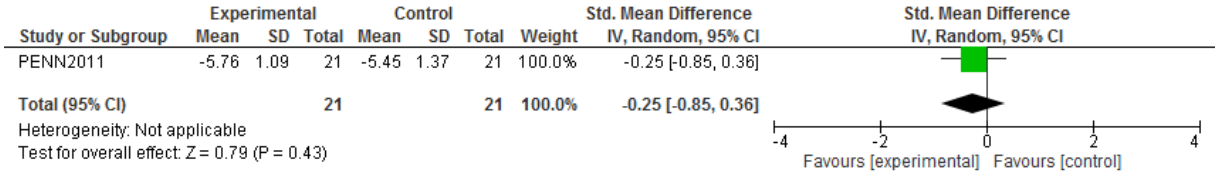


Vergelijking 2. Recovery CBT vs. TAU

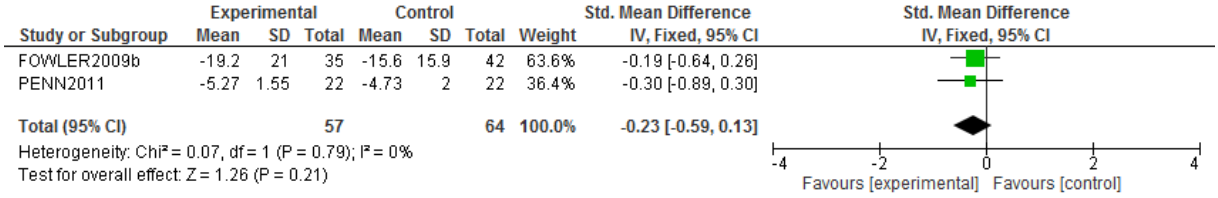
2.1 Social functioning (PT)



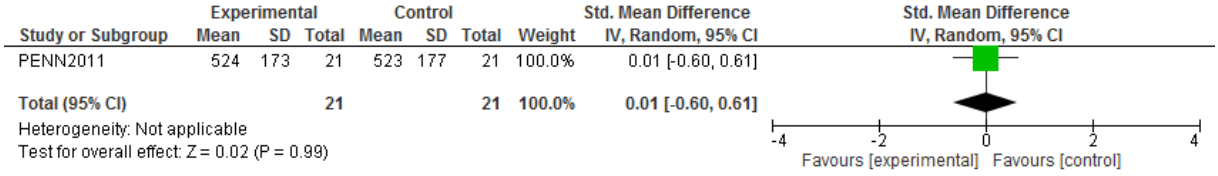
2.2 Social functioning (FU)



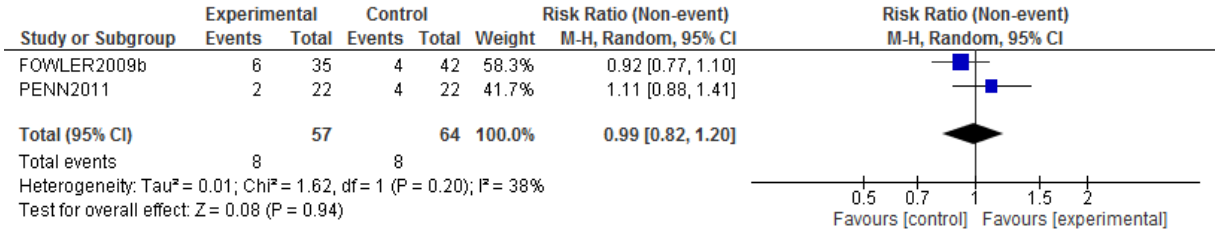
2.3 Constructive economic activity, including vocational & educational functioning (PT)



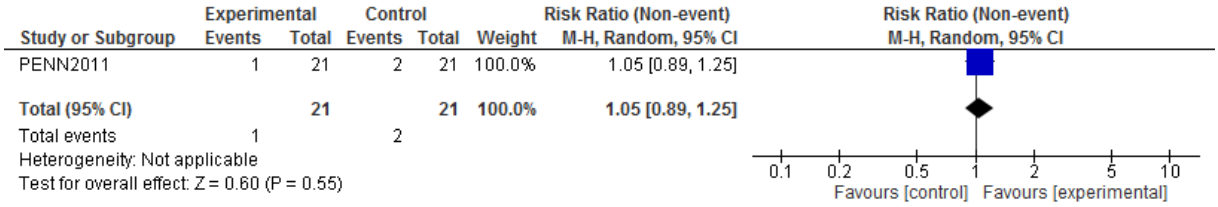
2.4 Constructive economic activity, including vocational & educational functioning (FU)



2.5 Hospitalization (number admitted) - PT



2.6 Hospitalization (number admitted) – FU

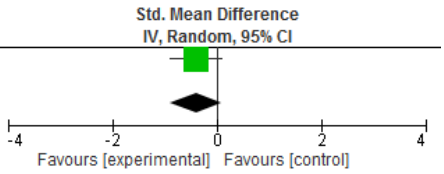


Vergelijking 3. Recovery CBT vs. befriending

3.1 Social functioning (PT)

Study or Subgroup	Experimental Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
JACKSON2008	-62.69	13.81	31	-57.6	11.37	31	100.0%	-0.40 [-0.90, 0.11]
Total (95% CI)			**31**			**31**	**100.0%**	**-0.40 [-0.90, 0.11]**

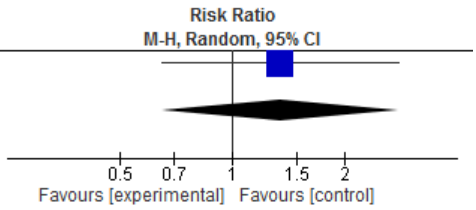
Heterogeneity: Not applicable
Test for overall effect: Z = 1.55 (P = 0.12)



3.2 Hospitalization (number admitted) (FU 52 weken)

Study or Subgroup	Experimental Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
JACKSON2008	12	30	8	27	100.0%	1.35 [0.65, 2.80]
Total (95% CI)		**30**		**27**	**100.0%**	**1.35 [0.65, 2.80]**
Total events	12		8			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.81 (P = 0.42)



Bijlage 8.F GRADE profielen – Maatschappelijke particpatie

Question: Vocational therapy (IPS) vs TAU for [Early psychosis]

Bibliography: . [Vocational therapy (IPS)] for [Early psychosis]. Cochrane Database of Systematic Reviews [Year], Issue [Issue].

Quality assessment							Summary of Findings			
Participants (studies) Follow up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall quality of evidence	Study event rates (%)		Relative effect (95% CI)	Anticipated absolute effects	
							With TAU	With Vocational therapy (IPS)		Risk with TAU	Risk difference with Vocational therapy (95% CI)
Employed (number) PT 26 weken - Standardized therapy (IPS) (CRITICAL OUTCOME)											
167 (2 studies)	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[1]	undetected	⨁⨁⨁⊖ **MODERATE**[1] due to imprecision	30/80 (37.5%)	61/87 (70.1%)	**RR 0.48** (0.33 to 0.69)	**Study population**	
										375 per 1000	**195 fewer per 1000** (from 116 fewer to 251 fewer)
										Moderate	
										285 per 1000	**148 fewer per 1000** (from 88 fewer to 191 fewer)
Enrolled in education (number) PT 26 weken - Standardized therapy (IPS) (CRITICAL OUTCOME)											
167 (2 studies)	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	undetected	⨁⨁⨁⊖ **MODERATE**[2] due to imprecision	29/80 (36.3%)	43/87 (49.4%)	**RR 0.81** (0.63 to 1.05)	**Study population**	
										362 per 1000	**69 fewer per 1000** (from 134 fewer to 18 more)
										Moderate	
										322 per 1000	**61 fewer per 1000** (from 119 fewer to 16 more)
Employed, hours per week PT 26 weken - Standardized therapy (IPS) (CRITICAL OUTCOME; Better indicated by lower values)											
34 (1 study)	no serious	no serious inconsistency	no serious indirectness	very serious[3]	undetected	⨁⨁⊖⊖ **LOW**[3]	21	13	-		The mean employed, hours per

	risk of bias					due to imprecision				week pt 26 weken - standardized therapy (ips) in the intervention groups was **0.88 standard deviations lower** (1.6 to 0.15 lower)
Employed or enrolled (number) PT 26 weken - Standardized therapy (IPS) (CRITICAL OUTCOME)										
110 (2 studies)	serious [4]	no serious inconsistency	no serious indirectness	serious[5]	undetected	⨁⨁⨀⨀ **LOW**[4,5] due to risk of bias, imprecision	16/44 (36.4%)	55/66 (83.3%)	**RR 0.27** (0.15 to 0.5)	**Study population**
										364 per 1000	**265 fewer per 1000** (from 182 fewer to 309 fewer)
										Moderate	
										360 per 1000	**263 fewer per 1000** (from 180 fewer to 306 fewer)
Employed or enrolled (number) FU - 78 weken (CRITICAL OUTCOME)										
69 (1 study)	serious [6]	no serious inconsistency	no serious indirectness	very serious[7]	undetected	⨁⨀⨀⨀ **VERY LOW**[6,7] due to risk of bias, imprecision	10/23 (43.5%)	33/46 (71.7%)	**RR 0.5** (0.28 to 0.9)	**Study population**
										435 per 1000	**217 fewer per 1000** (from 43 fewer to 313 fewer)
										Moderate	
										435 per 1000	**218 fewer per 1000** (from 44 fewer to 313 fewer)

[1] Optimal information size for dichotomous measure was not met (<300 events)

[2] Optimal information size for dichotomous measure was not met (<300 events)

[3] 2x downgrade - Optimal information size for continuous measure was not met

[4] Risk of Bias is unsure for Nuechterlein2008

[5] Optimal information size for dichotomous measure was not met (<300 events)

[6] Risk of Bias is unsure for Nuechterlein2008

[7] 2x downgrade – Optimal information size for dichotomous measure was not met (<50 events)

Question: Recovery CBT vs TAU for [Early psychosis]

Bibliography: . [Recovery CBT] for [Early psychosis]. Cochrane Database of Systematic Reviews [Year], Issue [Issue].

Quality assessment							**Summary of Findings**				
Participants (studies) Follow up	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Publication bias**	**Overall quality of evidence**	**Study event rates (%)**		**Relative effect** (95% CI)	**Anticipated absolute effects**	
							With TAU	**With Recovery CBT**		**Risk with TAU**	**Risk difference with Recovery CBT** (95% CI)
Social functioning PT (CRITICAL OUTCOME; measured with: Questionnaires[1]; Better indicated by lower values)											
212 (3 studies)	no serious risk of bias	serious[2]	no serious indirectness	serious[3]	undetected	⨁⨁⨀⨀ **LOW**[2,3] due to inconsistency, imprecision	110	102	-		The mean social functioning pt in the intervention groups was **0.05 standard deviations lower** (0.54 lower to 0.44 higher)
Social functioning (FU - 37 weken) (CRITICAL OUTCOME; measured with: Questionnaire; Better indicated by lower values)											
42 (1 study)	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[4]	undetected	⨁⨁⨀⨀ **LOW**[4] due to imprecision	21	21	-		The mean social functioning (fu - 37 weken) in the intervention groups was **0.25 standard deviations lower** (0.85 lower to 0.36 higher)

Constructive economic activity, including vocational & educational functioning PT (CRITICAL OUTCOME; measured with: Continuous measure[5]; Better indicated by lower values)										
121 (2 studies) 24-39 weken	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[6]	undetected	⨁⨁⨁⊖ **MODERATE**[6] due to imprecision	64	57	-	The mean constructive economic activity, including vocational & educational functioning pt in the intervention groups was **0.23 standard deviations lower** (0.59 lower to 0.13 higher)
Constructive economic activity, including vocational & educational functioning FU (CRITICAL OUTCOME; measured with: Contonuous measure[7]; Better indicated by lower values)										
42 (1 study) 37 weken	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[8]	undetected	⨁⨁⊖⊖ **LOW**[8] due to imprecision	21	21	-	The mean constructive economic activity, including vocational & educational functioning fu in the intervention groups was **0.01 standard deviations higher** (0.6 lower to 0.61 higher)
Hospitalisation (number admitted) PT (CRITICAL OUTCOME; assessed with: Number admitted)										
										Study population

121 (2 studies)	no serious risk of bias	no serious inconsistency [9]	no serious indirectness	very serious[10]	undetected	⨁⨁⨀⨀ **LOW**[9,10] due to imprecision	8/64 (12.5%)	8/57 (14%)	**RR 0.99** (0.82 to 1.2)	**125 per 1000**	**1 fewer per 1000** (from 23 fewer to 25 more)
										Moderate	
										139 per 1000	**1 fewer per 1000** (from 25 fewer to 28 more)
Hospitalisation (number admitted) - FU (CRITICAL OUTCOME; assessed with: Number admitted)											
42 (1 study) 37 weken	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[11]	undetected	⨁⨁⨀⨀ **LOW**[11] due to imprecision	2/21 (9.5%)	1/21 (4.8%)	**RR 1.05** (0.89 to 1.25)	**Study population**	
										95 per 1000	**5 more per 1000** (from 10 fewer to 24 more)
										Moderate	
										95 per 1000	**5 more per 1000** (from 10 fewer to 24 more)

[1] Social and Occupational Functioning Assessment (SOFAS-2x), Role Functioning Scale - subscale Social Network (RFS - 1x)

[2] Statistical heterogenity (I2 > 50%, p<0,1)

[3] Optimal informations size for continuous measure was not met (< 400 patients)

[4] 2x downgrade - Optimal informations size for continuous measure was not met

[5] Hours per week spent in constructive economic activity, RFS-Subscal Work productivity

[6] Optimal informations size for continuous measure was not met (< 400 patients)

[7] RFS-Subscal Work productivity

[8] 2x downgrade - Optimal informations size for continuous measure was not met

[9] Etsimates of effect are on different sides of line of no effect, but CI's are overlapping considerably, there is no statistical heterogenity (I2>50%)

[10] 2x downgrade - OPtimal information size was not me for dichotomous measure (<50 events)

[11] 2x downgrade - OPtimal information size was not me for dichotomous measure (<50 events)

Question: Recovery CBT vs Befriending for [Early psychosis]

Bibliography: . [Recovery CBT] for [Early psychosis]. Cochrane Database of Systematic Reviews [Year], Issue [Issue].

Quality assessment							Summary of Findings				
Participants (studies) Follow up	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Publication bias**	**Overall quality of evidence**	**Study event rates (%)**		**Relative effect** (95% CI)	**Anticipated absolute effects**	
							With Befriending	**With Recovery CBT**		**Risk with Befriending**	**Risk difference with Recovery CBT** (95% CI)
Social functioning PT (CRITICAL OUTCOME; measured with: Questionnaire (SOFAS); Better indicated by lower values)											
62 (1 study)	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[1]	undetected	⨁⨁⨀⨀ **LOW**[1] due to imprecision	31	31	-		The mean social functioning pt in the intervention groups was **0.4 standard deviations lower** (0.9 lower to 0.11 higher)
Hospitalization (number admitted) FU 52 wkn (CRITICAL OUTCOME)											
57 (1 study)	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[2]	undetected	⨁⨁⨀⨀ **LOW**[2] due to imprecision	8/27 (29.6%)	12/30 (40%)	**RR 1.35** (0.65 to 2.8)	**Study population**	
										296 per 1000	**104 more per 1000** (from 104 fewer to 533 more)
										Moderate	
										296 per 1000	**104 more per 1000** (from 104 fewer to 533 more)

[1] 2x downgrade - Optimal information size for continuous measure was not met

[2] 2x downgrade - Optimal information size for dichotomous measure was not met (< 50 events)

Kwaliteits-
ontwikkeling
GGz

Netwerk voor goede zorg