Bijlage 5 Evidence tabellen

Voor de ontwikkeling van deze zorgstandaard zijn op systematische wijze wetenschappelijke studies over diagnostiek en behandeling van volwassenen, en over screening, diagnostiek en behandeling van kinderen en jongeren met een dissociatieve stoornis verzameld en beoordeeld. Deze beoordeling is in 2016 uitgevoerd door het Trimbos-instituut. De uitgangsvragen waren:

Met betrekking tot diagnostiek bij volwassenen:

- Welke effectieve diagnostische instrumenten kunnen in het diagnostisch onderzoek naar dissociatieve stoornissen gebruikt worden?
- Hoe kan de diagnose dissociatieve stoornis onderscheiden worden van andere stoornissen (differentiaaldiagnose)?
- Waaruit bestaat (welke componenten) een goed en degelijk diagnostisch onderzoek?

Met betrekking tot behandeling van volwassenen:

- Is er sprake van practice-based/clinical consensus behandeling? Zo ja, waarover is dan consensus? Zo nee, waarover gaat de discrepantie?
- Is er empirisch bewijs voor effectiviteit van behandelingen? Welke behandelingen zijn beschikbaar? Wat is de effectiviteit van de behandelingen?

Met betrekking tot screening, diagnostiek en behandeling van kinderen en jongeren:

- Hoe verbeter je de vroegsignalering van risicogroepen?
- Hoe verbeter je de herkenning van patiënten die mogelijk een dissociatieve stoornis hebben?

5.1 Diagnostiek volwassenen

5.1.1 Review protocol diagnostiek volwassenen

Topic	Screening
Review question(s)	2. Hoe verbeter je de herkenning van patiënten die mogelijk een dissociatieve stoornis hebben?
Sub-question(s)	2a) Wanneer en bij welke patiënt ga je screenen? 2b) Wie screent? (huisarts, POH-GGZ, basis ggz, specialistische ggz, blijf van mijn lijf, kinderarts, jeugdzorg/ BJZ) 2c) Hoe vindt herkenning/screening plaats? Welke screeningsinstrumenten zijn het beste te gebruiken en in welke situatie?
Objectives	Subvraag 2a en b wordt beantwoord door middel van Focusgroep patiënten en/of hulpverleners Subvraag 2c wordt mede beantwoord door middel van een literatuursearch, deze search levert ook informatie voor subvraag 2a en b. Dit protocol behandeld de criteria mbt subvraag 2c.
Criteria for considering studies for the review	

Types of participants	Kinderen, adolescenten en volwassenen waarbij een vermoeden bestaat op een dissociatieve stoornis (depersonalisatie en derealisatie, DIS en de DIS-NAO) volgens de definitie van de DSM-IV of DSM-5.
Intervention (Indextest)	Screeningsvragenlijsten
Comparator (Reference standard)	Longitudinal, Expert, All Data (LEAD) procedure (operationalisation of optimal clinical expert judgement) Clinical judgement based on the Diagnostic Statistical Manual (DSM IV / 5) Clinical judgement based on International Classification of Diseases (ICD) (Semi-)gestructureerde diagnostisch interviews (DSM IV / 5 / ICD)
Critical outcomes	Sensitiviteit: de kans dat de indextest bij de mensen met de ziekte een positieve uitslag geeft. Specificiteit: de kans dat bij gezonde mensen (afwezigheid van de ziekte die de indextest moet opsporen) het resultaat negatief is.
Important outcomes	Positive Predictive Value (PPV): the proportion of patients with positive test results who are correctly diagnosed. Negative Predictive Value (NPV): the proportion of patients with negative test results who are correctly diagnosed. Area under the Curve (AUC): are constructed by plotting the true positive rate as a function of the false positive rate for each threshold.
Time	-
Study design	Cross-sectional design RCT
Dosage	-
Study setting/country	Inclusie alle sectoren van zorg Exclusie van onderzoek in gevangenissen en forensische settingen Exclusie van onderzoek uit Azië of Afrika
Search strategy	Databases searched: CINAHL, Pubmed, PsycInfo Date limiters: 2000 Other limiters, e.g. design, language, age: Engels en Nederlands
Study design filter used	Nee
Question specific search strategy	Nee
Searching other resources	Ongepubliceerd werk aangeleverd door experts
The review strategy	De Literatuur wordt in een narratieve analyse geanalyseerd. Voor DIS en DIS-NAO wordt een update uitgevoerd van de ‘Guidelines for the Evaluation and Treatment of Dissociative Symptoms in Children and Adolescents (2004) en ‘Guidelines for Treating Dissociative Identity Disorder in

	Adults, Third Revision' (2011).Richtlijn 'Guideline for the Evaluation and Treatment of Dissociative Symptoms' en 'International Society for the Study of Trauma and Dissociation (2011). Voor andere diagnoses (depersonalisatie en derealisatie) moet een aparte search gedaan worden, tenzij er in de search ook recente richtlijnen worden gevonden. De informatie specialist voert de zoekstrategie uit. De reviewer zal in twee fasen de studies selecteren met behulp van 'Criteria for considering studies for the review' 1. Eerste selectie (title and abstract): bij twijfel en voorlopige inclusie de full text opvragen. 2. Tweede selectie (full text): bij twijfel artikelen bespreken met tweede onderzoeker De reviewers bepalen de methodologische kwaliteit van de individuele studies met behulp van de QUADAS II. Een tweede reviewer is beschikbaar voor cross-checking, hulp en advies. Optie A Mochter een review/richtlijn worden gevonden die de uitgangsvraag beantwoord dan zal worden bekeken of het recente aanvullend onderzoek de conclusies van zullen veranderen. Als dit zo is dan wordt de review/richtlijn geupdate, anders niet. Optie B Bestaande studies worden samengevat en narratief geanalyseerd.
Note.	

Topic	Diagnostiek
Review question(s)	1. Welke, effectieve diagnostische instrumenten kunnen in het diagnostisch onderzoek naar dissociatieve stoornissen gebruikt worden? 2. Hoe kan de diagnose dissociatieve stoornis onderscheiden worden van andere stoornissen (differentiaaldiagnose)? 3.Waaruit bestaat (welke componenten) een goed en degelijk diagnostisch onderzoek?
Sub-question(s)	-
Objectives	Het literatuuronderzoek wordt gedaan naar vraag 1. Er wordt beoogd om de vraag te beantwoorden door middel van een literatuursearch. Naar verwachting is er geen/weinig onderzoek naar instrumenten en zal de werkgroep het stuk voor een groot gedeelte moeten schrijven.
Criteria for considering studies for the review	
Types of participants	Kinderen, adolescenten en volwassenen met en zonder een dissociatieve stoornis (depersonalisatie en derealisatie, DIS en de DIS-NAO) volgens de definitie van de DSM-IV of DSM-5.
Intervention (Indextest)	(Semi-)gestructureerde diagnostisch interview

Comparator (Reference standard)	Longitudinal, Expert, All Data (LEAD) procedure (operationalisation of optimal clinical expert judgement) Clinical judgement based on the Diagnostic Statistical Manual (DSM IV / 5) Clinical judgement based on International Classification of Diseases (ICD)
Critical outcomes	Sensitiviteit: de kans dat de indextest bij de mensen met de ziekte een positieve uitslag geeft. Specificiteit: de kans dat bij gezonde mensen (afwezigheid van de ziekte die de indextest moet opsporen) het resultaat negatief is.
Important outcomes	Positive Predictive Value (PPV) / Positief Voorspellende Waarde (VW+): de kans dat iemand met een positieve uitkomst op de indextest ook de diagnose heeft. Negative Predictive Value (NPV) / Negatief Voorspellende Waarde (VW-): de kans dat iemand met een negatieve uitkomst op de indextest gezond is (de diagnose niet heeft, d.w.z., een negatieve uitkomst heeft op de referentietest). Area under the Curve (AUC): een curve die de accuraatheid van de test aangeeft, zonder rekening te houden met een specifieke cutoff score.
Time	-
Study design	Cross-sectional design RCT's
Dosage	-
Study setting/country	Inclusie alle sectoren van zorg Exclusie van onderzoek in gevangenissen en forensische settingen Exclusie van onderzoek uit Azië of Afrika
Search strategy	Databases searched: CINAHL, Pubmed, PsycInfo Date limiters: 2000 Other limiters, e.g. design, language, age: Engels en Nederlands
Study design filter used	Nee
Question specific search strategy	Nee
Searching other resources	Ongepubliceerd werk aangeleverd door experts
The review strategy	De Literatuur wordt in een narratieve analyse geanalyseerd. Voor DIS en DS-NAO wordt de kennis uit 'Guidelines for the Evaluation and Treatment of Dissociative Symptoms in Children and Adolescents (2004) en 'Guidelines for Treating Dissociative Identity Disorder in Adults, Third Revision' (ISSTD, 2011) meegenomen. Richtlijn 'Guideline for the Evaluation and Treatment of Dissociative Symptoms' en 'International Society for the Study of Trauma and Dissociation (2011). Voor andere diagnoses (depersonalisatie en

	derealisatie) moet een aparte search gedaan worden, tenzij er in de search ook recente richtlijnen worden gevonden. De informatie specialist voert de zoekstrategie uit. De reviewer zal in twee fasen de studies selecteren met behulp van 'Criteria for considering studies for the review' 1. Eerste selectie (title and abstract): bij twijfel en voorlopige inclusie de full text opvragen. 2. Tweede selectie (full text): bij twijfel artikelen bespreken met tweede onderzoeker De reviewers bepalen de methodologische kwaliteit van de individuele studies met behulp van de QUADAS II. Een tweede reviewer is beschikbaar voor cross-checking, hulp en advies. Optie A Mochter een review/richtlijn worden gevonden die de uitgangsvraag beantwoord dan zal worden bekeken of het recente aanvullend onderzoek de conclusies van zullen veranderen. Als dit zo is dan wordt de review/richtlijn geupdate, anders niet. Optie B Bestaande studies worden samengevat en narratief geanalyseerd.
Note.	

5.1.2 Resultaten zoekstrategie Diagnostiek volwassenen

Zoekgeschiedenis screening en diagnostiek van dissociatieve stoornissen

Er is een zoekstrategie uitgevoerd in de databases PsycInfo, PubMed en CINAHL naar studies over screening en diagnostiek van dissociatieve stoornissen. Hierbij is geen beperking aangebracht op jaar van uitgave of taal. De searches zijn op 25 mei 2016 uitgevoerd.

PsycInfo

In PsycInfo is gezocht op de volgende thesaurustermen voor dissociatieve stoornissen: DE "Dissociative Disorders" OR DE "Depersonalization" OR DE "Depersonalization/Derealization Disorder" OR DE "Dissociative Identity Disorder" OR DE "Fugue Reaction" OR DE "Dissociation".

Deze thesaurustermen zijn aangevuld met woorden voor dissociatieve stoornissen in het titel-, keyword- of abstract-veld, te weten: dissociative OR dissociation OR depersonalisation OR depersonalization OR derealisation OR derealization OR fugue OR "multiple personality disorder*" OR "dual personality" OR "dual personalities" OR multiple personality" OR "multiple personalities".

Voor screening en diagnostiek is gezocht op de thesaurustermen: DE "Psychological Assessment" OR DE "Screening" or DE "Screening Tests" or DE "Psychological Screening Inventory" OR DE "Psychodiagnosis" OR DE "Psychodiagnostic Interview" OR DE "Diagnostic Interview Schedule" OR DE "Structured Clinical Interview" OR DE "Diagnosis" OR DE "Computer Assisted Diagnosis" OR DE "Rating Scales" OR DE "Questionnaires". Deze termen zijn aangevuld met de volgende woorden in titel-, keyword- of abstract-veld: screening OR assess* OR diagnos* OR classification OR psychodiagnos* OR sdq or "strengths and difficulties questionnaire" OR "Dissociative Experiences Scale".

Om verder te specificeren is de search gelimiteerd door het gebruik van de thesaurustermen: DE "Test Sensitivity" OR DE "Test Specificity" OR DE "Test Validity" OR DE "Statistical Validity" en de termen "test

accuracy" OR "diagnostic accuracy" OR "diagnostic test accuracy" OR "true positive*" OR "true negative*" OR "false positive*" OR "false negative*" OR "predictive validity" OR sensitivity OR specificity OR "area under the curve" OR "test performance" in titel-, keyword- of abstract-veld.

PubMed

In PubMed is voor dissociatieve stoornissen gezocht op de thesaurustermen "Dissociative Disorders"[Mesh] OR "Multiple Personality Disorder"[Mesh], aangevuld met de volgende woorden in titel of abstract: dissociative [tiab] OR dissociation [tiab] OR depersonalisation[tiab] OR depersonalization[tiab] OR derealisation[tiab] OR derealization[tiab] OR fugue[tiab] OR "multiple personality disorder"[tiab] OR "multiple personality disorders"[tiab] OR "dual personality"[tiab] OR "dual personalities"[tiab] OR “multiple personality"[tiab] OR "multiple personalities"[tiab].

Voor screening en diagnostiek is gezocht op de volgende thesaurustermen:

"Diagnosis"[Mesh:NoExp] OR "Psychological Tests"[Mesh:NoExp] OR "Psychiatric Status Rating Scales"[Mesh], aangevuld met de volgende woorden in de titel: screening [TI] OR assessment [TI] OR assessing [TI] OR diagnosis [TI] OR diagnoses [TI] OR diagnostic [TI] OR classification [TI] OR psychodiagnosis [TI] OR psychodiagnoses [TI] OR psychodiagnostic [TI].

Om de search verder te specificeren is gelimiteerd door de thesaurusterm "Sensitivity and Specificity"[Mesh] te gebruiken in combinatie met dezelfde woorden in titel en abstract als die in PsycInfo gebruikt zijn.

CINAHL

In CINAHL is gezocht op de thesaurustermen: MH "Dissociative Disorders" OR MH "Multiple-Personality Disorder" OR MH "Depersonalization". Deze termen zijn aangevuld in titel en abstract met dezelfde termen die gebruikt zijn in de andere databases.

Voor screening en diagnostiek is gezocht op de volgende thesaurustermen: MH "Questionnaires" OR MH "Psychological Tests" OR MH "Scales" OR MH "Behavior Rating Scales" OR MH "Checklists" OR MH "Clinical Assessment Tools+" OR MH "Diagnosis" OR MH "Clinical Assessment Tools" OR MH "Diagnosis, Psychosocial+" OR MH "Early Diagnosis" OR MH "Nursing Diagnosis" OR MH "Nursing Assessment" OR MH "Prognosis" OR MH "Self Diagnosis". Deze thesaurustermen zijn aangevuld met dezelfde termen in titel en abstract die gebruikt zijn in de andere databases.

Om verder te specificeren is gelimiteerd met de thesaurusterm MH "Sensitivity and Specificity" in combinatie met dezelfde woorden in titel en abstract als in de andere databases gebruikt zijn.

Resultaat

Er zijn in PsycInfo 598 referenties gevonden, in PubMed 414 en in CINAHL 35. Dit zijn er in totaal 1047. Deze resultaten zijn ontdubbeld en na verwijdering van 76 duplicaten bleven er 971 referenties over.

5.1.3: Tabel studiekenmerken en diagnostische accuratesse

Referentie	# Items (afkap-punt)	Land, Taal	Setting	N, % vrouwen, gem. leeftijd in jaren, prevalentie	Resultaten (Se (95%BI), Sp(95%BI))	Bijzonderheden
Dissociative Experiences Scale (DES)						
Mueller-Pfeiffer et al., 2013	28 items (optimaal posthoc ≥12 voor DD, optimaal posthoc ≥20 voor DD-NOS-I/DID)	Zwitserland, Duits	Extramuraal en dagbehandeling	N = 160 Vr = 67% Leeftijd = med. 33 Prev = 19% DD, waarvan 14% DD-NOS-I/DID	*DD* Se = .80 (95%CI: NA) Sp = .69 (95%CI: NA) AUC = 0.84 (95%CI: .74-.90) *DD-NOS-I/DID* Se = .82 (95%CI: NA) Sp = .80 (95%CI: NA) AUC = 0.89 (95%CI: .78-.95)	Referentietest: SCID-D-R en SCID-I en SCID II
Steinberg et al., 1991	28 items (≥15)	VS, Engels	Extramuraal	N = 24 Vr = meerderheid vrouw Leeftijd = 34.3 (DD), 41.2 (zonder DD), 32.6 (controle)	*Vergelijking met patiënten zonder DD:* Se = .95 (95%CI: NA) Sp = .93(95%CI: NA) *Vergelijking met gezonde controle groep:* Se = .95 (95%CI: NA)	Referentietest: SCID-D

					Sp = 1.0 (95%CI: NA)	
Somatoform Dissociation Questionnaire (SDQ)						
Mueller-Pfeiffer et al., 2013	20 items (optimaal posthoc ≥30 voor DD, optimaal posthoc ≥33 voor DD-NOS-I/DID)	Zwitserland, Duits	Extramuraal en dagbehandeling	N = 160 Vr = 67% Leeftijd = med. 33 Prev = 19% DD, waarvan 14% DD-NOS-I/DID	*DD* Se = .83 (95%CI: NA) Sp = .74 (95%CI: NA) AUC = 0.83 (95%CI: .73-.89) *DD-NOS-I/DID* Se = .82 (95%CI: NA) Sp = .80 (95%CI: NA) AUC = 0.86 (95%CI: .78-.92)	Referentietest: SCID-D-R en SCID-I en SCID II
Nijenhuis et al., 1998	5 items (≥8)	Nederland, Nederlands	Extramuraal	N = 76 Vr = meerderheid vrouw Leeftijd = 32.1 Prev = 41%	Se = .94 (95%CI: NA) Sp = .93 (95%CI: NA)	Referentietest: SCID-D
Nijenhuis et al., 1997	5 items (≥7)	Nederland, Nederlands	Extramuraal	N = 100 Vr. = 88% Leeftijd = 34.8	Se = .96 (95%CI: NA) Sp = .88 (95%CI: NA) *Crossvalidatie* Se = .82 (95%CI: NA) Sp = .88(95%CI: NA)	Referentietest: SCID-D en DIS-Q

				Prev. = 50%		
Multidimensional Inventory for Dissociation (MID)						
Mueller-Pfeiffer et al., 2013	28 items (optimaal posthoc ≥28 voor DD, optimaal posthoc ≥28 voor DD-NOS-I/DID)	Zwitserland, Duits	Extramuraal en dagbehandeling	N = 160 Vr = 67% Leeftijd = med. 33 Prev = 19% DD, waarvan 14% DD-NOS-I/DID	*DD* Se = .80 (95%CI: NA) Sp = .82 (95%CI: NA) AUC = 0.84 (95%CI: .75-.90) *DD-NOS-I/DID* Se = .86 (95%CI: NA) Sp = .80 (95%CI: NA) AUC = 0.86 (95%CI: .76-.92)	Referentietest: SCID-D-R en SCID-I en SCID II

5.1.4: TQuadas 2 – Evidence table for diagnostic accuracy studies

Methods	Patients	Instruments	Results	Quality Assesment
Reference: Mueller-Pfeiffer C, Rufibach K, Wyss D, Perron N, Pitman RK, Rufer M. Screening for dissociative disorders in psychiatric out- and day care-patients. Journal of Psychopathology and Behavioral Assessment 2013; 35(4):592-602. Study aim: This study evaluated the performance of three well known and internationally used dissociation scales in screening for dissociative disorders. Study design: DTA Setting: Consecutively treated out- and day care-patients Location: Two public psychiatric outpatients units, one	Number of patients: 160 Age: median of 33 (18-65) Sex: 0.67 female (n=107) Ethnicity: mostly swiss (82,4%) Inclusion : consecutive subjects between 18 and 65 years with sufficient fluency in the German language, who were in treatment for three or more sessions during 1/2009 to 12/2010, were eligible. Exclusion: mental retardation acute psychosis, psychiatric disorder due to an underlying medical condition, acute suicidal ideation, intoxication or withdrawal Co-morbidity: There was no significant influence of the presence of a comorbid affective disorder, anxiety disorder, or personality disorder on intercept and slope of the probit-transformed ROC curves for DES, SDQ-20, and MID summary scores with regard	Index test: Dissociative Experiences Scale (DES), Somatoform Dissociation Questionnaire (SDQ-20), and Multidimensional Inventory for Dissociation (MID) Reference test: The Structured Clinical Interview for DSM-IV Dissociative Disorders-Revised (SCID-D-R) and the Structured Clinical Interview for DSM-IV Axis I and Axis II Disorders Time interval and treatment in between both tests: 0	Target condition: Any dissociative disorder (DD) (and dissociative disorder not otherwise specified-I (DDNOS-I)/dissociative identity disorder (DID)) Prevalence in sample: DD = 0.1875, of which n=22 had DDNOS/DID = 0.1375 (so the 22 was a subset of the DD group) Results: <u>DES</u> AUC .84 (95 % CI [.74, .90]) <u>SDQ-20</u> AUC .83 (95 % CI [.73, .89]) <u>MID</u> AUC .84 (95 % CI [.75, .90]) See table 4 under this evidenc table for post-hoc optimal Se/Sp/PV+/NV-	DOMAIN 1: PATIENT SELECTION Could the selection of patients have introduced bias (selection bias)?RISK: LOW Is there concern that the included patients do not match the review question (spectrum bias)? CONCERN: LOW DOMAIN 2: INDEX TEST(S) Could the conduct or interpretation of the index test have introduced bias? RISK: LOW Is there concern that the index test, its conduct, or interpretation differ from the review question? CONCERN: LOW DOMAIN 3: REFERENCE STANDARD Could the reference standard, its conduct, or its interpretation have introduced bias? RISK: LOW Is there concern that the target condition as defined by the reference standard does not

Methods	Patients	Instruments	Results	Quality Assesment
private practice, and two psychiatric day care unitsin Switzerland Training of assessors: SCID-D-R and the Structured Clinical Interview for DSM-IV Axis I and Axis II Disorders (First et al. 1997a, b) were administered by trained interviewers with a B.Sc. or a M.Sc. degree who were blinded for the results of the self-rating scales.	to presence of a DD. This suggests that our results are not confounded by psychiatric comorbidity Other: limitation is the application of the three dissociation scales in the same sequence, so that order effects cannot be excluded. Moreover, administration of all three scales within the same session might have inflated concordance among them.		There was no significant influence of the presence of a comorbid affective disorder, anxiety disorder, or personality disorder on intercept and slope of the probit-transformed ROC curves for DES, SDQ-20, and MID summary scores with regard to presence of a DD. This suggests that our results are not confounded by psychiatric comorbidity.	match the review question? CONCERN: LOW DOMAIN 4: FLOW AND TIMING Could the patient flow have introduced bias? RISK: UNCLEAR *16 recruited subjects (9.1 % of the 176) were excluded from the analysis due to incomplete participation or doubtful validity of the results (e.g., suspected dissimulation or difficulties in understanding the questions)*

Se= Sensitivity

Sp= Specificity

PV+= Positive Predictive Value

NV-= Negative Predictive Value

LR+, LR-= Likelihood ratio's

AUC= Area under the ROC curve

Table 4 Test performance of the Dissociative Experiences Scale (DES), the Somatoform Dissociation Questionnaire (SDQ-20), and the Multidimensional Inventory of Dissociation (MID) summary scales for the detection of any dissociative disorder (DD) and dissociative disorder not otherwise specified-I (DDNOS-I)/dissociative identity disorder (DID), respectively, at indicated cut-off scores providing a minimal sensitivity of .80 in a sample of 160 psychiatric out- and day care-patients

Scale	Cut-Off	Sensitivity	Specificity	PPV	NPV	PPV	NPV	PPV	NPV	CCR	Kappa
				Sample prevalence[a]		Prevalence=10 %		Prevalence=1 %			
DD (n=30)											
DES	12	.80	.69	.38	.94	.22	.97	.03	1.00	.70	.33
SDQ-20	30	.83	.74	.42	.95	.26	.98	.03	1.00	.76	.42
MID	28	.80	.82	.51	.95	.33	.97	.04	1.00	.82	.51
DDNOS-I/DID (n=22)											
DES	20	.82	.80	.40	.97	.32	.98	.04	1.00	.81	.43
SDQ-20	33	.82	.80	.39	.96	.31	.98	.04	1.00	.80	.42
MID	28	.86	.80	.40	.97	.32	.98	.04	1.00	.81	.45

[a] DD=19 %; DDNOS-I/DID=14 %. *PPV* positive predictive value; *NPV* negative predictive value; *CCR* correct classification rate

Relation between the outcome of the index test and the outcome of the reference test

Threshold(s) index test	
Threshold(s) reference test	

	referentietest		Totaal
indextest	ziekte +	ziekte -	
Uitslag indextest +			0
Uitslag indextest -			0
totaal	0	0	0
Parameters voor de in	**waarde**	95% BI	
sensitiviteit	#DEEL/0!	#DEEL/0!	#DEEL/0!
specificiteit	#DEEL/0!	#DEEL/0!	#DEEL/0!
prevalentie (prior kans)	#DEEL/0!		
Voorspellende waarde po	#DEEL/0!		
Voorspellende waarde ne	#DEEL/0!		
Likelihoodratio positieve	#DEEL/0!		
Likelihoodratio negatieve	#DEEL/0!		
percentage correct	#DEEL/0!		

Nijenhuis et al. (1998)

Methods	Patients	Instruments	Results	Quality Assesment
Reference: Nijenhuis ER, Spinhoven P, van DR, van der Hart O, Vanderlinden J. Psychometric characteristics of the somatoform dissociation questionnaire: a replication study. Psychother Psychosom 1998; 67(1):17-23 Study aim: Replicate the results of previous studies concerning the development of two versions of the Somatoform Dissociation Questionnaire (SDQ).	Number of patients: 76 (Thirty-one patients with dissociative disorders and 45 consecutive psychiatric outpatients with other DSM-IV diagnoses completed) Dissociative disorder group Age: Mean 32.1 (SD = 10.3, range 18–53) Sex: 18/3 (F/M) Comparisongroup	Index test: The SDQ-20 *evaluates the severity of somatoform dissociative phenomena,* and the SDQ-5 is a dissociative disorders screening instrument. Dissociation Questionnaire which measures psychological dissociation (DIS-Q) Reference test: DSM-IV Dissociative Disorders (SCID-D) Time interval and treatment in between both tests: A subgroup of these patients	Target condition: DDNOS and DID Prevalence in sample: 41% Results: SDQ-5 (recommended cutoff point is ≥8) Se 0.94 Sp 0.98 PV+ 0.84 PV- 0.99	DOMAIN 1: PATIENT SELECTION Could the selection of patients have introduced bias (selection bias)?RISK: HIGH *Suspected diagnosis was probably known to patients before they filled-out the SDQ. Control group was a selection of non-DD patients.* Is there concern that the included patients do not match the review question (spectrum bias)? CONCERN: LOW

Methods	Patients	Instruments	Results	Quality Assesment
Study design: patient-control Setting: outpatient Location: Netherlands Training of assessors: All SCID-D interviewers were trained in the administration and interpretation of this instrument.	Age: 27/18 Sex: 34.6 (SD = 10.1, range 19–53) Ethnicity: Inclusion :- Exclusion:- Co-morbidity: - Other:-	with dissociative disorders had been diagnosed and had received treatment of their dissociative condition in advance of obtaining their responses to the SDQ-20, SDQ-5, and DIS-Q	See table 1 underneath for other scores They also recalcultated the scores to ‘real world’ prevalence of 10%.	DOMAIN 2: INDEX TEST(S) Could the conduct or interpretation of the index test have introduced bias? RISK: LOW Is there concern that the index test, its conduct, or interpretation differ from the review question? CONCERN: LOW DOMAIN 3: REFERENCE STANDARD Could the reference standard, its conduct, or its interpretation have introduced bias? RISK: LOW Is there concern that the target condition as defined by the

Methods	Patients	Instruments	Results	Quality Assesment
				reference standard does not match the review question? CONCERN: LOW DOMAIN 4: FLOW AND TIMING Could the patient flow have introduced bias? RISK: Unclear Due to time-lag

Table 1. Sensitivity, specificity, preditive values and likelihood ratios of the SDQ-5 at essential cutoff scores discriminating between 31 DSM-IV dissociative disorder patients and 45 psychiatric patients without a dissociative disorder

Cutoff score	Sensitivity	Specificity	Positive predictive value	Negative predictive value	Predictive value estimated at prevalence 10%		Likelihood rate	
					pos.	neg.	pos.	neg
10	0.77	0.98	0.96	0.86	0.81	0.97	38.5	0.23
9	0.87	0.98	0.96	0.92	0.83	0.98	43.5	0.13
8	0.94	0.98	0.97	0.96	0.84	0.99	47.0	0.06
7	0.97	0.89	0.86	0.98	0.49	0.99	8.8	0.03

Sensitivity, specificity, and predictive values are expressed as proportions.
Positive predictive value (corrected for prevalence) =
[sensitivity × prevalence]/[(sensitivity × prevalence) + (1 – specificity) × (1 – prevalence)].
Negative predictive value (corrected for prevalence) =
[specificity × (1 – prevalence)]/[specificity × (1 – prevalence) + (1 – sensitivity) × prevalance].
Likelihood ratio (positive) = sensitivity/ 1 – specificity. Likelihood ratio (negative) =
1 – sensitivity/specificity.

Nijenhuis et al. (1997)

Methods	Patients	Instruments	Results	Quality Assesment
Reference: Nijenhuis ER, Spinhoven P, van DR, van der Hart O, Vanderlinden J. The development of the somatoform dissociation questionnaire (SDQ-5) as a SCREENing INSTRUMENT for DISSOCIATIVE DISORDERs. Acta Psychiatr Scand 1997; 96(5):311-318. Study aim: the capacity of a short list of somatoform dissociation items to discriminate between patients with dissociative disorder and those with other psychiatric diagnoses was assessed.	Number of patients:50 vs. 50 Age: 34.8 (9.7) vs. 34.7 (12.7) Sex: 88% vs. 78% women Ethnicity: - Inclusion : Patients with dissociative disorder as diagnosed with SCID-D. Control patients who received psychiatric treatment with a non-dissociative DSM-IV diagnosis, who scored below 2.5 on the DIS-Q. Exclusion:- Co-morbidity: - Other:	Index test: SDQ-5 Reference test: SCID-D + DIS-Q Time interval and treatment in between both tests: not reported	Target condition: somatoform dissociation Prevalence in sample: 50% Results: In original sample at cut of ≥7: Se = 96% Sp = 88% PV+ = 89% PV- = 96% LR+ = 8.0 LR- = 0.0 AUC = - In cross validation at cut of ≥8: Se = 82% Sp = 88% PV+ = 84% PV- = 86%	DOMAIN 1: PATIENT SELECTION Could the selection of patients have introduced bias (selection bias)?RISK: HIHG *Diagnosis was already known, not a random selection of suspected patients. Control group was a selection of non-DD patients.* Is there concern that the included patients do not match the review question (spectrum bias)? CONCERN: LOW DOMAIN 2: INDEX TEST(S) Could the conduct or interpretation of the index test have introduced bias? RISK: LOW Is there concern that the index test, its conduct, or interpretation differ from the review question? CONCERN: LOW DOMAIN 3: REFERENCE STANDARD

Methods	Patients	Instruments	Results	Quality Assesment
Study design: patient vs. control Setting: outpatients Location: The Netherlands Training of assessors: not reported only mentioned experienced clinicians			LR+ = 6.8 LR- = 0.1 AUC = -	Could the reference standard, its conduct, or its interpretation have introduced bias? RISK: LOW Is there concern that the target condition as defined by the reference standard does not match the review question? CONCERN: LOW DOMAIN 4: FLOW AND TIMING Could the patient flow have introduced bias? RISK: UNCLEAR

Steinberg et al. (1991)

Methods	Patients	Instruments	Results	Quality Assesment
Reference: Steinberg M, Rounsaville B, Cicchetti D. Detection of DISSOCIATIVE DISORDERs in psychiatric patients by a SCREENing INSTRUMENT and a structured diagnostic interview. Am J Psychiatry 1991; 148(8):1050-1054.	Number of patients: 24 psychiatric patients vs. 8 healthy controls Age: - Patients with DD 34.3(7.7) - Patients without DD 41.2 (9.9) - Controls 32.6 (13.1)	Index test: Dissociative Experiences Scale (DES) a self-report instrument for dissociative experiences Reference test:SCID-D Time interval and treatment in between both tests: no time interval	Target condition: dissociative disorders Prevalence in sample: 47% Results: Patients with other psychiatric diagnoses as comparison & cut-off 15: Se =95% Sp =93%	DOMAIN 1: PATIENT SELECTION Could the selection of patients have introduced bias (selection bias)?RISK: HIGH *Diagnosis was already know, not a random selection of suspected patients.* Is there concern that the included patients do not match

Methods	Patients	Instruments	Results	Quality Assesment
Study aim: to investigate the utility of the Disoociative Experiences Scale (DES), in detecting patients at high risk for dissociative disorder, as a screening instrument. Study design: psychiatric patient vs control Setting: outpatients Location: US Training of assessors: not reported	Sex: mainly women Ethnicity: - Inclusion : *Patients* Outpatients in active treatment in a mental health center or private therapy. In treatment with referring physician for at least 6 months. Referring clinicians diagnoses were based on DSM-III. Exclusion: *Patients*: Very agitated, gravely disabled, or at risk for suicide patients. *Controls*: history of outpatient treatment for a psychiatric disorder, psychiatric hospitalization or suicide attempt. Co-morbidity: no evidence of organic brain syndrome or mental retardation in included patients.		PV+ = - PV- = - LR+ = - LR- = - AUC = - Healthy controls as comparison & cut-off 15: Se = 95% Sp = 100% PV+ = - PV- = - LR+ = - LR- = - AUC = - “The results of the present study indicate that with appropriate cutoffs (i.e., ≥15-20), the DES can be used successfully to screen for cases of dissociative disorders, particularly multiple personality disorder. However, it requires the use of a confirmatory instrument such as the SCID-D in order to diagnose definitively the presence of a dissociative disorder and to	the review question (spectrum bias)? CONCERN: LOW DOMAIN 2: INDEX TEST(S) Could the conduct or interpretation of the index test have introduced bias? RISK: LOW Is there concern that the index test, its conduct, or interpretation differ from the review question? CONCERN: LOW DOMAIN 3: REFERENCE STANDARD Could the reference standard, its conduct, or its interpretation have introduced bias? RISK: LOW Is there concern that the target condition as defined by the reference standard does not match the review question? CONCERN:LOW DOMAIN 4: FLOW AND TIMING Could the patient flow have introduced bias? RISK: LOW

Methods	Patients	Instruments	Results	Quality Assesment
			identify the specific disorder and symptom severity.	

Se= Sensitivity

Sp= Specificity

PV+= Positive Predictive Value

PV-= Negative Predictive Value

LR+, LR-= Likelihood ratio’s

AUC= Area under the ROC curve

Carlson, E.B., Putnam, F.W et al. (1993).

Reference: Carlson, E.B., Putnam, F.W., Ross, C.A., Torem, M., Coons, P., Dill, D.L., … & Braun, B.G. (1993). Validity of the Dissociative Experiences Scale in Screening for Multiple Personality Disorder: A Multicenter Study. *American Journal of Psychiatry, 150,* 1030-1036.	
Methods	Study aim: To assess the capacity of the Dissociative Experiences Scale to blindly predict a diagnosis of multiple personality disorder in a large pool of general psychiatric patients. Study design: A multicenter cross-sectional study design Setting: seven research and clinical centers in diverse locations Location: clinical centers in Washington, D.C., Atlanta, National Institute of Mental Health, Canada, Ohio, Indiana, Illinois and the Northeast region of the United States Training of assessors: Data were collected in each center as part of standard assessment procedures or research projects. There was no information about the expertise of the assessors
Patients	Number of patients: N = 1051 for the total study group; N = 883 for the subgroup selected to more accurately reflect a mental health treatment population (i.e., fewer patients with dissociative disorders) Inclusion: At least 18 years of age, specifically given informed consent to participate in the study Exclusion: unclear Age: Mean age total population = 34.8 years (SD = 11.6), mean age MPD patients = 33.5 years (SD = 9.8), mean age of non-MPD patients = 35.3 years (SD = 12.1) Sex: total population = 63% women, MPD patients = 87% women, non-MPD patients = 55% women Ethnicity: no information available Co-morbidity: no information available Other: In center 1 some subjects were from a specialized outpatient treatment for dissociative disorders in Washington D.C. For this reason a subgroup (created using Bayes's theorem) has also been analyzed to control for the relative high prevalence of dissociative disorders in the sample
Instruments	Index test: Dissociative Experiences Scale, a 28-item screening instrument measuring the frequency of dissociative experiences. The test-retest reliability ranged between 0.84 and 0.96, the inter-rater reliability was 0.96, internal consistency test yielded a Cronbach's Alpha of 0.95. Total scores are ranging between 0 and 100. Cut-off score for dissociative disorder is 30. Reference test: DSM-III or DSM-III-R diagnosis for psychiatric illnesses in the mental health care centers Time interval and treatment in between both tests: unclear
Results	Target condition: all psychiatric patients within the seven clinical centers Prevalence in sample: 9.6% affective disorder, 9.2% anxiety disorder, 11.1% dissociative disorder other than MPD, 11.4% eating disorder, 21.7% MPD, 12.5% neurological disorder, 11.0% PTSD, 5.8% Schizophrenic disorder, 7.6% other diagnosis Cut-off point (prespecified or optimal): prespecified cut-off point of 30 Results:

	Se: 76% in the total study group, 76% in subgroup **Sp**: 76% in the total study group, 85% in subgroup **PPV**: 46.63% in total study group, 27.22% in subgroup **NPV**: 91.91% in total study group, 98.04% in subgroup **LR+**: 3.17 in total study group, 5.07 in subgroup **LR-**: 0.32 in total study group, 0.28 in subgroup **PC**: 76% in total study group, 84.48% in subgroup AUC Summary: The DES has shown sufficient sensitivity and specificity as well in the total study sample with a high prevalence of MPD patients as in the subgroup with lower prevalence of MPD patients. The tool is especially successful in correctly screening the non-MPD patients (reducing the false-positives). Conclusion: The DES as screening tool can greatly increase the probability of identifying patients with MPD

QUADAS-2 questions for assessing risk of bias in diagnostic accuracy studies

Domain 1: Patient Selection

Was a consecutive or random sample of patients enrolled? (Yes/No/Unclear)

Yes, no random sampling but all patients who are willing to participate in the seven centers were included if they were willing to participate, so there was consecutive sampling

Was a case-control design avoided? (Yes/No/Unclear)

No, current study is a case-control study

Did the study avoid inappropriate exclusions? (Yes/No/Unclear)

Yes, the only inclusion criteria were 18 years or older, willing to give informed consent and psychiatric population. So patients were not unnecessarily excluded.

Could the selection of patients have introduced bias? Risk: HIGH/LOW/UNCLEAR

Low, patients were selected from different mental health clinics, among them some specialized in treatment of dissociative disorders so the prevalence of dissociative patients in the total sample is overestimated. However, in the subgroup analysis Bayes's theorem has controlled for this overestimation, so in the subgroup analysis the sample had a proper and representative distribution.

Is there concern that the included patients do not match the review question (spectrum bias)? CONCERN: HIGH/LOW/UNCLEAR

High, only MPD patients were separately analyzed in the main analysis, while in the non-MPD group also PTSD patients and patients with other dissociative disorders were included, these two disordered groups could have an increased chance of or comorbidity with MPD

Domain 2: Index Test(s) (complete for each index test used)

Were the index test results interpreted without knowledge of the reference standard? (Yes/No/Unclear)

Unclear, there is no information about the assessors of the DES and their foreknowledge of the diagnosis of the patient population.

If a threshold was used, was it pre-specified? (Yes/No/Unclear)

Yes, threshold was specified before analysis

Could the conduct or interpretation of the index test have introduced bias? Risk: HIGH/LOW/UNCLEAR

Low, unclear if the assessors were biased but the threshold was predefined

Is there concern that the index test, its conduct, or interpretation differ from the review question? CONCERN: HIGH/LOW/UNCLEAR

Low, the index test is a suitable screening instrument for dissociative disorders

Domain 3: Reference Standard

Is the reference standard likely to correctly classify the target condition? (Yes/No/Unclear)

Yes, the DSM III is an appropriate diagnostic instrument

Were the reference standard results interpreted without knowledge of the results of the index test? (Yes/No/Unclear)

Unclear, there is no information if the assessors of the DSM III are also the assessors of the DES and if there is any diagnostic foreknowledge

Could the reference standard, its conduct, or its interpretation have introduced bias?

Risk: HIGH/LOW/UNCLEAR

Unclear, interpretation of the reference test and the influence on the assessment of the DES is not reported

Is there concern that the target condition as defined by the reference standard does not match the review question? CONCERN: HIGH/LOW/UNCLEAR

Low, the DSM III correctly identifies psychiatric disorders and the distribution of disorders in the total population were reported.

Domain 4: Flow and Timing

Was there an appropriate interval between index test(s) and reference standard? (Yes/No/Unclear)

Unclear, no information about the interval between the assessment of the reference test and the index test

Did all patients receive a reference standard? (Yes/No/Unclear)

Yes, all patients had a DSM III diagnosis

Did all patients receive the same reference standard? (Yes/No/Unclear)

No, some patients were diagnosed using the DSM-III and some patients were diagnosed using the DSM-III-R

Were all patients included in the analysis? (Yes/No/Unclear)

Yes

Could the patient flow have introduced bias? RISK: HIGH/LOW/UNCLEAR

Low, all patients were diagnosed using the DSM-III or DSM-III-R, these differences were minimal so the risk of bias is also low, despite the two different reference tests

Conclusion:

Risk of Bias is low in current study, only concern is the fact that no information has been supplied about the independence and the blinding of the assessors of the index and the reference test.

Frischholz et al. (1990)

Reference: Frischholz, E.J., Braun, B.G., Sachs, R.G., Hopkins, L., Shaeffer, D.M., Lewis, J., … & Schwartz, D.R. (1990). The Dissociative Experiences Scale: Further Replication and Validation. *Dissociation, 3,* 151-153.	
Methods	Study aim: to estimate inter-rater reliability, temporal stability and internal consistency of DES scores in both normal and clinical groups; to compare DES scores between normal population and patients with dissociative psychopathology and between MPD and DDNOS patients; and examining the consequence of using different DES cut-off scores to discriminate between normal and dissociative disorder patients Study design: cross-sectional study design Setting: Dissociative Disorders Inpatient Unit, Rush North Shore Medical Center, Skokie, Illinois and University of Illinois, Chicago Location: Skokie (Illinois) and Chicago (Illinois) Training of assessors: DES has been administered by a psychologist, nurse or mental health worker, there was no information available about the training and expertise of the assessors. Twenty DES protocols were independently rated by four raters, ICC of absolute agreement was 0.96 and ICC of relative agreement was 0.99, there was no information available about the expertise of the raters
Patients	Number of patients: Total sample: N = 321; N = 62 dissociative disorder patients, among which N = 33 MPD patients and N = 29 DDNOS patients; N = 259 healthy college students Inclusion: for the patient population a DSM-III or DSM-III-R diagnosis of a dissociative disorder, for the healthy university undergraduates no inclusion criteria have been reported Exclusion: no exclusion criteria have been reported Age: Mean age of the patient group = 35.1 years; mean age of the healthy population = 19.8 years; mean age of the total sample = 22.8 years of age Sex: 59% of the patient group was female, 75% of the healthy population was female and 71.9% of the total sample is female Ethnicity: no ethnicity data reported Co-morbidity: no information about comorbidity Other: no further information
Instruments	Index test: The Dissociative Experiences Scale (DES), a 28-item self-report inventory of both normal and abnormal experiences to offer a means of reliably measuring dissociation in normal and clinical populations. Scores were relatively stable and the DES successfully discriminated patients with MPD from normal and other pathological groups Reference test: For the patient group: DSM-III or DSM-III-R, for the healthy control group no reference test has been reported Time interval and treatment in between both tests: no information about the interval time between the assessment of the DES and the DSM-III or DSM-III-R
Results	Target condition: patients with dissociative pathology versus healthy controls Prevalence in sample: 33 (10.3%) MPD patients, 29 (9.0%) DDNOS patients and 259 (80.7%) healthy undergraduate students Cut-off point (prespecified or optimal): no prespecified cut-off point, the optimal cut-off point is a DES score between 45 and 55 Results:

	Se: Cut off =10: 99%; Cut-off =15: 99%; Cut-off =20: 98%; Cut-off =25: 97%; Cut-off =30: 95%; Cut-off =35: 94%; Cut-off =40: 94%; Cut-off =45: 93%; Cut-off =50: 90%; Cut-off =55: 89%; Cut-off =60: 86% **Sp**: Cut off =10: 35%; Cut-off =15: 46%; Cut-off =20: 57%; Cut-off =25: 66%; Cut-off =30: 75%; Cut-off =35: 82%; Cut-off =40: 88%; Cut-off =45: 94%; Cut-off =50: 97%; Cut-off =55: 98%; Cut-off =60: 99% **PPV**: Cut off =10: 26.72%; Cut-off =15: 30.50%; Cut-off =20: 35.30%; Cut-off =25: 40.58%; Cut-off =30: 47.63%; Cut-off =35: 55.56%; Cut-off =40: 65.22%; Cut-off =45: 78.77%; Cut-off =50: 87.78%; Cut-off =55: 91.42%; Cut-off =60: 95.37% **NPV**: Cut off =10: 99.32%; Cut-off =15: 99.48%; Cut-off =20: 99.17%; Cut-off =25: 98.92%; Cut-off =30: 98.43%; Cut-off =35: 98.28%; Cut-off =40: 98.39%; Cut-off =45: 98.25%; Cut-off =50: 97.59%; Cut-off =55: 97.38%; Cut-off =60: 96.73% **LR+**: Cut off =10: 1.52; Cut-off =15: 1.83; Cut-off =20: 2.28; Cut-off =25: 2.85; Cut-off =30: 3.8; Cut-off =35: 5.22; Cut-off =40: 7.83; Cut-off =45: 15.5; Cut-off =50: 30; Cut-off =55: 44.5; Cut-off =60: 86 **LR-**: Cut off =10: 0.03; Cut-off =15: 0.02; Cut-off =20: 0.04; Cut-off =25: 0.05; Cut-off =30: 0.07; Cut-off =35: 0.07; Cut-off =40: 0.07; Cut-off =45: 0.07; Cut-off =50: 0.10; Cut-off =55: 0.11; Cut-off =60: 0.14 **PC**: Cut off =10: 34%; Cut-off =15: 45%; Cut-off =20: 54%; Cut-off =25: 63%; Cut-off =30: 70%; Cut-off =35: 76%; Cut-off =40: 82%; Cut-off =45: 87%; Cut-off =50: 87%; Cut-off =55: 87%; Cut-off =60: 85% AUC Summary: specificity and PPV are growing when the cut-off point is higher, sensitivity and NPV are minimally decreasing with a higher cut-off point Conclusion: a DES cut-off of 35 and higher will lead to good sensitivity and specificity, the optimal cut-off points depends on the preferred rate of false positives and false negatives in the test.
QUADAS-2 questions for assessing risk of bias in diagnostic accuracy studies **Domain 1: Patient Selection** Was a consecutive or random sample of patients enrolled? (Yes/No/Unclear)	

Unclear, no random sampling but unclear if it is consecutive sampling

Was a case-control design avoided? (Yes/No/Unclear)

No, current study had a case-control design

Did the study avoid inappropriate exclusions? (Yes/No/Unclear)

Unclear, no specific inclusion criteria were reported for the healthy control group so it is unclear if participants were inappropriately excluded

Could the selection of patients have introduced bias? Risk: HIGH/LOW/UNCLEAR

High, it is a case control design and information about sampling and avoiding inappropriate exclusions were too limited

Is there concern that the included patients do not match the review question (spectrum bias)? CONCERN: HIGH/LOW/UNCLEAR

Low, patients match the review question

Domain 2: Index Test(s) (complete for each index test used)

Were the index test results interpreted without knowledge of the reference standard? (Yes/No/Unclear)

Unclear, the psychiatric patients were assessed by psychologists and mental health workers affiliated with the inpatient setting, but it is unclear if they are blind for the DSM diagnosis

If a threshold was used, was it pre-specified? (Yes/No/Unclear)

No, the threshold was not pre-specified

Could the conduct or interpretation of the index test have introduced bias? Risk: HIGH/LOW/UNCLEAR

Low, there was no pre-specified threshold, but this study was executed with the goal of indicating a diagnostic screening threshold of the DES. Because the DES was a new instrument in this study the risk of bias is not very high

Is there concern that the index test, its conduct, or interpretation differ from the review question? CONCERN: HIGH/LOW/UNCLEAR

Low, the DES is a suitable diagnostic screening instrument

Domain 3: Reference Standard

Is the reference standard likely to correctly classify the target condition? (Yes/No/Unclear)

Yes, the DSM-III is a suitable diagnostic instrument

Were the reference standard results interpreted without knowledge of the results of the index test? (Yes/No/Unclear)

Yes, all patients were already diagnosed before the DES was executed, it was unclear if the healthy university undergraduates were diagnosed

Could the reference standard, its conduct, or its interpretation have introduced bias?

Risk: HIGH/LOW/UNCLEAR

Low, the DSM-III is an appropriate reference test

Is there concern that the target condition as defined by the reference standard does not match the review question? CONCERN: HIGH/LOW/UNCLEAR

High, it is unclear if all university undergraduates have undergone a DSM-III diagnosis, so it remains unclear if these undergraduates were healthy controls

Domain 4: Flow and Timing

Was there an appropriate interval between index test(s) and reference standard? (Yes/No/Unclear)

Unclear, there was no information about the interval between the DSM-III and the DES

Did all patients receive a reference standard? (Yes/No/Unclear)

Unclear, not evident if the undergraduates had undergone a DSM-III diagnostic screening

Did all patients receive the same reference standard? (Yes/No/Unclear)

Yes, the only reference standard was the DSM-III or DSM-III-R which are practically equal

Were all patients included in the analysis? (Yes/No/Unclear)

Yes

Could the patient flow have introduced bias? RISK: HIGH/LOW/UNCLEAR

Unclear, too few information about the use of the reference test for the undergraduates

Conclusion: Current study is lacking a lot of information to assess risk of bias. This makes current study an unreliable study with a high risk of bias.

Bijlage 5 Deel 2: behandeling volwassenen

Bijlage 5.2a Review protocol EBRO module Behandeling en Begeleiding

Topic	Interventions/ epidemiology
Review question(s)	1. Is er sprake van practice-based/clinical consensus behandeling? En zo ja, waarover is dan consensus? Zo nee, waarover gaat de discrepantie? 2. Is er empirisch bewijs voor effectiviteit van behandelingen? - Welke behandelingen zijn beschikbaar? - Wat is de effectiviteit van de behandelingen? 3. Wat is gepaste zorg (vanuit hulpverleners of cliënten) Op welke manier kan de bejegening worden verbeterd? (vanuit patiënten)
Sub-question(s)	-
Objectives	Vraag 1 wordt door middel van een focusgroep met Professionals beantwoord Vraag 2 wordt beantwoord door middel van een literatuursearch. Vraag 3 door middel van een Focusgroep/Conjunct analyse met cliënten Dit protocol behandelt de criteria mbt vraag 2.
Criteria for considering studies for the review	
Types of participants	Kinderen, adolescenten en volwassenen met een dissociatieve stoornis (depersonalisatie en derealisatie, DIS en de DIS-NAO) volgens de definitie van de DSM-IV of DSM-5. (exclusie: dissociatieve symptomen voortkomend uit een andere psychische comorbiditeit, zoals PTSS of Borderline Persoonlijkheidsstoornis; setting:, verslavingszorg of zorg voor verstandelijk gehandicapten.)
Intervention	Farmacologische,psychologische interventies en/ of (toevoeging) vaktherapeutische interventies. Herstelgerichte zorg.
Comparator	Wachtlijst, gebruikelijk zorg, andere psychologische of farmacologische interventies.
Critical outcomes	1. symptoomreductie zowel wat betreft de dissociatieve stoornis als wat betreft de comorbide stoornis 2. lijdensdruk 3. nivo van functioneren (bestaande uit mate van zelfstandig het dagelijks leven kunnen leiden, rol in maatschappij, belastbaarheid, en zorgconsumptie) 4. persoonlijk herstel
Important outcomes	Kwaliteit van leven Dropout (therapie of studie)
Time	-

Study design	1. Systematic review (met Meta-analyse) / Andere Internationale richtlijnen 2. RCT's
Dosage	-
Study setting/country	-
Search strategy	**Databases searched**: CINAHL, Pubmed, PsycInfo, Cochrane **Date limiters:** 1990 **Other limiters, e.g. design, language, age:** Engels en Nederlands
Study design filter used	Nee
Question specific search strategy	Nee
Searching other resources	Ongepubliceerd werk aangeleverd door experts
The review strategy	Voor DIS en DIS-NAO wordt een update uitgevoerd van de 'Guidelines for the Evaluation and Treatment of Dissociative Symptoms in Children and Adolescents (2004) en 'Guidelines for Treating Dissociative Identity Disorder in Adults, Third Revision' (2011). Voor andere diagnoses (depersonalisatie en derealisatie) moet een aparte search gedaan worden, tenzij er in de search ook recente richtlijnen worden gevonden. 1. Eerste selectie (title and abstract): bij twijfel en voorlopige inclusie de full text opvragen. 2. Tweede selectie (full text): bij twijfel artikelen bespreken met tweede onderzoeker 3. Zie kopje 'Study design' aflopend in voorkeur: 1. Heeft sterk de voorkeur ter beantwoording van de de uitgansvragen (eventueel met update); 4. Data extractie en kwaliteitsbeoordeling (RoB of AMSTAR) in bewijstabel 5. Als er voldoende bewijs wordt gevonden van goede kwaliteit dan kan eventueel een meta-analyse worden overwogen. In het geval dit niet zo is of er een artikel van 'Study design' type 1. wordt gevonden dan volgt een narratieve analyse. 6. Conclusies volgens GRADE-methodiek
Note.	

Bijlage 5.2b Resultaten zoekstrategie

Zoekgeschiedenis behandeling van dissociatieve stoornissen

Er is een zoekstrategie uitgevoerd in de databases PsycInfo, PubMed en CINAHL naar randomised controlled studies (RCT's), systematic reviews en meta-analyses over de behandeling van dissociatieve stoornissen.

Hierbij is geen beperking aangebracht op jaar van uitgave of taal. De searches zijn op 11 april en 25 mei 2016 uitgevoerd.

PsycInfo

In PsycInfo is gezocht op de volgende thesaurustermen voor dissociatieve stoornissen:

DE "Dissociative Disorders" OR DE "Depersonalization" OR DE "Depersonalization/Derealization Disorder" OR DE "Dissociative Identity Disorder" OR DE "Fugue Reaction" OR DE "Dissociation".

Deze thesaurustermen zijn aangevuld met woorden voor dissociatieve stoornissen in het titel-, keyword- of abstract-veld, te weten: dissociative OR dissociation OR depersonalisation OR depersonalization OR derealisation OR derealization OR fugue OR "multiple personality disorder*" OR "dual personality" OR "dual personalities" OR multiple personality" OR "multiple personalities".

Om te beperken tot RCT's, systematic reviews en meta-analyses is gebruik gemaakt van het methodologie filter in PsycInfo, aangevuld met rct or random* in het titel-, keyword- en abstract-veld.

PubMed

In PubMed is voor dissociatieve stoornissen gezocht op de thesaurustermen "Dissociative Disorders"[Mesh] OR "Multiple Personality Disorder"[Mesh], aangevuld met de volgende woorden in titel of abstract: dissociative [tiab] OR dissociation [tiab] OR depersonalisation[tiab] OR depersonalization[tiab] OR derealisation[tiab] OR derealization[tiab] OR fugue[tiab] OR "multiple personality disorder"[tiab] OR "multiple personality disorders"[tiab] OR "dual personality"[tiab] OR "dual personalities"[tiab] OR "multiple personality"[tiab] OR "multiple personalities"[tiab].

Om te beperken tot RCT's, systematic reviews en meta-analyses is gebruik gemaakt van het Clinical Queries filter 'therapy narrow' en die voor systematic reviews.

CINAHL

In CINAHL is gezocht op de thesaurustermen: MH "Dissociative Disorders" OR MH "Multiple-Personality Disorder" OR MH "Depersonalization". Deze termen zijn aangevuld in titel en abstract met dezelfde termen die gebruikt zijn in de andere databases.

Om te beperken tot RCT's is gebruik gemaakt van het filter voor publicatie type in CINAHL.

Resultaat

Er zijn in PsycInfo 544 RCT's gevonden, in PubMed 627 en in CINAHL 150. Dit zijn er in totaal 1321. Deze resultaten zijn ontdubbeld en na verwijdering van 193 dubbelen bleven er 1128 RCT's over.

In PsycInfo zijn 122 systematic reviews en meta-analyses gevonden, in PubMed 302. Dit zijn in totaal 424 referenties. Deze zijn ontdubbeld en er zijn 67 duplicaten verwijderd. Dit betekent dat er 357 referenties overbleven.

In de search is ook vaktherapie meegenomen; echter er zijn geen RCTs en systematische reviews gevonden naar vaktherapie bij dissociatieve stoornissen.

Bijlage 2c Evidence tabellen behandeling volwassenen

Systematische reviews en meta-analyses

Reference: Donaldson PH, Rinehart NJ, Enticott PG. Noninvasive stimulation of the temporoparietal junction: A systematic review. Neuroscience and Biobehavioral Reviews 2015; 55:547-572.	
Methods	Study aim: This review examined studies that use noninvasive transcranial stimulation (NTS) to explore temporoparietal junction (TPJ) function and to examine the potential clinical utility of NTS technologies as applied to the TPJ. Study design: Randomized clinical trials with and without (sham) control groups Analysis: Descriptive summary of studies and results Setting: outpatients
Patients	Number of studies: K= 3 (but only two samples, because on study used data from one of the other studies retrospectively). Number of patients: N= 29 unique patients suffering from depersonalistation disorder, 20 healthy controls Age: 33.6 (12.9) and 33.2 (7.8) Sex: 22 female, 27 male Inclusion: To be included in the review, the paper needed to be a full, published, empirical study, where transcranial stimulation was applied to the human TPJ (either as a focus of the study or as an active control site). Exclusion: not explicitly stated TPJ stimulation, case reports or case series, TJP as an inactive control site only. Baseline characteristics: the sample that was used in two studies consisted of 12 right-handed outpatients with DSM-IV DD diagnosis, of which 2 used no further medication and 10 did (SSRIs, anti-convulsants). The other study included 17 DD patients of which 8 used some type of medication (not reported which ones).
Interventions	Intervention: TPJ stimulation (daily 1 Hz rTMS to the rTPJ for 3 – 6 weeks, the other study 1 Hz rTMS (15 min, 900 pulses) applied to rVLPFC or rTPJ. Control: no Follow-up time: -
Outcome	Primary: DD symptomology (anomalous body experiences, alienation from surroundings, emotional numbing, anomalous subjective recall).
Results	Of the 12 patients that received stimulation 6 responded positively, 5 of them received 3 extra weeks of stimulation, showing 68% improvement in DD symptomatology. Some partial/non-responders were then treated with lTPJ stimulation without success. This sample was reanalyzed in another study in which the responses were examined in 4 clusters. The five responders had reductions in anomalous body experience (76%), alienations from surroundings (54%), emotional numbing (52%), and anomalous subjective recall (57%).

	In the other study patients who received rTMS to rVLPFC or rTPJ showed a similar reduction in DD symptoms.
Quality Assessment **(AMSTAR)**	**+**; **-**; **?**; **NA** (Not applicable), Yes, No, Can't answer (Not applicable) 1. Was an 'a priori' design provided? - 2. Was there duplicate study selection and data extraction? - 3. Was a comprehensive literature search performed? + 4. Were limitations in the literature search reported? - 5. Was a list of studies (included and excluded) provided? - 6. Were the characteristics of the included studies provided? + 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? + 10. Was the likelihood of publication bias assessed? - 11. Was the conflict of interest stated? + General conclusion: A large thorough search was performed, including efforts to find grey literature. The quality of the included studies was assessed and accounted for in the interpretation of the results. Overall the quality of the review was considered moderate. GRADE: High initial level of evidence: systematic review of RCTs. Lowered level due to moderate risk of bias and imprecision. Final level of evidence is low.

Reference: Schoenberg PLA, David AS. Biofeedback for psychiatric disorders: A systematic review. Applied Psychophysiology and Biofeedback 2014; 39(2):109-135.	
Methods	Study aim: how biofeedback interventions have been used to treat select psychiatric disorders [anxiety, autistic spectrum disorders, depression, *dissociation*, eating disorders, schizophrenia and psychoses] Study design: systematic review with narrative synthesis Analysis: *Search until February 2014* Setting:
Patients	Number of studies: K=63; **K=1 on Dissociative identy disorder Manchester et al. (1998), data on this study will be described in bold.**

	K=1 Depersonalization disorder Schoenberg et al. (2012), data on this study will be described in italic. Number of patients: **N=11** *and 32* Age: **range 26-50 (mean 41.1)** *and 19-59* Sex: **100%** *and 25% women* Inclusion: Exclusion: Baseline characteristics:
Interventions	Intervention: α-θ **regulation Biofeedback (30 sessions of 30 minutes)** *Skin conductance level (SCL) Biofeedback (8 sessions of 20 minutes)* Control: *Sham Biofeedback* Follow-up time: **7-25** *and 3 months*
Outcome	**Pre and post outcome: Millon clinical multiaxial inventory (MCMI-II), Global Assessment Scale (GAF), Dissociative Experiences Scale (DES)** *Cambridge depersonalization scale CDS (trait and state)* *version), Dissociative Experiences Scale (DES), Beck anxiety inventory (BAI), Beck depression inventory (BDI)*
Results	**Manchester et al. (1998) reported significant clinical improvement from the BF intervention. All met Kluft's criterion for unification after BF. Mean GAF scores sig improved:. 'Normal' range DES scores at follow-up** *Schoenberg et al. (2012) investigated the effects of eight sessions of skin conductance level (SCL) enhancement BF in patients with Depersonalization Disorder (DPD) randomly allocated to either a real-time or sham (placebo) group. Unexpectedly, the patients' baseline SCLs were significantly high, thus, marshalling further increase appeared difficult, suggesting the inclusion of an SCL decrease protocol would have been apt from the outset. As such, SCL reduction was evident across the BF-trial, which coincided with significant reduction in 'state' depersonalization symptoms (recorded after each session of biofeedback) in the real-time BF group only, not the sham/placebo. Thus, a transient ameliorating effect on dissociative symptoms was evident, but not necessarily linked to the investigated SCL-increase protocol.* FROM THE ORIGINAL ARTICLE *Depersonalization symptomatology. CDS Trait scores showed that neither the real-time nor sham condition yielded a significant change in depersonalization symptoms globally. Comparing CDS State scores, completed immediately after every session of biofeedback, a main effect of time, F(1, 27) = 6.38, p = .02, and Time × Condition interaction, F(1, 27) = 4.11, p = .05, showed a significant decrease in depersonalization symptoms when analyzed by the phase contrast (36.0 [SD = 16.9] falling to 29.9 [SD = 18.9]) for the real-time condition only, t(15) = 2.84, p = .01 (see Table 2).* *Exploring whether biofeedback specifically targeted disembodiment* *and emotional numbing symptoms, we found that the State CDS anomalous body experience (ABE) subscale scores showed a main effect of time (pre, post), F(1, 23) =*

	12.5, p = .002, reflecting a significant decrease in experienced ABE in both the real-time, t(14) = 2.65, p = .02, and sham, t(9) = 2.27, p = .05, conditions. No main effect of condition or Condition × Time interaction was found. The State CDS emotional numbing (EN) subscale scores also revealed a significant main effect of time, F(1, 24) = 5.01, p = .04, and no main effect of condition or *Condition × Time interaction. However, within-group analysis showed that EN significantly decreased in the real-time condition, t(14) = 2.26, p = .02, and marginally increased in the sham condition pre- to post trial (see Table 2). No significant change in ABE or EN scores were found for the Trait CDS.* *EIGEN Meta anlayse*
Quality Assessment **(AMSTAR)**	**+**; **-**; **?**; **NA** (Not applicable), Yes, No, Can't answer (Not applicable) 1. Was an 'a priori' design provided? + 2. Was there duplicate study selection and data extraction? ? 3. Was a comprehensive literature search performed? + A systematic search of EMBASE, MEDLINE, PsycINFO, and WOK databases 4. Were limitations in the literature search reported?* + 5. Was a list of studies (included and excluded) provided? +/- 6. Were the characteristics of the included studies provided? + 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? – narrative analysis, but there was only 1 study for dissociation. 10. Was the likelihood of publication bias assessed? - 11. Was the conflict of interest stated? General conclusion: Thorough search and selection. Assessment of study quality and accounted for in the interpretation of the result. Overall the quality of the review was considered good. GRADE: High initial level of evidence: systematic review of RCTs. Lowered level due to imprecision and inconsistency. Final level of evidence is low.
Manchester, C. F., Allen, T., & Tachiki, K. H. (1998). Treatment of dissociative identity disorder with neurotherapy and group selfexploration. Journal of Neurotherapy, 2(4), 40–52. *Schoenberg, P. L. A., Sierra, M., & David, A. S. (2012). Psychophysiological* *investigations in Depersonalization Disorder and effects of electrodermal biofeedback. Journal of Trauma and Dissociation, 13(3), 311–329.*	

Reference: Brand BL, Loewenstein RJ, Spiegel DA. Review of Dissociative Disorders Treatment Studies. J Nerv Ment Dis 2009; 197:646-654.	
Methods	[Niet gevonden met search, later toegevoegd] Study aim: The goal of this article is to review literature on DD treatment, including treatment of DID, DDNOS, depersonalization disorder (DPD), and dissociative seizures. Study design: studies that report on systematically collected treatment outcome data on the dissociative disorders: case studies and case series, treatment outcome studies. Analysis: Descriptive synthesis for results of all included studies added with mixed effects model to pool effect sizes (Hedges' g) across 8 studies that reported sufficient data. Setting: inpatient/outpatient
Patients	Number of studies: K = 8 non-randomized treatment outcome studies Number of patients: N = 476 patients with DD Age: NA Sex: unclear (not always reported) Inclusion: studies that report on systematically collected treatment outcome data on the dissociative disorders. Exclusion: - Baseline characteristics: -
Interventions	Intervention: various treatments aimed at dissociative disorder Control: wait list / other treatment (no randomization) Follow-up time: -
Outcome	Primary: clinical diagnosis of dissociative disorder (e.g., DDIS), and symptoms of DD like depersonalization (e.g., CDS-S), dissociative experiences (e.g., DES). Secondary: various comorbid psychological problems, for example: depression (e.g., BDI, HAM-D), anxiety (e.g., BAI, HADS).
Results	FROM THE ORIGINAL ARTICLE These studies provide preliminary evidence that treatment is effective in reducing a range of symptoms associated with dissociative disorders, including depression, anxiety, Axis I and Axis II diagnoses, and dissociative symptoms. DID patients who became integrated appear to show greater improvement across measures compared with those who remained unintegrated (Ellason and Ross, 1996, 1997, 2004), although diagnostic changes were less common. Integrated patients showed better outcome scores on depression, dissociation, somatization, first-rank symptoms, borderline features, and number of axis I and II disorders (Ellason and Ross, 1997). Across the case series and treatment studies, estimates of full integration range from 16.7% to 33% of DID patients (Coons and Sterne, 1986; Coons and Bowman, 2001; Ellason and Ross, 1997) with shorter follow-up associated with lower rates of integration (Coons and Sterne, 1986;

	Ellason and Ross, 1997). Case series that have not used standardized measures have reported higher rates of integration (e.g., 66% in Kluft, 1984). Although these preliminary findings are encouraging, it is important to recognize that these outcome studies have a number of methodological limitations. The lack of a control condition makes it difficult to know whether changes occurred due to treatment or some other variable such as the passage of time or regression to the mean. In many of these studies there is a selection bias. Patients are not randomly selected and often they are not systematically selected, although in some studies inclusion was based on consecutive admissions (Goldstein, et al., 2004; Ross and Haley, 2004). Drop-out rates are known to be a problem for several studies (Ellason and Ross, 1996, 1997, 2004; Gantt and Tinnin, 2007), but in others, the drop-out rates are not reported (Ross and Burns, 2007; Ross and Ellason, 2001). One outpatient study reported no drop-outs (Hunter et al., 2005). A small sample size is a limitation for some of these studies, which is not surprising given the population being sampled. Multiple testing without adjusting the p value is another limitation. Given these limitations, the generalizability of the findings are in question. Eight studies yielded sufficient outcome data to generate effect sizes (ES). The type of ES used was Hedges g, which makes a less restrictive assumption about standard deviations for both time periods (Kline, 2005). ES are reported such that a positive ES indicates change in the desired direction and a negative ES indicates change in the opposite direction. Ninety-four ES were from discharge outcomes and 24 were from longer term follow-up. Using MiMa, software (Viechtbauer, 2006) developed for the language and statistical computing environment R (R Development Core Team, 2008), ES across studies, outcome types, and follow-up length were calculated using a mixed-effects model. The overall ES was 0.71, with discharge ES slightly larger (0.72) and longer term follow-up ES slightly smaller (0.66). The range of ES across studies ranged from a maximum ES of 1.82 (Ross and Burns, 2007) to a minimum ES of 0.36 (Goldstein et al., 2004). Of the 118 ES, 64 were from outcomes that could be classified into 8 distinct types as follows: anxiety symptoms ES _ 0.94, BPD symptoms ES _ 0.95, depression symptoms ES _ 1.12, dissociation symptoms ES _ 0.70, general distress ES _ 1.09, somatoform symptoms ES _ 0.83, and substance use symptoms ES _ 0.78.
Quality Assessment **(AMSTAR)**	**+**; **-**; **?**; **NA** (Not applicable), Yes, No, Can't answer (Not applicable) 1. Was an 'a priori' design provided? - 2. Was there duplicate study selection and data extraction? - 3. Was a comprehensive literature search performed? + 4. Were limitations in the literature search reported? - 5. Was a list of studies (included and excluded) provided? - 6. Were the characteristics of the included studies provided? + 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? + 10. Was the likelihood of publication bias assessed? - 11. Was the conflict of interest stated? +

	General conclusion: the selection studies was not described into detail: no inclusion/exclusion criteria were listed. The methodological weaknesses of each study are reported and are accounted for in the interpretation of the results. For some studies it was possible to pool the quantitative results: only overall effect sizes were reported while associated standard errors were not presented, making the interpretation of the effect sizes impossible. Due to these limitations the quality of this review is considered moderate. GRADE: Low initial level of evidence: systematic review of non-randomized trials. Lowered level due to risk of bias, imprecision and indirectedness. Final level of evidence is very low.

Gerandomiseerde onderzoeken

Reference: Sierra M, Phillips ML, Ivin G, Krystal J, David AS. A placebo-controlled, cross-over trial of lamotrigine in DEPERSONALIzation disorder. J Psychopharmacol 2003; 17(1):103-105.	
Methods	Study aim: To test the efficacy of lamotrigine as a treatment for patients with depersonalization disorder. Study design: double-blind, placebo-controlled, cross-over design Analysis: Analysis of Variance (ANOVA) Study duration: 12 weeks Setting: patients recruited from a single specialized center Location: London, UK
Patients	Number of patients: N=14 included, N=9 completed Inclusion: patients with diagnosed DSM-IV depersonalization disorder (ascertained by a semi-structured interview using the Present State Examination (Wing et al. 1974), Exclusion: patients with comorbid psychiatric disorders, neurological conditions, substance or alcohol use. Baseline characteristics: N_{women}=4, N_{men}=5, age range 30-42 (mean=35.2, SD=3.4). 6 patients previously on SSRI's but not at the time of the study.
Interventions	Comparison between lamotrigine and placebo in a crossover trial with two treatment groups as follows: Group 1 (n=7): 1) 2 week wash-out; 2) 6 weeks of treatment with **lamotrigine** in increasing dose: 25mg/day week 1, 50mg/day week 2, 100mg/day week 3, 100mg/day week 4; 3) for the remaining 6 weeks: 200mg/day week 5, 200mg/day week 6, and then 250mg/day; 4) 2 week wash-out 5) 6 weeks of treatment with **placebo** in increasing dose: 25mg/day week 1, 50mg/day week 2, 100mg/day week 3, 100mg/day week 4; 6) for the remaining 6 weeks: 200mg/day week 5, 200mg/day week 6, and then 250mg/day;

	Group 1 (n=7): 1) 2 week wash-out; 2) 6 weeks of treatment with **placebo** in increasing dose: 25mg/day week 1, 50mg/day week 2, 100mg/day week 3, 100mg/day week 4; 3) for the remaining 6 weeks: 200mg/day week 5, 200mg/day week 6, and then 250mg/day; 4) 2 week wash-out 5) 6 weeks of treatment with **lamotrigine** in increasing dose: 25mg/day week 1, 50mg/day week 2, 100mg/day week 3, 100mg/day week 4; 6) for the remaining 6 weeks: 200mg/day week 5, 200mg/day week 6, and then 250mg/day; Duration of follow-up: NA Considerations: • Comparability of treatment groups at baseline *The nature of the design (crossover) deals with this problem, since outcomes are compared within patients.* • Group received the same care apart from the interventions studied *No information is provided, but assumed: yes* • Sufficient duration of follow up *12 weeks treatment without follow-up* • Funding by pharmacist / researcher is developer of experimental intervention (possible allegiance bias) *Not stated*
Outcome measures	Critical/primary: these were not operationalised, only the measurement instruments were listed as follows 1. Present State Examination (PSE) - structured interview 2. Cambridge Depersonalisation Scale (CDS): 3. Dissociative Experiences Scale (DES) 4. Beck's Depression Inventory (BDI) Important/secondary: 1. Side effects 2. Plasma levels of lamotrigine 3. White cell counts
Results	Treatment outcome: No significant differences between the treatments Carry-over: No significant carry-over effect Drop out: 5 patients failed to complete the study: 3 due to non-compliance with the treatment, 1 due to missed assessments, 1 due to neutropenie (while on placebo). Adverse events: - Lamotrigine: 3 patients reported dizziness, muscle aches and nausea - Placebo: 4 patients reported sedation, fatigue, muscle aches, neutropenie (as mentioned in drop-out section) - Plasma levels were within accepted range for all patients on lamotrigine Conclusion:

	No support for beneficial effect of lamotrigine when used as mono-therapy in treatment of depersonalization disorder. High drop-out reduced the statistical power of the study by 29%. However, the fact that no single patents had a reduction of than 12% from his baseline CDS or PSE scores makes it unlikely that the negative findings were due to this power reduction.
RoB Assessment **(Cochrane)** **+;-;?**	+ = Yes = low RoB, - = no = high RoB, ? = can't answer = RoB uncertain *Selection bias:* 1. Random sequence generation + 2. Allocation concealment + *Performance bias:* 3. Masking patients and professionals + *Detection bias:* 4. Masking of outcome assessment + *Attrition bias:* 5. Complete outcome data - *Reporting bias:* 6. Selective reporting - *Other bias: NA* Conclusion: Risk of bias due to design issues was low, however due to large drop-out the risk of bias is considered moderate. Due to this and small sample size the overall level of evidence is considered low.

Reference: Simeon D, Guralnik O, Schmeidler J, Knutelska M. Fluoxetine therapy in DEPERSONALIsation disorder: RANDOMised controlled trial. Br J Psychiatry 2004; 185:31-36	
Methods	Study aim: To investigate the efficacy of fluoxetine in the treatment of depersonalisation disorder. Study design: double-blind, randomized, parallel, placebo-controlled trial. Analysis: Analysis of Covariance (ANCOVA) Study duration: 10 weeks Setting: - Location: New York, USA
Patients	Number of patients: N=50 Inclusion: adults (age 18-65 years), meeting DSM-IV diagnostic criteria for current depersonalization disorder (as diagnosed by semi-structured clinical interview and the

	Structured Interview for DSM-IV Dissociative Disorders. No psychotropic medication for a period of at least 2 weeks. Exclusion: persons who previously had undergone an adequate fluoxetine trial, or if they reported fluoxetine intolerance or hypersensitivity. People with lifetime diagnosis of schizophrenia, schizoaffective disorder, bipolar disorder, or organic mental disorder, substance use disorder, eating disorder. People were included if they received psychotherapy for at least 3 months, but not if they just started it, or received specialized treatment such as cognitive-behavioral therapy or hypnosis. Acute or unstable medical illnesses, history of seizure disorder or major head trauma. Pregnant and lactating women. Baseline characteristics: -
Interventions	Intervention: 1) 2 week (single-blinded) placebo run-in phase 2) 10 mg/day fluoxetine in first week 3) Flexible increase of dosage (20mg/40mg/60mg per day) over the following 3 weeks 4) Continuation until end of trial Control: 1) 2 week (single-blinded) placebo run-in phase 2) Continuation with placebo until end of trial Duration of follow-up: - Considerations: • Comparability of treatment groups at baseline *The baseline table shows the two groups did not significantly differed at baseline on demographic and clinical variables.* • Group received the same care apart from the interventions studied *No detailed information on the treatment of the control group is presented.* • Sufficient duration of follow up *10 weeks of treatment with no follow-up.* • Funding by pharmacist / researcher is developer of experimental intervention (possible allegiance bias) *No*
Outcome measures	Critical/primary: - Clinical Global Impression (CGI-I) - Dissociative Experiences Scale (DES) - Depersonalization Severity Scale (DSS) Important/secondary: - Depression (Hamilton Rating Scale for Depression, HRSD) - Anxiety (Hamilton Rating Scale for Anxiety, HRSA) - Social phobia symptoms (Liebowitz Social Anxiety Scale, LSAS) - Obsessive compulsive symptoms (Yale-Brown Obsessive Compulsive Severity Scale - Panic attack diary - CGI-I scores were applied to all existent comorbid disorders

Results	Treatment outcome: fluoxetine was not superior to placebo in treating depersonalisation as measured by DES and DDS. However, a clinically small but statistically significant difference in CGI-I endpoint scores (not covaried for depression and anxiety) was found (mean improvement for fluoxetine 2.9 (SD=1.2) and for control 3.6 (SD=0.9), F(1,47)=6.02, *p*=0.02). Adverse events: side-effects that occurred at a frequency of at least 10% in one of the two groups were: - Decreased appetite: fluoxetine 36%, placebo 4% - Muscle stiffness or cramping: fluoxetine 16%, placebo 12% - Tremor: fluoxetine 16%, placebo 0% - Nervousness: fluoxetine 28%, placebo 40% - Excitation or hyperactivity: fluoxetine 8%, placebo 12% - Fatigue: fluoxetine 48%, placebo 16% - Sedation: fluoxetine 20%, placebo 0% - Headaches: fluoxetine 28%, placebo 28% - Diarrhea: fluoxetine 16%, placebo 16% - Nausea: fluoxetine 40%, placebo 20% - Stomach ache: fluoxetine 12%, placebo 12% - Urinary frequency: fluoxetine 20%, placebo 8% - Palpitations: fluoxetine 4%, placebo 20% - Dizziness/lightheadedness: fluoxetine 16%, placebo 16% - Blurry vision: fluoxetine 12%, placebo 8% - Sweating: fluoxetine 16%, placebo 12% - Insomnia: fluoxetine 48%, placebo 24% - Decreased libido: fluoxetine 48%, placebo 20% - Decreases sexual arousal: fluoxetine 24%, placebo 4% Only one person from the fluoxetine group discontinued the trial because of adverse events (heightened anxiety). 9 persons dropped out in the fluoxetine group, versus 4 persons in the placebo group. Only one person from the fluoxetine group discontinued the trial because of adverse events (heightened anxiety).
RoB Assessment **(Cochrane)** **+;-;?**	+ = Yes = low RoB, - = no = high RoB, ? = can't answer = RoB uncertain *Selection bias:* 1. Random sequence generation + 2. Allocation concealment + *Performance bias:* 3. Masking patients and professionals + *Detection bias:* 4. Masking of outcome assessment + *Attrition bias:* 5. Incomplete outcome data - *Reporting bias:* 6. Selective reporting +

	Other bias: NA Conclusion: Risk of bias due to design issues was low, however due to large drop-out the risk of bias is considered moderate. Due to this the overall level of evidence is considered moderate. For CGI-I the level of evidence is considered low since the found effect size is small and only present without correcting for anxiety and depression.

3. Jongeren

Screening en diagnostiek

Voor de wetenschappelijke onderbouwing is in de EBRO-module Screening & Diagnostiek – Volwassenen een algemene search gedaan waarbij niet gelimiteerd is op volwassenen. Echter de resultaten bevatten geen systematic reviews of DTA-onderzoeken op het gebied van kinderen/jongeren.

Behandeling

Voor de wetenschappelijke onderbouwing is in de EBRO-module Screening & Diagnostiek – Volwassenen een algemene search gedaan waarbij niet gelimiteerd is op volwassenen. Echter de resultaten bevatten geen systematic reviews of randomized controlled trials op het gebied van kinderen/jongeren.