

Supplementary Appendix 4| Examples of in-depth analysis of disagreements conducted with the support of the study report

Risk of bias item	Study Name	Support for judgement*	Information in the study report^	Category of disagreement	Reason of disagreement
Random sequence generation	ABCD 2004	Review 4136: Generated the randomisation list using SAS, stratified by sex and SCr; Low Risk	<i>“The (...) statistician generated the randomization list using SAS (...) stratified by sex and baseline serum creatinine concentration (...).”</i>	Missed information from the study report	
		Review 8277: Method not reported; Unclear Risk			
	Cho 2006	Review 7566: Stated that it is a quasi-randomized study but details not given; High Risk	<i>“... using a quasi-experimental design with a non-equivalent control group.”</i> <i>“They were randomly assigned to participate in the experimental group (...) or a waiting-list control group (...).”</i>	Different interpretation	Consider differently incomplete or unclear description
		Review 9553: Participants randomly allocated to treatment or control group; Unclear Risk			
	Petersen 2005	Review 9132: Quote: “[P]atients were randomly assigned...”Quote: “We used an adaptive allocation scheme for the treatment assignment, with the MMSE score, age and APOE e4 status as balancing covariates”; Low Risk	<i>“We used an adaptive allocation scheme for the treatment assignment, with the MMSE score, age, and APOE e 4 status as balancing covariates.”</i>	Different interpretation	Confusion or misknowledge
		Review 7176: The trial is described as randomised, but the method of sequence generation was not specified. Unclear Risk			

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Risk of bias item	Study Name	Support for judgement*	What is reported in the study report^	Category of disagreement	Reason of disagreement
Allocation concealment	Burge 2000	Review 2991: Participants were randomly assigned sequentially from a list comprising treatment numbers only; Low Risk	<i>"We used a computer generated allocation schedule stratified by centre (block size of six). Patients were randomised sequentially from a list comprising treatment numbers only".</i>	Different interpretation	Consider differently incomplete or unclear description
		Review 10115: Information not available; Unclear Risk			
	McMurdo 1993	Review 4294: Quote: "Randomisation was by opening sealed envelopes supplied in sequence by the study co-ordinator; Low Risk	<i>"Randomization was by opening sealed envelopes supplied in sequence by the study co-ordinator (...), and prepared from a computer-generated random numbers table."</i>	Different interpretation	Consider differently envelopes description
		Review 4963: Unclear, insufficient reporting to permit judgement; Unclear Risk			
	Draper 2007	Review 8179: "... and alternating between treatment or wait list control groups."; High Risk	<i>"On each occasion that a least eight patients had been recruited, their names were selected at random by a blinded investigator to be allocated alternately to the immediate treatment group or a wait-list control group."</i>	Different interpretation	Consider differently incomplete or unclear description
		Review 1919: "Reported as concealed but specific method for concealment not reported"; Unclear Risk			

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Risk of bias item	Study Name	Support for judgement*	What is reported in the study report^	Category of disagreement	Reason of disagreement
Blinding of participants and personnel	Nielsen 2006	Review 9672: "Double-blind"; Low Risk	<p><i>"This study was a randomized, placebo-controlled, double blind, Danish, multi-center (two centers) study."</i></p> <p><i>"The treatment was applied by a nasal spray with one puff in each nostril every day either in the morning or evening."</i></p>	Different information	One review accessed additional data through another study report
		Review 4143: Although "All treatments were supplied as identical intranasal sprays..." the 2004 publication describes a higher rate of withdrawal due to adverse effects in the intervention groups [11.7% in the placebo group, 21.7% in the 150 gm group and 28.7% in the 300 gm group} which may have affected blinding status; Unclear Risk			
	Gersel 1979	Review 10562: Described as double-blind [presumed participants and personnel/investigators]; Low Risk	<p><i>"A double-blind experimental design was used, employing each patient as his own control."</i></p>	Different interpretation	Consider differently information of "double blind"
		Review 6968: Not mentioned and no information to suggest this was done.; Unclear Risk			
	Stein 2011	Review 7025: Not possible to blind participants to intervention. Insufficient information to make a judgement about blinding of therapists; High Risk	<p><i>"Follow-up assessment was made 3 months after release (research staff conducting assessments were blind to treatment assignment)."</i></p> <p><i>"Randomization was accomplished via random numbers table in advance and placed in an envelope by the project coordinator. Following baseline assessment, research staff opened the envelope to learn of intervention assignment."</i></p>	Different interpretation	Consider differently incomplete or unclear description
		Review 10901: Researchers were blind until after the baseline assessment. Participants were not blinded.; Unclear Risk			

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Risk of bias item	Study Name	Support for judgement*	What is reported in the study report^	Category of disagreement	Reason of disagreement
Blinding of outcome assessment	Schoen 2007	Review 3603: Outcome assessor was not blinded.; High risk	<p><i>“In total 72 patients were screened by a maxillofacial surgeon (PJS) and prosthodontist (HR).”</i></p> <p><i>“All clinical assessments were performed by the investigator (PJS) who was not involved in treatment of the patients.”</i></p>	Different interpretation	Consider differently incomplete or unclear description
		Review 5005: Outcome assessor may have been unaware of allocation: "All clinical assessments were performed by the investigator (PJS) who was not involved in treatment of the patients."; Low risk			
	Geroin 2011	Review 6185: Not done; High risk	<p><i>“All patients were evaluated by the same examiner (an experienced internal coworker) who was not aware of the treatment received by the patients”;</i> Low Risk</p>	Missed information from the study report	
		Review 9645: Quote: "All patients were evaluated by the same examiner (an experienced internal coworker) who was not aware of the treatment received by the patients"; Low Risk			
	McCambridge 2004	Review 8969: As one interventionist was the study PI, a second independent interviewer who was blind to study condition was employed to conduct 3 month follow-ups, and an additional interviewer who was blind to initial group allocation was employed for 12 months follow-ups; Low Risk	<p><i>“further area of possible bias was that intervention recipients might report more favourable outcome data to the researcher who had delivered the intervention (J.M.). To study any such bias, a second independent interviewer who was blind to study condition, was employed to interview a sample of participants.”</i></p>	Different interpretation	Consider differently incomplete or unclear description
		Review 7025: A second independent interviewer who was blind to study condition was employed to interview a sample of participants, though not all participants; Unclear Risk			

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Incomplete outcome data	Altmaier 1992	Review 1822: All subjects recorded follow-up data; Low Risk	<i>[From table] “The n = 21 for control group and n = 24 for psychological group on all process measures.” [From table] The n = 21 for each group at each assessment.]</i>	Different interpretation	Consider differently incomplete or unclear description
		Review 7407: Inadequately reported; High Risk			
	Killen 1984	Review 146: 11/75 recruited dropped out before full treatment, and are excluded from analyses.; Low Risk	<i>“The first 75 were accepted into the study. Seven failed to attend (...) two dropped (...). The final sample (N = 64).”</i>	Missed information from the study report	
		Review 3999: Losses to follow-up not reported, all participants included; Unclear Risk			
	Creager 2008	Review 986: There was a huge loss to follow up (only 50% completed the 6 month follow up) in this study and therefore there is a high risk of attrition bias; High Risk	<i>“The remaining 525 patients met the inclusion criteria (...) The remaining 430 patients met their criteria for randomization (...).The ITT population consisted of 370 randomized patients (...). The per-protocol patient population consisted of 214 randomized patients”</i>	Different interpretation	Consider differently intention-to-treat analysis
		Review 5262: Unclear why of patients stopped medication, unclear whether data presented represents intention-to-treat or per-protocol analysis			

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