

## Appendix G: Excluded studies

### G.1 Information needs of people with Parkinson's disease and their families and carers

#### G.1.1 Impulse control disorders

Excluded studies – RQ8, 9, 10: Impulse control disorders	
Study	Reason for Exclusion
Warn patients treated for Parkinson's disease about gambling behaviour risk, Pharmaceutical Journal.271 (7262) (pp 200), 2003.Date of Publication: 16 Aug 2003., 200-, 2003	Comment article; no primary data
Parkinson's and gambling, Pharmaceutical Journal.275 (7358) (pp 74), 2005.Date of Publication: 16 Jul 2005., 74-, 2005	Short comment
Parkinson's drugs can cause compulsive gambling, Nature Reviews Drug Discovery.4 (8) (pp 619), 2005.Date of Publication: August 2005., 619-, 2005	No primary data, short comment paragraph
Abosch,A., Gupte,A., Eberly,L.E., Tuite,P.J., Nance,M., Grant,J.E., 20110624, Impulsive behavior and associated clinical variables in Parkinson's disease, Psychosomatics, 52, 41-47, 2011	Study examines prevalence of ICD; does not address any outcomes of interest identified in review protocol
Ambermoon,P., Carter,A., Hall,W.D., Dissanayaka,N.N., O'Sullivan,J.D., 20110525, Impulse control disorders in patients with Parkinson's disease receiving dopamine replacement therapy: evidence and implications for the addictions field. [Review], Addiction, 106, 283-293, 2011	Review is not up to date and only sources information from 2 databases
Avanzi,M., Baratti,M., Cabrini,S., Uber,E., Brighetti,G., Bonfa,F., 20070220, Prevalence of pathological gambling in patients with Parkinson's disease, Movement Disorders, 21, 2068-2072, 2006	Study examines prevalence of gambling in PD; not predictive factor, treatment, of information needs
Avila,A., Cardona,X., Bello,J., Maho,P., Sastre,F., Martin-Baranera,M., 20120731, Impulse control disorders and punning in Parkinson's disease: the need for a structured interview, Neurologia, 26, 166-172, 2011	Unable to retrieve full text in English (Spanish only)
Avila,A., Cardona,X., Martin-Baranera,M., Bello,J., Sastre,F., Impulsive and compulsive behaviors in Parkinson's disease: A one-year follow-up study, Journal of the Neurological Sciences.310 (1-2) (pp 197-201), 2011.Date of Publication: 15 Nov 2011., 197-201, 2011	Observational case series data - des not inform information needs or management strategies for ICD as outlined in review protocols.
Barake,M., Evins,A.E., Stoeckel,L., Pachas,G.N., Nachtigall,L.B., Miller,K.K., Biller,B.M.K., Tritos,N.A., Klibanski,A., Investigation of impulsivity in patients on dopamine agonist therapy for hyperprolactinemia: A pilot study, Pituitary.17 (2) (pp 150-156), 2014.Date of Publication: 2014.,	Study population is not Parkinson's disease

<b>Excluded studies – RQ8, 9, 10: Impulse control disorders</b>	
150-156, 2014	
Barns,M.P.N., Rickards,H., Cavanna,A.E., The prevalence and clinical characteristics of pathological gambling in Parkinson's disease: An evidence-based review, <i>Functional Neurology</i> .25 (1) (pp 9-13), 2010.Date of Publication: January-March 2010., 9-13, 2010	Systematic review to determine prevalence of ICD: study does not report on outcomes of interest in review protocol
Bermejo,P.E., Ruiz-Huete,C., Anciones,B., 20110126, Zonisamide in managing impulse control disorders in Parkinson's disease, <i>Journal of Neurology</i> , 257, 1682-1685, 2010	This study was not an RCT; any other design was deemed inappropriate to examine drug effectiveness, as stipulated in review protocol.
Bodi,N., Keri,S., Nagy,H., Moustafa,A., Myers,C.E., Daw,N., Dibo,G., Takats,A., Bereczki,D., Gluck,M.A., Reward-learning and the novelty-seeking personality: A between-and within-subjects study of the effects of dopamine agonists on young parkinsons patients, <i>Brain</i> .132 (9) (pp 2385-2395), 2009.Date of Publication: September 2009., 2385-2395, 2009	Study does not address any outcome of interest as identified in review protocol
Catalan,M.J., de Pablo-Fernandez,E., Villanueva,C., Fernandez-Diez,S., Lapena-Montero,T., Garcia-Ramos,R., Lopez-Valdes,E., Levodopa infusion improves impulsivity and dopamine dysregulation syndrome in Parkinson's disease, <i>Movement Disorders</i> .28 (14) (pp 2007-2010), 2013.Date of Publication: December 2013., 2007-2010, 2013	Population did not have ICD diagnosis; patients had dopamine dysregulation syndrome
Ceravolo,R., Frosini,D., Rossi,C., Bonuccelli,U., Impulse control disorders in Parkinson's disease: definition, epidemiology, risk factors, neurobiology and management, <i>Parkinsonism and Related Disorders</i> .15 (SUPPL.4) (pp S111-S115), 2010.Date of Publication: January 2010., S111-S115, 2010	Narrative review
Cilia,R., Siri,C., Canesi,M., Zecchinelli,A.L., De,Gaspari D., Natuzzi,F., Tesei,S., Meucci,N., Mariani,C.B., Sacilotto,G., Zini,M., Ruffmann,C., Pezzoli,G., Dopamine dysregulation syndrome in Parkinson's disease: From clinical and neuropsychological characterisation to management and long-term outcome, <i>Journal of Neurology, Neurosurgery and Psychiatry</i> .85 (3) (pp 311-318), 2014.Date of Publication: March 2014., 311-318, 2014	Study examines dopamine dysregulation syndrome (DDS), not ICD's
Dodd,M.L., Klos,K.J., Bower,J.H., Geda,Y.E., Josephs,K.A., Ahlskog,J.E., 20051114, Pathological gambling caused by drugs used to treat Parkinson disease, <i>Archives of Neurology</i> , 62, 1377-1381, 2005	Case series - N=11 patients described individually
Driver-Dunckley,E., Samanta,J., Stacy,M., 20040325, Pathological gambling associated with dopamine agonist therapy in Parkinson's disease, <i>Neurology</i> , 61, 422-423, 2003	Case series. Study reports on n=9 individual patients
Fantini,M.L., Macedo,L., Zibetti,M., Sarchioto,M., Vidal,T., Pereira,B., Marques,A., Debilly,B., Derost,P., Ulla,M., Vitello,N., Cicolin,A., Lopiano,L., Durif,F., 20150327, Increased risk of	Study does not examine predictors for ICD; focus is on relationship between RBD and ICD, which is not population of interest identified within the review protocol

<b>Excluded studies – RQ8, 9, 10: Impulse control disorders</b>	
impulse control symptoms in Parkinson's disease with REM sleep behaviour disorder, <i>Journal of Neurology, Neurosurgery &amp; Psychiatry</i> , 86, 174-179, 2015	
Farnikova,K., Obereigneru,R., Kanovsky,P., Prasko,J., 20120717, Comparison of personality characteristics in Parkinson disease patients with and without impulse control disorders and in healthy volunteers, <i>Cognitive &amp; Behavioral Neurology</i> , 25, 25-33, 2012	Study assessed personality characteristics of PD patient with ICD vs. without ICD - not predictive factors for development.
Gallagher,D.A., O'Sullivan,S.S., Evans,A.H., Lees,A.J., Schrag,A., 20080109, Pathological gambling in Parkinson's disease: risk factors and differences from dopamine dysregulation. An analysis of published case series, <i>Movement Disorders</i> , 22, 1757-1763, 2007	Case-series analysis with no primary data
Garcia-Ruiz,P.J., Martinez Castrillo,J.C., Alonso-Canovas,A., Herranz,Barcenas A., Vela,L., Sanchez,Alonso P., Mata,M., Olmedilla,Gonzalez N., Mahillo,Fernandez,I, 20140825, Impulse control disorder in patients with Parkinson's disease under dopamine agonist therapy: a multicentre study, <i>Journal of Neurology, Neurosurgery &amp; Psychiatry</i> , 85, 840-844, 2014	Study did not examine any outcomes of interest identified in review protocol.
Hui,J., Yang,L., Gomez,M., Togasaki,D., Impulse-control behaviors in parkinson's disease are not dose-dependent, <i>Neurology</i> , 80, -, 2013	Abstract only - no primary data
Hui,J.S., Cen,S., Gomez,M., Yang,L., Association of psychological symptoms with impulse-control behaviors after dopamine agonist therapy for Parkinson's disease: A longitudinal study, <i>Annals of Neurology</i> , 70, S18-S19, 2011	Duplicate reference
Lee,J.Y., Kim,H.J., Jeon,B.S., 20110316, Is pathological gambling in Parkinson's disease reduced by amantadine?, <i>Annals of Neurology</i> , 69, 213-214, 2011	Comment article; no primary data
Leroi,I., Barraclough,M., McKie,S., Hinest,N., Evans,J., Elliott,R., McDonald,K., 20141009, Dopaminergic influences on executive function and impulsive behaviour in impulse control disorders in Parkinson's disease, <i>Journal of Neuropsychology</i> , 7, 306-325, 2013	Study does not examine predictors for development of ICD; examines neuropsychological correlates of ICD
Lim,S.-Y., Tan,Z.K., Ngam,P.I., Lor,T.L., Mohamed,H., Schee,J.P., Tan,A.K., Goh,J.Y., Ooi,E., Soh,P.C.H., Impulsive-compulsive behaviors are common in Asian Parkinson's disease patients: Assessment using the QUIP, <i>Parkinsonism &amp; Related Disorders</i> , 17, 761-764, 2011	ICD diagnosis not confirmed, 'ICD positivity' on new questionnaire only
Limotai,N., Oyama,G., Go,C., Bernal,O., Ong,T., Moum,S.J., Bhidayasiri,R., Foote,K.D., Bowers,D., Ward,H., Okun,M.S., Addiction-like manifestations and Parkinson's disease: A large single center 9-year experience, <i>International</i>	Study did not examine any outcomes of interest identified in review protocol.

Excluded studies – RQ8, 9, 10: Impulse control disorders	
Journal of Neuroscience.122 (3) (pp 145-153), 2012.Date of Publication: March 2012., 145-153, 2012	
Macphee,G.J., Copeland,C., Stewart,D., Grosset,K., Grosset,D.G., 20100304, Clinical follow up of pathological gambling in Parkinson's disease in the West Scotland study, Movement Disorders, 24, 2430-2431, 2009	Letter to the editor
Mamikonyan,E., Siderowf,A.D., Duda,J.E., Potenza,M.N., Horn,S., Stern,M.B., Weintraub,D., 20080414, Long-term follow-up of impulse control disorders in Parkinson's disease, Movement Disorders, 23, 75-80, 2008	Study did not examine any outcomes of interest identified in review protocol.
Moore,T.J., Glenmullen,J., Mattison,D.R., 20150225, Reports of pathological gambling, hypersexuality, and compulsive shopping associated with dopamine receptor agonist drugs, JAMA Internal Medicine, 174, 1930-1933, 2014	Population not Parkinson's disease - population-wide study of ICD's
Nguyen,F.N., Chang,Y.L., Okun,M.S., Rodriguez,R.L., Shapiro,M.A., Jacobson,C.E., Swartz,C.L., Fernandez,H.H., 20110126, Prevalence and characteristics of punding and repetitive behaviors among Parkinson patients in North-Central Florida, International Journal of Geriatric Psychiatry, 25, 540-541, 2010	Letter to the editor
O'Callaghan,C., Hornberger,M., Screening for impulse control symptoms in patients with de novo Parkinson disease: A case-control study, Neurology.81 (7) (pp 694-695), 2013.Date of Publication: 13 Aug 2013., 694-695, 2013	Editorial
Poletti,M., Bonuccelli,U., 20130822, Impulse control disorders in Parkinson's disease: the role of personality and cognitive status. [Review], Journal of Neurology, 259, 2269-2277, 2012	Narrative review
Potenza,M.N., How central is dopamine to pathological gambling or gambling disorder?, Frontiers in Behavioral Neuroscience.7 (DEC) , 2013.Article Number: 206.Date of Publication: 23 Dec 2013., -, 2013	Narrative review; no primary data
Potenza,M.N., Voon,V., Weintraub,D., 20080123, Drug Insight: impulse control disorders and dopamine therapies in Parkinson's disease. [Review] [99 refs], Nature Clinical Practice Neurology, 3, 664-672, 2007	Narrative review
Sarathchandran,P., Soman,S., Sarma,G., Krishnan,S., Kishore,A., 20140627, Impulse control disorders and related behaviors in Indian patients with Parkinson's disease, Movement Disorders, 28, 1901-1902, 2013	Letter to editor
Singh,A., Kandimala,G., Dewey,R.B.,Jr., O'Suilleabhain,P., 20080102, Risk factors for pathologic gambling and other compulsions among Parkinson's disease patients taking dopamine agonists, Journal of Clinical Neuroscience, 14, 1178-1181, 2007	Raw data not presented - OR for predictors of ICD cannot be calculated

<b>Excluded studies – RQ8, 9, 10: Impulse control disorders</b>	
Vitale,C., Santangelo,G., Trojano,L., Verde,F., Rocco,M., Grossi,D., Barone,P., 20110824, Comparative neuropsychological profile of pathological gambling, hypersexuality, and compulsive eating in Parkinson's disease, <i>Movement Disorders</i> , 26, 830-836, 2011	Study examines cognitive correlates of different ICD's - not predictive factors of ICD development
Voon,V., Gao,J., Brezing,C., Symmonds,M., Ekanayake,V., Fernandez,H., Dolan,R.J., Hallett,M., 20110722, Dopamine agonists and risk: impulse control disorders in Parkinson's disease, <i>Brain</i> , 134, 5-46, 2011	Study did not examine any outcomes of interest identified in review protocol.
Voon,V., Sohr,M., Lang,A.E., Potenza,M.N., Siderowf,A.D., Whetteckey,J., Weintraub,D., Wunderlich,G.R., Stacy,M., Impulse control disorders in parkinson disease: A multicenter case-control study, <i>Annals of Neurology</i> , 69, 986-996, 2011	Duplicate paper
Weintraub,D., Koester,J., Potenza,M.N., Siderowf,A.D., Stacy,M., Voon,V., Whetteckey,J., Wunderlich,G.R., Lang,A.E., Impulse control disorders in Parkinson disease: A cross-sectional study of 3090 patients, <i>Archives of Neurology</i> .67 (5) (pp 589-595), 2010.Date of Publication: May 2010., 589-595, 2010	Duplicate reference
Weintraub,D., Mamikonyan,E., Papay,K., Shea,J.A., Xie,S.X., Siderowf,A., 20120614, Questionnaire for Impulsive-Compulsive Disorders in Parkinson's Disease-Rating Scale, <i>Movement Disorders</i> , 27, 242-247, 2012	Study does not report on any outcome of interest identified in review protocol. Study is designed to validate ICD questionnaire
Weintraub,D., Papay,K., Siderowf,A., Parkinson's Progression Markers Initiative, 20130301, Screening for impulse control symptoms in patients with de novo Parkinson disease: a case-control study, <i>Neurology</i> , 80, 176-180, 2013	Study examines prevalence of ICD in PD vs ICD in healthy controls to examine whether PD is a risk factor for ICD - not in line with outcome of interest in review protocol.
Wu,K., Politis,M., Piccini,P., 20100312, Parkinson disease and impulse control disorders: a review of clinical features, pathophysiology and management. [Review] [79 refs], <i>Postgraduate Medical Journal</i> , 85, 590-596, 2009	Narrative review
Okai D, Askey-Jones S, Samuel M, David A S, and Brown R G. 2015. "Predictors of response to a cognitive behavioral intervention for impulse control behaviors in Parkinson's disease". <i>Movement Disorders</i> 30(5):736-739.	Study design
Saez-Francas N, Marti Andres, G , Ramirez N, de Fabregues , O , Alvarez-Sabin J, Casas M, and Hernandez-Vara J. 2016. "Clinical and psychopathological factors associated with impulse control disorders in Parkinson's disease". <i>Neurologia</i> 31(4):231-238.	Not clear if all patients were on dopaminergic medication
Sharma A, Goyal V, Behari M, Srivastva A, Shukla G, and Vibha D. 2015. "Impulse control disorders and related behaviours (ICD-RBs) in Parkinson's disease patients: Assessment using	Study design



<b>Excluded studies – RQ8, 9, 10: Impulse control disorders</b>	
"Questionnaire for impulsive-compulsive disorders in Parkinson's disease" (QUIP).[Erratum appears in Ann Indian Acad Neurol. 2015 Jul-Sep;18(3):366; PMID: 26425030]". Annals of Indian Academy of Neurology 18(1):49-59.	
Todorova A, Samuel M, Brown R G, and Chaudhuri K R. 2015. "Infusion Therapies and Development of Impulse Control Disorders in Advanced Parkinson Disease: Clinical Experience After 3 Years' Follow-up". Clinical Neuropharmacology 38(4):132-4.	Not an intervention of interest
Tanwani P, Fernie B A, Nikcevic A V, and Spada M M. 2015. "A systematic review of treatments for Impulse Control Disorders and related behaviours in Parkinson's disease". Psychiatry Research 225(3):402-6.	Study design

### G.1.2 Women of childbearing age

<b>Excluded studies - 10. RQ22: What are the information needs specific to women of child bearing age with Parkinson's disease?</b>	
Study	Reason for Exclusion
Greene,N., Lassen,C.F., Rugbjerg,K., Ritz,B., Reproductive factors and Parkinson's disease risk in Danish women, European Journal of Neurology, 21, 1168-1177, 1968	Study examines reproductive factors that are associated with developing PD; not information about potential reproductive complications associated with PD
Kranick,S.M., Mowry,E.M., Colcher,A., Horn,S., Golbe,L.I., Movement disorders and pregnancy: A review of the literature, Movement Disorders.25 (6) (pp 665-671), 2010.Date of Publication: 30 Apr 2010., 665-671, 2010	Review: no primary data
Martignoni,E., Nappi,R.E., Citterio,A., Calandrella,D., Corengia,E., Fignon,A., Zangaglia,R., Riboldazzi,G., Pacchetti,C., Nappi,G., 20030328, Parkinson's disease and reproductive life events, Neurological Sciences, 23, Suppl-6, 2002	Only 25% of cohort interviewed was of childbearing age. Factors examined were reproductive factors i.e. age of onset menarche; not information needs
Martignoni,E., Nappi,R.E., Citterio,A., Calandrella,D., Zangaglia,R., Mancini,F., Corengia,E., Riboldazzi,G., Polatti,F., Nappi,G., 20040427, Reproductive life milestones in women with Parkinson's disease, Functional Neurology, 18, 211-217, 2003	Study does not examine information needs specific to women of childbearing age with PD; focus is relationship between hormones and risk of development of PD
Nicoletti,A., Nicoletti,G., Arabia,G., Annesi,G., De,Mari M., Lamberti,P., Grasso,L., Marconi,R., Epifanio,A., Morgante,L., Cozzolino,A., Barone,P., Quattrone,A., Zappia,M., 20120228, Reproductive factors and Parkinson's disease: a multicenter case-control study, Movement Disorders, 26, 2563-2566, 2011	Study does not examine information needs of women of childbearing age; focus is examining link between oestrogen and PD
Yadav,R., Shukla,G., Goyal,V., Singh,S., Behari,M., 20130212, A case control study of women with Parkinson's disease and their fertility characteristics, Journal of the Neurological Sciences, 319, 135-138, 2012	Study does not examine information needs of women of childbearing age; focus is fertility characteristics and risk of PD



## G.2 Pharmacological management of motor symptoms

### G.2.1 First-line treatment of motor symptoms

#### Excluded studies from systematic review

Excluded studies	
Study	Reason for Exclusion
"A multicenter Italian randomised study on early treatment of Parkinson disease: comparison of L-dopa, l-deprenyl and dopaminoagonists. Study design and short term results (1992). The Italian Parkinson Study Group". Italian Journal of Neurological Sciences 13:735-9.	Duplicate reference
Alobaidi Hajar, and Pall Hardev. 2013. "The role of dopamine replacement on the behavioural phenotype of Parkinson's disease". Behavioural Neurology 26:225-35.	Permitted patients on dopaminergic therapy for <6 months or amantadine, selegiline & anticholinergics prior and throughout the study. Washout period required for dopaminergic therapy: 2 weeks prior to study entry.
Antonini A, Bauer L, Dohin E, Oertel W H, Rascol O, Reichmann H, Schmid M, Singh P, Tolosa E, and Chaudhuri K Ray. 2015. "Effects of rotigotine transdermal patch in patients with Parkinson's disease presenting with non-motor symptoms - results of a double-blind, randomised, placebo-controlled trial". European Journal of Neurology 22:1400-7.	Permitted patients on anticholinergics, MAOB, and amantadine at stable doses for at least 28 days prior to baseline. These were maintained throughout the study.
Baker William L, Silver Dee, White C Michael, Kluger Jeffrey, Aberle Jeffrey, Patel Aarti A, and Coleman Craig I. 2009. "Dopamine agonists in the treatment of early Parkinson's disease: a meta-analysis". Parkinsonism & Related Disorders 15:287-94.	All included studies included non drug-naïve patients.
Barone P, Bravi D, Bermejo-Pareja F, Marconi R, Kulisevsky J, Malagu S, Weiser R, and Rost N. 1999. "Pergolide monotherapy in the treatment of early PD: a randomised, controlled study. Pergolide Monotherapy Study Group". Neurology 53:573-9.	Permitted patients on selegiline, amantadine, anticholinergics, DA prior to study start (no duration given). Levodopa was also permitted if no more than 12 weeks in total treatment. Washout period required for all treatments: At least 4 weeks (or 8 weeks for selegiline) prior to study entry.
Barone P, Santangelo G, Morgante L, Onofri M, Meco G, Abbruzzese G, Bonuccelli U, Cossu G, Pezzoli G, Stanzione P, Lopiano L, Antonini A, and Tinazzi M. 2015. "A randomised clinical trial to evaluate the effects of rasagiline on depressive symptoms in non-demented Parkinson's disease patients". European Journal of Neurology 22:1184-1191.	Permitted patients under stable doses of dopaminergic treatments at least 4 weeks prior to study entry. All stable doses of DA, levodopa/carbidopa, levodopa/benserazide and COMT inhibitors were permitted.
Caslake Robert, Macleod Angus, Ives Natalie, Stowe Rebecca, and Counsell Carl. 2009. "Monoamine oxidase B inhibitors versus other dopaminergic agents in early Parkinson's disease". Cochrane Database of Systematic Reviews :CD006661.	Only 1 relevant study included in this review but the study permitted patients on previous treatment for less than 4 months with study drug.
Chen Jack J, Swope David M, and Dashtipour Khashayar. 2007. "Comprehensive review of rasagiline, a second-generation monoamine oxidase inhibitor, for the treatment of Parkinson's disease". Clinical Therapeutics	Narrative review.



Excluded studies	
29:1825-49.	
Chondrogiorgi M, Tatsioni A, Reichmann H, and Konitsiotis S. 2014. "Dopamine agonist monotherapy in Parkinson's disease and potential risk factors for dyskinesia: a meta-analysis of levodopa-controlled trials". <i>European Journal of Neurology</i> 21:433-40.	Included studies that permitted patients on previous PD treatment for less than 6 months, including selegiline, amantadine and anticholinergics.
Constantinescu R, Romer M, McDermott M P, Kamp C, and Kieburtz K. 2007. "Impact of pramipexole on the onset of levodopa-related dyskinesias". <i>Movement disorders : official journal of the Movement Disorder Society</i> 22:1317-9.	Permitted patients on previous levodopa or DA treatments (no duration given).
Cooper J A, Sagar H J, Doherty S M, Jordan N, Tidswell P, and Sullivan E V. 1992. "Different effects of dopaminergic and anticholinergic therapies on cognitive and motor function in Parkinson's disease. A follow-up study of untreated patients". <i>Brain</i> 115:1701-25.	Reports results of a phase 2 study where patients have already been treated in phase 1 + wrong interventions: levodopa vs. bromocriptine vs. anticholinergics.
Crosby Niall, J , Deane Katherine, Clarke Carl, and E . 2003. "Amantadine in Parkinson's disease". <i>Cochrane Database of Systematic Reviews</i> :.	All apart from one parallel study were crossover studies + all studies included patients on other antiparkinsonian drugs prior and during the trial periods (no duration or details reported). Included in the previous guideline (CG35) but no statistical analysis could be performed as only data for the trials' means were given.
Elmer L, Schwid S, Eberly S, Goetz C, Fahn S, Kieburtz K, Oakes D, Blindauer K, Salzman P, Oren S, Prisco U L, Stern M, Shoulson I, Parkinson Study Group, Tempo , and Investigators Presto. 2006. "Rasagiline-associated motor improvement in PD occurs without worsening of cognitive and behavioral symptoms". <i>Journal of the Neurological Sciences</i> 248:78-83.	Permitted patients on anticholinergics prior and throughout the study.
Elmer Lawrence W, Surmann Erwin, Boroojerdi Babak, and Jankovic Joseph. 2012. "Long-term safety and tolerability of rotigotine transdermal system in patients with early-stage idiopathic Parkinson's disease: a prospective, open-label extension study". <i>Parkinsonism &amp; Related Disorders</i> 18:488-93.	Extension, single arm study.
Fahn S. 2006. "Levodopa in the treatment of Parkinson's disease". <i>Journal of Neural Transmission, and Supplement</i> :1-15.	Narrative review.
Fregni Felipe, Boggio Paulo S, Bermpohl Felix, Maia Fernanda, Rigonatti Sergio P, Barbosa Egberto R, and Pascual-Leone Alvaro. 2006. "Immediate placebo effect in Parkinson's disease--is the subjective relief accompanied by objective improvement?". <i>European Neurology</i> 56:222-9.	Included patients who had a response to levodopa – All patients were put through a 'levodopa challenge' prior to study entry – no duration given.
Fung V S, Herawati L, and Wan Y. 2009. "Quality of life in early Parkinson's disease treated with levodopa/carbidopa/entacapone". <i>Movement disorders : official journal of the Movement Disorder Society</i> 24:25-31.	Permitted patients on prior treatment with DAs, selegiline, anticholinergics or amantadine at stable doses (no duration given).
Ghys L, Surmann E, Whitesides J, and Boroojerdi B. 2011. "Effect of rotigotine on sleep and quality of life in Parkinson's disease patients: Post hoc analysis of RECOVER patients who were symptomatic at baseline". <i>Expert Opinion on Pharmacotherapy</i> 12:1985-1998.	81.6% of study population were on L-dopa at baseline (duration of treatment not reported).

Excluded studies	
Giladi Nir, Borojojerdi Babak, and Surmann Erwin. 2013. "The safety and tolerability of rotigotine transdermal system over a 6-year period in patients with early-stage Parkinson's disease". <i>Journal of Neural Transmission</i> 120:1321-9.	Extension study.
Giladi Nir, Ghys Liesbet, Surmann Erwin, Borojojerdi Babak, and Jankovic Joseph. 2014. "Effects of long-term treatment with rotigotine transdermal system on dyskinesia in patients with early-stage Parkinson's disease". <i>Parkinsonism &amp; Related Disorders</i> 20:1345-51.	Extension study.
Giladi Nir, Asgharnejad Mahnaz, Bauer Lars, Grieger Frank, Borojojerdi Babak. 2016. "Rotigotine in combination with the MAO-B inhibitor selegiline in early Parkinson's disease: a post hoc analysis". <i>Journal of Parkinson's Disease</i> 6:401-11	Post-hoc study pooling 2 phase 3 trials
Hauser Robert A, McDermott Michael P, and Messing Susan. 2006. "Factors associated with the development of motor fluctuations and dyskinesias in Parkinson disease". <i>Archives of Neurology</i> 63:1756-60.	Permitted patients on stable doses of selegiline, amantadine and anticholinergics prior and throughout the study (no duration given).
Hauser R A, Rascol O, and Korczyn A D. 2008. "Evaluation of the responsive of patients with parkinson's disease to initial therapy with ropinirole or L-dopa". <i>Focus on Parkinson's Disease</i> 20:11-13.	Study not available electronically.
Hauser R A, Schapira A H. V, Barone P, Mizuno Y, Rascol O, Busse M, Debieuvre C, Fraessdorf M, Poewe W, and Pramipexole E R. Studies Group. 2014. "Long-term safety and sustained efficacy of extended-release pramipexole in early and advanced Parkinson's disease". <i>European Journal of Neurology</i> 21:736-43.	Extension study.
Holloway R. 2000. "A randomised controlled trial comparing pramipexole with levodopa in early Parkinson's disease: Design and methods of the CALM-PD study". <i>Clinical Neuropharmacology</i> 23:34-44.	Permitted patients on previous levodopa or DA treatments (no duration given).
Holloway R G, Shoulson I, Fahn S, Kiebertz K, Lang A, Marek K, McDermott M, Seibyl J, Weiner W, Musch B, Kamp C, Welsh M, Shinaman A, Pahwa R, Barclay L, Hubble J, LeWitt P, Miyasaki J, Suchowersky O, Stacy M, Russell D S, Ford B, Hammerstad J, Riley D, Standaert D, Wooten F, Factor S, Jankovic J, Atassi F, Kurlan R, Panisset M, Rajput A, Rodnitzky R, Shults C, Petsinger G, Waters C, Pfeiffer R, Biglan K, Borchert L, Montgomery A, Sutherland L, Weeks C, DeAngelis M, Sime E, Wood S, Pantella C, Harrigan M, Fussell B, Dillon S, Alexander-Brown B, Rainey P, Tennis M, Rost-Ruffner E, Brown D, Evans S, Berry D, Hall J, Shirley T, Dobson J, Fontaine D, Pfeiffer B, Brocht A, Bennett S, Daigneault S, Hodgeman K, O'Connell C, Ross T, Richard K, and Watts A. 2004. "Pramipexole vs levodopa as initial treatment for Parkinson disease: a 4-year randomised controlled trial". <i>Archives of neurology</i> 61:1044-53.	Duplicate reference.
Imamura K, Okayasu N, and Nagatsu T. 2011. "The relationship between depression and regional cerebral blood flow in Parkinson's disease and the effect of selegiline treatment.[Erratum appears in <i>Acta Neurol Scand.</i> 2011 Sep;124(3):221-2]". <i>Acta Neurologica Scandinavica</i> 124:28-39.	Permitted patients on prior dopaminergic treatments (no duration given).

Excluded studies	
Jankovic Joseph, Berkovich Elijah, Eyal Eli, and Tolosa Eduardo. 2014. "Symptomatic efficacy of rasagiline monotherapy in early Parkinson's disease: post-hoc analyses from the ADAGIO trial". <i>Parkinsonism &amp; Related Disorders</i> 20:640-3.	Reported no extractable outcomes of interest (NPDRS Total). AEs were reported in p-values only.
Katzenschlager R, Head J, Schrag A, Ben-Shlomo Y, Evans A, Lees A J, Parkinson's Disease Research Group of the United, and Kingdom . 2008. "Fourteen-year final report of the randomised PDRG-UK trial comparing three initial treatments in PD". <i>Neurology</i> 71:474-80.	Permitted patients on anticholinergics and amantadine already (no duration given).
Kulisevsky Jaime, and Pagonabarraga Javier. 2010. "Tolerability and safety of ropinirole versus other dopamine agonists and levodopa in the treatment of Parkinson's disease: meta-analysis of randomised controlled trials". <i>Drug Safety</i> 33:147-61.	No extractable data. Do not report data separately for early and advance PD.
Kurth M C, Tetrud J W, Tanner C M, Irwin I, Stebbins G T, Goetz C G, and Langston J W. 1993. "Double-blind, placebo-controlled, crossover study of duodenal infusion of levodopa/carbidopa in Parkinson's disease patients with 'on-off' fluctuations". <i>Neurology</i> 43:1698-1703.	Cross-over trial.
Leentjens Albert F. G. 2011. "The role of dopamine agonists in the treatment of depression in patients with Parkinson's disease: a systematic review". <i>Drugs</i> 71:273-86.	No relevant outcomes of interest - Only report data on mood.
Marek K, Seibyl J, Shoulson I, Holloway R, Kieburtz K, McDermott M, Kamp C, Shinaman A, Fahn S, Lang A, Weiner W, and Welsh M. 2002. "Dopamine transporter brain imaging to assess the effects of pramipexole vs levodopa on Parkinson disease progression". <i>Journal of the American Medical Association</i> 287:1653-1661.	Duplicate of reference number 52.
Marquez-Cruz M, Diaz-Martinez JP, Soto-Molina H et al. 2016. "A systematic review and mixed treatment comparison of monotherapy in early Parkinson's disease: implications for Latin America". <i>Expert review of Pharmacoeconomics and Outcomes Research</i> 16(1):97-102	Systematic review from which relevant primary studies have been included
Martinez-Martin P, and Kurtis M M. 2010. "Systematic review of the effect of dopamine receptor agonists on patient health-related quality of life". <i>Parkinsonism and Related Disorders</i> 15:S58-S64.	This systematic review also included DAs that were not within the scope of the guideline – references of the potentially relevant articles were therefore retrieved for full text review but this systematic review is excluded.
Minguez-Minguez Sara, Solis-Garcia Del Pozo, Julian , and Jordan Joaquin. 2013. "Rasagiline in Parkinson's disease: a review based on meta-analysis of clinical data". <i>Pharmacological Research</i> 74:78-86.	Permitted patients on other antiparkinsonian drugs – potentially relevant references were retrieved for full text review.
Mizuno Y, Yanagisawa N, Kuno S, Yamamoto M, Hasegawa K, Origasa H, and Kowa H. 2003. "Randomised, double-blind study of pramipexole with placebo and bromocriptine in advanced Parkinson's disease". <i>Movement disorders : official journal of the Movement Disorder Society</i> 18:1149-56.	Patients had received an individual dosage of levodopa plus a decarboxylase inhibitor and were stable for at least 28 days before the administration of the study medication.
Mizuno Y, Abe T, Hasegawa K, Kuno S, Kondo T, Yamamoto M, Nakashima M, and Kanazawa I. 2007. "Ropinirole is effective on motor function when used as an adjunct to levodopa in Parkinson's disease: STRONG study". <i>Movement disorders : official journal of the</i>	All patients had been receiving levodopa for at least 4 weeks at the time of informed consent.

Excluded studies	
Movement Disorder Society 22:1860-5.	
Navan P, Findley L J, Undy M B, Pearce R K. B, and Bain P G. 2005. "A randomly assigned double-blind cross-over study examining the relative anti-Parkinsonian tremor effects of pramipexole and pergolide". <i>European Journal of Neurology</i> 12:1-8.	Pergolide vs. pramipexole.
Noyes K, Dick A W, and Holloway R G. 2006. "Pramipexole versus levodopa in patients with early Parkinson's disease: effect on generic and disease-specific quality of life". <i>Value in health : the journal of the International Society for Pharmacoeconomics and Outcomes Research</i> 9:28-38.	Permitted patients who had previously taken levodopa or a DA < 2 months prior to baseline + MAOB, pramipexole, selegiline, amantadine and anticholinergics (no duration given).
Olanow C W, Fahn S, Muentner M, Klawans H, Hurtig H, Stern M, Shoulson I, Kurlan R, Grimes J D, and Jankovic J. 1994. "A multicenter double-blind placebo-controlled trial of pergolide as an adjunct to Sinemet in Parkinson's disease". <i>Movement disorders : official journal of the Movement Disorder Society</i> 9:40-7.	Patients were required to have been on stable doses of levodopa for $\geq 2$ weeks prior to the baseline visit.
Pahwa R, Stacy M A, Factor S A, Lyons K E, Stocchi F, Hersh B P, Elmer L W, Truong D D, Earl N L, and Investigators Ease-Pd Adjunct Study. 2007. "Ropinirole 24-hour prolonged release: randomised, controlled study in advanced Parkinson disease". <i>Neurology</i> 68:1108-15.	Required patients to have a stable dose of levodopa for at least 4 weeks prior to screening.
Pahwa R, Tanner C M, Hauser R A, Sethi K, Isaacson S, Truong D, Struck L, Ruby A E, McClure N L, Went G T, and Stempien M J. 2015. "Amantadine extended release for levodopa-induced dyskinesia in Parkinson's disease (EASED Study)". <i>Movement Disorders</i> 30:788-795.	Permitted patients on any antiparkinsonian medications, including levodopa preparations at stable dosages for at least 30 days prior to screening and unchanged throughout study.
Palhågen S, Heinonen E, Hagglund J, Kaugesaar T, Maki-Ikola O, Palm R, Swedish Parkinson Study, and Group . 2006. "Selegiline slows the progression of the symptoms of Parkinson disease". <i>Neurology</i> 66:1200-6.	Reports Phase 2 data of an early vs. delayed selegiline trial.
Parkinson Study, and Group. 2002. "Dopamine transporter brain imaging to assess the effects of pramipexole vs levodopa on Parkinson disease progression". <i>JAMA</i> 287:1653-61.	Follow-up study (original study excluded due to patients being permitted on prior PD treatments).
Parkinson Study Group, and Calm Cohort Investigators. 2009. "Long-term effect of initiating pramipexole vs levodopa in early Parkinson disease". <i>Archives of Neurology</i> 66:563-70.	Extended follow-up study.
Przuntek H, Welzel D, Blumner E, Danielczyk W, Letzel H, Kaiser H J, Kraus P H, Riederer P, Schwarzmann D, and Wolf H. 1992. "Bromocriptine lessens the incidence of mortality in L-dopa-treated parkinsonian patients: prado-study discontinued". <i>European Journal of Clinical Pharmacology</i> 43:357-63.	Levodopa/benserazide vs. levodopa/benserazide + bromocriptine
Ramaker C, Beek W J. T. van d e, Finken M Jj, and van Hilten. 1998. "Bromocriptine for levodopa-induced motor complications in Parkinson's disease". <i>Cochrane Database of Systematic Reviews</i> .:	Bromocriptine review.
Rascol O, Goetz C, Koller W, Poewe W, and Sampaio C. 2002. "Treatment interventions for Parkinson's disease: An evidence based assessment". <i>Lancet</i> 359:1589-1598.	Narrative review.
Rektorova I, Rektor I, Bares M, Dostal V, Ehler E, Fanfrdlova Z, Fiedler J, Klajblova H, Kulist'ak P, Ressler	All patients were treated with levodopa and their treatment was stable for at

Excluded studies	
P, Svatova J, Urbanek K, and Veliskova J. 2003. "Pramipexole and pergolide in the treatment of depression in Parkinson's disease: a national multicentre prospective randomised study". <i>European Journal of Neurology</i> 10:399-406.	least 4 weeks prior to inclusion in the study.
Sawada H, Oeda T, Kuno S, Nomoto M, Yamamoto K, Yamamoto M, Hisanaga K, and Kawamura T. 2010. "Amantadine for dyskinesias in Parkinson's disease: a randomised controlled trial". <i>PLoS one</i> 5:e15298.	Permitted patients on fixed doses of L-dopa and/or LDED of dopamine agonists prior and throughout the study (no duration given).
Schapira A H. V, Barone P, Hauser R A, Mizuno Y, Rascol O, Busse M, Debieuvre C, Fraessdorf M, Poewe W, and Pramipexole E R. Studies Group. 2013. "Patient-reported convenience of once-daily versus three-times-daily dosing during long-term studies of pramipexole in early and advanced Parkinson's disease". <i>European Journal of Neurology</i> 20:50-6.	Extension study.
Stowe R L, Ives N J, Clarke C, van Hilten J, Ferreira J, Hawker R J, Shah L, Wheatley K, and Gray R. 2008. "Dopamine agonist therapy in early Parkinson's disease". <i>Cochrane Database of Systematic Reviews</i> :CD006564.	Of those potentially relevant studies included in the review – patients on PD drugs prior to enrolment were permitted (>6 weeks or more depending on trial).
Thorlund Kristian, Wu Ping, Druyts Eric, Eapen Shawn, and Mills Edward J. 2014. "Nonergot dopamine-receptor agonists for treating Parkinson's disease - a network meta-analysis". <i>Neuropsychiatric Disease &amp; Treatment</i> 10:767-76.	All apart from 1 study (already included in the guideline review) included patients who were on other active PD drugs prior to study entry.
Tolosa E, and Stern M B. 2012. "Efficacy, safety and tolerability of rasagiline as adjunctive therapy in elderly patients with Parkinson's disease". <i>European Journal of Neurology</i> 19:258-64.	Patients must have received an optimized and stable dosage of levodopa for at least 2 weeks before their screening evaluation. Concomitant treatment with stable dosages of dopamine agonists, amantadine hydrochloride, anticholinergics, and entacapone was allowed (no duration given).
Trenkwalder C, Kies B, Rudzinska M, Fine J, Nikl J, Honczarenko K, Dioszeghy P, Hill D, Anderson T, Myllyla V, Kassubek J, Steiger M, Zucconi M, Tolosa E, Poewe W, Surmann E, Whitesides J, Boroojerdi B, and Chaudhuri K R. 2011. "Rotigotine effects on early morning motor function and sleep in Parkinson's disease: a double-blind, randomised, placebo-controlled study (RECOVER)". <i>Movement disorders : official journal of the Movement Disorder Society</i> 26:90-9.	Permitted patients on levodopa, anticholinergics, MAOB, entacapone and other treatments at stable dosages for at least 28 days prior to baseline and throughout the study.
van Hilten, Ramaker Claudia, C, Stowe Rebecca, and Ives Natalie. 2007. "Bromocriptine/levodopa combined versus levodopa alone for early Parkinson's disease". <i>Cochrane Database of Systematic Reviews</i> .	Bromocriptine review.
van Hilten J J, Ramaker C C, Stowe R I, and Ives N J. 2007. "Bromocriptine versus levodopa in early Parkinson's disease". <i>Cochrane Database of Systematic Reviews</i> :CD002258.	Bromocriptine review.
Vershuur CVM, Suwijn SR, Posr B et al. 2015. "Protocol of a randomised delayed-start double-blind placebo-controlled multi-centre trial for levodopa in early Parkinson's disease: the LEAP-study" <i>BMC Neurology</i> 15:236	Study protocol



Excluded studies	
Visser M, Marinus J, Stiggelbout A M, van Hilten , and J J. 2006. "Responsiveness of impairments and disabilities in Parkinson's disease". <i>Parkinsonism &amp; Related Disorders</i> 12:314-8.	Narrative review.
Warren Olanow, C , Kieburtz K, Rascol O, Poewe W, Schapira A H, Emre M, Nissinen H, Leinonen M, and Stocchi F. 2013. "Factors predictive of the development of Levodopa-induced dyskinesia and wearing-off in Parkinson's disease". <i>Movement disorders : official journal of the Movement Disorder Society</i> 28:1064-71.	Levodopa/carbidopa vs. levodopa/carbidopa/entacapone
Wilson R E, Seeberger L C, Silver D, Griffith A, Conner J B, and Salzman P M. 2011. "Rasagiline: Time to onset of antiparkinson effect is similar when used as a monotherapy or adjunct treatment". <i>Neurologist</i> 17:318-324.	Permitted patients on levodopa, DA, COMT inhibitor, anticholinergics, or amantadine prior to baseline and throughout the study (no duration given).
Wong K S, Lu C S, Shan D E, Yang C C, Tsoi T H, and Mok V. 2003. "Efficacy, safety, and tolerability of pramipexole in untreated and levodopa-treated patients with Parkinson's disease". <i>Journal of the Neurological Sciences</i> 216:81-87.	Permitted patients on levodopa at stable dose for at least 1 month prior to study entry.
Zhang Lina, Zhang Zhiqin, Chen Yangmei, Qin Xinyue, Zhou Huadong, Zhang Chaodong, Sun Hongbin, Tang Ronghua, Zheng Jinou, Yi Lin, Deng Liying, and Li Jinfang. 2013. "Efficacy and safety of rasagiline as an adjunct to levodopa treatment in Chinese patients with Parkinson's disease: a randomised, double-blind, parallel-controlled, multi-centre trial". <i>International Journal of Neuropsychopharmacology</i> 16:1529-37.	All patients must have received levodopa for at least 2 weeks prior to screening.
Zhou C Q, Li S S, Chen Z M, Li F Q, Lei P, and Peng G G. 2013. "Rotigotine Transdermal Patch in Parkinson's Disease: A Systematic Review and Meta-Analysis". <i>PLoS ONE</i> 8:no pagination.	This systematic review included both early and advanced PD trials. 3 out of 6 trials were early PD trials but all included patients with prior treatment to baseline.
Zhou C Q, Lou J H, Zhang Y P, Zhong L, Chen Y L, Lu F J, and Peng G G. 2014. "Long-Acting Versus Standard Non-Ergot Dopamine Agonists in Parkinson's Disease: A Meta-Analysis of Randomised Controlled Trials". <i>CNS Neuroscience and Therapeutics</i> 20:368-376.	Only 1 trial from this systematic review was potentially relevant and was retrieved for full text review.
Zhou Chang-Qing, Zhang Jiang-Wei, Wang Min, and Peng Guo-Guang. 2014. "Meta-analysis of the efficacy and safety of long-acting non-ergot dopamine agonists in Parkinson's disease". <i>Journal of Clinical Neuroscience</i> 21:1094-101.	4 trials were potentially relevant from this systematic review and were retrieved for full text review.
Elrington G M. 2015. "Review on initial drug treatment in Parkinson's disease did not mention entacapone". <i>BMJ</i> 351:h5843.	Letter
Verschuur C V, Suwijn S R, Post B, Dijkgraaf M, Bloem B R, van Hilten , J J, van Laar , T , Tissingh G, Deuschl G, Lang A E, de Haan , R J, de Bie , and R M. 2015. "Protocol of a randomised delayed-start double-blind placebo-controlled multi-centre trial for Levodopa in EARly Parkinson's disease: the LEAP-study". <i>BMC Neurology</i> 15:236.	Protocol
Zhang Z, Asgharnejad M, Du X, Surmann E, and Bauer L. 2015. "Efficacy and safety of rotigotine transdermal patch in Chinese patients with early-stage Parkinson's disease: A randomized, double-blind, placebo-controlled	Abstract only



Excluded studies	
study". Movement disorders 30:S137-s138.	

### Excluded studies from previous guideline

Excluded studies	
Study	Reason for Exclusion
Ives NJ, Stowe RL, Marro J et al. Monoamine oxidase type B inhibitors in early Parkinson's disease: meta analysis of 17 randomised trials involving 3525 patients. British Medical Journal. 2004; 329(7466): 593–596.	Permitted patients on <12 months exposure to anti-parkinsonian medication – relevant references were retrieved for full text review.
Macleod AD, Counsell CE, Ives N et al. Monoamine oxidase B inhibitors for early Parkinson's disease. The Cochrane Database of Systematic Reviews. 2005;(3):CD004898.	Included patients who had started PD treatments in the last 12 months – relevant references were retrieved for full text review.
Lees AJ, Katzenschlager R, Head J et al. Ten-year follow-up of three different initial treatments in de-novo PD: a randomised trial. Neurology. 2001; 57(9):1687–1694.	Permitted patients on anticholinergics, amantadine (no duration given) + patients who had been considered to be intolerant of levodopa after a treatment period of <2 weeks.
Przuntek H, Welzel D, Gerlach M et al. Early institution of bromocriptine in Parkinson's disease inhibits the emergence of levodopa-associated motor side effects. Long-term results of the PRADO study. Journal of Neural Transmission. 1996; 103(6):699–715.	Levodopa/benserazide vs. bromocriptine.
Rinne UK, Bracco F, Chouza C et al. Early treatment of Parkinson's disease with Cabergoline delays the onset of motor complications. Results of a double-blind levodopa controlled trial. Drugs. 1998; 55(Suppl 1):23–3TxCM 20.	Cabergoline vs. levodopa.
Presthus J, Berstad J, Lien K. Selegiline (1-deprenyl) and low-dose levodopa treatment of Parkinson's disease. A double-blind crossover trial. Acta Neurologica Scandinavica. 1987; 76:200–203.	Crossover trial.
Kieburtz K. Safety and efficacy of pramipexole in early Parkinson disease: A randomised dose-ranging study. Journal of the American Medical Association. 1997; 278(2):125–130.	Permitted patients on selegiline, anticholinergics or amantadine prior to study entry (no duration given).
Barone P, Bravi D, Bermejo-Pareja F et al. Pergolide monotherapy in the treatment of early PD: a randomised, controlled study. Pergolide Monotherapy Study Group. Neurology. 1999; 53(3):573–579.	Pergolide vs. placebo.
Hubble JP, Koller WC, Cutler NR et al. Pramipexole in patients with early Parkinson's disease. Clinical Neuropharmacology. 1995; 18(4):338–347.	Permitted patients on anticholinergics prior and throughout study (no duration given).
Hely MA, Morris JG, Reid WG et al. The Sydney Multicentre Study of Parkinson's disease: a randomised, prospective five year study comparing low dose bromocriptine with low dose levodopa-carbidopa. Journal of Neurology, Neurosurgery & Psychiatry. 1994; 57(8):903–910.	Levodopa/carbidopa vs. bromocriptine.
Shannon KM, Bennett JPJ, Friedman JH. Efficacy of pramipexole, a novel dopamine agonist, as monotherapy in mild to moderate Parkinson's disease. Neurology. 1997; 49(3):724–728.	Permitted patients on up to 180 days (6 months) of levodopa but required washout period of 60 days prior to study entry.
Brooks DJ, Abbott RJ, Lees AJ et al. A placebo-controlled	Permitted patients on levodopa or DA

Excluded studies	
evaluation of ropinirole, a novel D2 agonist, as sole dopaminergic therapy in Parkinson's disease. <i>Clinical Neuropharmacology</i> . 1998; 21(2):101–107.	for ≤6 months prior to study + patients on anticholinergics, amantadine or selegiline at stable dosages prior and throughout the study. Washout period for levodopa and DA required: 2 weeks prior to screening.
Riopelle RJ, Gawel MJ, Libman I et al. A double-blind study of bromocriptine and L-dopa in de novo Parkinson's disease. Short-term results. <i>European Neurology</i> . 1988; 28(SUPPL. 1):11–14.	Bromocriptine vs. levodopa.
Hely MA, Morris JG, Traficante R et al. The sydney multicentre study of Parkinson's disease: progression and mortality at 10 years. <i>Journal of Neurology, Neurosurgery &amp; Psychiatry</i> . 1999; 67(3):300–307.	Bromocriptine vs. levodopa/carbidopa.
Herskovits E, Yorio A, Leston J. Long term bromocriptine treatment in de novo parkinsonian patients. <i>Medicina</i> . 1988; 48(4):345–350.	Bromocriptine vs. levodopa.
Kulisevsky J, Garcia-Sanchez C, Berthier ML et al. Chronic effects of dopaminergic replacement on cognitive function in Parkinson's disease: a two-year follow-up study of previously untreated patients. <i>Movement Disorders</i> . 2000; 15(4):613–626.	Pergolide vs. levodopa
Weiner WJ, Factor SA, Sanchez-Ramos JR et al. Early combination therapy (bromocriptine and levodopa) does not prevent motor fluctuations in Parkinson's disease. <i>Neurology</i> . 1993; 43(1):21–27.	Bromocriptine vs. levodopa.
Olanow CW, Hauser RA, Gauger L et al. The effect of deprenyl and levodopa on the progression of Parkinson's disease. <i>Annals of Neurology</i> . 1995; 38:771–777.	Full-text not available
Caraceni T, Musicco M. Levodopa or dopamine agonists, or deprenyl as initial treatment for Parkinson's disease. A randomised multicenter study. <i>Parkinsonism &amp; Related Disorders</i> . 2001; 7(2):107–114.	Permitted patients on previous treatment for <4 months with any of the studied drugs (levodopa plus dopa decarboxylase, selegiline, bromocriptine or lisuride).
Alarcon F, Cevallos N, Lees AJ. Does combined levodopa and bromocriptine therapy in Parkinson's disease prevent late motor complications? <i>European Journal of Neurology</i> . 1998; 5(3):255–263.	Levodopa/carbidopa vs. levodopa/carbidopa + bromocriptine.
Allain H, Destee A, Petit H et al. Five-year follow-up of early lisuride and levodopa combination therapy versus levodopa monotherapy in de novo Parkinson's disease. <i>European Neurology</i> . 2000; 44(1):22–30.	Levodopa + lisuride vs. levodopa.
Gimenez-Roldan S, Tolosa E, Burguera JA et al. Early combination of bromocriptine and levodopa in Parkinson's disease: a prospective randomised study of two parallel groups over a total follow-up period of 44 months including an initial 8-month double-blind stage. <i>Clinical Neuropharmacology</i> . 1997; 20(1):67–76.	Bromocriptine vs. levodopa.
Przuntek H, Welzel D, Blumner E et al. Bromocriptine lessens the incidence of mortality in L-dopa- treated parkinsonian patients: prado-study discontinued. <i>European Journal of Clinical Pharmacology</i> . 1992; 43(4):357–363.	Bromocriptine vs. levodopa.
Crosby N, Deane KHO, Clarke CE. Amantadine in Parkinson's disease (Cochrane Review). <i>The Cochrane</i>	All apart from one parallel study were crossover studies + all studies included

Excluded studies	
Database of Systematic Reviews. 2003;(1):CD003468.	patients on other antiparkinsonian drugs prior and during the trial periods (no duration or details reported).
Cox B, Danta G, Schnieden H et al. Interactions of L-dopa and amantadine in patients with Parkinsonism. Journal of Neurology, Neurosurgery & Psychiatry. 1973; 36(3):354–361.	Levodopa without decarboxylase inhibitor and permitted patients on anticholinergics (no duration given).

## G.2.2 Adjuvant treatment of motor symptoms

### Excluded studies from systematic review

Excluded studies	Reasons for exclusion
References	Reasons for exclusion
Agro A; Dubow J; Toong-Chow L; Giovinazzo A. 2015 Pharmacokinetics, safety and tolerability of high-dose sublingually administered APL-130277 in healthy volunteers. Movement disorders 30:S65-66	Study in healthy individuals, not people with Parkinson's disease
Ahlskog J E; Muentner M D. 1988. Treatment of Parkinson's disease with pergolide: a double-blind study. Mayo Clinic Proceedings 63:969-78	Non-retrievable
Antonini A; Isaias IU; Rodolfi G; Landi A; Natuzzi F; Siri C; Pezzoli G. 2011 A 5-year prospective assessment of advanced Parkinson disease patients treated with subcutaneous apomorphine infusion or deep brain stimulation. Journal of Neurology 258:579-85	Not a randomised controlled trial
Bonnet A M, Serre I, Marconi R, Agid Y, and Dubois B. 1995. "A "combined" levodopa test as a useful method for evaluating the efficacy of dopamine agonists: application to pergolide and bromocriptine". Movement disorders : official journal of the Movement Disorder Society 10:668-71.	Crossover study
Brodsky Matthew A, Park Byung S, and Nutt John G. 2010. "Effects of a dopamine agonist on the pharmacodynamics of levodopa in Parkinson disease". Archives of Neurology 67:27-32.	No outcomes of interest
Brusa Livia, Pavino Valentina, Massimetti Maria Carla, Bove Raffaele, Iani Cesare, and Stanzione Paolo. 2013. "The effect of dopamine agonists on cognitive functions in non-demented early-mild Parkinson's disease patients". Functional Neurology 28:13-7.	Cross-over study
Chen JJ; Obering C. 2005 A review of intermittent subcutaneous apomorphine injections for the rescue management of motor fluctuations associated with advanced Parkinson's disease. Clinical Therapeutics 27:1710-24	Review not providing any relevant studies
Clarke Carl, E , and Speller Julie. 1999. "Pergolide versus bromocriptine for levodopa-induced complications in Parkinson's disease". Cochrane Database of Systematic Reviews :.	Cross-over studies
Clarke C E, and Speller J M. 2000. "Pergolide versus bromocriptine for levodopa-induced motor complications in Parkinson's disease". Cochrane database of systematic reviews (Online) :CD000236.	Crossover studies
Clarke CE; Worth P; Grosset D; Stewart D. 2009 Systematic review of apomorphine infusion, levodopa infusion and deep brain stimulation in advanced Parkinson's disease. Parkinsonism & Related Disorders 15:728-41	Review not providing any relevant studies
Constantinescu R, Romer M, McDermott M P, Kamp C, and Kieburtz K. 2007. "Impact of pramipexole on the onset of	Monotherapy/ early PD

Excluded studies	
levodopa-related dyskinesias". Movement disorders: official journal of the Movement Disorder Society 22:1317-9.	
Crosby Niall, J , Deane Katherine, Clarke Carl, and E . 2003. "Amantadine in Parkinson's disease". Cochrane Database of Systematic Reviews .	Not in patients who are experiencing inadequate symptomatic control.
Dewey RB, Jr., Hutton JT, LeWitt PA, Factor SA. A randomized, double-blind, placebo-controlled trial of subcutaneously injected apomorphine for parkinsonian off-state events. Archives of Neurology 2001;58:1385-92	Control group were on both levodopa and a dopamine agonist
Dixit S N; Behari M ; Ahuja G K. 1999. Effect of selegiline on cognitive functions in Parkinson's disease. Journal of the Association of Physicians of India 47:784-6	No L-dopa placebo group
Elmer L, Schwid S, Eberly S, Goetz C, Fahn S, Kieburtz K, Oakes D, Blindauer K, Salzman P, Oren S, Prisco U L, Stern M, Shoulson I, Parkinson Study Group, Tempo , and Investigators Presto. 2006. "Rasagiline-associated motor improvement in PD occurs without worsening of cognitive and behavioral symptoms". Journal of the Neurological Sciences 248:78-83.	Monotherapy
Elmer Lawrence W, Surmann Erwin, Borojerdj Babak, and Jankovic Joseph. 2012. "Long-term safety and tolerability of rotigotine transdermal system in patients with early-stage idiopathic Parkinson's disease: a prospective, open-label extension study". Parkinsonism & Related Disorders 18:488-93.	Monotherapy
Ferreira J J, Rascol O, Poewe W, Sampaio C, Rocha J F, Nunes T, Almeida L, and Soares-Da-Silva P. 2010. "A double-blind, randomized, placebo and active-controlled study of nebicapone for the treatment of motor fluctuations in parkinson's disease". CNS Neuroscience and Therapeutics 16:337-347.	Nebicapone – new COMT inhibitor – not an intervention of interest
Giladi Nir, Borojerdj Babak, and Surmann Erwin. 2013. "The safety and tolerability of rotigotine transdermal system over a 6-year period in patients with early-stage Parkinson's disease". Journal of Neural Transmission 120:1321-9.	Monotherapy/ early PD
Giladi Nir, Ghys Liesbet, Surmann Erwin, Borojerdj Babak, and Jankovic Joseph. 2014. "Effects of long-term treatment with rotigotine transdermal system on dyskinesia in patients with early-stage Parkinson's disease". Parkinsonism & Related Disorders 20:1345-51.	Monotherapy/ early PD
Gimenez-Roldan S, Tolosa E, Burguera J A, Chacon J, Liano H, and Forcadell F. 1997. "Early combination of bromocriptine and levodopa in Parkinson's disease: a prospective randomized study of two parallel groups over a total follow-up period of 44 months including an initial 8-month double-blind stage". Clinical Neuropharmacology 20:67-76.	Early combination therapy
Grosset KA; Malek N; Morgan F; Grosset DG. 2013. Phase IIa randomized double-blind, placebo-controlled study of inhaled apomorphine as acute challenge for rescuing 'off' periods in patients with established Parkinson's disease. European Journal of Neurology 20:1445-50	Only measures the response to a single dose of apomorphine
Gunzler SA; Koudelka C; Carlson NE; Pavel M; Nutt JG. 2008. Effect of low concentrations of apomorphine on parkinsonism in a randomized, placebo-controlled, crossover study. Archives of Neurology 65:193-8	Control group were not taking levodopa monotherapy
Hattori N; Nomoto M; Kimura T; et al. 2014. Sustained efficacy of apomorphine in Japanese patients with advanced Parkinson's disease. Parkinsonism and Related Disorders 20:819-23	Control group were not taking levodopa monotherapy
Hauser R A, Schapira A H. V, Barone P, Mizuno Y, Rascol O,	Monotherapy

Excluded studies	
Busse M, Debievre C, Fraessdorf M, Poewe W, and Pramipexole E R. Studies Group. 2014. "Long-term safety and sustained efficacy of extended-release pramipexole in early and advanced Parkinson's disease". <i>European Journal of Neurology</i> 21:736-43.	
Hauser RA; Olanow CW; Dzyngel B; et al. 2016. Sublingual apomorphine (APL-130277) for the acute conversion of OFF to ON in Parkinson's disease. <i>Movement disorders</i> 31:1366-72	Only measures the response to a single dose of apomorphine
Imamura K, Okayasu N, and Nagatsu T. 2011. "The relationship between depression and regional cerebral blood flow in Parkinson's disease and the effect of selegiline treatment.[Erratum appears in <i>Acta Neurol Scand</i> . 2011 Sep;124(3):221-2]". <i>Acta Neurologica Scandinavica</i> 124:28-39.	Not in patients who are experiencing inadequate symptomatic control.
Kanovsky P, Kubova D, Bares M, Hortova H, Streitova H, Rektor I et al. Levodopa-induced dyskinesias and continuous subcutaneous infusions of apomorphine: results of a two-year, prospective follow-up. <i>Movement Disorders</i> 2002;17 :188-91	Not a randomised controlled trial
Kassubek Jan, Chaudhuri Kallol Ray, Zesiewicz Theresa, Surmann Erwin, Boroojerdi Babak, Moran Kimberly, Ghys Liesbet, and Trenkwalder Claudia. 2014. "Rotigotine transdermal system and evaluation of pain in patients with Parkinson's disease: a post hoc analysis of the RECOVER study". <i>BMC Neurology</i> 14:42.	Not all patients were on levodopa prior to study start
Katzenschlager R; Hughes A; Evans A; et al. 2005. Continuous subcutaneous apomorphine therapy improves dyskinesias in Parkinson's disease: a prospective study using single-dose challenges. <i>Movement disorders</i> 20: 151-7	Not a randomised controlled trial
Kulisevsky Jaime, and Pagonabarraga Javier. 2010. "Tolerability and safety of ropinirole versus other dopamine agonists and levodopa in the treatment of Parkinson's disease: meta-analysis of randomized controlled trials". <i>Drug Safety</i> 33:147-61.	Not in patients who are experiencing inadequate symptomatic control/ monotherapy
Kuoppamaki M, Vahteristo M, Ellmen J, and Kiebertz K. 2014. "Pooled analysis of phase III with entacapone in Parkinson's disease". <i>Acta Neurologica Scandinavica</i> 130:239-47.	A retrospective, pooled analysis of four phase III RCTs – Not a meta-analysis or SR
Marsala Sandro Zambito, Gioulis Manuela, Ceravolo Roberto, and Tinazzi Michele. 2012. "A systematic review of catechol-O-methyltransferase inhibitors: efficacy and safety in clinical practice". <i>Clinical Neuropharmacology</i> 35:185-90.	Population in the included interventions were not necessarily on l-dopa prior to study start.
Martinez-Martin P, and Kurtis M M. 2010. "Systematic review of the effect of dopamine receptor agonists on patient health-related quality of life". <i>Parkinsonism and Related Disorders</i> 15:S58-S64.	Includes early and advanced PD – potentially relevant references were requested for full text review.
Navan P, Findley L J, Undy M B, Pearce R K. B, and Bain P G. 2005. "A randomly assigned double-blind cross-over study examining the relative anti-Parkinsonian tremor effects of pramipexole and pergolide". <i>European Journal of Neurology</i> 12:1-8.	Monotherapy
Nomoto M; Kubo S; Nagai M; et al. 2015. A Randomized Controlled Trial of Subcutaneous Apomorphine for Parkinson Disease: A Repeat Dose and Pharmacokinetic Study. <i>Clinical Neuropharmacology</i> 38:241-7	Only measures the response to single doses of apomorphine
Nyholm D; Constantinescu R; Holmberg B; Dizdar N; Askmark H. 2009. Comparison of apomorphine and levodopa infusions in four patients with Parkinson's disease with symptom fluctuations. <i>Acta Neurologica Scandinavica</i> 119:345-8	Post-hoc analysis of a randomised controlled trial
Nyholm D, Johansson A, Lennernas H, and Askmark H. 2012. "Levodopa infusion combined with entacapone or tolcapone in	Pilot cross-over study



Excluded studies	
Parkinson disease: a pilot trial". European Journal of Neurology 19:820-6.	
Ostergaard L, Werdelin L, Odin P, Lindvall O, Dupont E, Christensen PB et al. Pen injected apomorphine against off phenomena in late Parkinson's disease: a double blind, placebo controlled study. Journal of Neurology, Neurosurgery & Psychiatry 1995; 58:681-7	Cross-over study of only 8 days duration
Pahwa R; Koller WC; Trosch RM; Sherry JH; Investigators APO. Study. 2007. Subcutaneous apomorphine in patients with advanced Parkinson's disease: a dose-escalation study with randomized, double-blind, placebo-controlled crossover evaluation of a single dose. Journal of the Neurological Sciences 258:137-43	Control group were not taking levodopa monotherapy
Palhagen S, Heinonen E, Hagglund J, Kaugesaar T, Maki-Ikola O, Palm R, Swedish Parkinson Study, and Group . 2006. "Selegiline slows the progression of the symptoms of Parkinson disease". Neurology 66:1200-6.	Not in patients who are experiencing inadequate symptomatic control/ monotherapy. Population: drug-naïve patients on selegiline or placebo.
Pappert EJ; Dzyngel B; Bilbault T; Agro A. 2016. Pharmacokinetic-pharmacodynamic effects of apomorphine sublingual film (APL-130277) for the rapid management of OFF episodes in patients with Parkinson's disease. Movement Disorders. Conference: 20th International Congress of Parkinson's Disease and Movement Disorders. Germany. Conference Start: 20160619. Conference End: 20160623	Conference abstract
Perez-Lloret S. 2013. Apomorphine for the treatment of refractory motor fluctuations in late stage Parkinson's disease: An old drug revisited. European Journal of Neurology 20:1427-8	Not a randomised controlled trial
Pfeiffer RF; Gutmann L; Hull KL; Bottini PB; Sherry JH. 2007. Continued efficacy and safety of subcutaneous apomorphine in patients with advanced Parkinson's disease. Parkinsonism & related disorders 13:93-100	Control group were not taking levodopa monotherapy
Przuntek H, Welzel D, Blumner E, Danielczyk W, Letzel H, Kaiser H J, Kraus P H, Riederer P, Schwarzmann D, and Wolf H. 1992. "Bromocriptine lessens the incidence of mortality in L-dopa-treated parkinsonian patients: prado-study discontinued". European Journal of Clinical Pharmacology 43:357-63.	Early PD - Not in patients who are experiencing inadequate symptomatic control/ monotherapy.
Rascol O, Brooks D J, Korczyn A D, De Deyn , P P, Clarke C E, and Lang A E. 2000. "A five-year study of the incidence of dyskinesia in patients with early Parkinson's disease who were treated with ropinirole or levodopa". New England Journal of Medicine 342:1484-91.	Monotherapy/ early PD
Rascol O, Goetz C, Koller W, Poewe W, and Sampaio C. 2002. "Treatment interventions for Parkinson's disease: An evidence based assessment". Lancet 359:1589-1598.	Narrative review
Rektorova I, Rektor I, Bares M, Dostal V, Ehler E, Fanfrdlova Z, Fiedler J, Klajblova H, Kulist'ak P, Ressler P, Svatova J, Urbanek K, and Veliskova J. 2005. "Cognitive performance in people with Parkinson's disease and mild or moderate depression: effects of dopamine agonists in an add-on to L-dopa therapy". European Journal of Neurology 12:9-15.	No extractable data
Ries Vincent, Selzer Roland, Eichhorn Tobias, Oertel Wolfgang H, Eggert Karla, German Tolcapone Study, and Group . 2010. "Replacing a dopamine agonist by the COMT-inhibitor tolcapone as an adjunct to L-dopa in the treatment of Parkinson's disease: a	Short-term vs. long-term replacement therapy (tolcapone vs. tolcapone)



Excluded studies	
randomized, multicenter, open-label, parallel-group study". Clinical Neuropharmacology 33:142-50.	
Sawada H, Oeda T, Kuno S, Nomoto M, Yamamoto K, Yamamoto M, Hisanaga K, and Kawamura T. 2010. "Amantadine for dyskinesias in Parkinson's disease: a randomized controlled trial". PloS one 5:e15298.	Crossover trial
Schapira A H. V, Barone P, Hauser R A, Mizuno Y, Rascol O, Busse M, Debievre C, Fraessdorf M, Poewe W, and Pramipexole E R. Studies Group. 2013. "Patient-reported convenience of once-daily versus three-times-daily dosing during long-term studies of pramipexole in early and advanced Parkinson's disease". European Journal of Neurology 20:50-6.	ER-Pramipexole vs. IM-Pramipexole (with levodopa being permitted)
Schapira A H. V, Barone P, Hauser R A, Mizuno Y, Rascol O, Busse M, Debievre C, Fraessdorf M, and Poewe W. 2013. "Success rate, efficacy, and safety/tolerability of overnight switching from immediate- to extended-release pramipexole in advanced Parkinson's disease". European Journal of Neurology 20:180-7.	Extension study
Stacy M; Silver D. 2008. Apomorphine for the acute treatment of "off" episodes in Parkinson's disease. Parkinsonism and Related Disorders 14:85-92	Not a randomised controlled trial
Stocchi Fabrizio, Hsu Ann, Khanna Sarita, Ellenbogen Aaron, Mahler Andreas, Liang Grace, Dillmann Ulrich, Rubens Robert, Kell Sherron, and Gupta Suneel. 2014. "Comparison of IPX066 with carbidopa-levodopa plus entacapone in advanced PD patients". Parkinsonism & Related Disorders 20:1335-40.	Crossover study
Thorlund Kristian, Wu Ping, Druyts Eric, Eapen Shawn, and Mills Edward J. 2014. "Nonergot dopamine-receptor agonists for treating Parkinson's disease - a network meta-analysis". Neuropsychiatric Disease & Treatment 10:767-76.	Monotherapy with levodopa being permitted
Trenkwalder C, Kies B, Rudzinska M, Fine J, Nikl J, Honczarenko K, Dioszeghy P, Hill D, Anderson T, Myllyla V, Kassubek J, Steiger M, Zucconi M, Tolosa E, Poewe W, Surmann E, Whitesides J, Boroojerdi B, and Chaudhuri K R. 2011. "Rotigotine effects on early morning motor function and sleep in Parkinson's disease: a double-blind, randomized, placebo-controlled study (RECOVER)". Movement disorders: official journal of the Movement Disorder Society 26:90-9.	Patients on levodopa were permitted; hence not all had it at baseline/throughout the study.
Utsumi H, Okuma Y, Kano O, Suzuki Y, Iijima M, Tomimitsu H, Hashida H, Kubo S, Suzuki M, Nanri K, Matsumura M, Murakami H, and Hattori N. 2013. "Evaluation of the efficacy of pramipexole for treating levodopa-induced dyskinesia in patients with Parkinson's disease". Internal medicine (Tokyo, and Japan) 52:325-32.	Switch group study + no extractable outcomes
van Hilten, Ramaker Claudia, C , Stowe Rebecca, and Ives Natalie. 2007. "Bromocriptine/levodopa combined versus levodopa alone for early Parkinson's disease". Cochrane Database of Systematic Reviews :.	Early PD - Not in patients who are experiencing inadequate symptomatic control/ monotherapy.
van Hilten , J J, Ramaker C C, Stowe RI, and Ives N J. 2007. "Bromocriptine versus levodopa in early Parkinson's disease". Cochrane Database of Systematic Reviews :CD002258.	Monotherapy
T. van Laar, E. N. Jansen, A. W. Essink, C. Neef, S. Oosterloo, and R. A. Roos. A double-blind study of the efficacy of apomorphine and its assessment in 'off'-periods in Parkinson's disease. Clinical Neurology & Neurosurgery 95 (3):231-235, 1993	Only measures the response to a single dose
Warren Olanow, C , Kieburtz K, Rascol O, Poewe W, Schapira A	Monotherapy/ early PD

Excluded studies	
H, Emre M, Nissinen H, Leinonen M, and Stocchi F. 2013. "Factors predictive of the development of Levodopa-induced dyskinesia and wearing-off in Parkinson's disease". <i>Movement disorders : official journal of the Movement Disorder Society</i> 28:1064-71.	
Wilson R E, Seeberger L C, Silver D, Griffith A, Conner J B, and Salzman P M. 2011. "Rasagiline: Time to onset of antiparkinson effect is similar when used as a monotherapy or adjunct treatment". <i>Neurologist</i> 17:318-324.	Not an RCT
Wolf Elisabeth, Seppi Klaus, Katzenschlager Regina, Hochschorner Guenter, Ransmayr Gerhard, Schwingenschuh Petra, Ott Erwin, Kloiber Iris, Haubenberger Dietrich, Auff Eduard, and Poewe Werner. 2010. "Long-term antidyskinetic efficacy of amantadine in Parkinson's disease". <i>Movement Disorders</i> 25:1357-63.	Not clear if it's an adjunct treatment to L-dopa
Wong K S, Lu C S, Shan D E, Yang C C, Tsoi T H, and Mok V. 2003. "Efficacy, safety, and tolerability of pramipexole in untreated and levodopa-treated patients with Parkinson's disease". <i>Journal of the Neurological Sciences</i> 216:81-87.	Not in patients who are experiencing inadequate symptomatic control/ monotherapy.
Zhang Zhenxin, Wang Jian, Zhang Xiaoying, Chen Shengdi, Wang Zhenfu, Zhang Baorong, Liu Chunfeng, Qu Qiumin, Cheng Yan, Li Jie, Cao Haijun, Cai Meng, and Zhu Rongxuan. 2013. "The efficacy and safety of ropinirole prolonged release tablets as adjunctive therapy in Chinese subjects with advanced Parkinson's disease: a multicenter, double-blind, randomized, placebo-controlled study.[Erratum appears in <i>Parkinsonism Relat Disord</i> . 2014 Aug;20(8):943-4]". <i>Parkinsonism &amp; Related Disorders</i> 19:1022-6.	Corrigendum
Zhou C Q, Li S S, Chen Z M, Li F Q, Lei P, and Peng G G. 2013. "Rotigotine Transdermal Patch in Parkinson's Disease: A Systematic Review and Meta-Analysis". <i>PLoS ONE</i> 8:no pagination.	Include both early and advanced PD – potentially relevant articles are requested for full text review
Zhou C Q, Lou J H, Zhang Y P, Zhong L, Chen Y L, Lu F J, and Peng G G. 2014. "Long-Acting Versus Standard Non-Ergot Dopamine Agonists in Parkinson's Disease: A Meta-Analysis of Randomized Controlled Trials". <i>CNS Neuroscience and Therapeutics</i> 20:368-376.	Include both early and advanced PD – potentially relevant articles are requested for full text review

### Excluded studies from previous guideline

Excluded studies	
References	Reasons for exclusion
Brodersen P, Philbert A, Gulliksen G et al. The effect of l-deprenyl on on-off phenomena in Parkinson's disease. <i>Acta Neurologica Scandinavica</i> . 1985; 71:494–497.	Not properly randomised, crossover trial – data not split by treatment period
Clarke CE, Speller JM. Lisuride for levodopa-induced complications in Parkinson's disease (Cochrane Review). <i>The Cochrane Database of Systematic Reviews</i> . 1999;(1):CD001515	Not an intervention of interest
Hubble JP, Koller WC, Waters C. Effects of selegiline dosing on motor fluctuations in Parkinson's disease. <i>Clinical Neuropharmacology</i> . 1993; 16:83–87. Ref ID: 2752	crossover trial – data not split by treatment period
Mizuno Y, Yanagisawa N, Kuno S et al. Randomized, double-blind study of pramipexole	Not sure if all patients suffered from inadequate symptomatic control

Excluded studies	
with placebo and bromocriptine in advanced Parkinson's disease. <i>Movement Disorders</i> . 2003; 18(10):1149–1156	
Olanow CW, Kieburtz K, Stern M et al. Double-blind, placebo-controlled study of entacapone in levodopa-treated patients with stable Parkinson disease. <i>Archives of Neurology</i> . 2004; 61(10):1563–1568.	Not in patients who suffered from inadequate symptomatic control
Pogarell O, Gasser T, Van Hilten JJ et al. Pramipexole in patients with Parkinson's disease and marked drug resistant tremor: a randomised, double blind, placebo controlled multicentre study. <i>Journal of Neurology, Neurosurgery &amp; Psychiatry</i> . 2002; 72(6):713–720.	Not all patients were treated with levodopa at baseline/prior to study start
Sivertsen B, Dupont E, Mikkelsen B et al. Selegiline and levodopa in early or moderately advanced Parkinson's disease: A double-blind controlled short- and long-term study. <i>Acta Neurologica Scandinavica Supplementum</i> . 1989; 80(126):147–152	Not an RCT

**Studies (both from previous guideline and the new search) already included in relevant Cochrane reviews and included in the systematic review**

Included studies	Cochrane reviews
References	Cochrane reviews
Adler C H, Singer C, O'Brien C, Hauser R A, Lew M F, Marek K L, Dorflinger E, Pedder S, Deptula D, and Yoo K. 1998. "Randomized, placebo-controlled study of tolcapone in patients with fluctuating Parkinson disease treated with levodopa-carbidopa". <i>Archives of Neurology</i> 55:1089-1095.	Included in Stowe 2010
Ahlskog J E, Wright K F, Muentner M D, and Adler C H. 1996. "Adjunctive cabergoline therapy of Parkinson's disease: comparison with placebo and assessment of dose responses and duration of effect". <i>Clinical Neuropharmacology</i> 19:202-12.	Patients in included in the multicentre USA 1 trial (Hutton et al 1996), which is included in Stowe 2010
Brunt E R; Brooks D J; Korczyn A D; Montastruc J L; Stocchi F; Study Group. 2002. A six-month multicentre, double-blind, bromocriptine-controlled study of the safety and efficacy of ropinirole in the treatment of patients with Parkinson's disease not optimally controlled by L-dopa. <i>Journal of Neural Transmission</i> 109:489-502	Included in Stowe 2010
Cai J P, Chen W J, Lin Y, Cai B, and Wang N. 2014. "Safety and efficacy of rasagiline in addition to levodopa for the treatment of idiopathic parkinson's disease: A meta-analysis of randomised controlled trials". <i>European Neurology</i> 73:5-12.	Studies in this meta-analysis are included in Stowe 2010
Clarke C E, and Speller Julie. 1999. "Pergolide for levodopa-induced complications in Parkinson's disease". <i>Cochrane Database of Systematic Reviews</i> .	Studies in this SR are included in Stowe 2010
Clarke C, E, Speller J, M, Clarke J, and A. 2000. "Pramipexole for levodopa-induced complications in Parkinson's disease". <i>Cochrane Database of Systematic Reviews</i> :CD002261.	Studies in this SR are included in Stowe 2010
Clarke C E, Speller J M, and Clarke J A. 2000. "Pramipexole versus bromocriptine for levodopa-induced complications in Parkinson's disease". <i>Cochrane database of systematic reviews (Online)</i> :CD002259.	Studies in this SR are included in Stowe 2010
Clarke C E, and Deane K H. 2001. "Cabergoline for levodopa-	Studies in this SR are

Included studies	
induced complications in Parkinson's disease". Cochrane Database of Systematic Reviews :CD001518.	included in Stowe 2010
Clarke C E, and Deane K H. 2001. "Ropinirole for levodopa-induced complications in Parkinson's disease". Cochrane Database of Systematic Reviews :CD001516.	Studies in this SR are included in Stowe 2010
Deane K H. O, Spieker S, and Clarke C E. 2004. "Catechol-O-methyltransferase inhibitors for levodopa-induced complications in Parkinson's disease". Cochrane Database of Systematic Reviews :CD004554.	Studies in this SR are included in Stowe 2010
Diamond S G, Markham C H, and Treciokas L J. 1985. "Double-blind trial of pergolide for Parkinson's disease". Neurology 35:291-5.	Formed part of a large multi-centre study (N America) which has now been published in full (Olanow et al., 1994) and included in Stowe 2010
Elmer Lawrence W. 2013. "Rasagiline adjunct therapy in patients with Parkinson's disease: post hoc analyses of the PRESTO and LARGO trials". Parkinsonism & Related Disorders 19:930-6.	Studies in this study are included in Stowe 2010
Hersh Bonnie P, Earl Nancy L, Hauser Robert A, and Stacy Mark. 2010. "Early treatment benefits of ropinirole prolonged release in Parkinson's disease patients with motor fluctuations". Movement Disorders 25:927-31.	A retrospective analysis of Pahwa et al., 2007 population, which is included in the Stowe 2010 SR – No new data.
Hutton J T, Koller W C, Ahlskog J E, Pahwa R, Hurtig H I, Stern M B, Hiner B C, Lieberman A, Pfeiffer R F, Rodnitzky R L, Waters C H, Muenter M D, Adler C H, and Morris J L. 1996. "Multicenter, placebo-controlled trial of cabergoline taken once daily in the treatment of Parkinson's disease". Neurology 46:1062-5.	Included in Clarke 2001a
Im Joo-Hyuk, Ha Jeong-Ho, Cho In-Sook, and Lee Myoung C. 2003. "Ropinirole as an adjunct to levodopa in the treatment of Parkinson's disease: a 16-week bromocriptine controlled study". Journal of Neurology 250:90-6.	Included in Clarke 2001b
Inzelberg R, Nisipeanu P, Rabey J M, Orlov E, Catz T, Kippervasser S, Schechtman E, and Korczyn A D. 1996. "Double-blind comparison of cabergoline and bromocriptine in Parkinson's disease patients with motor fluctuations". Neurology 47:785-8.	Included in Stowe 2010
Koller W, Lees A, Doder M, Hely M, Burns R, Hughes A, Morris J, Bowman C E, Capildeo R, Clark C E, Forsyth D R, Lees A J, Mondal B K, Sharma J C, Steiger M J, Comella C L, Davis T L, Hauser R A, Hutton J T, Koller W C, Kurth M C, Langston J W, Olanow C W, Riley D E, Roduitzky R L, Saint-Hilaire M H, Waters C H, and Watts R L. 2001. "Randomized trial of tolcapone versus pergolide as add-on to levodopa therapy in Parkinson's disease patients with motor fluctuations". Movement Disorders 16:858-866.	Included in Dean 2004
Korchounov Alexei, and Bogomazov Gregory. 2006. "Employment, medical absenteeism, and disability perception in Parkinson's disease: A pilot double-blind, randomized, placebo-controlled study of entacapone adjunctive therapy". Movement Disorders 21:2220-4.	Included in Stowe 2010
Kunig G, Pogarell O, Moller J C, Delf M, and Oertel W H. 1999. "Pramipexole, a nonergot dopamine agonist, is effective against rest tremor in intermediate to advanced Parkinson's disease". Clinical Neuropharmacology 22:301-305.	Included in Stowe 2010
Lieberman A, Olanow C W, Sethi K, Swanson P, Waters C H, Fahn S, Hurtig H, and Yahr M. 1998. "A multicenter trial of ropinirole as adjunct treatment for Parkinson's disease. Ropinirole Study Group.[Erratum appears in Neurology 1999 Jan 15;52(2):435]".	Included in Stowe 2010

Included studies	
Neurology 51:1057-62.	
Minguez-Minguez Sara, Solis-Garcia Del Pozo, Julian , and Jordan Joaquin. 2013. "Rasagiline in Parkinson's disease: a review based on meta-analysis of clinical data". Pharmacological Research 74:78-86.	Relevant references included in Stowe 2010 + 1 individual RCT included separately from search
Mizuno Yoshikuni, Kanazawa Ichiro, Kuno Sadako, Yanagisawa Nobuo, Yamamoto Mitsutoshi, and Kondo Tomoyoshi. 2007. "Placebo-controlled, double-blind dose-finding study of entacapone in fluctuating parkinsonian patients". Movement Disorders 22:75-80.	Included in Stowe 2010
Molho E S, Factor S A, Weiner W J, Sanchez-Ramos J R, Singer C, Shulman L, Brown D, and Sheldon C. 1995. "The use of pramipexole, a novel dopamine (DA) agonist, in advanced Parkinson's disease". Journal of Neural Transmission Supplementum 45:225-30.	Formed part of a large multicentre study (US/Canada) which has now been published in full (Lieberman et al., 1997) and included in Stowe 2010
Moller J Carsten, Oertel Wolfgang H, Koster Jurgen, Pezzoli Gianni, and Provinciali Leandro. 2005. "Long-term efficacy and safety of pramipexole in advanced Parkinson's disease: results from a European multicenter trial". Movement Disorders 20:602-10.	Included in Stowe 2010
Olanow C W, Fahn S, Muentner M, Klawans H, Hurtig H, Stern M, Shoulson I, Kurlan R, Grimes J D, and Jankovic J. 1994. "A multicenter double-blind placebo-controlled trial of pergolide as an adjunct to Sinemet in Parkinson's disease". Movement disorders : official journal of the Movement Disorder Society 9:40-7.	Included in Stowe 2010
Parkinson Study, and Group . 2005. "A randomized placebo-controlled trial of rasagiline in levodopa-treated patients with Parkinson disease and motor fluctuations: the PRESTO study". Archives of Neurology 62:241-8.	Included in Stowe 2010
Pinter M M, Pogarell O, and Oertel W H. 1999. "Efficacy, safety, and tolerance of the non-ergoline dopamine agonist pramipexole in the treatment of advanced Parkinson's disease: a double blind, placebo controlled, randomised, multicentre study". Journal of neurology, neurosurgery, and and psychiatry 66:436-41.	Included in Stowe 2010
Ramaker C, Beek W J. T. van d e, Finken M Jj, and van Hilten. 1998. "Bromocriptine for levodopa-induced motor complications in Parkinson's disease". Cochrane Database of Systematic Reviews : .	All relevant articles included in Stowe 2010 Cochrane Systematic Review
Rascol O, Lees A J, Senard J M, Pirtosek Z, Brefel C, Montastruc J L, and Fuell D. 1996. "A placebo-controlled study of ropinirole, a new D2 agonist, in the treatment of motor fluctuations of L-DOPA-treated parkinsonian patients". Advances in Neurology 69:531-4.	Included in Stowe 2010
Rascol O, Lees A J, Senard J M, Pirtosek Z, Montastruc J L, and Fuell D. 1996. "Ropinirole in the treatment of levodopa-induced motor fluctuations in patients with Parkinson's disease". Clinical Neuropharmacology 19:234-45.	Included in Stowe 2010
Rascol O, Brooks D J, Melamed E, Oertel W, Poewe W, Stocchi F, and Tolosa E. 2005. "Rasagiline as an adjunct to levodopa in patients with Parkinson's disease and motor fluctuations (LARGO, Lasting effect in Adjunct therapy with Rasagiline Given Once daily, study): a randomised, double-blind, parallel-group trial". Lancet (London, and England) 365:947-54.	Included in Stowe 2010
Ray Chaudhuri, K , Martinez-Martin P, Rolfe K A, Cooper J, Rockett C B, Giorgi L, and Ondo W G. 2012. "Improvements in nocturnal symptoms with ropinirole prolonged release in patients with advanced Parkinson's disease". European Journal of Neurology 19:105-13.	Included in Stowe 2010
Reichmann H, Boas J, Macmahon D, Myllyla V, Hakala A,	Included in Stowe 2010



Included studies	
Reinikainen K, ComQol Study, and Group . 2005. "Efficacy of combining levodopa with entacapone on quality of life and activities of daily living in patients experiencing wearing-off type fluctuations". <i>Acta Neurologica Scandinavica</i> 111:21-8.	
Steiger M J, El-Debas T, Anderson T, Findley L J, and Marsden C D. 1996. "Double-blind study of the activity and tolerability of cabergoline versus placebo in parkinsonians with motor fluctuations". <i>Journal of Neurology</i> 243:68-72.	Included in Stowe 2010
Stocchi F, and Rabey J M. 2011. "Effect of rasagiline as adjunct therapy to levodopa on severity of OFF in Parkinson's disease". <i>European Journal of Neurology</i> 18:1373-8.	Included in Stowe 2010
Stowe Rebecca, Ives Natalie, Clarke Carl E, Handley Kelly, Furnston Alexandra, Deane Katherine, van Hilten , J J, Wheatley Keith, and Gray Richard. 2011. "Meta-analysis of the comparative efficacy and safety of adjuvant treatment to levodopa in later Parkinson's disease". <i>Movement Disorders</i> 26:587-98.	All but one study are included in Stowe 2010. The additional study is included separately from search.
Talati R, Baker W L, Patel A A, Reinhart K, and Coleman C I. 2009. "Adding a dopamine agonist to preexisting levodopa therapy vs. levodopa therapy alone in advanced Parkinson's disease: a meta analysis". <i>International Journal of Clinical Practice</i> 63:613-23.	Included in Stowe 2010
Talati Ripple, Reinhart Kurt, Baker William, White C Michael, and Coleman Craig I. 2009. "Pharmacologic treatment of advanced Parkinson's disease: a meta-analysis of COMT inhibitors and MAO-B inhibitors". <i>Parkinsonism &amp; Related Disorders</i> 15:500-5.	Included in Stowe 2010
Tolosa E, and Stern M B. 2012. "Efficacy, safety and tolerability of rasagiline as adjunctive therapy in elderly patients with Parkinson's disease". <i>European Journal of Neurology</i> 19:258-64.	Post-hoc analysis of 2 included studies in Stowe 2010 (PRESTO and LARGO studies)
Wermuth L. 1998. "A double-blind, placebo-controlled, randomized, multi-center study of pramipexole in advanced Parkinson's disease". <i>European Journal of Neurology</i> 5:235-242.	Included in Stowe 2010
Zhou Chang-Qing, Zhang Jiang-Wei, Wang Min, and Peng Guo-Guang. 2014. "Meta-analysis of the efficacy and safety of long-acting non-ergot dopamine agonists in Parkinson's disease". <i>Journal of Clinical Neuroscience</i> 21:1094-101.	All relevant articles included in Stowe 2010 Cochrane Systematic Review



## G.3 Pharmacological management of non-motor symptoms

### G.3.1 Daytime hypersomnolence

Excluded studies	Reason for exclusion
Chahine,Lama M., Daley,Joseph, Horn,Stacy, Duda,John E., Colcher,Amy, Hurtig,Howard, Cantor,Charles, Dahodwala,Nabila, Association between dopaminergic medications and nocturnal sleep in early-stage Parkinson's disease. [References], Parkinsonism & Related Disorders, 19, 859-863, 2013	Not an RCT
Chaudhuri,K.Ray, Logishetty,Kartik, Dopamine receptor agonists and sleep disturbances in Parkinson's disease. [References], Parkinsonism & Related Disorders, 15, Jan-S104, 2010	Narrative review
Fabbrini,G., Barbanti,P., Aurilia,C., Pauletti,C., Vanacore,N., Meco,G., 20040106, Excessive daytime somnolence in Parkinson's disease. Follow-up after 1 year of treatment, Neurological Sciences, 24, 178-179, 2003	Not an RCT
Kumar,R., Approved and investigational uses of modafinil: An evidence-based review, Drugs.68 (13) (pp 1803-1839), 2008.Date of Publication: 2008., 1803-1839, 2008	All 3 studies reviewed here for PD are covered in guideline update
Lohr,J.B., Liu,L., Caligiuri,M.P., Kash,T.P., May,T.A., Murphy,J.D., Ancoli-Israel,S., 20140508, Modafinil improves antipsychotic-induced parkinsonism but not excessive daytime sleepiness, psychiatric symptoms or cognition in schizophrenia and schizoaffective disorder: a randomized, double-blind, placebo-controlled study, Schizophrenia Research, 150, 289-296, 2013	Population not PD
Lokk,Johan, Daytime sleepiness in elderly Parkinson's disease patients and treatment with the psychostimulant modafinil: A preliminary study. [References], Neuropsychiatric Disease and Treatment, 6, ArtID-97, 2010	Not an RCT
Romigi,A., Marciani,M.G., Placidi,F., 20040810, L-dopa-induced excessive daytime sleepiness in PD: a placebo-controlled case with MSLT assessment, Neurology, 62, 1454-1455, 2004	Letter
Sheng,P., Hou,L., Wang,X., Huang,C., Yu,M., Han,X., Dong,Y., Efficacy of modafinil on fatigue and excessive daytime sleepiness associated with neurological disorders: A systematic review and meta-analysis, PLoS ONE.8 (12) , 2013.Article Number: e81802.Date of Publication: 03 Dec 2013., -, 2013	Population not exclusively PD
Thorpy,M.J., 20040824, Sleep disorders in Parkinson's disease. [Review] [56 refs], Clinical Cornerstone, 6, Suppl-15, 2004	Review
Valentino,R.M., Foldvary-Schaefer,N., 20071016, Modafinil in the treatment of excessive daytime sleepiness. [Review] [50 refs], Cleveland Clinic Journal of Medicine, 74, 561-566, 568	Narrative review
Rodrigues T M, Caldas A C, and Ferreira J J. 2016. "Pharmacological interventions for daytime sleepiness and sleep disorders in Parkinson's disease: Systematic review and meta-analysis". Parkinsonism and Related Disorders 27(pp 25-34)	Crossover trials

### G.3.2 Nocturnal akinesia

Excluded studies - 3. sleep disorders in PD	
Study	Reason for Exclusion
Bruin,V.M.S., Bittencourt,L.R.A., Tufik,S., Sleep-wake disturbances in Parkinson's disease: Current evidence regarding diagnostic and therapeutic decisions, <i>European Neurology</i> .67 (5) (pp 257-267), 2012.Date of Publication: May 2012., 257-267, 2012	Review - no primary data
Bruin,Veralice Meireles Sales, Bittencourt,Lia Rita Azeredo, Tufik,Sergio, Sleep-wake disturbances in Parkinson's disease: Current evidence regarding diagnostic and therapeutic decisions. [References], <i>European Neurology</i> , 67, 257-267, 2012	Narrative review
Chahine,Lama M., Daley,Joseph, Horn,Stacy, Duda,John E., Colcher,Amy, Hurtig,Howard, Cantor,Charles, Dahodwala,Nabila, Association between dopaminergic medications and nocturnal sleep in early-stage Parkinson's disease. [References], <i>Parkinsonism &amp; Related Disorders</i> , 19, 859-863, 2013	Not an RCT
Chaudhuri,K.R., Friedman,J.H., Surmann,E., Ghys,L., Trenkwalder,C., The effects of transdermal rotigotine on mood/cognition: Interpretations from a post-hoc analysis of the RECOVER study using the Parkinson's disease non-motor symptom scale, <i>Movement DisordersMov.Disord.</i> , 26, S123-, 2011	Post-hoc analysis of RECOVER study: Trenkwalder et al 2011
Chaudhuri,K.Ray, Logishetty,Kartik, Dopamine receptor agonists and sleep disturbances in Parkinson's disease. [References], <i>Parkinsonism &amp; Related Disorders</i> , 15, Jan-S104, 2010	Narrative review
Diederich,N.J., Paolini,V., Vaillant,M., Slow wave sleep and dopaminergic treatment in Parkinson's disease: A polysomnographic study. [References], <i>Acta Neurologica Scandinavica</i> , 120, 308-313, 2009	Study not an RCT - observational assessment of relationship between influence of dopaminergic medication on slow wave sleep
Fabbrini,G., Barbanti,P., Aurilia,C., Pauletti,C., Vanacore,N., Mecco,G., 20040106, Excessive daytime somnolence in Parkinson's disease. Follow-up after 1 year of treatment, <i>Neurological Sciences</i> , 24, 178-179, 2003	Not an RCT
Giladi,N., Fichtner,A., Poewe,W., Borojerdi,B., 20111114, Rotigotine transdermal system for control of early morning motor impairment and sleep disturbances in patients with Parkinson's disease, <i>Journal of Neural Transmission</i> , 117, 1395-1399, 2010	Not an RCT
Kaynak,D., Kiziltan,G., Kaynak,H., Benbir,G., Uysal,O., 20050429, Sleep and sleepiness in patients with Parkinson's disease before and after dopaminergic treatment, <i>European Journal of Neurology</i> , 12, 199-207, 2005	Not RCT study design.
Kumar,R., Approved and investigational uses of modafinil: An evidence-based review, <i>Drugs</i> .68 (13) (pp 1803-1839), 2008.Date of Publication:	All 3 studies reviewed for PD are covered here in update

<b>Excluded studies - 3. sleep disorders in PD</b>	
2008., 1803-1839, 2008	
Lohr,J.B., Liu,L., Caligiuri,M.P., Kash,T.P., May,T.A., Murphy,J.D., Ancoli-Israel,S., 20140508, Modafinil improves antipsychotic-induced parkinsonism but not excessive daytime sleepiness, psychiatric symptoms or cognition in schizophrenia and schizoaffective disorder: a randomized, double-blind, placebo-controlled study, Schizophrenia Research, 150, 289-296, 2013	Population not PD
Lokk,Johan, Daytime sleepiness in elderly Parkinson's disease patients and treatment with the psychostimulant modafinil: A preliminary study. [References], Neuropsychiatric Disease and Treatment, 6, ArtID-97, 2010	Not an RCT
Lyons,K.E., Pahwa,R., Outcomes of rotigotine clinical trials. Effects on motor and nonmotor symptoms of parkinson's disease, Neurologic Clinics.31 (3 S) (pp S51-S59), 2013.Date of Publication: August 2013., S51-S59, 2013	Not an RCT
Reichmann,H., Cooper,J., Rolfe,K., Martinez-Martin,P., Sleep duration and on time during different periods of the day and night in patients with advanced parkinson's disease receiving adjunctive ropinirole prolonged release, Parkinson's Disease, , 2011. Article Number: 354760. Date of Publication: 2011., -, 2011	Not an RCT
Romigi,A., Marciani,M.G., Placidi,F., 20040810, L-dopa-induced excessive daytime sleepiness in PD: a placebo-controlled case with MSLT assessment, Neurology, 62, 1454-1455, 2004	Letter
Sheng,P., Hou,L., Wang,X., Huang,C., Yu,M., Han,X., Dong,Y., Efficacy of modafinil on fatigue and excessive daytime sleepiness associated with neurological disorders: A systematic review and meta-analysis, PLoS ONE.8 (12) , 2013.Article Number: e81802.Date of Publication: 03 Dec 2013., -, 2013	Population not exclusively PD
Stocchi,F., Stirpe,P., The relevance of dopaminergic level in nocturnal disability in Parkinson's disease: Implications of continuous dopaminergic stimulation at night to treat the symptoms, Journal of Neural Transmission.121 (SUPPL.1) (pp S79-S83), 2014.Date of Publication: August 2014., S79-S83, 2014	Review - not primary study
Swick,T., Surmann,E., Borojerdj,B., Moran,K., Ghys,L., Trenkwalder,C., Association between early morning motor symptoms and nocturnal sleep disturbance in patients with Parkinson's disease - A post hoc analysis of the randomized evaluation of the 24- hour coverage: Efficacy of rotigotine (RECOVER) study, Movement Disorders, 26, S303-, 2011	Post-hoc analysis of RECOVER study: Trenkwalder et al 2011
Thorpy,M.J., 20040824, Sleep disorders in Parkinson's disease. [Review] [56 refs], Clinical Cornerstone, 6, Suppl-15, 2004	Review
Trenkwalder,C., Kies,B., Dioszeghy,P., Hill,D.,	Open-label; not an RCT

<b>Excluded studies - 3. sleep disorders in PD</b>	
Surmann,E., Boroojerdi,B., Whitesides,J., Chaudhuri,K.R., Rotigotine transdermal system for the management of motor function and sleep disturbances in Parkinson's disease: Results from a 1-year, open-label extension of the RECOVER study, <i>Basal ganglia</i> , 2, 79-85, 2012	
Valentino,R.M., Foldvary-Schaefer,N., 20071016, Modafinil in the treatment of excessive daytime sleepiness. [Review] [50 refs], <i>Cleveland Clinic Journal of Medicine</i> , 74, 561-566, 568	Narrative review
Slow E J, Postuma R B, and Lang A E. 2014. "Implications of nocturnal symptoms towards the early diagnosis of Parkinson's disease". <i>Journal of Neural Transmission</i> 121 Suppl 1:S49-57.	Pre-PD diagnosis

### G.3.3 Orthostatic hypotension

<b>Excluded studies - 13. RQ12: what is the effectiveness of pharmacological interventions for orthostatic hypotension in Parkinson's disease?</b>	
Study	Reason for Exclusion
Biaggioni,I., Freeman,R., Mathias,C.J., Low,P., Hewitt,L.A., Kaufmann,H., Droxidopa 302 Investigators, 20150225, Randomized withdrawal study of patients with symptomatic neurogenic orthostatic hypotension responsive to droxidopa, <i>Hypertension</i> , 65, 101-107, 2015	Not all participants in study had Parkinson's disease
Biaggioni,I., Low,P., Rowse,G., Kaufmann,H., Analysis of efficacy in patients with symptomatic neurogenic orthostatic hypotension treated with droxidopa and dopadecarboxylase inhibitors, <i>Movement DisordersMov.Disord.</i> , 27, S422-S423, 2012	Conference Abstract - No Primary Data
Fox,S.H., Marras,C., Orthostatic hypotension in Parkinsonism: What is it and how can we treat it?, <i>Movement Disorders</i> .30 (5) (pp 601-603), 2015.Date of Publication: 15 Apr 2015., 601-603, 2015	Review - no primary data
Hauser,R.A., Isaacson,S., Kaufmann,H., Hewitt,L.A., Integrated efficacy of droxidopa for neurogenic orthostatic hypotension, <i>Movement Disorders</i> , 29, S562-, 2014	Conference abstract - No Primary Data
Isaacson,S., Shill,H., Vernino,S., Cioffi,C., Hutchman,R., Durability of effect with long-term, open-label droxidopa treatment in patients with symptomatic neurogenic orthostatic hypotension (NOH 303), <i>Movement Disorders</i> , 27, S424-S425, 2012	Conference Abstract - No Primary Data
Kaufmann,H., L-dihydroxyphenylserine (Droxidopa): A new therapy for neurogenic orthostatic hypotension: The US experience, <i>Clinical Autonomic Research</i> .18 (SUPPL.1) (pp 19-24), 2008.Date of Publication: March 2008., 19-24, 2008	Review - No primary data
Kaufmann,H., Freeman,R., Biaggioni,I., Low,P., Pedder,S., Hewitt,L.A., Mauney,J., Feirtag,M., Mathias,C.J., NOH301 Investigators, 20140909,	Not all patients had Parkinson's disease

<b>Excluded studies - 13. RQ12: what is the effectiveness of pharmacological interventions for orthostatic hypotension in Parkinson's disease?</b>	
Droxidopa for neurogenic orthostatic hypotension: a randomized, placebo-controlled, phase 3 trial, <i>Neurology</i> , 83, 328-335, 2014	
Low,P., Nelson,J., Stacy,M., Safety and efficacy of droxidopa in patients previously treated with midodrine, <i>Movement Disorders</i> , 27, S426-, 2012	Conference Abstract - No Primary Data
Mathias,C., Low,P., Freeman,R., Hewitt,A., Kaufmann,H., Integrated efficacy analysis of droxidopa in 2 double-blind, placebo-controlled phase 3 studies in patients with neurogenic orthostatic hypotension, <i>Movement Disorders</i> , 27, S426-, 2012	Conference Abstract - No Primary Data
Perez-Lloret,S., Rey,M.V., Pavy-Le,Traon A., Rascol,O., Droxidopa for the treatment of neurogenic orthostatic hypotension and other symptoms of neurodegenerative disorders, <i>Expert Opinion on Orphan Drugs</i> .2 (5) (pp 509-522), 2014.Date of Publication: May 2014., 509-522, 2014	Review, no primary data
Shill,H., Vernino,S., Hutchman,R., Adkins,L., Isaacson,S., A multicenter, open-label study to assess the long-term safety of droxidopa in patients with symptomatic neurogenic orthostatic hypotension (NOH 304), <i>Movement Disorders</i> , 27, S428-, 2012	Conference Abstract - No Primary Data
Wenning,G., Low,P., Szakacs,C., Kaufmann,H., Subgroup efficacy analysis: Orthostatic hypotension questionnaire composite score in patients with neurogenic orthostatic hypotension treated with droxidopa, <i>Movement Disorders</i> , 27, S429-, 2012	Conference Abstract - No Primary Data
Dewey R B, Jr , Rao S D, Holmburg S L, and Victor R G. 1998. "Ergotamine/caffeine treatment of orthostatic hypotension in parkinsonism with autonomic failure". <i>Eur J Neurol</i> 5(6):593-599.	Study design
Isaacson S, Liang G, Lisk J P, and Rowse G J. 2015. "Durability of effect with long-term droxidopa treatment in patients with symptomatic NOH". <i>Movement disorders</i> 30:S93.	Abstract only
Rowse G, Heritier S, and Hewitt L A. 2014. "Falls during a 10-week placebo-controlled study of droxidopa for neurogenic orthostatic hypotension in Parkinson's disease". <i>Clinical autonomic research</i> 24(5):229-30.	Abstract only
Rowse G J, Hewitt L A, Shields A, Freeman R, and Kaufmann H. 2015. "Responder analyses of droxidopa in patients with symptomatic neurogenic orthostatic hypotension". <i>Movement disorders</i> 30:S116-s117.	Abstract only



### G.3.4 Psychotic symptoms (hallucinations and delusions)

Excluded studies - 1. What is the comparative effectiveness of pharmacological interventions for psychotic symptoms associated with PD?	
Study	Reason for Exclusion
Figiel,G., Sadowsky,C., 20080227, A systematic review of the effectiveness of rivastigmine for the treatment of behavioral disturbances in dementia and other neurological disorders. [Review] [62 refs], Current Medical Research & Opinion, 24, 157-166, 2008	Not in patients with PD and psychosis.
Frieling,H., Hillemacher,T., Ziegenbein,M., Neundorfer,B., Bleich,S., 20070226, Treating dopamimetic psychosis in Parkinson's disease: structured review and meta-analysis. [Review] [55 refs], European Neuropsychopharmacology, 17, 165-171, 2007	Not all included studies in this review meet our inclusion criteria for RQ21. Those articles that do meet our inclusion criteria have already been picked up by our search strategy and are included.
Kurlan,R., Cummings,J., Raman,R., Thal,L., Alzheimer's Disease Cooperative Study Group, 20070510, Quetiapine for agitation or psychosis in patients with dementia and parkinsonism, Neurology, 68, 1356-1363, 2007	Data not reported separately for PDD.
Rolinski,M., Fox,C., Maidment,I., McShane,R., 20120607, Cholinesterase inhibitors for dementia with Lewy bodies, Parkinson's disease dementia and cognitive impairment in Parkinson's disease. [Review], Cochrane Database of Systematic Reviews, 3, CD006504- , 2012	Not in patients with PD and psychosis.
The French Clozapine Parkinson Study Group, Clozapine in drug-induced psychosis in Parkinson's disease, The Lancet, 353, 2041-2042, 1999	No data to extract.
Wang,H.-F., Yu,J.-T., Tang,S.-W., Jiang,T., Tan,C.-C., Meng,X.-F., Wang,C., Tan,M.-S., Tan,L., Efficacy and safety of cholinesterase inhibitors and memantine in cognitive impairment in Parkinson's disease, Parkinson's disease dementia, and dementia with Lewy bodies: Systematic review with meta-analysis and trial sequential analysis, Journal of Neurology, Neurosurgery and Psychiatry.86 (2) (pp 135-143), 2015.Date of Publication: 01 Feb 2015., 135-143, 2015	Not in patients with PD and psychosis.
Desmarais P, Massoud F, Filion J, Nguyen Q D, and Bajsarowicz P. 2016. "Quetiapine for Psychosis in Parkinson Disease and Neurodegenerative Parkinsonian Disorders: A Systematic Review". J Geriatr Psychiatry Neurol ..	Qualitative review

### G.3.5 REM sleep behaviour disorder

A single search was conducted for this question and for the question on nocturnal akinesia. For the full list of excluded studies for both questions, please see the section on nocturnal akinesia

### G.3.6 Thermoregulatory dysfunction

<b>Excluded studies - 14. RQ13: what is the effectiveness of pharmacological interventions for thermoregulatory dysfunction associated with Parkinson's disease?</b>	
Study	Reason for Exclusion
Asahina,M., Vichayanrat,E., Low,D.A., Iodice,V., Mathias,C.J., 20130712, Autonomic dysfunction in parkinsonian disorders: assessment and pathophysiology. [Review], Journal of Neurology, Neurosurgery & Psychiatry, 84, 674-680, 2013	Narrative review
Hirayama,M., 20070831, Sweating dysfunctions in Parkinson's disease. [Review] [43 refs], Journal of NeurologyJ Neurol, 253, Suppl-47, 2006	Narrative review
Kaufmann,H., Goldstein,D.S., 20140401, Autonomic dysfunction in Parkinson disease. [Review], Handbook of Clinical Neurology, 117, 259-278, 2013	Narrative review. No primary data
Mills,R., Bahroo,L., Pagan,F., An Update on the Use of Botulinum Toxin Therapy in Parkinson's Disease, Current Neurology and Neuroscience Reports.15 (1) , 2014.Date of Publication: 2014., -, 2014	Narrative review
Perez-Lloret,S., Rey,M.V., Pavy-Le,Traon A., Rascol,O., Droxidopa for the treatment of neurogenic orthostatic hypotension and other symptoms of neurodegenerative disorders, Expert Opinion on Orphan Drugs.2 (5) (pp 509-522), 2014.Date of Publication: May 2014., 509-522, 2014	No evidence for thermoregulatory dysfunction presented in the paper
Perez-Lloret,S., Rey,M.V., Pavy-Le,Traon A., Rascol,O., 20130821, Emerging drugs for autonomic dysfunction in Parkinson's disease. [Review], Expert Opinion on Emerging Drugs, 18, 39-53, 2013	No evidence for thermoregulatory dysfunction presented in the paper
Pursiainen,V., Lyytinen,J., Pekkonen,E., 20130128, Effect of duodenal levodopa infusion on blood pressure and sweating, Acta Neurologica Scandinavica, 126, e20-e24, 2012	Study not a RCT. Duodenal levodopa infusion not an intervention of interest for treatment of thermoregulatory dysfunction

## G.4 Pharmacological management of dementia associated with Parkinson's disease

Study	Reason for exclusion
Cholinesterase inhibitors and atypical antipsychotics may help manage dementia and psychosis in Parkinson's disease, <i>Drugs and Therapy Perspectives</i> .23 (3) (pp 7-10), 2007.Date of Publication: March 2007., 7-10, 2007	Not a relevant study
Cholinesterase inhibitors: Tremor and exacerbation of Parkinson's disease, <i>Prescrire International</i> .16 (91) (pp 197-198), 2007.Date of Publication: October 2007., 197-198, 2007	Not a relevant study
Rivastigmine patches: No therapeutic advantage and less convenient than capsules, <i>Prescrire International</i> <i>Prescrire Int.</i> , 18, 19-, 2009	Not a relevant study
Multicentre UK study of the acetylcholinesterase inhibitor donepezil in early dementia associated with Parkinson's disease (MUSTARDD-PD) (Project record), <i>Health Technology Assessment Database</i> , -, 2010	Not published version of study
20070514, Rivastigmine: new indication. Dementia and Parkinson's disease: no thank you!, <i>Prescrire International</i> , 16, 66-, 2007	Not a relevant study
Aarsland,D., Ballard,C., Rongve,A., Broadstock,M., Svenningsson,P., 20130403, Clinical trials of dementia with Lewy bodies and Parkinson's disease dementia, <i>Current Neurology &amp; Neuroscience Reports</i> , 12, 492-501, 2012	Systematic review – eligible studies already identified
Aarsland,D., Bronnick,K., Ehrt,U., De Deyn,P.P., Tekin,S., Emre,M., Cummings,J.L., 20061220, Neuropsychiatric symptoms in patients with Parkinson's disease and dementia: frequency, profile and associated care giver stress, <i>Journal of Neurology, Neurosurgery &amp; Psychiatry</i> , 78, 36-42, 2007	Not relevant comparison
Aarsland,D., Ehrt,U., Gauthier,S., Rivastigmine for the treatment of Parkinson's disease dementia, <i>Aging Health</i> .6 (3) (pp 277-284), 2010.Date of Publication: June 2010., 277-284, 2010	Systematic review – eligible studies already identified
Aarsland,D., Emre,M., Lees,A., Poewe,W., Ballard,C., Practice Parameter: Evaluation and treatment of depression, psychosis, and dementia in Parkinson disease (an evidence-based review): Report of the Quality Standards Subcommittee of the American Academy of Neurology [5], <i>Neurology</i> .68 (1) (pp 80), 2007.Date of Publication: January 2007., 80-, 2007	Not a relevant study
Aarsland,D., Taylor,J.-P., Weintraub,D., Psychiatric issues in cognitive impairment, <i>Movement Disorders</i> .29 (5) (pp 651-662), 2014.Date of Publication: 15 Apr 2014., 651-662, 2014	Not a relevant study
Aarsland,T., A double-blind, placebo-controlled multicentre trial of memantine in patients with Parkinson's disease dementia or dementia with Lewy bodies, <i>ISRCTN</i> : <i>ISRCTN89624516</i> , -, 2006	Not published version of study
Almaraz,A.C., Driver-Dunckley,E.D., Woodruff,B.K., Wellik,K.E., Caselli,R.J., Demaerschalk,B.M., Adler,C.H., Caviness,J.N., Wingerchuk,D.M., 20091009, Efficacy of rivastigmine for cognitive symptoms in Parkinson disease with dementia, <i>Neurologist</i> , 15, 234-237, 2009	Systematic review – eligible studies already identified
Anon, Randomised controlled trial of memantine versus placebo in Parkinson's disease dementia, <i>ISRCTN Register</i> [ <a href="http://www.controlled-trials.com/mrct">www.controlled-trials.com/mrct</a> ], -, 2005	Not relevant comparison
Anon, [Public title] Memantine versus placebo in Parkinson's disease dementia or dementia with Lewy bodies; [Scientific title] A randomised, double-blind, placebo-controlled, 6-month study of the efficacy and safety of memantine in patients with Parkinson's disease dementia or dementia with Lewy bodies, <i>ClinicalTrials.gov</i> [ <a href="http://clinicaltrials.gov">http://clinicaltrials.gov</a> ], -, 2007	Not published version of study

Study	Reason for exclusion
Anon, Long-term safety of rivastigmine capsule and patch in patients with mild to moderately-severe dementia associated with parkinson's disease (pdd) or a 76-week prospective, open-label, multicenter study to evaluate the long-term effect of rivastigmine capsule and transdermal patch on worsening of the underlying motor symptoms of pd in patients with mild to moderately severe dementia associated with parkinson's disease (pdd), ClinicalTrials.gov [http://clinicaltrials.gov], -, 2008	Not published version of study
Anon, [Public title] Donepezil in early dementia associated with Parkinson's disease; [Scientific title] Multicentre UK study of the acetylcholinesterase inhibitor donepezil in early dementia associated with Parkinson's disease, ISRCTN Register [http://www.controlled-trials.com], -, 2009	Not published version of study
Ballard,C., Kahn,Z., Corbett,A., Treatment of dementia with lewy bodies and Parkinson's disease dementia, Drugs and Aging.28 (10) (pp 769-777), 2011.Date of Publication: 2011., 769-777, 2011	Systematic review – eligible studies already identified
Ballard,C., Lane,R., Barone,P., Ferrara,R., Tekin,S., 20070405, Cardiac safety of rivastigmine in Lewy body and Parkinson's disease dementias.[Erratum appears in Int J Clin Pract. 2006 Sep;60(9):1146], International Journal of Clinical Practice, 60, 639-645, 2006	Systematic review – eligible studies already identified
Ballard,C.G., Chalmers,K.A., Todd,C., McKeith,I.G., O'Brien,J.T., Wilcock,G., Love,S., Perry,E.K., 20070607, Cholinesterase inhibitors reduce cortical Abeta in dementia with Lewy bodies, Neurology, 68, 1726-1729, 2007	No relevant outcomes; not a randomised controlled trial
Barone,P., Burn,D.J., van,Laar T., Hsu,C., Poewe,W., Lane,R.M., 20090408, Rivastigmine versus placebo in hyperhomocysteinemic Parkinson's disease dementia patients, Movement DisordersMov.Disord., 23, 1532-1540, 2008	Not a relevant comparison – sub-group analysis
Beverdorf,D.Q., Warner,J.L., Davis,R.A., Sharma,U.K., Nagaraja,H.N., Scharre,D.W., Donepezil in the treatment of dementia with Lewy bodies [1], American Journal of Geriatric PsychiatryAm.J.Geriatr.Psychiatry, 12, 542-544, 2004	Not a relevant study
Bhasin,M., Rowan,E., Edwards,K., McKeith,I., 20080501, Cholinesterase inhibitors in dementia with Lewy bodies: a comparative analysis, International Journal of Geriatric Psychiatry, 22, 890-895, 2007	Not a relevant study
Borghammer,P., Vafae,M., Ostergaard,K., Rodell,A., Bailey,C., Cumming,P., 20080612, Effect of memantine on CBF and CMRO2 in patients with early Parkinson's disease, Acta Neurologica Scandinavica, 117, 317-323, 2008	Not relevant population; no relevant outcomes
Brennan,L., Pantelyat,A., Duda,JE., Morley,JE., Weintraub,D., Wilkinson,JR., Moberg,PJ., Memantine and cognition in Parkinson's disease dementia/Dementia with Lewy Bodies: A meta-analysis, Movement Disorders, 3(2), 161-167, 2016	Systematic review – eligible studies already identified
Burn,D., Emre,M., McKeith,I., De Deyn,P.P., Aarsland,D., Hsu,C., Lane,R., 20070220, Effects of rivastigmine in patients with and without visual hallucinations in dementia associated with Parkinson's disease, Movement Disorders, 21, 1899-1907, 2006	Not a relevant comparison – sub group analysis
Burn,D., Emre,M., McKeith,I., Hsu,C., Lane,R., Response to Rivastigmine in Patients with and without Visual Hallucinations in Dementia Associated with Parkinson's Disease (EXPRESS Study Group), 57th Annual Meeting of the American Academy of Neurology, Miami Beach, April 2005 [S25.004], -, 2005	Unable to source
Burn,D.J., 20110104, The treatment of cognitive impairment associated with Parkinson's disease. [Review] [68 refs], Brain Pathology, 20, 672-678, 2010	Not a relevant study

Study	Reason for exclusion
Ceravolo,R., Volterrani,D., Frosini,D., Bernardini,S., Rossi,C., Logi,C., Manca,G., Kiferle,L., Mariani,G., Murri,L., Bonuccelli,U., 20070905, Brain perfusion effects of cholinesterase inhibitors in Parkinson's disease with dementia, Journal of Neural TransmissionJ.Neural Transm., 113, 1787-1790, 2006	Not relevant comparison
Chitnis,S., Rao,J., 20090928, Rivastigmine in Parkinson's disease dementia. [Review] [70 refs], Expert Opinion On Drug Metabolism & Toxicology, 5, 941-955, 2009	Not a relevant study
Cummings,J., Cholinesterase inhibitors for treatment of dementia associated with Parkinson's disease, Journal of Neurology, Neurosurgery and Psychiatry, 76, 903-904, 2005	Not a relevant study
Cummings,J., Winblad,B., 20080102, A rivastigmine patch for the treatment of Alzheimer's disease and Parkinson's disease dementia. [Review] [26 refs], Expert Review of Neurotherapeutics, 7, 1457-1463, 2007	Not a relevant study
Darreh-Shori,T., Jelic,V., Safety and tolerability of transdermal and oral rivastigmine in Alzheimer's disease and Parkinson's disease dementia, Expert Opinion on Drug Safety.9 (1) (pp 167-176), 2010.Date of Publication: 10 Jan 2010., 167-176, 2010	Not a relevant study
Deyn,P.P., Barone,P., Poewe,W., Kulisevsky,J., Laar,T., Pourcher,E., Callegari,F., Tenenbaum,N., Graf,A., Assessment of motor symptoms in a long-term safety study of rivastigmine capsules and patch in patients with dementia associated with Parkinson's disease, European Journal of Neurology, 18, 496-, 2011	Abstract only
Dujardin,K., Devos,D., Duhem,S., Destee,A., Marie,R.M., Durif,F., Lacomblez,L., Touchon,J., Pollak,P., Pere,J.J., 20070313, Utility of the Mattis dementia rating scale to assess the efficacy of rivastigmine in dementia associated with Parkinson's disease, Journal of Neurology, 253, 1154-1159, 2006	Not a relevant study – secondary reanalysis of data from Emre 2004
Dumbrava,L.P., Fischer,T., Medrea,R., Use of a rivastigmine transdermic patch in Alzheimer's disease and Parkinson's disease dementia, Romanian Journal of Neurology/ Revista Romana de NeurologieRom.J.Neurol.Rev.Rom.Neurol., 8, 38-42, 2009	Not a relevant study
Edwards,K., Royall,D., Hershey,L., Lichter,D., Hake,A., Farlow,M., Pasquier,F., Johnson,S., 20070724, Efficacy and safety of galantamine in patients with dementia with Lewy bodies: a 24-week open-label study, Dementia & Geriatric Cognitive Disorders, 23, 401-405, 2007	No relevant comparator
Emre,M., Treatment of dementia associated with Parkinson's disease, Parkinsonism and Related Disorders.13 (SUPPL.3) (pp S457-S461), 2007.Date of Publication: 2007., S457-S461, 2007	Not relevant study
Emre,M., Cummings,J.L., Lane,R.M., 20071102, Rivastigmine in dementia associated with Parkinson's disease and Alzheimer's disease: similarities and differences. [Review] [48 refs], Journal of Alzheimer's Disease, 11, 509-519, 2007	Not relevant comparison
Emre,M., Poewe,W., Deyn,P.P., Barone,P., Kulisevsky,J., Pourcher,E., Laar,T., Callegari,F., Tenenbaum,N., Graf,A., A 76-week study on the long-term safety of rivastigmine capsules and patch in patients with dementia associated with Parkinson's disease, Movement Disorders, 26, S125-, 2011	Abstract only
Emre,M., 20090401, Treatment of dementia associated with Parkinson's disease. [Review] [38 refs], Parkinsonism & Related Disorders, 13, Suppl-61, 2007	Evidence summary – not a randomised controlled trial
Emre,M., 20090814, Memantine: a new hope for treatment of Lewy body-related dementias?, Lancet Neurology, 8, 594-595, 2009	Not a study



Study	Reason for exclusion
Emre,P., A 24 week prospective, randomized, multicenter, double-blind, placebo-controlled, parallel-group study of the efficacy, tolerability and safety of 3-12 mg/day of rivastigmine capsules in patients with Parkinson's dementia, <a href="http://www.wifpma.org/clinicaltrials.html">http://www.wifpma.org/clinicaltrials.html</a> , -, 2005	Unable to source
Fischer,C., Bozanovic,R., Atkins,J.H., Rourke,S.B., 20070620, Treatment of delusions in dementia with Lewy bodies - response to pharmacotherapy. [Review] [19 refs], <i>Dementia &amp; Geriatric Cognitive Disorders</i> , 23, 307-311, 2007	Systematic review – eligible studies already identified
Fong,T.G., Inouye,S.K., Dai,W., Press,D.Z., Alsop,D.C., Association cortex hypoperfusion in mild dementia with Lewy bodies: A potential indicator of cholinergic dysfunction?, <i>Brain Imaging and Behavior</i> Brain Imaging Behav., 5, 25-35, 2011	Not relevant population
Gaskell,H., Burns,A., Fox,C., Maidment,I., Pettit,T.A.C.L., Wild,R., McShane,R., Boustani,M., Cholinesterase inhibitors for dementia with Lewy bodies, Parkinson's disease dementia and cognitive impairment in Parkinson's disease, <i>Cochrane Database of Systematic Reviews</i> , -, 2007	Updated Cochrane Review published (2012)
Gauthier,S., Giannakopoulos,P., Hof,P.R., Pharmacotherapy of parkinson disease dementia and lewy body dementia, <i>Dementia in Clinical Practice.Frontiers of Neurology and Neuroscience</i> .24 (pp 135-139), 2009.Date of Publication: 2009., -139, 2009	Not a relevant study
Hussl,A., Seppi,K., Poewe,W., Nonmotor symptoms in Parkinson's disease, <i>Expert Review of Neurotherapeutics</i> .13 (6) (pp 581-583), 2013.Date of Publication: June 2013., 581-583, 2013	Not a relevant study
Ikeda,M., Mori,E., Kosaka,K., Iseki,E., Hashimoto,M., Matsukawa,N., Matsuo,K., Nakagawa,M., Katayama,S., Higashi,Y., Yamada,T., Maruki,Y., Orimo,S., Yoshiiwa,A., Hanyu,H., Yokochi,M., Kimura,T., Mizoguchi,K., Nakanishi,A., Tsukamoto,T., Taniguchi,N., Okamoto,K., Kitamura,T., Nakano,Y., Kato,T., Shimada,K., Hiji,M., Yoshiyama,Y., Kitamura,Y., Takahashi,S., Akishita,M., Washimi,Y., Yamamoto,Y., Kobayashi,M., Udaka,F., Osaki,Y., Hino,H., Kanda,T., Kishimoto,T., Oguro,H., Matsuoka,T., Tsugu,Y., Fujii,N., Kawase,Y., Long-term safety and efficacy of donepezil in patients with dementia with lewy bodies: Results from a 52-week, open-label, multicenter extension study, <i>Dementia and geriatric cognitive disorders</i> Dementia Geriatr.Cogn.Disord., 36, 229-241, 2013	No relevant comparator
Johansson,C., Ballard,C., Hansson,O., Palmqvist,S., Minthon,L., Aarsland,D., Londos,E., 20110505, Efficacy of memantine in PDD and DLB: an extension study including washout and open-label treatment, <i>International Journal of Geriatric Psychiatry</i> , 26, 206-213, 2011	Not a relevant comparison
Jones,R.W., A review comparing the safety and tolerability of memantine with the acetylcholinesterase inhibitors, <i>International Journal of Geriatric Psychiatry</i> .25 (6) (pp 547-553), 2010.Date of Publication: June 2010., 547-553, 2010	Not a relevant study
Josif,S., Graham,K., 20080718, Diagnosis and treatment of dementia with Lewy bodies. [Review] [24 refs], <i>JAAPA</i> , 21, 22-26, 2008	Not a relevant study
Kim,D.H., Brown,R.T., Ding,E.L., Kiel,D.P., Berry,S.D., Review: Cholinesterase inhibitors but not memantine increase syncope in older adults with mild cognitive impairment or dementia, <i>Annals of Internal Medicine</i> .155 (10) (pp JC5-10), 2011.Date of Publication: 20111115., JC5-10, 2011	Not a relevant study
Klingelhoefer,L., Reichmann,H., Dementia - The real problem for patients with Parkinson's disease, <i>Basal Ganglia</i> .4 (1) (pp 9-13), 2014.Date of Publication: June 2014., 9-13, 2014	Not a relevant study
Larsson,V., Aarsland,D., Ballard,C., Minthon,L., Londos,E., 20110314,	Not a relevant study –

Study	Reason for exclusion
The effect of memantine on sleep behaviour in dementia with Lewy bodies and Parkinson's disease dementia, <i>International Journal of Geriatric Psychiatry</i> , 25, 1030-1038, 2010	secondary reanalysis of data from Aarsland 2009
Larsson,V., Engedal,K., Aarsland,D., Wattmo,C., Minthon,L., Londos,E., Quality of life and the effect of memantine in dementia with lewy bodies and Parkinson's disease dementia, <i>Dementia and geriatric cognitive disorders</i> <i>Dementia Geriatr.Cogn.Disord.</i> , 32, 227-234, 2011	Not a relevant study – secondary reanalysis of data from Aarsland 2009
Lee,P.H., Yong,S.W., An,Y.S., 20090212, Changes in cerebral glucose metabolism in patients with Parkinson disease with dementia after cholinesterase inhibitor therapy, <i>Journal of Nuclear Medicine</i> , 49, 2006-2011, 2008	Not a relevant comparison; no relevant outcomes
Leroi,I., Atkinson,R., Overshott,R., 20150511, Memantine improves goal attainment and reduces caregiver burden in Parkinson's disease with dementia, <i>International Journal of Geriatric Psychiatry</i> , 29, 899-905, 2014	Not a relevant study – secondary reanalysis of data from Leroi 2009
Leroi,I., Collins,D., Marsh,L., 20070123, Non-dopaminergic treatment of cognitive impairment and dementia in Parkinson's disease: a review. [Review] [91 refs], <i>Journal of the Neurological Sciences</i> , 248, 104-114, 2006	Systematic review – eligible studies already identified
Levin,O.S., Batukaeva,L.A., [Efficacy of memantine in Parkinson's disease with dementia], <i>Zhurnal neurologii i psikiatrii imeni S.S.Korsakova / Ministerstvo zdravookhraneniia i meditsinsko? promyshlennosti Rossi?sko? Federatsii, Vserossi?skoe obshchestvo nevrologov [i] Vserossi?skoe obshchestvo psikiatrov</i> , 108, 16-23, 2008	Not English language
Levin,O.S., Batukaeva,L.A., Smolentseva,I.G., Amosova,N.A., [Efficacy and safety of memantine in dementia with Lewy bodies], <i>Zhurnal neurologii i psikiatrii imeni S.S.Korsakova / Ministerstvo zdravookhraneniia i meditsinsko? promyshlennosti Rossi?sko? Federatsii, Vserossi?skoe obshchestvo nevrologov [i] Vserossi?skoe obshchestvo psikiatrov</i> , 108, 39-46, 2008	Not English language
Levin,O.S., Batukaeva,L.A., Smolentseva,I.G., Amosova,N.A., 20090827, Efficacy and safety of memantine in Lewy body dementia, <i>Neuroscience &amp; Behavioral Physiology</i> , 39, 597-604, 2009	Not a randomised controlled trial
Li,W., Zhao,J.H., Sun,S.G., Zhang,J.W., Suo,A.Q., Ma,M.M., [Clinical rehabilitative effect of memantine on cognitive and motor disorders in patients with Parkinson's disease], <i>Zhonghua yi xue za zhi</i> , 91, 301-303, 2011	Not English language
Liepelt,I., Maetzler,W., Blaicher,H.P., Gasser,T., Berg,D., 20070724, Treatment of dementia in parkinsonian syndromes with cholinesterase inhibitors. [Review] [176 refs], <i>Dementia &amp; Geriatric Cognitive Disorders</i> , 23, 351-367, 2007	Systematic review – eligible studies already identified
Linazasoro,G., Lasa,A., Van,Blercom N., 20051207, Efficacy and safety of donepezil in the treatment of executive dysfunction in Parkinson disease: a pilot study, <i>Clinical Neuropharmacology</i> , 28, 176-178, 2005	Not relevant population
Litvinenko,I.V., Odinak,M.M., Mogil'naya,V.I., Emelin,A.Y., 20090402, Efficacy and safety of galantamine (reminyl) for dementia in patients with Parkinson's disease (an open controlled trial), <i>Neuroscience &amp; Behavioral Physiology</i> , 38, 937-945, 2008	Comparator is no treatment rather than placebo
Litvinenko,I.V., Odinak,M.M., Mogil'naia,V.I., Emelin,A.I., [Efficacy and safety of galantamine (reminyl) in the treatment of dementia in patients with Parkinson's disease (open-label controlled trial)], <i>Zhurnal neurologii i psikiatrii imeni S.S.Korsakova / Ministerstvo zdravookhraneniia i meditsinsko.? promyshlennosti Rossi?sko?</i>	Not English language

Study	Reason for exclusion
Federatsii, Vserossi?skoe.obshchestvo nevrologov [i] Vserossi?skoe.obshchestvo psikhiatrov, 107, 25-33, 2007	
Litvinenko,I.V., Odinak,M.M., Mogil'naya,V.I., Perstnev,S.V., 20100322, Use of memantine (akatinol) for the correction of cognitive impairments in Parkinson's disease complicated by dementia, Neuroscience & Behavioral Physiology, 40, 149-155, 2010	Not a randomised controlled trial; population unclear
MacMahon,D., DONEPEZIL 318 - A 52 week, multicentre, open label extension study of the safety, tolerability and efficacy of donepezil (Aricept) in Parkinson's Disease patients with dementia, National Research Register, -, 2005	Not published version of study
Maidment,I., Fox,C., Boustani,M., 20060407, Cholinesterase inhibitors for Parkinson's disease dementia. [Review] [60 refs], Cochrane Database of Systematic Reviews, CD004747-, 2006	Updated Cochrane Review published (2012)
Maidment,I.D., Fox,C., Boustani,M., 20051011, A review of studies describing the use of acetyl cholinesterase inhibitors in Parkinson's disease dementia. [Review] [40 refs], Acta Psychiatrica Scandinavica, 111, 403-409, 2005	Evidence summary – eligible studies already identified
Mamikonyan,E., Xie,S.X., Melvin,E., Weintraub,D., Rivastigmine for mild cognitive impairment in Parkinson disease: a placebo-controlled study, Movement DisordersMov.Disord., 30, 912-918, 2015	Not relevant population
Marsh,L., Double-Blind Placebo-Controlled Trial of Memantine for Treatment of Cognitive Impairment in Patients With Parkinson's Disease and Dementia, ClinicalTrials.gov [http://clinicaltrials.gov], -, 2006	Not published version of study
Marsh,L., Treatment of Lewy-body dementias and psychopathology, The Lancet Neurology.9 (10) (pp 943-944), 2010.Date of Publication: October 2010., 943-944, 2010	Not a relevant study
Massano,J., Rivastigmine for the treatment of Parkinson's disease dementia, Sinapse, 14, 21-25, 2014	Unable to source
Matsunaga,S., Kishi,T., Iwata,N., Memantine for Lewy body disorders: systematic review and meta-analysis (Provisional abstract), Database of Abstracts of Reviews of Effects, epub-, 2013	Systematic review – eligible studies already identified
McKeith,I., 20090323, Top cited papers in International Psychogeriatrics: 1. Long-term use of rivastigmine in patients with dementia with Lewy bodies: an open-label trial, International PsychogeriatricsInt.Psychogeriatr., 21, 5-6, 2009	Not a relevant study
MEMPDD 2008, Efficacy and safety of memantine for Parkinson's disease dementia (PDD) and dementia with Lewy Bodies (DLB), ClinicalTrials.gov [http://clinicaltrials.gov], -, 2008	Not published version of study
Molho,E., Barba,A., Feustel,P., Higgins,D., Factor,S., Double-blind, placebo-controlled trial of donepezil for dementia or mild cognitive impairment in Parkinson disease, Journal of Parkinson's DiseaseJ.Parkinson's Dis., Conference: 3rd World Parkinson Congress Montreal, QC Canada. Conference Start: 20131001 Conference End: 20131004. Conference Publication:, 106-, 2013	Abstract only
Moreau,C., Delval,A., Dujardin,K., Delliaux,M., Tiffreau,V., Kreisler,A., Simonin,C., Blatt,J.-L., Bordet,R., Destee,A., Defebvre,L., Devos,D., Memantine for gait disorders, axial rigidity and attention deficit in Parkinson's disease? A double blind placebo controlled study, Movement DisordersMov.Disord., 26, S257-, 2011	Abstract only
Moreau,C., Delval,A., Tiffreau,V., Defebvre,L., Dujardin,K., Duhamel,A., Petyt,G., Hossein-Foucher,C., Blum,D., Sablonniere,B., Schraen,S., Allorge,D., Destee,A., Bordet,R., Devos,D., 20130531, Memantine for axial signs in Parkinson's disease: a randomised, double-blind, placebo-controlled pilot study, Journal of Neurology, Neurosurgery & Psychiatry, 84, 552-555, 2013	Not relevant population

Study	Reason for exclusion
Morgan,J., Sethi,K.D., 20051028, Rivastigmine for dementia associated with Parkinson's disease, Current Neurology & Neuroscience Reports, 5, 263-265, 2005	Not a relevant study
Mori,E., Ikeda,M., Nagai,R., Matsuo,K., Nakagawa,M., Kosaka,K., 20150225, Long-term donepezil use for dementia with Lewy bodies: results from an open-label extension of Phase III trial, Alzheimer's Research & Therapy, 7, 5-, 2015	No relevant comparator
Mori,S., Mori,E., Iseki,E., Kosaka,K., 20060606, Efficacy and safety of donepezil in patients with dementia with Lewy bodies: preliminary findings from an open-label study, Psychiatry & Clinical Neurosciences, 60, 190-195, 2006	No relevant comparator
Muller,T., Welnic,J., Fuchs,G., Baas,H., Ebersbach,G., Reichmann,H., 20070517, The DONPAD-study--treatment of dementia in patients with Parkinson's disease with donepezil, Journal of Neural Transmission, Supplementum., 27-30, 2006	Not a randomised controlled trial
NCT01014858, Multi-centre UK study of the acetylcholinesterase inhibitor donepezil in early dementia associated with Parkinson's disease (MUSTARDD-PD), ClinicalTrials.gov [http://clinicaltrials.gov], -, 2009	Not published version of study
NCT02345213, A Post-Marketing Clinical Study of Aricept in Patients With Dementia With Lewy Bodies (DLB), Http://clinicaltrials.gov/show/NCT02345213, -, 2015	Not published version of study
Novartis, An open-label, 24 week extension to a 24-week prospective, randomized, multicenter, double-blind, placebo-controlled, parallel-group study of the efficacy, tolerability and safety of 3-12 mg/day of rivastigmine capsules in patients with Parkinson's Disease dementia, IFPMA Register, -, 2006	Unable to source
Oertel,W., Poewe,W., Wolters,E., De Deyn,P.P., Emre,M., Kirsch,C., Hsu,C., Tekin,S., Lane,R., 20080505, Effects of rivastigmine on tremor and other motor symptoms in patients with Parkinson's disease dementia: a retrospective analysis of a double-blind trial and an open-label extension, Drug Safety, 31, 79-94, 2008	Not a relevant study
Oh,Y.S., Kim,J.S., Lee,P.H., 20150619, Effect of Rivastigmine on Behavioral and Psychiatric Symptoms of Parkinson's Disease Dementia, Journal of Movement Disorders, 8, 98-102, 2015	Not a randomised controlled trial
Olin,J.T., Aarsland,D., Meng,X., 20101208, Rivastigmine in the treatment of dementia associated with Parkinson's disease: effects on activities of daily living, Dementia & Geriatric Cognitive Disorders, 29, 510-515, 2010	Not a relevant study – secondary reanalysis of data from Emre 2004
Ondo,W.G., Shinawi,L., Davidson,A., Lai,D., 20110607, Memantine for non-motor features of Parkinson's disease: a double-blind placebo controlled exploratory pilot trial, Parkinsonism & Related Disorders, 17, 156-159, 2011	Not relevant population
Pagano,G., Rengo,G., Pasqualetti,G., Femminella,G.D., Monzani,F., Ferrara,N., Tagliati,M., Cholinesterase inhibitors for Parkinson's disease: a systematic review and meta-analysis (Provisional abstract), Database of Abstracts of Reviews of Effects, epub-, 2014	Systematic review – eligible studies already identified
Pakrasi,S., Thomas,A., Mosimann,U.P., Cousins,D.A., Lett,D., Burn,D.J., O'Brien,J.T., McKeith,I.G., 20070608, Cholinesterase inhibitors in advanced Dementia with Lewy bodies: increase or stop?, International Journal of Geriatric Psychiatry, 21, 719-721, 2006	Not a randomised controlled trial
Peng,D., Yuan,X., Zhu,R., 20140606, Memantine hydrochloride in the treatment of dementia subtypes. [Review], Journal of Clinical Neuroscience, 20, 1482-1485, 2013	Not a relevant study
Poewe,W., Long-Term Benefits of Rivastigmine in Dementia	Unable to source

Study	Reason for exclusion
Associated with Parkinson's Disease: An Open-Label Extension Study, 57th Annual Meeting of the American Academy of Neurology, Miami Beach, April 2005 [P02.096], -, 2005	
Pourcher,E., Nadeau,A., Jaime,M., Corbeil,P., Does rivastigmine improve balance control in parkinson's dementia?, European journal of neurologyEur.J.Neurol., 19, 309-, 2012	Abstract only
Reingold,J.L., Morgan,J.C., Sethi,K.D., Rivastigmine for the treatment of dementia associated with Parkinson's disease, Neuropsychiatric Disease and Treatment.3 (6) (pp 775-783), 2007.Date of Publication: 2007., 775-783, 2007	Not a relevant study
Rodda,J., Carter,J., Cholinesterase inhibitors and memantine for symptomatic treatment of dementia, BMJ (Online).344 (7856) , 2012.Article Number: e2986.Date of Publication: 12 May 2012., -, 2012	Not a relevant study
Rolinski,M., Fox,C., Maidment,I., McShane,R., 20120607, Cholinesterase inhibitors for dementia with Lewy bodies, Parkinson's disease dementia and cognitive impairment in Parkinson's disease. [Review], Cochrane Database of Systematic Reviews, 3, CD006504-, 2012	Systematic review – eligible studies already identified
Rosengarten,B., Dannhardt,V., Burr,O., Pohler,M., Rosengarten,S., Oechsner,M., Reuter,I., 20110309, Neurovascular coupling in Parkinson's disease patients: effects of dementia and acetylcholinesterase inhibitor treatment, Journal of Alzheimer's DiseaseJ.Alzheimer's Dis., 22, 415-421, 2010	Not relevant comparison
Rowan,E., McKeith,I.G., Saxby,B.K., O'Brien,J.T., Burn,D., Mosimann,U., Newby,J., Daniel,S., Sanders,J., Wesnes,K., 20070426, Effects of donepezil on central processing speed and attentional measures in Parkinson's disease with dementia and dementia with Lewy bodies, Dementia & Geriatric Cognitive Disorders, 23, 161-167, 2007	Not a randomised controlled trial
Russ,T.C., Morling,J.R., Review: Cholinesterase inhibitors do not reduce progression to dementia from mild cognitive impairment, Annals of Internal MedicineAnn.Intern.Med., 158, JC3-, 2013	Not a relevant study; not relevant population
Sadowsky,C.H., Micca,J.L., Grossberg,G.T., Velting,D.M., 20150210, Rivastigmine from capsules to patch: therapeutic advances in the management of Alzheimer's disease and Parkinson's disease dementia. [Review], The Primary Care Companion to CNS Disorders, 16, 2014-, 2014	Not a relevant study
Sandoval-Rincon,M., Saenz-Farret,M., Miguel-Puga,A., Micheli,F., Arias-Carrion,O., Rational pharmacological approaches for cognitive dysfunction and depression in Parkinson's disease, Frontiers in Neurology.6 (MAR) , 2015.Article Number: 71.Date of Publication: 2015., -, 2015	Systematic review – eligible studies already identified
Satoh,M., Ishikawa,H., Meguro,K., Kasuya,M., Ishii,H., Yamaguchi,S., 20110411, Improved visual hallucination by donepezil and occipital glucose metabolism in dementia with Lewy bodies: the Osaki-Tajiri project, European NeurologyEur.Neurol., 64, 337-344, 2010	Not a randomised controlled trial
Schmitt,F., Farlow,M., Olin,J., Effects of rivastigmine on executive function in Parkinson's disease dementia: Results from a 24-week placebo-controlled clinical trial, Annals of NeurologyAnn.Neurol., 66, S48, Abstract-66, 2009	Abstract only
Schmitt,F.A., Aarsland,D., Bronnick,K.S., Meng,X., Tekin,S., Olin,J.T., 20101104, Evaluating rivastigmine in mild-to-moderate Parkinson's disease dementia using ADAS-cog items, American Journal of Alzheimer's Disease & Other Dementias, 25, 407-413, 2010	Not a relevant study – secondary reanalysis of data from Emre 2004
Schmitt,F.A., Aarsland,D., Bronnick,K.S., Olin,J.T., Meng,X.,	Abstract only



Study	Reason for exclusion
Evaluating cognitive effects of oral rivastigmine using Subscales and Items of the ADAS-cog in Patients with mild to moderate Parkinson's disease dementia, <i>Journal of the American Geriatrics Society</i> J.Am.Geriatr.Soc., 58, S23-, 2010	
Schmitt,F.A., Farlow,M.R., Meng,X., Tekin,S., Olin,J.T., Efficacy of rivastigmine on executive function in patients with parkinson's disease dementia, <i>CNS Neuroscience and Therapeutics</i> .16 (6) (pp 330-336), 2010.Date of Publication: December 2010., 330-336, 2010	Not a relevant study – secondary reanalysis of data from Emre 2004
Siddiqui,M.A., Wagstaff,A.J., 20061128, Rivastigmine: in Parkinson's disease dementia. [Review] [31 refs], <i>CNS Drugs</i> , 20, 739-747, 748	Not a relevant study
Stinton,C., McKeith,I., Taylor,J.-P., Lafortune,L., Mioshi,E., Mak,E., Cambridge,V., Mason,J., Thomas,A., O'Brien,J.T., Pharmacological management of lewy body dementia: A systematic review and meta-analysis, <i>American Journal of Psychiatry</i> .172 (8) (pp 731-742), 2015.Date of Publication: 01 Aug 2015., 731-742, 2015	Systematic review – eligible studies already identified
Stubendorff,K., Larsson,V., Ballard,C., Minthon,L., Aarsland,D., Londos,E., Treatment effect of memantine on survival in dementia with Lewy bodies and Parkinson's disease with dementia: A prospective study, <i>BMJ Open</i> , 4, -, 2014	Not a relevant study
Thomas,A.J., Burn,D.J., Rowan,E.N., Littlewood,E., Newby,J., Cousins,D., Pakrasi,S., Richardson,J., Sanders,J., McKeith,I.G., 20060222, A comparison of the efficacy of donepezil in Parkinson's disease with dementia and dementia with Lewy bodies, <i>International Journal of Geriatric Psychiatry</i> , 20, 938-944, 2005	Not relevant comparison
Van Der Putt,R., Dineen,C., Janes,D., Series,H., McShane,R., 20070608, Effectiveness of acetylcholinesterase inhibitors: diagnosis and severity as predictors of response in routine practice, <i>International Journal of Geriatric Psychiatry</i> Int.J.Geriatr.Psychiatry, 21, 755-760, 2006	Not relevant comparison
van,Laar T., De Deyn,P.P., Aarsland,D., Barone,P., Galvin,J.E., 20120703, Effects of cholinesterase inhibitors in Parkinson's disease dementia: a review of clinical data. [Review], <i>CNS Neuroscience &amp; Therapeutics</i> , 17, 428-441, 2011	Systematic review – eligible studies already identified
Wang,H.-F., Yu,J.-T., Tang,S.-W., Jiang,T., Tan,C.-C., Meng,X.-F., Wang,C., Tan,M.-S., Tan,L., Efficacy and safety of cholinesterase inhibitors and memantine in cognitive impairment in Parkinson's disease, Parkinson's disease dementia, and dementia with Lewy bodies: Systematic review with meta-analysis and trial sequential analysis, <i>Journal of Neurology, Neurosurgery and Psychiatry</i> .86 (2) (pp 135-143), 2015.Date of Publication: 01 Feb 2015., 135-143, 2015	Systematic review – eligible studies already identified
Weintraub,D., Somogyi,M., Meng,X., 20120424, Rivastigmine in Alzheimer's disease and Parkinson's disease dementia: an ADAS-cog factor analysis, <i>American Journal of Alzheimer's Disease &amp; Other Dementias</i> , 26, 443-449, 2011	Systematic review – eligible studies already identified
Wesnes,K., Aarsland,D., Ballard,C., Londos,E., Memantine improves attention and verbal episodic memory in parkinson's disease dementia and dementiawith lewy bodies: A double-blind, placebo-controlled multicentre trial, <i>Alzheimer's &amp; dementia</i> , 9, 890-, 2013	Abstract only
Wesnes,K.A., Aarsland,D., Ballard,C., Londos,E., Memantine improves attention and episodic memory in Parkinson's disease dementia and dementia with Lewy bodies, <i>International Journal of Geriatric Psychiatry</i> Int.J.Geriatr.Psychiatry, No-, 2014	Not a relevant study – secondary reanalysis of data from Aarsland 2009
Wesnes,K.A., Aarsland,D., Ballard,C., Londos,E., Improvements to attention and verbal episodic memory with memantine in Parkinson's disease dementia and dementia with lewy bodies, <i>Journal of Nutrition, Health and Aging</i> J.Nutr.Health Aging, 17, 781-782, 2013	Abstract only

Study	Reason for exclusion
Wesnes, K.A., McKeith, I., Edgar, C., Emre, M., Lane, R., 20060227, Benefits of rivastigmine on attention in dementia associated with Parkinson disease, <i>Neurology</i> , 65, 1654-1656, 2005	Not a relevant study – secondary reanalysis of data from Emre 2004
Wezenberg, E., Verkes, R.J., Sabbe, B.G., Ruigt, G.S., Hulstijn, W., 20060215, Modulation of memory and visuospatial processes by biperiden and rivastigmine in elderly healthy subjects, <i>Psychopharmacology</i> , 181, 582-594, 2005	Not relevant population
Brennan L, Pantelyat A, Duda J E, Morley J F, Weintraub D, Wilkinson J R, and Moberg P J. 2016. "Memantine and Cognition in Parkinson's Disease Dementia/Dementia With Lewy Bodies: A Meta-Analysis". <i>Movement Disorders Clinical Practice</i> 3(2):161-167.	Not RCTs
Leroi I, Atkinson R, and Overshott R. 2014. "Memantine improves goal attainment and reduces caregiver burden in Parkinson's disease with dementia". <i>International Journal of Geriatric Psychiatry</i> 29(9):899-905.	Not RCTs
Matsunaga S, Kishi T, and Iwata N. 2015. "Memantine for Lewy body disorders: systematic review and meta-analysis". <i>American Journal of Geriatric Psychiatry</i> 23(4):373-83.	Study design
Stubendorff K, Larsson V, Ballard C, Minthon L, Aarsland D, and Londos E. 2014. "Treatment effect of memantine on survival in dementia with Lewy bodies and Parkinson's disease with dementia: A prospective study". <i>BMJ Open</i> 4(7):.	Study design
Wesnes K A, Aarsland D, Ballard C, and Londos E. 2015. "Memantine improves attention and episodic memory in Parkinson's disease dementia and dementia with Lewy bodies". <i>International journal of geriatric psychiatry</i> 30(1):46-54.	Study design

## G.5 Non-pharmacological management of motor and non-motor symptoms

### G.5.1 Physiotherapy and physical activity

Excluded studies - 1. What is the effectiveness of physiotherapy compared to usual care?	
Study	Reason for Exclusion
Allen, N.E., Canning, C.G., Sherrington, C., Lord, S.R., Latt, M.D., Close, J.C., O'Rourke, S.D., Murray, S.M., Fung, V.S., 20101104, The effects of an exercise program on fall risk factors in people with Parkinson's disease: a randomized controlled trial, <i>Movement Disorders</i> , 25, 1217-1225, 2010	Included within Tomlinson 2013 Cochrane review
Allen, N.E., Sherrington, C., Paul, S.S., Canning, C.G., 20111208, Balance and falls in Parkinson's disease: a meta-analysis of the effect of exercise and motor training. [Review], <i>Movement Disorders</i> , 26, 1605-1615, 2011	Meta analyses includes studies in Tomlinson Cochrane review
Ashburn, A., Fazakarley, L., Ballinger, C., Pickering, R., McLellan, L.D., Fitton, C., 20070709, A randomised controlled trial of a home based exercise programme to reduce the risk of falling among people with Parkinson's disease, <i>Journal of Neurology, Neurosurgery &amp; Psychiatry</i> , 78, 678-684, 2007	Already included within Tomlinson 2013 Cochrane review
Brichetto, G., Pelosin, E., Marchese, R., Abbruzzese, G., 20060517, Evaluation of physical therapy in parkinsonian patients with freezing of gait: a pilot study, <i>Clinical Rehabilitation</i> , 20, 31-35, 2006	Study design: not an RCT. Uncontrolled pilot study
Cakit, B.D., Saracoglu, M., Genc, H., Erdem, H.R., Inan, L., 20071108, The effects of incremental speed-dependent treadmill training on postural instability and fear of falling in Parkinson's disease, <i>Clinical Rehabilitation</i> , 21, 698-705, 2007	Already included within Tomlinson 2013 Cochrane review
Canning, C.G., Allen, N.E., Dean, C.M., Goh, L., Fung, V.S.C., Minimally-supervised treadmill training for individuals with Parkinson's disease: A randomized controlled trial, <i>Neurorehabilitation and neural repair</i> , 26, 703-704, 2012	Abstract only
Canning, C.G., Sherrington, C., Lord, S.R., Close, J.C.T., Heller, G., Heritier, S., Howard, K., Allen, N.E., Paul, S.S., Murray, S.M., O'Rourke, S.D., Fung, V.S.C., Exercise for falls prevention in Parkinson's disease: A randomised controlled trial, <i>Movement Disorders</i> , 28, S158-, 2013	Abstract only
Clarke, C.E., Patel, S., Woolley, R., Ives, N.J., Rick, C.E., Dowling, F., Wheatley, K., Walker, M.F., Sackley, C.M., PD REHAB: A large pragmatic randomised controlled trial of physiotherapy and occupational therapy versus no therapy in mild to moderate Parkinson's disease, <i>Movement Disorders</i> , 29, S231-S232, 2014	Published in abstract form only - unable to extract full dataset or methods

<b>Excluded studies - 1. What is the effectiveness of physiotherapy compared to usual care?</b>	
Comella,C.L., Stebbins,G.T., Brown-Toms,N., Goetz,C.G., Physical therapy and Parkinson's disease: a controlled clinical trial, <i>Neurology</i> , 44, 376-378, 1994	Date precedes date limit imposed post previous guideline (1994)
Crizzle,A.M., Newhouse,I.J., 20070223, Is physical exercise beneficial for persons with Parkinson's disease?. [Review] [12 refs], <i>Clinical Journal of Sport Medicine</i> , 16, 422-425, 2006	Review
de Dreu,M.J., van der Wilk,A.S., Poppe,E., Kwakkel,G., van Wegen,E.E., 20120827, Rehabilitation, exercise therapy and music in patients with Parkinson's disease: a meta-analysis of the effects of music-based movement therapy on walking ability, balance and quality of life, <i>Parkinsonism &amp; Related Disorders</i> , 18, Suppl-9, 2012	Review includes studies that are included within Tomlinson 2014 Cochrane review
Dereli,E.E., Yaliman,A., 20100715, Comparison of the effects of a physiotherapist-supervised exercise programme and a self-supervised exercise programme on quality of life in patients with Parkinson's disease, <i>Clinical Rehabilitation</i> , 24, 352-362, 2010	Study design: not an RCT, only quasi random design
Dowling,F.P., Rick,C., Sackley,C., Ives,N., Patel,S., Yao,G.L., Wheatley,K., Clarke,C.E., Parkinson's disease REHAB: Randomised controlled trial to study the effectiveness and cost-effectiveness of physiotherapy and occupational therapy for people with PD, <i>Movement Disorders</i> , 27, S115-, 2012	Old version of PD REHAB abstract - current abstract Clarke et al., 2014
Duncan,R.P., Earhart,G.M., 20120521, Randomized controlled trial of community-based dancing to modify disease progression in Parkinson disease, <i>Neurorehabilitation &amp; Neural Repair</i> , 26, 132-143, 2012	Already included within Tomlinson 2013 Cochrane review
Ebersbach,G., Ebersbach,A., Gandor,F., Wegner,B., Wissel,J., Kupsch,A., 20140610, Impact of physical exercise on reaction time in patients with Parkinson's disease-data from the Berlin BIG Study, <i>Archives of Physical Medicine &amp; Rehabilitation</i> , 95, 996-999, 2014	Paper included in Tomlinson 2014 Cochrane review
Ebersbach,G., Edler,D., Kauffhold,O., Wissel,J., Whole body vibration versus conventional physiotherapy to improve balance and gait in Parkinson's disease, <i>Archives of physical medicine and rehabilitation</i> , 89, 399-403, 2008	Not intervention of interest as outlined in protocol.
Ellis,T., de Goede,C.J., Feldman,R.G., Wolters,E.C., Kwakkel,G., Wagenaar,R.C., 20050512, Efficacy of a physical therapy program in patients with Parkinson's disease: a randomized controlled trial, <i>Archives of Physical Medicine &amp; Rehabilitation</i> , 86, 626-632, 2005	Date precedes previous guideline limit
Fernandez-del-Olmo,M.A., Sanchez,J.A., Bello,O., Lopez-Alonso,V., Marquez,G., Morenilla,L., Castro,X., Giraldez,M., Santos-Garcia,D., Treadmill training improves overground walking economy in Parkinson's disease: A randomized, controlled pilot study,	Does not report on clinical outcomes of interest pre-specified in review protocol

<b>Excluded studies - 1. What is the effectiveness of physiotherapy compared to usual care?</b>	
Frontiers in Neurology.5 (SEP) , 2014.Article Number: 191.Date of Publication: 2014., -, 2014	
Fietzek,U.M., Schroeteler,F.E., Ziegler,K., Zwosta,J., Ceballos-Baumann,A.O., Randomized cross-over trial to investigate the efficacy of a two-week physiotherapy programme with repetitive exercises of cueing to reduce the severity of freezing of gait in patients with Parkinson's disease, Clinical Rehabilitation, 28, 902-911, 2014	Study design not valid. Cross-over design does not permit accurate assessment of intervention whereby there is no guarantee that strategies taught to patients to improve gait and falling won't be utilised by those in 'no treatment' phase after training phase.
Frazzitta,G., Bertotti,G., Riboldazzi,G., Turla,M., Uccellini,D., Boveri,N., Guaglio,G., Perini,M., Comi,C., Balbi,P., Maestri,R., 20120521, Effectiveness of intensive inpatient rehabilitation treatment on disease progression in parkinsonian patients: a randomized controlled trial with 1-year follow-up, Neurorehabilitation & Neural Repair, 26, 144-150, 2012	Illogical comparator: comparator consists only of suggested home exercise and usual care - not well-matched to intensive inpatient physiotherapy.
Goodwin,V.A., Richards,S.H., Henley,W., Ewings,P., Taylor,A.H., Campbell,J.L., 20111213, An exercise intervention to prevent falls in people with Parkinson's disease: a pragmatic randomised controlled trial, Journal of Neurology, Neurosurgery & Psychiatry, 82, 1232-1238, 2011	Already included within Tomlinson 2013 Cochrane review
Harro,C.C., Shoemaker,M.J., Frey,O., Gamble,A.C., Harring,K.B., Karl,K.L., McDonald,J.D., Murray,C.J., VanDyke,J.M., Tomassi,E.M., VanHaitsma,R.J., 20141029, The effects of speed-dependent treadmill training and rhythmic auditory-cued overground walking on balance function, fall incidence, and quality of life in individuals with idiopathic Parkinson's disease: a randomized controlled trial, Neurorehabilitation, 34, 541-556, 2014	Does not compare physiotherapy to usual care as specified in protocol
Kurtais,Y., Kutlay,S., Tur,B.S., Gok,H., Akbostanci,C., 20080923, Does treadmill training improve lower-extremity tasks in Parkinson disease? A randomized controlled trial, Clinical Journal of Sport Medicine, 18, 289-291, 2008	Study does not report on outcomes of interest specified within the review protocol
Li,F., Fitzgerald,K., Postural stability in Parkinson's disease patients after Tai Chi training: A randomized controlled trial, Parkinsonism & Related Disorders, 18, S155-, 2012	Included in Tomlinson 2014 Cochrane review
Li,F., Harmer,P., Liu,Y., Eckstrom,E., Fitzgerald,K., Stock,R., Chou,L.S., A randomized controlled trial of patient-reported outcomes with tai chi exercise in Parkinson's disease, Movement Disorders, 29, 539-545, 2014	Original study included in Tomlinson 2014 Cochrane review. This study analysis focused on correlation between patient-reported outcomes and exercise adherence. Data on outcomes of interest as specified in review protocol not provided.
Mak,M.K., Hui-Chan,C.W., 20080722, Cued task-specific training is better than exercise in improving sit-to-stand in patients with Parkinson's disease: A randomized controlled trial, Movement Disorders, 23, 501-509, 2008	Included in Tomlinson 2014 Cochrane review



<b>Excluded studies - 1. What is the effectiveness of physiotherapy compared to usual care?</b>	
Mendes,F.A.D.S., Pompeu,J.E., Lobo,A.M., da Silva,K.G., Oliveira,T.D.P., Zomignani,A.P., Piemonte,M.E.P., Motor learning, retention and transfer after virtual-reality-based training in Parkinson's disease - effect of motor and cognitive demands of games: A longitudinal, controlled clinical study, <i>Physiotherapy (United Kingdom)</i> .98 (3) (pp 217-223), 2012.Date of Publication: September 2012., 217-223, 2012	Study design: Not an RCT
Munneke,M., Nijkrake,M.J., Keus,S.H., Kwakkel,G., Berendse,H.W., Roos,R.A., Borm,G.F., Adang,E.M., Overeem,S., Bloem,B.R., ParkinsonNet Trial Study Group, 20100217, Efficacy of community-based physiotherapy networks for patients with Parkinson's disease: a cluster-randomised trial, <i>Lancet Neurology</i> , 9, 46-54, 2010	Randomised trial of systems of healthcare for delivery of physiotherapy, not RCT of different physiotherapy interventions
Shulman,L.M., Katznel,L.I., Ivey,F.M., Sorkin,J.D., Favors,K., Anderson,K.E., Smith,B.A., Reich,S.G., Weiner,W.J., Macko,R.F., 20130416, Randomized clinical trial of 3 types of physical exercise for patients with Parkinson disease, <i>JAMA Neurology</i> , 70, 183-190, 2013	Does not compare physiotherapy to usual care, as specified in protocol
Sousa,A.V.C., Simao,C.R., Melo Santiago,L.M., Spaniol,A.P., Oliveira,D., Lindquist,R.R., Effects of treadmill training on dual-task gait in people with parkinson's disease, <i>Archives of physical medicine and rehabilitation</i> , 94, e14-e15, 2013	Poster description
Speelman,A.D., van,Nimwegen M., Bloem,B.R., Munneke,M., Evaluation of implementation of the ParkFit program: A multifaceted intervention aimed to promote physical activity in patients with Parkinson's disease, <i>Physiotherapy (United Kingdom)</i> .100 (2) (pp 134-141), 2014.Date of Publication: June 2014., 134-141, 2014	Evaluation of implementation of ParkFit program; analyses focused on patient and therapist experience, and subgroup analyses, rather than reporting on outcomes of interest as specified in review protocol
Stack,E., Roberts,H., Ashburn,A., 20111110, The PIT: SToPP Trial-A Feasibility Randomised Controlled Trial of Home-Based Physiotherapy for People with Parkinson's Disease Using Video-Based Measures to Preserve Assessor Blinding, <i>Parkinsons Disease</i> , 2012, 360231-, 2012	Feasibility study
Tomlinson,C.L., Patel,S., Meek,C., Herd,C.P., Clarke,C.E., Stowe,R., Shah,L., Sackley,C., Deane,K.O., Wheatley,K., Ives,N., Physiotherapy intervention in Parkinson's disease: Systematic review and meta-analysis, <i>BMJ (Online)</i> .345 (7872) , 2012.Article Number: e5004.Date of Publication: 01 Sep 2012., -, 2012	Updated in Tomlinson 2014 Cochrane review
Tomlinson,Claire L., Herd,Clare P., Clarke,Carl E., Meek,Charmaine, Patel,Smitaa, Stowe,Rebecca, Deane-Katherine,H.O., Shah,Laila, Sackley,Catherine M., Wheatley,Keith, Ives,Natalie, Physiotherapy for Parkinson's disease: a comparison of techniques, <i>Cochrane Database of Systematic Reviews</i> , -, 2014	Does not compare physiotherapy to best supportive care, as outlined in protocol

<b>Excluded studies - 1. What is the effectiveness of physiotherapy compared to usual care?</b>	
Yen,C.Y., Lin,K.H., Hu,M.H., Wu,R.M., Lu,T.W., Lin,C.H., 20110811, Effects of virtual reality-augmented balance training on sensory organization and attentional demand for postural control in people with Parkinson disease: a randomized controlled trial, <i>Physical Therapy</i> , 91, 862-874, 2011	Study did not report on outcomes of interest specified in the review protocol
Agosti V, Vitale C, Avella D, Rucco R, Santangelo G, Sorrentino P, Varriale P, and Sorrentino G. 2016. "Effects of Global Postural Reeducation on gait kinematics in parkinsonian patients: a pilot randomized three-dimensional motion analysis study". <i>Neurological Sciences</i> 37(4):515-522.	No relevant outcomes
Barry G, Galna B, and Rochester L. 2014. "The role of exergaming in Parkinson's disease rehabilitation: a systematic review of the evidence (Provisional abstract)". <i>Journal of Neuroengineering and Rehabilitation</i> 11(1):33.	Relevant references retrieved and reviewed
Belton A, Walsh R, Murphy S, McCabe D, and Galvin R. 2014. "The effect of a balance exercise class on activity limitations in people with parkinson's disease". <i>Irish journal of medical science</i> 183(7 suppl. 1):S326.	MSc dissertation
Burcu Duyur Cakit, Meryem Saracoglu, Hakan Genc, and Hatice Rana Erdem. 2007. "The effects of incremental speed-dependent treadmill training on postural instability and fear of falling in Parkinson's disease". <i>Clinical Rehabilitation</i> 21:698-705.	Included in Cochrane review
Canning C G, Farag I, Sherrington C, Lord S R, Close J C. T, Howard K, Heritier S, Heller G Z, Hayes A, Allen N E, Latt M D, Murray S M, O'Rourke S D, Paul S S, Song J, and Fung V S. C. 2015. "Minimally-supervised exercise is effective and cost-saving in reducing falls in people with mild, but not more severe parkinson's disease". <i>Physiotherapy (United Kingdom)</i> 101:eS199.	Conference abstract
Capato T T, Tornai J, Avila P, Barbosa E R, and Piemonte M E. 2015. "Randomized controlled trial protocol: balance training with rhythmical cues to improve and maintain balance control in Parkinson's disease". <i>BMC Neurology</i> 15:162.	Study protocol
Chung C L, Thilarajah S, and Tan D. 2016. "Effectiveness of resistance training on muscle strength and physical function in people with Parkinson's disease: a systematic review and meta-analysis". <i>Clinical Rehabilitation</i> 30(1):11-23.	Relevant references retrieved and reviewed
Cruise KE et al. 2011. "Exercise and Parkinson's: benefits for cognition and quality of life". <i>Acta Neurol Scand</i> 123:13-19.	Not an RCT
da Silva , F C, Iop Rda, R , Dos Santos, P D, Bezerra L M, Gutierrez P J, da Silva , and R . 2016. "Effects of Physical Exercise Based Rehabilitation Programs on Quality of Life in	Relevant references retrieved and reviewed

<b>Excluded studies - 1. What is the effectiveness of physiotherapy compared to usual care?</b>	
Parkinson's Disease Patients: A Systematic Review of Randomized Controlled Trials". J Aging Phys Act :	
Dibble et al. 2009. "High intensity eccentric resistance training decreases bradykinesia and improves quality of life in persons with Parkinson's disease: A preliminary study". Parkinsonism and Related Disorders 15:752-757.	Not an RCT
Duncan R P, and Earhart G M. 2014. "Are the effects of community-based dance on Parkinson disease severity, balance, and functional mobility reduced with time? A 2-year prospective pilot study". Journal of Alternative & Complementary Medicine 20(10):757-63.	No standard deviations reported
Felippe L, Oliveira R, Guimaraes L, Silva T, Andrade T, Berton B, Silva A, Charro P, and Christofoletti G. 2015. "Benefits of physical therapy on the executive functions of people with Parkinson's disease: A controlled clinical trial". Journal of the neurological sciences 357:e350-e351.	Conference abstract
Fitton C, Kunkel D, Hulbert S, Robison J, Roberts L, Pickering R, Wiles R, Roberts H, and Ashburn A. 2015. "Dancing with parkinson's disease: Feasibility randomised controlled trial". Physiotherapy (United Kingdom) 101:eS384-eS385.	Conference abstract
Foster et al. 2013. "A community-based Argentine tango dance program is associated with increased activity participation among individuals with Parkinson disease". Arch Phys Med Rehabil 94:240-249.	No relevant outcomes
Franzen E, Conradsson D, Lefgren N, Nero H, Stahle A, and Hagstremmer M. 2014. "Efficacy of a highly challenging and systems-specific balance training program in elderly with Parkinson's disease". Movement disorders 29:S239.	Conference abstract
Frazzitta G, Riboldazzi G, Bertotti G, Ferrazzoli D, Boveri N, Bera R, Rovescala R, Gobbi L, Perini M, Comi C, Maestri R, and Pezzoli G. 2014. "Multidisciplinary intensive rehabilitation treatment and rotigotine in the early stages of Parkinson's disease: A randomized controlled study". Movement disorders 29:S239.	Conference abstracts
Ganesan M, Pal P K, Gupta A, and Sathyaprabha T N. 2014. "Treadmill gait training improves baroreflex sensitivity in Parkinson's disease". Clinical Autonomic Research 24(3):111-8.	No standard deviations reported
Ganesan M, Sathyaprabha T N, Gupta A, and Pal P K. 2014. "Effect of partial weight-supported treadmill gait training on balance in patients with Parkinson disease". PM & R : the journal of injury, function, and and rehabilitation 6(1):22-33.	Duplicate study

<b>Excluded studies - 1. What is the effectiveness of physiotherapy compared to usual care?</b>	
Goodwin V A, Pickering R, Ballinger C, Roberts H, McIntosh E, Lamb S, Nieuwboer A, Rochester L, Ashburn A, and Group Pdsafe Protocol Development. 2015. "A multi-centre, randomised controlled trial of the effectiveness of PDSAFE to prevent falls among people with Parkinson's: study protocol". BMC Neurology 15:81.	Study protocol
Hackney et al. 2008. "Tai Chi Improves Balance and Mobility in People with Parkinson Disease". Gait Posture 28(3):456-460.	Duplicate study
Harris D M, Rantalainen T, Muthalib M, Johnson L, and Teo W P. 2015. "Exergaming as a Viable Therapeutic Tool to Improve Static and Dynamic Balance among Older Adults and People with Idiopathic Parkinson's Disease: A Systematic Review and Meta-Analysis". Frontiers in aging neuroscience 7:167.	Not PD
Hass et al. 2012. "Progressive resistance training improves gait initiation in individuals with Parkinson's disease". Progressive resistance training improves gait initiation in individuals with 35:669-673.	No relevant outcomes
Hirsch et al. 2003. "The Effects of Balance Training and High-Intensity Resistance Training on Persons With Idiopathic Parkinson's Disease". Arch Phys Med Rehabil 84:1109-17.	Active control
Iris Bräuninger, PhD , and BT D . 2012. "The efficacy of dance movement therapy group on improvement of quality of life: A randomized controlled trial". The Arts in Psychotherapy 39:296-303.	No relevant outcomes
Jaywant A, Ellis T D, Roy S, Lin C C, Nearing S, and Cronin-Golomb A. 2016. "Randomized Controlled Trial of a Home-Based Action Observation Intervention to Improve Walking in Parkinson Disease". Archives of Physical Medicine & Rehabilitation 97(5):665-73.	No relevant intervention
Klamroth S, Steib S, Devan S, and Pfeifer K. 2016. "Effects of Exercise Therapy on Postural Instability in Parkinson Disease: A Meta-analysis". Journal of Neurologic Physical Therapy 40(1):3-14.	No relevant outcomes
Lee G H. 2015. "Effects of virtual reality exercise program on balance and quality of life among patients with Parkinson's disease". Movement disorders 30:S98-s99.	Conference abstract
Li et al. 2012. "Tai Chi and Postural Stability in Patients with Parkinson's Disease". N Engl J Med 366:511-9.	Active control group
Liao Y, Yang Y R, and Wang R Y. 2014. "Vr-based training using wii fit improve obstacle crossing performance and dynamic balance in patients with parkinson disease". Neurology 82(10 suppl. 1):.	Abstract
Lotzke D, Ostermann T, and Bussing A. 2015.	Relevant references retrieved and reviewed

<b>Excluded studies - 1. What is the effectiveness of physiotherapy compared to usual care?</b>	
"Argentine tango in Parkinson disease--a systematic review and meta-analysis". BMC Neurology 15:226.	
Mandelbaum Rosalind, and Lo Albert C. 2014. "Examining dance as an intervention in Parkinson's disease: A systematic review". American Journal of Dance Therapy 36(2):160-175.	Relevant references retrieved and reviewed
Mateos-Toset S, Cabrera-Martos I, Torres-Sanchez I, Ortiz-Rubio A, Gonzalez-Jimenez E, and Valenza M C. 2016. "Effects of a Single Hand-Exercise Session on Manual Dexterity and Strength in Persons with Parkinson Disease: A Randomized Controlled Trial". Pm & R 8(2):115-22.	No relevant outcomes
Mehrholz J, Kugler J, Storch A, Pohl M, Hirsch K, and Elsner B. 2016. "Treadmill training for patients with Parkinson's disease. An abridged version of a Cochrane Review". Eur J Phys Rehabil Med :.	Relevant references retrieved and reviewed
Mehrholz Jan, Kugler Joachim, Storch Alexander, Pohl Marcus, Hirsch Kathleen, and Elsner Bernhard. 2015. "Treadmill training for patients with Parkinson's disease". Cochrane Database of Systematic Reviews (9):.	Relevant references retrieved and reviewed
Melo Santiago, L M, Antunes D O, Macedo Ferreira, L G L, Brito Pinto, H Y, Spaniol A P, Trigueiro L C. L, and Lindquist R R. 2014. "Effects of mental practice and physical activity on gait of individuals with parkinson's disease: Randomized clinical trial". Archives of physical medicine and rehabilitation 95(10):e36.	Conference abstract
Monteiro E P, Franzoni L T, Cubillos D M, de Oliveira Fagundes, A , Carvalho A R, Oliveira H B, Pantoja P D, Schuch F B, Rieder C R, Martinez F G, and Peyre-Tartaruga L A. 2016. "Effects of Nordic walking training on functional parameters in Parkinson's disease: a randomized controlled clinical trial". Scand J Med Sci Sports :.	Active control group
Monticone M, Ambrosini E, Laurini A, Rocca B, and Foti C. 2015. "In-patient multidisciplinary rehabilitation for Parkinson's disease: A randomized controlled trial". Movement Disorders 30(8):1050-8.	Active control group
Morberg et al. 2014. "Tai Chi and Postural Stability in Patients on motor and non-motor symptoms in patients with Parkinson's disease (PIP): A preliminary study". Neurohabilitation :.	No standard deviations reported
Morris M E, Menz H B, McGinley J L, Watts J J, Huxham F E, Murphy A T, Danoudis M E, and Iansek R. 2015. "A Randomized Controlled Trial to Reduce Falls in People With Parkinson's Disease". Neurorehabilitation & Neural Repair 29(8):777-85.	Active control group
Nadeau A, Pourcher E, and Corbeil P. 2014. "Effects of 24 wk of treadmill training on gait	Active control group



<b>Excluded studies - 1. What is the effectiveness of physiotherapy compared to usual care?</b>	
performance in Parkinson's disease". <i>Medicine and science in sports and exercise</i> 46(4):645-55.	
Ni M, Mooney K, and Signorile J F. 2016. "Controlled pilot study of the effects of power yoga in Parkinson's disease". <i>Complementary Therapies in Medicine</i> 25:126-31.	Active control group
Ni X, Liu S, Lu F, Shi X, and Guo X. 2014. "Efficacy and safety of Tai Chi for Parkinson's disease: a systematic review and meta-analysis of randomized controlled trials". <i>PLoS ONE [Electronic Resource]</i> 9(6):e99377.	Relevant references retrieved and reviewed
Picelli A, Varalta V, Melotti C, Zatezalo V, Fonte C, Amato S, Saltuari L, Santamato A, Fiore P, and Smania N. 2016. "Effects of treadmill training on cognitive and motor features of patients with mild to moderate Parkinson's disease: a pilot, single-blind, randomized controlled trial". <i>Functional Neurology</i> 31(1):25-31.	Active control group
Piemonte M E. P, Mendes F A. S, Pikel M, Lopes A, and Maciel L. 2015. "Improvement of the gait stability after cognitive strategy patients with Parkinson's disease: A single-blind, randomised clinical trial". <i>Movement disorders</i> 30:S111-s112.	Conference abstracts
Pompeu et al. 2012. "Effect of Nintendo Wii™-based motor and cognitive training on activities of daily living in patients with Parkinson's disease: A randomised clinical trial". <i>Physiotherapy</i> 98:196-204.	Active control group
Rios Romenets, S , Anang J, Fereshtehnejad S M, Pelletier A, and Postuma R. 2015. "Tango for treatment of motor and non-motor manifestations in Parkinson's disease: a randomized control study". <i>Complementary Therapies in Medicine</i> 23(2):175-84.	Active control group
Roeder L, Costello J T, Smith S S, Stewart I B, and Kerr G K. 2015. "Effects of Resistance Training on Measures of Muscular Strength in People with Parkinson's Disease: A Systematic Review and Meta-Analysis". <i>PLoS ONE [Electronic Resource]</i> 10(7):e0132135.	Relevant references retrieved and reviewed
Saltychev M, Barlund E, Paltamaa J, Katajapuu N, and Laimi K. 2016. "Progressive resistance training in Parkinson's disease: a systematic review and meta-analysis". <i>BMJ Open</i> 6(1):e008756.	Relevant references retrieved and reviewed
Sang-Myung Cheon, Bo-Kyung Chae, Hye-Ryun Sung, Geon Cheol Lee, and Jae Woo Kima. 2013. "The Efficacy of Exercise Programs for Parkinson's Disease: Tai Chi versus Combined Exercise". <i>J Clin Neurol</i> 9:237-243.	Only reports results for significant outcomes
Schilling et al. 2010. "Effects of Moderate-Volume, High-Load Lower-Body Resistance Training on Strength and Function in Persons with Parkinson's Disease: A Pilot Study".	Secondary publication (Schilling 2008)

<b>Excluded studies - 1. What is the effectiveness of physiotherapy compared to usual care?</b>	
Parkinson's disease :	
Sharma N K, Robbins K, Wagner K, and Colgrove Y M. 2015. "A randomized controlled pilot study of the therapeutic effects of yoga in people with Parkinson's disease". <i>International Journal of Yoga</i> 8(1):74-9.	Active control group
Sharp K, and Hewitt J. 2014. "Dance as an intervention for people with Parkinson's disease: a systematic review and meta-analysis". <i>Neuroscience &amp; Biobehavioral Reviews</i> 47:445-56.	Relevant references retrieved and reviewed
Shen X, and Mak M K. 2014. "Balance and Gait Training With Augmented Feedback Improves Balance Confidence in People With Parkinson's Disease: A Randomized Controlled Trial". <i>Neurorehabil Neural Repair</i> 28(6):524-535.	Active control group
Shen X, Wong-Yu I S, and Mak M K. 2015. "Effects of Exercise on Falls, Balance, and Gait Ability in Parkinson's Disease: A Meta-analysis". <i>Neurorehabil Neural Repair</i> :	Relevant references retrieved and reviewed
Shu H F, Yang T, Yu S X, Huang H D, Jiang L L, Gu J W, and Kuang Y Q. 2014. "Aerobic exercise for Parkinson's disease: a systematic review and meta-analysis of randomized controlled trials". <i>PLoS ONE [Electronic Resource]</i> 9(7):e100503.	Relevant references retrieved and reviewed
Smania et al. 2010. "Effect of balance training on postural instability in patients with idiopathic Parkinson's disease". <i>Neurorehabilitation and Neural Repair</i> 24(9):826-834.	Active control group
Smulders K, King L, Mancini M, Peterson D S, Carlson-Kuhta P, Fleming M, Schlueter H, Fling B W, Nutt J G, and Horak F B. 2015. "Effects of exercise on mobility, cognition and locomotor circuit connectivity in Parkinsonism". <i>Movement disorders</i> 30:S124-s125.	Conference abstract
Sumec R, Filip P, Sheardova K, and Bares M. 2015. "Psychological Benefits of Nonpharmacological Methods Aimed for Improving Balance in Parkinson's Disease: A Systematic Review". <i>Behavioural Neurology</i> 2015:620674.	Qualitative SR
Tambosco L, Percebois-Macadre L, Rapin A, Nicomette-Bardel J, and Boyer F C. 2014. "Effort training in Parkinson's disease: a systematic review". <i>Annals of Physical &amp; Rehabilitation Medicine</i> 57(2):79-104.	Active control group
Teixeira-Machado L, Araujo F, Cunha F, Menezes M, Menezes T, and DeSantana J. 2015. "Feldenkrais method-based exercise improves quality of life in individuals with Parkinson's disease: A controlled, randomized clinical trial". <i>Journal of pain</i> 16(4 suppl. 1):S113.	No standard deviations reported
Tillman A, Muthalib M, Hendy A M, Johnson L G, Rantalainen T, Kidgell D J, Enticott P G, and Teo W P. 2015. "Lower limb progressive	Relevant references retrieved and reviewed

<b>Excluded studies - 1. What is the effectiveness of physiotherapy compared to usual care?</b>	
resistance training improves leg strength but not gait speed or balance in Parkinson's disease: a systematic review and meta-analysis". <i>Frontiers in aging neuroscience</i> 7:40.	
Tomlinson Claire, L , Herd Clare, P , Clarke Carl, E , Meek Charmaine, Patel Smitaa, Stowe Rebecca, Deane Katherine, H O, Shah Laila, Sackley Catherine, M , Wheatley Keith, and Ives Natalie. 2014. "Physiotherapy for Parkinson's disease: a comparison of techniques". <i>Cochrane Database of Systematic Reviews</i> (6):.	Active control group
Tramontano M, Bonni S, Martino Cinnera, A , Marchetti F, Caltagirone C, Koch G, and Peppe A. 2016. "Blindfolded Balance Training in Patients with Parkinson's Disease: A Sensory-Motor Strategy to Improve the Gait". <i>Parkinson's disease</i> 2016(no pagination):.	Active control group
Trigueiro L C, Gama G L, Simao C R, Sousa A V, Godeiro Junior Cde, O , and Lindquist A R. 2015. "Effects of Treadmill Training with Load on Gait in Parkinson Disease: A Randomized Controlled Clinical Trial". <i>American Journal of Physical Medicine &amp; Rehabilitation</i> 94(10 Suppl 1):830-7.	Active control group
Uhrbrand A, Stenager E, Pedersen M S, and Dalgas U. 2015. "Parkinson's disease and intensive exercise therapy--a systematic review and meta-analysis of randomized controlled trials". <i>Journal of the Neurological Sciences</i> 353(1-2):9-19.	Relevant references retrieved and reviewed
Villegas I L, and Israel V. 2014. "Effect of the ai-chi method on functional activity, quality of life, and posture in patients with parkinson disease". <i>Topics in geriatric rehabilitation</i> 30(4):282-9.	Non-randomised
Wang X Q, Pi Y L, Chen B L, Wang R, Li X, and Chen P J. 2016. "Cognitive motor intervention for gait and balance in Parkinson's disease: systematic review and meta-analysis". <i>Clinical Rehabilitation</i> 30(2):134-44.	Relevant references retrieved and reviewed
Wong-Yu I S. K, and Mak M K. Y. 2014. "Long-term effects of the hopeful outdoor Parkinson's exercise (HOPE) program on enhancing the dynamic balance and gait performance in people with Parkinson's disease". <i>Movement disorders</i> 29:S274-s275.	Conference abstract
Wong-Yu I S, and Mak M K. 2015. "Task- and Context-Specific Balance Training Program Enhances Dynamic Balance and Functional Performance in Parkinsonian Nonfallers: A Randomized Controlled Trial With Six-Month Follow-Up". <i>Archives of Physical Medicine &amp; Rehabilitation</i> 96(12):2103-11.	Active control group
Yang W C, Wang H K, Wu R M, Lo C S, and Lin K H. 2015. "Home-based virtual reality balance training and conventional balance training in Parkinson's disease: A randomized controlled trial". <i>J Formos Med Assoc</i> .:	Active control group

<b>Excluded studies - 1. What is the effectiveness of physiotherapy compared to usual care?</b>	
Yang Y, Hao Y, Tian W, Gong L, Zhang K, Shi Q, Sun D, Li C, and Zhao Z. 2015. "The effectiveness of Tai Chi for patients with Parkinson's disease: Study protocol for a randomized controlled trial". <i>Trials</i> . 16 (1) (no pagination), and 2015 Article Number:111. Date of Publication: March 24.	Study protocol
Yang Y, Li X Y, Gong L, Zhu Y L, and Hao Y L. 2014. "Tai Chi for improvement of motor function, balance and gait in Parkinson's disease: a systematic review and meta-analysis". <i>PLoS ONE [Electronic Resource]</i> 9(7):e102942.	Relevant references retrieved and reviewed
Yang Y, Qiu W Q, Hao Y L, Lv Z Y, Jiao S J, and Teng J F. 2015. "The efficacy of traditional Chinese Medical Exercise for Parkinson's disease: a systematic review and meta-analysis". <i>PLoS ONE [Electronic Resource]</i> 10(4):e0122469.	Relevant references retrieved and reviewed

## G.5.2 Occupational therapy

<b>Excluded studies - 11. RQ7: What is the effectiveness of occupational therapy compared with usual care in the treatment of symptoms of Parkinson's disease</b>	
Study	Reason for Exclusion
Advocat,J., Russell,G., Enticott,J., Hased,C., Hester,J., Vandenberg,B., 20131011, The effects of a mindfulness-based lifestyle programme for adults with Parkinson's disease: protocol for a mixed methods, randomised two-group control study, <i>BMJ Open</i> , 3, e003326-, 2013	Intervention not an OT intervention; feasibility study only not primary RCT
Ayan,C., Cancela,J., Feasibility of 2 different water-based exercise training programs in patients with parkinson's disease: A pilot study, <i>Archives of Physical Medicine and Rehabilitation</i> .93 (10) (pp 1709-1714), 2012.Date of Publication: October 2012., 1709-1714, 2012	Feasibility study only. Not an RCT design
Belton,A., Walsh,R., Murphy,S., McCabe,D., Galvin,R., The effect of a balance exercise class on activity limitations in people with parkinson's disease, <i>Irish journal of medical science</i> , 183, S326-, 2014	Conference abstract only
Clarke,C.E., Furnston,A., Morgan,E., Patel,S., Sackley,C., Walker,M., Bryan,S., Wheatley,K., 20090902, Pilot randomised controlled trial of occupational therapy to optimise independence in Parkinson's disease: the PD OT trial, <i>Journal of Neurology, Neurosurgery &amp; Psychiatry</i> , 80, 976-978, 2009	Pilot study only. Full dataset yet to be published
Clarke,C.E., Patel,S., Woolley,R., Ives,N.J., Rick,C.E., Dowling,F., Wheatley,K., Walker,M.F., Sackley,C.M., PD REHAB: A large pragmatic randomised controlled trial of physiotherapy and occupational therapy versus no therapy in mild to moderate Parkinson's	Abstract only - full data and methodological details to come

<b>Excluded studies - 11. RQ7: What is the effectiveness of occupational therapy compared with usual care in the treatment of symptoms of Parkinson's disease</b>	
disease, Movement Disorders, 29, S231-S232, 2014	
Deane KHO, Ellis-Hill C, Playford ED, Ben Shlomo Y, Clarke CE. Occupational therapy for Parkinson's disease.(Cochrane Review). The Cochrane Library 2003.	No statistical data for confidence intervals was provided within the studies, rendering it impossible to derive meaningful conclusions from the results. Studies included within this review contained both physiotherapy and occupational therapy elements, and were therefore not explicitly designed to examine occupational therapy compared to no intervention.
Dixon,L., Duncan,D., Johnson,P., Kirkby,L., O'Connell,H., Taylor,H., Deane,K.H., 20071018, Occupational therapy for patients with Parkinson's disease. [Review] [77 refs][Update of Cochrane Database Syst Rev. 2001;(3):CD002813; PMID: 11687028], Cochrane Database of Systematic Reviews, CD002813-, 2007	Author update only of 2003 Deane et al., Cochrane review. No new data presented.
Foster,E.R., Bedekar,M., Tickle-Degnen,L., 20140915, Systematic review of the effectiveness of occupational therapy-related interventions for people with Parkinson's disease. [Review], American Journal of Occupational Therapy, 68, 39-49, 2014	Criteria for inclusion in systematic review did not meet current inclusion and inclusion criteria.
Meshack,R.P., Norman,K.E., A randomized controlled trial of the effects of weights on amplitude and frequency of postural hand tremor in people with Parkinson's disease, Clinical rehabilitation, 16, 481-492, 2002	Study does not examine outcomes of interest as specified in review protocol
Morris,M.E., Iansek,R., Kirkwood,B., 20090604, A randomized controlled trial of movement strategies compared with exercise for people with Parkinson's disease, Movement Disorders, 24, 64-71, 2009	Study does not match study design as specified in review protocol: not compared to usual care.
Prodoehl,J., Rafferty,M.R., David,F.J., Poon,C., Vaillancourt,D.E., Comella,C.L., Leurgans,S.E., Kohrt,W.M., Corcos,D.M., Robichaud,J.A., Two-year exercise program improves physical function in Parkinson's disease: The PRET-PD randomized clinical trial, Neurorehabilitation and neural repair, 29, 112-122, 2015	Study intervention is physiotherapy not occupational therapy
Rose,M.H., Lokkegaard,A., Sonne-Holm,S., Jensen,B.R., 20130516, Improved clinical status, quality of life, and walking capacity in Parkinson's disease after body weight-supported high-intensity locomotor training, Archives of Physical Medicine & Rehabilitation, 94, 687-692, 2013	Study design is not an RCT
Schenkman,M., Hall,D.A., Baron,A.E., Schwartz,R.S., Mettler,P., Kohrt,W.M., 20130109, Exercise for people in early- or mid-stage Parkinson disease: a 16-month randomized controlled trial, Physical Therapy, 92, 1395-1410, 2012	Intervention is not OT; physiotherapy intervention
Shaw,J.A., Huffman,J.L., Frank,J.S., Jog,M.S.,	Study design is not an RCT



<b>Excluded studies - 11. RQ7: What is the effectiveness of occupational therapy compared with usual care in the treatment of symptoms of Parkinson's disease</b>	
Adkin,A.L., 20110428, The effects of skill focused instructions on walking performance depend on movement constraints in Parkinson's disease, <i>Gait &amp; Posture</i> , 33, 119-123, 2011	
Shen,X., Mak,M.K., 20130415, Repetitive step training with preparatory signals improves stability limits in patients with Parkinson's disease, <i>Journal of Rehabilitation Medicine</i> , 44, 944-949, 2012	Study does not report on outcomes of interest specified in review protocol
Shen,X., Mak,M.K.Y., Balance and gait training with augmented feedback improves balance confidence in people with parkinson's disease: A randomized controlled trial, <i>Neurorehabilitation and Neural Repair</i> .28 (6) (pp 524-535), 2014.Date of Publication: July-August 2014., 524-535, 2014	Intervention not OT; physiotherapy intervention
Sturkenboom,I., Graff,M., Veenhuizen,Y., Hendriks,J., Bloem,B., Nijhuis,Van Der-Sanden, Munneke,M., The effectiveness of occupational therapy in Parkinson's disease, <i>Journal of Parkinson's Disease</i> , 3, 157-, 2013	Primary data presented in included study Sturkenboom et al., 2014
Foster Erin R, Bedekar Mayuri, and Tickle-Degnen Linda. 2014. "Systematic review of the effectiveness of occupational therapy-related interventions for people with Parkinson's disease". <i>American Journal of Occupational Therapy</i> 68(1):39-49.	Qualitative review
Leung I H, Walton C C, Hallock H, Lewis S J, Valenzuela M, and Lampit A. 2015. "Cognitive training in Parkinson disease: A systematic review and meta-analysis". <i>Neurology</i> 85(21):1843-51.	Cognitive therapy vs. both active and non-active treatments
Monticone M, Ambrosini E, Laurini A, Rocca B, and Foti C. 2015. "In-patient multidisciplinary rehabilitation for Parkinson's disease: A randomized controlled trial". <i>Movement Disorders</i> 30(8):1050-8.	Active control group

### G.5.3 Speech and language therapy

<b>Excluded studies - 3. RQ14: What is the effectiveness of speech and language therapy (SLT) compared with usual care?</b>	
Study	Reason for Exclusion
Baijens,L.W., Speyer,R., 20090605, Effects of therapy for dysphagia in Parkinson's disease: systematic review. [Review] [31 refs], <i>Dysphagia</i> , 24, 91-102, 2009	Systematic review: criteria for review inclusion does not match current protocol inclusion and exclusion criteria for studies
Ciucci,M.R., Grant,L.M., Rajamanickam,E.S., Hilby,B.L., Blue,K.V., Jones,C.A., Kelm-Nelson,C.A., 20140703, Early identification and treatment of communication and swallowing deficits in Parkinson disease. [Review], <i>Seminars in Speech &amp; Language</i> , 34, 185-202, 2013	Narrative review, no primary data
Constantinescu,G., Theodoros,D., Russell,T., Ward,E., Wilson,S., Wootton,R., Treating	Study compares two different methods of administration of Lee Silverman technique

<b>Excluded studies - 3. RQ14: What is the effectiveness of speech and language therapy (SLT) compared with usual care?</b>	
disordered speech and voice in Parkinson's disease online: a randomized controlled non-inferiority trial, International journal of language & communication disorders / Royal College of Speech & Language Therapists, 46, 1-16, 2011	(LST), no comparison of LST to usual care, as specified in review protocol
Dowling,F., Clarke,C.E., Patel,S., Woolley,R., Ives,N.J., Rick,C.E., PD COMM pilot: A pilot randomised controlled trial of Lee Silverman voice treatment versus standard NHS speech and language therapy versus control in Parkinson's disease, Movement disorders, 29, S234-S235, 2014	Conference abstract - no primary data
Herd,C.P., Tomlinson,C.L., Deane,K.H., Brady,M.C., Smith,C.H., Sackley,C.M., Clarke,C.E., 20120926, Comparison of speech and language therapy techniques for speech problems in Parkinson's disease. [Review][Update of Cochrane Database Syst Rev. 2001;(2):CD002814; PMID: 11406045], Cochrane Database of Systematic Reviews, 8, CD002814-, 2012	Review provides a comparison of techniques, does not examine effectiveness of techniques compared to usual care, as stipulated in review protocol
Logemann,J.A., Gensler,G., Robbins,J., Lindblad,A.S., Brandt,D., Hind,J.A., Kosek,S., Dikeman,K., Kazandjian,M., Gramigna,G.D., Lundy,D., McGarvey-Toler,S., Miller Gardner,P.J., A randomized study of three interventions for aspiration of thin liquids in patients with dementia or Parkinson's disease, Journal of speech, language, and hearing research : JSLHR, 51, 173-183, 2008	Study population not exclusively PD: participants had dementia and/or PD
Redecker,B., Neuhauser,S., Simpson,A.P., Redecker,C., Speech and voice treatment with literary texts in advanced Parkinson's disease patients: Assessment of intelligibility and acoustic changes, Movement disorders, 29, S169-S170, 2014	Conference abstract - no primary data
Sackley,C.M., Smith,C.H., Rick,C., Brady,M.C., Ives,N., Patel,R., Lee Silverman voice treatment versus standard NHS speech and language therapy versus control in Parkinson's disease (PD COMM pilot): study protocol for a randomized controlled trial, Trials, 15, -, 2014	Narrative of research design and prospective goals of PDCOMM study
Sapir,S., Spielman,J.L., Ramig,L.O., Story,B.H., Fox,C., 20070912, Effects of intensive voice treatment (the Lee Silverman Voice Treatment [LSVT]) on vowel articulation in dysarthric individuals with idiopathic Parkinson disease: acoustic and perceptual findings.[Erratum appears in J Speech Lang Hear Res. 2007 Dec;50(6):1652], Journal of Speech Language & Hearing Research, 50, 899-912, 2007	Study design: case-control study, not RCT
Atkinson-Clement C, Sadat J, and Pinto S. 2015. "Behavioral treatments for speech in Parkinson's disease: meta-analyses and review of the literature". Neurodegenerative Disease Management 5(3):233-48.	Study design

<b>Excluded studies - 3. RQ14: What is the effectiveness of speech and language therapy (SLT) compared with usual care?</b>	
Mahler L A, Ramig L O, and Fox C. 2015. "Evidence-based treatment of voice and speech disorders in Parkinson disease". <i>Current Opinion in Otolaryngology &amp; Head &amp; Neck Surgery</i> 23(3):209-15.	Narrative review
Ramig L A, Fox C M, Halpern A E, Spielman J L, and Freeman K. 2014. "Randomized clinical trial (RCT) of speech and voice treatment for Parkinson's disease". <i>Movement disorders</i> 29:S260.	Abstract only
Ramig L A, Levy E S, Fox C M, Halpern A, Spielman J, Moya-Gale G, and Goudarzi A. 2015. "Impact of LSVT LOUD and LSVT ARTIC on speech intelligibility in Parkinson's disease". <i>Movement disorders</i> 30:S112-s113.	Abstract only
Stegemoller E L, Radig H, Hibbing P, Wingate J, and Sapienza C. 2016. "Effects of singing on voice, respiratory control and quality of life in persons with Parkinson's disease". <i>Disabil Rehabil</i> :1-7.	2 active groups
van Hooren , M R, Baijens L W, Voskuilen S, Oosterloo M, and Kremer B. 2014. "Treatment effects for dysphagia in Parkinson's disease: a systematic review". <i>Parkinsonism &amp; Related Disorders</i> 20(8):800-7.	Qualitative review

#### G.5.4 Nutrition

<b>Excluded studies - RQ3: What is the effectiveness of nutritional support compared with usual care?</b>	
Study	Reason for Exclusion
Andersson,I., Granerus,A.K., Jagenburg,R., Svanborg,A., 19760226, Intestinal decarboxylation of orally administered L-dopa. Influence of pharmacological preparations, dose magnitude, dose sequence and food intake, <i>Acta Medica Scandinavica</i> , 198, 415-420, 1975	Parkinsonian patients of different conditions, not confirmed Parkinson's disease, non-separable
Ates,K., 20081028, Salt and water in PD: the Turkish contribution, <i>Peritoneal Dialysis International</i> , 28, 224-228, 2008	Narrative Review
Balk,E., Chung,M., Raman,G., Tatsioni,A., Chew,P., Ip,S., DeVine,D., Lau,J., 20071012, B vitamins and berries and age-related neurodegenerative disorders. [Review] [197 refs], <i>Evidence Report/Technology Assessment</i> , 1-161, 2006	Review: non-systematic
Barichella,M., Cereda,E., Pezzoli,G., 20100111, Major nutritional issues in the management of Parkinson's disease. [Review] [110 refs], <i>Movement Disorders</i> , 24, 1881-1892, 2009	Narrative review
Bega,D., Zadikoff,C., 20141031, Complementary & alternative management of Parkinson's disease: an evidence-based review of eastern influenced practices. [Review], <i>Journal of Movement Disorders</i> , 7, 57-66, 2014	Review, non-systematic
Bender,A., Samtleben,W., Elstner,M.,	Secondary study based on primary trial.

<b>Excluded studies - RQ3: What is the effectiveness of nutritional support compared with usual care?</b>	
Klopstock,T., 20090306, Long-term creatine supplementation is safe in aged patients with Parkinson disease, Nutrition Research, 28, 172-178, 2008	Examined for useful data further to the primary publication.
Boldyrev,A., Fedorova,T., Stepanova,M., Dobrotvorskaya,I., Kozlova,E., Boldanova,N., Bagyeva,G., Ivanova-Smolenskaya,I., Illarioshkin,S., 20081118, Carnosine [corrected] increases efficiency of DOPA therapy of Parkinson's disease: a pilot study.[Erratum appears in Rejuvenation Res. 2008 Oct;11(5):988], Rejuvenation Research, 11, 821-827, 2008	Non-randomised
Carter,J.H., Nutt,J.G., Woodward,W.R., Hatcher,L.F., Trotman,T.L., 19890510, Amount and distribution of dietary protein affects clinical response to levodopa in Parkinson's disease, Neurology, 39, 552-556, 1989	Data only reported in means with no indication of variance
Casetta,I., Govoni,V., Granieri,E., Oxidative stress, antioxidants and neurodegenerative diseases, Current Pharmaceutical Design.11 (16) (pp 2033-2052), 2005.Date of Publication: 2005., 2033-2052, 2005	Narrative review
Cereda,E., Barichella,M., Pedrolli,C., Pezzoli,G., 20110126, Low-protein and protein-redistribution diets for Parkinson's disease patients with motor fluctuations: a systematic review. [Review], Movement Disorders, 25, 2021-2034, 2010	Review 1 database searched
DiFrancisco-Donoghue,J., Lamberg,E.M., Rabin,E., Elokda,A., Fazzini,E., Werner,W.G., 20120829, Effects of exercise and B vitamins on homocysteine and glutathione in Parkinson's disease: a randomized trial, Neurodegenerative Diseases, 10, 127-134, 2012	No outcomes of interest
Evatt,M.L., 20110714, Nutritional therapies in Parkinson's disease, Current Treatment Options in Neurology, 9, 198-204, 2007	Narrative review
Ferraz,H.B., Quagliato,E.A.B., Rieder,C.R.M., Silva,D.J., Teive,H.A.G., Barbosa,E.R., Cardoso,F., Limongi,J.C.P., Bezerra,J.M.F., Andrade,L.A.F., Allam,N., Prado,R.C.P., Tumas,V., Coimbra,C.G., "High doses of riboflavin and the elimination of dietary red meat promote the recovery of some motor functions in Parkinson's disease patients. C.G. Coimbra and V.B.C. Junqueira. Brazilian Journal of Medical and Biological Research, 36: 1409-1417, 2003", Brazilian Journal of Medical and Biological Research.37 (9) (pp 1297-1299), 2004.Date of Publication: September 2004., 1297-1299, 2004	Inappropriate control group (people with dementia)
Gillespie,N.G., Mena,I., Cotzias,G.C., Bell,M.A., 19730619, Diets affecting treatment of parkinsonism with levodopa, Journal of the American Dietetic Association, 62, 525-528, 1973	Non-randomised study
Hubbard,R., Dietary soy protein reduces 3-	Abstract only

<b>Excluded studies - RQ3: What is the effectiveness of nutritional support compared with usual care?</b>	
methyl dopa in patients with Parkinson disease, American Journal of Clinical Nutrition, 70, 630S-, 1999	
Khan,M.S., Tabrez,S., Priyadarshini,M., Priyamvada,S., Khan,M.M., 20121203, Targeting Parkinson's - tyrosine hydroxylase and oxidative stress as points of interventions. [Review], CNS & Neurological Disorders Drug Targets, 11, 369-380, 2012	Review, non-systematic
Kones,R., 20110217, Parkinson's disease: mitochondrial molecular pathology, inflammation, statins, and therapeutic neuroprotective nutrition. [Review], Nutrition in Clinical Practice, 25, 371-389, 2010	Narrative review
Liu,J., Wang,L., Zhan,S., Tan,J., Xia,Y., Coenzyme Q10 for Parkinson's disease, Cochrane Database of Systematic Reviews, -, 2009	Study protocol
Liu,J., Wang,L.N., Zhan,S.Y., Xia,Y., 20120801, WITHDRAWN: Coenzyme Q10 for Parkinson's disease. [Review][Update of Cochrane Database Syst Rev. 2011;(12):CD008150; PMID: 22161420], Cochrane Database of Systematic Reviews, 5, CD008150-, 2012	Study withdrawn due to methodological shortcomings
Muller,T., Jugel,C., Muhlack,S., Klostermann,F., 20131213, Methyl group-donating vitamins elevate 3-O-methyl dopa in patients with Parkinson disease, Clinical Neuropharmacology, 36, 52-54, 2013	Cohort study
Peterson,A.L., A review of vitamin D and Parkinson's disease, Maturitas, 78, 40-44, 2014	Review paper, only one database searched
Pham,D.Q., Plakogiannis,R., 20060315, Vitamin E supplementation in Alzheimer's disease, Parkinson's disease, tardive dyskinesia, and cataract: Part 2. [Review] [73 refs], Annals of Pharmacotherapy, 39, 2065-2072, 2005	Review, non-systematic
Postuma,R.B., Espay,A.J., Zadikoff,C., Suchowersky,O., Martin,W.R., Lafontaine,A.L., Ranawaya,R., Camicioli,R., Lang,A.E., 20060719, Vitamins and entacapone in levodopa-induced hyperhomocysteinemia: a randomized controlled study, Neurology, 66, 1941-1943, 2006	No outcomes of interest reported. A study of the protective effect of vitamins on levodopa induced hyperhomocysteinemia
Saint-Hilaire,M., Carbohydrate-protein ratio of 7:1 optimizes effects of levodopa, American Family Physician.50 (1) (pp 166), 1994.Date of Publication: 1994., 166-, 1994	Abstract only
Seidl,S.E., Santiago,J.A., Bilyk,H., Potashkin,J.A., The emerging role of nutrition in Parkinson's disease, Frontiers in Aging Neuroscience.6 (MAR) , 2014.Article Number: Article 36.Date of Publication: 2014., -, 2014	Narrative review
Shen,L., Ji,H.-F., Vitamin E: Supplement versus diet in neurodegenerative diseases, Trends in Molecular Medicine.18 (8) (pp 443-445), 2012.Date of Publication: August 2012., 443-	Narrative review



<b>Excluded studies - RQ3: What is the effectiveness of nutritional support compared with usual care?</b>	
445, 2012	
Spindler,M., Beal,M.F., Henschcliffe,C., 20110426, Coenzyme Q10 effects in neurodegenerative disease, Neuropsychiatric Disease & Treatment, 5, 597-610, 2009	Narrative review
Thalamos,C., Rayet,S., Brefel,C., Eagle,S., Lopez-Gil,A., Fitzpatrick,K., Beerah,A., Montastruc,J.L., Rascol,O., Effects of food on the pharmacokinetics of ropinirole in parkinsonian patients, Fundamental & Clinical Pharmacology, 10, 94-, 1996	Duplicate reference
Tsao,W.-L., Chan,H.-Y., Lee,J.-T., Hsu,C.-H., Lin,C.-C., Nimit,Y., Peng,G.-S., Clinical efficacy of nutritional food supplement in non-motor symptoms of Parkinson's disease, Journal of Medical Sciences.31 (6) (pp 257-262), 2011.Date of Publication: 2011., 257-262, 2011	Case series
Weber,C.A., Ernst,M.E., 20060731, Antioxidants, supplements, and Parkinson's disease. [Review] [18 refs], Annals of Pharmacotherapy, 40, 935-938, 2006	Review, non-systematic
Beal M F. 2014. "A randomized clinical trial of high-dosage coenzyme q10 in early parkinson disease no evidence of benefit". JAMA Neurology 71(5):543-552.	Included in Negida review (2016)
Michela B, Pacchetti C, Bolliri C, Cassani E, Iorio L, Pusani C, Privitera G, Cesari I, Faierman S A, Caccialanza R, Pezzoli G, and Cereda E. 2015. "Double blind, placebo-controlled trial of a fermented milk containing multiple probiotics strains and prebiotic fiber for constipation associated with parkinson's disease". Journal of the neurological sciences 357:e260.	Conference abstract
Peterson Hiller, A L, Lobb B M, Murchison C, and Quinn J F. 2015. "The effects of vitamin D supplementation on balance, motor, and neuropsychiatric function in Parkinson's disease (PD)". Movement disorders 30:S111.	Abstract available only
Seet R C, Lim E C, Tan J J, Quek A M, Chow A W, Chong W L, Ng M P, Ong C N, and Halliwell B. 2014. "Does high-dose coenzyme Q10 improve oxidative damage and clinical outcomes in Parkinson's disease?". Antioxidants & Redox Signaling 21(2):211-7.	No extractable outcomes
Simon D K, Wu C, Tilley B C, Wills A M, Aminoff M J, Bainbridge J, Hauser R A, Schneider J S, Sharma S, Singer C, Tanner C M, Truong D, and Wong P S. 2015. "Caffeine and Progression of Parkinson Disease: A Deleterious Interaction With Creatine". Clinical Neuropharmacology 38(5):163-9.	Not an intervention of interest
Virmani T, Tazan S, Mazzoni P, Ford B, and Greene P E. 2016. "Motor fluctuations due to interaction between dietary protein and levodopa in Parkinson's disease". J Clin Mov Disord 3:8.	Study design



## G.6 Deep brain stimulation and Duodopa

<b>Excluded studies - RQ15, RQ17 and RQ18: deep brain stimulation, levodopa–carbidopa intestinal gel and best medical treatment for advanced Parkinson's disease</b>	
Study	Reason for exclusion
Deep-brain stimulation significantly improves motor function in patients with PD, <i>Journal of Neurology</i> <i>J Neurol</i> , 248, 1113-1114, 2001	Comment
Antonini,A., Chatamra,K., Robieson,W., Pritchett,Y., Widnell,K., Benesh,J., Lenz,R., Randomized, double-blind, double-dummy study of levodopa-carbidopa intestinal gel in patients with advanced parkinson's disease: Efficacy analyses by subgroups, <i>Neurology</i> , 80, -, 2013	Conference abstract
Antonini,A., Chatamra,K., Robieson,W.Z., Pritchett,Y., Widnell,K.L., Benesh,J., Lenz,R.A., Randomized, double-blind, doubledummy study of levodopa-carbidopa intestinal gel in patients with advanced Parkinson's disease: Efficacy analyses by subgroups, <i>European Journal of Neurology</i> <i>Eur.J.Neurol.</i> , 19, 291- , 2012	Conference abstract only
Bakay,Roy A.E., Freeman,Alan, Evatt,Marian, Green,Joanne, McDonald,William, Haber,Michael, Barnhart,Huiman, Wahlay,Natalie, Triche,Shirley, Mewes,Klaus, Chockkan,Vijay, Zhang,Jian Yu, DeLong,Mahlon R., Randomized trial of pallidotomy versus medical therapy for Parkinson's disease, <i>Annals of Neurology</i> <i>Ann Neurol</i> , 53, 558-569, 2003	Pallidotomy – not a relevant intervention
Bie,R.M., Haan,R.J., Nijssen,P.C., Rutgers,A.W., Beute,G.N., Bosch,D.A., Haaxma,R., Schmand,B., Schuurman,P.R., Staal,M.J., Speelman,J.D., Unilateral pallidotomy in Parkinson's disease: a randomised, single-blind, multicentre trial, <i>Lancet</i> , 354, 1665-1669, 1999	Pallidotomy – not a relevant intervention
Charles,D., Tolleson,C., Davis,T.L., Gill,C.E., Molinari,A.L., Bliton,M.J., Tramontana,M.G., Salomon,R.M., Kao,C., Wang,L., Hedera,P., Phibbs,F.T., Neimat,J.S., Konrad,P.E., Pilot study assessing the feasibility of applying bilateral subthalamic nucleus deep brain stimulation in very early stage Parkinson's disease: study design and rationale, <i>Journal of Parkinson's disease</i> <i>J Parkinsons Dis</i> , 2, 215-223, 2012	Secondary publication for included study (Charles et al. 2014)
Charles,P.D., Dolhun,R.M., Gill,C.E., Davis,T.L., Bliton,M.J., Tramontana,M.G., Salomon,R.M., Wang,L., Hedera,P., Phibbs,F.T., Neimat,J.S., Konrad,P.E., Deep brain stimulation in early Parkinson's disease: Enrollment experience from a pilot trial, <i>Parkinsonism and Related Disorders</i> . 18 (3) (pp 268-273), 2012. Date of Publication: March 2012., 268-273, 2012	Secondary publication for included study (Charles et al. 2014)
de Bie,R.M., de Haan,R.J., Nijssen,P.C., Rutgers,A.W., Beute,G.N., Bosch,D.A., Haaxma,R., Schmand,B., Schuurman,P.R., Staal,M.J., Speelman,J.D., 1999 1130, Unilateral pallidotomy in Parkinson's disease: a randomised, single-blind, multicentre trial, <i>Lancet</i> , 354, 1665-1669, 1999	Study does not examine DBS - lesioning study
Deuschl,G., Schupbach,M., Knudsen,K., Pinsker,M.O., Cornu,P., Rau,J., Agid,Y., Schade-Brittinger,C., 2013 0807, Stimulation of the subthalamic nucleus at an earlier disease stage of Parkinson's disease: concept and standards of the EARLYSTIM-study, <i>Parkinsonism &amp; Related Disorders</i> <i>Parkinsonism Relat Disord</i> , 19, 56-61, 2013	Pilot feasibility study - no primary data
D'Haese,Pierre Francois, Dawant,Benoit, Allen,Laura, Kao,Chris, Charles,P.David, Konrad,Peter, Deep brain stimulation in early stage Parkinson's disease: operative experience from a prospective randomised clinical trial, <i>Journal of neurology</i> ,	Paper does not report on clinical efficacy, reports on operative experience only

<b>Excluded studies - RQ15, RQ17 and RQ18: deep brain stimulation, levodopa-carbidopa intestinal gel and best medical treatment for advanced Parkinson's disease</b>	
neurosurgery, and psychiatry <i>J Neurol Neurosurg Psychiatry</i> , 83, 164-170, 2012	
Dolhun,R.M., Gill,C.E., Davis,T.L., Bliton,M.J., Tramontana,M.G., Salomon,R.M., Wang,L., Hedera,P., Phibbs,F.T., Neimat,J.S., Konrad,P.E., Deep brain stimulation in early Parkinson's disease: enrollment experience from a pilot trial, <i>Parkinsonism &amp; Related Disorders</i> <i>Parkinsonism Relat Disord</i> , 18, 268-273, 2012	Secondary publication for included study (Charles et al. 2014)
Eggington,S., Valldeoriola,F., Chaudhuri,K.R., Ashkan,K., Annoni,E., Deuschl,G., 20140919, The cost-effectiveness of deep brain stimulation in combination with best medical therapy, versus best medical therapy alone, in advanced Parkinson's disease, <i>Journal of Neurology</i> , 261, 106-116, 2014	Cost-effectiveness study: no primary clinical effectiveness data
Fernandez,H.H., Vanagunas,A., Odin,P., Espay,A.J., Hauser,R.A., Standaert,D.G., Chatamra,K., Benesh,J., Pritchett,Y., Hass,S.L., Lenz,R.A., Levodopa-carbidopa intestinal gel in advanced Parkinson's disease open-label study: Interim results, <i>Parkinsonism &amp; Related Disorders</i> , 19, 339-345, 2013	Open label study, not an RCT
Follett,Kenneth A., Stern,Matthew, Luo,Ping, Harris,Crystal L., Hur,Kwan, Marks,William J.J., Rothlind,Johannes, Sagher,Oren, Moy,Claudia, Pahwa,Rajesh, Burchiel,Kim, Hogarth,Penelope, Lai,Eugene C., Duda,John E., Holloway,Kathryn, Samii,Ali, Horn,Stacy, Bronstein,Jeff M., Stoner,Gatana, Starr,Philip A., Simpson,Richard, Baltuch,Gordon, De Salles,Antonio, Huang,Grant D., Reda,Domenic J., Study Group, Randomized trial of deep brain stimulation for Parkinson disease: thirty-six-month outcomes, <i>Neurology</i> , 79, 55-65, 2012	Patients randomised to receive 2 different DBS targets, not comparing DBS to BSC
Follett,Kenneth, Weaver,Frances, Stern,Matthew, Marks,William, Hogarth,Penelope, Holloway,Katherine, Bronstein,Jeff, Duda,John, Horn,Stacy, Lai,Eugene, Samii,Ali, Multisite randomized trial of deep brain stimulation, <i>Archives of Neurology</i> <i>Arch Neurol</i> , 62, 1643-1645, 2005	Comment. No primary data
Gallo,B.V., Okun,M.S., Mandybur,G., Arle,J., Elias,J., Ford,B., Horn,S., Hung,S., Jankovic,J., Junn,F.S., Marshall,F., Stewart,R.M., Swope,D., Verhagen,L., Tagliati,M., Constant current DBS: A randomized controlled clinical trial in Parkinson's disease: 12 month results, <i>Movement Disorders</i> , 26, S128-, 2011	Study does not compare DBS vs best supported medial therapy- design is to compare
Gallo,Bruno V., Mandybur,George, Jagid,Jonathan, Foote,Kelly D., Revilla,Fredy J., Alterman,Ron, Jankovic,Joseph, Simpson,Richard, Junn,Fred, Verhagen,Leo, Arle,Jeff E., Ford,Blair, Goodman,Robert R., Stewart,R.Malcolm, Horn,Stacy, Baltuch,Gordon H., Kopell,Brian H., Marshall,Frederick, Peichel,Delea, Pahwa,Rajesh, Lyons,Kelly E., Troster,Alexander I., Vitek,Jerrold L., Tagliati,Michele, SJM DBS Study Group, Subthalamic deep brain stimulation with a constant-current device in Parkinson's disease: an open-label randomised controlled trial, <i>The Lancet</i> . <i>Neurology</i> <i>Lancet neurol.</i> , 11, 140-149, 2012	Study does not compare DBS vs best supported medial therapy- design is to compare immediate vs 3 month delay DBS
Granert,Oliver, Daniels,Christine, Volkmann,Jens, Falk,Daniela, van Eimeren,Thilo, Deuschl,Gunther, Relation of lead trajectory and electrode position to neuropsychological outcomes of subthalamic neurostimulation in Parkinson's disease: results from a randomized trial, <i>Brain : a journal of neurology</i> , 136, 2109-2119, 2013	Duplication - Witt et al., 2013
Kamusheva,M.S., Gerasimov,N., Petrova,G.I., Intestinal gel Levodopa + Carbidopa in Parkinson's patients with frequent and prolonged akinesia - an economic evaluation, <i>International Journal of Pharmaceutical Sciences Review and</i>	Not an RCT

<b>Excluded studies - RQ15, RQ17 and RQ18: deep brain stimulation, levodopa-carbidopa intestinal gel and best medical treatment for advanced Parkinson's disease</b>	
ResearchIntl.J.Pharm.Sci.Rev.Res., 22, 244-246, 2013	
Katzenschlager,R., Poewe,W., Intestinal levodopa infusion in PD - the first randomized trial, Nature Reviews Neurology, 10, 128-129, 2014	Study is not an RCT
Khoo,H.M., Kishima,H., Hosomi,K., Maruo,T., Tani,N., Oshino,S., Shimokawa,T., Yokoe,M., Mochizuki,H., Saitoh,Y., Yoshimine,T., Low-frequency subthalamic nucleus stimulation in Parkinson's disease: A randomized clinical trial, Movement Disorders.29 (2) (pp 270-274), 2014.Date of Publication: February 2014., 270-274, 2014	Not an RCT of DBS vs BSC
Kiebertz,K., Antonini,A., Olanow,C.W., Fernandez,H.H., Espay,A.J., Standaert,D.G., Hass,S., Widnell,K.L., Robieson,W.Z., Pritchett,Y., Chatamra,K., Benesh,J., Randomized, phase 3, double-blind, double-dummy study of levodopa-carbidopa intestinal gel in patients with advanced Parkinson's disease: Functional and quality-of-life outcomes, Movement Disorders, 27, S124-, 2012	Abstract only
Lew,M.F., Fung,V.S.C., Robieson,W.Z., Dubow,J., Chatamra,K., Benesh,J., Levodopa-carbidopa intestinal gel titration with and without a nasojejunal titration period in advanced Parkinson's disease patients, Movement DisordersMov.Disord., 29, S248-, 2014	Abstract only
Li,Weina, Tan,Changhong, Liu,Xi, Wang,Xin, Gui,Yuejiang, Qin,Lu, Deng,Fen, Hu,Changlin, Chen,Lifen, Meta-analysis comparing deep brain stimulation of the globus pallidus and subthalamic nucleus to treat advanced Parkinson disease, Journal of NeurosurgeryJ Neurosurg, 121, 709-718, 2014	Meta-analysis: inclusion criteria differed to current review criteria
Mehdorn,M.H., Cornu,P., Deep brain stimulation for parkinson disease - results of the earlystim study, Stereotactic and functional neurosurgeryStereotact Funct Neurosurg, 91, 65-, 2013	Results of earlystim reported in Deuschl et al and Schiepbach et al., 2013.
Nyholm,D., Nilsson Remahl,A.I., Dizdar,N., Constantinescu,R., Holmberg,B., Jansson,R., Aquilonius,S.M., Askmark,H., 20050920, Duodenal levodopa infusion monotherapy vs oral polypharmacy in advanced Parkinson disease, Neurology, 64, 216-223, 2005	Only duodopa used in tmt arm, no other meds permitted. Only nasoduodenal, so not abdominal. 3 week cross over trial per arm
Nyholm,D., 20130617, Duodopa treatment for advanced Parkinson's disease: a review of efficacy and safety. [Review], Parkinsonism & Related DisordersParkinsonism Relat Disord, 18, 916-929, 2012	Non-systematic review
Obeso,J.A., Lang,A.E., Houeto,J.L., Pollak,P., Rehnrona,S., Kulisevsky,J., Albanese,A., Volkmann,J., Hariz,M.I., Quinn,N.P., Speelman,J.D., Guridi,J., Zamarbide,I., Gironell,A., Molet,J., Pascual-Sedano,B., Pidoux,B., Bonnet,A.M., Agid,Y., Xie,J., Benabid,A.L., Lozano,A.M., Saint-Cyr,J., Romito,L., Contarino,M.F., Scerrati,M., Fraix,V., Van Blercom,N., Bilateral deep brain stimulation in Parkinson's disease: a multicentre study with 4 years follow-up, Brain : a journal of neurology, 128, 2240-2249, 2005	Not an RCT of DBS vs BMC
Odekerken,V.J., Hoogland,J., Geurtsen,G.J., Munckhof,P., Schuurman,P.R., Schmand,B.A., Bie,R.M., Neuropsychological and psychiatric outcome after bilateral deep brain stimulation of the globus pallidus and subthalamic nucleus for advanced Parkinson's disease: A randomized controlled trial, Movement DisordersMov.Disord., 29, S447-S448, 2014	Not an RCT comparing DBS vs BMC
Odekerken,V.J., Laar,T., Mosch,A., Vugt,J., Nijssen,P.C., Schmand,B.A., Schuurman,P.R., Bie,R.M., Randomized	Abstract only



<b>Excluded studies - RQ15, RQ17 and RQ18: deep brain stimulation, levodopa–carbidopa intestinal gel and best medical treatment for advanced Parkinson's disease</b>	
multicenter trial comparing bilateral subthalamic nucleus DBS and bilateral globus pallidus internus DBS for advanced Parkinson's disease (NSTAPS), <i>Movement Disorders</i> , 27, S165-, 2012	
Olanow,C.W., Antonini,A., Kieburtz,K., Fernandez,H.H., Espay,A.J., Standaert,D.G., Vanaganas,A., Widnell,K.L., Freeman,S., Robieson,W.Z., Pritchett,Y., Chatamra,K., Benesh,J., Lenz,R.A., Randomized, double-blind, double-dummy study of levodopa-carbidopa intestinal gel in patients with advanced Parkinson's disease: Efficacy and safety, <i>Annals of Neurology</i> Ann Neurol, 72, S102-, 2012	Abstract only
Ottridge,R.S., Rick,C.E., Daniels,J., Patel,S., Ives,N., Gill,S., Varma,T.R.K., Jenkinson,C., Mitchell,R., Quinn,N., Williams,A., Wheatley,K., Implantable pulse generator lifespan in the PD SURG trial, <i>Movement Disorders</i> , 27, S132-, 2012	Abstract only
Puig-Junoy,Jaume, Puig-Peiro,Ruth, Workgroup of the SCOPE study, Cost analysis of the treatments for patients with advanced Parkinson's disease: SCOPE study, <i>Journal of Medical Economics</i> J Med Econ, 16, 191-201, 2013	Cost analysis, no clinical effectiveness primary data
Rodriguez-Oroz,M.C., Obeso,J.A., Lang,A.E., Houeto,J.L., Pollak,P., Rehnrcrona,S., Kulisevsky,J., Albanese,A., Volkmann,J., Hariz,M.I., Quinn,N.P., Speelman,J.D., Guridi,J., Zamarbide,I., Gironell,A., Molet,J., Pascual-Sedano,B., Pidoux,B., Bonnet,A.M., Agid,Y., Xie,J., Benabid,A.L., Lozano,A.M., Saint-Cyr,J., Romito,L., Contarino,M.F., Scerrati,M., Fraix,V., Van,Blercom N., 20051229, Bilateral deep brain stimulation in Parkinson's disease: a multicentre study with 4 years follow-up, <i>Brain</i> , 128, 10-19, 2005	Study is not an RCT of surgery vs. BSC
Santos-Garcia,D., Sanjurjo,L.F., Macias,M., Llanaez,M., Carpintero,P., Fuente-Fernandez,R., 20121015, Long-term exposure to duodenal levodopa/carbidopa infusion therapy improves quality of life in relation especially to mobility, activities of daily living, and emotional well-being, <i>Acta Neurologica Scandinavica</i> , 125, 187-191, 2012	Study design: not an RCT
Schade-Brittinger,Carmen, Krack,Paul, Volkmann,Jens, Schafer,Helmut, Botzel,Kai, Daniels,Christine, Deutschlander,Angela, Dillmann,Ulrich, Eisner,Wilhelm, Gruber,Doreen, Hamel,Wolfgang, Herzog,Jan, Hilker,Rudiger, Klebe,Stephan, Kloss,Manja, Koy,Jan, Krause,Martin, Kupsch,Andreas, Lorenz,Delia, Lorenzl,Stefan, Mehdorn,H.Maximilian, Moringlane,Jean Richard, Oertel,Wolfgang, Pinsker,Marcus O., Reichmann,Heinz, Reuss,Alexander, Schneider,Gerd Helge, Schnitzler,Alfons, Steude,Ulrich, Sturm,Volker, Timmermann,Lars, Tronnier,Volker, Trottenberg,Thomas, Wojtecki,Lars, Wolf,Elisabeth, Poewe,Werner, Voges,Jurgen, German Parkinson Study Group,Neurostimulation Section, A randomized trial of deep-brain stimulation for Parkinson's disease, <i>The New England journal of medicine</i> N Engl J Med, 355, 896-908, 2006	Duplicate - Deuschl et al
Schuepbach,W.M., Rau,J., Knudsen,K., Volkmann,J., Krack,P., Timmermann,L., Halbig,T.D., Hesekamp,H., Navarro,S.M., Meier,N., Falk,D., Mehdorn,M., Paschen,S., Maarouf,M., Barbe,M.T., Fink,G.R., Kupsch,A., Gruber,D., Schneider,G.H., Seigneuret,E., Kistner,A., Chaynes,P., Ory-Magne,F., Brefel,Courbon C., Vesper,J., Schnitzler,A., Wojtecki,L., Houeto,J.L., Bataille,B., Maltete,D., Damier,P., Raoul,S., Sixel-Doering,F., Hellwig,D., Gharabaghi,A., Kruger,R., Pinsker,M.O., Amtage,F., Regis,J.M., Witjas,T., Thobois,S., Mertens,P., Kloss,M., Hartmann,A., Oertel,W.H., Post,B., Speelman,H.,	Duplication of Rau et al., paper

<b>Excluded studies - RQ15, RQ17 and RQ18: deep brain stimulation, levodopa–carbidopa intestinal gel and best medical treatment for advanced Parkinson's disease</b>	
Agid,Y., Schade-Brittinger,C., Deuschl,G., EARLYSTIM Study Group, 20130226, Neurostimulation for Parkinson's disease with early motor complications, New England Journal of Medicine, 368, 610-622, 2013	
Schupbach,Michael, Knudsen,Karina, Pinsker,Marcus O., Cornu,Philippe, Rau,Jorn, Agid,Yves, Schade-Brittinger,Carmen, Stimulation of the subthalamic nucleus at an earlier disease stage of Parkinson's disease: concept and standards of the EARLYSTIM-study, Parkinsonism & Related DisordersParkinsonism Relat Disord, 19, 56-61, 2013	Duplicate
Slevin,J.T., Fernandez,H.H., Zadikoff,C., Hall,C., Eaton,S., Dubow,J., Chatamra,K., Benesh,J., Long-term safety and maintenance of efficacy of levodopa-carbidopa intestinal gel: an open-label extension of the double-blind pivotal study in advanced Parkinson's disease patients, Journal of Parkinsons Disease Print, 5, 165-174, 2015	Open-label study from Olanow et al., 2014 publication
Stroupe,Kevin T., Cao,Lishan, Holloway,Robert G., Vickrey,Barbara G., Simuni,Tanya, Hendricks,Ann, Ippolito,Dolores, Parkinson's disease medication use and costs following deep brain stimulation, Movement disorders : official journal of the Movement Disorder SocietyMov Disord, 27, 1398-1403, 2012	Excluded from clinical review due to lack of clinical RCT data - considered for cost analysis
Tolleson,Christopher, Davis,Thomas L., Gill,Chandler E., Molinari,Anna L., Bliton,Mark J., Tramontana,Michael G., Salomon,Ronald M., Kao,Chris, Wang,Lily, Hedera,Peter, Phibbs,Fenna T., Neimat,Joseph S., Konrad,Peter E., Pilot study assessing the feasibility of applying bilateral subthalamic nucleus deep brain stimulation in very early stage Parkinson's disease: study design and rationale, Journal of Parkinson's diseaseJ Parkinsons Dis, 2, 215-223, 2012	Secondary publication for included study (Charles et al. 2014)
Tramontana,M.G., Molinari,A.L., Konrad,P.E., Davis,T.L., Wylie,S.A., Neimat,J.S., May,A.T., Phibbs,F.T., Hedera,P., Gill,C.E., Salomon,R.M., Wang,L., Song,Y., Charles,D., Neuropsychological effects of deep brain stimulation in subjects with early stage Parkinson's disease in a randomized clinical trial, Journal of Parkinson's Disease.5 (1) (pp 151-163), 2015.Date of Publication: 2015., 151-163, 2015	Follow-on from Charles et al., 2015 paper. Feasibility safety study only (limited to N=30)
Valldeoriola,Francesc, Chaudhuri,K.Ray, Ashkan,Keyoumars, Annoni,Elena, Deuschl,Gunther, The cost-effectiveness of deep brain stimulation in combination with best medical therapy, versus best medical therapy alone, in advanced Parkinson's disease, Journal of NeurologyJ Neurol, 261, 106-116, 2014	Cost-effectiveness assessment, to be examined by HE analysis
Vercruyse,S., Vandenberghe,W., Munks,L., Nuttin,B., Devos,H., Nieuwboer,A., 20140825, Effects of deep brain stimulation of the subthalamic nucleus on freezing of gait in Parkinson's disease: a prospective controlled study, Journal of Neurology, Neurosurgery & Psychiatry, 85, 871-877, 2014	Not an RCT: patients were free to choose between DBS and BMC
Vitek,J.L., Bakay,R.A., Freeman,A., Evatt,M., Green,J., McDonald,W., Haber,M., Barnhart,H., Wahlay,N., Triche,S., Mewes,K., Chockkan,V., Zhang,J.Y., DeLong,M.R., 20030604, Randomized trial of pallidotomy versus medical therapy for Parkinson's disease, Annals of Neurology, 53, 558-569, 2003	Pallidotomy – not a relevant intervention
Weaver,F.M., Follett,K., Stern,M., Hur,K., Harris,C., Marks,Jr, Rothlind,J., Sagher,O., Reda,D., Moy,C.S., Pahwa,R., Burchiel,K., Hogarth,P., Lai,E.C., Duda,J.E., Holloway,K., Samii,A., Horn,S., Bronstein,J., Stoner,G., Heemskerk,J., Huang,G.D., Bilateral deep	Duplicate reference

<b>Excluded studies - RQ15, RQ17 and RQ18: deep brain stimulation, levodopa–carbidopa intestinal gel and best medical treatment for advanced Parkinson's disease</b>	
brain stimulation vs best medical therapy for patients with advanced parkinson disease: A randomized controlled trial, JAMA - Journal of the American Medical Association.301 (1) (pp 63-73), 2009.Date of Publication: 07 Jan 2009., 63-73, 2009	
Weaver,F.M., Stroupe,K.T., Cao,L., Holloway,R.G., Vickrey,B.G., Simuni,T., Hendricks,A., Ippolito,D., 20130306, Parkinson's disease medication use and costs following deep brain stimulation, Movement DisordersMov.Disord., 27, 1398-1403, 2012	Not an RCT, cost data to be assessed for HE analysis
Zadikoff,C., Fernandez,H.H., Hall,C., Eaton,S., Dubow,J., Benesh,J., Safety of levodopa-carbidopa intestinal gel (LCIG) initiation in advanced Parkinson's patients who received immediate vs. delayed LCIG after gastrointestinal procedure, Movement DisordersMov.Disord., 29, S275-S276, 2014	Abstract only
Zhu,X.L., Chan,D.T., Lau,C.K., Poon,W.S., Mok,V.C., Chan,A.Y., Wong,L.K., Yeung,J.H., Leung,M.C., Tang,V.Y., Wong,R.K., Yeung,C., Cost-effectiveness of subthalamic nucleus deep brain stimulation for the treatment of advanced Parkinson disease in Hong Kong: a prospective study, World NeurosurgeryWorld Neurosurg, 82, 987-993, 2014	Cost-effectiveness data to be assessed for HE analysis

## **G.7 Managing and monitoring impulse control disorder as an adverse effect of dopaminergic treatment**

### **G.7.1 Predictors for the development of impulse control disorders**

A single search was conducted for all three questions on impulse control disorders. For the full list of excluded studies for all three questions, please see the section on information needs about impulse control disorders.

### **G.7.2 Managing dopaminergic treatment in people who have developed impulse control disorder**

A single search was conducted for all three questions on impulse control disorders. For the full list of excluded studies for all three questions, please see the section on information needs about impulse control disorders.

## G.8 Palliative Care

<b>Excluded studies - 9. RQ21: What are the needs of people with Parkinson's disease for advance directives and palliative care plans throughout the course of their disease?</b>	
Study	Reason for Exclusion
Chase,T.N., Engber,T.M., Mouradian,M.M., 19940826, Palliative and prophylactic benefits of continuously administered dopaminomimetics in Parkinson's disease. [Review] [24 refs], Neurology, 44, Suppl-8, 1994	Information review, no primary data
Ghoche,R., The conceptual framework of palliative care applied to advanced Parkinson's disease, Parkinsonism and Related Disorders.18 (SUPPL.3) (pp S2-S5), 2012.Date of Publication: December 2012., S2-S5, 2012	Information review, no primary data
Gonsalkorale,M., Palliative care in Parkinson's disease, CME Journal Geriatric Medicine.7 (1) (pp 22-28), 2005.Date of Publication: 2005., 22-28, 2005	Information review, no primary data
Habermann,B., Davis,L.L., 20051108, Caring for family with Alzheimer's disease and Parkinson's disease: needs, challenges and satisfaction, Journal of Gerontological Nursing, 31, 49-54, 2005	Study examines needs of AD and PD carers; population not solely PD.
Hatano,T., Kubo,S.-I., Shimo,Y., Nishioka,K., Hattori,N., Unmet needs of patients with Parkinson's disease: Interview survey of patients and caregivers, Journal of International Medical Research.37 (3) (pp 717-726), 2009.Date of Publication: 2009., 717-726, 2009	Paper does not explore palliation needs of patients and their carers
Lanoix,M., 20090617, Palliative care and Parkinson's disease: managing the chronic-palliative interface. [Review] [34 refs], Chronic Illness, 5, 46-55, 2009	Information review, no primary data
Lokk,J., Delbari,A., Clinical aspects of palliative care in advanced Parkinson's disease, BMC Palliative Care.11 , 2012.Article Number: 20.Date of Publication: 2012., -, 2012	Information review, no primary data
Lokk,J., Fereshtehnejad,S.-M., Managing palliative care in Parkinson's disease from diagnosis to end-stage disease: What the clinician should know, Neurodegenerative Disease Management.3 (2) (pp 169-183), 2013.Date of Publication: April 2013., 169-183, 2013	Information review, no primary data
Mallick,S., 20110714, Palliative care in Parkinson's disease: role of cognitive behavior therapy, Indian Journal of Palliative Care, 15, 51-56, 2009	Review on CBT in PD - does not meet criteria or report on outcomes of interest as outlined in review protocol
Midlov,P., Bondesson,A., Eriksson,T., Petersson,J., Minthon,L., Hoglund,P., Descriptive study and pharmacotherapeutic intervention in patients with epilepsy or Parkinson's disease at nursing homes in southern Sweden, European journal of clinical pharmacologyEur J Clin Pharmacol, 57, 903-910, 2001	Study describes drug use in patients with epilepsy and PD in care homes, not palliation needs; population not solely PD
Miyasaki,J.M., Long,J., Mancini,D., Moro,E.,	Validation summary of symptom assessment



<b>Excluded studies - 9. RQ21: What are the needs of people with Parkinson's disease for advance directives and palliative care plans throughout the course of their disease?</b>	
Fox,S.H., Lang,A.E., Marras,C., Chen,R., Strafella,A., Arshinoff,R., Ghoche,R., Hui,J., Palliative care for advanced Parkinson disease: An interdisciplinary clinic and new scale, the ESAS-PD, Parkinsonism and Related Disorders.18 (SUPPL.3) (pp S6-S9), 2012.Date of Publication: December 2012., S6-S9, 2012	tool - does not investigate needs of people with PD for advance directives. Does not report on any outcomes of interest as specified in review protocol
Miyasaki,J.M., 20140907, Palliative care in Parkinson's disease, Current Neurology & Neuroscience Reports, 13, 367-, 2013	Information review, no primary data
Thomas,S., MacMahon,D., 20040428, Parkinson's disease, palliative care and older people: Part 1. [Review] [17 refs], Nursing Older People, 16, 22-26, 2004	Information review, no primary data
Walker,R.W., 20131025, Palliative care and end-of-life planning in Parkinson's disease. [Review], Journal of Neural Transmission, 120, 635-638, 2013	Information review, no primary data
Bruno V, Mancini D, Ghoche R, Arshinoff R, and Miyasaki J M. 2016. "High prevalence of physical and sexual aggression to caregivers in advanced Parkinson's disease. Experience in the Palliative Care Program". Parkinsonism and Related Disorders 24(pp 141-142):.	Letter
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Ross G W, and Abbott R D. 2014. "Living and dying with Parkinson's disease". Movement Disorders 29(13):1571-3.	Editorial
Veronese S, Gallo G, Valle A, Cugno C, Chio A, Calvo A, Rivoiro C, and Oliver D J. 2015. "The palliative care needs of people severely affected by neurodegenerative disorders: A qualitative study". Progress in Palliative Care 23(6):331-342.	Not PD specific