

Appendix 3_References for excluded studies

Review questions 1-3

Reference	Reason for exclusion
Comi G, Filippi M, Barkhof F, Durelli L, Edan G, Fernández O, et al. Effect of early interferon treatment on conversion to definite multiple sclerosis: a randomised study. <i>Lancet</i> . 2001;357(9268):1576-82.	Investigated an unlicensed dose of interferon
Demina TL, Khachanova NV, Davydovskaia MV. The interferon beta therapy after the first clinical episode of demyelination in multiple sclerosis. <i>Zh Nevrol Psikhiatr Im S S Korsakova</i> . 2006;106(3):15-9.	Non English language paper
Filippi M, Rovaris M, Inglese M, Barkhof F, De Stefano N, Smith S, et al. Interferon beta-1a for brain tissue loss in patients at presentation with syndromes suggestive of multiple sclerosis: A randomised, double-blind, placebo-controlled trial. <i>Lancet</i> . 2004;364(9444):1489-96.	Investigated an unlicensed dose of interferon
Hartung HP, Freedman MS, Polman CH, Edan G, Kappos L, Miller DH, et al. Interferon β -1b-neutralizing antibodies 5 years after clinically isolated syndrome. <i>Neurology</i> . 2011;77(9):835-43.	Trial already included. Outcomes reported not relevant
Nagtegaal GJ, Pohl C, Wattjes MP, Hulst HE, Freedman MS, Hartung HP, et al. Interferon beta-1b reduces black holes in a randomised trial of clinically isolated syndrome. <i>Mult Scler</i> . 2014;20(2):234-42.	Trial already included. Outcomes reported not relevant
Siddiqui MA, Wellington K. Intramuscular interferon-beta-1a: in patients at high risk of developing clinically definite multiple sclerosis. <i>CNS Drugs</i> . 2005;19(1):55-61; discussion 63-4.	Not a primary intervention study
De Stefano N, Sormani MP, Stubinski B, Blevins G, Drulovic JS, Issard D, et al. Efficacy and safety of subcutaneous interferon β -1a in relapsing-remitting multiple sclerosis: further outcomes from the IMPROVE study. <i>J Neurol Sci</i> . 2012;312(1-2):97-101.	16 week follow-up
Goodman AD, Rossman H, Bar-Or A, Miller A, Miller DH, Schmierer K, et al. GLANCE: results of a phase 2, randomized, double-blind, placebo-controlled study. <i>Neurology</i> . 2009;72(9):806-12.	24 week follow-up
Kappos L, Li D, Calabresi PA, O'Connor P, Bar-Or A, Barkhof F, et al. Ocrelizumab in relapsing-remitting multiple sclerosis: a phase 2, randomised, placebo-controlled, multicentre trial. <i>Lancet</i> . 2011;378(9805):1779-87.	24 week follow-up

Reference	Reason for exclusion
Cascione M, Wynn D, Barbato LM, Pestreich L, Schofield L, McCague K. Randomized, open-label study to evaluate patient-reported outcomes with fingolimod after changing from prior disease-modifying therapy for relapsing multiple sclerosis: EPOC study rationale and design. <i>J Med Econ.</i> 2013;16(7):859-65.	24 week follow-up
Comi G, O'Connor P, Montalban X, Antel J, Radue EW, Karlsson G, et al. Phase II study of oral fingolimod (FTY720) in multiple sclerosis: 3-year results. <i>Mult Scler.</i> 2010 ;16(2):197-207.	24 week follow-up
Kappos L, Antel J, Comi G, Montalban X, O'Connor P, Polman CH, et al. Oral fingolimod (FTY720) for relapsing multiple sclerosis. <i>N Engl J Med.</i> 2006;355(11):1124-40.	24 week follow-up
Kappos L, Gold R, Miller DH, MacManus DG, Havrdova E, Limmroth V, et al. Effect of BG-12 on contrast-enhanced lesions in patients with relapsing--remitting multiple sclerosis: subgroup analyses from the phase 2b study. <i>Mult Scler.</i> 2012;18(3):314-21.	24 week follow-up
Kappos L, Gold R, Miller DH, Macmanus DG, Havrdova E, Limmroth V, et al. Efficacy and safety of oral fumarate in patients with relapsing-remitting multiple sclerosis: a multicentre, randomised, double-blind, placebo-controlled phase IIb study. <i>Lancet.</i> 2008;372(9648):1463-72.	24 week follow-up
Montalban X, Comi G, O'Connor P, Gold S, de Vera A, Eckert B, et al. Oral fingolimod (FTY720) in relapsing multiple sclerosis: impact on health-related quality of life in a phase II study. <i>Mult Scler.</i> 2011;17(11):1341-50.	24 week follow-up
Polman C, Barkhof F, Kappos L, Pozzilli C, Sandbrink R, Dahlke F, et al. Oral interferon beta-1a in relapsing-remitting multiple sclerosis: a double-blind randomized study. <i>Mult Scler.</i> 2003;9(4):342-8.	24 week follow-up
Radue EW, O'Connor P, Polman CH, Hohlfeld R, Calabresi P, Selmaj K, et al. Impact of fingolimod therapy on magnetic resonance imaging outcomes in patients with multiple sclerosis. <i>Arch Neurol.</i> 2012;69(10):1259-69.	24 week follow-up
Saida T, Kikuchi S, Itoyama Y, Hao Q, Kurosawa T, Nagato K, et al. A randomized, controlled trial of fingolimod (FTY720) in Japanese patients with multiple sclerosis. <i>Mult Scler.</i> 2012;18(9):1269-77.	24 week follow-up
O'Connor PW, Li D, Freedman MS, Bar-Or A, Rice GP, Confavreux C, et al. A Phase II study of the safety	34 week follow-up

Reference	Reason for exclusion
and efficacy of teriflunomide in multiple sclerosis with relapses. <i>Neurology</i> . 2006;66(6):894-900.	
Comi G, Filippi M, Wolinsky JS. European/Canadian multicenter, double-blind, randomized, placebo-controlled study of the effects of glatiramer acetate on magnetic resonance imaging--measured disease activity and burden in patients with relapsing multiple sclerosis. European/Canadian Glatiramer Acetate Study Group. <i>Ann Neurol</i> . 2001;49(3):290-7.	39 week follow-up
Rovaris M, Comi G, Rocca MA, Valsasina P, Ladkani D, Pieri E, et al. Long-term follow-up of patients treated with glatiramer acetate: a multicentre, multinational extension of the European/Canadian double-blind, placebo-controlled, MRI-monitored trial. <i>Mult Scler</i> . 2007;13(4):502-8.	39 week follow-up
Sormani MP, Bruzzi P, Comi G, Filippi M. The distribution of the magnetic resonance imaging response to glatiramer acetate in multiple sclerosis. <i>Mult Scler</i> . 2005;11(4):447-9.	39 week follow-up
Edan G, Miller D, Clanet M, Confavreux C, Lyon-Caen O, Lubetzki C, et al. Therapeutic effect of mitoxantrone combined with methylprednisolone in multiple sclerosis: a randomised multicentre study of active disease using MRI and clinical criteria. <i>J Neurol Neurosurg Psychiatry</i> . 1997;62(2):112-8.	Combination of drugs
Lublin FD, Cofield SS, Cutter GR, Conwit R, Narayana PA, Nelson F, et al. Randomized study combining interferon and glatiramer acetate in multiple sclerosis. <i>Ann Neurol</i> . 2013;73(3):327-40.	Combination of drugs
Rudick RA, Stuart WH, Calabresi PA, Confavreux C, Galetta SL, Radue EW, et al. Natalizumab plus interferon beta-1a for relapsing multiple sclerosis. <i>N Engl J Med</i> . 2006;354(9):911-23.	Combination of drugs
Wynn D, Kaufman M, Montalban X, Vollmer T, Simon J, Elkins J, et al. Daclizumab in active relapsing multiple sclerosis (CHOICE study): a phase 2, randomised, double-blind, placebo-controlled, add-on trial with interferon beta. <i>Lancet Neurol</i> . 2010;9(4):381-90.	Combination of drugs
Fischer JS, Priore RL, Jacobs LD, Cookfair DL, Rudick RA, Herndon RM, et al. Neuropsychological effects of interferon beta-1a in relapsing multiple sclerosis. Multiple Sclerosis Collaborative Research Group. <i>Ann Neurol</i> . 2000;48(6):885-92.	Data not available
Cohen JA, Rovaris M, Goodman AD, Ladkani D, Wynn D, Filippi M. Randomized, double-blind, dose-comparison study of glatiramer acetate in relapsing-remitting MS. <i>Neurology</i> . 2007;68(12):939-44.	Dose comparison study

Reference	Reason for exclusion
Comi G, Cohen JA, Arnold DL, Wynn D, Filippi M; FORTE Study Group. Phase III dose-comparison study of glatiramer acetate for multiple sclerosis. <i>Ann Neurol</i> . 2011;69(1):75-82.	Dose comparison study
Wolinsky JS, Borresen TE, Dietrich DW, Wynn D, Sidi Y, Steinerman JR, et al. GLACIER: An open-label, randomized, multicenter study to assess the safety and tolerability of glatiramer acetate 40 mg three-times weekly versus 20 mg daily in patients with relapsing-remitting multiple sclerosis. <i>Mult Scler Relat Disord</i> . 2015;4(4):370-6.	Dose comparison study
Bonavita S, Dinacci D, Lavorgna L, Savettieri G, Quattrone A, Livrea P, et al. Treatment of multiple sclerosis with interferon beta in clinical practice: 2-year follow-up data from the South Italy Mobile MRI Project. <i>Neurol Sci</i> . 2006;27 Suppl 5:S365-8.	Dose comparison trial
Durelli L, Verdun E, Barbero P, Bergui M, Versino E, Ghezzi A, et al. Every-other-day interferon beta-1b versus once-weekly interferon beta-1a for multiple sclerosis: results of a 2-year prospective randomised multicentre study (INCOMIN). <i>Lancet</i> . 2002;359(9316):1453-60.	Dose comparison trial
Freedman MS, Francis GS, Sanders EA, Rice GP, O'Connor P, Comi G, et al. Randomized study of once-weekly interferon beta-1a therapy in relapsing multiple sclerosis: three-year data from the OWIMS study. <i>Mult Scler</i> . 2005;11(1):41-5	Dose comparison trial
Mazdeh M, Afzali S, Jaafari MR. The therapeutic effect of Avonex, Rebif and Betaferon on EDSS and relapse in multiple sclerosis: a comparative study. <i>Acta Med Iran</i> . 2010;48(2):83-8.	Dose comparison trial
Mokhber N, Azarpazhooh A, Orouji E, Rao SM, Khorram B, Sahraian MA, et al. Cognitive dysfunction in patients with multiple sclerosis treated with different types of interferon beta: a randomized clinical trial. <i>J Neurol Sci</i> . 2014;342(1-2):16-20.	Dose comparison trial
Nafissi S, Azimi A, Amini-Harandi A, Salami S, shahkarami MA, Heshmat R. Comparing efficacy and side effects of a weekly intramuscular biogeneric/biosimilar interferon beta-1a with Avonex in relapsing remitting multiple sclerosis: a double blind randomized clinical trial. <i>Clin Neurol Neurosurg</i> . 2012;114(7):986-9.	Dose comparison trial
Oger J, Francis G, Chang P; PRISMS Study Group. Prospective assessment of changing from placebo to IFN beta-1a in relapsing MS: the PRISMS study. <i>J Neurol Sci</i> . 2005;237(1-2):45-52.	Dose comparison trial

Reference	Reason for exclusion
Panitch H, Goodin DS, Francis G, Chang P, Coyle PK, O'Connor P, et al. Randomized, comparative study of interferon beta-1a treatment regimens in MS: The EVIDENCE Trial. <i>Neurology</i> . 2002;59(10):1496-506.	Dose comparison trial
Havrdova E, Zivadinov R, Krasensky J, Dwyer MG, Novakova I, Dolezal O. Randomized study of interferon beta-1a, low-dose azathioprine, and low-dose corticosteroids in multiple sclerosis. <i>Mult Scler</i> . 2009;15(8):965-76.	Drug combination trial
Double-blind controlled trial of azathioprine in the treatment of multiple sclerosis. <i>J Neurol Neurosurg Psychiatry</i> . 1987;50(10):1387.	Drug not licensed for MS
Double-masked trial of azathioprine in multiple sclerosis. British and Dutch Multiple Sclerosis Azathioprine Trial Group. <i>Lancet</i> . 1988;2(8604):179-83.	Drug not licensed for MS
Ellison GW, Myers LW, Mickey MR, Graves MC, Tourtellotte WW, Syndulko K, et al. A placebo-controlled, randomized, double-masked, variable dosage, clinical trial of azathioprine with and without methylprednisolone in multiple sclerosis. <i>Neurology</i> . 1989;39(8):1018-26.	Drug not licensed for MS
Massacesi L, Tramacere I, Amoroso S, Battaglia MA, Benedetti MD, Filippini G, et al. Azathioprine versus beta interferons for relapsing-remitting multiple sclerosis: a multicentre randomized non-inferiority trial. <i>PLoS One</i> . 2014;9(11):e113371.	Drug not licensed for MS
Mertin J, Knight SC, Rudge P, Thompson EJ, Healy MJ. Double-blind, controlled trial of immunosuppression in treatment of multiple sclerosis. <i>Lancet</i> . 1980;2(8201):949-51.	Drug not licensed for MS
Milanese C, La Mantia L, Salmaggi A, Campi A, Bortolami C, Tajoli L, et al. Double blind controlled randomized study on azathioprine efficacy in multiple sclerosis. Preliminary results. <i>Ital J Neurol Sci</i> . 1988;9(1):53-7.	Drug not licensed for MS
Millefiorini E, Gasperini C, Pozzilli C, D'Andrea F, Bastianello S, Trojano M, et al. Randomized placebo-controlled trial of mitoxantrone in relapsing-remitting multiple sclerosis: 24-month clinical and MRI outcome. <i>J Neurol</i> . 1997;244(3):153-9.	Drug not prioritized for RRMS
Minderhoud JM1, Prange AJ, Luyckx GJ. A long-term double-blind controlled study on the effect of	Drug not licensed for MS

Reference	Reason for exclusion
azathioprine in the treatment of multiple sclerosis. Clin Neurol Neurosurg. 1988;90(1):25-8.	
Rivera VM, Jeffery DR, Weinstock-Guttman B, Bock D, Dangond F. Results from the 5-year, phase IV RENEW (Registry to Evaluate Novantrone Effects in Worsening Multiple Sclerosis) study. BMC Neurol. 2013;13:80.	Drug not prioritized for RRMS
Tindall RS, Walker JE, Ehle AL, Near L, Rollins J, Becker D. Plasmapheresis in multiple sclerosis: prospective trial of pheresis and immunosuppression versus immunosuppression alone. Neurology. 1982;32(7):739-43.	Drug not prioritized for RRMS
Csépany T. [Natalizumab retreatment: effectiveness and long-term safety in multiple sclerosis in the STRATA study]. Ideggyogy Sz. 2014;67(7-8):277-9.	Non English language paper
Demina TL, Khachanova NV, Davydovskaia MV, Popova NF, Gusev EI. [Clinical efficacy and safety of long-term immunomodulating therapy with interferon beta]. Zh Nevrol Psikhiatr Im S S Korsakova. 2008;108(4):24-6.	Non English language paper
Klotz L, Meuth SG, Kieseier B, Wiendl H. [Alemtuzumab for relapsing-remitting multiple sclerosis. Results of two randomized controlled phase III studies]. Nervenarzt. 2013;84(8):984-94.	Non English language paper
Komoly S. [Better life expectations of SM patients: 21 years follow up of patients treated with interferon beta-1b]. Ideggyogy Sz. 2013;66(3-4):143-4.	Non English language paper
López-Ruiz Minerva, Ruiz-Sandoval José Luis, Barroso-Rodríguez Noé Saúl, Cantú-Brito Carlos Gerardo, Violante-Villanueva José Arturo, Molina-Pérez Aarón, et al. Open label, extension-of-PRO-3209 trial to assess efficacy and safety of Probioglat® (glatiramer acetate) in Mexican patients with relapsing-remitting multiple sclerosis. Interim report of the first 12 months of treatment (Study PRO-4109). Rev Mex Neuroci. 2014;15(6):307-14.	Non English language paper
Magdolna S. [Effectiveness and safety of natalizumab in multiple sclerosis: data of the first five years from the TOP (Tysabri Observational Program)]. Ideggyogy Sz. 2014;67(5-6):211-2	Non English language paper
Popova EV, Boïko AN, Davydovskaia MV, Demina TL, Kukel' TM, Lashch Niu, et al. [The first experience of the use the Russian B-interferon-1b biosimilar (infibeta) in the daily practice of the Moscow Center of Multiple Sclerosis]. Zh Nevrol Psikhiatr Im S S Korsakova. 2013;113(10 Pt 2):93-6.	Non English language paper

Reference	Reason for exclusion
Ruiz Sandoval José Luis, López-Ruiz Minerva, Barroso-Rodríguez Noé, Cantú-Brito Carlos, Violante-Villanueva Arturo, Hernández-Hernández Marisela, et al. Safety and pharmacodynamics comparative study to evaluate the effect of glatiramer acetate (Probioglat® and Copaxone®) study drug and reference over response Th1, Th2 and sVCAM in patients with Relapsing-Remitting Multiple Sclerosis. . Rev Mex Neuroci. 2013;14(6):306-13.	Non English language paper
Millefiorini E, Gasperini C, Pozzilli C, D'Andrea F, Bastianello S, Trojano M, et al. Randomized placebo-controlled trial of mitoxantrone in relapsing-remitting multiple sclerosis: 24-month clinical and MRI outcome. J Neurol. 1997;244(3):153-9.	Drug not prioritized for RRMS
Minderhoud JM1, Prange AJ, Luyckx GJ. A long-term double-blind controlled study on the effect of azathioprine in the treatment of multiple sclerosis. Clin Neurol Neurosurg. 1988;90(1):25-8.	Drug not licensed for MS
Rivera VM, Jeffery DR, Weinstock-Guttman B, Bock D, Dangond F. Results from the 5-year, phase IV RENEW (Registry to Evaluate Novantrone Effects in Worsening Multiple Sclerosis) study. BMC Neurol. 2013;13:80.	Drug not prioritized for RRMS
Tindall RS, Walker JE, Ehle AL, Near L, Rollins J, Becker D. Plasmapheresis in multiple sclerosis: prospective trial of pheresis and immunosuppression versus immunosuppression alone. Neurology. 1982;32(7):739-43.	Drug not prioritized for RRMS
Csépany T. [Natalizumab retreatment: effectiveness and long-term safety in multiple sclerosis in the STRATA study]. Ideggyogy Sz. 2014;67(7-8):277-9.	Non English language paper
Demina TL, Khachanova NV, Davydovskaia MV, Popova NF, Gusev EI. [Clinical efficacy and safety of long-term immunomodulating therapy with interferon beta]. Zh Nevrol Psikhiatr Im S S Korsakova. 2008;108(4):24-6.	Non English language paper
Klotz L, Meuth SG, Kieseier B, Wiendl H. [Alemtuzumab for relapsing-remitting multiple sclerosis. Results of two randomized controlled phase III studies]. Nervenarzt. 2013;84(8):984-94.	Non English language paper
Komoly S. [Better life expectations of SM patients: 21 years follow up of patients treated with interferon beta-1b]. Ideggyogy Sz. 2013;66(3-4):143-4.	Non English language paper

Reference	Reason for exclusion
López-Ruiz Minerva, Ruiz-Sandoval José Luis, Barroso-Rodríguez Noé Saúl, Cantú-Brito Carlos Gerardo, Violante-Villanueva José Arturo, Molina-Pérez Aarón, et al. Open label, extension-of-PRO-3209 trial to assess efficacy and safety of Probioglat® (glatiramer acetate) in Mexican patients with relapsing-remitting multiple sclerosis. Interim report of the first 12 months of treatment (Study PRO-4109). <i>Rev Mex Neuroci.</i> 2014;15(6):307-14.	Non English language paper
Magdolna S. [Effectiveness and safety of natalizumab in multiple sclerosis: data of the first five years from the TOP (Tysabri Observational Program)]. <i>Ideggyogy Sz.</i> 2014;67(5-6):211-2	Non English language paper
Popova EV, Boïko AN, Davydovskaia MV, Demina TL, Kukul' TM, Lashch Niu, et al. [The first experience of the use the Russian B-interferon-1b biosimilar (infibeta) in the daily practice of the Moscow Center of Multiple Sclerosis]. <i>Zh Nevrol Psikhiatr Im S S Korsakova.</i> 2013;113(10 Pt 2):93-6.	Non English language paper
Ruiz Sandoval José Luis, López-Ruiz Minerva, Barroso-Rodríguez Noé, Cantú-Brito Carlos, Violante-Villanueva Arturo, Hernández-Hernández Marisela, et al. Safety and pharmacodynamics comparative study to evaluate the effect of glatiramer acetate (Probioglat® and Copaxone®) study drug and reference over response Th1, Th2 and sVCAM in patients with Relapsing-Remitting Multiple Sclerosis. . <i>Rev Mex Neuroci.</i> 2013;14(6):306-13.	Non English language paper
Grieb P1, Stelmasiak Z. [Treatment of multiple sclerosis with cladribine (2-CDA), a new immunosuppressant agent. Theoretical basis and preliminary results]. <i>Neurol Neurochir Pol.</i> 1995 Jan-Feb;29(1):69-76.	Non English language paper
Cocco E, Marchi P, Sardu C, Russo P, Paolillo A, Mascia M, et al. Mitoxantrone treatment in patients with early relapsing-remitting multiple sclerosis. <i>Mult Scler.</i> 2007;13(8):975-80.	Not an RCT
Ghezzi A; Immunomodulatory Treatment of Early Onset MS (ITEMS) Group. Immunomodulatory treatment of early onset multiple sclerosis: results of an Italian Co-operative Study. <i>Neurol Sci.</i> 2005;26 Suppl 4:S183-6.	Not an RCT
Hamzehloo A, Etemadifar M. Mitoxantrone reduced disability in Iranian patients with multiple sclerosis. <i>Arch Iran Med.</i> 2007;10(1):59-64.	Not an RCT

Reference	Reason for exclusion
Lang C, Reiss C, Mäurer M. Natalizumab may improve cognition and mood in multiple sclerosis. <i>Eur Neurol.</i> 2012;67(3):162-6.	Not an RCT
Mattioli F, Stampatori C, Capra R. The effect of natalizumab on cognitive function in patients with relapsing-remitting multiple sclerosis: preliminary results of a 1-year follow-up study. <i>Neurol Sci.</i> 2011;32(1):83-8.	Not an RCT
McFarland HF. Alemtuzumab versus interferon beta-1a: implications for pathology and trial design. <i>Lancet Neurol.</i> 2009;8(1):26-8.	Not an RCT
Comi G, Hartung HP, Kurukulasuriya NC, Greenberg SJ, Scaramozza M. Cladribine tablets for the treatment of relapsing-remitting multiple sclerosis <i>Expert Opin Pharmacother.</i> 2013 Jan;14(1):123-36.	Not an RCT
Khan O, Shen Y, Caon C, Bao F, Ching W, Reznar M, et al. Axonal metabolic recovery and potential neuroprotective effect of glatiramer acetate in relapsing-remitting multiple sclerosis. <i>Mult Scler.</i> 2005;11(6):646-51.	Pilot study (n=18)
Arnold DL, Gold R, Kappos L, Bar-Or A, Giovannoni G, Selmaj K, et al. Effects of delayed-release dimethyl fumarate on MRI measures in the Phase 3 DEFINE study. <i>J Neurol.</i> 2014;261(9):1794-802.	Trial already included. No additional relevant outcomes
Miller DH, Fox RJ, Phillips JT, Hutchinson M, Havrdova E, Kita M, et al. Effects of delayed-release dimethyl fumarate on MRI measures in the phase 3 CONFIRM study. <i>Neurology.</i> 2015;84(11):1145-52.	Trial already included. No additional relevant outcomes
Miller DH, Soon D, Fernando KT, MacManus DG, Barker GJ, Yousry TA, et al. MRI outcomes in a placebo-controlled trial of natalizumab in relapsing MS. <i>Neurology.</i> 2007;68(17):1390-401.	Trial already included. No additional relevant outcomes
Arnold DL, Gold R, Kappos L, Bar-Or A, Giovannoni G, Selmaj K, et al. Magnetization transfer ratio in the delayed-release dimethyl fumarate DEFINE study. <i>J Neurol.</i> 2014;261(12):2429-37.	Trial already included. Outcomes reported not relevant
Arnold DL, Narayanan S, Antel S. Neuroprotection with glatiramer acetate: evidence from the PreCISe trial.	Trial already included.

Reference	Reason for exclusion
J Neurol. 2013;260(7):1901-6.	Outcomes reported not relevant
Cadavid D, Cheriyan J, Skurnick J, Lincoln JA, Wolansky LJ, Cook SD. New acute and chronic black holes in patients with multiple sclerosis randomised to interferon beta-1b or glatiramer acetate. J Neurol Neurosurg Psychiatry. 2009;80(12):1337-43.	Trial already included. Outcomes reported not relevant
Devonshire V, Havrdova E, Radue EW, O'Connor P, Zhang-Auberson L, Agoropoulou C, et al. Relapse and disability outcomes in patients with multiple sclerosis treated with fingolimod: subgroup analyses of the double-blind, randomised, placebo-controlled FREEDOMS study. Lancet Neurol. 2012;11(5):420-8.	Trial already included. Outcomes reported not relevant
Graves J, Galetta SL, Palmer J, Margolin DH, Rizzo M, Bilbruck J, et al. Alemtuzumab improves contrast sensitivity in patients with relapsing-remitting multiple sclerosis. Mult Scler. 2013;19(10):1302-9.	Trial already included. Outcomes reported not relevant
Kappos L, Giovannoni G, Gold R, Phillips JT, Arnold DL, Hotermans C, et al. Time course of clinical and neuroradiological effects of delayed-release dimethyl fumarate in multiple sclerosis. Eur J Neurol. 2015;22(4):664-71.	Trial already included. Outcomes reported not relevant
Kappos L, O'Connor PW, Polman CH, Vermersch P, Wiendl H, Pace A, et al. Clinical effects of natalizumab on multiple sclerosis appear early in treatment course. J Neurol. 2013;260(5):1388-95.	Trial already included. Outcomes reported not relevant
Zivadinov R, Dwyer M, Barkay H, Steinerman JR, Knappertz V, Khan O. Effect of glatiramer acetate three-times weekly on the evolution of new, active multiple sclerosis lesions into T1-hypointense "black holes": a post hoc magnetic resonance imaging analysis. J Neurol. 2015;262(3):648-53.	Trial already included. Outcomes reported not relevant
Zivadinov R, Dwyer MG, Ramasamy DP, Davis MD, Steinerman JR, Khan O. The Effect of Three Times a Week Glatiramer Acetate on Cerebral T1 Hypointense Lesions in Relapsing-Remitting Multiple Sclerosis. J Neuroimaging. 2015;25(6):989-95.	Trial already included. Outcomes reported not relevant
Phillips JT, Giovannoni G, Lublin FD, O'Connor PW, Polman CH, Willoughby E, et al. Sustained improvement in Expanded Disability Status Scale as a new efficacy measure of neurological change in multiple sclerosis: treatment effects with natalizumab in patients with relapsing multiple sclerosis.	Trial already included. Post-hoc analysis not relevant

Reference	Reason for exclusion
Mult Scler. 2011;17(8):970-9.	
Uitdehaag B, Constantinescu C, Cornelisse P, Jeffery D, Kappos L, Li D, et al. Impact of exposure to interferon beta-1a on outcomes in patients with relapsing-remitting multiple sclerosis: exploratory analyses from the PRISMS long-term follow-up study. Ther Adv Neurol Disord. 2011;4(1):3-14.	Trial already included. Post-hoc analysis not relevant
Arnold DL, Calabresi PA, Kieseier BC, Sheikh SI, Deykin A, Zhu Y, et al. Effect of peginterferon beta-1a on MRI measures and achieving no evidence of disease activity: results from a randomized controlled trial in relapsing-remitting multiple sclerosis. BMC Neurol. 2014;14:240.	Trial already included. Sensitivity analysis not relevant
Agius M, Meng X, Chin P, Grinspan A, Hashmonay R. Fingolimod therapy in early multiple sclerosis: an efficacy analysis of the TRANSFORMS and FREEDOMS studies by time since first symptom. CNS Neurosci Ther. 2014;20(5):446-51.	Trial already included. Subgroup analyses not relevant
Cree BA, Stuart WH, Tornatore CS, Jeffery DR, Pace AL, Cha CH. Efficacy of natalizumab therapy in patients of African descent with relapsing multiple sclerosis: analysis of AFFIRM and SENTINEL data. Arch Neurol. 2011;68(4):464-8.	Trial already included. Sub-group analysis not relevant
Cohen JA, Barkhof F, Comi G, Izquierdo G, Khatri B, Montalban X, et al. Fingolimod versus intramuscular interferon in patient subgroups from TRANSFORMS. J Neurol. 2013;260(8):2023-32.	Trial already included. Sub-set of included participants not relevant
Gold R, Giovannoni G, Phillips JT, Fox RJ, Zhang A, Meltzer L, et al. Efficacy and safety of delayed-release dimethyl fumarate in patients newly diagnosed with relapsing-remitting multiple sclerosis (RRMS). Mult Scler. 2015;21(1):57-66.	Trial already included. Sub-set of included participants not relevant
Rammohan K, Giovannoni G, Comi G, Cook S, Rieckmann P, Soelberg Sørensen P et al. Cladribine tablets for relapsing-remitting multiple sclerosis: Efficacy across patient subgroups from the phase III CLARITY study. Mult Scler Relat Disord. 2012 Jan;1(1):49-54.	No relevant outcomes
De Stefano N, Giorgio A, Battaglini M, De Leucio A, Hicking C, Dangond F. Reduced brain atrophy rates are associated with lower risk of disability progression in patients with relapsing multiple sclerosis treated with cladribine tablets. Mult Scler. 2017 Jan 1:1352458517690269.	No relevant outcomes
Giovannoni G, Cook S, Rammohan K, Rieckmann P, Sørensen PS, Vermersch P. Sustained disease-activity-	No relevant outcomes

Reference	Reason for exclusion
free status in patients with relapsing-remitting multiple sclerosis treated with cladribine tablets in the CLARITY study: a post-hoc and subgroup analysis. <i>Lancet Neurol.</i> 2011 Apr;10(4):329-37.	
Muir VJ1, Plosker GL. Cladribine tablets: in relapsing-remitting multiple sclerosis. <i>CNS Drugs.</i> 2011 Mar;25(3):239-49.	Descriptive review of CLARITY trial
Stelmasiak Z, Solski J, Nowicki J, Jakubowska B, Ryba M, Grieb P. Effect of parenteral cladribine on relapse rates in patients with relapsing forms of multiplesclerosis: results of a 2-year, double-blind, placebo-controlled, crossover study. <i>Mult Scler.</i> 2009 Jun;15(6):767-70.	Intervention not relevant
Rice GP, Filippi M, Comi G. Cladribine and progressive MS Clinical and MRI outcomes of a multicenter controlled trial. <i>Neurology.</i> 2000 Mar 14;54(5):1145-55.	Participants had progressive MS
Janiec K1, Wajgt A, Kondera-Anasz Z. Effect of immunosuppressive cladribine treatment on serum leucocytes system in two-year clinical trial in patients with chronic progressive multiple sclerosis. <i>Med Sci Monit.</i> 2001 Jan-Feb;7(1):93-8.	Participants had progressive MS
Selby R1, Brandwein J, O'Connor P. Safety and tolerability of subcutaneous cladribine therapy in progressive multiple sclerosis. <i>Can J Neurol Sci.</i> 1998 Nov;25(4):295-9.	Participants had progressive MS
Filippi M1, Rovaris M, Iannucci G, Mennea S, Sormani MP, Comi G. Whole brain volume changes in patients with progressive MS treated with cladribine. <i>Neurology.</i> 2000 Dec 12;55(11):1714-8.	Participants had progressive MS
Beutler E, Sipe JC, Romine JS, Koziol JA, McMillan R, Zyroff J. The treatment of chronic progressive multiple sclerosis with cladribine. <i>Proc Natl Acad Sci U S A.</i> 1996 Feb 20;93(4):1716-20.	Participants had progressive MS

Review question 4-5

Reference	Reason for exclusion
-----------	----------------------

Arnold DL, Calabresi PA, Kieseier BC, Sheikh SI, Deykin A, Zhu Y, et al. Effect of peginterferon beta-1a on MRI measures and achieving no evidence of disease activity: results from a randomized controlled trial in relapsing-remitting multiple sclerosis. BMC Neurol. 2014;14:240.	Comparison not relevant
<u>Kappos L, De Stefano N, Freedman MS, Cree BA, Radue EW, Sprenger T, et al. Inclusion of brain volume loss in a revised measure of 'no evidence of disease activity' (NEDA-4) in relapsing-remitting multiple sclerosis. Mult Scler. 2016;22(10):1297-305.</u>	Comparison not relevant
Damasceno A, Damasceno BP, Cendes F. No evidence of disease activity in multiple sclerosis: Implications on cognition and brain atrophy. Mult Scler. 2016;22(1):64-72.	No relevant data
Nygaard GO, Celius EG, de Rodez Benavent SA, Sowa P, Gustavsen MW, Fjell AM, et al. A longitudinal study of disability, cognition, and gray matter atrophy in early multiple sclerosis patients according to evidence of disease activity. PLoS One. 2015;10(8):e0135974.	No relevant data
Prosperini L, Fanelli F, Pozzilli C. Long-term assessment of No Evidence of Disease Activity with natalizumab in relapsing multiple sclerosis. J Neurol Sci. 2016;364:145-7.	No relevant data
Rio J, Rovira A, Blanco Y, Sainz A, Perkal H, Robles R, et al. Response to treatment with interferon beta in patients with multiple sclerosis. Validation of the Rio Score. Revista De Neurologia. 2016;63(4):145-150.	Non-English language paper

Review question 6

Reference	Reason for exclusion
Braune S, Lang M, Bergmann A; NTC Study Group. Second line use of Fingolimod is as effective as Natalizumab in a German out-patient RRMS-cohort. J Neurol. 2013;260(12):2981-5.	Comparison not relevant
Castillo-Trivino T, Mowry EM, Gajofatto A, Chabas D, Crabtree-Hartman E, Cree BA, et al. Switching multiple sclerosis patients with breakthrough disease to second-line therapy. PLoS One. 2011;6(2):e16664.	Comparison not relevant
Healy BC, Glanz BI, Stankiewicz J, Buckle G, Weiner H, Chitnis T. A method for evaluating	Comparison not relevant

Reference	Reason for exclusion
treatment switching criteria in multiple sclerosis. <i>Mult Scler.</i> 2010;16(12):1483-9.	
Carrá A, Onaha P, Luetic G, Burgos M, Crespo E, Deri N, et al. Therapeutic outcome 3 years after switching of immunomodulatory therapies in patients with relapsing–remitting multiple sclerosis in Argentina. <i>Eur J Neurol.</i> 2008;15(4):386-93.	Drug not relevant
Caon C, Din M, Ching W, Tselis A, Lisak R, Khan O. Clinical course after change of immunomodulating therapy in relapsing-remitting multiple sclerosis. <i>Eur J Neurol.</i> 2006;13(5):471-4.	No comparison group
Gajofatto A, Bacchetti P, Grimes B, High A, Waubant E. Switching first-line disease-modifying therapy after failure: impact on the course of relapsing-remitting multiple sclerosis. <i>Mult Scler.</i> 2009;15(1):50-8.	No relevant comparison
Kalincik T, Horakova D, Spelman T, Jokubaitis V, Trojano M, Lugaresi A, et al.; MSBase Study Group. Switch to natalizumab versus fingolimod in active relapsing-remitting multiple sclerosis. <i>Ann Neurol.</i> 2015;77(3):425-35.	No relevant comparison
Lanzillo R, Bonavita S, Quarantelli M, Vacca G, Lus G, Amato L, et al. Natalizumab is effective in multiple sclerosis patients switching from other disease modifying therapies in clinical practice. <i>Neurological Sciences.</i> 2013;34(4):521-8.	No relevant comparison
Meng X, Chin PS, Hashmonay R, Zahur Islam M, Cutter G. Effect of switching from intramuscular interferon beta-1a to oral fingolimod on time to relapse in patients with relapsing-remitting multiple sclerosis enrolled in a 1-year extension of TRANSFORMS. <i>Contemp Clin Trials.</i> 2015;41:69-74.	No relevant comparison
Putzki N, Yaldizli O, Maurer M, Cursiefen S, Kuckert S, Klawe C, et al. Efficacy of natalizumab in second line therapy of relapsing-remitting multiple sclerosis: Results from a multi-center study in German speaking countries. <i>European Journal of Neurology.</i> 2010;17(1):31-7.	No relevant comparison
Spelman T, Mekhael L, Burke T, Butzkueven H, Hodgkinson S, Havrdova E, et al. Risk of early relapse following the switch from injectables to oral agents for multiple sclerosis. <i>European Journal of Neurology.</i> 2016;23(4):729-36.	No relevant comparison

Reference	Reason for exclusion
<p>Ziemssen T, Bajenaru OA, Carrá A, de Klippel N, de Sá JC, Edland A, et al. A 2-year observational study of patients with relapsing-remitting multiple sclerosis converting to glatiramer acetate from other disease-modifying therapies: the COPTIMIZE trial. J Neurol. 2014;261(11):2101-11.</p>	<p>No relevant comparison</p>
<p>Gajofatto A, Bianchi MR, Deotto L, Benedetti MD. Are natalizumab and fingolimod analogous second-line options for the treatment of relapsing-remitting multiple sclerosis? a clinical practice observational study. Eur Neurol. 2014;72(3-4):173-80.</p>	<p>Population not relevant (participants did not have to have evidence of disease activity and could be treatment naïve)</p>

Review question 7

Reference	Reason for exclusion
Baumgartner A, Stich O, Rauer S. Clinical and radiological disease reactivation after cessation of long-term therapy with natalizumab. <i>Int J Neurosci.</i> 2012;122(1):35-9.	<10 participants per arm
Berger B, Baumgartner A, Rauer S, Mader I, Luetzen N, Farenkopf U, et al. Severe disease reactivation in four patients with relapsing-remitting multiple sclerosis after fingolimod cessation. <i>J Neuroimmunol.</i> 2015;282:118-22.	<10 participants per arm
Hakiki B, Portaccio E, Giannini M, Razzolini L, Pastò L, Amato MP. Withdrawal of fingolimod treatment for relapsing-remitting multiple sclerosis: report of six cases. <i>Mult Scler.</i> 2012;18(11):1636-9	<10 participants per arm
Havla J, Gerdes LA, Meinl I, Krumbholz M, Faber H, Weber F, et al. De-escalation from natalizumab in multiple sclerosis: recurrence of disease activity despite switching to glatiramer acetate. <i>J Neurol.</i> 2011;258(9):1665-9	<10 participants per arm
Gobbi C, Meier DS, Cotton F, Sintzel M, Leppert D, et al. Interferon beta 1b following natalizumab discontinuation: one year, randomized, prospective, pilot trial. <i>BMC Neurol.</i> 2013;13:101.	<10 participants per arm
Zecca C, Riccitelli GC, Calabrese P, Pravatà E, Candrian U, Guttmann CR, et al. Treatment satisfaction, adherence and behavioral assessment in patients de – escalating from natalizumab to interferon beta. <i>BMC Neurol.</i> 2014;14:38.	<10 participants per arm
Bianco A, Patanella AK, Nociti V, Marti A, Frisullo G, Plantone D, et al. Second-line therapy with fingolimod for relapsing-remitting multiple sclerosis in clinical practice: The effect of previous exposure to natalizumab. <i>Eur Neurol.</i> 2015;73(1-2):57-65	Comparison not relevant
Comi G, Gold R, Dahlke F, Sinha A, von Rosenstiel P, Tomic D. Relapses in patients treated with fingolimod after previous exposure to natalizumab. <i>Mult Scler.</i> 2015;21(6):786-90.	Comparison not relevant
Rieckmann P, Heidenreich F, Sailer M, Zettl UK, Zessack N, Hartung HP, et al. Treatment de-	Drug not prioritized for RRMS

Reference	Reason for exclusion
escalation after mitoxantrone therapy: Results of a phase IV, multicentre, open-label, randomized study of subcutaneous interferon beta-1a in patients with relapsing multiple sclerosis. <i>Ther Adv Neurol Disord.</i> 2012;5(1):3-12.	
Kappos L, Radue EW, Comi G, Montalban X, Butzkueven H, Wiendl H, et al. Switching from natalizumab to fingolimod: a randomized, placebo-controlled study in RRMS. <i>Neurology.</i> 2015;85(1):29-39.	No relevant comparison
O'Connor P, Goodman A, Kappos L, Lublin F, Polman C, Rudick RA, et al. Long-term safety and effectiveness of natalizumab redosing and treatment in the STRATA MS study. <i>Neurology.</i> 2014;83(1):78-86.	No relevant comparison
Putzki N, Yaldizli O, Bühler R, Schwegler G, Curtius D, Tettenborn B. Natalizumab reduces clinical and MRI activity in multiple sclerosis patients with high disease activity: results from a multicenter study in Switzerland. <i>Eur Neurol.</i> 2010;63(2):101-6.	No relevant comparison
Stüve O, Cravens PD, Frohman EM, Phillips JT, Remington GM, von Geldern G, et al. Immunologic, clinical, and radiologic status 14 months after cessation of natalizumab therapy. <i>Neurology.</i> 2009;72(5):396-401.	No relevant outcomes
Capobianco M, di Sapio A, Malentacchi M, Malucchi S, Matta M, Sperli F, et al. No impact of current therapeutic strategies on disease reactivation after natalizumab discontinuation: a comparative analysis of different approaches during the first year of natalizumab discontinuation. <i>Eur J Neurol.</i> 2015;22(3):585-7.	NTZ < 12 months
Kaufman MD, Lee R, Norton HJ. Course of relapsing-remitting multiple sclerosis before, during and after natalizumab. <i>Mult Scler.</i> 2011;17(4):490-4.	NTZ < 12 months
Kerbrat A, Le Page E, Leray E, Anani T, Coustans M, Desormeaux C, et al. Natalizumab and drug holiday in clinical practice: an observational study in very active relapsing remitting multiple sclerosis patients. <i>J Neurol Sci.</i> 2011;308(1-2):98-102.	NTZ < 12 months
O'Connor PW, Goodman A, Kappos L, Lublin FD, Miller DH, Polman C, et al. Disease activity	NTZ < 12 months

Reference	Reason for exclusion
return during natalizumab treatment interruption in patients with multiple sclerosis. <i>Neurology</i> . 2011;76(22):1858-65.	
Sorensen PS, Koch-Henriksen N, Petersen T, Ravnborg M, Oturai A, Sellebjerg F. Recurrence or rebound of clinical relapses after discontinuation of natalizumab therapy in highly active MS patients. <i>J Neurol</i> . 2014;261(6):1170-7.	NTZ < 12 months
Rossi S, Motta C, Studer V, De Chiara V, Barbieri F, Monteleone F, et al. Effect of glatiramer acetate on disease reactivation in MS patients discontinuing natalizumab. <i>Eur J Neurol</i> . 2013;20(1):87-94.	Population not relevant
Klotz L, Grützke B, Eveslage M, Deppe M, Gross CC, Kirstein L. Assessment of immune functions and MRI disease activity in relapsing-remitting multiple sclerosis patients switching from natalizumab to fingolimod (ToFingo-Successor). <i>BMC Neurology</i> . 2015;15:96.	Study protocol

Review question 8

Reference	Reason for exclusion
Sempere AP, Martin-Medina P, Berenguer-Ruiz L, Perez-Carmona N, Sanchez-Perez R, Polache-Vengud J, et al. Switching from natalizumab to fingolimod: An observational study. <i>Acta Neurologica Scandinavica</i> . 2013;128(2):e6-e10.	<10 participants per arm
Killestein J, Vennegoor A, Strijbis EM, Seewann A, Van Oosten BW, Uitdehaag BMJ, et al. Natalizumab drug holiday in multiple sclerosis: Poorly tolerated. <i>Annals of Neurology</i> . 2010;68(3):392-5.	<10 participants per arm
Barroso B, Miquel M, Marasescu R, Demasles S, Krim E, Bonnan M. Natalizumab is effective in controlling the inflammatory rebound after its discontinuation and failure of an alternative	Design not relevant. Case study

Reference	Reason for exclusion
treatment. <i>Multiple Sclerosis and Related Disorders</i> . 2015;4(4):380-2.	
Centonze D, Rossi S, Rinaldi F, Gallo P. Severe relapses under fingolimod treatment prescribed after natalizumab. <i>Neurology</i> . 2012;79(19):2004-5.	Design not relevant. Case study
Ghezzi A, Rocca MA, Baroncini D, Annovazzi P, Zaffaroni M, Minonzio G, et al. Disease reactivation after fingolimod discontinuation in two multiple sclerosis patients. <i>J Neurol</i> . 2013;260(1):327-9.	Design not relevant. Case study
Gunduz T, Kurtuncu M, Eraksoy M. Severe rebound after withdrawal of fingolimod treatment in patients with multiple sclerosis. <i>Multiple Sclerosis and Related Disorders</i> . 2017;11:1-3.	Design not relevant. Case study
Habek M. Severe relapse after stopping natalizumab for multiple sclerosis. <i>Neurologia Croatica</i> . 2014;63(1-2):61-2.	Design not relevant. Case study
Vecchio D, Naldi P, Stecco A, Cantello R, Leone MA. Severe rebound of spinal cord multiple sclerosis activity after fingolimod withdrawal. <i>Clinical and Experimental Neuroimmunology</i> . 2014;5(3):378-9.	Design not relevant. Case study
Ferrè L, Moiola L, Sangalli F, Radaelli M, Barcella V, Comi G, et al. Recurrence of disease activity after repeated Natalizumab withdrawals. <i>Neurol Sci</i> . 2015;36(3):465-7.	No relevant comparison
Lanzillo R, Bonavita S, Quarantelli M, Vacca G, Lus G, Amato L, et al. Natalizumab is effective in multiple sclerosis patients switching from other disease modifying therapies in clinical practice. <i>Neurological Sciences</i> . 2013;34(4):521-8.	No relevant comparison
Putzki N, Yaldizli O, Maurer M, Cursiefen S, Kuckert S, Klawe C, et al. Efficacy of natalizumab in second line therapy of relapsing-remitting multiple sclerosis: Results from a multi-center study in German speaking countries. <i>European Journal of Neurology</i> . 2010;17(1):31-7.	No relevant comparison
Fragoso YD, Alves-Leon SV, Becker J, Brooks JBB, Correa EC, Damasceno A, et al. Safety of switching from natalizumab straight into fingolimod in a group of JCV-positive patients with multiple sclerosis. <i>Arquivos de Neuro-Psiquiatria</i> . 2016;74(8):650-2.	No relevant outcomes

Reference	Reason for exclusion
Iaffaldano P, Viterbo RG, Trojano M. Natalizumab discontinuation is associated with a rebound of cognitive impairment in multiple sclerosis patients. <i>J Neurol</i> . 2016;263(8):1620-5.	No relevant outcomes
Laroni A, Brogi D, Milesi V, Abate L, Uccelli A, Mancardi GL. Early switch to fingolimod may decrease the risk of disease recurrence after natalizumab interruption. <i>Multiple Sclerosis Journal</i> . 2013;19(9):1236-7.	No relevant outcomes
Prosperini L, Annovazzi P, Capobianco M, Capra R, Buttari F, Gasperini C, et al. Natalizumab discontinuation in patients with multiple sclerosis: Profiling risk and benefits at therapeutic crossroads. <i>Mult Scler</i> . 2015;21(13):1713-22.	No relevant outcomes
Iuliano G, Napoletano R. Switching from drug to drug in multiple sclerosis: A longitudinal evaluation. <i>Rivista Italiana di Neurobiologia</i> . 2008;5(3):167-73.	Non-English language paper
Klotz L, Grutze B, Eveslage M, Deppe M, Gross CC, Kirstein L, et al. Assessment of immune functions and MRI disease activity in relapsing-remitting multiple sclerosis patients switching from natalizumab to fingolimod (ToFingo-Successor). <i>BMC Neurology</i> . 2015;15(96).	Study protocol

Review question 9

Reference	Reason for exclusion
Kister I, Spelman T, Alroughani R, Lechner-Scott J, Duquette P, Grand'maison F, et al. Are stable MS patients who stop their disease-modifying therapy (DMT) at increased risk for relapses and disability progression compared to patients who continue on DMTs? A propensity-score matched analysis of the MSBase registrants. <i>Multiple Sclerosis</i> . 2015;1:17-18.	Same sample as Kister 2016

Review question 10

Reference	Reason for exclusion
Hellwig K, Gold R. Glatiramer acetate and interferon-beta throughout gestation and postpartum in women with multiple sclerosis. <i>J Neurol</i> . 2011;258: 502–503.	<10 participants per arm
Schneider H, Weber CE, Hellwig K, Schrotten H, Tenenbaum T. Natalizumab treatment during pregnancy - effects on the neonatal immune system. <i>Acta Neurol Scand</i> . 2013;127(1):e1-4.	<10 participants per arm
Vukusic S, Durand-Dubief F, Benoit A, Marignier R, Frangoulis B, Confavreux C. Natalizumab for the prevention of post-partum relapses in women with multiple sclerosis. <i>Mult Scler</i> . 2015;21(7):953-5.	<10 participants per arm
Fragoso YD, Finkelsztejn A, Comini-Frota ER, et al. Pregnancy and multiple sclerosis: the initial results from a Brazilian database. <i>Arq Neuropsiquiatr</i> . 2009;67:657– 660.	Case series design
Fragoso YD, Finkelsztejn A, Kaimen-Maciel DR, et al. Long-term use of glatiramer acetate by 11 pregnant women with multiple sclerosis: a retrospective, multicentre case series. <i>CNS Drugs</i> . 2010;24:969 –976.	Case series design
Finkelsztejn A, Fragoso YD, Ferreira ML, et al. The Brazilian database on pregnancy in multiple sclerosis. <i>Clin Neurol Neurosurg</i> . 2011;113:277–280	Case series design
Haghikia A, Langer-Gould A, Rellensmann G, Schneider H, Tenenbaum T, Elias-Hamp B, et al. Natalizumab use during the third trimester of pregnancy. <i>JAMA Neurol</i> . 2014;71(7):891-5.	Case series design
Salminen HJ, Leggett H, Boggild M. Glatiramer acetate exposure in pregnancy: preliminary safety and birth outcomes. <i>J Neurol</i> . 2011;257:2020 –2023.	Case series design
Sandberg-Wollheim M, Frank D, Goodwin TM, et al. Pregnancy outcomes during treatment with interferon -1a in patients with multiple sclerosis. <i>Neurology</i> . 2005;65:802–806	Case series design
Sandberg-Wollheim M, Alteri E, Stam Moraga M, Kornmann G. Pregnancy outcomes in	Case series design

multiple sclerosis following subcutaneous interferon beta-1a therapy. <i>Mult Scler.</i> 2011;17:423– 430.	
Sempere AP, Berenguer-Ruiz L, Feliu-Rey E. Rebound of disease activity during pregnancy after withdrawal of fingolimod. <i>Eur J Neurol.</i> 2013;20(8):e109-10.	Letter to the editor - no data available
Portaccio E, Ghezzi A, Hakiki B, Sturchio A, Martinelli V, Moiola L, et al. Postpartum relapses increase the risk of disability progression in multiple sclerosis: the role of disease modifying drugs. <i>J Neurol Neurosurg Psychiatry.</i> 2014;85(8):845-50.	No relevant outcomes
Hellwig K, Haghikia A, Gold R. Parenthood and immunomodulation in patients with multiple sclerosis. <i>J Neurol.</i> 2010;257:580 –583.	Population not relevant