

Appendix 2_ Search strategies

Review Questions 1-3

Databases: Central, Embase, Medline, PreMedline, PsycINFO
Date Range: inception to December 2015
<p>Hits Deduped: 6217 (Central: 1808; Other: 4409) Undeduped: 9532 (Central: 2250; Other: 7282)</p> <p><i>Notes: references excluded from Central's screen for reports of trials (n2940) imported into a separate EndNote Library; these are unlikely to need a sift.</i></p>

- Embase, Medline, PreMedline, PsycINFO - OVID

#	searches
1	exp *multiple sclerosis/ or *myelitis/
2	1 use emez
3	exp multiple sclerosis/ or myelitis, transverse/
4	3 use mesz, prem
5	exp multiple sclerosis/ or myelitis/
6	5 use psyh
7	(((disseminated or insular or multiple or multiplex) adj2 scleros*) or chariot disease or encephalomyelitis disseminate or transverse myelitis).ti,ab. or ms.ti.
8	or/2,4,6-7
9	((disease adj2 modif* adj2 (agent* or drug* or therap* or treat*)) or ((immunomodulat* or immunosuppress* or (immun* adj (modulat* or suppress*))) adj2 (agent* or drug* or therap* or treat*))).ti,ab.
10	interferon beta serine.sh. use emez
11	interferon-beta.sh. use mesz, prem or interferon type i.sh. use mesz, prem
12	<u>(beneseron or beta 1b interferon or beta1b interferon or beta interferon or betaferon or betaseron or extavia or fiblaferon or fibroblast interferon or ifnb or ifn b or ifn beta or ifnbeta or interferon beta or interferon fibroblast or rifn beta 1b or rifn beta1b).ti,ab.</u>
13	or/10-12
14	beta1a interferon.sh. use emez or recombinant interferon.sh. use emez
15	interferon-beta.sh. use mesz, prem or interferon type i.sh. use mesz, prem

#	searches
16	(avonex or beta 1a interferon or beta1a interferon or cinnovex or ifn a or ifna or rebif or rifn beta).ti,ab.
17	or/14-16
18	peginterferon beta1a.sh. use emez
19	(beta 1a peginterferon or beta1a peginterferon or peginterferon beta 1a or peginterferon beta1a or (pegylated adj2 interferon beta 1a) or (pegylated adj2 interferon beta1a) or plegridy or (peginf or peg inf)).ti,ab.
20	or/18-19
21	glatiramer.sh. use emez
22	(cop 1 or copaxone or copolymer 1 or copolymer cop 1 or copolymer i or glatiramer or glatopa).ti,ab.
23	or/21-22
24	teriflunomide.sh. use emez
25	(aubagio or teriflunomid*).ti,ab.
26	or/24-25
27	fumaric acid dimethyl ester.sh. use emez
28	fumarates.sh. use mesz, prem
29	(dimethyl fumarate or dimetil fumarate or dimethylfumarate or dimetilfumarate or panaclar or tecfidera or trans butenedioic acid dimethyl ester or tecfidera).ti,ab.
30	or/27-29
31	fingolimod.sh. use emez
32	(fingolimod* or gilenia or gilenya).ti,ab.
33	or/31-32
34	natalizumab.sh. use emez
35	(antegren or natalizumab or tysabri).ti,ab.
36	or/34-35
37	alemtuzumab.sh. use emez
38	(alemtuzumab or campath or cd52 monoclonal antibody or emtrada or lemtrada or mabcampath or monoclonal antibody cd52).ti,ab.
39	or/37-38
40	daclizumab.sh. use emez
41	(daclizumab or dacliximab or dacluzimab or zenapax).ti,ab.
42	or/40-41
43	ocrelizumab.sh. use emez
44	(monoclonal antibod* or ocrelizumab or rhumab 2h7).ti,ab.

#	searches
45	or/43-44
46	mitoxantrone.sh. use emez,mesz
47	(dhad or dhaq or domitrone or elsep or formyxan or misostol or mitoxanthron* or mitoxantron* or mitoxigen or mitozantron* or mitroxantron* or mitroxon* or neotalem or norexan or novanthron* or novantron* or oncotron* or onkotron* or quinizarin* or ralenova or pralifan*).ti,ab.
48	or/46-47
49	cyclophosphamide.sh. use emez,mesz
50	(alkyroxan or carloxan or ciclofosfamida or ciclolen or cicloxal or clafen or cyclo cell or cycloblastin* or cyclofos amide or cyclofosfamid* or cyclofosfamid* or cyclophar or cyclophosphamid* or cyclophosphan* or cyclostin or cycloxan or cyphos or cytophosphan* or cytoxan or endocyclo phosphate or endoxan* or endoxon asta or enduxan or genoxal or ledoxan or ledoxina or mitoxan or neosan or neosar or noristan or procytox or procytoxide or semdoxan or sendoxan or syklofosfamid).ti,ab.
51	or/49-50
52	azathioprine*.sh. use emez,mesz
53	(arathioprin or arathioprine or aza q or azafalk or azahexal or azamedac or amazun or amazune or azanin or azapin or azapress or azaprine or azarex or azasan or azathiodura or azathiopine or azathioprim or azathioprin* or azathiopurin* or azathropsin* or azatioprina or azatox or azatilem or azopi or azoran or azothioprin* or colinsan or immuran or immurel or immuthera or imunen or imuprin or imuran or imurane or imurek or imurel or imuren or thioazeprin* or thioprin* or transimun* or zytrim).ti,ab.
54	or/52-53
55	((corticosteroid* or steroid*) adj2 puls*).ti,ab.
56	or/9,13,17,20,23,26,30,33,36,39,42,45,48,51,54-55
57	exp "clinical trial (topic)"/ or exp clinical trial/ or crossover procedure/ or double blind procedure/ or placebo/ or randomization/ or random sample/ or single blind procedure/
58	57 use emez
59	exp clinical trial/ or exp "clinical trials as topic"/ or cross-over studies/ or double-blind method/ or placebos/ or random allocation/ or single-blind method/
60	59 use mesz, prem
61	(clinical trials or placebo or random sampling).sh,id.
62	61 use psych
63	(clinical adj2 trial*).ti,ab.
64	(crossover or cross over).ti,ab.
65	((single* or doubl* or trebl* or tripl*) adj2 blind*) or mask* or dummy or doubleblind* or singleblind* or trebleblind* or tripleblind*).ti,ab.

#	searches
66	(placebo* or random*).ti,ab.
67	treatment outcome*.md. use psych
68	animals/ not human*.mp. use emez
69	animal*/ not human*/ use mesz, prem
70	(animal not human).po. use psych
71	(or/58,60,62-67) not (or/68-70)
72	8 and 56 and 71
73	(2010* or 2011* or 2012* or 2013* or 2014* or 2015* or 2016*).dd,yr. use emez
74	(2005* or 2006* or 2007* or 2008* or 2009* or 2010* or 2011* or 2012* or 2013* or 2014* or 2015* or 2016*).dd,yr. use mesz, prem
75	72 and (73 or 74)
76	72
77	limit 76 to yr="1860 - 2010"
78	76 not 77
79	remove duplicates from 77
80	remove duplicates from 78
81	from 79 keep 3938-3995
82	from 80 keep 3212-3317
83	from 72 keep 9037-9458
84	or/75,81-83

- CENTRAL - Wiley

#	searches
1	MeSH descriptor: [Multiple Sclerosis] explode all trees
2	MeSH descriptor: [Myelitis, Transverse] this term only
3	((disseminated or insular or multiple or multiplex) near/2 scleros*) or "chariot disease" or "encephalomyelitis disseminate" or "transverse myelitis"):ti,ab,kw. or ms:ti
4	#1 or #2 or #3
5	((disease near/2 modif* near/2 (agent* or drug* or therap* or treat*)) or ((immunomodulat* or immunosuppress* or (immun* near/1 (modulat* or suppress*))) near/2 (agent* or drug* or therap* or treat*)):ti,ab,kw.
6	MeSH descriptor: [Interferon-beta] this term only

#	searches
7	MeSH descriptor: [Interferon Type I] this term only
8	(beneseron or "beta 1b interferon" or "beta1b interferon" or "beta interferon" or betaferon or betaseron or extavia or fiblaferon or "fibroblast interferon" or "ifn b" or ifnb or "ifn beta" or ifnbeta or "interferon beta" or "interferon fibroblast" or "rifn beta 1b" or "rifn beta1b"):ti,ab,kw.
9	#6 or #7 or #8
10	MeSH descriptor: [Interferon-beta] this term only
11	MeSH descriptor: [Interferon Type I] this term only
12	(avonex or "beta 1a interferon" or "beta1a interferon" or cinnovex or "ifn a" or ifna or rebif or "rifn beta"):ti,ab,kw.
13	#10 or #11 or #12
14	("beta 1a peginterferon" or "beta1a peginterferon" or "peginterferon beta 1a" or "peginterferon beta1a" or (pegylated near/2 "interferon beta 1a") or (pegylated near/2 "interferon beta1a") or plegridy or (peginf or "peg inf")):ti,ab,kw.
15	("cop 1" or copaxone or "copolymer 1" or "copolymer cop 1" or "copolymer I" or glatiramer or glatopa):ti,ab,kw.
16	(aubagio or teriflunomid*):ti,ab,kw.
17	MeSH descriptor: [Fumarates] this term only
18	("dimethyl fumarate" or "dimetil fumarate" or dimethylfumarate or dimetilfumarate or panaclar or tecfidera or "trans butenedioic acid dimethyl ester" or tecfidera):ti,ab,kw.
19	#17 or #18
20	(fingolimod* or gilenia or gilenya):ti,ab,kw.
21	(antegren or natalizumab or tysabri):ti,ab,kw.
22	(alemtuzumab or campath or "cd52 monoclonal antibody" or emtrada or lemtrada or mabcampath or "monoclonal antibody cd52"):ti,ab,kw.
23	(daclizumab or dacliximab or dacluzimab or zenapax):ti,ab,kw.
24	("monoclonal antibod*" or ocrelizumab or "rhumab 2h7"):ti,ab,kw.
25	MeSH descriptor: [Mitoxantrone] this term only
26	(dhad or dhaq or domitrone or elsep or formyxan or misostol or mitoxanthron* or mitoxantron* or mitoxgen or mitozantron* or mitroxantron* or mitroxon* or neotalem or norexan or novanthron* or novantron* or oncotron* or onkotron* or quinizarin* or ralenova or pralifan*):ti,ab,kw.
27	#25 or #26
28	MeSH descriptor: [Cyclophosphamide] this term only
29	(alkyroxan or carloxan or ciclofosfamida or ciclolen or cicloxal or clafen or "cyclo cell" or cycloblastin* or "cyclofos amide" or cyclofosamid* or cyclofosphamid* or cyclophar or cyclophosphamid* or

#	searches
	cyclophosphan* or cyclostin or cyclozan or cyphos or cytophosphan* or cytoxan or endocyclo phosphate or endoxan* or “endoxon asta” or enduxan or genoxal or ledoxan or ledoxina or mitoxan or neosan or neosar or noristan or procytox or procytoxide or semdoxan or sendoxan or syklofosfamid):ti,ab,kw.
30	#28 or #29
31	MeSH descriptor: [Azathioprine] this term only
32	(arathioprin or arathioprine or “aza q” or azafalk or azahexal or azamedac or azamun or azamune or azanin or azapin or azapress or azapriner or azarex or azasan or azathiodura or azathiopine or azathioprim or azathioprin* or azathiopurin* or azathropsin* or azatioprina or azatox or azatrim or azopi or azoran or azothioprin* or colinsan or immuran or immurel or immuthera or imunen or imuprin or imuran or imurane or imurek or imurel or imuren or thioazeprin* or thioprin* or transimun* or zytrim):ti,ab,kw.
33	#31 or #32
34	((corticosteroid* or steroid*) near/2 puls*):ti,ab,kw.
35	#5 or #9 or #13 or #14 or #15 or #16 or #19 or #20 or #21 or #22 or #23 or #24 or #27 or #30 or #33 or #34
36	#4 and #35

Databases: Embase, Medline, PsycINFO (OVID)
Date Range: inception to June 2017
Hits Deduped: 596 Undeduped: 710

- **Embase**

#	Searches
1	exp *multiple sclerosis/ or *myelitis/
2	((disseminated or insular or multiple or multiplex) adj2 scleros*) or chariot disease or encephalomyelitis disseminate or transverse myelitis).ti,ab. or ms.ti.
3	#1 or #2
4	cladribine/
5	(cladribin* or litak or leustat* or Biodribin or Hemobine or Intocel or Movectro).mp.
6	(2-Chloro-2'-deoxyadenosine or CdA or 2-CdA).mp.

#	Searches
7	#4 or #5 or #6
8	exp "clinical trial (topic)"/ or exp clinical trial/ or crossover procedure/ or double blind procedure/ or placebo/ or randomization/ or random sample/ or single blind procedure/
9	(clinical adj2 trial*).ti,ab.
10	(crossover or cross over).ti,ab.
11	(((single* or doubl* or trebl* or tripl*) adj2 blind*) or mask* or dummy or doubleblind* or singleblind* or trebleblind* or tripleblind*).ti,ab.
12	(placebo* or random*).ti,ab.
13	animals/ not human*.mp.
14	(or/#8-12) not #13
15	#3 and #7 and #14

- **Medline**

#	Searches
1	exp multiple sclerosis/ or myelitis, transverse/
2	(((disseminated or insular or multiple or multiplex) adj2 scleros*) or chariot disease or encephalomyelitis disseminate or transverse myelitis).ti,ab. or ms.ti.
3	#1 or #2
4	Cladribine/
5	(cladribin* or litak or leustat* or Biodribin or Hemobine or Intocel or Movectro).mp.
6	(2-Chloro-2'-deoxyadenosine or CdA or 2-CdA).mp.
7	#4 or #5 or #6
8	exp clinical trial/ or exp "clinical trials as topic"/ or cross-over studies/ or double-blind method/ or placebos/ or random allocation/ or single-blind method/
9	(clinical adj2 trial*).ti,ab.
10	(crossover or cross over).ti,ab.
11	(((single* or doubl* or trebl* or tripl*) adj2 blind*) or mask* or dummy or doubleblind* or singleblind* or trebleblind* or tripleblind*).ti,ab.
12	(placebo* or random*).ti,ab.
14	#8 or #9 or #10 or #11 or #12
15	#3 and #7 and #13

- PsychINFO

#	Searches
1	exp multiple sclerosis/ or myelitis/
2	(((disseminated or insular or multiple or multiplex) adj2 scleros*) or chariot disease or encephalomyelitis disseminate or transverse myelitis).ti,ab. or ms.ti.
3	#1 or #2
4	(cladribin* or litak or leustat* or Biodribin or Hemobine or Intocel or Movectro).mp.
5	(2-Chloro-2'-deoxyadenosine or CdA or 2-CdA).mp.
6	#4 or #5
7	(clinical trials or placebo or random sampling).sh,id.
8	(clinical adj2 trial*).ti,ab.
9	(crossover or cross over).ti,ab.
10	(((single* or doubl* or trebl* or tripl*) adj2 blind*) or mask* or dummy or doubleblind* or singleblind* or trebleblind* or tripleblind*).ti,ab.
11	(placebo* or random*).ti,ab.
12	treatment outcome*.md.
14	#7 or #8 or #9 or #10 or #11 or #12
15	#5 and #6 and #13

Review Question 4

Update of Rio 2016 review
Databases: PubMed, Medline, Embase, Web of SCIENCE
Date Range: Jan 2014 until December 2016
Hits Deduped: 1470 Undeduped: 1653

- Pubmed

#	Searches
1	((("Multiple Sclerosis"[Mesh]) OR ("Myelitis, Transverse"[Mesh:noexp]) OR ("Demyelinating Diseases"[Mesh:noexp]) OR ("Encephalomyelitis, Acute Disseminated"[Mesh:noexp]) OR ("Optic Neuritis"[Mesh])) OR (("multiple sclerosis") OR ("neuromyelitis optica") OR ("transverse myelitis") OR (encephalomyelitis) OR (devic) OR ("optic neuritis")) OR ("demyelinating disease*") OR ("acute disseminated encephalomyelitis")))
2	((("Interferon-beta"[Mesh]) OR ("Interferon-beta*") OR (rebif OR avonex OR betaseron OR betaferon)) OR ((copolymer-1 OR cop-1 OR copaxone OR "glatiramer acetate" OR glatiramer))
3	#1 AND #2
4	((response OR respond* OR failure OR non-respon* OR resist* OR fail* OR refractory) AND ((Expanded Disability Status Scale OR EDSS) OR ("magnetic resonance imaging" OR "MRI" OR "magnetic resonance" OR "MR" OR "nuclear magnetic resonance" OR "NMR") OR relapse))
5	#3 AND #4
6	(randomized controlled trial [pt] OR controlled clinical trial[pt] OR randomized[tiab] OR randomised[tiab] OR randomization[tiab] OR randomisation[tiab] OR placebo[tiab] OR drug therapy[sh] OR randomly[tiab] OR trial[tiab] OR groups[tiab] OR Clinical trial[pt] OR "clinical trial"[tw] OR "clinical trials"[tw] OR "evaluation studies"[Publication Type] OR "evaluation studies as topic"[MeSH Terms] OR "evaluation study"[tw] OR evaluation studies[tw] OR "intervention studies"[MeSH Terms] OR "intervention study"[tw] OR "intervention studies"[tw] OR "cohort studies"[MeSH Terms] OR cohort[tw] OR "longitudinal studies"[MeSH Terms] OR "longitudinal"[tw] OR longitudinally[tw] OR "prospective"[tw] OR prospectively[tw] OR "follow up"[tw] OR "comparative study"[PT] OR "comparative study"[tw] OR systematic[subset] OR " meta-analysis "[PT] OR " meta-analysis as topic"[MeSH Terms] OR " meta-analysis "[tw] OR "meta-analyses"[tw]) NOT (Editorial[PT] OR Letter[PT] OR Case Reports[PT] OR Comment[PT]) NOT (animals[Mesh] NOT humans[Mesh])

#	Searches
7	#5 AND #6
8	((Epidemiologic Studies[Mesh:noexp] OR case-control studies[Mesh] OR cohort studies[Mesh] OR seroepidemiologic studies[Mesh]) OR cohort OR cohorts OR observ* OR case-control OR non-randomized OR nonrandomized OR unrandomized OR prospectiv* OR retrospectiv* OR follow* OR longitudinal OR (cases AND controls)) AND (odds ratio[Mesh] OR "odds ratio" OR "relative risk" OR risk OR risks OR associat* OR causality OR etiology OR epidemiology OR ethnology OR probability OR inciden*)
9	#5 AND #8
10	#7 OR #9

- Medline, Embase (SCOPUS)

#	Searches
1	TITLE-ABS-KEY (((("Multiple Sclerosis") OR ("Myelitis, Transverse") OR ("Demyelinating Diseases") OR ("Encephalomyelitis, Acute Disseminated") OR ("Optic Neuritis"))) OR (((("multiple sclerosis") OR ("neuromyelitis optica") OR ("transverse myelitis") OR (encephalomyelitis) OR (devic) OR ("optic neuritis"))) OR ("demyelinating disease*") OR ("acute disseminated encephalomyelitis"))))
2	TITLE-ABS-KEY (((("Interferon-beta") OR ("Interferon-beta*") OR (rebif OR avonex OR betaseron OR betaferon)) OR ((copolymer-1 OR cop-1 OR copaxone OR "glatiramer acetate" OR glatiramer)))
3	#1 AND #2
4	TITLE-ABS-KEY ((response OR respond* OR failure OR non-respon* OR resist* OR fail* OR refractory) AND ((Expanded Disability Status Scale OR EDSS) OR ("magnetic resonance imaging" OR "MRI" OR "magnetic resonance" OR "MR" OR "nuclear magnetic resonance" OR "NMR")))
5	#3 AND #4
6	TITLE-ABS-KEY (" randomized controlled trial " OR "controlled clinical trial" OR randomized OR randomised OR randomization OR randomisation OR placebo OR "drug therapy" OR randomly OR trial OR groups OR "clinical trial" OR "clinical trials" OR "evaluation studies" OR "evaluation study" OR "intervention study" OR "intervention studies" OR cohort OR longitudinal OR longitudinally OR "prospective" OR prospectively OR "follow up" OR "comparative study" OR systematic OR " meta-analysis " OR "meta-analyses") AND (LIMIT-TO(DOCTYPE, "ar") OR LIMIT-TO(DOCTYPE, "re") OR LIMIT-TO(DOCTYPE, "sh"))
7	#5 AND #6

#	Searches
8	TITLE-ABS-KEY (("Epidemiologic Stud*" OR "seroepidemiologic stud*") OR cohort OR cohorts OR observ* OR "case-control" OR non-randomized OR nonrandomized OR unrandomized OR prospectiv* OR retrospectiv* OR follow* OR longitudinal OR (cases AND controls)) AND ("odds ratio" OR "relative risk" OR risk OR risks OR associat* OR causality OR etiology OR epidemiology OR ethnology OR probability OR inciden*)
9	#5 AND #8
10	#7 OR #9

- Web of SCIENCE (Web of Science™ Core Collection, BIOSIS Previews®, MEDLINE®, Current Contents Connect)

#	Searches
1	TS = (((("Multiple Sclerosis") OR ("Myelitis, Transverse") OR ("Demyelinating Diseases") OR ("Encephalomyelitis, Acute Disseminated") OR ("Optic Neuritis")) OR (((("multiple sclerosis") OR ("neuromyelitis optica") OR ("transverse myelitis") OR (encephalomyelitis) OR (devic) OR ("optic neuritis")) OR ("demyelinating disease*") OR ("acute disseminated encephalomyelitis"))))
2	TS = (((("Interferon-beta") OR ("Interferon-beta*") OR (rebif OR avonex OR betaseron OR betaferon)) OR ((copolymer-1 OR cop-1 OR copaxone OR "glatiramer acetate" OR glatiramer)))
3	#1 AND #2
4	TS = ((response OR respond* OR failure OR non-respon* OR resist* OR fail* OR refractory) AND ((Expanded Disability Status Scale OR EDSS) OR ("magnetic resonance imaging" OR "MRI" OR "magnetic resonance" OR "MR" OR "nuclear magnetic resonance" OR "NMR")))
5	#3 AND #4
6	TS = (" randomized controlled trial " OR "controlled clinical trial" OR randomized OR randomised OR randomization OR randomisation OR placebo OR "drug therapy" OR randomly OR trial OR groups OR "clinical trial" OR "clinical trials" OR "evaluation studies" OR "evaluation study" OR "intervention study" OR "intervention studies" OR cohort OR longitudinal OR longitudinally OR "prospective" OR prospectively OR "follow up" OR "comparative study" OR systematic OR " meta-analysis " OR "meta-analyses")
7	#5 AND #6
8	TS = (("Epidemiologic Stud*" OR "seroepidemiologic stud*") OR cohort OR cohorts OR observ* OR "case-control" OR non-randomized OR nonrandomized OR unrandomized OR prospectiv* OR retrospectiv* OR follow* OR longitudinal OR (cases AND controls)) AND ("odds ratio" OR "relative risk" OR risk OR

#	Searches
	risks OR associat* OR causality OR etiology OR epidemiology OR ethnology OR probability OR inciden*)
9	#5 AND #8
10	#7 OR #9

Search for 'No Evidence of Disease Activity'

Databases: Embase, Medline, PsycINFO

Date Range: inception until January 2017

Hits

Deduped: 244

Undeduped: 267

- Embase

#	searches
1	exp *multiple sclerosis/ or *myelitis/
2	((disseminated or insular or multiple or multiplex) adj2 scleros*) or chariot disease or encephalomyelitis disseminate or transverse myelitis).ti,ab. or ms.ti.
3	1 or 2
4	((disease adj2 modif* adj2 (agent* or drug* or therap* or treat*)) or ((immunomodulat* or immunosuppress* or (immun* adj (modulat* or suppress*))) adj2 (agent* or drug* or therap* or treat*))).ti,ab.
5	interferon beta serine.sh.
6	(beneseron or beta 1b interferon or beta1b interferon or beta interferon or betaferon or betaseron or extavia or fiblaferon or fibroblast interferon or ifnb or ifn b or ifn beta or ifnbeta or interferon beta or interferon fibroblast or rifn beta 1b or rifn beta1b).ti,ab.
7	4 or 5 or 6
8	(beta1a interferon or recombinant interferon).sh.
9	(avonex or beta 1a interferon or beta1a interferon or cinnovex or ifn a or ifna or rebif or rifn beta).ti,ab.
10	8 or 9
11	peginterferon beta1a.sh.
12	<u>(beta 1a peginterferon or beta1a peginterferon or peginterferon beta 1a or peginterferon beta1a or (pegylated adj2 interferon beta 1a) or (pegylated adj2 interferon beta1a) or plegridy or (peginf or peg inf)).ti,ab.</u>
13	11 or 12
14	glatiramer.sh.
15	(cop 1 or copaxone or copolymer 1 or copolymer cop 1 or copolymer i or glatiramer or glatopa).ti,ab.
16	14 or 15

17	teriflunomide.sh.
18	(aubagio or teriflunomid*).ti,ab.
19	17 or 18
20	fumaric acid dimethyl ester.sh.
21	(dimethyl fumarate or dimetil fumarate or dimethylfumarate or dimetilfumarate or panaclar or tecfidera or trans butenedioic acid dimethyl ester or tecfidera).ti,ab.
22	20 or 21
23	fingolimod.sh.
24	(fingolimod* or gilenia or gilenya).ti,ab.
25	natalizumab.sh.
26	(antegren or natalizumab or tysabri).ti,ab.
27	23 or 24
28	25 or 26
29	alemtuzumab.sh.
30	(alemtuzumab or campath or cd52 monoclonal antibody or emtrada or lemtrada or mabcampath or monoclonal antibody cd52).ti,ab.
31	29 or 30
32	daclizumab.sh.
33	(daclizumab or dacliximab or dacluzimab or zenapax).ti,ab.
34	32 or 33
35	mitoxantrone.sh.
36	(dhad or dhaq or domitrone or elsep or formyxan or misostol or mitoxanthron* or mitoxantron* or mitoxgen or mitozantron* or mitroxantron* or mitroxon* or neotalem or norexan or novanthron* or novantron* or oncotron* or onkotron* or quinizarin* or ralenova or pralifan*).ti,ab.
37	35 or 36
38	7 or 10 or 13 or 16 or 19 or 22 or 27 or 28 or 31 or 34 or 37
39	(evidence of disease activity or NEDA or EDA or disease free status or disease-free status).mp.
40	3 and 38 and 39

- Medline

#	searches
1	exp multiple sclerosis/ or myelitis, transverse/
2	((disseminated or insular or multiple or multiplex) adj2 scleros*) or chariot disease or encephalomyelitis disseminate or transverse myelitis).ti,ab. or ms.ti.

#	searches
3	1 or 2
4	((disease adj2 modif* adj2 (agent* or drug* or therap* or treat*)) or ((immunomodulat* or immunosuppress* or (immun* adj (modulat* or suppress*))) adj2 (agent* or drug* or therap* or treat*))).ti,ab.
5	(interferon-beta or interferon type i).sh.
6	(beneseron or beta 1b interferon or beta1b interferon or beta interferon or betaferon or betaseron or extavia or fiblaferon or fibroblast interferon or ifnb or ifn b or ifn beta or ifnbeta or interferon beta or interferon fibroblast or rifn beta 1b or rifn beta1b).ti,ab.
7	(interferon-beta or interferon type i).sh.
8	(avonex or beta 1a interferon or beta1a interferon or cinnovex or ifn a or ifna or rebif or rifn beta).ti,ab.
9	(beta 1a peginterferon or beta1a peginterferon or peginterferon beta 1a or peginterferon beta1a or (pegylated adj2 interferon beta 1a) or (pegylated adj2 interferon beta1a) or plegridy or (peginf or peg inf)).ti,ab.
10	(cop 1 or copaxone or copolymer 1 or copolymer cop 1 or copolymer i or glatiramer or glatopa).ti,ab.
11	(aubagio or teriflunomid*).ti,ab.
12	<u>fumarates.sh.</u>
13	(dimethyl fumarate or dimetil fumarate or dimethylfumarate or dimetilfumarate or panaclar or tecfidera or trans butenedioic acid dimethyl ester or tecfidera).ti,ab.
14	(fingolimod* or gilenia or gilenya).ti,ab.
15	(antegren or natalizumab or tysabri).ti,ab.
16	(alemtuzumab or campath or cd52 monoclonal antibody or emtrada or lemtrada or mabcampath or monoclonal antibody cd52).ti,ab.
17	(daclizumab or dacliximab or dacluzimab or zenapax).ti,ab.
18	mitoxantrone.sh.
19	(dhad or dhaq or domitrone or elsep or formyxan or misostol or mitoxanthron* or mitoxantron* or mitoxgen or mitozantron* or mitroxantron* or mitroxon* or neotalem or norexan or novanthron* or novantron* or oncotron* or onkotron* or quinizarin* or ralenova or pralifan*).ti,ab.
20	4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19
21	(evidence of disease activity or NEDA or EDA or disease free status or disease-free status).mp.
22	3 and 20 and 21

- PsychInfo

#	searches
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#	searches
1	exp multiple sclerosis/ or myelitis/
2	((disseminated or insular or multiple or multiplex) adj2 scleros*) or chariot disease or encephalomyelitis disseminate or transverse myelitis).ti,ab. or ms.ti.
3	1 or 2
4	((disease adj2 modif* adj2 (agent* or drug* or therap* or treat*)) or ((immunomodulat* or immunosuppress* or (immun* adj (modulat* or suppress*))) adj2 (agent* or drug* or therap* or treat*))).ti,ab.
5	(beneseron or beta 1b interferon or beta1b interferon or beta interferon or betaferon or betaseron or extavia or fiblaferon or fibroblast interferon or ifnb or ifn b or ifn beta or ifnbeta or interferon beta or interferon fibroblast or rfn beta 1b or rfn beta1b).ti,ab.
6	(avonex or beta 1a interferon or beta1a interferon or cinnovex or ifn a or ifna or rebif or rfn beta).ti,ab.
7	(beta 1a peginterferon or beta1a peginterferon or peginterferon beta 1a or peginterferon beta1a or (pegylated adj2 interferon beta 1a) or (pegylated adj2 interferon beta1a) or plegridy or (peginf or peg inf)).ti,ab.
8	(cop 1 or copaxone or copolymer 1 or copolymer cop 1 or copolymer i or glatiramer or glatopa).ti,ab.
9	(aubagio or teriflunomid*).ti,ab.
10	(dimethyl fumarate or dimetil fumarate or dimethylfumarate or dimetilfumarate or panaclar or tecfidera or trans butenedioic acid dimethyl ester or tecfidera).ti,ab.
11	(fingolimod* or gilenia or gilenya).ti,ab.
12	<u>(alemtuzumab or campath or cd52 monoclonal antibody or emtrada or lemtrada or mabcampath or monoclonal antibody cd52).ti,ab.</u>
13	(daclizumab or dacliximab or dacluzimab or zenapax).ti,ab.
14	(dhad or dhaq or domitrone or elsep or formyxan or misostol or mitoxanthron* or mitoxantron* or mitoxgen or mitozantron* or mitroxantron* or mitroxon* or neotalem or norexan or novanthron* or novantron* or oncotron* or onkotron* or quinizarin* or ralenova or pralifan*).ti,ab.
15	4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14
16	(evidence of disease activity or NEDA or EDA or disease free status or disease-free status).mp.
17	3 and 15 and 16

Review Question 6-8

Databases: Embase, Medline, PsycINFO
Date Range: inception to December 2015
Hits Deduped: 3779 Undeduped: 3853

#	searches
1	exp *multiple sclerosis/ or *myelitis/
2	1 use emez
3	exp multiple sclerosis/ or myelitis, transverse/
4	3 use mesz
5	exp multiple sclerosis/ or myelitis/
6	5 use psych
7	((disseminated or insular or multiple or multiplex) adj2 scleros*) or chariot disease or encephalomyelitis disseminate or transverse myelitis).ti,ab. or ms.ti.
8	or/56,58,60-61
9	((disease adj2 modif* adj2 (agent* or drug* or therap* or treat*)) or ((immunomodulat* or immunosuppress* or (immun* adj (modulat* or suppress*))) adj2 (agent* or drug* or therap* or treat*))).ti,ab.
10	interferon beta serine.sh. use emez
11	interferon-beta.sh. use mesz or interferon type i.sh. use mesz
12	<u>(beneseron or beta 1b interferon or beta1b interferon or beta interferon or betaferon or betaseron or extavia or fiblaferon or fibroblast interferon or ifnb or ifn b or ifn beta or ifnbeta or interferon beta or interferon fibroblast or rifn beta 1b or rifn beta1b).ti,ab.</u>
13	or/64-66
14	beta1a interferon.sh. use emez or recombinant interferon.sh. use emez
15	interferon-beta.sh. use mesz or interferon type i.sh. use mesz
16	(avonex or beta 1a interferon or beta1a interferon or cinnovex or ifn a or ifna or rebif or rifn beta).ti,ab.
17	or/68-70
18	peginterferon beta1a.sh. use emez
19	(beta 1a peginterferon or beta1a peginterferon or peginterferon beta 1a or peginterferon beta1a or

	(pegylated adj2 interferon beta 1a) or (pegylated adj2 interferon beta1a) or plegridy or (peginf or peg inf).ti,ab.
20	or/72-73
21	glatiramer.sh. use emez
22	(cop 1 or copaxone or copolymer 1 or copolymer cop 1 or copolymer i or glatiramer or glatopa).ti,ab.
23	or/75-76
24	teriflunomide.sh. use emez
25	(aubagio or teriflunomid*).ti,ab.
26	or/78-79 (1940)
27	fumaric acid dimethyl ester.sh. use emez
28	fumarates.sh. use mesz
29	(dimethyl fumarate or dimetil fumarate or dimethylfumarate or dimetilfumarate or panaclar or tecfidera or trans butenedioic acid dimethyl ester or tecfidera).ti,ab.
30	or/81-83
31	fingolimod.sh. use emez
32	(fingolimod* or gilenia or gilenya).ti,ab.
33	or/85-86
34	natalizumab.sh. use emez
35	(antegren or natalizumab or tysabri).ti,ab.
36	or/88-89
37	alemtuzumab.sh. use emez
38	(alemtuzumab or campath or cd52 monoclonal antibody or entrada or lemtrada or mabcampath or monoclonal antibody cd52).ti,ab.
39	or/91-92
40	daclizumab.sh. use emez
41	(daclizumab or dacliximab or dacluzimab or zenapax).ti,ab.
42	or/94-95
43	ocrelizumab.sh. use emez
44	(monoclonal antibod* or ocrelizumab or rhumab 2h7).ti,ab.
45	or/97-98
46	mitoxantrone.sh. use emez,mesz
47	(dhad or dhaq or domitron or elsep or formyxan or misostol or mitoxanthron* or mitoxantron* or mitoxgen or mitozantron* or mitroxantron* or mitroxon* or neotalem or norexan or novanthron* or novantron* or oncotron* or onkotron* or quinizarin* or ralenova or pralifan*).ti,ab.

48	or/100-101
49	or/63,67,71,74,77,80,84,87,90,93,96,99,102
50	(switch* or cessat* or suspen* or stop* or withdraw* or interrupt* or discontin* or treatment strateg* or restart* or re-start* or initiate or de-escalat* or escalat* or second line or second-line).ti,ab.
51	62 and 103 and 104
52	remove duplicates from 105

Review Question 9

Databases: Embase, Medline, PsycINFO (OVID)
Date Range: inception to December 2016
Hits Deduped: 3066 Undeduped: 4323

#	Searches
1	exp *multiple sclerosis/ or *myelitis/
2	1 use emez
3	exp multiple sclerosis/ or myelitis, transverse/
4	3 use mesz
5	exp multiple sclerosis/ or myelitis/
6	5 use psych
7	((disseminated or insular or multiple or multiplex) adj2 scleros*) or chariot disease or encephalomyelitis disseminate or transverse myelitis).ti,ab. or ms.ti.
8	or/2,4,6-7
9	((disease adj2 modif* adj2 (agent* or drug* or therap* or treat*)) or ((immunomodulat* or immunosuppress* or (immun* adj (modulat* or suppress*))) adj2 (agent* or drug* or therap* or treat*))).ti,ab.
10	interferon beta serine.sh. use emez
11	interferon-beta.sh. use mesz or interferon type i.sh. use mesz
12	(beneseron or beta 1b interferon or beta 1b interferon or beta interferon or betaferon or betaseron or extavia or fiblaferon or fibroblast interferon or ifnb or ifn b or ifn beta or ifnbeta or interferon beta or interferon fibroblast or rifn beta 1b or rifn beta 1b).ti,ab. (33090)
13	or/10-12 (49488)
14	beta 1a interferon.sh. use emez or recombinant interferon.sh. use emez (8232)
15	interferon-beta.sh. use mesz or interferon type i.sh. use mesz (23192)
16	(avonex or beta 1a interferon or beta 1a interferon or cinnovex or ifn a or ifna or rebif or rifn beta).ti,ab. (4334)
17	or/14-16 (34429)
18	peginterferon beta 1a.sh. use emez (242)
19	(beta 1a peginterferon or beta 1a peginterferon or peginterferon beta 1a or peginterferon beta 1a or (pegylated adj2 interferon beta 1a) or (pegylated adj2 interferon beta 1a) or plegridy or peginf or peg inf).ti,ab. (466)
20	or/18-19 (590)
21	glatiramer.sh. use emez (6866)
22	(cop 1 or copaxone or copolymer 1 or copolymer cop 1 or copolymer i or glatiramer or glatopa).ti,ab. (5131)
23	or/21-22 (8947)
24	teriflunomide.sh. use emez (1683)
25	(aubagio or teriflunomid*).ti,ab. (912)
26	or/24-25 (1940)
27	fumaric acid dimethyl ester.sh. use emez (1967)
28	fumarates.sh. use mesz (4243)
29	(dimethyl fumarate or dimetil fumarate or dimethylfumarate or dimetilfumarate or panaclar or tecfidera or trans butenedioic acid dimethyl ester or tecfidera).ti,ab. (1821)
30	or/27-29 (6570)
31	fingolimod.sh. use emez (6495)

32	(fingolimod* or gilenia or gilenya).ti,ab. (3841)
33	or/31-32 (7689)
34	or/9,13,17,20,23,26,30,33 (217637)
35	(clinically stable or clinically-stable or stable or clinical stability or clinical-stability or stability or long term or long-term).ti,ab. (3007791)
36	8 and 34 and 35 (4323)
37	remove duplicates from 36 (3066)

Review Question 10

Databases: Embase, Medline, PsycINFO (OVID)
Date Range: inception to December 2016
Hits Deduped: 808 Undeduped: 2033

#	Searches
1	exp *multiple sclerosis/ or *myelitis/
2	1 use emez
3	exp multiple sclerosis/ or myelitis, transverse/
4	3 use mesz
5	exp multiple sclerosis/ or myelitis/
6	5 use psyh
7	((disseminated or insular or multiple or multiplex) adj2 scleros*) or chariot disease or encephalomyelitis disseminate or transverse myelitis).ti,ab. or ms.ti.
8	or/2,4,6-7
9	((disease adj2 modif* adj2 (agent* or drug* or therap* or treat*)) or ((immunomodulat* or immunosuppress* or immun* adj (modulat* or suppress*))) adj2 (agent* or drug* or therap* or treat*))).ti,ab.
10	interferon beta serine.sh. use emez
11	interferon-beta.sh. use mesz or interferon type i.sh. use mesz
12	(beneseron or beta 1b interferon or beta 1b interferon or beta interferon or betaferon or betaseron or extavia or fiblaferon or fibroblast interferon or ifnb or ifn b or ifn beta or ifnbeta or interferon beta or interferon fibroblast or rfn beta 1b or rfn beta 1b).ti,ab.
13	or/10-12
14	beta 1a interferon.sh. use emez or recombinant interferon.sh. use emez
15	interferon-beta.sh. use mesz or interferon type i.sh. use mesz)
16	(avonex or beta 1a interferon or beta 1a interferon or cinnovex or ifn a or ifna or rebif or rfn beta).ti,ab.
17	or/14-16
18	peginterferon beta 1a.sh. use emez
19	(beta 1a peginterferon or beta 1a peginterferon or peginterferon beta 1a or peginterferon beta 1a or (pegylated adj2 interferon beta 1a) or (pegylated adj2 interferon beta 1a) or plegridy or (peginf or peg inf)).ti,ab.
20	or/18-19
21	glatiramer.sh. use emez
22	(cop 1 or copaxone or copolymer 1 or copolymer cop 1 or copolymer i or glatiramer or glatopa).ti,ab.
23	or/21-22
24	teriflunomide.sh. use emez
25	(aubagio or teriflunomid*).ti,ab.)
26	or/24-25
27	fumaric acid dimethyl ester.sh. use emez
28	fumarates.sh. use mesz
29	(dimethyl fumarate or dimetil fumarate or dimethylfumarate or dimetilfumarate or panaclar or tecfidera or trans butenedioic acid dimethyl ester or tecfidera).ti,ab.
30	or/27-29
31	fingolimod.sh. use emez
32	(fingolimod* or gilenia or gilenya).ti,ab.
33	or/31-32

34	natalizumab.sh. use emez
35	(antegren or natalizumab or tysabri).ti,ab.
36	or/34-35
37	alemtuzumab.sh. use emez
38	(alemtuzumab or campath or cd52 monoclonal antibody or emtrada or lemtrada or mabcampath or monoclonal antibody cd52).ti,ab.
39	or/37-38
40	daclizumab.sh. use emez
41	(daclizumab or dacliximab or dacluzimab or zenapax).ti,ab.
42	or/40-41
43	ocrelizumab.sh. use emez
44	(monoclonal antibod* or ocrelizumab or rhumab 2h7).ti,ab.
45	or/43-44
46	mitoxantrone.sh. use emez,mesz
47	(dhad or dhaq or domitrone or elsep or formyxan or misostol or mitoxanthron* or mitoxantron* or mitoxgen or mitozantron* or mitroxantron* or mitroxon* or neotalem or norexan or novanthron* or novantron* or oncotron* or onkotron* or quinizarin* or ralenova or pralifan*).ti,ab.
48	or/46-47
49	or/9,13,17,20,23,26,30,33,36,39,42,45,48
50	(Pregnan* or conception or child development or teratogen* or spermatozoa or ovum or reproduc* or birth or delivery or fetal or foetal or fetus or foetus or neonatal or obstetric* or abortion).mp. [mp=ti, ab, hw, tn, ot, dm, mf, dv, kw, fs, nm, kf, px, rx, ui, tc, id, tm]
51	8 and 49 and 50
52	limit 51 to yr="2012 -Current"
53	remove duplicates from 52