ECTRIMS
EUROPEAN COMMITTEE FOR TREATMENT AND RESEARCH IN MULTIPLE SCLEROSIS

MRI and the diagnosis of MS:
from MAGNIMS 2016 to the 2017 revision of the McDonald criteria

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Disclosures

Prof. Massimo Filippi

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Outline of the presentation

- Background
- 2016 MAGNIMS MRI criteria
- 2017 Revised McDonald criteria
- Possible future markers
- Conclusions

Background / What is MS?

«Multiple sclerosis is a chronic, inflammatory, demyelinating multifocal disease of the CNS»

Dissemination in space (DIS)

Dissemination in time (DIT)

How?

- Clinical assessment
- Laboratory tests (e.g., CSF analysis)
- Paraclinical tests (e.g., EPs, MRI)

Background / History of MS criteria

« de l'**altération scléreuse** en plaques **disséminées**, est surtout relative à la **substance blanche**, niais elle peut s'appliquer également, d'une manière générale au moins, à la **substance grise** »

Jean-Martin Charcot, Leçons du mardi, 1868

HISTOLOGIE

Clinically definite multiple sclerosis

SPECIAL REPORT

Diagnostic Criteria for Multiple Sclerosis: 2010 Revisions to the McDonald Criteria

Chris H. Polman, MD, PhD,[1] Stephen C. Reingold, PhD,[2] Brenda Banwell, MD,[3] Michel Clanet, MD,[4] Jeffrey A. Cohen, MD,[5] Massimo Filippi, MD,[6] Kazuo Fujihara, MD,[7] Eva Havrdova, MD, PhD,[8] Michael Hutchinson, MD,[9] Ludwig Kappos, MD,[10] Fred D. Lublin, MD,[11] Xavier Montalban, MD,[12] Paul O'Connor, MD,[13] Magnhild Sandberg-Wollheim, MD, PhD,[14] Alan J. Thompson, MD,[15] Emmanuelle Waubant, MD, PhD,[16] Brian Weinshenker, MD,[17] and Jerry S. Wolinsky, MD[18]

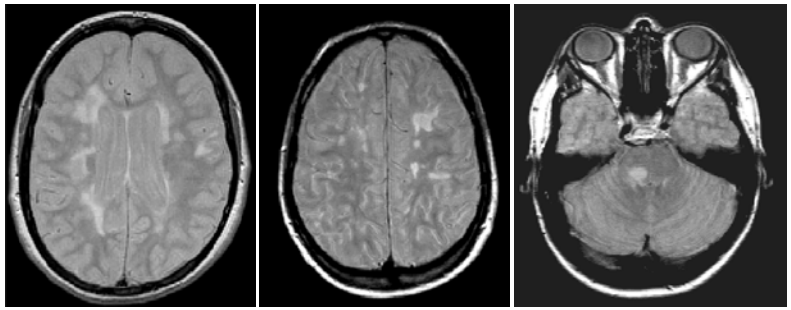
New evidence and consensus has led to further revision of the McDonald Criteria for diagnosis of multiple sclerosis. The use of imaging for demonstration of dissemination of central nervous system lesions in space and time has been simplified, and in some circumstances dissemination in space and time can be established by a single scan. These revisions simplify the Criteria, preserve their diagnostic sensitivity and specificity, address their applicability across populations, and may allow earlier diagnosis and more uniform and widespread use.

ANN NEUROL 2011;69:292–302

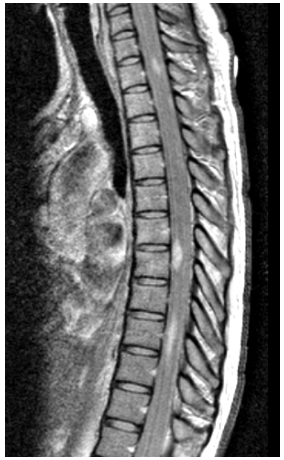
2010 Revised McDonald criteria

DIS

≥1 T2 asymptomatic lesion in at least 2 of 4 CNS areas:

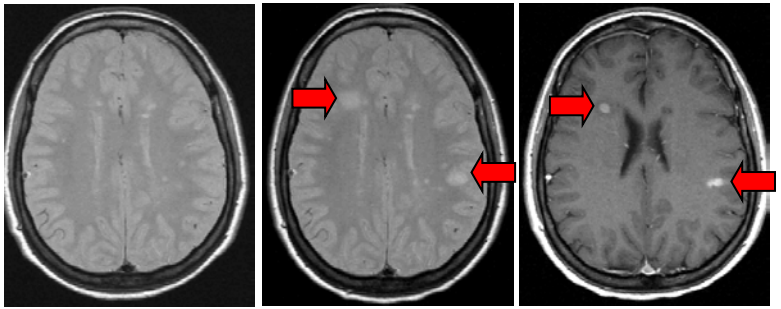


PERIVENTRICULAR JUXTACORTICAL INFRATENTORIAL



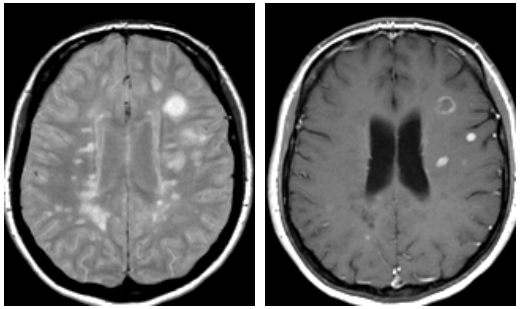
SPINAL CORD

DIT



BASELINE FOLLOW-UP

1) A **new T2 and/or GD-enhancing lesion** on follow-up MRI, irrespective of the timing of the baseline MRI



2) Simultaneous presence of **asymptomatic Gd-enhancing and non-enhancing lesions** at any time

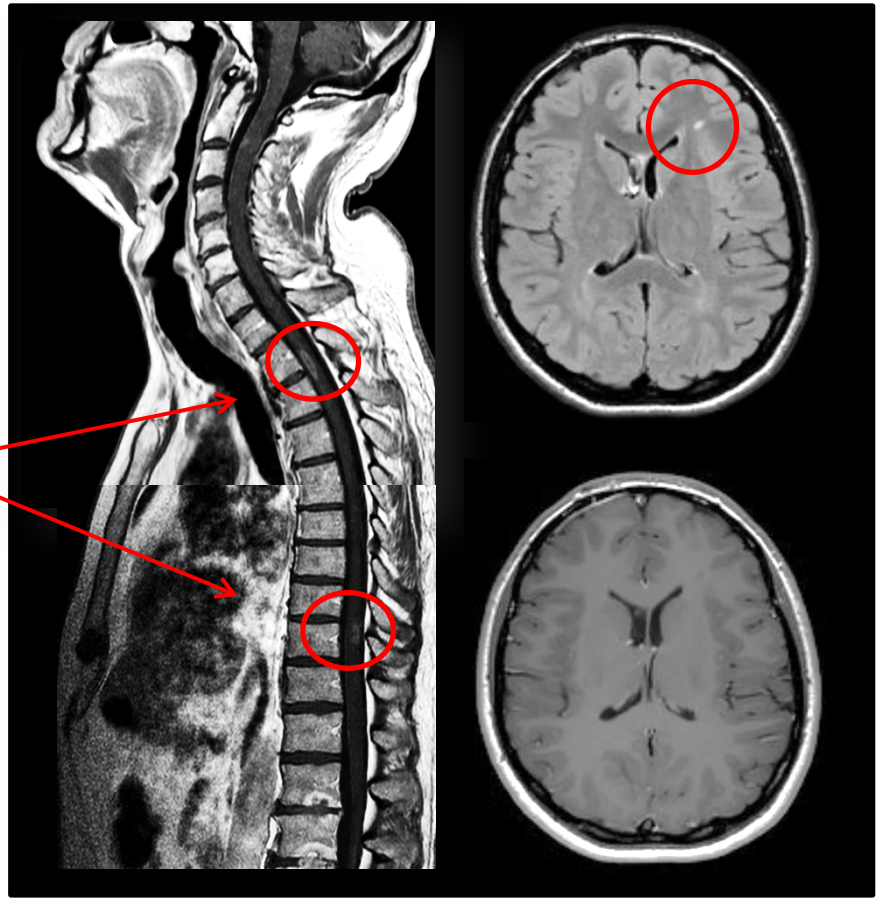
Polman et al., Ann Neurol 2011

Clinical case 1

- 45 year-old man
- No previous neurological history
- 4 limb hyposthenia and sphincteric dysfunction

Two spinal cord enhancing lesions

One non-enhancing JC lesion



Is this MS (2010 Revised McDonald criteria)?

1) The patient satisfies both criteria for DIS and DIT

2) The patient satisfies criteria for DIS, but not DIT

3) The patient does not satisfy criteria for DIS, but satisfies criteria for DIT

4) The patient does not satisfy neither criteria for DIS nor DIT

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MAGNIMS 2016 criteria

MRI criteria for the diagnosis of multiple sclerosis: MAGNIMS consensus guidelines

*Massimo Filippi, Maria A Rocca, Olga Ciccarelli, Nicola De Stefano, Nikos Evangelou, Ludwig Kappos, Alex Rovira, Jaume Sastre-Garriga, Mar Tintorè, Jette L Frederiksen, Claudio Gasperini, Jacqueline Palace, Daniel S Reich, Brenda Banwell, Xavier Montalban, Frederik Barkhof, on behalf of the MAGNIMS Study Group**

Lancet Neurol 2016; 15: 292–303

Panel 2: Recommended 2016 MAGNIMS MRI criteria to establish disease dissemination in space in multiple sclerosis

Dissemination in space can be shown by involvement* of at least two of five areas of the CNS as follows:

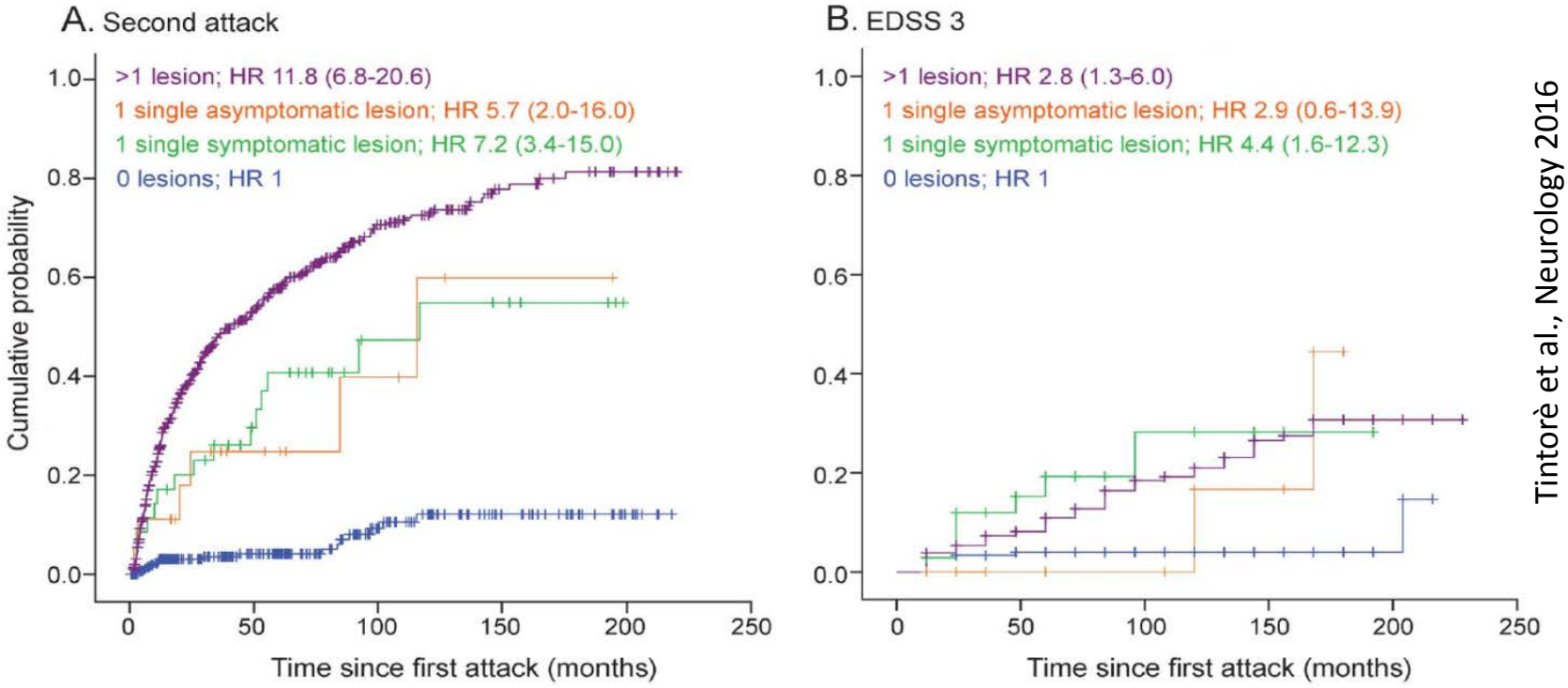
- Three or more periventricular lesions
- One or more infratentorial lesion
- One or more spinal cord lesion
- One or more optic nerve lesion
- One or more cortical or juxtacortical lesion†

*If a patient has a brainstem or spinal cord syndrome, or optic neuritis, the symptomatic lesion (or lesions) are not excluded from the criteria and contribute to the lesion count. †This combined terminology indicates the involvement of the white matter next to the cortex, the involvement of the cortex, or both, thereby expanding the term juxtacortical lesion.

MAGNIMS 2016 criteria / Rationale for modifications

- No distinction between symptomatic and asymptomatic lesions

(Brownlee et al., Neurology 2016; Tintorè et al., Neurology 2016)



MAGNIMS 2016 criteria / Rationale for modifications

- No distinction between symptomatic and asymptomatic lesions

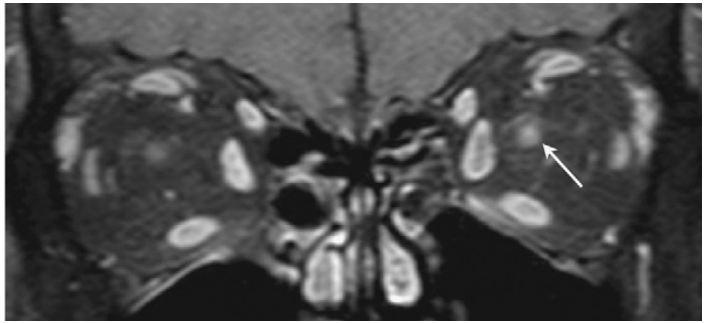
(Brownlee et al., Neurology 2016; Tintorè et al., Neurology 2016)

↓

- No reason any more to exclude the optic nerve

(The Optic Neuritis Study Group, Arch Neurol 2008; Simò et al., MSJ 2008; Lebrun et al., Ann Neurol 2009; Swanton et al., MSJ 2010)

MAGNIMS 2016 criteria / Rationale for modifications



OPTIC NERVE

Clinical documentation of optic nerve atrophy or pallor, neurophysiological confirmation of optic nerve dysfunction (slowed conduction), or imaging features of clinically silent optic nerve inflammation (MRI lesions or retinal nerve fibre layer thinning) support dissemination in space and, in patients without concurrent visual symptoms, dissemination in time

- Optic nerve lesions are reported in **94–99%** of MS autopsy cases (Kolappan et al. J Neurol 2009)
- Optic neuritis is the presenting symptom of MS in **25%** of cases and occurs during the disease in about **70%** of cases (Toosy et al., Lancet Neurol 2014)
- The cumulative probability of developing MS by **15 years** after onset of optic neuritis was **50%** (95% CI, 44%-56%) (Optic Neuritis Study G., Arch Neurol 2008)

MAGNIMS 2016 criteria / Rationale for modifications

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(Brownlee et al., Neurology 2016; Tintorè et al., Neurology 2016)

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↓

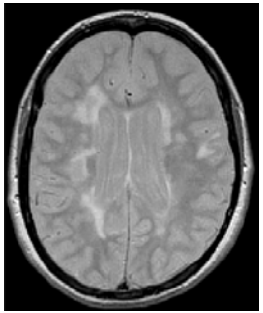
- To reduce the risk of FP: increased number of PV required (1→3)

(Barkhof et al., Brain 1997; Nielsen et al., Ann Neurol 2005; Neema et al., Am J Neuroradiol 2009; Absinta et al., J Neurol 2012; Liu et al., MSJ 2013; Kim et al., MSJ 2014; Brownlee et al., MSJ 2016)

MAGNIMS 2016 criteria / Rationale for modifications

MRI criterion	Cut-off point	Prevalence (*n*)	CDMS (*n*)	PPV (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)
Periventricular lesions	3	35	24	69	73	73	73
Basal ganglia and internal capsule lesions	1	15	10	67	30	89	62
Hypointense lesions on T1	1	20	14	70	44	85	65
Callosal/subcallosal lesions	1	38	26	69	79	71	74
Juxtacortical lesions	1	38	24	63	73	66	74
Gadolinium-enhancement	1	28	20	71	61	80	72
Infratentorial lesion	1	28	19	68	58	78	69
Lesions > 6 mm	2	30	21	70	64	78	72
Large gadolinium-enhancing lesion	1	10	6	60	18	90	58
Occipital lesions	1	30	12	40	64	78	72
Parietal lesions	3	33	23	70	70	76	73
Temporal lesions	1	39	26	67	79	68	73
Frontal lesions	3	35	24	69	77	73	73
Oval	NA	39	25	64	76	66	70
Total number of lesions	9	30	24	80	73	80	77

Barkhof et al., Brain 1997



PERIVENTRICULAR

Capping hyperintensity anterior to the frontal horns of the lateral ventricles was present in **all HC** Neema et al., Am J Neuroradiol 2009

Periventricular lesions can be detected in **healthy individuals** and up to **30% of migraine patients** Absinta et al., J Neurol 2012

34% patients with migraine met DIS 2010 Mc Donald criteria
Liu et al., MSJ 2013

	Prevalence
Barkhof 3 mm criteria	12/168 (7.1%)
McDonald 3 mm criteria	58/168 (34.5%)

MAGNIMS 2016 criteria / Rationale for modifications

- No distinction between symptomatic and asymptomatic lesions

(Brownlee et al., Neurology 2016; Tintorè et al., Neurology 2016)

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- No reason any more to exclude the optic nerve

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↓

- In addition: cortical lesions (new sequences)

(Filippi et al., Neurology 2010)

MAGNIMS 2016 criteria / Rationale for modifications

Revised McDonald 2010 *vs* Filippi 2010*

	Sensitivity	Specificity	Accuracy	PPV	NPV	PLR	NLR	OR	p value
DIS only									
Revised McDonald 2010	0.91 (0.81-0.97)	0.34 (0.18-0.54)	0.72 (0.61-0.81)	0.73 (0.61-0.83)	0.67 (0.38-0.88)	1.39 (1.06-1.84)	0.25 (0.10-0.68)	6.22 (1.50-32.21)	0.016
Filippi 2010	0.82 (0.70-0.91)	0.54 (0.34-0.72)	0.73 (0.62-0.82)	0.78 (0.66-0.88)	0.60 (0.39-0.79)	1.78 (1.17-2.69)	0.33 (0.17-0.63)	5.67 (1.81-19.39)	0.004
DIS + DIT									
Revised McDonald 2010	0.81 (0.68-0.90)	0.59 (0.39-0.76)	0.73 (0.63-0.82)	0.79 (0.67-0.89)	0.61 (0.41-0.78)	1.95 (1.24-3.06)	0.33 (0.18-0.61)	5.14 (1.73-16.37)	0.004
Filippi 2010	0.74 (0.60-0.84)	0.66 (0.46-0.82)	0.71 (0.60-0.80)	0.81 (0.67-0.90)	0.56 (0.38-0.73)	2.14 (1.26-3.61)	0.40 (0.24-0.67)	5.14 (1.77-16.24)	0.003

Preziosa et al., JNNP 2017

***Filippi 2010 DIS**: ≥2 of: **≥1 ICL**, ≥1 PF, ≥1 SC or ≥1 Gd-enhancing lesion

DIT: Simultaneous presence of asymptomatic Gd-enhancing and non-enhancing lesions or a new T2/Gd-enhancing lesion on the follow-up MRI

N=86 CIS
Follow-up = 36 months

MAGNIMS 2016 criteria / Rationale for modifications

- A **new T2 and/or GD-enhancing** lesion on follow-up MRI
- Simultaneous presence of ~~asymptomatic~~ **Gd-enhancing and non-enhancing lesions**

		2010 McDonald DIS criteria		
		Met	Not met	Total
2010 McDonald DIT Criteria	Met	33	4	37 (33.9%)
	Not met	43	29	72 (66.1%)
	Total	76 (69.7%)	33 (30.3%)	*N* = 109
2010 Modified McDonald DIT criteria[a]	Met	36	4	40 (36.7%)
	Not met	40	29	69 (63.3%)
	Total	76 (69.7%)	33 (30.3%)	*N* = 109

Kang et al., MSJ 2014

Revised 2010 McDonald and MAGNIMS 2016

Prediction of a multiple sclerosis diagnosis in patients with clinically isolated syndrome using the 2016 MAGNIMS and 2010 McDonald criteria: a retrospective study

Massimo Filippi, Paolo Preziosa, Alessandro Meani, Olga Ciccarelli, Sarlota Mesaros, Alex Rovira, Jette Frederiksen, Christian Enzinger, Frederik Barkhof, Claudio Gasperini, Wallace Brownlee, Jelena Drulovic, Xavier Montalban, Stig P Cramer, Alexander Pichler, Marloes Hagens, Serena Ruggieri, Vittorio Martinelli, Katherine Miszkiel, Mar Tintorè, Giancarlo Comi, Iris Dekker, Bernard Uitdehaag, Irena Dujmovic-Basuroski, Maria A Rocca

Background In 2016, the Magnetic Resonance Imaging in Multiple Sclerosis (MAGNIMS) network proposed modifications to the MRI criteria to define dissemination in space (DIS) and time (DIT) for the diagnosis of multiple sclerosis in patients with clinically isolated syndrome (CIS). Changes to the DIS definition included removal of the distinction between symptomatic and asymptomatic lesions, increasing the number of lesions needed to define periventricular involvement to three, combining cortical and juxtacortical lesions, and inclusion of optic nerve evaluation. For DIT, removal of the distinction between symptomatic and asymptomatic lesions was suggested. We compared the performance of the 2010 McDonald and 2016 MAGNIMS criteria for multiple sclerosis diagnosis in a large multicentre cohort of patients with CIS to provide evidence to guide revisions of multiple sclerosis diagnostic criteria.

Interpretation The 2016 MAGNIMS criteria showed similar accuracy to the 2010 McDonald criteria in predicting the development of clinically definite multiple sclerosis. Inclusion of symptomatic lesions is expected to simplify the clinical use of MRI criteria without reducing accuracy, and our findings suggest that needing three lesions to define periventricular involvement might slightly increase specificity, suggesting that these two factors could be considered during further revisions of multiple sclerosis diagnostic criteria.

Filippi et al., Lancet Neurol 2018

Revised 2010 McDonald and MAGNIMS 2016

	Sensitivity	Specificity	AUC	PPV	NPV
DIS + DIT (36 months)					
Revised McDonald 2010	**0.73 (0.66-0.80)**	**0.50 (0.42-0.59)**	**0.62 (0.56-0.67)**	**0.58 (0.51-0.65)**	**0.67 (0.58-0.75)**
Inclusion of symptomatic lesions	**0.76 (0.69-0.83)**	0.49 (0.40-0.58)	0.62 (0.57-0.68)	0.58 (0.51-0.65)	0.68 (0.60-0.77)
Inclusion of 3 PV lesions	0.70 (0.63-0.77)	**0.55 (0.46-0.63)**	0.62 (0.56-0.68)	0.59 (0.51-0.67)	0.66 (0.57-0.74)
Inclusion of CL	**0.75 (0.67-0.81)**	0.50 (0.42-0.60)	0.63 (0.57-0.68)	0.59 (0.51-0.66)	0.68 (0.59-0.76)
Inclusion of ON	**0.75 (0.67-0.81)**	0.48 (0.39-0.57)	0.61 (0.56-0.67)	0.57 (0.50-0.65)	0.67 (0.57-0.75)
MAGNIMS 2016	**0.77 (0.70-0.83)**	**0.50 (0.41-0.59)**	**0.64 (0.58-0.69)**	**0.60 (0.52-0.67)**	**0.70 (0.61-0.78)**

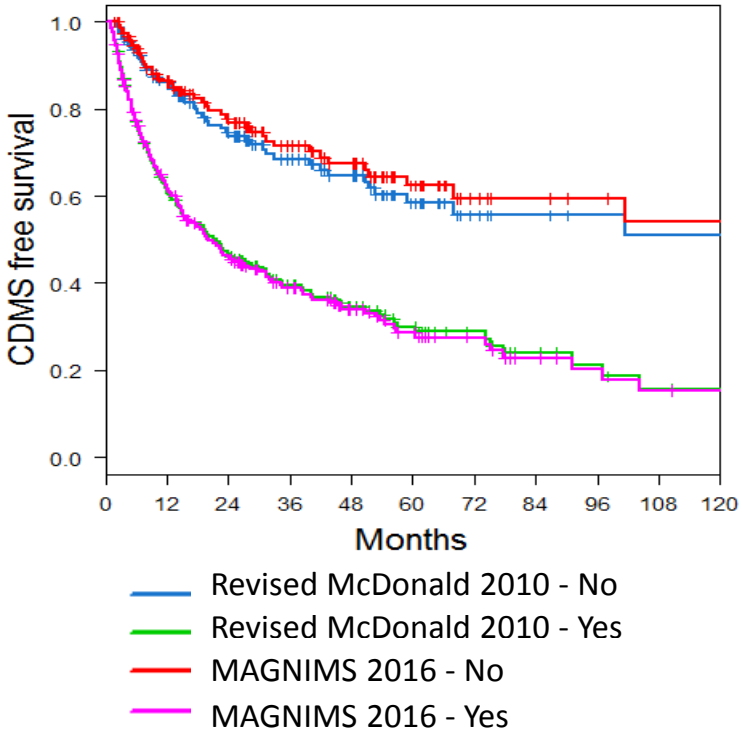
Filippi et al., Lancet Neurol 2018

Revised 2010 McDonald and MAGNIMS 2016

	aHR (95% CI)	p value
DIS + DIT (36 months)		
Revised McDonald 2010	**2.52 (1.78-3.58)**	<0.0001
Inclusion of symptomatic lesions	2.54 (1.77-3.65)	<0.0001
Inclusion of 3 PV lesions	2.54 (1.80-3.58)	<0.0001
Inclusion of CL	2.60 (1.83-3.71)	<0.0001
Inclusion of ON	2.58 (1.81-3.67)	<0.0001
MAGNIMS 2016	**2.95 (2.04-4.26)**	<0.0001

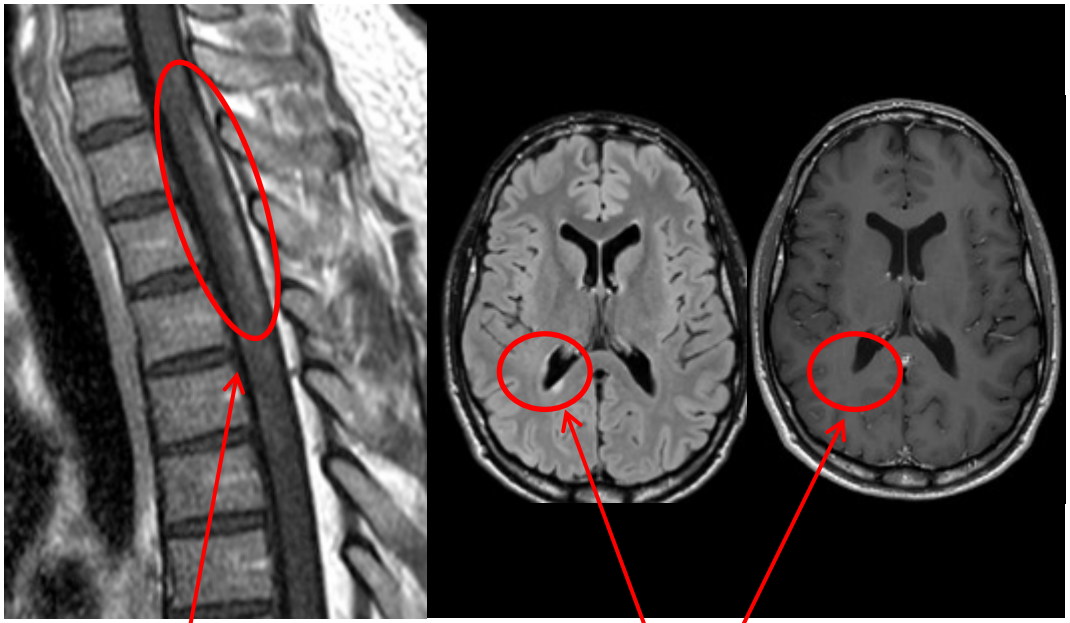
Filippi et al., Lancet Neurol 2018

DIS + DIT



Clinical case 2

- 37 year-old woman
- No previous neurological history
- Sudden onset of paraparesis and sensory ataxia



One (probably) symptomatic spinal cord enhancing lesion

One non-enhancing PV lesion

Is this MS (MAGNIMS 2016 criteria)?

1) The patient satisfies both criteria for DIS and DIT

2) The patient satisfies criteria for DIS, but not DIT

3) The patient does not satisfy criteria for DIS, but satisfies criteria for DIT

4) The patient does not satisfy neither criteria for DIS nor DIT

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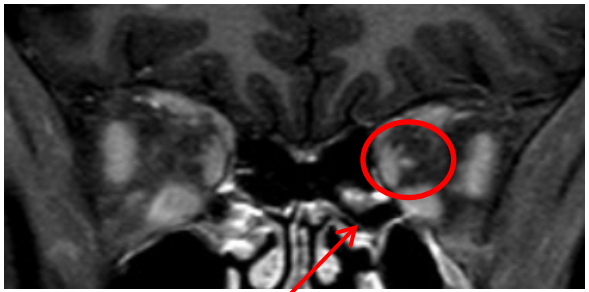
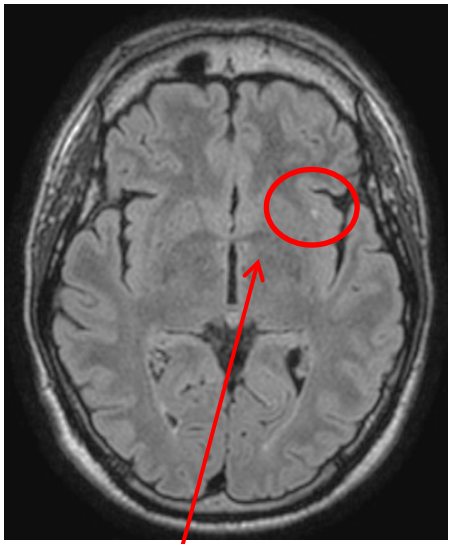
Clinical case 3

- 17 year-old woman
- No previous neurological history
- Progressive left visual loss within 3 days and pain with ocular movements





Left optic nerve enhancing lesion

One JC lesion

Is this MS (MAGNIMS 2016 criteria)?

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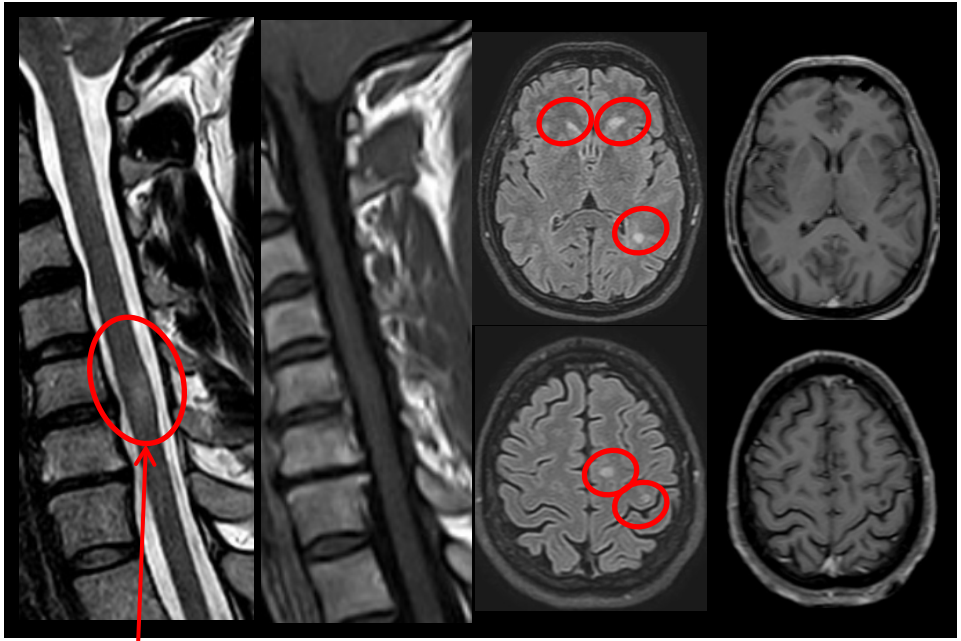
Clinical case 4

- 29 year-old man
- No previous neurological history
- Bilateral hand paresthesias started almost one month ago



One symptomatic spinal cord non-enhancing lesion

≥ 3 PV and JC non-enhancing lesions

Is this MS (MAGNIMS 2016 criteria)?

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4) The patient does not satisfy neither criteria for DIS nor DIT

Is this MS (MAGNIMS 2016 criteria)?

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4) The patient does not satisfy neither criteria for DIS nor DIT

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MAGNIMS 2016 and 2017 McDonald Revision

Diagnosis of multiple sclerosis: 2017 revisions of the McDonald criteria

Alan J Thompson, Brenda L Banwell, Frederik Barkhof, William M Carroll, Timothy Coetzee, Giancarlo Comi, Jorge Correale, Franz Fazekas, Massimo Filippi, Mark S Freedman, Kazuo Fujihara, Steven L Galetta, Hans Peter Hartung, Ludwig Kappos, Fred D Lublin, Ruth Ann Marrie, Aaron E Miller, David H Miller, Xavier Montalban, Ellen M Mowry, Per Soelberg Sorensen, Mar Tintoré, Anthony L Traboulsee, Maria Trojano, Bernard M J Uitdehaag, Sandra Vukusic, Emmanuelle Waubant, Brian G Weinshenker, Stephen C Reingold, Jeffrey A Cohen

The 2010 McDonald criteria for the diagnosis of multiple sclerosis are widely used in research and clinical practice. Scientific advances in the past 7 years suggest that they might no longer provide the most up-to-date guidance for clinicians and researchers. The International Panel on Diagnosis of Multiple Sclerosis reviewed the 2010 McDonald criteria and recommended revisions. The 2017 McDonald criteria continue to apply primarily to patients experiencing a typical clinically isolated syndrome, define what is needed to fulfil dissemination in time and space of lesions in the CNS, and stress the need for no better explanation for the presentation. The following changes were made: in patients with a typical clinically isolated syndrome and clinical or MRI demonstration of dissemination in space, the presence of CSF-specific oligoclonal bands allows a diagnosis of multiple sclerosis; symptomatic lesions can be used to demonstrate dissemination in space or time in patients with supratentorial, infratentorial, or spinal cord syndrome; and cortical lesions can be used to demonstrate dissemination in space. Research to further refine the criteria should focus on optic nerve involvement, validation in diverse populations, and incorporation of advanced imaging, neurophysiological, and body fluid markers.

Thompson et al., Lancet Neurol 2018

MAGNIMS 2016 and 2017 McDonald Revision

MAGNIMS 2016

- No distinction between symptomatic and asymptomatic lesions

(Brownlee et al., Neurology 2016; Tintorè et al., Neurology 2016)

↓

- No reason any more to exclude the optic nerve

(The ONS Group, Arch Neurol 2008; Simò et al., MSJ 2008; Lebrun et al., Ann Neurol 2009; Swanton et al., MSJ 2010)

↓

- To reduce the risk of FP: increased number of PV required (1→3)

(Barkhof et al., Brain 1997; Nielsen et al., Ann Neurol 2005; Neema et al., Am< J Neuroradiol 2009; Absinta et al., J Neurol 2012; Liu et al., MSJ 2013; Kim et al., MSJ 2014; Brownlee et al., MSJ 2016)

↓

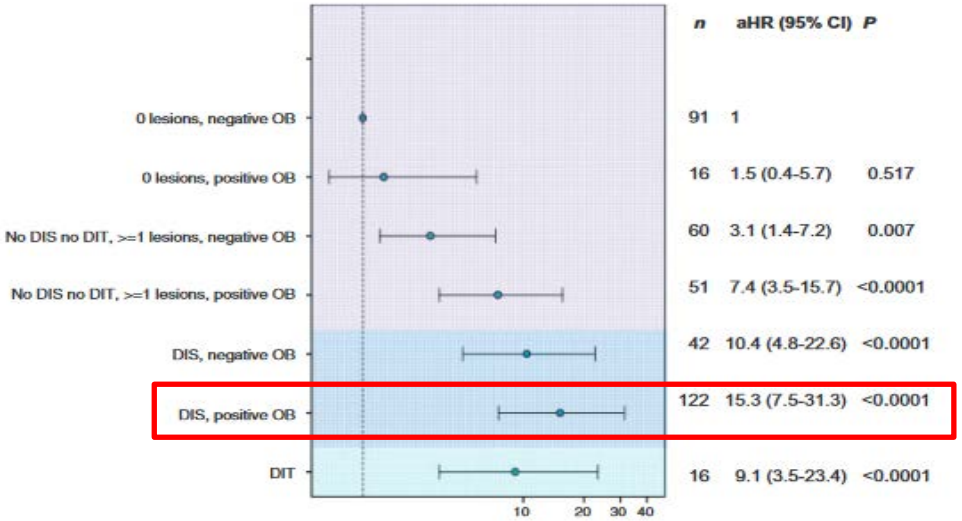
- In addition: cortical lesions (new sequences)

(Filippi et al., Neurology 2010)

2017 McDonald Revision

With a typical CIS, fulfillment of clinical or MRI criteria for DIS, and no better explanation, demonstration of CSF OCBs in the absence of atypical CSF findings allows a diagnosis of MS to be made, even if the MRI findings on the baseline scan do not meet the criteria for DIT

Thompson et al., Lancet Neurol 2018



Arrambide et al., Brain 2018

n = 314	n	McDonald MS at 3 years n (%)	Sensitivity (95% CI)	Specificity (95% CI)	Accuracy (95% CI)	PPV (95% CI)	NPV (95% CI)
All DIS	137	111/137 (81.0)	61.7 (54.1–68.8)	80.6 (72.9–86.9)	69.7 (64.3–74.8)	81.0 (74.8–86.0)	61.0 (56.1–65.7)
DIS with +OB	101	85/101 (84.2)	47.2 (39.8–54.8)	88.1 (81.3–93.0)	64.6 (59.1–69.9)	84.2 (76.6–89.6)	55.4 (51.6–59.1)

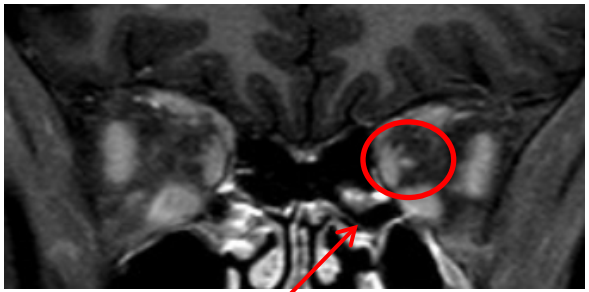
2017 McDonald Revision

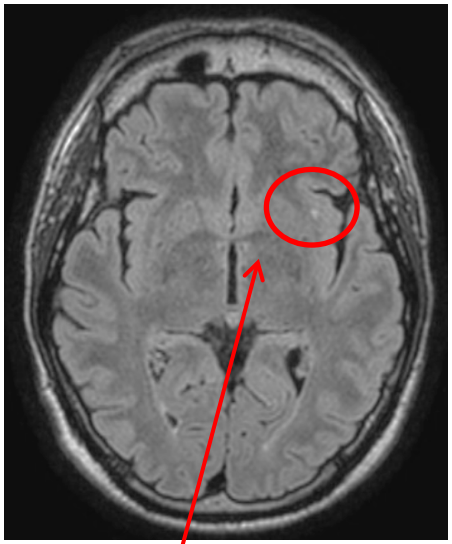
	DIS	DIT
CIS	≥1 T2 lesion (**both symptomatic and asymptomatic**) in at least 2 of 4 CNS areas: PV, JC/**CL**, spinal cord, infratentorial	Simultaneous presence of Gd+ and Gd- lesions at any time (**both symptomatic and asymptomatic**) OR A new T2 and/or Gd+ lesion on follow-up MRI OR Presence of **CSF-specific OCBs**
PPMS	**One year of disability progression** (retrospectively or prospectively determined) independent of clinical relapse + **> 2/3 of:**	• ≥1 T2 lesion (**symptomatic and asymptomatic**) both in ≥1 areas in the brain characteristic of MS (PV, JC/CL or infratentorial) • ≥2 T2-hyperintense lesions in the **spinal cord** • Presence of **CSF-specific OCBs**

Thompson et al., Lancet Neurol 2018

Clinical case 3 (revisited)

- 17 year-old woman
- No previous neurological history
- Progressive left visual loss within 3 days and pain with ocular movements





Left optic nerve enhancing lesion

One JC lesion

Positive OCBs

Is this MS (McDonald 2017 criteria)?

1) The patient satisfies both criteria for DIS and DIT

2) The patient satisfies criteria for DIS, but not DIT

3) The patient does not satisfy criteria for DIS, but satisfies criteria for DIT

4) The patient does not satisfy neither criteria for DIS nor DIT

Is this MS (McDonald 2017 criteria)?

1) The patient satisfies both criteria for DIS and DIT

2) The patient satisfies criteria for DIS, but not DIT

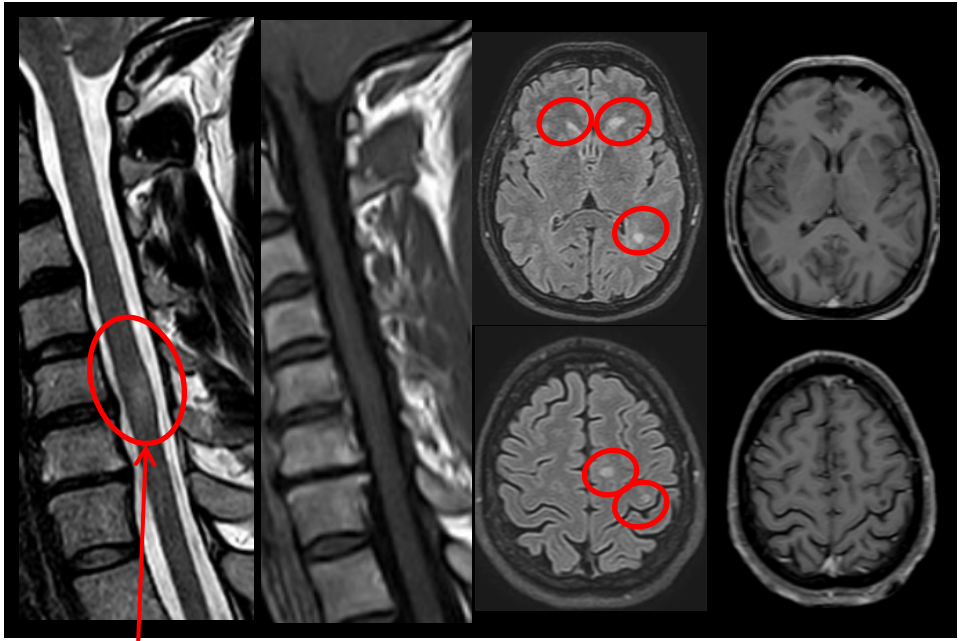
3) The patient does not satisfy criteria for DIS, but satisfies criteria for DIT

4) The patient does not satisfy neither criteria for DIS nor DIT

Clinical case 4 (revisited)

- 29 year-old man
- No previous neurological history
- Bilateral hand paresthesias started almost one month ago

→ **Positive OCBs**



One symptomatic spinal cord non-enhancing lesion

≥ 3 PV and JC non-enhancing lesions

Is this MS (McDonald 2017 criteria)?

1) The patient satisfies both criteria for DIS and DIT

2) The patient satisfies criteria for DIS, but not DIT

3) The patient does not satisfy criteria for DIS, but satisfies criteria for DIT

4) The patient does not satisfy neither criteria for DIS nor DIT

Is this MS (McDonald 2017 criteria)?

1) The patient satisfies both criteria for DIS and DIT

2) The patient satisfies criteria for DIS, but not DIT

3) The patient does not satisfy criteria for DIS, but satisfies criteria for DIT

4) The patient does not satisfy neither criteria for DIS nor DIT

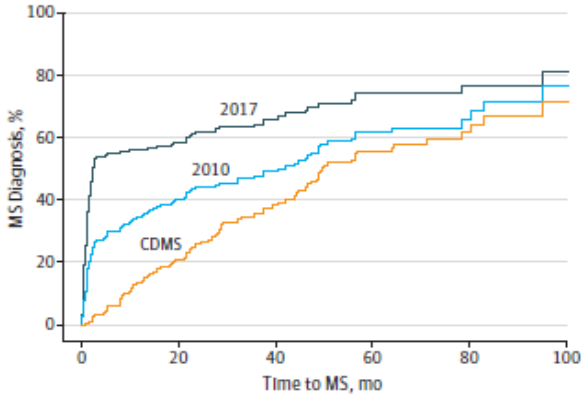
MAGNIMS 2016 vs 2017 McDonald Revision

	Description	MAGNIMS 2016	McDonald 2017
Case 3	• One **optic nerve enhancing** lesion • One **juxtacortical non-enhancing** lesion • Positive **OCBs**	**MS**	**DIT**
Case 4	• One **spinal cord non-enhancing** lesion • **> 3 PV and JC non-enhancing** lesions • Positive **OCBs**	**DIS**	**MS**
		Filippi et al., Lancet Neurol 2016	Thompson et al., Lancet Neurol 2018

2017 McDonald Revision

van der Vuurst de Vries et al., JAMA Neurol 2018

Survival curves for time from CIS to MS for CDMS with 2010 and 2017 criteria



Characteristic	DIS (n = 229)	DIT (n = 180)	DIS+DIT (n = 180)
2010			
Sensitivity (95% CI)	66 (56-74)	36 (27-47)	36 (27-47)
Specificity (95% CI)	57 (47-66)	85 (76-92)	85 (76-92)
Accuracy (95% CI)	52 (45-58)	61 (54-68)	61 (54-68)
Hazard ratio (95% CI)	2.0 (1.3-2.9)	1.9 (1.2-2.9)	1.9 (1.2-2.9)
2017			
Sensitivity (95% CI)	79 (70-86)	84 (74-90)	68 (57-77)
Specificity (95% CI)	48 (39-58)	44 (34-55)	61 (50-71)
Accuracy (95% CI)	44 (38-51)	64 (57-71)	64 (57-71)
Hazard ratio (95% CI)	2.7 (1.7-4.2)	2.6 (1.5-4.6)	2.0 (1.3-3.1)

Brownlee et al., Neurology 2018

	160 CIS with 15 year-follow-up	
Clinical	With ON (n=129)	Without ON (n=31)
Abnormal VEPs	25/26	3/16
Abnormal MRI	104	23

	Sensitivity (95% CI), %	Specificity (95% CI), %	Accuracy (95% CI), %	PPV (95% CI),	NPV (95% CI), %
		DIS alone			
2017	83 (73–90)	68 (53–81)	78 (69–84)	82 (72–90	70 (54–82)
2017+ON	95 (88–99)	57 (42–72)	81 (74–88)	80 (70–87	87 (70–96)
		DIS plus DIT			
2017	74 (64–83)	77 (62–88)	75 (67–82)	85 (74–92	63 (49–76)
2017+ON	83 (73–90)	77 (62–88)	81 (73–87)	86 (76–93	72 (58–84)

The inclusion of ON involvement in the **group without ON did not identify additional patients** and the performance of **McDonald 2017 remained the same**

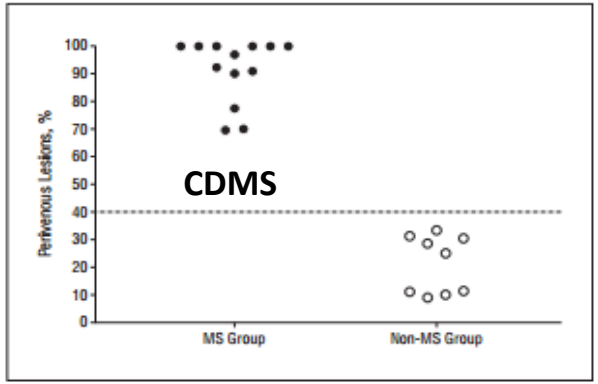
Outline of the presentation

- Background
- 2016 MAGNIMS MRI criteria
- 2017 Revised McDonald criteria
- Possible future markers
- Conclusions

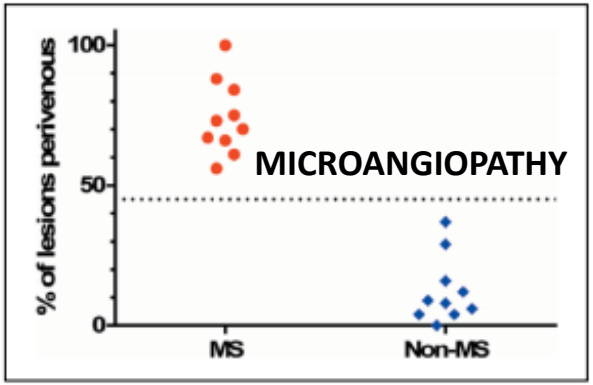
Future directions?

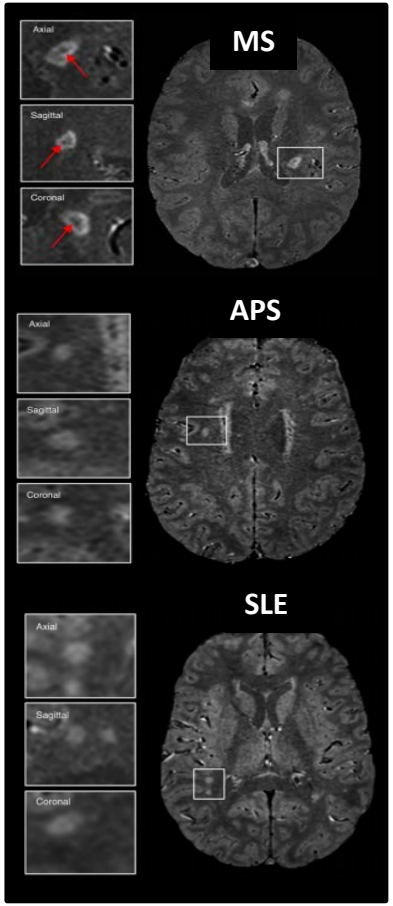
Central vein sign

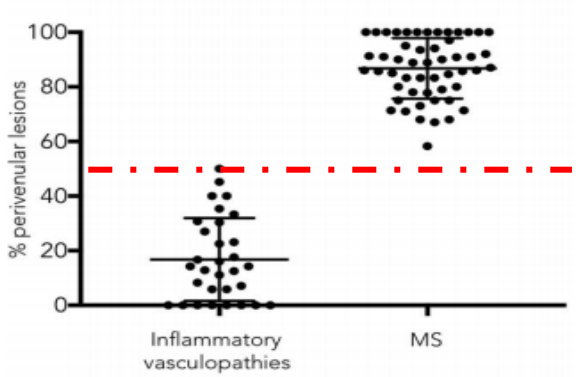
Mistry et al., JAMA Neurol 2013

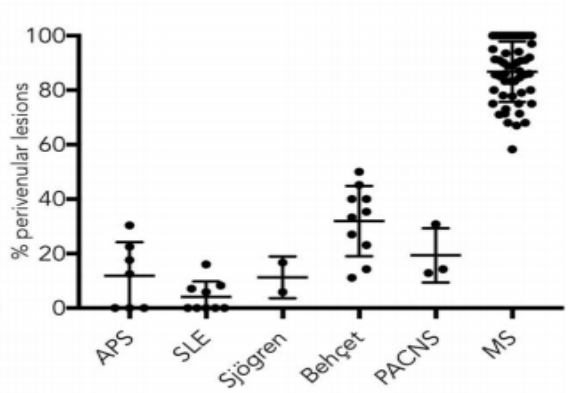


Mistry et al., MSJ 2016





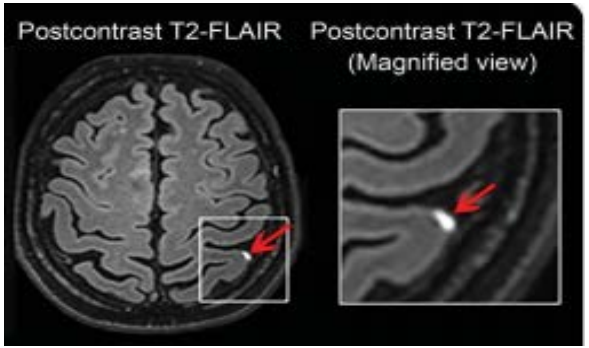


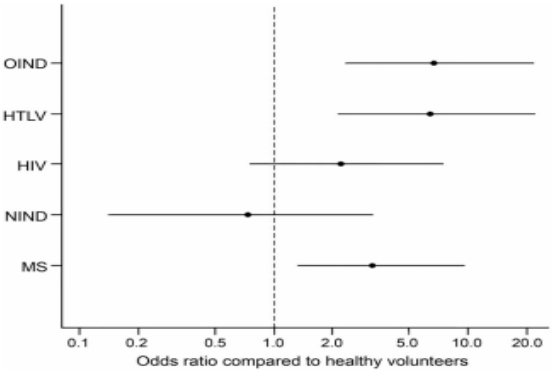


Maggi et al., Ann Neurol 2018

Future directions?

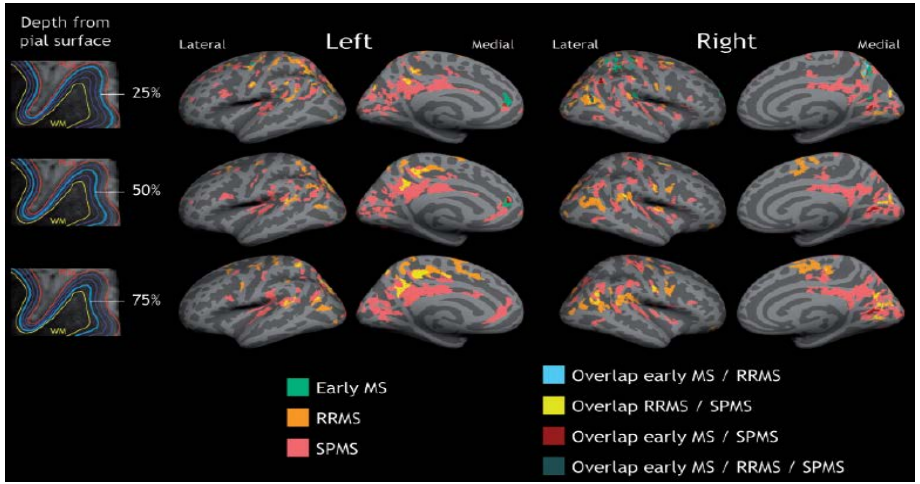
Leptomeningal enhancement





Absinta et al., Neurology 2017

Subpial demyelination



Mainero et al., Brain 2015

Conclusions

- Refinement of MRI criteria to show DIS and DIT in MS patients with a simplified (“unified”) approach
- The clinical context remains central
- Validation studies to assess 2017 McDonald criteria are urgently needed
- New specific MRI hallmarks of MS are under investigation