

Supplementary Online Content

Almusalam N, Oh J, Terzaghi M, et al. Comparison of physician therapeutic inertia for management of patients with multiple sclerosis in Canada, Argentina, Chile, and Spain. *JAMA Netw Open*. 2019;2(7):e197093. doi:10.1001/jamanetworkopen.2019.7093

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This supplementary material has been provided by the authors to give readers additional information about their work.

eAppendix. Case Vignette Answered by Participating Physicians

- 1- A 40-year old woman diagnosed of RRMS 5 years ago has been under intramuscular interferon beta 1a treatment. Her last relapse was 2 years ago. She noticed progressive memory difficulties and lack of attention in the last 12 months.
No recent relapses. Her husband noticed she has been forgetful affecting her daily activities. She denied depression. Her EDSS has been stable. Her cognitive assessment (Symbol Digit Modalities Test) score of 44. A score of below 55 is indicative of cognitive impairment in MS patients. Current brain MRI: 5 new T2 periventricular lesions.

What would you do? Please select one option from the screen:

- . Continue on the same DMT and perform a new neuropsychological evaluation in 6 months
- . Stop interferon and start her on a monoclonal antibody agent (Natalizumab/Alemtuzumab)
- . Stop interferon and start her on Fingolimod
- . Stop interferon and start her on Glatiramer acetate
- . Stop interferon and start her on teriflunomide

- 2- A 27-year old woman had an episode of double vision that resolved within 3 weeks, and another episode of unsteady gait, both in the last 18 months. Her EDSS is 1.0. An MRI revealed 5 T2 bilateral periventricular lesions and one subcortical lesion. There is no gadolinium enhancement. Your clinical diagnosis is RRMS.

What would you do? Please select one option:

- . Initiate treatment with Glatiramer or Interferon
- . Initiate Vitamin D supplementation
- . Initiate treatment with Dimethyl Fumarate
- . Initiate treatment with Fingolimod
- . clinical reassessment within 6 months prior to treatment initiation
- . Clinical reassessment and MRI with gadolinium within 6 months prior to treatment initiation

- 3- A 28-year old woman with a diagnosis of RRMS has been on subcutaneous interferon beta 1a (interferon) for 16 months. She had two non-disabling recurrent events since the initiation of interferon. Her EDSS score is 1.5. A repeated brain MRI revealed 5 new T2 bilateral periventricular lesions and one subcortical Gadolinium-enhanced lesion compared to the MRI prior to the initiation of interferon.

What would you do? Please select one option from the screen:

- . Stop interferon and start her on Teriflunomide.
- . Stop interferon and start her on Glatiramer
- . Stop interferon and start her on Fingolimod.
- . Stop interferon and start her on a monoclonal antibody agent (e.g. Natalizumab, alemtuzumab)
- . Continue the same treatment
- . Continue on interferon and reassess in 6 months.

- 4- A 38-year old man diagnosed of RRMS 4 years ago. His EDSS score was 2.5. He developed a new onset of imbalance and double vision. He had 2 previous relapses (optic neuritis and hypoesthesia in right upper limb). He has been on subcutaneous interferon beta 1a since the diagnosis. A new brain MRI showed two T1 Gadolinium-enhanced lesions involving the pons and cerebellar peduncle.

What would you do? Please select one option from the screen:

- Stop interferon and start him on Teriflunomide
- Stop interferon and start him on Fingolimod
- Stop interferon and start him on Dimethyl fumarate
- Stop interferon and start him on a monoclonal antibody (Natalizumab/Alemtuzumab)
- Stop interferon and start him on Glatiramer acetate
- Continue with the current therapy and reassess in 6 months.

- 5- A 28-years old woman developed facial numbness and mild headaches. Her neurological examination showed a subjective diminished sensation on the left face affecting her forehead and cheek and hypoesthesia on the right upper limb. An MRI showed a T1 Gadolinium-enhancing lesion in the right-pons and 6 T2 periventricular and juxtacortical hyperintense lesions. You treated her with methylprednisolone and then started interferon beta 1A. Six months later, she developed loss of strength in the left arm.

What would you do? Please select one option from the screen:

- Continue interferon and re-assess in 6 months
- Stop interferon and start her on Fingolimod
- Stop interferon and start her on Glatiramer
- Stop interferon and start her on a monoclonal antibody agent (Natalizumab/Alemtuzumab)
- Stop interferon and start her on Teriflunomide
- Continue on interferon

- 6- A 43-year old woman was diagnosed with RRMS 6 years ago. In total, she has had 4 new relapses. Has been stable on interferon B1a subcutaneous. Her EDSS 3.0. She has been feeling unwell noticing fatigue, and generalized weakness in the last 6 months.

A recent MRI revealed a 12 old periventricular and 1 new subcortical lesion on right frontal lobe. There were no GAD-enhancing lesions.

What would you do? Please select one option from the screen:

- Stop interferon and start her on Fingolimod
- Stop interferon and start her on Dimethyl Fumarate
- Stop interferon and start her on a Monoclonal agent (e.g. Natalizumab, Alemtuzumab)
- Continue with the current therapy and reassess in 6 months.
- Stop interferon and start her on Teriflunomide
- Stop interferon B1a and start treatment with PEG Interferon B1a (Plegridy)

- 7- A 33-year old woman was diagnosed with RRMS 4 years ago. She came to your clinic for a follow-up. In total, she had 3 relapses prior starting on intramuscular interferon once weekly. She has been clinically stable in the last 2 years. Her EDSS score is 4.5. A new brain MRI revealed a new 14 mm subcortical lesion in T1 that enhanced with Gadolinium in addition to the old confluent periventricular lesions in T2.

What would you do? Please select one option from the screen:

- Continue with the current therapy
- Stop interferon and start her on Fingolimod
- Stop interferon and start her on Dimethyl fumarate
- Stop interferon and start her on a monoclonal antibody agent (Natalizumab/Alemtuzumab)
- Continue with the current therapy and reassess in 6 months.
- Stop interferon and start her on Teriflunomide

- 8- A 31-year old woman had an episode of optic neuritis and numbness on the left had 2 months ago.

Her EDSS is 0. The CSF revealed positive oligoclonal bands. An MRI revealed five small T2 periventricular lesions. What would you do? Please select one option:

- Initiate treatment with Glatiramer or Interferon
- Initiate Vitamin D supplementation
- Initiate treatment with Dimethyl Fumarate
- Initiate treatment with Fingolimod
- Clinical reassessment within 6 months prior to treatment initiation
- Clinical reassessment and MRI with gadolinium within 6 months prior to treatment initiation

9- A 25-year old woman was diagnosed with RRMS 4 years ago. She had one relapse while being on Glatiramer two years ago. Three month ago, she developed an episode of right sided weakness. A brain MRI revealed 6 small new T2 periventricular lesions. None enhanced with gadolinium.

What would you do? Please select one option from the screen:

- Continue with the current therapy and reassess in 6 months.
- Stop Glatiramer and start her on Fingolimod
- Stop Glatiramer and start her on Teriflunomide
- Stop Glatiramer and start her on Peg-interferon β -1a (Plegridy)
- Stop Glatiramer and start her on a monoclonal antibody agent (Natalizumab/Alemtuzumab)
- Continue with Glatiramer

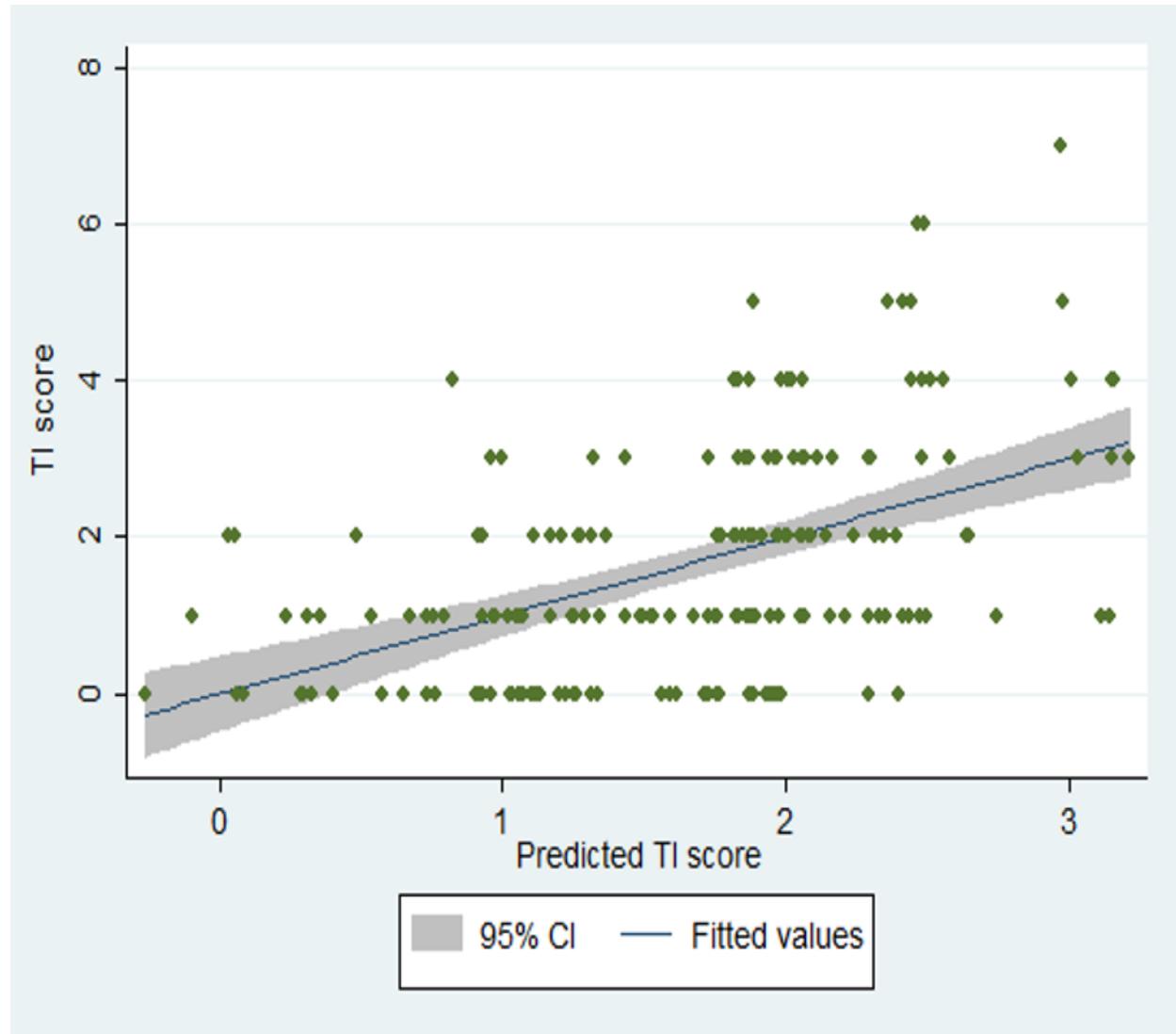
10- A 28-year old woman was diagnosed with RRMS 2 years ago. She had two relapses while being on Glatiramer. She was switched to Dimethyl Fumarate 10 months ago. Recently, she developed an episode of double vision (left INO) and right sided weakness that resolved in 3 weeks. A brain MRI revealed a 15 mm gadolinium-enhanced lesion in the left paramedian pons.

What would you do? Please select one option from the screen:

- Continue with the current therapy and reassess in 6 months.
- Stop Dimethyl Fumarate and start her on Fingolimod
- Stop Dimethyl Fumarate and start her on Teriflunomide
- Stop Dimethyl Fumarate and start her on Pegilated-interferon β -1a
- Stop Dimethyl Fumarate and start her on a monoclonal antibody agent (Natalizumab/Alemtuzumab)
- Continue with Dimethyl Fumarate

eFigure. Observed vs Predicted TI Score After Adjustment for Covariates

This figure represent the observed (dots) vs. predicted TI score after adjustment for age, specialty, years of practice, volume of MS patients seen per week and aversion to ambiguity.



eTable 1. Mixed Linear Regression Model Adjusted for Clustering

Linear regression

Number of obs = 195
 F(6, 194) = 9.63
 Prob > F = 0.0000
 R-squared = 0.2022
 Root MSE = 1.3487

(Std. Err. adjusted for 195 clusters in pid)

TI score	Coef.	Robust Std. Err.	[95% Conf. Interval]
age	0.040	0.024	-0.007 0.086
MS per week	-0.025	0.009	-0.042 -0.007
MS specialist	-0.423	0.212	-0.840 -0.005
yrs of practice	-0.045	0.024	-0.093 0.002
Canada vs other	-0.900	0.193	-1.281 -0.519
Aversion to ambiguity	0.390	0.229	-0.061 0.841
Constant	1.518	0.704	0.131 2.906

eTable 2. Bootstrap Linear Regression to Compare Normal vs Bias-Corrected 95% CI

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Linear regression

Number of obs = 195
Replications = 1000

(Replications based on 195 clusters in pid)

TI score	Coef.	Observed Bias	Bootstrap Std. Err.	[95% Conf. Interval]	
age	.03958388	.0011745	.02491887	-.0092562 -.0030797 -.0024686 -1.75e-06	.088424 (N) .0960786 (P) .09875 (BC) .1007133 (BCa)
MS per week	-.02476726	-.0000247	.00913559	-.0426727 -.0432226 -.0431453 -.0434144	-.0068618 (N) -.0072979 (P) -.0071524 (BC) -.0078095 (BCa)
MS specialist 	-.42267544	-.0184136	.21270927	-.8395779 -.8629452 -.8131921 -.808783	-.0057729 (N) -.0256341 (P) .0108584 (BC) .018469 (BCa)
Yrs practice	-.04539291	-.0015491	.02517197	-.0947291 -.1004555 -.1004224 -.1033896	.0039432 (N) -.0022204 (P) -.0021897 (BC) -.0026762 (BCa)
Canada vs O	-.89995784	-.0029067	.20068173	-1.293287 -1.290103 -1.255636 -1.254455	-.5066289 (N) -.4966192 (P) -.454275 (BC) -.4531753 (BCa)
Aversion Amb	.38997183	.0022838	.2253716	-.0517484 -.0424694 -.0465826 -.0365294	.831692 (N) .83175 (P) .8271382 (BC) .8369908 (BCa)
cons	1.5182215	-.0129152	.74293783	.0620902 -.0301683 -.0398558 -.1557113	2.974353 (N) 2.824306 (P) 2.811678 (BC) 2.776518 (BCa)

(N) normal confidence interval
(P) percentile confidence interval
(BC) bias-corrected confidence interval
(BCa) bias-corrected and accelerated confidence interval

References: Aversion Amb: aversion to ambiguity; O: other countries (Argentina, Chile, Spain), MS: multiple sclerosis; yrs: years.

Note that 95%CI for each variable are similar irrespective of the analytical estimation method (e.g normal CI, percentile CI, and biased-corrected CI).