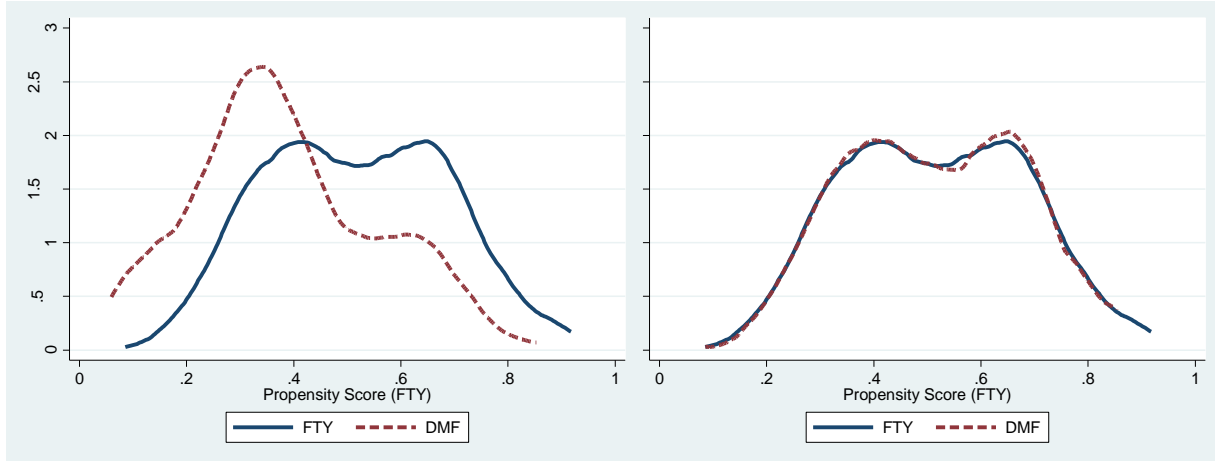


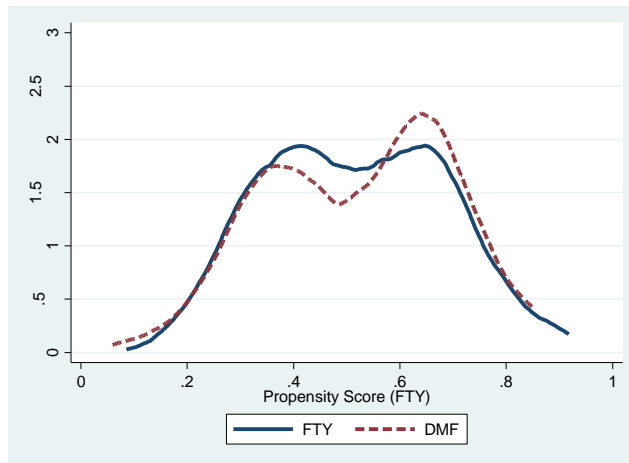
## Supplemental Appendix

**Figure S1.** Density plot of propensity scores (propensity of DMF) demonstrating overlap of propensity scores between DMF and FTY achieved through 2:1 matching with replacement and ATT doubly robust weighting. FTY: fingolimod, DMF: dimethyl fumarate.



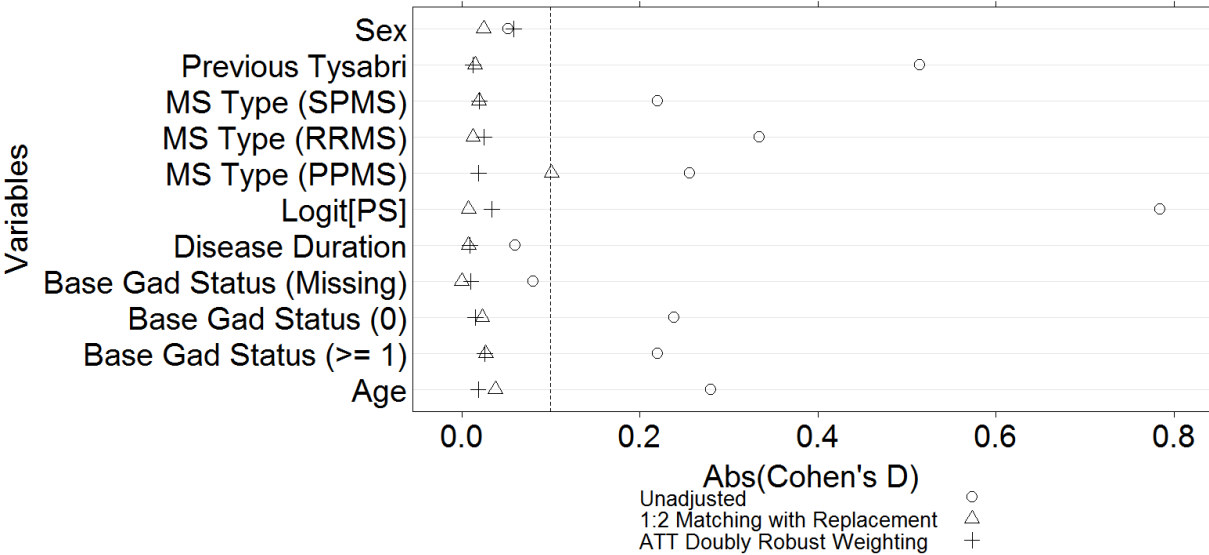
Entire Cohort

2:1 Matching with Replacement



ATT Doubly Robust Weighting

**Figure S2.** Cohen’s D values for effect sizes comparing baseline covariates between FTY and DMF for unadjusted, 1:2 propensity score matching and ATT doubly robust weighting. FTY: fingolimod, DMF: dimethyl fumarate.



*Relapsing-Remitting Multiple Sclerosis Only Cohort*

**Table S1.** Baseline characteristics of RRMS\* only

	Fingolimod (N=271)		Dimethyl fumarate (N=265)		P-value
	N or Mean	% or SD	N or Mean	% or SD	
<b>Disease Duration (Years, SD)</b>	10.4	6.3	9.9	6.6	0.101
<b>Age (Years, SD)</b>	41.5	11.2	43.5	12.0	0.046
<b>Gender - Female</b>	178	73.0%	192	72.5%	0.900
<b>Previous DMT**</b>					<0.001
Interferons	35	14.3%	39	14.7%	
Glatiramer acetate	46	18.9%	91	34.3%	
Natalizumab	97	39.8%	48	18.1%	
Rituximab	1	0.4%	5	1.9%	
Fingolimod	1	0.4%	0	0.0%	
Dimethyl fumarate	0	0.0%	17	6.4%	
None	61	25.0%	60	22.6%	
Other	3	1.2%	5	1.9%	
<b>Mean time between Previous DMT and study drug (SD)</b>	1.05 (N=183)	1.22	0.76 (N=205)	1.31	<0.001
<b>Baseline MRI Available for Review</b>					0.004
Available	211	86.5%	249	94.0%	
Unavailable	33	13.5%	16	6.0%	
<b>Contrast Enhancement on Baseline MRI</b>	53 (N=208)	25.5%	37 (N=233)	15.9%	0.013
<b>Disease Burden on Baseline MRI</b>					<0.001
Mild	92	37.7%	140	52.8%	
Moderate	70	28.7%	71	26.8%	
Severe	37	15.2%	16	6.0%	
Missing	45	18.4%	38	14.3%	

\* relapsing-remitting multiple sclerosis

\*\* Within 6 months prior to starting study drug

**Table S2.** Unadjusted discontinuation outcomes for RRMS\* only

	Fingolimod (N=271)		Dimethyl fumarate (N=265)		P-value
	N or Mean	% or SD	N or Mean	% or SD	
<b>Discontinued drug ≤24 months</b>	79	32.4%	121	45.7%	0.002
Disease activity**	21	8.6%	25	9.4%	0.745
Adverse events	41	16.8%	62	23.4%	0.064
Insurance	1	0.4%	3	1.1%	0.625
Loss to follow up	13	5.3%	22	8.3%	0.221
Other	3	1.2%	9	3.4%	0.145
<b>Mean time to discontinuation (Months)***</b>	10.6	7.0	10.4	7.4	0.654

\*relapsing-remitting multiple sclerosis

\*\*includes discontinuation of drug due to clinical relapse, MRI activity or disease progression

\*\*\*for those who discontinue

**Table S3.** Unadjusted efficacy outcomes for RRMS\* only

	Fingolimod (N=271)		Dimethyl fumarate (N=265)		P-value
	N or Mean	% or SD	N or Mean	% or SD	
<b>Patients with a relapse during first 2 years of study drug</b>	23	9.4%	38	14.3%	0.088
<b>MRI Available while on drug in first 2 years</b>	195	79.9%	207	78.1%	0.618
Mean number of available MRIs	1.66	0.69	1.64	0.66	0.823
Patients with Contrast enhancement	25	12.8%	23	11.1%	0.597
Patients with New T2 lesions	70	35.9%	70	33.8%	0.662
<b>Composite Efficacy Measure*</b>	87	35.7%	98	37.0%	0.756

\*relapsing-remitting multiple sclerosis

\*\*Patients who had a clinical relapse, contrast enhancement or a new T2 lesion on follow-up MRI

**Table S4.** Unadjusted & adjusted odds ratios for discontinuation for any reason at ≤24 months, discontinuation due to adverse events only and disease activity (DMF versus FTY), RRMS patients

	N	Discontinuation				Efficacy	
		Due to Any Reason		Due to Adverse Events		Composite Measure**	
		Odds Ratio (95% CI)	p-value	Odds Ratio (95% CI)	p-value	Odds Ratio (95% CI)	p-value
<b>Simple Logistic Regression</b>	509	<b>1.76</b> (1.22, 2.52)	0.002	<b>1.52</b> (0.97, 2.35)	0.066	<b>1.06</b> (0.74, 1.52)	0.756
<b>Adjusted Logistic Regression*</b>	509	<b>2.01</b> (1.36, 2.97)	<0.001	<b>1.51</b> (0.95, 2.41)	0.079	<b>1.10</b> (0.74, 1.63)	0.628
<b>Propensity Matching with 1:1 greedy matching without replacement*</b>	488	<b>1.86</b> (1.29, 2.69)	0.001	<b>1.54</b> (0.99, 2.41)	0.057	<b>1.05</b> (0.73, 1.53)	0.778
<b>Propensity Matching with 1:2 nearest neighbor matching with replacement*</b>	732 (431 unique)	<b>1.79</b> (1.14, 2.80)	0.011	<b>1.63</b> (0.96, 2.78)	0.072	<b>1.13</b> (0.72, 1.78)	0.597
<b>ATT Doubly Robust Weighting Estimator*</b>	509	<b>1.86</b> (1.25, 2.77)	0.002	<b>1.43</b> (0.89, 2.29)	0.145	<b>1.17</b> (0.80, 1.72)	0.424

\*controlling for age, disease duration, previous natalizumab use, gender, and contrast enhancement on baseline MRI

\*\*includes clinical relapse, new T2 lesion on follow-up MRI, or contrast enhancement on follow-up MRI regardless of the event leading to discontinuation of drug

*Patients who initiated fingolimod in first half versus second half of observation period*

**Table S5.** Unadjusted discontinuation outcomes for fingolimod patients who began before and on/after April 1<sup>st</sup>, 2012

	Before April 1 <sup>st</sup> , 2012 (N=181)		On/After April 1 <sup>st</sup> , 2012 (N=90)		P-value
	N or Mean	% or SD	N or Mean	% or SD	
<b>Discontinued drug ≤24 months</b>	57	31.5%	36	40.0%	0.164
Disease activity*	17	9.4%	10	11.1%	0.656
Adverse events	28	15.5%	18	20.0%	0.349
Insurance	1	0.6%	1	1.1%	0.613
Loss to follow up	9	5.0%	6	6.7%	0.566
Other	2	1.1%	1	1.1%	0.996
<b>Mean time to discontinuation (Months)**</b>	12.1	7.1	7.5	6.2	0.003

\*includes discontinuation of drug due to clinical relapse, MRI activity or disease progression

\*\*for those who discontinue

*Patients who initiated dimethyl fumarate in first half versus second half of observation period*

**Table S6.** Unadjusted discontinuation outcomes for dimethyl fumarate patients before and on/after July 1<sup>st</sup>, 2013

	Before July 1 <sup>st</sup> , 2013 (N=192)		On/after July 1 <sup>st</sup> , 2013 (N=150)		P-value
	N or Mean	% or SD	N or Mean	% or SD	
<b>Discontinued drug ≤24 months</b>	91	47.4%	70	46.7%	0.893
Disease activity*	25	13.0%	13	8.7%	0.204
Adverse events	46	24.0%	36	24.0%	0.993
Insurance	2	1.0%	2	1.3%	0.803
Loss to follow up	13	6.8%	14	9.3%	0.383
Other	5	2.6%	5	3.3%	0.691
<b>Mean time to discontinuation (Months)**</b>	11.0	7.1	8.6	7.1	0.025

\*includes discontinuation of drug due to clinical relapse, MRI activity or disease progression

\*\*for those who discontinue

**Table S7.** Cohen's D values for FTY vs DMF before and after propensity matching

	Unadjusted	1:1 Greedy Matching	1:2 Matching with Replacement	1:1 Matching with Replacement	ATT Doubly Robust Weighting
<b>Age</b>	0.280	0.089	0.038	0.048	0.018
<b>Disease Duration</b>	0.060	0.094	0.008	0.075	0.009
<b>MS Type (RRMS)</b>	0.339	0.038	0.012	0.078	0.025
<b>MS Type (SPMS)</b>	0.221	0.013	0.020	0.041	0.020
<b>MS Type (PPMS)</b>	0.258	0.070	0.100	0.116	0.019
<b>Previous Tysabri</b>	0.531	0.417	0.015	0.015	0.012
<b>Sex</b>	0.052	0.017	0.024	0.067	0.058
<b>Base Gad Status (0)</b>	0.240	0.151	0.023	0.015	0.015
<b>Base Gad Status (≥ 1)</b>	0.221	0.143	0.027	0.018	0.026
<b>Base Gad Status (Missing)</b>	0.080	0.043	0.000	0.000	0.010