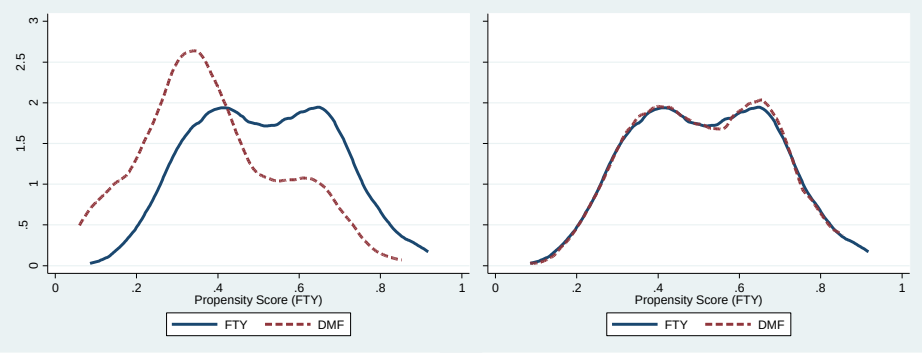
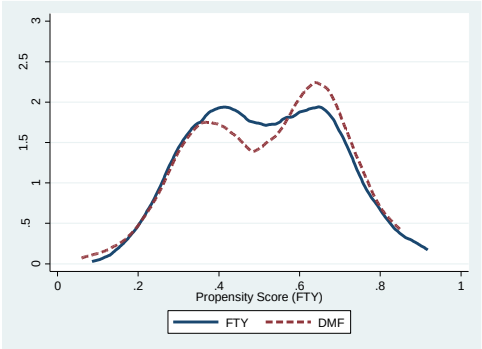
Supplemental Appendix

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.



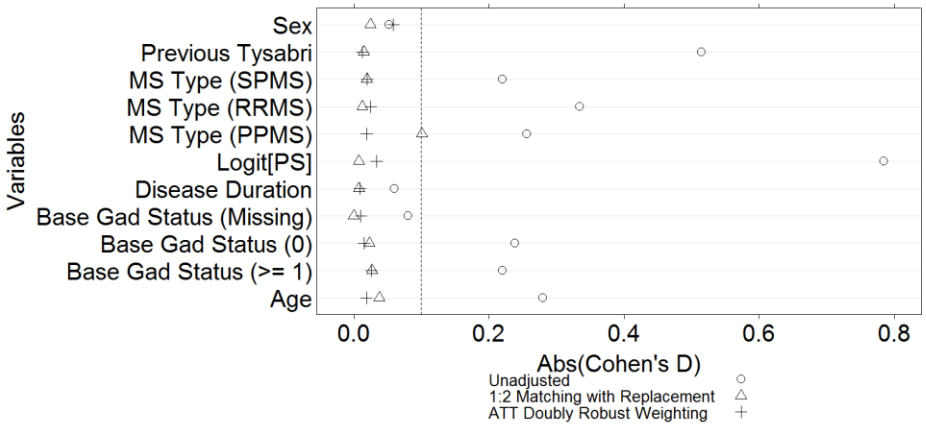
Entire Cohort

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)		
	N or Mean	**% or SD**	**N or Mean**	**% or SD**	**P-value**
Disease Duration (Years, SD)	10.4	6.3	9.9	6.6	0.101
Age (Years, SD)	41.5	11.2	43.5	12.0	0.046
Gender - Female	178	73.0%	192	72.5%	0.900
Previous DMT**					<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%	
Mean time between Previous DMT and study drug (SD)	1.05 (N=183)	1.22	0.76 (N=205)	1.31	<0.001
Baseline MRI Available for Review					0.004
Available	211	86.5%	249	94.0%	
Unavailable	33	13.5%	16	6.0%	
Contrast Enhancement on Baseline MRI	53 (N=208)	25.5%	37 (N=233)	15.9%	0.013
Disease Burden on Baseline MRI					<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)		
	N or Mean	**% or SD**	**N or Mean**	**% or SD**	**P-value**
Discontinued drug ≤24 months	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
Mean time to discontinuation (Months)*	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)		
	N or Mean	**% or SD**	**N or Mean**	**% or SD**	**P-value**
Patients with a relapse during first 2 years of study drug	23	9.4%	38	14.3%	0.088
MRI Available while on drug in first 2 years	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
Composite Efficacy Measure*	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

		Discontinuation				Efficacy	
		Due to Any Reason		Due to Adverse Events		Composite Measure**	
	N	Odds Ratio (95% CI)	p-value	Odds Ratio (95% CI)	p-value	Odds Ratio (95% CI)	p-value
Simple Logistic Regression	509	**1.76** (1.22, 2.52)	0.002	**1.52** (0.97, 2.35)	0.066	**1.06** (0.74, 1.52)	0.756
Adjusted Logistic Regression*	509	**2.01** (1.36, 2.97)	<0.001	**1.51** (0.95, 2.41)	0.079	**1.10** (0.74, 1.63)	0.628
Propensity Matching with 1:1 greedy matching without replacement*	488	**1.86** (1.29, 2.69)	0.001	**1.54** (0.99, 2.41)	0.057	**1.05** (0.73, 1.53)	0.778
Propensity Matching with 1:2 nearest neighbor matching with replacement*	732 (431 unique)	**1.79** (1.14, 2.80)	0.011	**1.63** (0.96, 2.78)	0.072	**1.13** (0.72, 1.78)	0.597
ATT Doubly Robust Weighting Estimator*	509	**1.86** (1.25, 2.77)	0.002	**1.43** (0.89, 2.29)	0.145	**1.17** (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 1st, 2012

	Before April 1st, 2012 (N=181)		On/After April 1st, 2012 (N=90)		
	N or Mean	**% or SD**	**N or Mean**	**% or SD**	**P-value**
Discontinued drug ≤24 months	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
Mean time to discontinuation (Months)**	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 1st, 2013

	Before July 1st, 2013 (N=192)		On/after July 1st, 2013 (N=150)		
	N or Mean	**% or SD**	**N or Mean**	**% or SD**	**P-value**
Discontinued drug ≤24 months	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
Mean time to discontinuation (Months)**	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
Age	0.280	0.089	0.038	0.048	0.018
Disease Duration	0.060	0.094	0.008	0.075	0.009
MS Type (RRMS)	0.339	0.038	0.012	0.078	0.025
MS Type (SPMS)	0.221	0.013	0.020	0.041	0.020
MS Type (PPMS)	0.258	0.070	0.100	0.116	0.019
Previous Tysabri	0.531	0.417	0.015	0.015	0.012
Sex	0.052	0.017	0.024	0.067	0.058
Base Gad Status (0)	0.240	0.151	0.023	0.015	0.015
Base Gad Status (≥ 1)	0.221	0.143	0.027	0.018	0.026
Base Gad Status (Missing)	0.080	0.043	0.000	0.000	0.010

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