Comorbidity and Persistence of Disease-Modifying Therapy Use for Relapsing Remitting Multiple Sclerosis

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Background

- Comorbidity is more common among individuals with multiple sclerosis (MS) compared to controls[1]
- Comorbidity influences MS:
  - Delays MS diagnosis[2]
  - Increases risk of relapse[3]
  - Increases risk of disability progression[4]
- Comorbidity influences MS treatment:
  - Decreases likelihood of starting disease modifying therapy (DMT)[5]
  - Increases risk of discontinuing initial DMT due to lack of tolerability[6]

Objectives

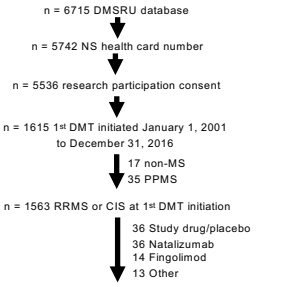
Evaluate effect of comorbidity on initial DMT persistence along with reasons for discontinuation

Methods

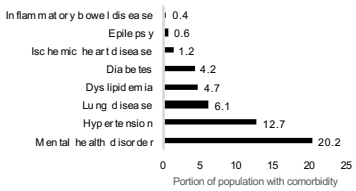
- Research ethics board approval obtained from Nova Scotia Health Authority Research Ethics Board (#1023555)
- Secondary data analysis using Dalhousie Multiple Sclerosis Research Unit (DMSRU) and Health Data Nova Scotia (HDNS) databases
- Population: Relapsing remitting multiple sclerosis/Clinically isolated syndrome starting initial platform DMT (glatiramer acetate, interferon-β, dimethyl fumarate, teriflunomide) between January 1 2001 to December 31 2016
- Comorbidity based on validated administrative case definitions

Comorbidity	ICD-9 codes	ICD-10 codes	Years of Data	Number and type of hospital (H) or physician (P) claims
Hypertension	401, 402, 403, 404, 405	I10, I11, I12, I13, I15	2	≥1H or ≥2P
Hyperlipidemia	272	E78.0, E78.2, E78.4, E78.5	5	≥1H or ≥2P
Diabetes	250	E10, E11, E12, E13, E14	5	≥1H or ≥2P
Chronic lung disease	491, 492, 493, 496	J40, J42, J43, J44, J45, J46	5	≥1H or ≥2P
Ischemic heart disease	410, 411, 412, 413, 414	I20, I21, I22, I23, I24, I25	5	≥1H or ≥2P
Epilepsy	345	G40, G41	3	≥1H or ≥2P
Inflammatory bowel disease	555,556	K50, K51		≥5H or P; or if resident in province <2 years ≥3H or P
Mental health disorder (anxiety, depression, bipolar disorder, schizophrenia)	300.0, 300.2, 296.2, 296.3, 298.0, 300.4, 311, 296.0, 296.1, 296.04, 296.14, 296.4, 296.44, 296.5, 296.54, 296.6, 296.7, 296.8, 295	F40, F41, F32, F33, F34, F31, F20, F25	5	≥1H or ≥5P

Results



Cohort Characteristics	n	
MS Subtype (most recent) (n,%)	1464	
RRMS		1280 (87.4%)
SPMS		177 (12.1%)
CIS		7 (0.5%)
Age symptom onset, years (median, IQR)	1459	33.0 (26.4-40.6)
Age MS diagnosis, years (median, IQR)	1445	36.6 (29.3-44.6)
Sex (n,%)	1463	
Male		341 (23.3%)
Female		1122 (76.7%)
Delay MS diagnosis to first DMT, years (median, IQR)	1445	0 (0-2)
EDSS at DMT initiation (median, IQR)	1343	2.0 (1.5-3.0)
Neighbourhood income quintile (n,%)	1408	
1 (lowest)		263 (18.7%)
2		280 (19.9%)
3		295 (21.0%)
4		294 (20.9%)
5 (highest)		276 (19.6%)
First DMT (n,%)	1464	
Interferon-β		814 (55.6%)
Glatiramer acetate		478 (32.7%)
Dimethyl fumarate 240 mg bid		117 (8.0%)
Teriflunomide 14 mg daily		55 (3.8%)
Comorbidity count (n,%)	1464	
0		904 (61.7%)
1		422 (28.8%)
≥2		138 (9.4%)

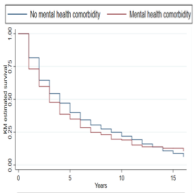


Cox Proportional Hazards Regression for Persistence of DMT According to Comorbidity Count (n=1140)

	HR	95% CI	SE	Wald	p value
Comorbidity Count					
0	1	-	-	-	-
1	1.07	0.92-1.25	0.08	0.89	0.4
≥2	1.03	0.80-1.32	0.13	0.22	0.8
Age MS diagnosis	**0.98**	**0.97-0.99**	**0.004**	**-5.30**	**<0.01**
Diagnostic lag	1.00	0.98-1.01	0.01	-0.44	0.7
EDSS at DMT initiation	1.05	1.00-1.10	0.03	1.78	0.07
Sex					
Male	1	-	-	-	-
Female	0.96	0.82-1.12	0.08	-0.54	0.6
Income quintile					
1 (lowest)	1	-	-	-	-
2	0.92	0.74-1.15	0.10	-0.73	0.5
3	1.01	0.82-1.25	0.11	0.12	0.9
4	1.06	0.86-1.31	0.11	0.52	0.6
5 (highest)	1.08	0.87-1.34	0.12	0.69	0.5

Cox Proportional Hazards Regression for Persistence of DMT According to Specific Comorbidity (n=1140)

	HR	95% CI	SE	Wald	p value
Comorbidity					
Mental health disorder	**1.20**	**1.02-1.41**	**0.10**	**2.15**	**0.03**
Hypertension	0.97	0.78-1.19	0.10	-0.33	0.7
Hyperlipidemia	0.80	0.56-1.14	0.14	-1.24	0.2
Diabetes	0.82	0.57-1.17	0.15	-1.11	0.3
Ischemic heart disease	1.10	0.59-2.03	0.34	0.30	0.8
Lung disease	1.08	0.82-1.43	0.15	0.56	0.6
Other*	0.48	0.21-1.10	0.20	-1.74	0.1
Age MS diagnosis	**0.98**	**0.97-0.99**	**0.004**	**-4.75**	**<0.01**
Diagnostic lag	1.00	0.98-1.01	0.01	-0.38	0.7
EDSS at DMT initiation	1.05	1.00-1.11	0.03	2.00	0.05
Sex					
Male	1	-	-	-	-
Female	0.94	0.80-1.10	0.08	-0.75	0.5
Income quintile					
1 (lowest)	1	-	-	-	-
2	0.91	0.73-1.14	0.10	-0.82	0.4
3	1.01	0.82-1.25	0.11	0.12	0.9
4	1.04	0.84-1.28	0.11	0.35	0.7
5 (highest)	1.07	0.86-1.33	0.12	0.59	0.6



Median DMT Persistence by Mental Health Comorbidity
No = 4 years (95% CI 4-5)
Yes = 3 years(95% CI 3-4)

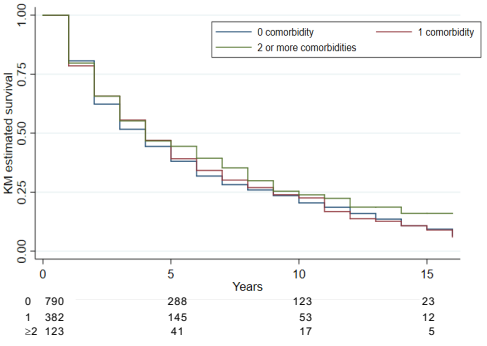
Logistic Regression for Stopping DMT Due to Tolerability According to Comorbidity Count (n=1012)

	OR	95% CI	SE	Wald	P value
Comorbidity Count					
0	1	-	-	-	-
1	1.10	0.82-1.47	0.16	0.63	0.5
≥2	**1.72**	**1.05-2.82**	**0.43**	**2.14**	**0.03**
Age MS diagnosis	**0.98**	**0.97-1.00**	**0.01**	**-2.19**	**0.03**
Diagnostic lag	1.00	0.98-1.03	0.01	0.28	0.8
EDSS at DMT initiation	**0.80**	**0.72-0.88**	**0.04**	**-4.52**	**<0.001**
Sex					
Male	1	-	-	-	-
Female	**1.54**	**1.14-2.09**	**0.24**	**2.79**	**0.01**
Income quintile					
1	1	-	-	-	-
2	0.87	0.58-1.32	0.19	-0.64	0.5
3	0.92	0.62-1.37	0.19	-0.41	0.7
4	1.04	0.70-1.56	0.21	0.21	0.8
5	0.93	0.61-1.40	0.19	-0.36	0.7

Logistic Regression for Stopping DMT Due to Efficacy According to Comorbidity Count (n=1012)

	OR	95% CI	SE	Wald	P value
Comorbidity Count					
0	1	-	-	-	-
1	1.11	0.80-1.54	0.18	0.62	0.5
≥2	0.67	0.38-1.18	0.19	-1.38	0.2
Age MS diagnosis	**1.02**	**1.00-1.04**	**0.01**	**2.30**	**0.02**
Diagnostic lag	1.00	0.97-1.03	0.02	0.12	0.9
EDSS at DMT initiation	**1.37**	**1.23-1.53**	**0.07**	**5.86**	**<0.001**
Sex					
Male	1	-	-	-	-
Female	**0.70**	**0.50-0.97**	**0.12**	**-2.12**	**0.03**
Income quintile					
1	1	-	-	-	-
2	0.96	0.59-1.57	0.24	-0.17	0.9
3	1.03	0.64-1.63	0.24	0.10	0.9
4	1.43	0.91-2.24	0.33	1.55	0.1
5	1.31	0.82-2.10	0.31	1.15	0.3

Kaplan Meier survival analysis of disease-modifying therapy persistence by comorbidity count



Median DMT Persistence by Comorbidity
0 = 4 years (95% CI 3-4)
1 = 4 years (95% CI 4-5)
≥2 = 4 years (95% CI 3-6)

Conclusion

Individuals with higher comorbidity burden, and particularly mental health comorbidity should be monitored for barriers to continuing DMT after treatment initiation

References

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