

Appendix

Table e1. Years for which each data source was available in the study provinces

| Data Source | British Columbia | Manitoba |
|-------------------------------------|------------------|-----------------|
| Discharge Abstract Database | 1991/92-2015/16 | 1979/80-2016/17 |
| Physician (medical services) visits | 1991/92-2015/16 | 1979/80-2016/17 |
| Prescription claims | 1996-2015/16 | 1995-2016/17 |
| Home care utilization | - | 1998-2015 |

Slash between years designates fiscal years. For example, 1991/92 indicates fiscal year 1991 which is from April 1, 1991 to March 31, 1992

Table e2. Diagnosis, procedure and drug identification codes/numbers used to identify participants with multiple sclerosis, cardiac diagnoses and procedures

| Diagnosis/ Procedure | Code |
|---|--|
| Prescription claims for multiple sclerosis | 02169649; 02337819; 02237770, 02269201; 02281708, 02277492, 02237317, 02237319, 02237320, 02318253, 02318261, 02233014, 02245619; 02286386; 02365480, 02404508, 02416328; 02418320 |
| Demyelinating disease claims [ICD-9/10-CA] | optic neuritis [377.3/H46], transverse myelitis [323.82/G37], acute disseminated encephalomyelitis [323/G36.9], demyelinating disease of CNS unspecified [341.9/G37.8], other acute disseminated demyelination [G36], MS [340/G35], or neuromyelitis optica [341.0/G36.0] |
| Cardiac catheterization [ICD-9/CCI] | 37.21, 37.22, 37.23, 88.52-88.57 / 3.IP.10 |
| Angioplasty with or without stent insertion [ICD-9/CCI] | 36.01, 36.02, 36.05, 36.06 / 1.IJ.50.GQ-BD, 1.IJ.50.GU-BD, 1.IJ.50.GT-BD, 1.IJ.50.GQ-BF, 1.IJ.50.GU-BF, 1.IJ.50.GT-BF, 1.IJ.50.GQ-OD, 1.IJ.50.GU-OD, 1.IJ.50.GT-OD, 1.IJ.57.GQ, 1.IJ.50.GQ-NR, 1.IJ.50.GQ-OA, 1.IJ.50.GU-OA, 1.IJ.50.GT-OA, 1.IJ.50.GQ-OB, 1.IJ.50.GU-OB, 1.IJ.50.GT-OB, 1.IJ.50.GQ-OE, 1.IJ.50.GU-OE, 1.IJ.50.GT-OE |
| Coronary artery bypass grafting [ICD-9/CCI] | 36.1x / 1.IJ.76 |

ICD = International Classification of Disease, CCI = Canadian Classification of Interventions

Table e3. Proportion of participants who filled a prescription for pharmacotherapy within 30 days after hospitalization for acute myocardial infarction

| Pharmacotherapy | Multiple Sclerosis | Matches | Difference of Proportions (95% CI) | P-value |
|--|--------------------|------------------|------------------------------------|-------------------|
| <i>Beta-blocker use, n (%)</i> | | | | |
| Any use, all participants* | 354/541 (65.4) | 1768/2390 (74.0) | -8.6 (-13.0, -4.2) | <0.0001 |
| Any use, excluding participants taking a beta-blocker or with lung disease pre-admission | 247/394 (62.7) | 1235/1678 (73.6) | -10.9 (-16.1, -5.7) | <0.0001 |
| Any use among participants with ≥1 year follow-up | 310/423 (73.3) | 1541/1925 (80.1) | -6.8 (-11.4, -2.2) | 0.0025 |
| Any use among participants with ≥1 year follow-up, excluding participants taking a beta-blocker or with lung disease pre-admission | 220/309 (71.2) | 1116/1404 (79.5) | -8.3 (-13.8, -2.8) | 0.0019 |
| <i>High dose statin use, n (%)</i> | | | | |
| Any use, all participants* | 245/541 (45.3) | 1188/2390 (49.7) | -8.9 (-13.4, -4.4) | <0.0001 |
| Any use, excluding those taking a statin pre-admission | 252/438 (57.5) | 1154/1776 (65.0) | -7.5 (-12.6, -2.4) | 0.0038 |
| Any use among participants with ≥1 year follow-up | 300/423 (70.9) | 1476/1925 (76.7) | -5.8 (-10.5, -1.1) | 0.013 |
| Any use among participants with ≥1 year follow-up, excluding participants taking statin pre-admission | 232/340 (68.2) | 1044/1445 (72.2) | -4.0 (-9.3, 1.3) | 0.14 |
| <i>Dual anti-platelet therapy, n (%)</i> | | | | |
| Any use, all participants | 309/541 (57.1) | 1461/2390 (61.1) | -4.0 (-8.6, 0.6) | 0.085 |
| Any use among participants with ≥1 year follow-up | 269/423 (63.6) | 1925/1486 (77.2) | -13.6 (-18.6, -8.6) | 0.0002 |
| <i>ACEI/ARB use, n (%)</i> | | | | |
| Any use, all participants* | 319/541 (59.0) | 1958/2390 (81.9) | -22.9 (-27.3, -18.5) | <0.0001 |
| Any use, excluding participants taking ACEI/ARB pre-admission | 177/370 (47.8) | 1244/1503 (82.8) | -35.0 | <0.0001 |

| | | | | |
|---|----------------|------------------|-------------------------|-------------------|
| Any use among participants with ≥ 1 year follow-up | 276/423 (65.2) | 1640/1925 (91.1) | (-40.4, -29.6) -25.9 | <0.0001 |
| Any use among participants with ≥ 1 year follow-up, excluding participants taking ACEI/ARB pre-admission | 166/291 (57.0) | 1027/1272 (80.7) | (-30.6, -21.2) -23.7 | <0.0001 |

*Participants with an AMI index year in ≥ 1995 (Manitoba) or ≥ 1996 (British Columbia). Bold indicates statistical significance

Table e4. Pooled adjusted^a odds ratios and 95% confidence intervals for association of multiple sclerosis with discontinuation of pharmacotherapy within 12 months and of good adherence

| Pharmacotherapy^b | Discontinuation | Good adherence |
|------------------------------------|--------------------------------|--------------------------------|
| Beta-blocker | 0.86 (0.66, 1.12) ^d | 1.18 (0.89, 1.56) ^d |
| Statin | 1.00 (0.75, 1.32) ^d | 0.99 (0.75, 1.32) ^d |
| Anti-platelet ^c | 1.13 (0.75, 1.71) ^e | 1.02 (0.77, 1.36) ^d |
| ACEI/ARB | 0.83 (0.58, 1.18) ^f | 1.08 (0.80, 1.46) ^d |

Adjusted for age group, sex, index year, SES, number of physician visits, number of drug classes (ATC 4th level), diabetes, hypertension, hyperlipidemia, chronic lung disease; b- Sample sizes for pharmacotherapy analyses were: beta-blocker (British Columbia [BC]: 216 MS, 1045 matches; Manitoba [MB]: 112 MS, 566 matches), statins (BC: 216 MS, 1042 matches; MB: 113 MS, 567 matches), anti-platelets (BC: 195 MS, 876 matches; MB: 107 MS, 521 matches), ACEI/ARB (BC: 209 MS, 1030 matches; MB: 110 MS, 554 matches); c- In Manitoba adjusted only for sex, age due to small number of events; d- $I^2 = 0$; e- $I^2 = 58.2\%$; f- $I^2 = 31.5\%$

Table e5. Odds ratios (95% confidence intervals) for the association between multiple sclerosis and death within 30 or 365 days post-discharge after acute myocardial infarction (AMI)

| Model | British Columbia |
|--|-------------------------|
| <i>Death within 30 days</i> | |
| Unadjusted | 1.94 (0.92, 4.12) |
| Adjusted for demographics*, index year | 1.95 (0.92, 4.16) |
| Adjusted for demographics*, index year, comorbidities, † acute complications‡ | 1.96 (0.88, 4.19) |
| Adjusted for demographics*, index year, comorbidities, † acute complications‡, AMI management§ | 1.47 (0.65, 3.33) |
| <i>Death within 365 days</i> | |
| Unadjusted | 1.31 (0.88, 1.96) |
| Adjusted for demographics*, index year | 1.33 (0.87, 2.02) |
| Adjusted for demographics*, index year, comorbidities, † acute complications‡ | 1.36 (0.88, 2.10) |
| Adjusted for demographics*, index year, comorbidities, † acute complications‡, AMI management§ | 1.16 (0.73, 1.85) |

SES = socioeconomic status; *- demographics = age (20-54, ≥55), sex, SES; †- diabetes, congestive heart failure, cancer, cerebrovascular disease, chronic renal failure; ‡- shock, pulmonary edema, acute renal failure, cardiac dysrhythmia; §-revascularization within 30 days of AMI admission, use of each of beta-blockers, statins, ACE-inhibitors/Angiotensin-receptor blocker and dual anti-platelets within 30 days post-discharge