

Supplemental Methods and Results

Case Definitions: Immune-mediated inflammatory diseases

The case definitions used to identify Manitobans with multiple sclerosis, inflammatory bowel disease and rheumatoid arthritis are delineated below. Each case definition was developed then validated using medical records review where diagnoses were affirmed according to prevailing clinical diagnostic criteria. Two of the definitions have also been validated against self-report data.^{1,2}

Table e1 Case Definitions for Immune-mediated Inflammatory Diseases^{1,3,4}

Name	ICD9/10 codes	Case Definition	Date of Diagnosis
MS	340/ G35 DIN 02169649, 02337819 02281708, 02277492 02237317, 02237319 02237320, 02318253 02318261, 02237770 02269201, 02233014 02245169, 02286386 02365480, 02404508 02416328, 02418320	≥3 H or P or Rx ever	Based on first CNS demyelinating disease claim. After identifying those who meet MS definition look to see if any of the following codes appear in hospital or physician claims earlier: G36, 341.0, G37.8, 323, G36.9, 377.3, H46, 323.82, G37, 340, G35, 323,83, 341.9
IBD	555.xx, 556.xx, K50, K51	If resident in Manitoba ≥2 years: ≥5 H or P If resident in Manitoba <2 years: ≥3 H or P	Based on first IBD claim
RA	714.0, M05, M06	If resident in Manitoba ≥2 years: ≥5 H or P If resident in Manitoba <2 years: ≥3 H or P	Based on first RA claim

DIN = drug identification number, MS = multiple sclerosis, IBD = inflammatory bowel disease, RA = rheumatoid arthritis, H = hospital claims, P = physician claims, Rx = prescription claims

General Population Cohort Definition

As previously described, we identified a general population cohort without the immune-mediated inflammatory diseases of interest. The source population was all Manitobans. We excluded individuals with any diagnosis codes for inflammatory bowel disease, multiple sclerosis or rheumatoid arthritis or use of any multiple sclerosis-specific disease-modifying therapies. The full case definitions for these diseases have negative predictive values of 92.4%-97.5%.^{1,3,4} By requiring only one claim, we could

exclude individuals in whom the diagnosis had been considered, as well as individuals who might meet the diagnostic criteria in the future with negative predictive values of 99-100%.

Administrative Definitions: Mood and Anxiety Disorders

The case definitions for mood and anxiety disorders, depression, anxiety disorders were developed and validated against medical records in the multiple sclerosis population,⁵ then subsequently re-validated in the inflammatory bowel disease population using the Composite International Diagnostic Interview.⁶ The case definitions require a specific combination of hospital, physician and prescription claims (Table e2), and rely on diagnoses identified using ICD-9/10 codes and medications identified using Anatomical Therapeutic Chemical Classification codes (Table e3). Compared to medical records, the specificity for all case definitions exceeded 90%, except for anxiety (82%).

Table e2. Administrative case definitions for identifying psychiatric comorbidity^{5,7}

Psychiatric Comorbidity	No. Years of Data	No. & Type of Claims
Any mood or anxiety disorder	2	≥1 H or ≥5 P OR (≥1 P AND ≥4 Rx)
Depression	2	≥1 H or ≥5 P OR (≥1 P AND ≥7 Rx)
Anxiety	2	≥1 H or ≥2 P OR (≥1 P AND ≥2 Rx)
Bipolar disorder	5	≥1 H or ≥3 P

*Use ICD-9/10 codes and ATC codes from Table e3; H = hospital claims; P = physician claims, Rx = prescription claims

Table e3. Diagnosis and medication codes used to identify psychiatric comorbidities^{6,8,9}

Comorbidity	ICD ^a -9 codes	ICD ^a -10 codes	ATC ^b codes	Other Considerations
Any mood or anxiety disorder	300.0, 300.2, 296.0, 296.1, 296.04, 296.14, 296.4, 296.44, 296.5, 296.5, 296.54, 296.6, 296.7, 296.8, 296.2, 296.3, 298.0, 300.4, 311	F40, F41, F31, F32, F33, F34	Antidepressants, anticonvulsants/ mood stabilizers, anxiolytics including N06AA01, N06AA02, N06AA04, N06AA11, N06AA12, N06AA17, N06AA21, N06AB03, N06AB04, N06AB05, N06AB06 N06AB08, N06AB10, N06AF03, N06AF04, N06AG02, N06AX06, N06AX11, N06AX16,	Anticonvulsants used were restricted to lamotrigine, carbamazepine, and valproate which are used as mood stabilizers, after excluding persons with epilepsy. Antidepressants excluded amitriptyline, nortriptyline and buspirone because

Appendix 1, as supplied by the authors. Appendix to: Marrie RA, Walld R, Bolton JM, et al.; CIHR Team in Defining the Burden and Managing the Effects of Psychiatric Comorbidity in Chronic Immunoinflammatory Disease. Uptake of influenza vaccination among persons with inflammatory bowel disease, multiple sclerosis or rheumatoid arthritis: a population-based matched cohort study. *CMAJ Open* 2021. doi:10.9778/cmajo.20200105. Copyright © 2021 The Author(s) or their employer(s). To receive this resource in an accessible format, please contact us at cmajgroup@cmaj.ca. Appendices are posted as supplied by authors.

			N06AX21, N06AX23, N05AB12, N05AB06, N05AN01, N03AF01, N03AG01, N03AX09	of their frequent off-label uses.
Depression	296.2, 296.3, 298.0, 300.4, 311	F32, F33, F34	Antidepressants including N06AA01, N06AA02, N06AA04, N06AA11, N06AA12, N06AA17, N06AA21, N06AB03, N06AB04, N06AB05, N06AB06 N06AB08, N06AB10, N06AF03, N06AF04, N06AG02, N06AX06, N06AX11, N06AX16, N06AX21, N06AX23	Antidepressants excluded amitriptyline, nortriptyline and buspirone because of their frequent off-label uses.
Anxiety	300.0, 300.2	F40, F41	Anxiolytics including N05AB12 (Alprazolam), N05AB06 (Lorazepam)	None of the antidepressants were considered specific for anxiety. Most benzodiazepines were also considered not to be adequately specific for anxiety disorders.

a – ICD: International Classification of Disease; b – ATC: Anatomic Therapeutic Chemical System

Table e4 Tariff and procedure codes to identify surgeries for inflammatory bowel disease^{8,10}

Procedure	Physician Claim Tariff Codes
Intestinal suture	3221, 3223
Colostomy	3195
Colectomy	3179
Colectomy, proctectomy	3180, 3181, 3182, 3183, 3184
Proctosigmoidectomy	3286
Proctosigmoidectomy, proctectomy	3288, 3289, 3290
Rectal surgery	3301
Small bowel resection	3201, 3174

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Ileostomy	3193
	Hospital Procedures
Incision, excision & anastomosis of intestine	45, excluding 451 & 452 diagnostic procedures 1NM – colon + 59, 87, 89, 92 excision

Table e5 Diagnostic and procedure codes to identify joint-related procedures for rheumatoid arthritis^{6,8}

Procedure	ICD-9-CM code	CCI code
Hip replacement (incl. Partial, total, revisions)	81.50, 81.51, 81.53, 81.52	1.VA.53.LA-PN^^ or 1.VA.53.PN-PN^^ 1.VA.53.LA-PM^^ or 1.VA.53.PN-PM^^
Knee replacement	81.54, 81.55	1.VG.53.LA-PN or 1.VG.53.LA-PP
Elbow replacement	81.84	1.TM.80.^^
Shoulder replacement	81.80, 81.81, 81.83	1.TA.53.^^
Wrist fusion	81.25, 81.26	1.UB.75.^^, 1.UG.75.^^
Ankle fusion	81.1	1.WA.75.^^
Foot joint fusion	81.1	1.WE.75.^^
Foot joint replacement	81.57	1.WJ.53.^^
Cervical spine fusion	81.01, 81.02, 81.03	1.SA.75.^^
Hand joint replacement	81.7	1.UC.53.^^, 1.UC.55. ^^

ICD-9-CM = International Classification of Diseases, 9th revision, Clinical Modification; CCI = Canadian Classification of Intervention code. ^ CCI codes are 10 characters long and broken into components. The first number in the code followed by 2 letters indicates anatomical location or development stage. Subsequent codes provide more specific information about the intervention. The ^ indicates that ll of the codes with more specific indicators were included.

Table e6. Immune therapies used for management of inflammatory bowel disease, multiple sclerosis and rheumatoid arthritis (including Anatomic Therapeutic Chemical Classification Codes)

Treatment	Inflammatory Bowel Disease	Multiple Sclerosis	Rheumatoid Arthritis
Disease			
Corticosteroids¹	Methylprednisolone (H02AB04)	Methylprednisolone (H02AB04)	Methylprednisolone (H02AB04)
	Prednisolone (H02AB06)	Prednisolone (H02AB06)	Prednisolone (H02AB06)
	Prednisone (H02AB07)	Prednisone (H02AB07)	Prednisone (H02AB07)
	Budesonide		Triamcinolone (H02AB08)
	Hydrocortisone (enema)		Cortisone (H02AB10))
Anti-inflammatory or Immunomodulatory therapies²	5-ASA (A07EC02, A07EC03)	Glatiramer acetate (L03AX13)	Sulfasalazine (A07EC01)
	Sulfasalazine (A07EC01)	Interferon-beta 1a (L03AB07)	Sodium aurothiomalate (M01CB01)
		Interferon-beta 1b (L03AB08)	Auranofin (M01CB03)
		Dimethyl fumarate (N07XX09)	Aurothioglucose (M01CB04)
		Teriflunomide (L04AA31)	Penicillamine (M01CC01)
		Peg interferon-beta (L03AB13)	Hydroxychloroquine (P01BA02)
Traditional immunosuppressive therapies³	Azathioprine (L04AX01)	Azathioprine (L04AX01)	Azathioprine (L04AX01)
	Methotrexate (L04AX03)	Methotrexate (L04AX03)	Methotrexate (L04AX03)
	6-mercaptopurine (L01BB02)	Mitoxantrone (L01DB07)	Cyclophosphamide (L01AA01)

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	Cyclosporine (L04AA01)	Cyclophosphamide (L01AA01)	Cyclosporine (L04AA01)
	Tacrolimus (L04AD02)		Leflunomide (L04AA13)
Novel therapies/ Biologics³	Infliximab (L04AA12)	Natalizumab (L04AA23)	Infliximab (L04AA12)
	adalimumab (L04AA17)	Fingolimod (L04AA27)	adalimumab (L04AA17)
	Golimumab (L04AB06)	Alemtuzumab (L04AA34)	Etanercept (L04AA11)
	Ustekinumab (L04AC05)	Cladribine ⁴ (L04AA40)	Anakinra (L04AA14)
	Vedolizumab (L04AA33)	Ocrelizumab ⁴ (L04AA36)	Rituximab (L01XC02)
			Abatacept (L04AA24)
			Tocilizumab (L04AC07)
			Tofacitinib (L04AA29)
			Golimumab (L04AB06)
			Certolizumab (L04AB05)

- 1- Corticosteroids were not included as immune therapies for multiple sclerosis because they are not used as an chronic therapy, but exclusively for episodic treatment of relapses. 2- Therapies in this row in the multiple sclerosis column were considered first-line. 3- Therapies in this row in the multiple sclerosis column were considered second-line. 4- Not available during the study period.

Table e7. Crude percentage of persons with immune-mediated disease and matched controls who received influenza vaccinations annually, stratified according to mood/anxiety disorder status

Year	Matched Controls		Immune-Mediated Disease Cases	
	No Mood/Anxiety Disorder	With Mood/Anxiety Disorder	No Mood/Anxiety Disorder	With Mood/Anxiety Disorder
1984	3.74 (3.50, 4.00)	6.42 (5.19, 7.92)	6.71 (6.01, 7.50)	10.69 (7.74, 14.59)
1985	4.34 (4.11, 4.59)	7.81 (6.79, 8.96)	7.28 (6.62, 8.01)	9.02 (7.00, 11.54)
1986	5.18 (4.94, 5.43)	8.56 (7.67, 9.55)	8.44 (7.77, 9.17)	11.53 (9.60, 13.80)
1987	5.61 (5.36, 5.86)	9.34 (8.52, 10.24)	8.48 (7.82, 9.17)	10.12 (8.51, 12.00)
1988	6.41 (6.16, 6.67)	9.63 (8.87, 10.44)	10.08 (9.39, 10.81)	11.00 (9.49, 12.71)
1989	7.40 (7.14, 7.67)	11.19 (10.45, 11.98)	11.23 (10.53, 11.98)	13.15 (11.65, 14.80)
1990	9.23 (8.95, 9.52)	12.79 (12.06, 13.56)	13.77 (13.01, 14.56)	15.74 (14.23, 17.37)
1991	11.55 (11.24, 11.86)	15.85 (15.09, 16.63)	16.96 (16.15, 17.81)	19.16 (17.61, 20.80)
1992	12.79 (12.47, 13.11)	17.22 (16.48, 17.98)	18.02 (17.20, 18.88)	20.46 (18.96, 22.05)
1993	14.29 (13.97, 14.62)	18.33 (17.62, 19.07)	20.50 (19.64, 21.38)	21.77 (20.33, 23.29)
1994	14.21 (13.89, 14.54)	18.23 (17.56, 18.93)	21.26 (20.41, 22.15)	23.37 (21.96, 24.83)
1995	12.63 (12.33, 12.94)	16.21 (15.60, 16.83)	17.78 (16.99, 18.61)	18.92 (17.70, 20.20)

Table e8. Age- and sex-standardized* percentage of persons with immune-mediated disease and matched cohorts who received influenza vaccinations annually (*to 2010 Canadian population)

Year	Immune-mediated disease		Inflammatory bowel disease		Multiple sclerosis		Rheumatoid arthritis	
	Controls	Cases	Controls	Cases	Controls	Cases	Controls	Cases
1984	3.25 (3.03, 3.48)	6.08 (5.42, 6.83)	2.96 (2.46, 3.56)	6.00 (4.58, 7.86)	3.01 (2.53, 3.58)	6.07 (4.66, 7.89)	3.43 (3.13, 3.77)	5.73 (4.85, 6.79)
1985	3.91 (3.70, 4.14)	6.51 (5.90, 7.18)	3.89 (3.38, 4.47)	7.45 (6.01, 9.24)	3.52 (3.05, 4.07)	5.74 (4.55, 7.25)	4.14 (3.85, 4.46)	6.33 (5.51, 7.27)
1986	4.61 (4.40, 4.84)	7.77 (7.14, 8.45)	4.63 (4.11, 5.21)	8.46 (7.01, 10.21)	4.50 (4.01, 5.06)	7.71 (6.37, 9.32)	4.65 (4.37, 4.95)	7.43 (6.58, 8.39)
1987	4.99 (4.78, 5.21)	7.65 (7.06, 8.30)	5.06 (4.55, 5.62)	7.42 (6.16, 8.95)	4.49 (4.02, 5.02)	7.94 (6.57, 9.59)	5.19 (4.90, 5.50)	7.79 (6.93, 8.77)
1988	5.60 (5.38, 5.83)	8.93 (8.31, 9.59)	5.70 (5.20, 6.25)	9.40 (8.05, 10.98)	5.65 (5.13, 6.21)	8.60 (7.29, 10.13)	5.71 (5.39, 6.05)	8.69 (7.84, 9.63)
1989	6.41 (6.19, 6.64)	10.22 (9.58, 10.91)	6.69 (6.18, 7.25)	10.81 (9.44, 12.38)	6.15 (5.64, 6.71)	9.33 (7.99, 10.90)	6.58 (6.28, 6.91)	9.98 (9.09, 10.95)
1990	7.82 (7.59, 8.07)	12.40 (11.70, 13.14)	7.90 (7.37, 8.47)	13.89 (12.40, 15.55)	7.84 (7.28, 8.44)	11.44 (9.95, 13.16)	7.86 (7.53, 8.20)	11.83 (10.90, 12.82)
1991	9.78 (9.52, 10.05)	15.19 (14.44, 15.98)	9.98 (9.40, 10.59)	16.69 (15.12, 18.42)	9.60 (8.99, 10.24)	13.19 (11.63, 14.96)	9.86 (9.50, 10.23)	14.92 (13.87, 16.05)
1992	10.59 (10.33, 10.86)	15.98 (15.23, 16.77)	10.51 (9.95, 11.11)	15.99 (14.53, 17.59)	10.67 (10.05, 11.33)	14.38 (12.77, 16.21)	10.66 (10.31, 11.03)	16.26 (15.18, 17.40)
1993	11.75 (11.48, 12.02)	17.90 (17.13, 18.70)	11.71 (11.14, 12.31)	18.87 (17.35, 20.54)	11.49 (10.85, 12.17)	16.59 (14.83, 18.57)	12.19 (11.69, 12.72)	18.19 (17.01, 19.45)
1994	11.53 (11.27, 11.80)	18.37 (17.62, 19.15)	11.60 (11.05, 12.18)	18.98 (17.51, 20.56)	11.33 (10.73, 11.97)	17.21 (15.51, 19.10)	11.53 (11.16, 11.90)	18.40 (17.31, 19.55)
1995	9.91 (9.68, 10.14)	15.02 (14.36, 15.71)	9.96 (9.47, 10.48)	15.33 (14.05, 16.73)	9.92 (9.36, 10.52)	13.95 (12.47, 15.60)	9.97 (9.65, 10.30)	15.59 (14.55, 16.70)
1996	8.45 (8.25, 8.66)	13.82 (13.19, 14.50)	8.35 (7.91, 8.81)	14.31 (13.09, 15.64)	8.31 (7.80, 8.86)	12.83 (11.39, 14.44)	8.56 (8.29, 8.84)	13.79 (12.88, 14.76)
1997	8.28 (8.08, 8.48)	13.33 (12.74, 13.96)	8.31 (7.89, 8.76)	14.19 (13.04, 15.45)	8.27 (7.78, 8.80)	13.01 (11.34, 14.91)	8.33 (8.07, 8.61)	13.11 (12.29, 13.97)
1998	8.01 (7.82, 8.20)	12.84 (12.27, 13.44)	8.15 (7.76, 8.57)	13.32 (12.24, 14.49)	8.10 (7.62, 8.60)	12.38 (10.74, 14.28)	8.03 (7.77, 8.29)	12.88 (12.0, 13.73)

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1999	8.70 (8.50, 8.90)	14.64 (14.04, 15.27)	8.93 (8.52, 9.35)	15.20 (14.08, 16.42)	8.88 (8.39, 9.40)	14.08 (12.48, 15.90)	8.69 (8.41, 8.98)	15.24 (14.29, 16.26)
2000	13.98 (13.73, 14.24)	22.72 (21.94, 23.53)	14.01 (13.52, 14.52)	23.25 (21.90, 24.68)	14.25 (13.58, 14.95)	22.60 (20.59, 24.80)	14.17 (13.73, 14.63)	22.85 (21.61, 24.16)
2001	14.23 (13.98, 14.49)	22.95 (22.18, 23.75)	14.20 (13.72, 14.70)	23.26 (21.95, 24.65)	14.34 (13.70, 15.00)	22.67 (20.40, 25.20)	14.58 (14.20, 14.98)	23.44 (21.88, 25.12)
2002	15.14 (14.88, 15.40)	23.74 (22.99, 24.52)	14.89 (14.41, 15.39)	24.43 (23.12, 25.81)	15.31 (14.64, 16.01)	22.90 (21.15, 24.78)	15.63 (15.14, 16.14)	23.62 (22.44, 24.87)
2003	20.26 (19.96, 20.57)	31.46 (30.50, 32.45)	19.79 (19.25, 20.34)	32.36 (30.80, 34.01)	20.06 (19.37, 20.78)	29.66 (27.63, 31.83)	20.99 (20.43, 21.58)	30.59 (29.25, 31.98)
2004	20.94 (20.64, 21.26)	32.10 (31.16, 33.06)	21.04 (20.49, 21.60)	32.78 (31.26, 34.38)	20.67 (19.97, 21.39)	30.46 (28.39, 32.69)	21.18 (20.69, 21.67)	32.00 (30.57, 33.50)
2005	22.91 (22.59, 23.24)	35.79 (34.75, 36.86)	22.86 (22.30, 23.44)	36.13 (34.55, 37.78)	23.07 (22.25, 23.92)	36.87 (33.58, 40.49)	23.18 (22.63, 23.75)	35.69 (33.73, 37.77)
2006	22.05 (21.73, 22.38)	32.92 (31.97, 33.91)	22.12 (21.57, 22.68)	33.53 (32.04, 35.10)	22.15 (21.29, 23.04)	32.13 (29.67, 34.78)	22.05 (21.54, 22.57)	33.45 (31.37, 35.66)
2007	21.89 (21.58, 22.21)	32.69 (31.76, 33.65)	21.79 (21.26, 22.34)	33.31 (31.8, 34.84)	22.06 (21.34, 22.80)	32.36 (30.30, 34.56)	22.12 (21.51, 22.75)	32.33 (30.56, 34.20)
2008	21.34 (21.03, 21.65)	32.43 (31.48, 33.41)	21.10 (20.58, 21.63)	32.86 (31.39, 34.39)	21.09 (20.39, 21.81)	32.36 (30.25, 34.61)	21.43 (20.95, 21.92)	32.22 (30.46, 34.08)
2009	22.25 (21.93, 22.57)	34.44 (33.48, 35.44)	22.06 (21.54, 22.59)	34.37 (32.91, 35.89)	22.18 (21.44, 22.93)	37.23 (32.87, 42.17)	22.26 (21.73, 22.81)	33.98 (32.22, 35.82)
2010	23.31 (22.99, 23.63)	34.10 (33.16, 35.07)	22.62 (22.10, 23.15)	34.95 (33.49, 36.47)	23.08 (22.36, 23.82)	33.03 (30.89, 35.32)	23.80 (23.27, 24.36)	33.73 (32.04, 35.51)
2011	22.46 (22.15, 22.77)	32.38 (31.46, 33.33)	22.10 (21.60, 22.62)	32.97 (31.55, 34.45)	22.60 (21.85, 23.38)	32.47 (30.42, 34.65)	22.66 (22.07, 23.27)	31.82 (30.37, 33.33)
2012	22.40 (22.09, 22.72)	31.44 (30.52, 32.38)	22.34 (21.84, 22.86)	32.69 (31.31, 34.12)	21.75 (21.07, 22.45)	30.41 (28.37, 32.60)	22.18 (21.68, 22.68)	30.92 (29.42, 32.49)
2013	25.16 (24.82, 25.51)	34.18 (33.26, 35.12)	24.81 (24.28, 25.35)	35.50 (34.09, 36.96)	25.37 (24.56, 26.20)	33.42 (31.27, 35.71)	25.43 (24.66, 26.23)	33.59 (32.07, 35.17)
2014	24.71 (24.37, 25.05)	33.57 (32.63, 34.53)	24.45 (23.93, 24.98)	35.25 (33.82, 36.74)	25.24 (24.47, 26.04)	33.28 (31.17, 35.53)	24.60 (23.86, 25.35)	32.83 (30.42, 35.42)
2015	23.69 (23.36, 24.02)	31.53 (30.63, 32.45)	23.65 (23.14, 24.17)	33.12 (31.75, 34.54)	24.19 (23.43, 24.97)	31.37 (29.46, 33.41)	23.18 (22.65, 23.72)	30.98 (28.76, 33.38)

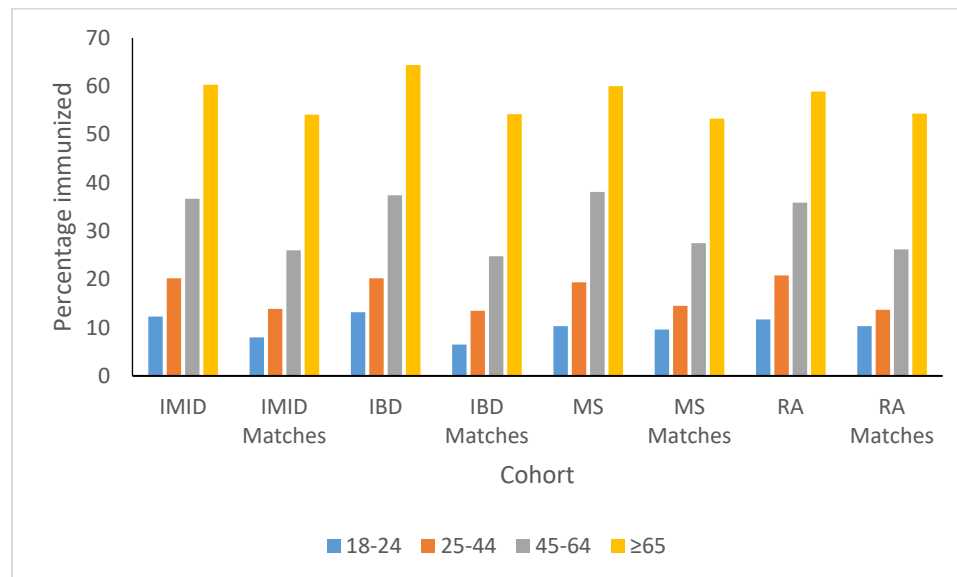
Appendix 1, as supplied by the authors. Appendix to: Marrie RA, Walld R, Bolton JM, et al.; CIHR Team in Defining the Burden and Managing the Effects of Psychiatric Comorbidity in Chronic Immuno-inflammatory Disease. Uptake of influenza vaccination among persons with inflammatory bowel disease, multiple sclerosis or rheumatoid arthritis: a population-based matched cohort study. *CMAJ Open* 2021. doi:10.9778/cmajo.20200105. Copyright © 2021 The Author(s) or their employer(s). To receive this resource in an accessible format, please contact us at cmajgroup@cmaj.ca. Appendices are posted as supplied by authors.

Table e9. Multivariable risk differences for the association of immune-mediated disease, any mood/anxiety disorder and uptake of influenza vaccination (Percentage; 95% confidence interval) adjusting for covariates including annual physician visits

Variable	Immune-mediated disease	Inflammatory bowel disease	Multiple sclerosis	Rheumatoid arthritis
Controls without a mood/anxiety disorder	0	0	0	0
Immune-mediated disease effect without a mood/anxiety disorder effect	5.34 (4.70, 5.98)	6.24 (5.20, 7.29)	5.75 (4.22, 7.29)	4.30 (3.35, 5.26)
Mood/anxiety disorder effect without an immune-mediated disease effect	3.53 (3.19, 3.87)	4.12 (3.55, 4.69)	4.34 (3.57, 5.11)	2.69 (2.19, 3.20)
Interaction contrast between case effect and mood/anxiety disorder effect*	-1.15 (-2.01, -0.28)	-1.28 (-2.72, 0.17)	0.26 (-1.75, 2.28)	-1.57 (-2.92, -0.32)

*A negative interaction contrast with a confidence interval that does not include zero indicates a subadditive effect; that is, the joint effect of immune-mediated disease and mood/anxiety disorder is less than the sum of their individual effects. A positive interaction with a confidence interval that does not include zero indicates a superadditive effect that is greater than the sum of the individual immune-mediated disease and mood/anxiety disorder effects.

Figure e1. Percentage of the Immune-mediated inflammatory disease (IMID) and matched cohorts immunized against influenza in 2015 stratified by age group



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