

**Supplemental Table 1a. The risk of incident cardiovascular comorbidity, stratified by sex and age, after diagnosis of multiple sclerosis (MS) compared with MS-free matched individuals, in a national, register-based cohort study in Sweden 2008-2016**

	MS-patients N=6602			MS-free individuals N=61628			
	Events	Person- years	IR (95% CI) <sup>a</sup>	Events	Person- years	IR (95% CI) <sup>a</sup>	IRR (95% CI)
<b>MACE</b>	75	31099.2	24.12 (18.66-29.57)	501	295936.5	16.93 (15.45-18.41)	1.42 (1.12-1.82)
Female	43	21509.2	19.99 (14.02-25.97)	246	204828.6	12.01 (10.51-13.51)	1.66 (1.20-2.30)
Male	32	9590.0	33.37 (21.81-44.93)	255	91108.0	27.99 (24.55-31.42)	1.19 (0.83-1.72)
Age <40	n < 10	15524.7	5.15 (2.22-10.15)	22	130761.3	1.68 (1.05-2.55)	3.06 (1.36-6.88)
Age 40-59	30	12855.4	23.34 (14.99-31.69)	215	131621.0	16.33 (14.15-18.52)	1.43 (0.98-2.09)
Age ≥ 60	37	2719.0	136.08 (92.23- 179.93)	264	33554.2	78.68 (69.19-88.17)	1.73 (1.23-2.44)
<b>Myocardial infarction</b>	35	31853.3	10.99 (7.35-14.63)	252	298201.0	8.45 (7.41-9.49)	1.30 (0.91-1.85)
Female	17	21978.2	7.73 (4.51-12.38)	100	206127.7	4.85 (3.90-5.80)	1.59 (0.95-2.67)
Male	18	9875.0	18.23 (10.80-28.81)	152	92073.4	16.51 (13.88-19.13)	1.10 (0.68-1.80)
Age <40	n < 10	15654.7	1.28 (0.15-4.62)	n < 10	130979.8	0.15 (0.02-0.55)	8.37 (1.18-59.40)
Age 40-59	15	13251.5	11.32 (6.34-18.67)	112	132693.8	8.44 (6.88-10.00)	1.34 (0.78-2.30)
Age ≥ 60	18	2947.0	61.08 (36.20-96.53)	138	34527.5	39.97 (33.30-46.64)	1.53 (0.94-2.50)
<b>Stroke, hemorrhagic and ischemic</b>	42	31332.1	13.40 (9.35-17.46)	274	298188.4	9.19 (8.10-10.28)	1.46 (1.05-2.02)
Female	27	21615.2	12.49 (8.23-18.17)	156	205592.1	7.59 (6.40-8.78)	1.65 (1.09-2.48)
Male	15	9716.9	15.44 (8.64-25.46)	118	92596.3	12.74 (10.44-15.04)	1.21 (0.71-2.07)
Age <40	n < 10	15533.1	3.86 (1.42-8.41)	19	130815.2	1.45 (0.87-2.27)	2.66 (1.06-6.66)
Age 40-59	15	12995.5	11.54 (6.46-19.04)	108	132659.8	8.14 (6.61-9.68)	1.42 (0.83-2.43)
Age ≥ 60	21	2803.5	74.91 (46.37-114.50)	147	34713.4	42.35 (35.50-49.19)	1.77 (1.12-2.79)
<b>Transient Ischemic attack</b>	26	31887.5	8.15 (5.33-11.95)	148	299505.0	4.94 (4.15-5.74)	1.65 (1.09-2.50)
Female	21	21945.5	9.57 (5.92-14.63)	93	206277.7	4.51 (3.59-5.42)	2.12 (1.32-3.41)
Male	n < 10	9942.0	5.03 (1.63-11.74)	55	93227.3	5.90 (4.34-7.46)	0.85 (0.34-2.13)
Age <40	n < 10	15609.1	2.56 (0.70-6.56)	n < 10	130959.4	0.46 (0.17-1.00)	5.59 (1.58-19.82)

	MS-patients N=6602			MS-free individuals N=61628			
	Events	Person- years	IR (95% CI) <sup>a</sup>	Events	Person- years	IR (95% CI) <sup>a</sup>	IRR (95% CI)
Age 40-59	11	13306.1	8.27 (4.13-14.79)	58	133254.9	4.35 (3.23-5.47)	1.90 (1.00-3.62)
Age >= 60	11	2972.2	37.01 (18.47-66.22)	84	35290.7	23.80 (18.71-28.89)	1.55 (0.83-2.91)
<b>Angina pectoris &amp; unspecified ischemic heart disease</b>							
	24	31732.8	7.56 (4.85-11.25)	263	296805.8	8.86 (7.79-9.93)	0.85 (0.56-1.30)
Female	10	21896.2	4.57 (2.19-8.40)	121	205050.7	5.90 (4.85-6.95)	0.77 (0.41-1.47)
Male	14	9836.6	14.23 (7.78-23.88)	142	91755.1	15.48 (12.93-18.02)	0.92 (0.53-1.59)
Age <40	0	15663.1	0.00 (N/A)	n < 10	130969.9	0.23 (0.05-0.67)	N/A
Age 40-59	14	13212.2	10.60 (5.79-17.78)	107	132255.3	8.09 (6.56-9.62)	1.31 (0.75-2.29)
Age >= 60	10	2857.6	34.99 (16.78-64.36)	153	33580.6	45.56 (38.34-52.78)	0.77 (0.41-1.46)
<b>Heart failure</b>							
	49	31885.7	15.37 (11.06-19.67)	296	298764.6	9.91 (8.78-11.04)	1.55 (1.15-2.10)
Female	22	22001.3	10.00 (6.27-15.14)	155	206097.5	7.52 (6.34-8.70)	1.33 (0.85-2.08)
Male	27	9884.4	27.32 (18.00-39.74)	141	92667.1	15.22 (12.70-17.73)	1.80 (1.19-2.71)
Age <40	n < 10	15627.2	3.20 (1.04-7.47)	13	130912.4	0.99 (0.53-1.70)	3.22 (1.15-9.04)
Age 40-59	16	13349.2	11.99 (6.85-19.46)	85	133048.3	6.39 (5.03-7.75)	1.88 (1.10-3.20)
Age >= 60	28	2909.3	96.24 (63.95-139.10)	198	34803.9	56.89 (48.97-64.81)	1.69 (1.14-2.51)
<b>Venous thromboembolism</b>							
	93	31824.0	29.22 (23.28-35.16)	615	298960.6	20.57 (18.95-22.20)	1.42 (1.14-1.77)
Female	60	21899.4	27.40 (20.47-34.33)	418	205876.4	20.30 (18.36-22.25)	1.35 (1.03-1.77)
Male	33	9924.6	33.25 (21.91-44.60)	197	93084.2	21.16 (18.21-24.12)	1.57 (1.09-2.27)
Age <40	19	15573.6	12.20 (7.35-19.05)	131	130434.9	10.04 (8.32-11.76)	1.21 (0.75-1.97)
Age 40-59	43	13210.0	32.55 (22.82-42.28)	291	133009.8	21.88 (19.36-24.39)	1.49 (1.08-2.05)
Age >= 60	31	3040.4	101.96 (66.07-137.85)	193	35515.9	54.34 (46.68-62.01)	1.88 (1.28-2.74)
<b>Peripheral vascular disease</b>							
	13	31960.4	4.07 (2.17-6.96)	90	299851.4	3.00 (2.38-3.62)	1.36 (0.76-2.42)
Female	n < 10	21988.0	4.09 (1.87-7.77)	63	206431.0	3.05 (2.30-3.81)	1.34 (0.67-2.70)
Male	n < 10	9972.4	4.01 (1.09-10.27)	27	93420.4	2.89 (1.90-4.21)	1.39 (0.49-3.97)

	MS-patients N=6602			MS-free individuals N=61628			
	Events	Person- years	IR (95% CI) <sup>a</sup>	Events	Person- years	IR (95% CI) <sup>a</sup>	IRR (95% CI)
Age <40	n < 10	15623.8	1.28 (0.16-4.62)	13	130852.3	0.99 (0.53-1.70)	1.29 (0.29-5.71)
Age 40-59	n < 10	13308.0	5.26 (2.11-10.84)	33	133437.8	2.47 (1.63-3.32)	2.13 (0.94-4.81)
Age ≥ 60	n < 10	3028.5	13.21 (3.60-33.82)	44	35561.3	12.37 (8.72-16.03)	1.07 (0.38-2.97)
<b>Pericardial disease</b>	12	32025.8	3.75 (1.94-6.55)	62	299946.7	2.07 (1.55-2.58)	1.81 (0.98-3.36)
Female	n < 10	22073.1	1.81 (0.49-4.64)	33	206649.2	1.60 (1.05-2.14)	1.13 (0.40-3.20)
Male	n < 10	9952.7	8.04 (3.47-15.84)	29	93297.5	3.11 (2.08-4.46)	2.59 (1.18-5.66)
Age <40	n < 10	15612.3	1.92 (0.40-5.62)	11	130803.2	0.84 (0.42-1.50)	2.28 (0.64-8.19)
Age 40-59	n < 10	13375.6	5.98 (2.58-11.79)	32	133465.7	2.40 (1.57-3.23)	2.49 (1.15-5.41)
Age ≥ 60	n < 10	3037.9	3.29 (0.08-18.34)	19	35677.8	5.33 (3.21-8.32)	0.62 (0.08-4.62)
<b>Bradycardia and heart block</b>	13	32039.8	4.06 (2.16-6.94)	76	300081.5	2.53 (1.96-3.10)	1.60 (0.89-2.89)
Female	n < 10	22046.3	3.63 (1.57-7.15)	36	206686.7	1.74 (1.17-2.31)	2.08 (0.97-4.48)
Male	n < 10	9993.6	5.00 (1.62-11.68)	40	93394.7	4.28 (2.96-5.61)	1.17 (0.46-2.96)
Age <40	n < 10	15641.6	2.56 (0.70-6.55)	n < 10	130956.1	0.53 (0.21-1.10)	4.78 (1.40-16.34)
Age 40-59	n < 10	13367.0	3.74 (1.21-8.73)	24	133549.5	1.80 (1.15-2.67)	2.08 (0.79-5.46)
Age ≥ 60	n < 10	3031.2	13.20 (3.60-33.79)	45	35575.9	12.65 (8.95-16.34)	1.04 (0.38-2.90)
<b>Paroxysmal tachycardia</b>	19	31922.8	5.95 (3.58-9.29)	165	298807.1	5.52 (4.68-6.36)	1.08 (0.67-1.73)
Female	12	21971.1	5.46 (2.82-9.54)	112	205651.1	5.45 (4.44-6.45)	1.00 (0.55-1.82)
Male	n < 10	9951.7	7.03 (2.83-14.49)	53	93156.0	5.69 (4.16-7.22)	1.24 (0.56-2.72)
Age <40	n < 10	15609.9	3.84 (1.41-8.37)	36	130520.5	2.76 (1.86-3.66)	1.39 (0.59-3.31)
Age 40-59	n < 10	13296.9	6.77 (3.09-12.85)	74	132908.9	5.57 (4.30-6.84)	1.22 (0.61-2.43)
Age ≥ 60	n < 10	3016.0	13.26 (3.61-33.96)	55	35377.8	15.55 (11.44-19.66)	0.85 (0.31-2.35)
<b>Atrial fibrillation and atrial flutter</b>	41	31777.8	12.90 (8.95-16.85)	466	296945.3	15.69 (14.27-17.12)	0.82 (0.60-1.13)
Female	21	21938.2	9.57 (5.93-14.63)	217	205417.6	10.56 (9.16-11.97)	0.91 (0.58-1.42)
Male	20	9839.6	20.33 (12.42-31.39)	249	91527.7	27.20 (23.83-30.58)	0.75 (0.47-1.18)
Age <40	n < 10	15611.2	2.56 (0.70-6.56)	18	130752.5	1.38 (0.82-2.18)	1.86 (0.63-5.50)

	<b>MS-patients N=6602</b>			<b>MS-free individuals N=61628</b>			
	<b>Events</b>	<b>Person- years</b>	<b>IR (95% CI)<sup>a</sup></b>	<b>Events</b>	<b>Person- years</b>	<b>IR (95% CI)<sup>a</sup></b>	<b>IRR (95% CI)</b>
Age 40-59	10	13225.6	7.56 (3.63-13.91)	132	132258.9	9.98 (8.28-11.68)	0.76 (0.40-1.44)
Age >= 60	27	2940.9	91.81 (60.50-133.57)	316	33933.8	93.12 (82.85-103.39)	0.99 (0.67-1.46)
<b>Other arrhythmias</b>	37	31823.2	11.63 (7.88-15.37)	309	297570.2	10.38 (9.23-11.54)	1.12 (0.80-1.57)
Female	27	21894.4	12.33 (8.13-17.94)	218	204820.4	10.64 (9.23-12.06)	1.16 (0.78-1.73)
Male	10	9928.9	10.07 (4.83-18.52)	91	92749.8	9.81 (7.80-11.83)	1.03 (0.53-1.97)
Age <40	n < 10	15563.4	5.78 (2.64-10.98)	68	130064.8	5.23 (3.99-6.47)	1.11 (0.55-2.22)
Age 40-59	15	13266.4	11.31 (6.33-18.65)	155	132312.2	11.71 (9.87-13.56)	0.97 (0.57-1.64)
Age >= 60	13	2993.4	43.43 (23.12-74.26)	86	35193.1	24.44 (19.27-29.60)	1.78 (0.99-3.18)

<sup>a</sup>Per 10,000 person-years; **crude IR and IRR**. CI: confidence interval; IR: incidence rate; IRR: incidence rate ratio; MACE: major adverse cardiovascular events; N/A: not applicable

**Supplemental Table 1b. The risk of incident non-infectious, non-cardiovascular comorbidity, stratified by sex and age, after diagnosis of multiple sclerosis (MS) compared with MS-free matched individuals, in a national, register-based cohort study in Sweden 2008-2016**

	MS-patients N=6602			MS-free individuals N=61628			
	Events	Person- years	IR (95% CI) <sup>a</sup>	Events	Person- years	IR (95% CI) <sup>a</sup>	IRR (95% CI)
<b>Autoimmune disease</b>	94	31383.9	29.95 (23.90-36.01)	233	297945.9	7.82 (6.82-8.82)	3.83 (3.01-4.87)
Female	70	21571.7	32.45 (24.85-40.05)	203	204680.4	9.92 (8.55-11.28)	3.27 (2.49-4.29)
Male	24	9812.1	24.46 (15.67-36.39)	30	93265.4	3.22 (2.07-4.37)	7.60 (4.45-13.01)
Age <40	41	15400.8	26.62 (18.47-34.77)	59	130223.1	4.53 (3.37-5.69)	5.88 (3.94-8.75)
Age 40-59	42	13046.7	32.19 (22.46-41.93)	87	132694.7	6.56 (5.18-7.93)	4.91 (3.40-7.10)
Age ≥ 60	11	2936.4	37.46 (18.70-67.03)	87	35028.1	24.84 (19.62-30.06)	1.51 (0.81-2.82)
<b>Bladder dysfunction, neuromuscular</b>	334	30603.5	109.14 (97.43- 120.84)	57	299814.4	1.90 (1.41-2.39)	57.41 (43.35-76.02)
Female	209	21152.8	98.80 (85.41-112.20)	31	206539.6	1.50 (0.97-2.03)	65.83 (45.14-96.00)
Male	125	9450.7	132.27 (109.08- 155.45)	26	93274.8	2.79 (1.82-4.08)	47.45 (31.10-72.40)
Age <40	105	15080.4	69.63 (56.31-82.94)	12	130823.1	0.92 (0.47-1.60)	75.91 (41.77-137.93)
Age 40-59	161	12707.4	126.70 (107.13- 146.27)	22	133408.0	1.65 (1.03-2.50)	76.83 (49.21-119.95)
Age ≥ 60	68	2815.7	241.50 (184.10- 298.90)	23	35583.3	6.46 (4.10-9.70)	37.36 (23.29-59.95)
<b>Optic neuritis</b>	279	26325.9	105.98 (93.54- 118.42)	12	300458.7	0.40 (0.21-0.70)	265.35 (148.89-472.91)
Female	212	17757.2	119.39 (103.32- 135.46)	n < 10	206831.5	0.39 (0.17-0.76)	308.67 (152.37-625.27)
Male	67	8568.7	78.19 (59.47-96.91)	n < 10	93627.2	0.43 (0.12-1.09)	183.02 (66.74-501.92)
Age <40	169	11781.2	143.45 (121.82- 165.08)	n < 10	130981.8	0.38 (0.12-0.89)	375.78 (154.41-914.54)
Age 40-59	95	11597.9	81.91 (65.44-98.38)	n < 10	133689.7	0.37 (0.12-0.87)	219.01 (89.11-538.32)

	MS-patients N=6602			MS-free individuals N=61628			
	Events	Person- years	IR (95% CI) <sup>a</sup>	Events	Person- years	IR (95% CI) <sup>a</sup>	IRR (95% CI)
Age >= 60	15	2946.8	50.90 (28.49-83.96)	n < 10	35787.2	0.56 (0.07-2.02)	91.08 (20.83-398.30)
<b>Chronic renal disease</b>	17	32011.6	5.31 (3.09-8.50)	171	299668.4	5.71 (4.85-6.56)	0.93 (0.57-1.53)
Female	n < 10	22044.3	2.72 (1.00-5.92)	95	206460.4	4.60 (3.68-5.53)	0.59 (0.26-1.35)
Male	11	9967.3	11.04 (5.51-19.75)	76	93208.0	8.15 (6.32-9.99)	1.35 (0.72-2.55)
Age <40	n < 10	15643.7	1.92 (0.40-5.60)	19	130808.7	1.45 (0.87-2.27)	1.32 (0.39-4.46)
Age 40-59	n < 10	13362.4	6.74 (3.08-12.79)	54	133296.2	4.05 (2.97-5.13)	1.66 (0.82-3.37)
Age >= 60	n < 10	3005.6	16.64 (5.40-38.82)	98	35563.5	27.56 (22.10-33.01)	0.60 (0.25-1.48)
<b>Diabetes Type I</b>	15	31665.3	4.74 (2.65-7.81)	141	297111.8	4.75 (3.96-5.53)	1.00 (0.59-1.70)
Female	11	21795.6	5.05 (2.52-9.03)	80	204874.1	3.90 (3.05-4.76)	1.29 (0.69-2.43)
Male	n < 10	9869.8	4.05 (1.10-10.38)	61	92237.8	6.61 (4.95-8.27)	0.61 (0.22-1.69)
Age <40	n < 10	15523.1	1.93 (0.40-5.65)	32	129920.4	2.46 (1.61-3.32)	0.78 (0.24-2.56)
Age 40-59	n < 10	13163.6	4.56 (1.67-9.92)	55	132114.4	4.16 (3.06-5.26)	1.09 (0.47-2.54)
Age >= 60	n < 10	2978.7	20.14 (7.39-43.84)	54	35077.0	15.39 (11.29-19.50)	1.31 (0.56-3.04)
<b>Diabetes Type II</b>	69	31436.4	21.95 (16.77-27.13)	654	294374.5	22.22 (20.51-23.92)	0.99 (0.77-1.27)
Female	34	21702.7	15.67 (10.40-20.93)	369	203510.8	18.13 (16.28-19.98)	0.86 (0.61-1.23)
Male	35	9733.7	35.96 (24.04-47.87)	285	90863.7	31.37 (27.72-35.01)	1.15 (0.81-1.63)
Age <40	10	15549.6	6.43 (3.08-11.83)	56	130399.2	4.29 (3.17-5.42)	1.50 (0.76-2.93)
Age 40-59	40	13008.5	30.75 (21.22-40.28)	322	130562.0	24.66 (21.97-27.36)	1.25 (0.90-1.73)
Age >= 60	19	2878.3	66.01 (39.74-103.08)	276	33413.3	82.60 (72.86-92.35)	0.80 (0.50-1.27)
<b>Dyslipidemia</b>	67	31390.5	21.34 (16.23-26.45)	701	294553.7	23.80 (22.04-25.56)	0.90 (0.70-1.15)
Female	37	21693.3	17.06 (11.56-22.55)	390	203763.0	19.14 (17.24-21.04)	0.89 (0.64-1.25)
Male	30	9697.2	30.94 (19.87-42.01)	311	90790.6	34.25 (30.45-38.06)	0.90 (0.62-1.31)
Age <40	n < 10	15600.5	1.28 (0.16-4.63)	28	130692.7	2.14 (1.42-3.10)	0.60 (0.14-2.51)
Age 40-59	33	12974.3	25.43 (16.76-34.11)	324	130721.8	24.79 (22.09-27.48)	1.03 (0.72-1.47)
Age >= 60	32	2815.7	113.65 (74.27-153.03)	349	33139.2	105.31 (94.26-116.36)	1.08 (0.75-1.55)
<b>Retinal disorders</b>	112	30961.6	36.17 (29.47-42.87)	606	295619.1	20.50 (18.87-22.13)	1.76 (1.44-2.16)

	MS-patients N=6602			MS-free individuals N=61628			
	Events	Person- years	IR (95% CI) <sup>a</sup>	Events	Person- years	IR (95% CI) <sup>a</sup>	IRR (95% CI)
Female	75	21355.1	35.12 (27.17-43.07)	408	203722.2	20.03 (18.08-21.97)	1.75 (1.37-2.24)
Male	37	9606.5	38.52 (26.11-50.93)	198	91896.9	21.55 (18.54-24.55)	1.79 (1.26-2.54)
Age <40	25	15319.1	16.32 (10.56-24.09)	48	130228.9	3.69 (2.64-4.73)	4.43 (2.73-7.18)
Age 40-59	43	12912.2	33.30 (23.35-43.26)	178	131696.1	13.52 (11.53-15.50)	2.46 (1.77-3.44)
Age >= 60	44	2730.3	161.16(113.54- 208.77)	380	33694.1	112.78(101.44- 124.12)	1.43 (1.05-1.95)
<b>Asthma</b>	93	30971.2	30.03 (23.92-36.13)	674	290583.9	23.19 (21.44-24.95)	1.29 (1.04-1.61)
Female	70	21222.4	32.98 (25.26-40.71)	523	199186.4	26.26 (24.01-28.51)	1.26 (0.98-1.61)
Male	23	9748.8	23.59 (14.96-35.40)	151	91397.5	16.52 (13.89-19.16)	1.43 (0.92-2.21)
Age <40	33	15045.0	21.93 (14.45-29.42)	249	125852.8	19.79 (17.33-22.24)	1.11 (0.77-1.59)
Age 40-59	46	12954.4	35.51 (25.25-45.77)	320	130035.4	24.61 (21.91-27.30)	1.44 (1.06-1.97)
Age >= 60	14	2971.8	47.11 (25.76-79.04)	105	34695.8	30.26 (24.47-36.05)	1.56 (0.89-2.72)
<b>Chronic Obstructive Pulmonary Disease</b>	38	31874.4	11.92 (8.13-15.71)	290	298635.3	9.71 (8.59-10.83)	1.23 (0.88-1.72)
Female	19	21963.0	8.65 (5.21-13.51)	198	205617.5	9.63 (8.29-10.97)	0.90 (0.56-1.44)
Male	19	9911.4	19.17 (11.54-29.94)	92	93017.8	9.89 (7.87-11.91)	1.94 (1.18-3.18)
Age <40	0	15655.1	0.00 (N/A)	n < 10	130952.9	0.46 (0.17-1.00)	N/A
Age 40-59	15	13252.8	11.32 (6.33-18.67)	98	132820.3	7.38 (5.92-8.84)	1.53 (0.89-2.64)
Age >= 60	23	2966.5	77.53 (49.15-116.34)	186	34862.1	53.35 (45.69-61.02)	1.45 (0.94-2.24)
<b>Bowel dysfunction</b>	217	30394.1	71.40 (61.90-80.89)	960	290499.7	33.05 (30.96-35.14)	2.16 (1.86-2.50)
Female	158	20747.6	76.15 (64.28-88.03)	732	198805.5	36.82 (34.15-39.49)	2.07 (1.74-2.46)
Male	59	9646.5	61.16 (45.56-76.77)	228	91694.2	24.87 (21.64-28.09)	2.46 (1.85-3.28)
Age <40	78	14831.3	52.59 (40.92-64.26)	373	126122.6	29.57 (26.57-32.58)	1.78 (1.39-2.27)
Age 40-59	91	12642.2	71.98 (57.19-86.77)	369	129700.5	28.45 (25.55-31.35)	2.53 (2.01-3.18)
Age >= 60	48	2920.6	164.35(117.86- 210.85)	218	34676.6	62.87 (54.52-71.21)	2.61 (1.91-3.57)
<b>Crohn disease</b>	11	31909.9	3.45 (1.72-6.17)	84	298976.1	2.81 (2.21-3.41)	1.23 (0.65-2.30)
Female	n < 10	21967.9	3.19 (1.28-6.57)	63	205733.6	3.06 (2.31-3.82)	1.04 (0.48-2.27)

	MS-patients N=6602			MS-free individuals N=61628			
	Events	Person- years	IR (95% CI) <sup>a</sup>	Events	Person- years	IR (95% CI) <sup>a</sup>	IRR (95% CI)
Male	n < 10	9941.9	4.02 (1.10-10.30)	21	93242.5	2.25 (1.39-3.44)	1.79 (0.61-5.20)
Age <40	n < 10	15559.6	3.21 (1.04-7.50)	43	130303.4	3.30 (2.31-4.29)	0.97 (0.39-2.46)
Age 40-59	n < 10	13322.0	3.75 (1.22-8.76)	26	133023.7	1.95 (1.28-2.86)	1.92 (0.74-5.00)
Age >= 60	n < 10	3028.3	3.30 (0.08-18.40)	15	35649.0	4.21 (2.36-6.94)	0.78 (0.10-5.94)
<b>Ulcerative colitis</b>	21	31838.0	6.60 (4.08-10.08)	147	298073.1	4.93 (4.13-5.73)	1.34 (0.85-2.11)
Female	20	21939.9	9.12 (5.57-14.08)	104	205291.9	5.07 (4.09-6.04)	1.80 (1.12-2.90)
Male	n < 10	9898.2	1.01 (0.03-5.63)	43	92781.2	4.63 (3.25-6.02)	0.22 (0.03-1.58)
Age <40	n < 10	15537.6	5.15 (2.22-10.15)	71	129908.1	5.47 (4.19-6.74)	0.94 (0.45-1.96)
Age 40-59	n < 10	13281.8	6.78 (3.10-12.86)	61	132552.8	4.60 (3.45-5.76)	1.47 (0.73-2.96)
Age >= 60	n < 10	3018.7	13.25 (3.61-33.93)	15	35612.2	4.21 (2.36-6.95)	3.15 (1.04-9.48)
<b>Cancer</b>	180	30770.6	58.50 (49.95-67.04)	1657	287073.1	57.72 (54.94-60.50)	1.01 (0.87-1.18)
Female	123	21148.6	58.16 (47.88-68.44)	1141	196960.5	57.93 (54.57-61.29)	1.00 (0.83-1.21)
Male	57	9622.0	59.24 (43.86-74.62)	516	90112.6	57.26 (52.32-62.20)	1.03 (0.79-1.36)
Age <40	21	15473.8	13.57 (8.40-20.75)	157	129142.9	12.16 (10.26-14.06)	1.12 (0.71-1.76)
Age 40-59	78	12601.7	61.90 (48.16-75.63)	757	127038.4	59.59 (55.34-63.83)	1.04 (0.82-1.31)
Age >= 60	81	2695.1	300.55 (235.09-366.00)	743	30891.7	240.52 (223.22-257.81)	1.25 (0.99-1.57)
<b>Breast cancer</b>	28	31806.2	8.80 (5.85-12.72)	342	297237.6	11.51 (10.29-12.73)	0.77 (0.52-1.12)
Female	28	21802.7	12.84 (8.53-18.56)	340	203601.2	16.70 (14.92-18.47)	0.77 (0.52-1.13)
Male	0	10003.5	0.00 (N/A)	n < 10	93636.4	0.21 (0.03-0.77)	N/A
Age <40	n < 10	15628.6	1.92 (0.40-5.61)	32	130813.4	2.45 (1.60-3.29)	0.78 (0.24-2.56)
Age 40-59	13	13227.1	9.83 (5.23-16.81)	187	131878.2	14.18 (12.15-16.21)	0.69 (0.40-1.22)
Age >= 60	12	2950.5	40.67 (21.02-71.04)	123	34546.0	35.60 (29.31-41.90)	1.14 (0.63-2.07)
<b>Prostate cancer</b>	15	32001.0	4.69 (2.62-7.73)	156	299631.5	5.21 (4.39-6.02)	0.90 (0.53-1.53)
Female	0	22089.5	0.00 (N/A)	0	206963.5	0.00 (N/A)	N/A
Male	15	9911.5	15.13 (8.47-24.96)	156	92668.0	16.83 (14.19-19.48)	0.90 (0.53-1.53)
Age <40	0	15663.1	0.00 (N/A)	n < 10	131026.2	0.08 (0.00-0.43)	N/A
Age 40-59	n < 10	13316.8	5.26 (2.11-10.83)	41	133477.3	3.07 (2.13-4.01)	1.71 (0.77-3.81)



	MS-patients N=6602			MS-free individuals N=61628			
	Events	Person- years	IR (95% CI) <sup>a</sup>	Events	Person- years	IR (95% CI) <sup>a</sup>	IRR (95% CI)
Age >= 60	n < 10	3021.1	26.48 (11.43-52.18)	114	35128.0	32.45 (26.50-38.41)	0.82 (0.40-1.67)
<b>Skin cancer</b>	78	31615.7	24.67 (19.20-30.15)	586	296215.3	19.78 (18.18-21.38)	1.25 (0.98-1.58)
Female	57	21755.2	26.20 (19.40-33.00)	428	203656.9	21.02 (19.02-23.01)	1.25 (0.95-1.64)
Male	21	9860.5	21.30 (13.18-32.55)	158	92558.4	17.07 (14.41-19.73)	1.25 (0.79-1.97)
Age <40	n < 10	15621.3	3.84 (1.41-8.36)	61	130462.3	4.68 (3.50-5.85)	0.82 (0.36-1.90)
Age 40-59	33	13146.6	25.10 (16.54-33.67)	271	131584.5	20.60 (18.14-23.05)	1.22 (0.85-1.75)
Age >= 60	39	2847.8	136.95 (93.97- 179.93)	254	34168.5	74.34 (65.20-83.48)	1.84 (1.32-2.58)
<b>Demyelinating disease other than MS</b>	197	24446.1	80.59 (69.33-91.84)	n < 10	300541.1	0.27 (0.11-0.52)	302.74 (149.30-613.86)
Female	143	16752.0	85.36 (71.37-99.35)	n < 10	206902.4	0.34 (0.14-0.70)	252.31 (118.15-538.82)
Male	54	7694.1	70.18 (51.46-88.90)	n < 10	93638.7	0.11 (0.00-0.60)	657.19 (90.91-4750.68)
Age <40	102	11603.1	87.91 (70.85-104.97)	n < 10	131016.8	0.23 (0.05-0.67)	383.91 (121.79-1210.20)
Age 40-59	80	10482.5	76.32 (59.59-93.04)	n < 10	133730.1	0.30 (0.08-0.77)	255.15 (93.47-696.49)
Age >= 60	15	2360.5	63.55 (35.57-104.81)	n < 10	35794.2	0.28 (0.01-1.56)	227.46 (30.05-1722.03)
<b>Epilepsy and seizure</b>	40	31563.9	12.67 (8.75-16.60)	161	297879.4	5.40 (4.57-6.24)	2.34 (1.66-3.31)
Female	26	21712.9	11.97 (7.82-17.55)	98	205095.7	4.78 (3.83-5.72)	2.51 (1.63-3.86)
Male	14	9851.0	14.21 (7.77-23.84)	63	92783.6	6.79 (5.11-8.47)	2.09 (1.17-3.73)
Age <40	15	15400.7	9.74 (5.45-16.06)	53	129774.2	4.08 (2.98-5.18)	2.38 (1.34-4.23)
Age 40-59	16	13164.0	12.15 (6.95-19.74)	69	132608.4	5.20 (3.98-6.43)	2.34 (1.36-4.02)
Age >= 60	n < 10	2999.2	30.01 (13.72-56.96)	39	35496.7	10.99 (7.54-14.44)	2.73 (1.32-5.64)
<b>Depression</b>	325	29131.4	111.56 (99.43- 123.69)	1326	282469.4	46.94 (44.42-49.47)	2.38 (2.11-2.68)
Female	228	19936.3	114.36 (99.52- 129.21)	979	193005.4	50.72 (47.55-53.90)	2.25 (1.95-2.60)
Male	97	9195.1	105.49 (84.50- 126.48)	347	89464.0	38.79 (34.71-42.87)	2.72 (2.17-3.41)

	MS-patients N=6602			MS-free individuals N=61628			
	Events	Person- years	IR (95% CI) <sup>a</sup>	Events	Person- years	IR (95% CI) <sup>a</sup>	IRR (95% CI)
Age <40	166	14084.4	117.86 (99.93-135.79)	670	121757.7	55.03 (50.86-59.19)	2.14 (1.81-2.54)
Age 40-59	126	12216.9	103.14 (85.13-121.14)	550	126076.6	43.62 (39.98-47.27)	2.36 (1.95-2.87)
Age ≥ 60	33	2830.1	116.60 (76.82-156.39)	106	34635.2	30.60 (24.78-36.43)	3.81 (2.58-5.63)
<b>Anxiety</b>	193	30015.3	64.30 (55.23-73.37)	1470	284539.2	51.66 (49.02-54.30)	1.24 (1.07-1.45)
Female	141	20531.3	68.68 (57.34-80.01)	1128	194418.6	58.02 (54.63-61.41)	1.18 (0.99-1.41)
Male	52	9484.0	54.83 (39.93-69.73)	342	90120.6	37.95 (33.93-41.97)	1.44 (1.08-1.93)
Age <40	105	14454.5	72.64 (58.75-86.54)	815	121803.0	66.91 (62.32-71.51)	1.09 (0.89-1.33)
Age 40-59	72	12650.3	56.92 (43.77-70.06)	544	127719.9	42.59 (39.01-46.17)	1.34 (1.05-1.71)
Age ≥ 60	16	2910.4	54.97 (31.42-89.28)	111	35016.4	31.70 (25.80-37.60)	1.73 (1.03-2.93)
<b>Fatigue</b>	n < 10	32055.5	0.31 (0.01-1.74)	18	300237.5	0.60 (0.36-0.95)	0.52 (0.07-3.90)
Female	n < 10	22053.1	0.45 (0.01-2.53)	15	206665.0	0.73 (0.41-1.20)	0.62 (0.08-4.73)
Male	0	10002.5	0.00 (N/A)	n < 10	93572.6	0.32 (0.07-0.94)	N/A
Age <40	n < 10	15650.1	0.64 (0.02-3.56)	n < 10	130854.0	0.61 (0.26-1.20)	1.05 (0.13-8.36)
Age 40-59	0	13367.0	0.00 (N/A)	10	133588.1	0.75 (0.36-1.38)	N/A
Age ≥ 60	0	3038.3	0.00 (N/A)	0	35795.4	0.00 (N/A)	N/A
<b>Schizophrenia</b>	17	31778.2	5.35 (3.12-8.57)	142	297649.5	4.77 (3.99-5.56)	1.12 (0.68-1.85)
Female	13	21898.3	5.94 (3.16-10.15)	93	205046.9	4.54 (3.61-5.46)	1.31 (0.73-2.34)
Male	n < 10	9879.9	4.05 (1.10-10.37)	49	92602.6	5.29 (3.81-6.77)	0.77 (0.28-2.12)
Age <40	n < 10	15531.1	3.22 (1.05-7.51)	70	129829.6	5.39 (4.13-6.65)	0.60 (0.24-1.48)
Age 40-59	10	13232.4	7.56 (3.62-13.90)	56	132250.3	4.23 (3.13-5.34)	1.78 (0.91-3.50)
Age ≥ 60	n < 10	3014.6	6.63 (0.80-23.97)	16	35569.6	4.50 (2.57-7.30)	1.47 (0.34-6.41)
<b>Bipolar affective disorders</b>	37	31694.7	11.67 (7.91-15.44)	273	297921.5	9.16 (8.08-10.25)	1.27 (0.90-1.80)
Female	32	21791.6	14.68 (9.60-19.77)	218	204860.8	10.64 (9.23-12.05)	1.38 (0.95-2.00)
Male	n < 10	9903.2	5.05 (1.64-11.78)	55	93060.7	5.91 (4.35-7.47)	0.85 (0.34-2.13)

	MS-patients N=6602			MS-free individuals N=61628			
	Events	Person- years	IR (95% CI) <sup>a</sup>	Events	Person- years	IR (95% CI) <sup>a</sup>	IRR (95% CI)
Age <40	15	15499.0	9.68 (5.42-15.96)	156	129678.1	12.03 (10.14-13.92)	0.80 (0.47-1.37)
Age 40-59	17	13215.5	12.86 (7.49-20.60)	110	132610.6	8.29 (6.74-9.85)	1.55 (0.93-2.58)
Age ≥ 60	n < 10	2980.3	16.78 (5.45-39.15)	n < 10	35632.7	1.96 (0.79-4.05)	8.54 (2.71-26.91)
<b>Fracture</b>	390	27249.6	143.12 (128.92- 157.33)	2846	262547.8	108.40 (104.42- 112.38)	1.32 (1.19-1.47)
Female	274	19087.8	143.55 (126.55- 160.54)	1965	183789.8	106.92 (102.19- 111.64)	1.34 (1.18-1.52)
Male	116	8161.8	142.13 (116.26- 167.99)	881	78758.0	111.86 (104.47- 119.25)	1.27 (1.05-1.54)
Age <40	104	13512.8	76.96 (62.17-91.76)	841	114250.3	73.61 (68.64-78.59)	1.05 (0.85-1.28)
Age 40-59	192	11371.4	168.85 (144.96- 192.73)	1328	117928.9	112.61 (106.55- 118.67)	1.50 (1.29-1.74)
Age ≥ 60	94	2365.4	397.40 (317.06- 477.74)	677	30368.5	222.93 (206.14- 239.72)	1.78 (1.44-2.21)
<b>Osteoporosis</b>	34	31826.3	10.68 (7.09-14.27)	181	299157.3	6.05 (5.17-6.93)	1.77 (1.22-2.55)
Female	28	21863.0	12.81 (8.51-18.51)	163	205650.5	7.93 (6.71-9.14)	1.62 (1.08-2.41)
Male	n < 10	9963.3	6.02 (2.21-13.11)	18	93506.8	1.92 (1.14-3.04)	3.13 (1.24-7.88)
Age <40	0	15638.9	0.00 (N/A)	n < 10	130930.3	0.46 (0.17-1.00)	N/A
Age 40-59	17	13265.3	12.82 (7.47-20.52)	67	133164.7	5.03 (3.83-6.24)	2.55 (1.50-4.34)
Age ≥ 60	17	2922.2	58.18 (33.89-93.14)	108	35062.3	30.80 (24.99-36.61)	1.89 (1.13-3.15)
<b>Viral liver disease (viral hepatitis)</b>	12	31974.9	3.75 (1.94-6.56)	110	298158.1	3.69 (3.00-4.38)	1.02 (0.56-1.85)
Female	n < 10	22010.1	3.18 (1.28-6.55)	56	205503.8	2.73 (2.01-3.44)	1.17 (0.53-2.56)
Male	n < 10	9964.8	5.02 (1.63-11.71)	54	92654.3	5.83 (4.27-7.38)	0.86 (0.34-2.15)
Age <40	n < 10	15629.8	2.56 (0.70-6.55)	42	130044.5	3.23 (2.25-4.21)	0.79 (0.28-2.21)
Age 40-59	n < 10	13310.8	6.01 (2.59-11.84)	56	132353.0	4.23 (3.12-5.34)	1.42 (0.68-2.98)
Age ≥ 60	0	3034.3	0.00 (N/A)	12	35760.7	3.36 (1.73-5.86)	N/A
<b>Alcoholic liver disease</b>	n < 10	32077.8	0.94 (0.19-2.73)	50	300396.7	1.66 (1.20-2.13)	0.56 (0.18-1.80)

	MS-patients N=6602			MS-free individuals N=61628			
	Events	Person- years	IR (95% CI) <sup>a</sup>	Events	Person- years	IR (95% CI) <sup>a</sup>	IRR (95% CI)
Female	n < 10	22085.6	0.45 (0.01-2.52)	24	206871.0	1.16 (0.74-1.73)	0.39 (0.05-2.89)
Male	n < 10	9992.2	2.00 (0.24-7.23)	26	93525.7	2.78 (1.82-4.07)	0.72 (0.17-3.03)
Age <40	0	15663.1	0.00 (N/A)	0	131028.6	0.00 (N/A)	N/A
Age 40-59	n < 10	13377.4	2.24 (0.46-6.55)	32	133604.4	2.40 (1.57-3.23)	0.94 (0.29-3.06)
Age ≥ 60	0	3037.4	0.00 (N/A)	18	35763.6	5.03 (2.98-7.95)	N/A
<b>Chronic liver disease /</b>							
<b>cirrhosis</b>	n < 10	32041.4	0.62 (0.08-2.25)	45	300219.2	1.50 (1.06-1.94)	0.42 (0.10-1.72)
Female	n < 10	22053.3	0.45 (0.01-2.53)	27	206706.3	1.31 (0.86-1.90)	0.35 (0.05-2.55)
Male	n < 10	9988.0	1.00 (0.03-5.58)	18	93512.9	1.92 (1.14-3.04)	0.52 (0.07-3.90)
Age <40	n < 10	15647.8	1.28 (0.15-4.62)	n < 10	130954.5	0.23 (0.05-0.67)	5.58 (0.93-33.39)
Age 40-59	0	13356.3	0.00 (N/A)	22	133492.0	1.65 (1.03-2.50)	N/A
Age ≥ 60	0	3037.4	0.00 (N/A)	20	35772.7	5.59 (3.42-8.63)	N/A
<b>Acute liver disease or</b>							
<b>failure</b>	n < 10	32085.1	0.94 (0.19-2.73)	35	300528.8	1.16 (0.78-1.55)	0.80 (0.25-2.61)
Female	n < 10	22081.7	0.91 (0.11-3.27)	15	206911.9	0.72 (0.41-1.20)	1.25 (0.29-5.46)
Male	n < 10	10003.5	1.00 (0.03-5.57)	20	93617.0	2.14 (1.30-3.30)	0.47 (0.06-3.49)
Age <40	n < 10	15660.4	0.64 (0.02-3.56)	n < 10	131006.4	0.15 (0.02-0.55)	4.18 (0.38-46.13)
Age 40-59	n < 10	13379.5	0.75 (0.02-4.16)	22	133721.6	1.65 (1.03-2.49)	0.45 (0.06-3.37)
Age ≥ 60	n < 10	3045.3	3.28 (0.08-18.30)	11	35800.9	3.07 (1.53-5.50)	1.07 (0.14-8.28)
<b>Toxic liver disease</b>							
	n < 10	32066.9	1.56 (0.51-3.64)	15	300443.2	0.50 (0.28-0.82)	3.12 (1.14-8.59)
Female	n < 10	22065.9	1.81 (0.49-4.64)	11	206838.5	0.53 (0.27-0.95)	3.41 (1.09-10.70)
Male	n < 10	10001.0	1.00 (0.03-5.57)	n < 10	93604.6	0.43 (0.12-1.09)	2.34 (0.26-20.94)
Age <40	n < 10	15662.4	0.64 (0.02-3.56)	n < 10	130978.8	0.38 (0.12-0.89)	1.67 (0.20-14.32)
Age 40-59	n < 10	13369.1	2.99 (0.82-7.66)	n < 10	133688.8	0.37 (0.12-0.87)	8.00 (2.15-29.79)
Age ≥ 60	0	3035.4	0.00 (N/A)	n < 10	35775.6	1.40 (0.45-3.26)	N/A
<b>Liver diseases without</b>							
<b>viral or alcoholic cause</b>	15	31984.5	4.69 (2.62-7.74)	99	299659.0	3.30 (2.65-3.95)	1.42 (0.82-2.44)
Female	11	22026.0	4.99 (2.49-8.94)	64	206358.4	3.10 (2.34-3.86)	1.61 (0.85-3.05)

	<b>MS-patients N=6602</b>			<b>MS-free individuals N=61628</b>			
	<b>Events</b>	<b>Person- years</b>	<b>IR (95% CI)<sup>a</sup></b>	<b>Events</b>	<b>Person- years</b>	<b>IR (95% CI)<sup>a</sup></b>	<b>IRR (95% CI)</b>
Male	n < 10	9958.4	4.02 (1.09-10.28)	35	93300.5	3.75 (2.51-4.99)	1.07 (0.38-3.01)
Age <40	n < 10	15614.6	4.48 (1.80-9.24)	20	130767.2	1.53 (0.93-2.36)	2.93 (1.24-6.93)
Age 40-59	n < 10	13345.1	4.50 (1.65-9.79)	47	133238.4	3.53 (2.52-4.54)	1.27 (0.54-2.98)
Age >= 60	n < 10	3024.8	6.61 (0.80-23.89)	32	35653.3	8.98 (5.87-12.09)	0.74 (0.18-3.07)

<sup>a</sup>Per 10,000 person-years, **crude IR and IRR**. CI: confidence interval; IR: incidence rate; IRR: incidence rate ratio; MACE: major adverse cardiovascular events; N/A: not applicable

**Supplemental Table 2. The risk of incident cardiovascular comorbidity (with no history of CV diseases (CVD) or CVD risk factors), stratified by sex and age, after diagnosis of multiple sclerosis (MS) compared with MS-free matched individuals, in a national, register-based cohort study in Sweden 2008-2016**

	MS patients N=4539			MS-free matched individuals N=47527			
	Events	Person- years	IR (95% CI) <sup>a</sup>	Events	Person- years	IR (95% CI) <sup>a</sup>	IRR (95% CI)
<b>MACE</b>	32	21835.6	14.65 (9.58-19.73)	234	227902.9	10.27 (8.95-11.58)	1.43 (0.99-2.07)
Female	20	15017.7	13.32 (8.13-20.57)	112	155220.0	7.22 (5.88-8.55)	1.85 (1.15-2.97)
Male	12	6817.8	17.60 (9.09-30.75)	122	72682.9	16.79 (13.81-19.76)	1.05 (0.58-1.90)
Age <40	n < 10	12344.3	4.05 (1.32-9.45)	19	113019.3	1.68 (1.01-2.63)	2.41 (0.90-6.45)
Age 40-59	14	8391.7	16.68 (9.12-27.99)	124	98316.1	12.61 (10.39-14.83)	1.32 (0.76-2.30)
Age ≥ 60	13	1099.5	118.23 (62.95-202.18)	91	16567.5	54.93 (43.64-66.21)	2.15 (1.20-3.85)
<b>Myocardial infarction</b>	16	21875.9	7.31 (4.18-11.88)	102	228231.3	4.47 (3.60-5.34)	1.64 (0.97-2.77)
Female	n < 10	15041.2	5.98 (2.74-11.36)	34	155381.4	2.19 (1.45-2.92)	2.73 (1.31-5.70)
Male	n < 10	6834.7	10.24 (4.12-21.10)	68	72849.9	9.33 (7.12-11.55)	1.10 (0.50-2.39)
Age <40	n < 10	12361.8	1.62 (0.20-5.84)	n < 10	113089.2	0.18 (0.02-0.64)	9.15 (1.29-64.95)
Age 40-59	n < 10	8402.7	8.33 (3.35-17.16)	52	98543.1	5.28 (3.84-6.71)	1.58 (0.72-3.48)
Age ≥ 60	n < 10	1111.4	62.98 (25.32-129.77)	48	16599.0	28.92 (20.74-37.10)	2.18 (0.99-4.81)
<b>Stroke, hemorrhagic and ischemic</b>	16	21887.0	7.31 (4.18-11.87)	133	228177.4	5.83 (4.84-6.82)	1.25 (0.75-2.11)
Female	11	15044.7	7.31 (3.65-13.08)	78	155313.2	5.02 (3.91-6.14)	1.46 (0.77-2.74)
Male	n < 10	6842.3	7.31 (2.37-17.05)	55	72864.3	7.55 (5.55-9.54)	0.97 (0.39-2.42)
Age <40	n < 10	12352.6	2.43 (0.50-7.10)	16	113036.5	1.42 (0.81-2.30)	1.72 (0.50-5.89)
Age 40-59	n < 10	8421.1	8.31 (3.34-17.13)	73	98505.7	7.41 (5.71-9.11)	1.12 (0.52-2.44)
Age ≥ 60	n < 10	1113.3	53.89 (19.78-117.30)	44	16635.2	26.45 (18.63-34.27)	2.04 (0.87-4.78)
<b>Transient Ischemic attack</b>	13	21882.5	5.94 (3.16-10.16)	62	228328.1	2.72 (2.04-3.39)	2.19 (1.20-3.98)
Female	11	15026.5	7.32 (3.65-13.10)	38	155378.0	2.45 (1.67-3.22)	2.99 (1.53-5.86)
Male	n < 10	6856.0	2.92 (0.35-10.54)	24	72950.1	3.29 (2.11-4.90)	0.89 (0.21-3.75)
Age <40	n < 10	12336.9	3.24 (0.88-8.30)	n < 10	113085.0	0.53 (0.19-1.15)	6.11 (1.72-21.66)

	MS patients N=4539			MS-free matched individuals N=47527			
	Events	Person- years	IR (95% CI) <sup>a</sup>	Events	Person- years	IR (95% CI) <sup>a</sup>	IRR (95% CI)
Age 40-59	n < 10	8408.0	8.33 (3.35-17.15)	28	98647.2	2.84 (1.89-4.10)	2.93 (1.28-6.71)
Age ≥ 60	n < 10	1137.5	17.58 (2.13-63.51)	28	16595.9	16.87 (11.21-24.38)	1.04 (0.25-4.37)
<b>Angina pectoris &amp; unspecified ischemic heart disease</b>							
	n < 10	21915.3	3.65 (1.58-7.19)	107	228183.3	4.69 (3.80-5.58)	0.78 (0.38-1.60)
Female	n < 10	15063.7	1.99 (0.41-5.82)	44	155347.9	2.83 (2.00-3.67)	0.70 (0.22-2.26)
Male	n < 10	6851.6	7.30 (2.37-17.03)	63	72835.4	8.65 (6.51-10.79)	0.84 (0.34-2.10)
Age <40	0	12370.1	0.00 (N/A)	n < 10	113069.5	0.27 (0.05-0.78)	N/A
Age 40-59	n < 10	8419.2	7.13 (2.62-15.51)	52	98562.0	5.28 (3.84-6.71)	1.35 (0.58-3.14)
Age ≥ 60	n < 10	1126.0	17.76 (2.15-64.16)	52	16551.8	31.42 (22.88-39.96)	0.57 (0.14-2.32)
<b>Heart failure</b>							
	13	21892.6	5.94 (3.16-10.15)	76	228287.3	3.33 (2.58-4.08)	1.78 (0.99-3.21)
Female	n < 10	15055.8	3.99 (1.46-8.67)	37	155383.1	2.38 (1.61-3.15)	1.67 (0.71-3.97)
Male	n < 10	6836.8	10.24 (4.12-21.10)	39	72904.1	5.35 (3.67-7.03)	1.91 (0.86-4.28)
Age <40	n < 10	12353.6	3.24 (0.88-8.29)	n < 10	113080.0	0.80 (0.36-1.51)	4.07 (1.25-13.21)
Age 40-59	n < 10	8420.3	5.94 (1.93-13.86)	39	98590.8	3.96 (2.71-5.20)	1.50 (0.59-3.81)
Age ≥ 60	n < 10	1118.7	35.76 (9.74-91.55)	28	16616.5	16.85 (11.20-24.35)	2.12 (0.74-6.05)
<b>Venous thromboembolism</b>							
	44	21804.3	20.18 (14.22-26.14)	307	227747.8	13.48 (11.97-14.99)	1.50 (1.09-2.05)
Female	32	14969.5	21.38 (13.97-28.78)	206	154980.0	13.29 (11.48-15.11)	1.61 (1.11-2.33)
Male	12	6834.8	17.56 (9.07-30.67)	101	72767.8	13.88 (11.17-16.59)	1.26 (0.70-2.30)
Age <40	11	12301.7	8.94 (4.46-16.00)	88	112738.2	7.81 (6.17-9.44)	1.15 (0.61-2.14)
Age 40-59	22	8351.4	26.34 (16.51-39.88)	154	98383.8	15.65 (13.18-18.13)	1.68 (1.08-2.63)
Age ≥ 60	11	1151.3	95.55 (47.70-170.96)	65	16625.7	39.10 (29.59-48.60)	2.44 (1.29-4.63)
<b>Peripheral vascular disease</b>							
	n < 10	21913.3	3.19 (1.28-6.58)	39	228407.8	1.71 (1.17-2.24)	1.87 (0.84-4.18)
Female	n < 10	15058.6	2.66 (0.72-6.80)	27	155406.7	1.74 (1.14-2.53)	1.53 (0.53-4.37)
Male	n < 10	6854.7	4.38 (0.90-12.79)	12	73001.1	1.64 (0.85-2.87)	2.66 (0.75-9.43)
Age <40	n < 10	12360.1	1.62 (0.20-5.85)	11	113053.4	0.97 (0.49-1.74)	1.66 (0.37-7.50)

	MS patients N=4539			MS-free matched individuals N=47527			
	Events	Person- years	IR (95% CI) <sup>a</sup>	Events	Person- years	IR (95% CI) <sup>a</sup>	IRR (95% CI)
Age 40-59	n < 10	8415.0	3.57 (0.74-10.42)	16	98697.1	1.62 (0.93-2.63)	2.20 (0.64-7.55)
Age ≥ 60	n < 10	1138.2	17.57 (2.13-63.48)	12	16657.3	7.20 (3.72-12.58)	2.44 (0.55-10.90)
<b>Pericardial disease</b>	n < 10	21904.3	2.74 (1.01-5.96)	35	228411.3	1.53 (1.02-2.04)	1.79 (0.75-4.25)
Female	n < 10	15067.7	1.33 (0.16-4.79)	16	155435.2	1.03 (0.59-1.67)	1.29 (0.30-5.61)
Male	n < 10	6836.6	5.85 (1.59-14.98)	19	72976.1	2.60 (1.57-4.07)	2.25 (0.76-6.61)
Age <40	n < 10	12346.3	1.62 (0.20-5.85)	10	113071.7	0.88 (0.42-1.63)	1.83 (0.40-8.36)
Age 40-59	n < 10	8433.3	3.56 (0.73-10.40)	17	98693.6	1.72 (1.00-2.76)	2.07 (0.61-7.05)
Age ≥ 60	n < 10	1124.7	8.89 (0.23-49.54)	n < 10	16646.0	4.81 (2.07-9.47)	1.85 (0.23-14.79)
<b>Bradycardia and heart block</b>	n < 10	21912.0	3.19 (1.28-6.58)	26	228455.6	1.14 (0.74-1.67)	2.81 (1.22-6.47)
Female	n < 10	15058.8	2.66 (0.72-6.80)	11	155456.0	0.71 (0.35-1.27)	3.75 (1.20-11.79)
Male	n < 10	6853.1	4.38 (0.90-12.79)	15	72999.5	2.05 (1.15-3.39)	2.13 (0.62-7.36)
Age <40	n < 10	12356.7	2.43 (0.50-7.10)	n < 10	113089.3	0.35 (0.10-0.91)	6.86 (1.54-30.67)
Age 40-59	n < 10	8433.2	2.37 (0.29-8.57)	n < 10	98731.7	0.91 (0.42-1.73)	2.60 (0.56-12.04)
Age ≥ 60	n < 10	1122.0	17.82 (2.16-64.39)	13	16634.5	7.82 (4.16-13.36)	2.28 (0.51-10.11)
<b>Paroxysmal tachycardia</b>	n < 10	21907.4	4.11 (1.88-7.80)	93	228231.3	4.07 (3.25-4.90)	1.01 (0.51-2.00)
Female	n < 10	15056.7	3.98 (1.46-8.67)	69	155261.9	4.44 (3.40-5.49)	0.90 (0.39-2.07)
Male	n < 10	6850.6	4.38 (0.90-12.80)	24	72969.4	3.29 (2.11-4.89)	1.33 (0.40-4.42)
Age <40	n < 10	12352.5	4.05 (1.31-9.45)	26	112991.9	2.30 (1.50-3.37)	1.76 (0.68-4.58)
Age 40-59	n < 10	8429.7	4.75 (1.29-12.15)	46	98599.6	4.67 (3.32-6.01)	1.02 (0.37-2.83)
Age ≥ 60	0	1125.2	0.00 (N/A)	21	16639.7	12.62 (7.81-19.29)	N/A
<b>Atrial fibrillation and atrial flutter</b>	14	21890.0	6.40 (3.50-10.73)	190	228022.5	8.33 (7.15-9.52)	0.77 (0.45-1.32)
Female	n < 10	15057.6	3.98 (1.46-8.67)	81	155284.2	5.22 (4.08-6.35)	0.76 (0.33-1.75)
Male	n < 10	6832.5	11.71 (5.06-23.07)	109	72738.3	14.99 (12.17-17.80)	0.78 (0.38-1.60)
Age <40	n < 10	12350.5	2.43 (0.50-7.10)	13	113051.0	1.15 (0.61-1.97)	2.11 (0.60-7.41)
Age 40-59	n < 10	8401.0	5.95 (1.93-13.89)	80	98439.4	8.13 (6.35-9.91)	0.73 (0.30-1.81)
Age ≥ 60	n < 10	1138.6	52.70 (19.34-114.70)	97	16532.1	58.67 (47.00-70.35)	0.90 (0.39-2.05)



	MS patients N=4539			MS-free matched individuals N=47527			
	Events	Person- years	IR (95% CI) <sup>a</sup>	Events	Person- years	IR (95% CI) <sup>a</sup>	IRR (95% CI)
<b>Other arrhythmias</b>	16	21886.0	7.31 (4.18-11.87)	161	228032.1	7.06 (5.97-8.15)	1.04 (0.62-1.73)
Female	12	15033.1	7.98 (4.12-13.94)	119	155111.2	7.67 (6.29-9.05)	1.04 (0.57-1.88)
Male	n < 10	6852.9	5.84 (1.59-14.94)	42	72920.9	5.76 (4.02-7.50)	1.01 (0.36-2.83)
Age <40	n < 10	12347.8	4.05 (1.31-9.45)	49	112892.1	4.34 (3.13-5.56)	0.93 (0.37-2.34)
Age 40-59	n < 10	8421.0	9.50 (4.10-18.72)	87	98503.0	8.83 (6.98-10.69)	1.08 (0.52-2.22)
Age ≥ 60	n < 10	1117.1	26.85 (5.54-78.48)	25	16637.0	15.03 (9.72-22.18)	1.79 (0.54-5.92)

<sup>a</sup>Per 10,000 person-years, crude IR and IRR. CI: confidence interval; IR: incidence rate; IRR: incidence rate ratio; MACE: major adverse cardiovascular events; N/A: not applicable

**Supplemental Table 3a. Hospitalizations after diagnosis of multiple sclerosis (MS) compared with MS-free matched individuals, stratified by sex and age, in a national, register-based cohort study in Sweden 2008-2016**

	MS patients N=6602			MS-free matched individuals N=61828			
	Events	Person-years	IR (95% CI) <sup>a</sup>	Events	Person-years	IR (95% CI) <sup>a</sup>	IRR (95% CI)
<b>Cause of hospitalization</b>							
<b>All hospitalizations</b>	3414	18499.5	1845.45 (1783.55-1907.36)	18242	239082.5	763.00 (751.93-774.07)	2.42 (2.33-2.51)
Female	2391	12632.2	1892.79 (1816.92-1968.66)	14221	158542.9	896.98 (882.24-911.72)	2.11 (2.02-2.20)
Male	1023	5867.4	1743.54 (1636.70-1850.38)	4021	80539.6	499.26 (483.83-514.69)	3.49 (3.26-3.74)
Age <40	1673	8118.2	2060.81 (1962.05-2159.56)	8896	104738.4	849.35 (831.70-867.00)	2.43 (2.30-2.56)
Age 40-59	1295	8366.5	1547.84 (1463.54-1632.14)	6220	109291.4	569.12 (554.98-583.26)	2.72 (2.56-2.89)
Age >= 60	446	2014.8	2213.57 (2008.13-2419.01)	3126	25052.7	1247.77 (1204.03-1291.51)	1.77 (1.61-1.96)
<b>MS-related</b>	1982	23576.9	840.65 (803.64-877.66)	0	300614.2	0.00 (N/A)	N/A
Female	1342	16343.2	821.14 (777.20-865.07)	0	206963.5	0.00 (N/A)	N/A
Male	640	7233.8	884.74 (816.19-953.29)	0	93650.6	0.00 (N/A)	N/A
Age <40	1060	10264.3	1032.71 (970.54-1094.88)	0	136087.3	0.00 (N/A)	N/A
Age 40-59	752	10335.7	727.57 (675.57-779.57)	0	130084.3	0.00 (N/A)	N/A
Age >= 60	170	2976.9	571.06 (485.22-656.91)	0	34442.6	0.00 (N/A)	N/A
<b>Cardiovascular-related</b>	138	31697.6	43.54 (36.27-50.80)	1205	297147.2	40.55 (38.26-42.84)	1.07 (0.90-1.28)
Female	81	21864.0	37.05 (28.98-45.12)	639	205152.7	31.15 (28.73-33.56)	1.19 (0.94-1.50)
Male	57	9833.7	57.96 (42.92-73.01)	566	91994.5	61.53 (56.46-66.59)	0.94 (0.72-1.24)
Age <40	13	14872.7	8.74 (4.65-14.95)	87	135767.3	6.41 (5.06-7.75)	1.36 (0.76-2.44)
Age 40-59	61	13374.6	45.61 (34.16-57.05)	459	128512.9	35.72 (32.45-38.98)	1.28 (0.98-1.67)
Age >= 60	64	3450.3	185.49 (140.05-230.94)	659	32867.0	200.51 (185.20-215.81)	0.93 (0.72-1.20)

<sup>a</sup>Per 10,000 person-years. CI: confidence interval; IR: incidence rate; IRR: incidence rate ratio; N/A: not applicable

**Supplemental Table 3b. Mortality after diagnosis of multiple sclerosis (MS) compared with MS-free matched individuals, stratified by sex and age, in a nationwide, register-based cohort study in Sweden 2008-2016**

Cause of death	MS patients N=6602			MS-free matched individuals N=61828			IRR (95% CI)
	Cases	Person-years	IR (95% CI) <sup>a</sup>	Cases	Person-years	IR (95% CI) <sup>a</sup>	
<b>All-cause deaths</b>	109	32093.0	33.96 (27.59-40.34)	663	300614.2	22.05 (20.38-23.73)	1.54 (1.26-1.89)
Female	61	22089.5	27.61 (20.68-34.55)	362	206963.5	17.49 (15.69-19.29)	1.58 (1.20-2.07)
Male	48	10003.5	47.98 (34.41-61.56)	301	93650.6	32.14 (28.51-35.77)	1.49 (1.10-2.02)
Age <40	n < 10	15663.1	3.19 (1.04-7.45)	57	141124.4	4.04 (2.99-5.09)	0.79 (0.32-1.97)
Age 40-59	36	13305.6	27.06 (18.22-35.89)	196	128904.2	15.21 (13.08-17.33)	1.78 (1.25-2.54)
Age ≥ 60	68	3124.3	217.65 (165.92-269.38)	410	30585.5	134.05 (121.07-147.03)	1.62 (1.26-2.10)
<b>Cardiovascular deaths</b>	11	32093.0	3.43 (1.71-6.13)	54	300614.2	1.80 (1.32-2.28)	1.91 (1.00-3.65)
Female	n < 10	22089.5	3.62 (1.56-7.14)	21	206963.5	1.01 (0.63-1.55)	3.57 (1.58-8.06)
Male	n < 10	10003.5	3.00 (0.62-8.76)	33	93650.6	3.52 (2.32-4.73)	0.85 (0.26-2.78)
Age <40	0	15663.1	0.00 (N/A)	n < 10	141124.4	0.21 (0.04-0.62)	N/A
Age 40-59	n < 10	13305.6	3.76 (1.22-8.77)	15	128904.2	1.16 (0.65-1.92)	3.23 (1.17-8.89)
Age ≥ 60	n < 10	3124.3	19.20 (7.05-41.80)	36	30585.5	11.77 (7.93-15.62)	1.63 (0.69-3.87)
<b>Cancer-related deaths</b>	27	32093.0	8.41 (5.54-12.24)	254	300614.2	8.45 (7.41-9.49)	1.00 (0.67-1.48)
Female	19	22089.5	8.60 (5.18-13.43)	155	206963.5	7.49 (6.31-8.67)	1.15 (0.71-1.85)
Male	n < 10	10003.5	8.00 (3.45-15.76)	99	93650.6	10.57 (8.49-12.65)	0.76 (0.37-1.55)
Age <40	n < 10	15663.1	1.92 (0.39-5.60)	12	141124.4	0.85 (0.44-1.49)	2.25 (0.64-7.98)
Age 40-59	n < 10	13305.6	6.76 (3.09-12.84)	80	128904.2	6.21 (4.85-7.57)	1.09 (0.55-2.17)
Age ≥ 60	15	3124.3	48.01 (26.87-79.19)	162	30585.5	52.97 (44.81-61.12)	0.91 (0.53-1.54)
<b>MS-related deaths</b>	30	32093.0	9.35 (6.00-12.69)	0	300614.2	0.00 (N/A)	N/A
Female	15	22089.5	6.79 (3.80-11.20)	0	206963.5	0.00 (N/A)	N/A
Male	15	10003.5	14.99 (8.39-24.73)	0	93650.6	0.00 (N/A)	N/A
Age <40	n < 10	15663.1	0.64 (0.02-3.56)	0	141124.4	0.00 (N/A)	N/A
Age 40-59	n < 10	13305.6	6.01 (2.60-11.85)	0	128904.2	0.00 (N/A)	N/A

Cause of death	MS patients N=6602			MS-free matched individuals N=61828			
	Cases	Person-years	IR (95% CI) <sup>a</sup>	Cases	Person-years	IR (95% CI) <sup>a</sup>	IRR (95% CI)
Age ≥ 60	21	3124.3	67.22 (41.61-102.75)	0	30585.5	0.00 (N/A)	N/A
<b>Suicide</b>	n < 10	32093.0	2.49 (1.08-4.91)	29	300614.2	0.96 (0.65-1.39)	2.58 (1.18-5.65)
Female	n < 10	22089.5	1.81 (0.49-4.64)	14	206963.5	0.68 (0.37-1.13)	2.68 (0.88-8.13)
Male	n < 10	10003.5	4.00 (1.09-10.24)	15	93650.6	1.60 (0.90-2.64)	2.50 (0.83-7.52)
Age <40	n < 10	15663.1	0.64 (0.02-3.56)	11	141124.4	0.78 (0.39-1.39)	0.82 (0.11-6.34)
Age 40-59	n < 10	13305.6	3.01 (0.82-7.70)	13	128904.2	1.01 (0.54-1.72)	2.98 (0.97-9.14)
Age ≥ 60	n < 10	3124.3	9.60 (1.98-28.06)	n < 10	30585.5	1.63 (0.53-3.81)	5.87 (1.40-24.58)

<sup>a</sup>Per 10,000 person-years, crude IR and IRR. CI: confidence interval; IR: incidence rate; IRR: incidence rate ratio; N/A: not applicable

## Supplemental Appendix A

### ICD-10 codes for non-infectious comorbidity in multiple sclerosis in a national, register-based cohort study in Sweden 2008-2016

<u>Category of comorbidity</u>	<u>ICD-10 code</u>
<u>Cardiovascular disease</u>	
<u>Myocardial infarction<sup>1</sup></u>	<u>I21, I22</u>
<u>Stroke, hemorrhagic, and ischemic<sup>1</sup></u>	<u>I61, I63, I64</u>
<u>Transient ischemic attack (TIA)</u>	<u>G45.8, G45.9</u>
<u>Angina pectoris &amp; unspecified ischemic heart disease</u>	<u>I20</u>
<u>Heart failure</u>	<u>I50</u>
<u>Venous thromboembolism</u>	<u>I26, I80, I81, I82</u>

**ICD-10 codes for non-infectious comorbidity in multiple sclerosis in a national, register-based cohort study in Sweden 2008-2016**

<b><u>Category of comorbidity</u></b>	<b><u>ICD-10 code</u></b>
<u>Peripheral vascular disease</u>	<u>I73</u>
<u>Pericardial disease</u>	<u>I30, I31</u>
<u>Bradycardia and heart block</u>	<u>I44</u>
<u>Paroxysmal tachycardia</u>	<u>I47</u>
<u>Atrial fibrillation and atrial flutter</u>	<u>I48</u>
<u>Other cardiac arrhythmias</u>	<u>I49</u>
<u>Sudden death<sup>1</sup></u>	<u>I46.1, R96</u>
<b><u>Non-cardiovascular disease</u></b>	
<u>Autoimmune disease</u>	<u>M30-M36</u>
<u>Bladder dysfunction, neuromuscular</u>	<u>N31</u>
<u>Optic neuritis</u>	<u>H46</u>
<u>Chronic renal disease</u>	<u>I68.8, N18, N19</u>
<u>Diabetes Type I</u>	<u>E10</u>
<u>Diabetes Type II</u>	<u>E11</u>
<u>Dyslipidemia</u>	<u>E78</u>
<u>Retinal disorders</u>	<u>H35, H36</u>
<u>Asthma</u>	<u>J45, J46</u>
<u>Chronic obstructive pulmonary disease</u>	<u>J44</u>
<u>Bowel dysfunction</u>	<u>K58, K59, R14</u>
<u>Crohn disease</u>	<u>K50</u>
<u>Ulcerative colitis</u>	<u>K51</u>
<u>Cancer</u>	<u>C00-C97</u>
<u>Breast cancer</u>	<u>C50</u>
<u>Prostate cancer</u>	<u>C61</u>
<u>Skin cancer</u>	<u>C43-44</u>
<u>Demyelinating disease other than MS</u>	<u>G36-G37</u>

**ICD-10 codes for non-infectious comorbidity in multiple sclerosis in a national, register-based cohort study in Sweden 2008-2016**

<b><u>Category of comorbidity</u></b>	<b><u>ICD-10 code</u></b>
<u>Epilepsy and seizure</u>	<u>G40</u>
<u>Depression</u>	<u>F32-F34</u>
<u>Anxiety</u>	<u>F40, F41</u>
<u>Fatigue</u>	<u>F48</u>
<u>Schizophrenia</u>	<u>F20-F29</u>
<u>Biopolar affective disorders</u>	<u>F31</u>
<u>Fracture</u>	<u>S02, S12, S22, S32, S42, S52, S62, S72, S82, S92, T02, T08, T10, T12</u>
<u>Osteoporosis</u>	<u>M80-M81</u>
<u>Viral liver disease (viral hepatitis)</u>	<u>B15-B19</u>
<u>Alcoholic liver disease</u>	<u>K70</u>
<u>Chronic liver disease / cirrhosis</u>	<u>K73, K74</u>
<u>Acute liver disease or failure</u>	<u>K72</u>
<u>Toxic liver disease</u>	<u>K71</u>
<u>Liver diseases without viral or alcoholic cause</u>	<u>K75, K76</u>

<sup>1</sup>Included in major adverse cardiovascular events (MACE) outcome.

**ICD-10 codes for cause of death in multiple sclerosis in a national, register-based cohort study in Sweden 2008-2016**

<b><u>Category of cause of death</u></b>	<b><u>ICD-10 code</u></b>
<u>MS</u>	<u>G35</u>

<a href="#"><u>Cardiovascular</u></a>	<a href="#"><u>I21, I22, I64, G45.8, G45.9, I20, I50, I26, I80, I81, I82, I73, I30, I31, I44, I47, I48, I49</u></a>
<a href="#"><u>Cancer</u></a>	<a href="#"><u>C00-C97</u></a>
<a href="#"><u>Suicide</u></a>	<a href="#"><u>Z91.5</u></a>

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