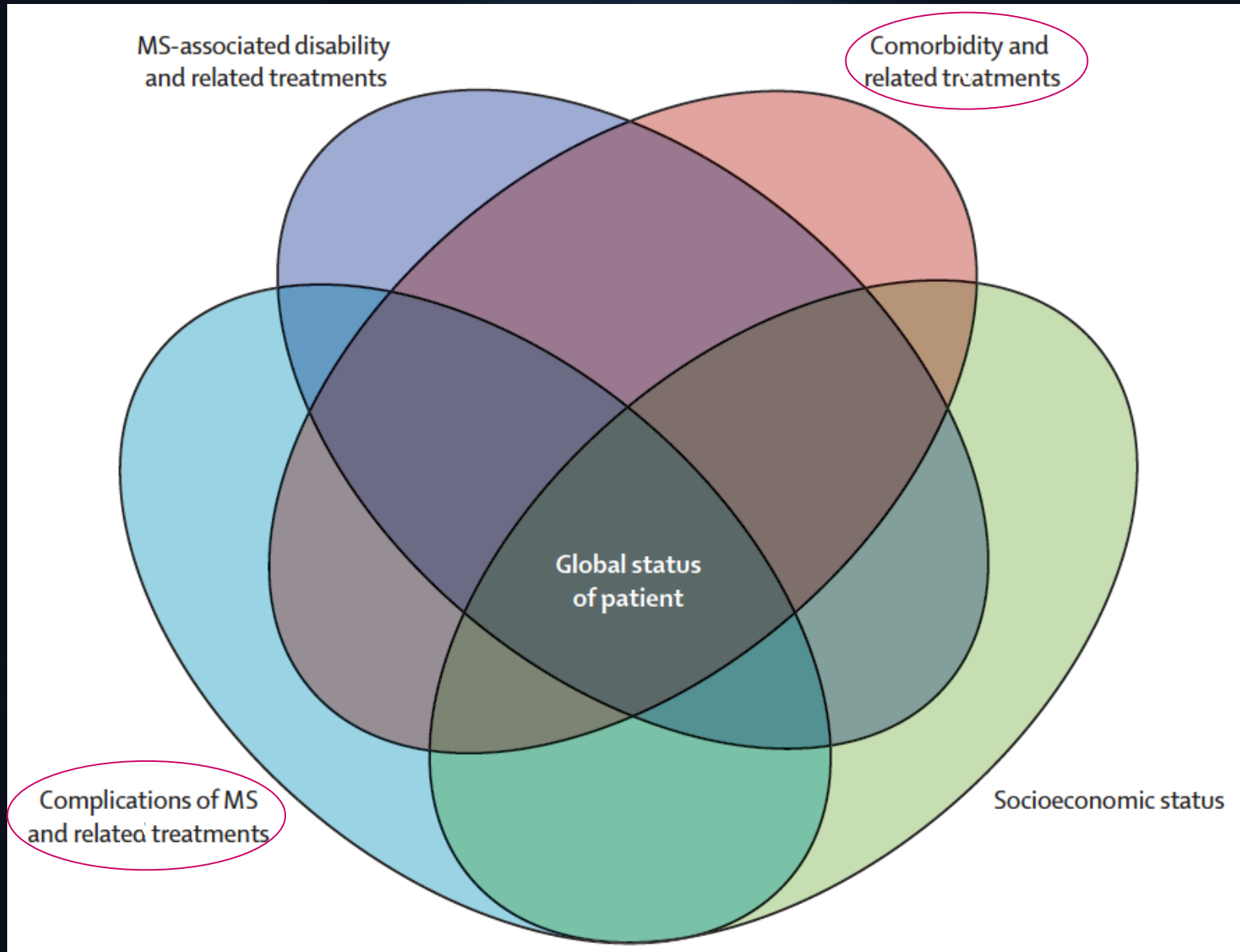


# SCLEROSI MULTIPLA: LE EMERGENZE/URGENZE LEGATE ALLA COMORBILITÀ

Eleonora Cocco  
Università di Cagliari



# Factors that affect the health status of patients with multiple sclerosis



**COMORBIDITY** refers to the total burden of (chronic) illness other than that specific disease of interest  
(Gikisen R et al 2001)

# Meccanismi comorbidità

- 👉 Associazione casuale
- 👉 Età
- 👉 Bias of care
- 👉 Condivisione del meccanismo etiologico:
  - ✓ causa diretta
    - ✓ malattia di base
    - ✓ trattamento
  - ✓ condivisione di fattori di rischio (genetica)
  - ✓ eterogeneità (altri fattori indipendenti)
  - ✓ Indipendenza (conseguenza di una terza malattia ignota)

# PROBLEMATICHE NELLA GESTIONE



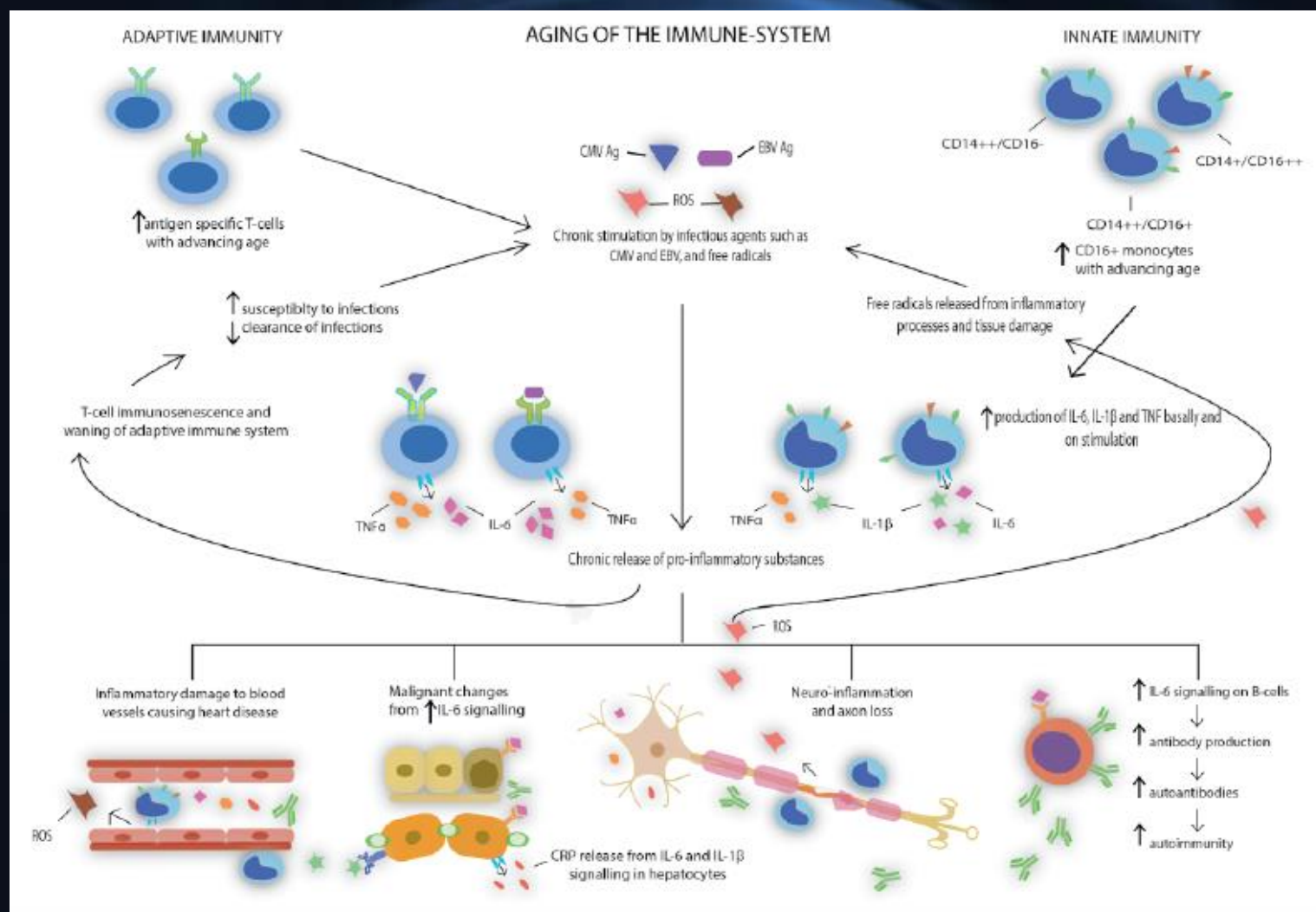
- ✓ Diagnosi
- ✓ Popolazione più longeva
- ✓ Lunga storia di malattia
- ✓ Esposizione a terapie diverse.....
- ✓ Sintomi (fatica, dolore)
- ✓ Disabilità
- ✓ Ricerca gravidanza
- ✓ Scelta e gestione delle terapie

# Aging and multiple sclerosis

Shaik Ahmed Sanai, Vasu Saini, Ralph HB Benedict, Robert Zivadinov, Barbara E Teter, Murali Ramanathan and Bianca Weinstock-Guttman

*Multiple Sclerosis Journal*

2016, Vol. 22(6) 717-725





# PATTERNS OF COMORBIDITY IN ELDERLY PATIENTS WITH MULTIPLE SCLEROSIS

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*(Received in revised form 29 March 1994)*

**Abstract**—This study explored the prevalence of comorbid conditions in hospitalized patients with multiple sclerosis (MS) who were 65 years of age or older. Using 1989 data from the Quality of Care Medicare Provider Analysis and Review (MEDPAR) file, hospitalized MS patients were compared with respect to discharge diagnoses to an age- and sex-matched group of hospitalized patients without MS. As expected, the following discharge diagnoses were more common ( $P < 0.05$ ) for MS patients: urinary tract infection, pneumonia, septicemia and cellulitis. In contrast, MS patients were less likely ( $P < 0.05$ ) to have discharge diagnoses of acute myocardial infarction, heart failure, hypertension, angina pectoris, cerebrovascular disease, diabetes mellitus and chronic obstructive pulmonary disease. Possible explanations include under-reporting of certain comorbid conditions on discharge records of MS patients, a protective effect of MS or its treatment, reduced prevalence of risk factors, disproportionate mortality in younger MS patients with comorbidity and the benefits of medical surveillance.

Multiple sclerosis/epidemiology    Comorbidity    Prevalence    Chronic disease/  
epidemiology    Cardiovascular diseases    Diabetes mellitus    Neoplasms

# Effetto della comorbidità sul trattamento

1. Impedire la cura (multiple barriere al self care, multiterapia)
2. Influenzare su frequenza e intensità del trattamento delle condizioni coesistenti
3. Influenzare su aderenza e persistenza
4. Influenzare efficacia, sicurezza e tollerabilità
5. Aumentare il rischio di interazione tra farmaci e tra farmaco e malattia



# A systematic review of the incidence and prevalence of comorbidity in multiple sclerosis: Overview

Ruth Ann Marrie, Jeffrey Cohen, Olaf Stuve, Maria Trojano, Per Soelberg-Sørensen, Stephen Reingold, Gary Cutter, and Nadia Reider

Multiple Sclerosis Journal  
2015, Vol. 21(3) 283–291  
DOI: 10.1177/  
1532298515584401



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**Table 2.** The prevalence of comorbidity in multiple sclerosis in population-based studies.

Comorbidity	No. studies	<i>I</i> <sup>2</sup> statistic	Meta-analysis estimate (95% CI)
Alcohol abuse	1	-	14.8*
Anxiety	8	99.2	21.9 (8.76-35)
Asthma	3	93.1	7.46 (2.50-12.4)
Autoimmune			
Ankylosing spondylitis	1	-	1.78*
Diabetes type I	4	66.7	0.02 (0-0.58)
IBD	1	-	0.78*
Myasthenia gravis	1	-	0.20*
Psoriasis	1	-	7.74*
Rheumatoid arthritis	2	3.94	2.92 (1.8-4.0)
SLE	1	-	2.90*
Thyroid disease	3	95.4	6.44 (0.19-12.7)
Bipolar disorder	1	-	5.83*
Cancer			
All types	5	90.8	2.23 (1.18–3.29)
Breast	1	-	2.01 <sup>a</sup>
Digestive system	1	-	-
Thyroid	1	-	0.48 <sup>a</sup>
Vulvar	1	-	0.67 <sup>a</sup>
Lung	1	-	-
Skin cancer	1	-	0.48 <sup>a</sup>
Multiple myeloma	0	-	0.97 <sup>a</sup>
Cardiac arrhythmia	1	-	4.5 <sup>a</sup>
Chronic lung disease	2	99.3	10.0 (0–20.9)
Congestive heart disease	1	-	1.8 <sup>a</sup>
Depression	15	97.3	23.7 (17.4–30)
Diabetes	8	98.0	0.76 (0.67–0.84)
Diabetes type II	1	-	8.57
Drug abuse	1	-	2.5 <sup>a</sup>
Epilepsy	11	93.9	3.09 (2.01–4.16)
Eye disease			
Cataracts	2	-	-
Glaucoma	2	-	-
Macular degeneration	-	-	-
Fibromyalgia	1	-	6.82 <sup>a</sup>
Gastrointestinal			
IBS	1	-	12.2 <sup>a</sup>
Viral hepatitis	1	-	3.45 <sup>a</sup>
Hyperlipidemia	3	94.9	10.9 (5.6–16.1)
Hypertension	2	89.9	18.6 (13.9–23.2)
Ischemic heart disease	3	97.6	2.50 (0–5.77)
Peripheral vascular disease	2	88.2	2.40 (0–5.14)
Psychosis	2	97.8	4.3 (0–10.3)
Stroke (any)	2	97.4	3.28 (0–8.98)

Systematic Review

## A systematic review of the incidence and prevalence of autoimmune disease in multiple sclerosis

Ruth Ann Marrie, Nadia Reider, Jeffrey Cohen, Olaf Stuve, Per S Sorensen, Gary Cutter, Stephen C Reingold and Maria Trojano

*Multiple Sclerosis Journal*  
2015, Vol. 21(3) 282–293

DOI: 10.1177/  
1352458514564400



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Systematic Review

## The incidence and prevalence of psychiatric disorders in multiple sclerosis: A systematic review

Ruth Ann Marrie, Stephen Reingold, Jeffrey Cohen, Olaf Stuve, Maria Trojano, Per Soelberg Sorensen, Gary Cutter and Nadia Reider

*Multiple Sclerosis Journal*  
2015, Vol. 21(3) 305–317

DOI: 10.1177/  
1352458514564487

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Original Research Paper

## Influence of hypertension, diabetes, hyperlipidemia, and obstructive lung disease on multiple sclerosis disease course

Devon S Conway, Nicolas R Thompson and Jeffrey A Cohen

*Multiple Sclerosis Journal*

1–9

DOI: 10.1177/  
1352458516650512

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Systematic Review

## A systematic review of the incidence and prevalence of cardiac, cerebrovascular, and peripheral vascular disease in multiple sclerosis

Ruth Ann Marrie, Nadia Reider, Jeffrey Cohen, Olaf Stuve, Maria Trojano, Gary Cutter, Stephen Reingold and Per Soelberg Sorensen

*Multiple Sclerosis Journal*

2015, Vol. 21(3) 318–331

DOI: 10.1177/  
1352458514564485

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Systematic Review

## The incidence and prevalence of comorbid gastrointestinal, musculoskeletal, ocular, pulmonary, and renal disorders in multiple sclerosis: A systematic review

Ruth Ann Marrie, Nadia Reider, Olaf Stuve, Maria Trojano, Per Soelberg Sorensen, Gary R Cutter, Stephen C Reingold and Jeffrey Cohen

*Multiple Sclerosis Journal*  
2015, Vol. 21(3) 332–341

DOI: 10.1177/  
1352458514564488

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Systematic Review

## A systematic review of the incidence and prevalence of sleep disorders and seizure disorders in multiple sclerosis

Ruth Ann Marrie, Nadia Reider, Jeffrey Cohen, Maria Trojano, Per Soelberg Sorensen, Gary Cutter, Stephen Reingold and Olaf Stuve

*Multiple Sclerosis Journal*  
2015, Vol. 21(3) 342–349

DOI: 10.1177/  
1352458514564486

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Systematic Review

## A systematic review of the incidence and prevalence of cancer in multiple sclerosis

Ruth Ann Marrie, Nadia Reider, Jeffrey Cohen, Olaf Stuve, Maria Trojano, Per Soelberg Sorensen, Stephen C Reingold and Gary Cutter

*Multiple Sclerosis Journal*  
2015, Vol. 21(3) 294–304

DOI: 10.1177/  
1352458514564489

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# Comorbidity delays diagnosis and increases disability at diagnosis in MS

Neurology® 2009;72: 117-124

R.A. Marrie, MD, PhD  
 R. Horwitz, MD  
 G. Cutter, PhD  
 T. Tyry, PhD  
 D. Campagnolo, MD  
 T. Vollmer, MD

**Table 2** Mean (SD) diagnostic delay in years among NARCOMS participants by age at symptom onset, and presence or absence of comorbidity at diagnosis of multiple sclerosis (n = 8,983)

Comorbidity category	Age at symptom onset								
	<25 y			≥25 y and <40 y			≥40 y		
	Unaffected, mean (SD)	Affected, mean (SD)	Difference (95% CI)	Unaffected, mean (SD)	Affected, mean (SD)	Difference (95% CI)	Unaffected, mean (SD)	Affected, mean (SD)	Difference (95% CI)
Vascular	9.9 (8.7)	18.7 (11.0)	8.8 (7.5-10.1)*	5.9 (6.1)	9.3 (7.6)	3.4 (2.9-4.0)*	3.6 (3.9)	4.9 (4.7)	1.3 (0.9-1.8)*
Autoimmune	10.1 (9.0)	16.4 (9.8)	6.3 (4.9-7.6)*	6.2 (6.4)	8.9 (7.1)	2.7 (2.0-3.4)*	3.7 (4.1)	5.2 (4.7)	1.4 (0.8-2.1)*
Musculoskeletal	10.1 (8.8)	19.0 (10.6)	8.9 (7.4-10.5)*	6.0 (6.3)	10.7 (7.4)	4.7 (3.9-5.4)*	3.7 (4.0)	6.0 (5.2)	2.3 (1.6-3.0)*
Gastrointestinal	10.1 (9.0)	14.6 (9.9)	4.5 (3.2-5.7)*	6.2 (6.4)	8.2 (7.0)	2.0 (1.4-2.7)*	3.9 (4.2)	4.5 (4.6)	0.6 (-0.06 to 1.3)*
Visual	9.9 (8.7)	20.2 (9.2)	10.3 (7.5-13.0)*	6.0 (6.2)	10.1 (7.8)	4.1 (2.7-5.5)*	3.7 (4.0)	5.6 (5.0)	1.9 (0.7-3.2)*
Mental	9.9 (8.9)	14.6 (10.0)	6.3 (4.9-7.6)*	6.0 (6.3)	8.0 (6.8)	2.0 (1.6-2.5)*	3.9 (4.2)	4.2 (4.3)	0.3 (-0.2 to 0.8) <sup>§</sup>

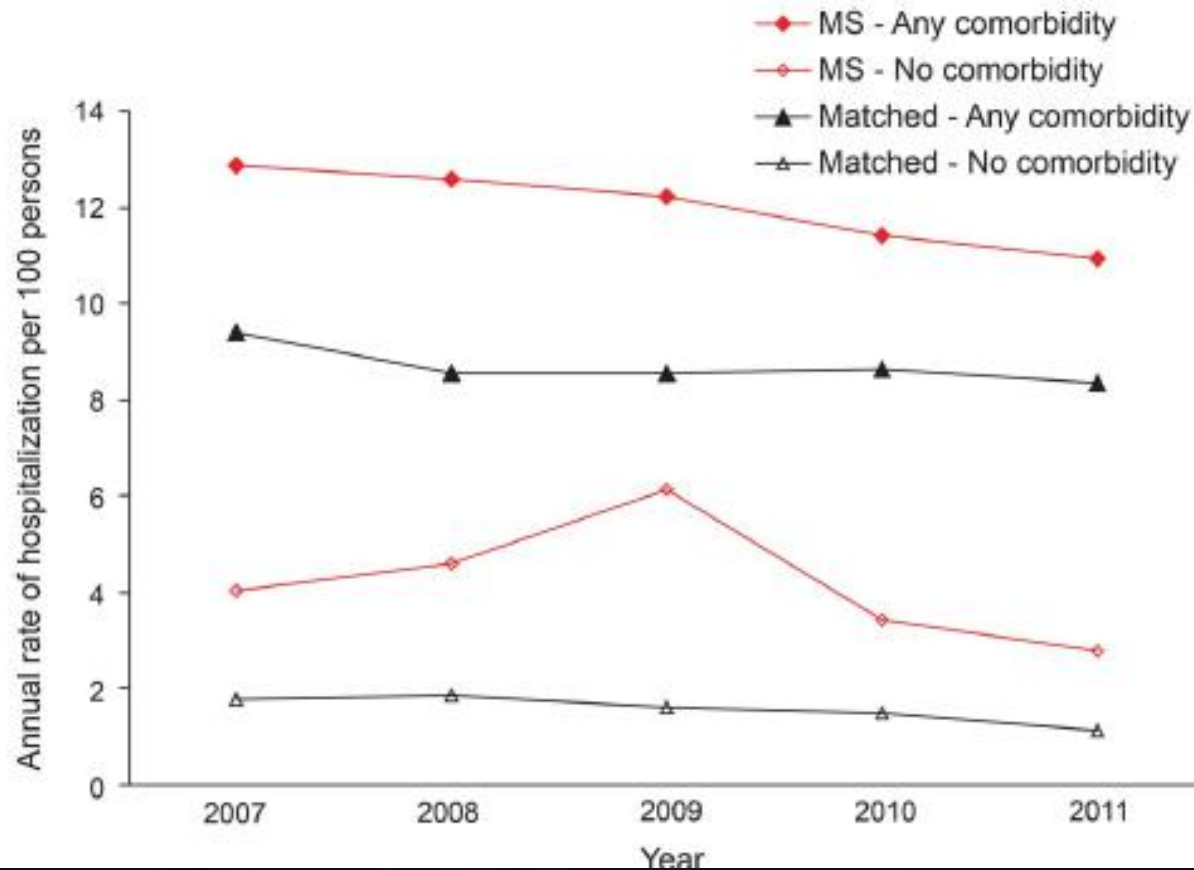
**Table 3** Odds ratios and 95% CIs for the association of comorbidity category at diagnosis and degree of disability at diagnosis in white NARCOMS participants enrolled within 2 years of diagnosis (n = 2,237)

Comorbidity category	Adjusted*				Adjusted for diagnostic delay*			
	Moderate vs mild		Severe vs mild		Moderate vs mild		Severe vs mild	
	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
Vascular	1.51	1.12-2.05	1.06	0.77-1.44	1.32	0.97-1.80	0.87	0.63-1.20
Musculoskeletal	1.54	1.04-2.28	1.81	1.25-2.63	1.35	0.91-2.01	1.55	1.06-2.27
Mental	1.29	0.97-1.71	1.62	1.23-2.14	1.23	0.92-1.63	1.53	1.16-2.02
Overweight <sup>†</sup>	1.08	0.78-1.50	1.03	0.74-1.42	1.02	0.74-1.43	0.93	0.68-1.29
Obesity <sup>†</sup>	1.38	1.02-1.87	1.24	0.91-1.67	1.33	0.98-1.80	1.16	0.86-1.57

# Comorbidity increases the risk of hospitalizations in multiple sclerosis

Neurology® 2015;84:350-358

**Figure 2** Annual age-standardized hospitalization rates in the multiple sclerosis (MS) and matched populations by comorbidity status from 2007 to 2011

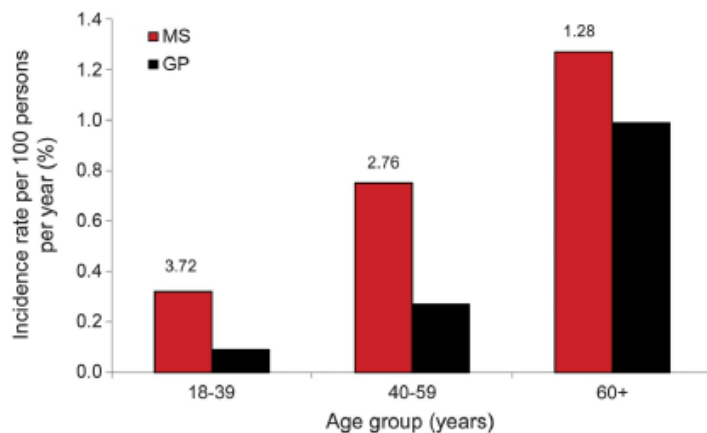


# Intensive care unit admission in multiple sclerosis

Increased incidence and increased mortality

Neurology® 2014;82:2112-2119

**Figure 1** Average annual age-specific incidence rates: MS population and the general population controls



Text boxes show incidence rate ratios comparing incidence of ICU admission by age group in MS with the matched GP cohort. GP = general population; ICU = intensive care unit; MS = multiple sclerosis.

**Table 4** Percent age-specific mortality 1 year after intensive care unit admission in multiple sclerosis as compared with the matched cohort from the general population

Age group, y	General population		Multiple sclerosis		Rate ratio (95% CI)
	No. at risk	Mortality (95% CI)	No. at risk	Mortality (95% CI)	
<40	98	13.3 (6.55-20.0)	14	50.0 (23.8-76.2)	3.77 (1.45-8.11)
40-59	881	12.8 (10.6-15.0)	110	17.3 (10.2-24.3)	1.34 (0.79-1.99)
≥60	1,381	21.9 (19.7-24.1)	91	33.0 (23.3-42.6)	1.50 (1.04-2.03)

Abbreviation: CI = confidence interval.



# Health care utilization before and after intensive care unit admission in multiple sclerosis

Ruth Ann Marrie <sup>a,b,\*</sup>, Charles N. Bernstein <sup>a,c</sup>, Christine A. Peschken <sup>a,b</sup>, Carol A. Hitchon <sup>a</sup>, Hui Chen <sup>d</sup>, Randall Fransoo <sup>b,c</sup>, Allan Garland <sup>a,b,d</sup> *Multiple Sclerosis and Related Disorders* 4 (2015) 296–303

Outcome	Unadjusted		Adjusted	
	Rate ratio	95% CI	Rate ratio	95% CI
Any hospitalization <sup>a</sup>	1.24	0.76, 2.01	1.17	0.69, 1.98
Number of hospital days <sup>a</sup>	1.18	0.76, 1.83	3.36	1.58, 7.15
Number of physician visits <sup>a</sup>	1.09	0.92, 1.30	1.10	0.92, 1.31

**Table 5**  
Health care utilization in the year after ICU admission in the MS population vs. the matched general population.

Outcome	Matched-ICU (n=284)	MS-ICU (n=93)	Crude rate ratio (95% CI)	Standardized <sup>a</sup> rate ratio (95% CI)
Any ICU hospitalizations, n (%)	20 (7.04)	7 (7.5)	1.07 (0.37, 2.31)	1.60 (0.42, 4.13)
Any hospitalizations after ICU, n (%)	96 (33.8)	36 (38.7)	1.14 (0.81, 1.54)	1.32 (0.85, 2.03)
No. hospital days after ICU per person-year, median (p25–p75)	0 (0–3)	0 (0–9)	2.14 (1.01, 4.05)	3.11 (1.34, 5.90)
No. physician visits per person-year, rate (std error)	7.8 (0.17)	16.7 (0.44)	1.12 (0.94, 1.35)	1.35 (1.05, 1.78)
Total prescription drug costs per person-year, rate (std error)	1916.1 (2.8)	3052.4 (6.5)	1.59 (1.22, 2.08)	2.06 (1.38, 13.7)
PCH before ICU, n (%)	s	s	7.63 (1.53, 27.5)	11.5 (2.10, 42.7)
PCH after ICU, n (%)	6 (2.11)	8 (8.6)	4.07 (1.31, 13.7)	5.85 (1.90, 20.9)

**Conclusions:** The incidence of ICU admission is higher among persons with MS who have higher prior health care utilization. Health care utilization remains high after ICU admission. Efforts to prevent ICU admission in this population are needed.



## Emergency Medical Care of Multiple Sclerosis Patients: Primary Data from the Mount Sinai Resource Utilization in Multiple Sclerosis Project

**Background and Purpose** There has been no systematic analysis of emergency department (ED) utilization in the multiple sclerosis (MS) population. We investigated the acute-care needs of MS patients using ED as a route for entry into healthcare services.

**Methods** ED visits made by MS patients were identified. Data extracted included demographics, medical/neurological history, and workup/management in the ED.

**Results** The Mount Sinai ED received 569 visits from 224 MS patients during a 3-year period, of whom 33.5% were covered by Medicaid and 12.9% were uninsured. Patients with an Expanded Disability Status Scale score of  $\geq 6$  accounted for 54%, 50.5% of relapsing remitting MS patients were being treated with disease-modifying therapies, and 74.5% of the ED visits were non-neurological. Patients with mild-to-moderate MS were more likely to present to the ED for issues directly related to MS such as acute exacerbations, while those with severe MS presented more often due to medical issues indirectly related to MS, such as urinary tract infections ( $p < 0.0001$ ).

**Conclusions** Most MS patients seeking ED care suffer from acute nonneurological problems. The MS patients presenting to the ED tended to be underinsured, had high levels of disability, and were undertreated with disease-modifying therapies. The acute-care needs of MS patients evolve over the disease course, as do the resources that must be utilized in providing emergency care across the spectrum of MS severity. Understanding the characteristics, problems, and needs of MS patients utilizing the ED is an important step in improving care in this population from both clinical and public health perspectives.

# Critical Illness in Patients with Multiple Sclerosis: A Matched Case-Control Study

PLOS ONE | DOI:10.1371/journal.pone.0155795 May 31, 2016

Anush Karamyan<sup>1</sup>, Martin W. Dünser<sup>2</sup>, Douglas J. Wiebe<sup>3</sup>, Georg Pilz<sup>1</sup>, Peter Wipfler<sup>1</sup>, Vaclav Chroust<sup>1</sup>, Helmut F. Novak<sup>1</sup>, Larissa Hauer<sup>4</sup>, Eugen Trinka<sup>1</sup>, Johann Sellner<sup>1,5\*</sup>

**Table 1. Reasons for ICU admission and clinical characteristics of patients with MS.**

Parameter	MS patients (n = 61)	Pre-planned admissions (n = 18)	Unplanned admissions (n = 43)	p value
Female, n (%)	39 (63.9)	10 (25.6)	29 (74.4)	0.28
Age at first admission, y	48 (29)	40.5 (17.5)	60 (20)	0.02
Age group, y, n (%)				0.02
<40	20 (33.3)	8 (40)	12 (60)	
40–59	21 (35)	9 (40.9)	13 (59.1)	
≥60	19 (31.7)	1 (5.3)	18 (94.7)	
Years since MS diagnosis	9 (13)	2 (6.8)	13 (23)	0.002
CCI, n (%)				0.07
0	26 (42.6)	11 (42.3)	15 (57.7)	
1–2	24 (39.3)	7 (26.9)	19 (73.1)	
>2	11 (18.1)	0 (0)	8 (100)	
EDSS score	4.5 (3.3)	3 (2.3)	8.5 (5.4)	0.002
Reason for admission				
Respiratory dysfunction	21 (34.4)	0 (0)	21 (100)	
Circulatory dysfunction	5 (8.2)	0 (0)	5 (100)	
Impaired consciousness	5 (8.2)	2 (40)	3 (60)	
Status epilepticus	5 (8.2)	0 (0)	5 (100)	
Infection	3 (4.9)	0 (0)	3 (100)	
Plasma exchange	13 (21.3)	13 (100)	0 (0)	
Drug administration	3 (4.9)	3 (100)	0 (0)	
PML	3 (4.9)	0 (0)	3 (100)	
Sepsis	2 (3.3)	0 (0)	2 (100)	
Trauma	1 (1.6)	0 (0)	1 (100)	
SAPS II score at first admission	20 (14.8)	13 (3.5)	22.5 (27)	0.002
TISS-28 score at first admission	26 (6)	24 (3.8)	26.5 (7)	0.02
ICU length of stay at first admission, d	5 (30.6)	5 (2.5)	4 (7.8)	0.6
Readmitted patients, n (%)	13 (21.3)	3 (23.1)	10 (76.9)	0.42
Cumulative number of admissions, n	86	27	59	
ICU length of stay in total, d	5 (33.9)	5 (4)	4 (9.5)	0.7
Respiratory support, n (%)	13 (21.7)	2 (14.3)	12 (85.7)	0.14
ICU mortality, n (%)	7 (11.7)	0 (0)	7 (100)	0.009
Post-ICU mortality, n (%)	12 (20)	0 (0)	12 (100)	0.09
3-month-mortality	7 (11.7)	0 (0)	7 (100)	0.08
6-month-mortality	8 (13.3)	0 (0)	8 (100)	0.06
1-year-mortality	9 (15)	0 (0)	9 (100)	0.04

**Table 2. Causes of admission, ICU characteristics and mortality in patients with MS and non-MS controls.**

	Crude OR	CI 95%	p value	Adjusted OR <sup>a</sup>	CI 95%	p value
<b>Causes of admission to the ICU</b>						
Respiratory disease/infection	8.52	3.63–20	<0.001	7.86	3.02–20.42	<0.001
Cardio-/cerebrovascular disease	0.09	0.03–0.23	<0.001	0.09	0.03–0.24	<0.001
Neuro-/psychiatric disease*	0.32	0.15–0.7	0.004	0.38	0.15–0.97	0.02
Infection**	4.32	1.63–11.46	0.003	3.71	1.29–10.68	0.02
Intervention***	15.77	4.33–56.97	<0.001	8.13	2.11–31.26	0.002
Other****	0.8	0.2–3.19	0.6	0.63	0.11–3.56	0.29
CCI	1	0.99–1	0.83	n.a.	n.a.	n.a.
SAPS II	0.98	0.97–0.99	<0.001	n.a.	n.a.	n.a.
TISS-28 for the first admission	0.999	0.998–0.999	0.005	n.a.	n.a.	n.a.
ICU length of stay for first admission, d	1.01	0.99–1.03	0.32	n.a.	n.a.	n.a.
Number of readmissions, n	2.53	1.05–6.05	0.04	n.a.	n.a.	n.a.
ICU length of stay in total, d	1.02	0.99–1.03	0.13	n.a.	n.a.	n.a.
ICU mortality	4.72	1.41–15.78	0.01	4.3	1.21–15.29	<0.001
3-month mortality	3.05	1–9.31	0.049	2.83	0.85–9.58	0.15
6-month mortality	2.94	1.02–8.46	0.046	2.73	0.87–8.58	0.14
1-year mortality	3.27	1.12–9.17	0.02	3.36	1.095–10.34	0.09
Mortality over the study period	4.02	1.57–10.35	0.004	4.21	1.49–11.85	0.04

# Comorbidity in multiple sclerosis is associated with diagnostic delays and increased mortality

Neurology® 2017;89:1668-1675

**Table 4** Hazard ratios (HRs) of death in multiple sclerosis (MS) cases with and without severe psychiatric or somatic comorbidity

	No. with comorbidity at or after MS onset	No. without comorbidity at or after MS onset	Starting point: MS onset		Starting point: MS diagnosis	
			HR (95% CI)	p	HR (95% CI)	p
Psychiatric comorbidity vs not	169	8,679	2.42 (1.67-3.01)	<0.0005	2.54 (1.75-3.68)	<0.0005
Cerebrovascular comorbidity vs not						
Male	365	2,603	1.43 (1.14-1.78)	0.002	1.44 (1.15-1.79)	0.001
Female	566	5,314	2.47 (2.05-2.98)	<0.0005	2.29 (1.90-2.76)	<0.0005
Cardiovascular comorbidity vs not						
Male	499	2,469	1.16 (0.93-1.44)	0.201	1.20 (0.96-1.49)	0.114
Female	772	5,108	1.69 (1.39-2.05)	<0.0005	1.54 (1.27-1.87)	<0.0005
Lung comorbidity vs not						
Male	325	2,643	1.68 (1.33-2.12)	0.0005	1.67 (1.32-2.11)	<0.0005
Female	978	4,902	1.28 (1.05-1.56)	0.015	1.10 (0.91-1.34)	0.319
Diabetes comorbidity vs not	465	8,383	1.39 (1.05-1.85)	0.021	1.39 (1.05-1.84)	0.022
Autoimmune comorbidity vs not	739	8,109	1.08 (0.84-1.38)	0.559	1.03 (0.81-1.32)	0.797
Cancer comorbidity vs not	828	8,020	3.51 (2.94-4.19)	<0.0005	3.23 (2.71-3.84)	<0.0005
Parkinson disease comorbidity vs not	34	8,814	2.85 (1.34-6.06)	0.007	2.67 (1.26-5.68)	0.011

# Causes of death among persons with multiple sclerosis

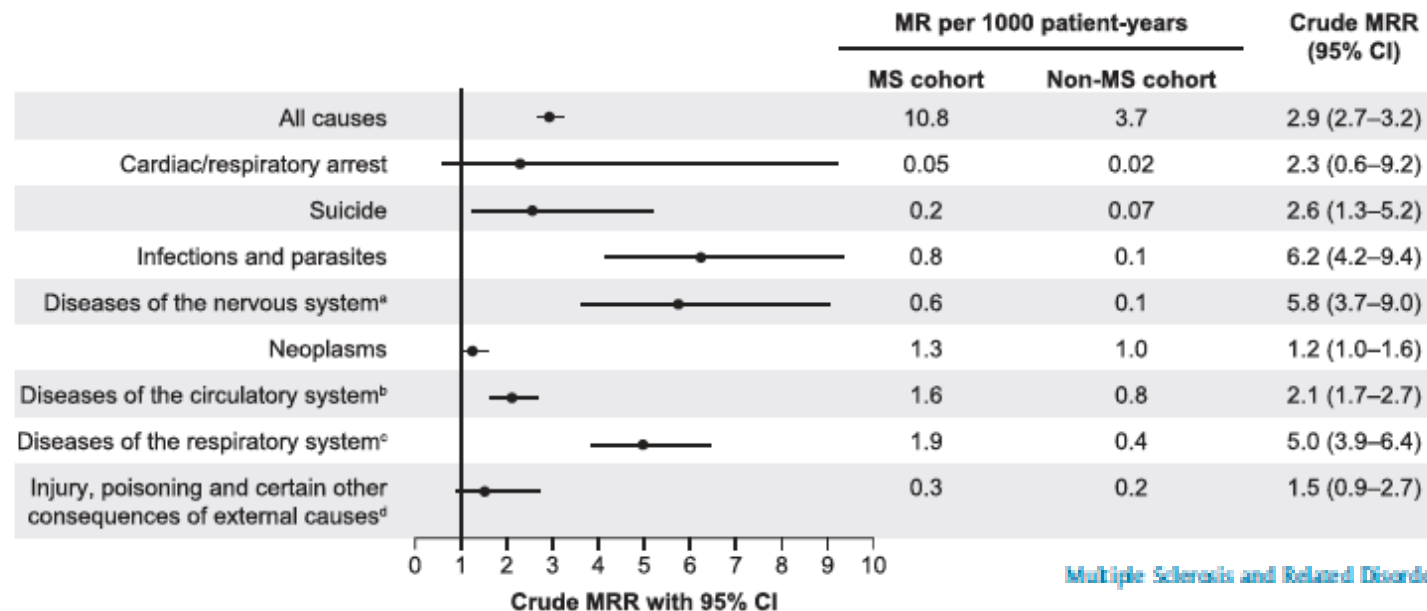
Gary R. Cutter <sup>a,\*</sup>, Jeffrey Zimmerman <sup>b</sup>, Amber R. Salter <sup>a</sup>, Volker Knappertz <sup>c,d</sup>, Gustavo Suarez <sup>e</sup>, John Waterbor <sup>b</sup>, Virginia J. Howard <sup>b</sup>, Ruth Ann Marrie <sup>f</sup>

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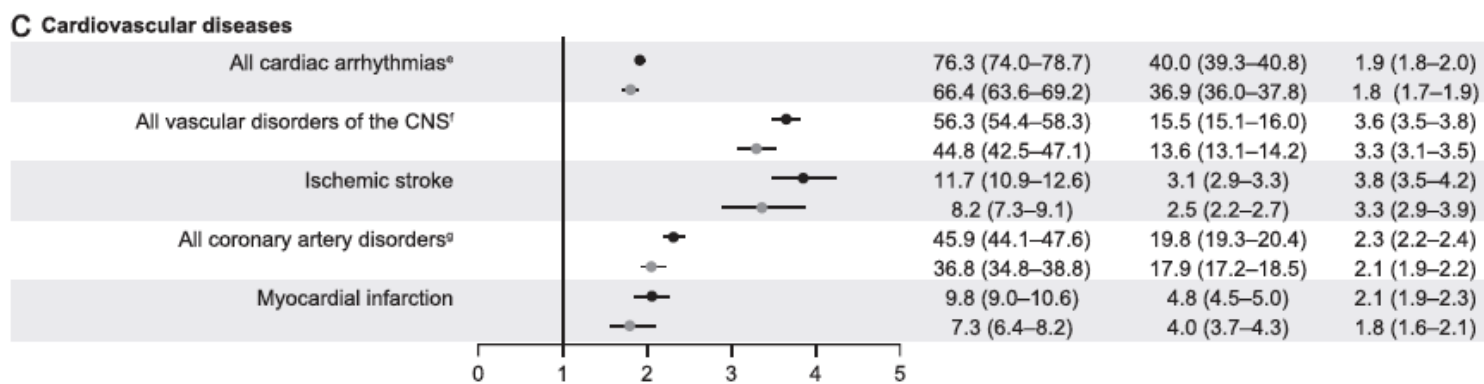
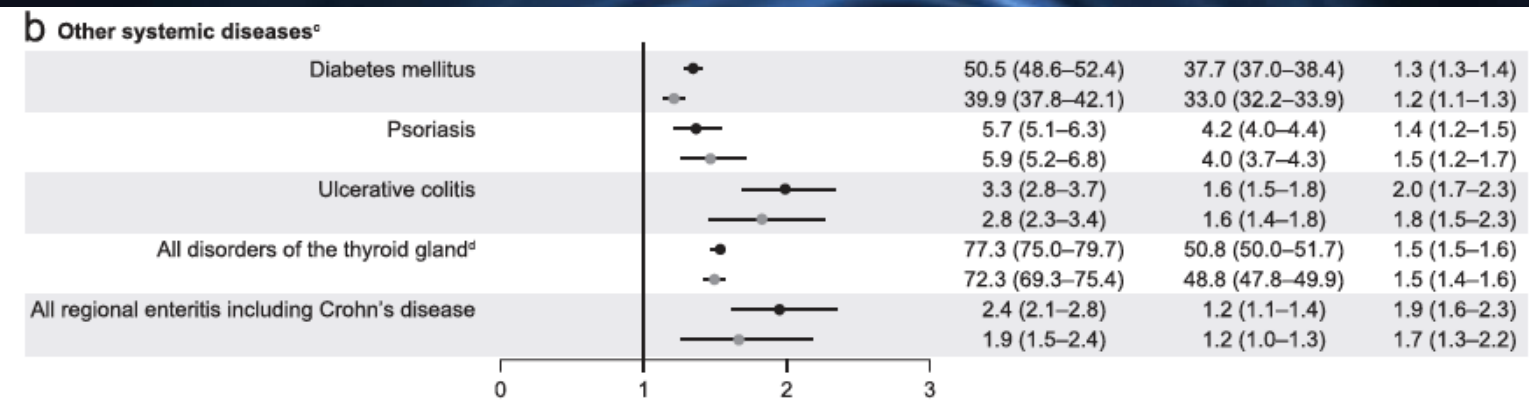
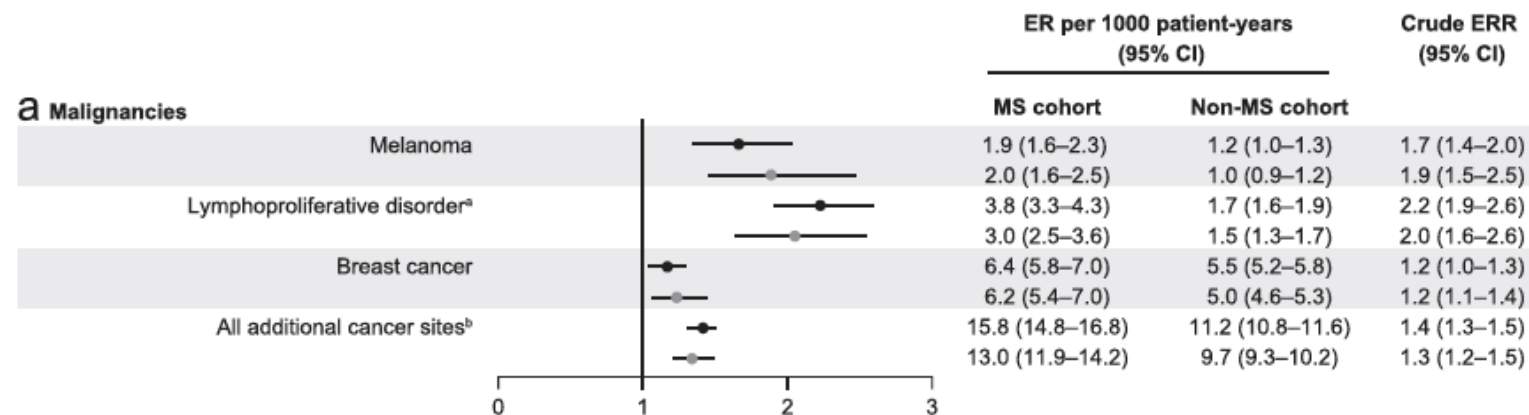
**Table 5.** Underlying Cause-Specific Deaths Among NARCOMS participants, n (% of deaths), for Selected Disease Categories Stratified by Age Group at Enrollment and Sex.

Age Group	Sex	Accidents	Cancer	MS	Major CV	Other	Pneumonia	Septicemia	Suicide
25-39	Female	3 (1.0)	21 (7.1)	141 (48.0)	29 (9.9)	72 (24.5)	10 (3.4)	8 (2.7)	10 (3.4)
	Male	6 (3.1)	9 (4.7)	110 (57.6)	23 (12.0)	24 (12.6)	6 (3.1)	7 (3.7)	6 (3.1)
40-54	Female	9 (1.8)	69 (14.0)	214 (43.3)	61 (12.3)	105 (21.3)	11 (2.2)	16 (3.2)	9 (1.8)
	Male	10 (2.3)	33 (7.7)	199 (46.4)	73 (17.0)	81 (18.9)	14 (3.3)	13 (3.0)	6 (1.4)
55-64	Female	4 (1.0)	64 (16.1)	147 (37.0)	71 (17.9)	88 (22.2)	15 (3.8)	5 (1.3)	3 (0.8)
	Male	9 (2.2)	52 (12.5)	161 (38.7)	76 (18.3)	81 (19.5)	20 (4.8)	5 (1.2)	12 (2.9)
65-74	Female	2 (1.1)	32 (16.8)	62 (32.5)	41 (21.5)	41 (21.5)	7 (3.7)	6 (3.1)	–(–)
	Male	3 (0.9)	39 (11.8)	123 (37.2)	76 (23.0)	61 (18.4)	23 (7.0)	4 (1.2)	2 (0.6)
75+	Female	–(–)	3 (4.4)	19 (27.5)	17 (24.6)	20 (29.0)	8 (11.6)	2 (2.9)	–(–)
	Male	1 (0.9)	12 (10.4)	36 (31.3)	24 (20.9)	33 (28.7)	9 (7.8)	–(–)	–(–)

NARCOMS=North American Research Committee on Multiple Sclerosis; MS=Multiple Sclerosis; CV=Cardiovascular

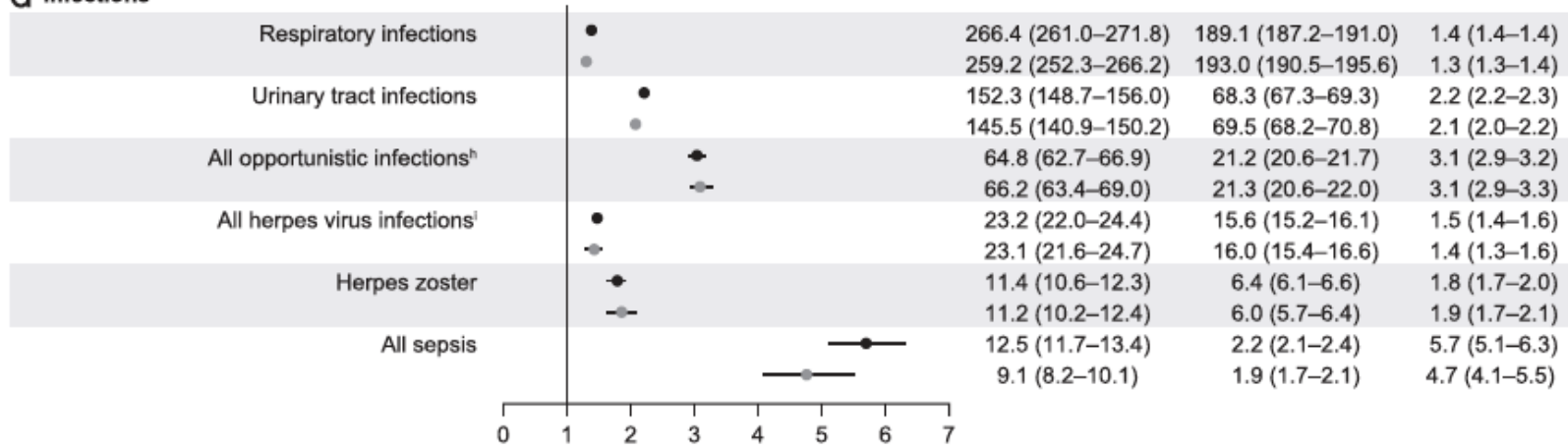


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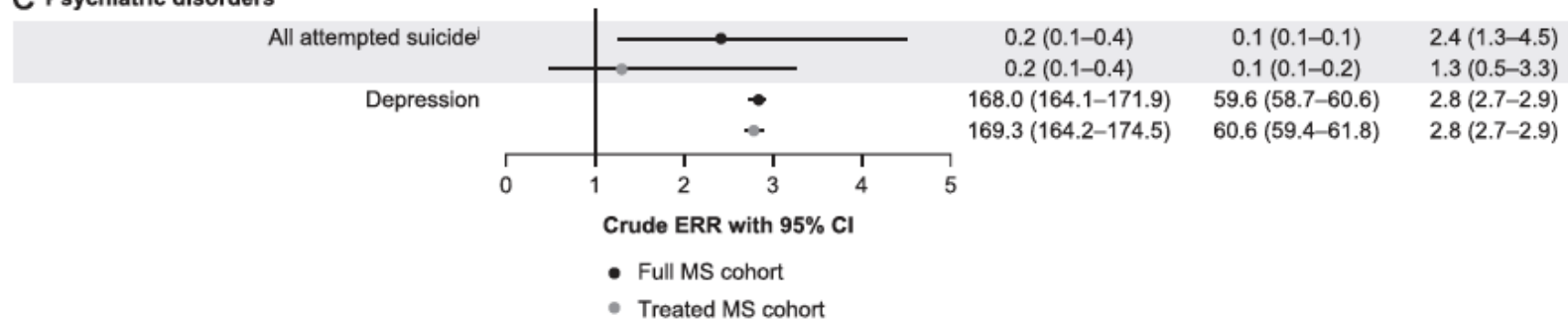




### d Infections



### e Psychiatric disorders



# Differences in the burden of psychiatric comorbidity in MS vs the general population

OPEN

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Impact of Comorbidity  
on Multiple Sclerosis

## ABSTRACT

**Objective:** We aimed to compare the incidence and prevalence of psychiatric comorbidity in the multiple sclerosis (MS) population and in controls matched for age, sex, and geographic area.

**Methods:** Using population-based administrative health data from 4 Canadian provinces, we identified 2 cohorts: 44,452 persons with MS and 220,849 controls matched for age, sex, and geographic area. We applied validated case definitions to estimate the incidence and prevalence of depression, anxiety, bipolar disorder, and schizophrenia from 1995 to 2005. We pooled the results across provinces using meta-analyses.

**Results:** Of the MS cases, 31,757 (71.3%) were women with a mean (SD) age at the index date of 43.8 (13.7) years. In 2005, the annual incidence of depression per 100,000 persons with MS was 979 while the incidence of anxiety was 638, of bipolar disorder was 328, and of schizophrenia was 60. The incidence and prevalence estimates of all conditions were higher in the MS population than in the matched population. Although the incidence of depression was higher among women than men in both populations, the disparity in the incidence rates between the sexes was lower in the MS population (incidence rate ratio 1.26; 95% confidence interval: 1.07-1.49) than in the matched population (incidence rate ratio 1.50; 95% confidence interval: 1.21-1.86). Incidence rates were stable over time while prevalence increased slightly.

**Conclusions:** Psychiatric comorbidity is common in MS, and more frequently affected the MS population than a matched population, although the incidence was stable over time. Men with MS face a disproportionately greater relative burden of depression when they develop MS than women. *Neurology*® 2015;85:1972-1979

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# Multiple sclerosis and suicide

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*Multiple Sclerosis Journal*

2017, Vol. 23(7) 923–927

**Abstract:** Mortality rates are elevated in people with multiple sclerosis (MS) relative to the general population. There is, however, some uncertainty whether suicide contributes to this. Epidemiological data suggest that the standardized mortality ratio (SMR) for suicide in MS is approximately twice that of the general population with younger males in the first few years following diagnosis most at risk. Rates of suicidal intent, a potential harbinger of more self-destructive behavior, are also elevated, but the frequency with which intent is followed by suicide is not known. Depression, severity of depression, social isolation, and alcohol abuse are associated with thoughts of suicide. The variables linked with suicide and suicidal intent are therefore well defined and should be readily available from routine clinical inquiry. While vigilance on the part of clinicians is required, particularly in the context of high-risk patients, it is also recognized that prevention is dependent on full disclosure of intent.



# Chronic lung disease and multiple sclerosis: Incidence, prevalence, and temporal trends



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Multiple Sclerosis and Related Disorders 8 (2016) 86–92

## A B S T R A C T

**Objectives:** We aimed to estimate the incidence and prevalence of chronic lung disease (CLD), including asthma and chronic obstructive pulmonary disease, in the MS population versus a matched cohort from the general population.

**Methods:** We used population-based administrative data from four Canadian provinces to identify 44,452 persons with MS and 220,849 age-, sex- and geographically-matched controls aged 20 years and older. We employed a validated case definition to estimate the incidence and prevalence of CLD over the period 1995–2005, and used Poisson regression to assess temporal trends.

**Results:** In 2005, the crude incidence of CLD per 100,000 persons was 806 (95%CI: 701–911) in the MS population, and 757 in the matched population (95%CI: 712–803). In 2005, the crude prevalence of CLD was 13.5% (95%CI: 13.1–14.0%) in the MS population, and 12.4% (95%CI: 12.3–12.6%) in the matched population. Among persons aged 20–44 years, the average annual incidence of CLD was higher in the MS population than in the matched population (RR 1.15; 95%CI: 1.02–1.30), but did not differ between populations for those aged  $\geq 45$  years. The incidence of CLD was stable, but the prevalence of CLD increased 60% over the study period.

**Conclusion:** CLD is relatively common in the MS population. The incidence of CLD has been stable over time, but the prevalence of CLD has increased. Among persons aged 20–44 years, CLD is more common in the MS population than in a matched population. Given the prevalence of CLD in the MS population, further attention to the effects of CLD on outcomes in MS and approaches to mitigating those effects are warranted.

# Risk of subsequent ischemic and hemorrhagic stroke in patients hospitalized for immune-mediated diseases: a nationwide follow-up study from Sweden

Bengt Zöller<sup>1\*</sup>, Xinjun Li<sup>1</sup>, Jan Sundquist<sup>1,2</sup> and Kristina Sundquist<sup>1</sup>

Zöller et al. *BMC Neurology* 2012, **12**:41

**Table 3 SIR for subsequent hemorrhagic stroke of patients with IMD**

	Follow-up interval (years)																			
	<1			1-5			5-10			>=10			All							
	O	SIR	95 % CI	O	SIR	95 % CI	O	SIR	95 % CI	O	SIR	95 % CI	O	SIR	95 % CI					
Immune-mediated diseases																				
Addison's disease	2	2.70	0.25	9.94	2	0.64	0.06	2.34	1	0.42	0.00	2.41	1	0.55	0.00	3.17	6	0.74	0.27	1.63
Amyotrophic lateral sclerosis	1	0.47	0.00	2.68	2	1.30	0.12	4.78	1	1.82	0.00	10.42	0				4	0.89	0.23	2.30
Ankylosing spondylitis	6	<b>8.11</b>	<b>2.92</b>	<b>17.76</b>	15	<b>3.43</b>	<b>1.92</b>	<b>5.68</b>	7	1.66	0.66	3.44	14	<b>2.28</b>	<b>1.24</b>	<b>3.84</b>	42	<b>2.72</b>	<b>1.96</b>	<b>3.67</b>
Autoimmune hemolytic anemia	1	3.13	0.00	17.91	4	2.96	0.77	7.66	1	1.15	0.00	6.59	2	2.99	0.28	10.98	8	<b>2.49</b>	<b>1.06</b>	<b>4.93</b>
Behcet's disease	1	33.33	0.01	191.08	0				0				0				1	1.67	0.00	9.55
Celiac disease	2	3.57	0.34	13.13	6	2.08	0.75	4.56	7	<b>2.69</b>	<b>1.07</b>	<b>5.58</b>	8	<b>2.65</b>	<b>1.13</b>	<b>5.25</b>	23	<b>2.54</b>	<b>1.61</b>	<b>3.81</b>
Chorea minor	0				0				0				0				0			
Crohn disease	5	1.47	0.46	3.46	47	<b>2.60</b>	<b>1.91</b>	<b>3.46</b>	19	1.19	0.72	1.87	24	<b>1.57</b>	<b>1.00</b>	<b>2.34</b>	95	<b>1.80</b>	<b>1.46</b>	<b>2.21</b>
Diabetes mellitus type I	0				2	2.50	0.24	9.19	1	1.11	0.00	6.37	2	1.01	0.09	3.70	5	1.32	0.42	3.10
Discoid lupus erythematosus	1	11.11	0.00	63.69	1	2.33	0.00	13.33	0				0				2	1.87	0.18	6.87
Grave's disease	8	1.53	0.65	3.02	58	<b>1.77</b>	<b>1.35</b>	<b>2.29</b>	48	<b>1.61</b>	<b>1.18</b>	<b>2.13</b>	41	<b>1.48</b>	<b>1.06</b>	<b>2.02</b>	155	<b>1.62</b>	<b>1.38</b>	<b>1.90</b>
Hashimoto's thyroiditis	4	1.47	0.38	3.79	27	<b>2.01</b>	<b>1.32</b>	<b>2.93</b>	19	<b>2.10</b>	<b>1.26</b>	<b>3.29</b>	11	1.37	0.68	2.46	61	<b>1.84</b>	<b>1.40</b>	<b>2.36</b>
Immune thrombocytopenic purpura	8	<b>8.60</b>	<b>3.67</b>	<b>17.03</b>	12	<b>2.81</b>	<b>1.45</b>	<b>4.92</b>	6	2.18	0.79	4.78	2	1.23	0.12	4.54	28	<b>2.93</b>	<b>1.94</b>	<b>4.23</b>
Localized scleroderma	0				1	0.93	0.00	5.36	1	0.85	0.00	4.90	6	<b>4.32</b>	<b>1.55</b>	<b>9.46</b>	8	2.11	0.90	4.17
Lupoid hepatitis	0				0				0				0				0			
Multiple sclerosis	4	1.82	0.47	4.70	15	1.36	0.76	2.25	9	1.09	0.49	2.08	6	0.94	0.34	2.06	34	1.22	0.84	1.71
Myasthenia gravis	1	1.22	0.00	6.99	8	2.09	0.89	4.14	6	2.17	0.78	4.76	0				15	1.62	0.90	2.68
Pernicious anemia	4	2.15	0.56	5.56	18	1.67	0.99	2.65	13	1.52	0.81	2.61	7	0.99	0.39	2.06	42	<b>1.49</b>	<b>1.07</b>	<b>2.01</b>
Polyarteritis nodosa	2	5.41	0.51	19.88	0	0.00	0.54	2.19	3	1.91	0.36	5.66	0				5	1.00	0.31	2.34
Polymyalgia rheumatica	21	<b>2.06</b>	<b>1.28</b>	<b>3.16</b>	78	<b>1.42</b>	<b>1.12</b>	<b>1.77</b>	65	<b>1.67</b>	<b>1.29</b>	<b>2.13</b>	40	<b>1.49</b>	<b>1.06</b>	<b>2.03</b>	204	<b>1.56</b>	<b>1.35</b>	<b>1.79</b>
Polymyositis/dermatomyositis	1	2.63	0.00	15.08	3	1.95	0.37	5.77	1	1.18	0.00	6.74	1	2.08	0.00	11.94	6	1.85	0.66	4.04
Primary biliary cirrhosis	1	2.08	0.00	11.94	3	1.76	0.33	5.22	2	2.17	0.20	7.99	0				6	1.87	0.67	4.10
Psoriasis	9	<b>2.88</b>	<b>1.31</b>	<b>5.50</b>	32	<b>1.83</b>	<b>1.25</b>	<b>2.59</b>	23	1.51	0.95	2.26	21	1.32	0.81	2.02	85	<b>1.64</b>	<b>1.31</b>	<b>2.03</b>
Reiter's disease	0				1	2.94	0.00	16.86	1	2.56	0.00	14.70	0				2	1.42	0.13	5.22
Rheumatic fever	1	7.69	0.00	44.09	0				0				1	1.72	0.00	9.88	2	1.04	0.10	3.81
Rheumatoid arthritis	65	<b>3.27</b>	<b>2.52</b>	<b>4.17</b>	191	<b>2.03</b>	<b>1.76</b>	<b>2.34</b>	109	<b>1.92</b>	<b>1.57</b>	<b>2.31</b>	61	<b>1.78</b>	<b>1.36</b>	<b>2.29</b>	426	<b>2.08</b>	<b>1.89</b>	<b>2.29</b>
Sarcoidosis	3	2.48	0.47	7.34	12	1.87	0.96	3.28	14	<b>2.26</b>	<b>1.23</b>	<b>3.80</b>	6	0.79	0.28	1.73	35	<b>1.64</b>	<b>1.14</b>	<b>2.28</b>
Sjögren's syndrome	0				3	1.35	0.25	4.00	2	1.03	0.10	3.77	0				5	0.81	0.26	1.90
Systemic lupus erythematosus	9	<b>8.65</b>	<b>3.92</b>	<b>16.50</b>	13	<b>2.89</b>	<b>1.53</b>	<b>4.95</b>	4	1.17	0.31	3.03	6	1.91	0.69	4.19	32	<b>2.65</b>	<b>1.81</b>	<b>3.74</b>
Systemic sclerosis	2	3.17	0.30	11.67	5	2.67	0.84	6.29	3	2.73	0.51	8.07	2	3.45	0.33	12.68	12	<b>2.87</b>	<b>1.48</b>	<b>5.03</b>
Ulcerative colitis	7	1.45	0.57	3.00	40	<b>1.45</b>	<b>1.03</b>	<b>1.97</b>	28	1.21	0.80	1.74	33	1.44	0.99	2.02	108	<b>1.37</b>	<b>1.13</b>	<b>1.66</b>
Wegener's granulomatosis	6	<b>5.83</b>	<b>2.10</b>	<b>12.76</b>	3	0.90	0.17	2.67	2	1.08	0.10	3.95	0				11	1.47	0.73	2.63
All	175	<b>2.65</b>	<b>2.27</b>	<b>3.08</b>	602	<b>1.83</b>	<b>1.69</b>	<b>1.98</b>	396	<b>1.63</b>	<b>1.47</b>	<b>1.80</b>	295	<b>1.47</b>	<b>1.31</b>	<b>1.65</b>	1468	<b>1.75</b>	<b>1.66</b>	<b>1.84</b>

O = observed number of cases; SIR = standardized incidence ratio; CI = confidence interval.

Bold type: 95 % CI does not include 1.00.

Adjusted for age, period, socioeconomic status, region of residence, hospitalization of chronic lower respiratory diseases, obesity, alcoholism, hypertension, diabetes, atrial fibrillation, heart failure, renal disease, sepsis, and coronary heart disease.

# Risk of subsequent ischemic and hemorrhagic stroke in patients hospitalized for immune-mediated diseases: a nationwide follow-up study from Sweden

Bengt Zöller<sup>1\*</sup>, Xinjun Li<sup>1</sup>, Jan Sundquist<sup>1,2</sup> and Kristina Sundquist<sup>1</sup>

Zöller et al. *BMC Neurology* 2012, **12**:41

**Table 4 SIR for subsequent ischemic stroke of patients with IMD**

	Follow-up interval (years)																			
	<1			1-5			5-10			>=10			All							
	O	SIR	95 % CI	O	SIR	95 % CI	O	SIR	95 % CI	O	SIR	95 % CI	O	SIR	95 % CI					
Immune-mediated diseases																				
Addison's disease	14	<b>2.71</b>	<b>1.48</b>	<b>4.56</b>	28	1.17	0.78	1.69	30	<b>1.90</b>	<b>1.28</b>	<b>2.72</b>	11	0.97	0.48	1.74	83	<b>1.48</b>	<b>1.18</b>	<b>1.83</b>
Amyotrophic lateral sclerosis	7	0.53	0.21	1.10	16	1.52	0.87	2.47	7	1.77	0.70	3.67	2	1.15	0.11	4.23	32	1.09	0.74	1.54
Ankylosing spondylitis	8	1.62	0.69	3.21	44	<b>1.55</b>	<b>1.13</b>	<b>2.08</b>	24	0.98	0.63	1.46	35	1.08	0.75	1.50	111	<b>1.23</b>	<b>1.01</b>	<b>1.48</b>
Autoimmune hemolytic anemia	4	1.45	0.38	3.75	12	1.00	0.51	1.75	19	<b>2.51</b>	<b>1.51</b>	<b>3.93</b>	5	1.23	0.39	2.90	40	<b>1.51</b>	<b>1.08</b>	<b>2.06</b>
Behcet's disease	1	4.00	0.00	22.93	1	0.65	0.00	3.70	0				1	1.43	0.00	8.19	3	0.78	0.15	2.29
Celiac disease	9	2.17	0.99	4.14	29	1.28	0.86	1.84	21	1.17	0.72	1.78	26	1.47	0.96	2.15	85	<b>1.36</b>	<b>1.09</b>	<b>1.68</b>
Chorea minor	0				1	2.27	0.00	13.03	0				0				1	1.11	0.00	6.37
Crohn disease	49	<b>2.15</b>	<b>1.59</b>	<b>2.84</b>	160	<b>1.33</b>	<b>1.13</b>	<b>1.55</b>	108	1.11	0.91	1.35	97	1.15	0.93	1.40	409	<b>1.28</b>	<b>1.16</b>	<b>1.41</b>
Diabetes mellitus type I	1	6.25	0.00	35.83	2	0.45	0.04	1.65	5	2.75	0.87	6.46	17	<b>5.00</b>	<b>2.91</b>	<b>8.02</b>	25	<b>2.54</b>	<b>1.64</b>	<b>3.76</b>
Discoid lupus erythematosus	3	4.23	0.80	12.51	3	0.99	0.19	2.92	1	0.47	0.00	2.70	3	1.55	0.29	4.60	10	1.28	0.61	2.37
Grave's disease	101	<b>2.15</b>	<b>1.76</b>	<b>2.62</b>	402	<b>1.39</b>	<b>1.26</b>	<b>1.53</b>	348	<b>1.36</b>	<b>1.22</b>	<b>1.51</b>	276	<b>1.27</b>	<b>1.12</b>	<b>1.43</b>	1127	<b>1.39</b>	<b>1.31</b>	<b>1.48</b>
Hashimoto's thyroiditis	77	<b>2.99</b>	<b>2.36</b>	<b>3.74</b>	211	<b>1.73</b>	<b>1.50</b>	<b>1.98</b>	115	<b>1.39</b>	<b>1.14</b>	<b>1.67</b>	82	<b>1.28</b>	<b>1.02</b>	<b>1.59</b>	485	<b>1.64</b>	<b>1.50</b>	<b>1.80</b>
Immune thrombocytopenic purpura	16	<b>2.35</b>	<b>1.34</b>	<b>3.83</b>	55	<b>1.77</b>	<b>1.33</b>	<b>2.30</b>	19	0.94	0.57	1.48	14	1.20	0.65	2.01	104	<b>1.49</b>	<b>1.22</b>	<b>1.81</b>
Localized scleroderma	2	1.28	0.12	4.71	13	1.25	0.66	2.14	18	<b>1.72</b>	<b>1.01</b>	<b>2.72</b>	11	1.04	0.51	1.86	44	1.33	0.97	1.79
Lupoid hepatitis	3	4.48	0.84	13.25	4	1.98	0.52	5.12	0				0				7	2.10	0.83	4.36
Multiple sclerosis	40	<b>3.05</b>	<b>2.18</b>	<b>4.15</b>	73	1.09	0.85	1.37	55	1.11	0.83	1.44	35	0.95	0.66	1.32	203	<b>1.22</b>	<b>1.06</b>	<b>1.40</b>
Myasthenia gravis	6	1.01	0.36	2.21	38	1.36	0.96	1.87	23	1.20	0.76	1.80	13	1.08	0.57	1.85	80	1.23	0.97	1.53
Pernicious anemia	25	<b>1.56</b>	<b>1.01</b>	<b>2.31</b>	138	<b>1.49</b>	<b>1.25</b>	<b>1.76</b>	89	1.23	0.99	1.52	74	<b>1.44</b>	<b>1.13</b>	<b>1.80</b>	326	<b>1.40</b>	<b>1.25</b>	<b>1.56</b>
Polyarteritis nodosa	5	1.23	0.39	2.89	20	1.30	0.79	2.02	11	1.05	0.52	1.88	10	1.13	0.54	2.08	46	1.19	0.87	1.58
Polymyalgia rheumatica	165	<b>1.76</b>	<b>1.50</b>	<b>2.05</b>	761	<b>1.50</b>	<b>1.39</b>	<b>1.61</b>	529	<b>1.54</b>	<b>1.41</b>	<b>1.68</b>	322	<b>1.53</b>	<b>1.37</b>	<b>1.71</b>	1777	<b>1.54</b>	<b>1.47</b>	<b>1.61</b>
Polymyositis/dermatomyositis	10	<b>3.46</b>	<b>1.65</b>	<b>6.39</b>	13	1.19	0.63	2.03	6	1.07	0.38	2.34	5	1.73	0.55	4.07	34	<b>1.52</b>	<b>1.05</b>	<b>2.13</b>
Primary biliary cirrhosis	4	1.54	0.40	3.98	11	1.45	0.72	2.60	4	0.91	0.24	2.35	1	2.17	0.00	12.46	20	1.33	0.81	2.05
Psoriasis	44	<b>1.92</b>	<b>1.39</b>	<b>2.58</b>	217	<b>1.65</b>	<b>1.44</b>	<b>1.89</b>	163	<b>1.53</b>	<b>1.30</b>	<b>1.78</b>	144	<b>1.41</b>	<b>1.19</b>	<b>1.66</b>	568	<b>1.56</b>	<b>1.44</b>	<b>1.70</b>
Reiter's disease	0				5	2.02	0.64	4.76	6	2.47	0.89	5.41	2	0.56	0.05	2.07	13	1.47	0.78	2.52
Rheumatic fever	5	<b>3.91</b>	<b>1.23</b>	<b>9.19</b>	10	1.66	0.79	3.06	14	<b>3.04</b>	<b>1.65</b>	<b>5.11</b>	7	1.81	0.72	3.75	36	<b>2.28</b>	<b>1.59</b>	<b>3.16</b>
Rheumatoid arthritis	345	<b>2.08</b>	<b>1.86</b>	<b>2.31</b>	1266	<b>1.66</b>	<b>1.57</b>	<b>1.75</b>	663	<b>1.45</b>	<b>1.34</b>	<b>1.56</b>	326	<b>1.30</b>	<b>1.16</b>	<b>1.45</b>	2600	<b>1.59</b>	<b>1.53</b>	<b>1.65</b>
Sarcoidosis	9	0.97	0.44	1.85	70	<b>1.43</b>	<b>1.12</b>	<b>1.81</b>	51	1.12	0.83	1.47	56	1.08	0.81	1.40	186	<b>1.19</b>	<b>1.03</b>	<b>1.38</b>
Sjögren's syndrome	10	<b>2.57</b>	<b>1.22</b>	<b>4.75</b>	28	1.38	0.92	1.99	15	0.96	0.54	1.59	15	1.26	0.70	2.08	68	<b>1.31</b>	<b>1.02</b>	<b>1.67</b>
Systemic lupus erythematosus	19	<b>2.21</b>	<b>1.33</b>	<b>3.46</b>	88	<b>2.33</b>	<b>1.87</b>	<b>2.87</b>	54	<b>1.92</b>	<b>1.44</b>	<b>2.51</b>	30	1.26	0.85	1.80	191	<b>1.94</b>	<b>1.68</b>	<b>2.24</b>
Systemic sclerosis	11	1.90	0.94	3.41	28	1.22	0.81	1.77	11	1.19	0.59	2.14	2	0.39	0.04	1.43	52	1.21	0.90	1.58
Ulcerative colitis	71	<b>2.15</b>	<b>1.68</b>	<b>2.71</b>	231	<b>1.27</b>	<b>1.11</b>	<b>1.45</b>	162	1.09	0.92	1.27	146	1.05	0.89	1.24	610	<b>1.21</b>	<b>1.12</b>	<b>1.31</b>
Wegener's granulomatosis	11	1.66	0.82	2.98	12	0.47	0.24	0.83	26	<b>1.54</b>	<b>1.00</b>	<b>2.25</b>	12	1.69	0.87	2.96	61	1.09	0.83	1.40
All	1075	<b>2.02</b>	<b>1.90</b>	<b>2.14</b>	3990	<b>1.50</b>	<b>1.46</b>	<b>1.55</b>	2592	<b>1.38</b>	<b>1.33</b>	<b>1.43</b>	1780	<b>1.29</b>	<b>1.23</b>	<b>1.35</b>	9437	<b>1.46</b>	<b>1.43</b>	<b>1.49</b>

O = observed number of cases; SIR = standardized incidence ratio; CI = confidence interval.

Bold type: 95 % CI does not include 1.00.

Adjusted for age, period, socioeconomic status, region of residence, hospitalization of chronic lower respiratory diseases, obesity, alcoholism, hypertension, diabetes, atrial fibrillation, heart failure, renal disease, sepsis, and coronary heart disease.



# Neurological comorbidity and survival in multiple sclerosis

Olga Krökki<sup>a</sup>, Risto Bloigu<sup>b</sup>, Hanna Ansakorpi<sup>a</sup>,  
Mauri Reunanen<sup>a</sup>, Anne M. Remes<sup>c,d,\*</sup>

Multiple Sclerosis and Related Disorders (2014) 3, 72-77

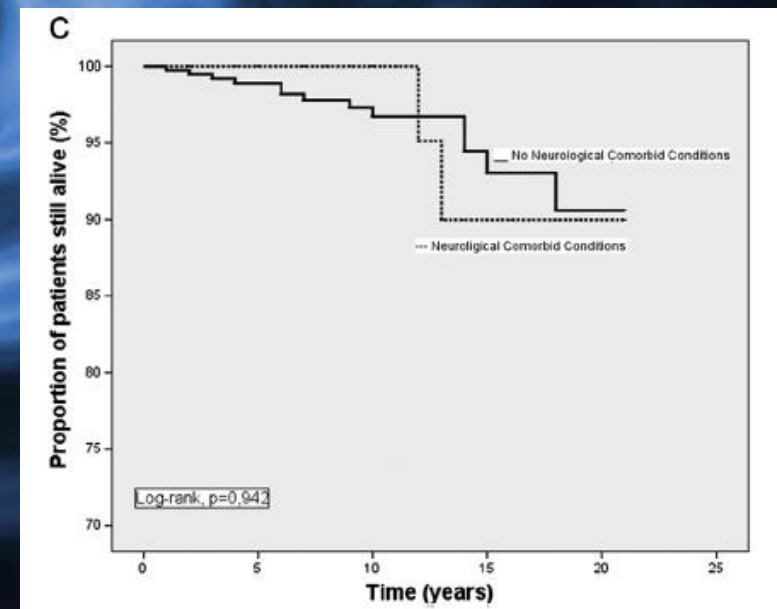
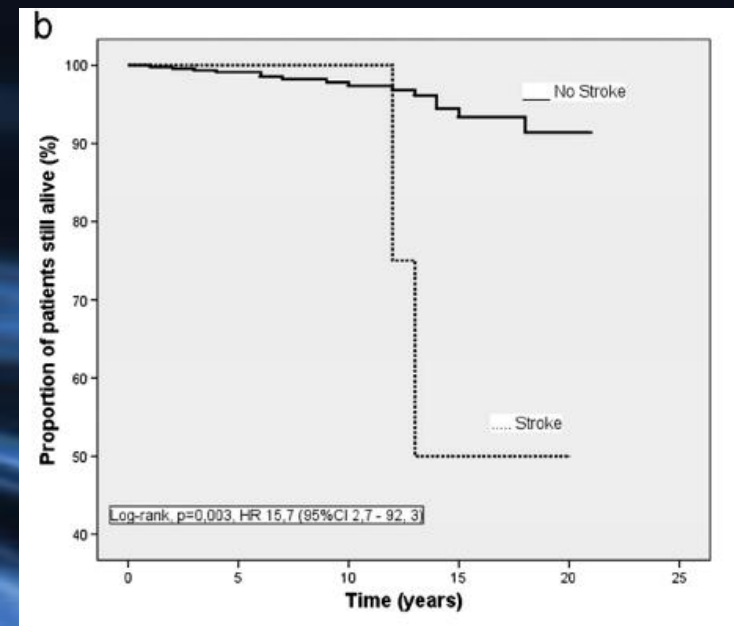
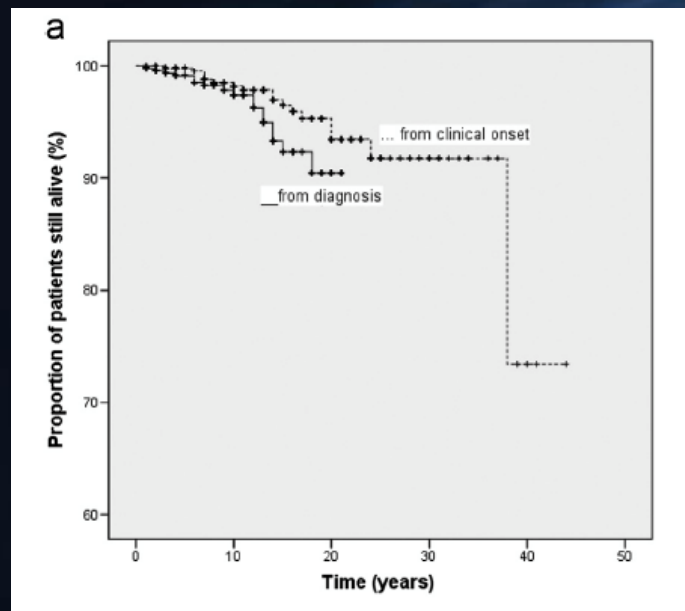
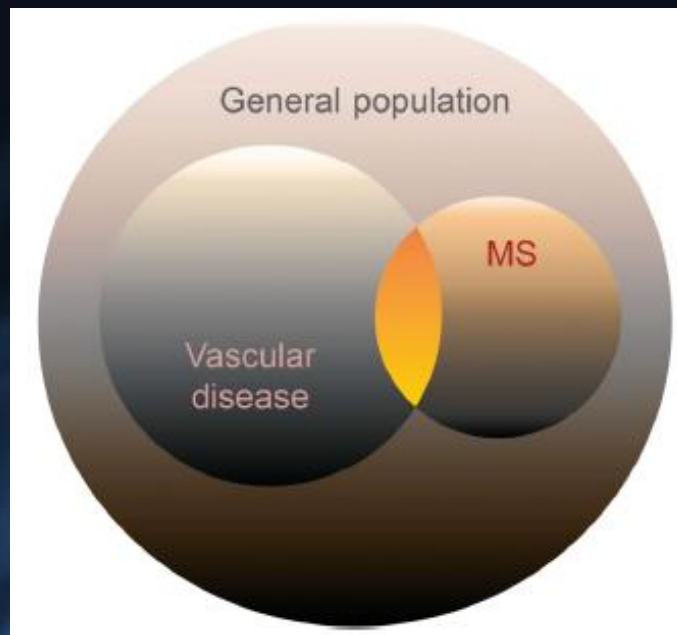
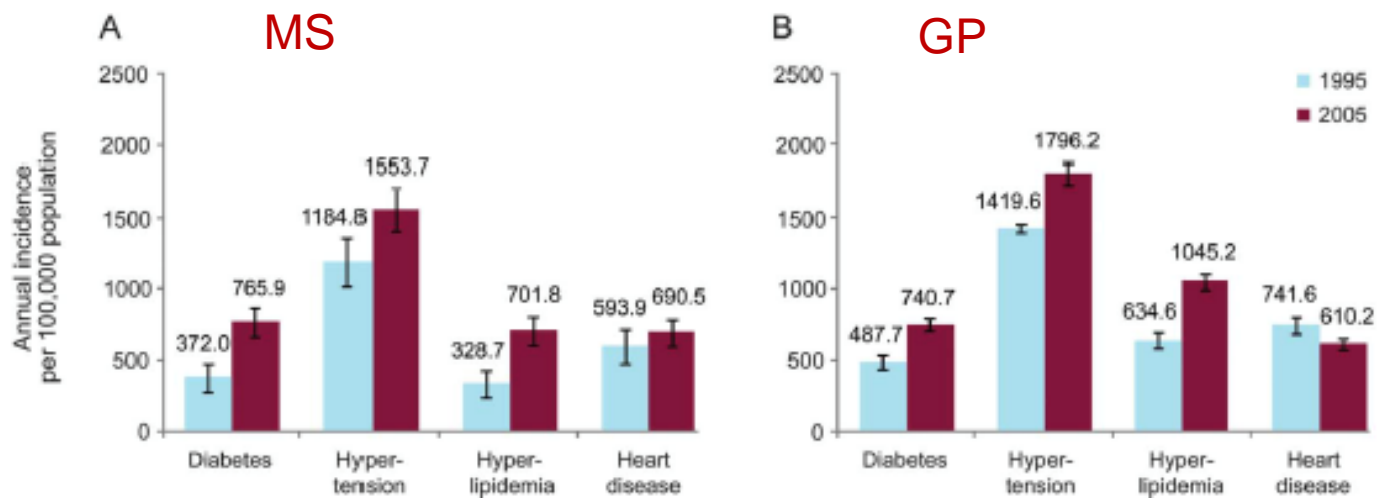


Fig. 1 21-Year survival rates (a) from time of MS onset and from time of MS-diagnosis in the Finnish Northern Ostrobothnia MS-cohort, (b) with stroke as neurological comorbid disease and (c) with neurological comorbid disease.



**Figure 1** Annual incidence of comorbidity per 100,000 persons with multiple sclerosis (A) and in 100,000 persons in the matched population (B) in 1995 and 2005



**Table 3. Associations between modifiable lifestyle factors and number of comorbidities,**

	Unadjusted regression				Adjusted regression *			
	B	Sig.	95% CI		B	Sig.	95% CI	
<b>Body Mass Index</b>								
Underweight	0.06	0.691	-0.24	0.37	-0.05	0.736	-0.35	0.24
Overweight	<b>0.35</b>	<b>&lt; .001</b>	0.20	0.51	<b>0.21</b>	<b>0.007</b>	0.06	0.36
Obese	<b>1.07</b>	<b>&lt; .001</b>	0.91	1.24	<b>0.81</b>	<b>&lt; .001</b>	0.64	0.98
Normal	#	.	.	.	#	.	.	.
<b>Physical activity</b>								
High	<b>-0.49</b>	<b>&lt; .001</b>	-0.65	-0.33	-0.15	0.054	-0.31	0.00
Moderate	<b>-0.33</b>	<b>&lt; .001</b>	-0.48	-0.17	-0.05	0.489	-0.20	0.09
Low	#	.	.	.	#	.	.	.
Diet score (1–100)	<b>-0.02</b>	<b>&lt; .001</b>	-0.03	-0.02	<b>-0.01</b>	<b>0.003</b>	-0.02	0.00
<b>Alcohol consumption</b>								
High	-0.15	0.694	-0.90	0.60	-0.33	0.355	-1.03	0.37
Moderate	<b>-0.44</b>	<b>&lt; .001</b>	-0.58	-0.31	<b>-0.33</b>	<b>&lt; .001</b>	-0.46	-0.20
Low	#	.	.	.	#	.	.	.
<b>Smoking status</b>								
Current	<b>0.86</b>	<b>&lt; .001</b>	0.65	1.06	<b>0.71</b>	<b>&lt; .001</b>	0.51	0.91
Former	<b>0.26</b>	<b>&lt; .001</b>	0.13	0.40	<b>0.21</b>	<b>0.002</b>	0.08	0.34
Never	#	.	.	.	#	.	.	.
<b>Vitamin D supplementation</b>								
>5000IU	<b>-0.40</b>	<b>&lt; .001</b>	-0.61	-0.19	-0.08	0.445	-0.29	0.13
2001-5000IU	<b>-0.41</b>	<b>&lt; .001</b>	-0.60	-0.23	-0.10	0.283	-0.30	0.09
1-2000IU	-0.17	0.098	-0.36	0.03	-0.07	0.445	-0.26	0.12
None	#	.	.	.	#	.	.	.
<b>Omega-3 supplementation</b>								
Yes	<b>-0.36</b>	<b>&lt; .001</b>	-0.49	-0.22	-0.08	0.271	-0.22	0.06
No	#	.	.	.	#	.	.	.

\* Covariates not displayed were age and gender

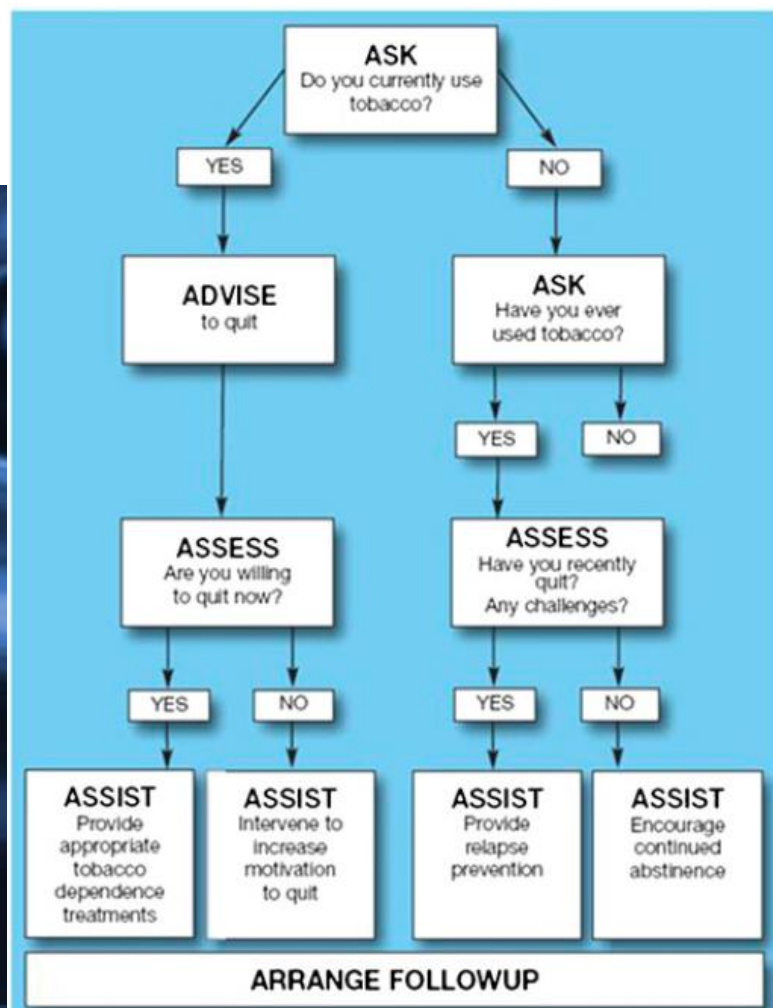
# Reference category. N = 1864

## Modifiable Comorbidities and Disability in Multiple Sclerosis

Shannon Overs • Christina M. Hughes •  
Jodie K. Haselkorn • Aaron P. Turner

Brief Counseling During a Provider Visit

Intervention Delivered in the Context of Chronic Illness  
Care



# Examining the joint effect of disability, health behaviors, and comorbidity on mortality in MS

Amber Salter, PhD; Tuula Tyry, PhD; Guoqiao Wang, PhD; Robert J. Fox, MD, MS; Gary Cutter, PhD; Ruth Ann Marrie, MD, PhD

**Neurol Clin Pract 2016;6:397-408**

## Abstract

**Background:** In multiple sclerosis (MS), comorbidities have been associated with disability progression and an increased risk of mortality. We investigated the association between comorbidities and mortality in MS after accounting for disability and health behaviors. **Methods:**

We followed North American Research Committee on Multiple Sclerosis (NARCOMS) Registry participants who completed the Fall 2006 survey on comorbidities until death (reported or matched in the National Death Index) or date of last follow-up in 2014. We used proportional hazards regression to investigate the association between comorbidities and mortality, controlling for demographic, clinical, health behavior, and disability factors. **Results:**

Of 9,496 participants meeting the inclusion criteria, 502 (5.3%) were deceased. Most participants reported having  $\leq 3$  comorbid conditions (70.9% survivors, 76.9% decedents). In individual regression models, vascular, visual, and mental comorbidities were associated with increased mortality risk after adjustment for factors associated with survival. When combined into a single model, vascular (hazard ratio 1.269; 1.041-1.547), visual (1.490; 1.199-1.852), and mental comorbidities (excluding anxiety, 1.239; 1.024-1.499) remained independently associated with an increased risk of mortality. **Conclusions:** Presence of comorbidities was independently associated with an increased risk of mortality as compared to absence of comorbidities after adjusting for factors associated with survival. Specifically, vascular, visual, and mental comorbidities increased the risk of mortality. This highlights the need for clinicians to attend to these comorbidities, which can be modified by treatments or other interventions, and potentially reduce the risk of mortality in persons with MS who have these conditions. **Neurol Clin Pract 2016;6:397-408**

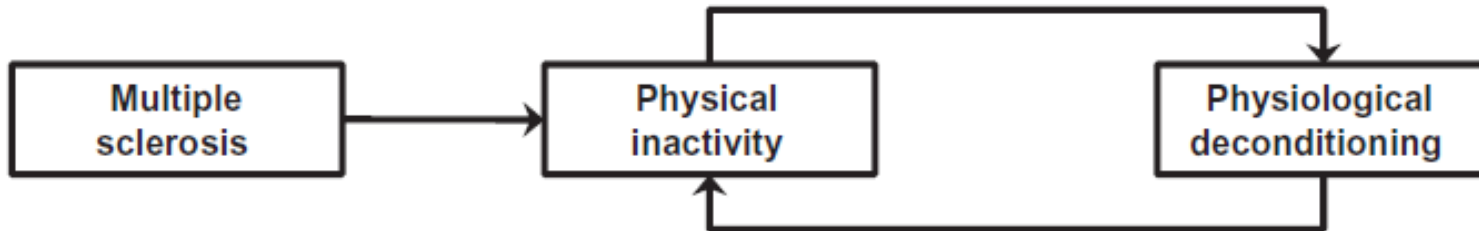




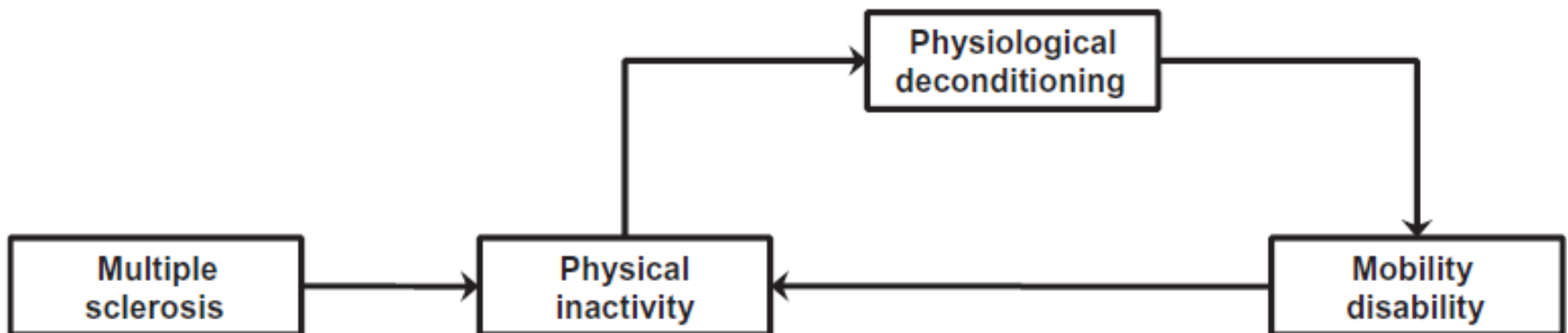
# DECONDIZIONAMENTO E DISABILITA'



## Stage 1



## Stage 2



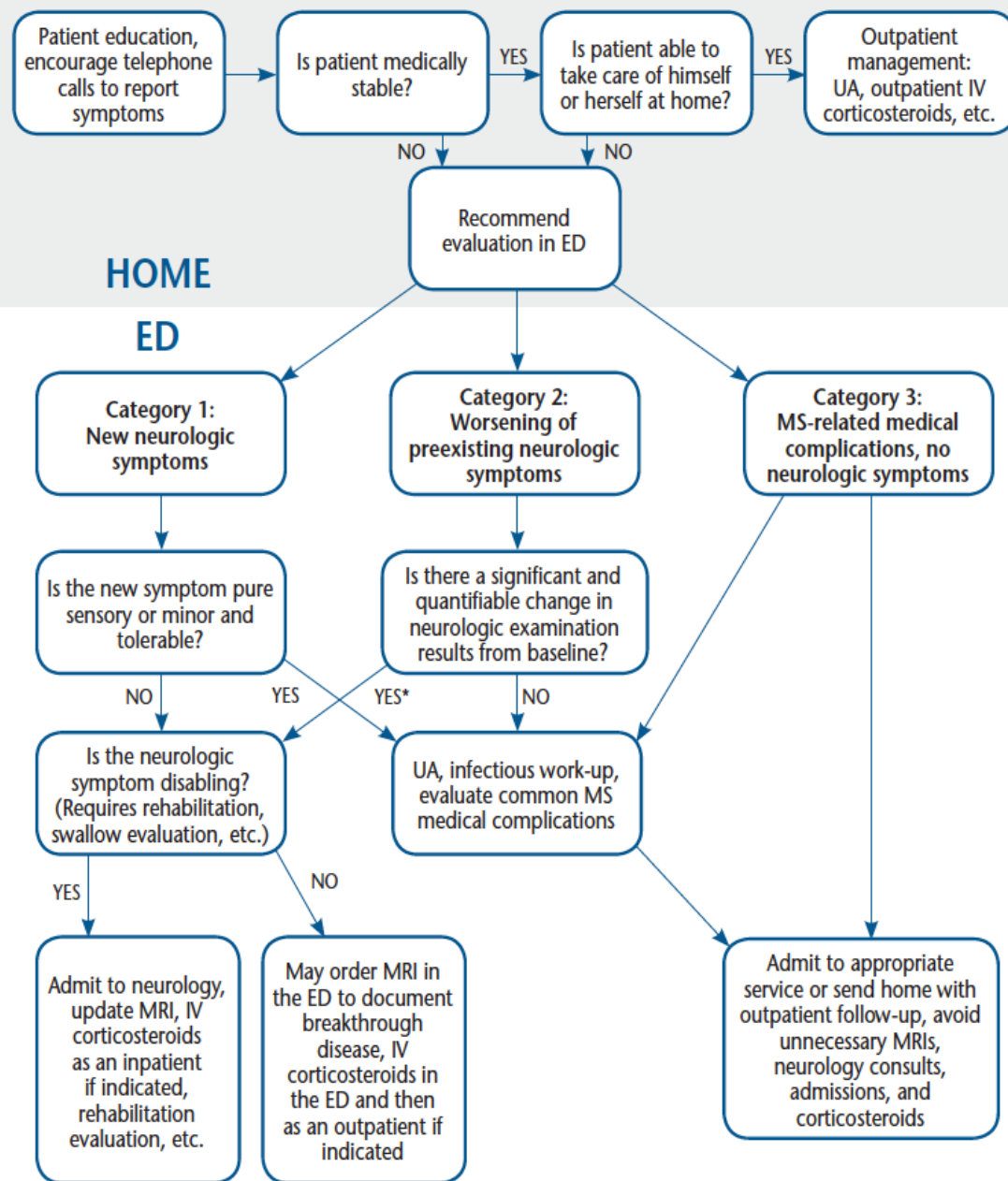


# Triaging Patients with Multiple Sclerosis in the Emergency Department

Room for Improvement

Hesham Abboud, MD, PhD; Karin Mente, MD; Meagan Seay, DO; Jeffrey Kim, MD; Ashhar Ali, DO;  
Robert Bermel, MD; Mary A. Willis, MD

*MS Care.* 2017;19:290–296.

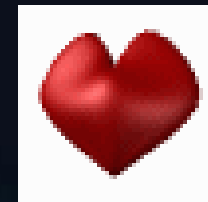


**Figure 1. Algorithm for appropriate management of patients with multiple sclerosis (MS) with new symptoms**



RICORDIAMOCI  
CHE NELLA  
PERSONA CON SM  
NON TUTTO È  
DOVUTO ALLA  
SM!!!

# Centro Regionale per la diagnosi e la cura della SM ASL 8/Università di Cagliari



Prof. Maria Giovanna Marrosu

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