

# **RESEARCH ARTICLE**

# PREVALENCE OF MULTIPLE SCLEROSIS IN SAUDI ARABIA

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#### Abstract

This study aimed at detecting a rough estimation of the prevalence of multiple sclerosis among citizens of Saudi Arabia.

# Methodology:

It is a cross sectional study purposed to estimate the prevalence of multiple sclerosis in KSA in 2016. It involved 633 individual from the society of Saudi Arabia.

#### **Results and conclusion:**

Most of the respondents (68.1%) were female, Also most of them (47.1%) aged between (20-24), (94.5%) of them were Saudi national, the largest proportion of them (34.4%) live in the eastern region, (69.8%) of them hold a university degree, and (57.7%) of the respondents are single.

Also, we found out that (66.2%) of the respondents don't know if they have MS or not, while (64.1%) of them don't have relatives suffer from MS, as (24.3%) of the relatives who suffer from MS were cousins, and the most common suspicious symptom of MS was Fatigue Exhaustion as (6.8%) of the respondents have that symptom, also (96.4%) of the respondents don't suffer from immune diseases, and most of those who suffer from immune diseases (26.1%) suffer from eczema.

Also, (86.1%) of the respondents don't suffer from Genetics diseases, while(18.2%) of the respondents who suffer from Genetic disease

suffer from diabetes, and (71.7) of the respondents who suffer MS are females, while 49.1%) of the respondents who suffer MS aged between 25-35, (84.9%) of the respondents who suffer MS are Saudi national, and (39.6%) of the respondents who suffer MS live in the

**Objectives:-**Central region, as (73.6%) of the respondents who suffer MS hold a university degree.

The analysis illustrated that (64.2%) of the respondents who suffer from MS don't have relatives suffer from MS, and (33.3%) of the respondents who suffer from MS who have relatives suffer from MS have a mother suffers from MS, also (5.7%) of the respondents who suffer from MS have a symptom of Weakness in arm or leg, Numbness in the extremities, Loss of Balance or Fatigue Exhaustion, while (83.0%) of the respondents who suffer from MS don't suffer from immune diseases, and (22.2%) of the respondents who suffer from MS and immune diseases suffer from rhumatic fever or erthymatosis, as (96.2%) of the respondents who suffer from MS don't suffer from Genetic disease, and (50%) of the respondents who suffer from MS and Genetics disease suffer from diabetes or hypertension.

The results of analysis illustrated that there were statistically significant differences between those with and without MS as regard to age, nationality and the region (P<0.05), while there were no statistically significant differences as regard to gender, education and marital status(P>0.05). Also, MS was more prevalent between 25 and 30 years (49.1%), in Saudi nation (84.9%) and the central region (39.6%).

Also, there were statistically significant differences at the level of significance (P <0.05), in the prevalence of MS in the relatives of the patients with and without MS in favor of no prevalence of MS in the relatives of (64.1%) patients with and without of respondents,

We found that there were statistically significant differences between those with and without MS as regard to absence of suspicious symptoms of MS of Weakness in arm or leg, Loss of Balance and Anxiety (P<0.05), while there were no statistically significant differences as regard to Numbness in the extremities, Muscles Cramps, Walking Difficulty, Fatigue Exhaustion, Vertigo, Headache, Convulsion(Epilepsy), Vision Problems, Bladder Problems, Intestinal Problems, Sexual Problems, Depression and Memory and Thinking Problems (P>0.05).as most of the respondents stated the absence of Weakness in arm or leg (99.5%), Loss of Balance (99.5%) and Anxiety (99.8%).

Finally, we indicated that there were statistically significant differences between those with and without MS as regard to absence of immune diseases and Genetics diseases (P<0.05), as (97.6%) of the respondents reported absence of immune diseases and (96.2%) of the respondents reported absence of Genetics diseases.

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#### Introduction:-

Multiple sclerosis (MS) is a neurological disorder that typically affects adults in their reproductive years mostly between 20 and 40 causing major disability <sup>1</sup>.Clinically there are no specific signs,but some feature are highly suggestive of MS such as relapsing an remitting course, optic neuritis, lhermitte sign, internuclearophthalmoplegia, fatigue and heat sensitivity (Uhthoff phenomenon). Symptoms varies including sensory deficits in the limbs or one side of the face, visual loss, acute or subacute motor weakness, diplopia, gait disturbance and balance problems, , vertigo, bladder problems, limb ataxia, acute transverse myelitis, and pain. The onset is often polysymptomatic. The most common presenting symptoms are sensory disturbances, then weakness and visual disturbances<sup>2</sup>.

On the other hand, a study done in the the Lazio region, Italy the overall prevalence rate standardized to the European Standard Population was 119.6/100,000 (95 % CI 116.8-122.4)1. In Leeds, UK, crude prevalence of MS in all ages was 97 per 100,000<sup>3</sup>. A study conducted in Santarém – a district in the center of Portugal the crude prevalence rate found was 46.3/100,000. According to a Canadian study conducted through tow decades the province of British Columbia founded to have a prevalence rate that is among the highest globally <sup>5</sup>.

In a cohort study conducted to estimate the mortality rate using prospectively collected data from the UK General Practice Research Database (GPRD) of the 1,822 MS cases, 130 (7.1 %) died during 14,295 person-years of follow-up, while 573 (3.1 %) referents died during 144,760 person-years of follow-up. The crude death rate for MS patients was 9.1 (95 % CI 7.6–10.8) per 1,000 person-years compared with 4.0 (95 % CI 3.6–4.3) per 1,000 person-years for

the non-MS counterparts. Mortality rates were higher in MS patients compared with their matched controls in each age group and for both males and females  $^{6}$ .

In Saudi Arabia as such population based evidence on prevalence of MS is not available. However the pervasiveness of MS in Saudis estimated to be approximately 40/100,000 in 2008. Though MS found to be rare in Saudis, it is currently clear that it is predominant, under-diagnosed and expanding we aim in this study to estimate the prevalence of multiple sclerosis among Saudi citizens <sup>3</sup>.

# Methodology:-

A cross sectional study was done to estimate the prevalence of multiple sclerosis in KSA during June-July 2016. A total of 633 participants were included from various areas of the Kingdom of Saudi Arabia to respond to this self-administered online questionnaire. The sample comprised of 202(31.9%) male, and 431(68.1%) females.



Figure no. (1) Illustrates the distribution of respondents according to Gender

Table (1):	Distribution	of respondents	according to Age
1 and (1).	Distribution	or respondents	according to figu

Age (years)	Frequencies	percentage
20-24	298	47.1%
25-35	216	34.1%
more than 35	119	18.8%
Total	633	100%

It's evident from Table (1) that (47.1%) of the respondents aged between (20-24), While (34.1%) of the respondents Aged between (25-35), While (18.8%) of the respondents Aged more than 35.

#### Table (2): Distribution of respondents according to Nationality

Nationality	Frequencies	percentage
Saudi	598	94.5%
non- Saudi	35	5.5%
Total	633	100%

It's evident from Table (2) that (94.5%) of the respondents are a Saudi national, While (5.5%) of the respondents aren't a Saudi national.

#### Table(3): Distribution of respondents according to Region

Region	Frequencies	percentage
eastern	218	34.4%
western	212	33.5%
central	129	20.4%
northern	28	4.4%
southern	46	7.3%
Total	633	100%

It's evident from Table (3) that (34.4%) of the respondents belong to the eastern region, while (33.5%) of them belong to the western region, (20.4%) of them belong to the Central Region, and (7.3%) of them belong to the southern district.

#### Table (4): Distribution of respondents according to education

Education	Frequencies	percentage	
			_

primary	6	0.9%
intermediate	22	3.5%
secondary	139	22.0%
academic	442	69.8%
postgraduate	24	3.8%
Total	633	100%

It's evident from Table (4) that (0.9%) of the respondents hold a primary degree, while (3.5%) of them hold an intermediate degree, (22.0%) of them hold a high school diploma, (69.8%) of them hold a university degree, while (3.8%) of them hold a Postgraduate degree.

# Results

#### Table (5): Distribution of respondents according to suffering from MS

Are you suffering from Multiple Sclerosis?	Frequencies	percentage
yes	53	8.4%
no	419	66.2%
I don't know	161	25.4%
Total	633	100%

It's evident from table (5) that (8.4%) of the respondents suffer from MS, while (66.2%) of them don't suffer from MS, and (66.2%) of the respondents don't know if they have MS or not. The following figure illustrates that.



Figure no. (2) Distribution of respondents according to suffering from MS

Table (6): Distribution of re	spondents according to having	ng relatives suffer from MS
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Do you have relatives suffer from multiple sclerosis	Frequencies	percentage
yes	70	11.1%
no	406	64.1%
I don't know	157	24.8%
Total	633	100%

It's evident from table (6) that (11.1%) of the respondents have relatives suffer from MS, while (64.1%) of them don't have relatives suffer from MS, and (24.8%) of them don't know if they have relatives suffer from MS or not. The following figure illustrates that.



Figure no. (3) Distribution of respondents according to having relatives suffer from MS

Table (7): Distribution of respondents according to the relationship with the relative who suffer from MS for
the respondents who have relatives suffer from MS

If yes, what is the relationship?	Frequencies	percentage
brother	4	5.7%
brother of my father	1	1.4%
brother of my mother	8	11.4%
cousin	17	24.3%
daughter	3	4.3%
father	2	2.9%
grand mother	1	1.4%
Grand daughter	1	1.4%
mother	10	14.3%
my brothers daughter	1	1.4%
my sisters daughter	2	2.9%
sister	11	15.7%
sister of my father	3	4.3%
sister of my mother	6	8.5%
Total	70	100%

It's evident from table (7) that (5.7%) of the respondents have a brother suffer from MS, while (1.4%) of the respondents have a brother of father suffer from MS, and (11.4%) of the respondents have a brother of mother suffer from MS, also (24.3%) of the respondents have a cousin suffer from MS, as(4.3%) of the respondents have a daughter suffer from MS, while (2.9%) of the respondents have a father suffer from MS, and (1.4%) of the respondents have a grand mother suffer from MS, also (1.4%) of the respondents have a Grand daughter suffer from MS, as(14.3%) of the respondents have a mother suffer from MS, while (1.4%) of the respondents have a brother's daughter suffer from MS, and (2.9%) of the respondents have a sister's daughter suffer from MS, also (15.7%) of the respondents have a sister suffer from MS, as(4.3%) of the respondents have a sister from MS, also (15.7%) of the respondents have a sister suffer from MS, as(4.3%) of the respondents have a sister from MS, and (8.5%) of the respondents have a sister of mother suffer from MS.

suspicious symptoms of MS in the studied group	Frequencies	percentage
Weakness in arm or leg	6	0.9%
Numbness in the extremities	17	2.7%
Loss of Balance	6	0.9%
Muscles Cramps	4	0.6%
Walking Difficulty	4	0.6%
Fatigue Exhaustion	43	6.8%
Vertigo	19	3.0%
Headache	29	4.6%
Convulsion Epilepsy	1	0.2%
Vision Problems	14	2.2%
Bladder Problems	4	0.6%
Intestinal Problems	5	0.8%
Sexual Problems	4	0.6%
Depression	19	3.0%
Anxiety	3	0.5%
Memory and Thinking Problems	4	0.6%
Increased Sensitivity of the Heat	1	0.2%
Palpitation	1	0.2%
Breathing Difficulties	2	0.3%
Total	186	29.3%

Table (8): Distribution of respondents according to suspicious symptoms of MS in the studied group

It's evident from table (8) that (5.7%) of the respondents have a symptom of Weakness in arm or leg, and (2.7%) of the respondents have a symptom of Numbness in the extremities, also (0.9%) of the respondents have a symptom of Loss of Balance, while (0.6%) of the respondents have a symptom of Muscles Cramps, as (0.6%) of the respondents have a symptom of Walking Difficulty, and (6.8%) of the respondents have a symptom of Fatigue Exhaustion, also (3.0%) of the respondents have a symptom of Vertigo, while (4.6%) of the respondents have a symptom of Headache, as (0.2%) of the respondents have a symptom of Convulsion Epilepsy, while (2.2%) of the respondents have a symptom of Vision Problems, as (0.6%) of the respondents have a symptom of Bladder Problems, and (0.8%) of the respondents have a symptom of Intestinal Problems, also (0.6%) of the respondents have a symptom of Sexual Problems, while (3.0%) of the respondents have a symptom of Memory and Thinking Problems, also (0.2%) of the respondents have a symptom of Increased Sensitivity of the Heat, while (0.2%) of the respondents have a symptom of Palpitation, as (0.3%) of the respondents have a symptom of Bladder Problems, also (0.2%) of the respondents have a symptom of Bladder Problems, also (0.2%) of the respondents have a symptom of Bladder Problems, also (0.2%) of the respondents have a symptom of Bladder Problems, also (0.2%) of the respondents have a symptom of Bladder Problems, also (0.2%) of the respondents have a symptom of Bladder Problems, also (0.2%) of the respondents have a symptom of Bladder Problems, also (0.2%) of the respondents have a symptom of Bladder Problems, also (0.2%) of the respondents have a symptom of Bladder Problems, also (0.2%) of the respondents have a symptom of Bladder Problems, also (0.2%) of the respondents have a symptom of Bladder Problems, also (0.2%) of the respondents have a symptom of Bladder Bladder Problems, also (0.2%) of the respondents have a symptom of Bla

Tuble ()). Distribution of respondents according to suffering it on minimute discuses
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Are you suffering from immune diseases?	Frequencies	percentage
yes	23	3.6%
no	610	96.4%
Total	633	100%

It's evident from table (9) that (3.6%) of the respondents suffer from immune diseases, while (96.4%) of the respondents don't suffer from immune diseases.

Table	(10):	Distribution	of res	nondents	according	to immune	diseases	type	if e	xist
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Are you suffering from immune diseases?	Frequencies	percentage
Adiopathicurticaria	1	4.3%
diapetes	2	8.7%
eczema	6	26.1%
hemolyticanemia	3	13%
hypothyrodism	2	8.7%
rhinitis	2	8.7%
rhumatic fever	2	8.7%
skin hypopigmintstion	1	4.3%
systemic lupus erthymatosis	4	17.4%
Total	23	100%

It's evident from table (10) that (4.3%) of the respondents suffer from Adiopathicurticaria, while (8.7%) of the respondents suffer from diabetes, also (26.1%) of the respondents suffer from hemolyticanemia, as (8.7%) of the respondents suffer from hypothyroidism, and (8.7%) of the respondents suffer from rhumatic fever, also (4.3%) of the respondents suffer from rhumatic fever, also (4.3%) of the respondents suffer from hypothyroidism, and (8.7%) of the respondents suffer from rhumatic fever, also (4.3%) of the respondents suffer from hypothyroidism.

Table (11), Distribution of respondence according to suffering from Ochetics diseases
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Are you suffering from Genetics diseases?	Frequencies	percentage
yes	88	13.9%
no	545	86.1%
Total	633	100%

It's evident from table (11) that (13.9%) of the respondents suffer from Genetics diseases, while (86.1%) of the respondents don't suffer from Genetics diseases.

Table (12): Distribution	of respondents	according t	to the type	e of Genetic	diseases	that th	ose who	suffer fron
Genetic disease have	_	_						

Are you suffering from Genetic disease?	Frequencies	percentage
anemia	3	3.4%
broncheal asthma	7	8.0%
color blindness	1	1.1%
diabetes	16	18.2%
eczema	10	11.4%
eye allergyccyc	1	1.1%
G6PDanemia	9	10.2%
gout	1	1.1%
hair falling	2	2.3%
Total	50	56.8%

It's evident from table (12) that (3.4%) of the respondents suffer from anemia, and (8.0%) of the respondents suffer from broncheal asthma, while (1.1%) of the respondents suffer from color blindness, and (18.2%) of the respondents suffer from diabetes, also (11.4%) of the respondents suffer from eczema, and (1.1%) of the respondents suffer from eye allergy, as (10.2%) of the respondents suffer from G6PD anemia, and (1.1%) of the respondents suffer from gout, while (2.3%) of the respondents suffer from hair falling.

		MS patients N=53	
		Frequencies	percentage
Gender	male	15	28.3%
	female	38	71.7%
	20-24	13	24.5%
age	25-35	26	49.1%
	more than 35	14	26.4%
Nationality	Saudi	45	84.9%
· ·	non-saudi	8	15.1%
	eastern	12	22.6%
	western	15	28.3%
Region	central	21	39.6%
	northean	3	5.7%
	southern	2	3.8%
Education	secondary	11	20.8%
	academic	39	73.6%
	postgraduate	3	5.7%
Material Status	married	22	41.5%
	single	31	58.5%

Table (13): Distribution of respondents according to socio-demographic characteristics of patients with MS

It's evident from table (13) that (28.3%) of the respondents who suffer MS are males, and (71.7) of the respondents who suffer MS are females, while (24.5%) of the respondents who suffer MS aged between 20-24, and (49.1%) of the respondents who suffer MS aged between 25-35, and (26.4%) of the respondents who suffer MS aged more than 35, also (84.9%) of the respondents who suffer MS are Saudi national, and (15.1%) of the respondents who suffer MS are not Saudi national, as (22.6%) of the respondents who suffer MS live in the eastern region, and (28.3%) of the respondents who suffer MS live in the western region, and (39.6%) of the respondents who suffer MS live in the central region, and (5.7%) of the respondents who suffer MS live in the southern region, while (20.8%) of the respondents who suffer MS hold a high school diploma, and (73.6%) of the respondents who suffer MS hold a university degree, and (5.7%) of the respondents who suffer MS hold a Postgraduate degree, while (41.5%) of the respondents who suffer MS are married, and (58.5%) of the respondents who suffer MS are single. The following figure illustrates that.



Figure no. (4) Distribution of respondents according to socio-demographic characteristics of patients with MS

- ····································					
Do you have relatives suffer from multiple sclerosis?	Frequencies	percentage			
yes	15	28.3%			
no	34	64.2%			
I don't know	4	7.5%			
Total	53	100%			

Table (14): Distribution of respondents according to relatives suffer from MS

It's evident from table (14) that (28.3%) of the respondents who suffer from MS have relatives suffer from MS, while (64.2%) of the respondents who suffer from MS don't have relatives suffer from MS, and (7.5%) of the respondents who suffer from MS don't know if they have relatives suffer from MS. The following figure illustrates that.



Figure no. (5) Distribution of respondents according to relatives suffer from MS

Table (15): Distribution of respondents according to suspicious sympt	oms of MS in the MS patients
suspicious symptoms of MS in the MS patients	MS nationts

suspicious symptoms of MS in the MS patients	MS patients N=53			
	Frequencies	percentage		
Weakness in arm or leg	3	5.7%		
Numbness in the extremities	3	5.7%		
Loss of Balance	3	5.7%		
Muscles Cramps	0.0	0.0%		
Walking Difficulty	0.0	0.0%		
Fatigue Exhaustion	3	5.7%		
Vertigo	0	0%		
Headache	1	1.9%		
Convulsion Epilepsy	0.0	0.0%		
Vision Problems	1	1.9%		
Bladder Problems	0.0	0.0%		
Intestinal Problems	0.0	0.0%		
Sexual Problems	0.0	0.0%		
Depression	0.0	0.0%		
Anxiety	2	3.8%		
Memory and Thinking Problems	0.0	0.0%		
Increased Sensitivity of the Heat	0.0	0.0%		
Palpitation	0.0	0.0%		
Breathing Difficulties	0.0	0.0%		

It's evident from table (15) that (5.7%) of the respondents who suffer from MS have a symptom of Weakness in arm or leg, and (5.7%) of the respondents who suffer from MS have a symptom of Numbness in the extremities, while (5.7%) of the respondents who suffer from MS have a symptom of Loss of Balance, and (5.7%) of the respondents who suffer from MS have a symptom of Fatigue Exhaustion, and (1.9 %) of the respondents who suffer from MS have a symptom of Headache, also (1.9%) of the respondents who suffer from MS have a symptom of Vision Problems, and (3.8%) of the respondents who suffer from MS have a symptom of Anxiety.

Table	(16):	Distribution	of respon	dents accordin	g to autoimmune	diseases in th	e patients	with MS
	< - / ·				0			

Are you suffering from immune diseases?	Frequencies	percentage
yes	9	17.0%
no	44	83.0%
Total	53	100%

It's evident from table (16) that (17.0 %) of the respondents who suffer from MS also suffer from immune diseases, while (83.0%) of the respondents who suffer from MS don't suffer from immune diseases.

		MS patients N=53	
The question	The answer	Frequencies	percentage
Are you suffering from Genetic diseases?	yes	2	3.8%
	no	51	96.2%
If Yes, Please write it (n=2)	diabetes	1	50%
	hypertension	1	50%

# Table (17): presence or absence of genetic diseases in the patients with MS, and it's type if exist

It's evident from table (17) that (3.8%) of the respondents who suffer from MS also suffer from Genetic disease, while (96.2%) of the respondents who suffer from MS don't suffer from Genetic disease. Also (50%) of the respondents who suffer from MS and Genetics disease suffer from diabetes, and (50%) of the respondents who suffer from MS and Genetics disease suffer from hypertension.

#### Table (18): Comparison between the socio-demographic characteristics in patients with and without MS

		have ms	don't have MS or don't know	X2	P-value
		n=53	n=580		
	male	15	187	0.347 <sup>a</sup>	0.556
		28.3%	32.2%		
Gender	female	38	393		
		71.7%	67.8%		
	20-24	13	285	11.812 <sup>a</sup>	0.003*
		24.5%	49.1%		
	25-35	26	190		
		49.1%	32.8%		
age	more than 35	14	105		
		26.4%	18.1%		
	Saudi	45	553	10.131 <sup>a</sup>	0.001*
		84.9%	95.3%		
	non-Saudi	8	27		
Nationality		15.1%	4.7%		
Region	eastern	12	206	14.485 <sup>a</sup>	0.006*
-		22.6%	35.5%		
	western	15	197		
		28.3%	34.0%		
	central	21	108		
		39.6%	18.6%		
	northern	3	25		
		5.7%	4.3%		
	southern	2	44		
		3.8%	7.6%		
Education	primary	0	6	3.247 <sup>a</sup>	0.517
	1 1	0.0%	1.0%		
	intermediate	0	22		
		0.0%	3.8%		
	secondary	11	128		
		20.8%	22.1%		
	academic	39	403		
		73.6%	69.5%		
	postgraduate	3	21		
	1 0	5.7%	3.6%		
Material Status	married	22	246	0.016 <sup>a</sup>	0.899
		41.5%	42.4%		
	single	31	334		
	Ũ	58.5%	57.6%		

Table (18) shows the following:

- There are no statistically significant differences at the level of significance (P <0.05), in the prevalence of MS according to the variable of "gender" ( $X^2 = 0.347$ , sig<0.556). Indicating a convergence of Prevalence rates of MS among male and female respondents with and without MS or don't know.
- There are statistically significant differences at the level of significance (P <0.05), in the prevalence of MS according to the variable of "age" ( $X^2 = 11.812$ ,sig<0.003). Indicating a Divergence of Prevalence rates of MS, among those with and without MS or don't know in favor of 20-24 years old respondents without MS or don't know and 25-35 years old respondents with MS.
- There are statistically significant differences at the level of significance (P <0.05), in the prevalence of MS according to the variable of "Nationality" ( $X^2 = 10.131$ ,sig<0.001). Indicating a Divergence of Prevalence rates of MS, among those with and without MS or don't know in favor of Saudis respondents.
- There are statistically significant differences at the level of significance (P <0.05), in the prevalence of MS according to the variable of "Region" ( $X^2 = 14.485$ , sig<0.006). Indicating a Divergence of Prevalence rates of MS, among those with and without MS or don't know in favor of central region respondents.
- There are no statistically significant differences at the level of significance (P <0.05), in the prevalence of MS according to the variable of "Education" ( $X^2 = 3.247$ , sig<0.517). Indicating a convergence of Prevalence rates of MS among primary, intermediate, secondary, academic and postgraduate educational level respondents with and without MS or don't know.
- There are no statistically significant differences at the level of significance (P <0.05), in the prevalence of MS according to the variable of "Material Status" ( $X^2 = 0.016$ ,sig<0.899). Indicating a convergence of Prevalence rates of MS among married and single respondents with and without MS or don't know.

#### Table (19): The prevalence of MS in the relatives of the patients with and without MS

		ms			
		have ms n=53	donnot have MS or donnot know n=580	X2	P-value
Do you have relatives suffer	yes	15	55	22.49	< 0.0001*
from multiple sclerosis?		28.3%	9.5%		
	no	34	372		
		64.2%	64.1%		
	i do not know	4	153		
		7.5%	26.4%		



Figure no. (6) The prevalence of MS in the relatives of the patients with and without MS

Table (19) shows the following:

There are statistically significant differences at the level of significance (P <0.05), in the prevalence of MS

in the relatives of the patients with and without MS (  $X^2 = 22.49$ , sig<0.0001). Indicating a Divergence of the prevalence of MS in the relatives of the patients with and without MS in favor of no prevalence of MS in the relatives of the patients with and without MS.

Table (20). Suspicious sympt	onis of Mis of the	e padents with			
		ms			
		have ms n=53	Don't have MS or don't know n=580	X2	P-value
Weakness in arm or leg	present	3	3	13.682 <sup>a</sup>	< 0.0001*
		5.7%	0.5%		
	absent	50	577		
		94.3%	99.5%		
Numbness in the extremities	present	3	14	1.959 <sup>a</sup>	0.162
		5.7%	2.4%		
	absent	50	566		
		94.3%	97.6%		
Loss of Balance	present	3	3	13.682 <sup>a</sup>	< 0.0001*
		5.7%	0.5%		
	absent	50	577		
		94.3%	99.5%		
Muscles Cramps	present	0	4	0.368 <sup>a</sup>	0.544
		0.0%	0.7%		
	absent	53	576		
		100.0%	99.3%		
Walking Difficulty	present	0	4	0.368 <sup>a</sup>	0.544
		0.0%	0.7%		
	absent	53	576		
		100.0%	99.3%		
Fatigue Exhaustion	present	3	40	0.117 <sup>a</sup>	0.732
		5.7%	6.9%		

	absent	50	540		
		94.3%	93.1%		
Vertigo	present	0	19	$1.790^{a}$	0.181
		0.0%	3.3%		
	absent	53	561		
		100.0%	96.7%		
Headache	present	1	28	0.961 <sup>a</sup>	0.327
		1.9%	4.8%		
	absent	52	552		
		98.1%	95.2%		
Convulsion(Epilepsy)	present	0	1	$0.092^{a}$	0.762
		0.0%	0.2%		
	absent	53	579		
		100.0%	99.8%		
Vision Problems	present	1	13	$0.028^{a}$	0.867
	_	1.9%	2.2%		
	absent	52	567		
		98.1%	97.8%		
Bladder Problems	present	0	4	$0.368^{a}$	0.544
	_	0.0%	0.7%		
	absent	53	576		
		100.0%	99.3%		
Intestinal Problems	present	0	5	0.461 <sup>a</sup>	0.497
	•	0.0%	0.9%		
	absent	53	575		
		100.0%	99.1%		
Sexual Problems	present	0	4	$0.368^{a}$	0.544
	•	0.0%	0.7%		
	absent	53	576		
		100.0%	99.3%		
Depression	present	0	19	$1.790^{a}$	0.181
*	•	0.0%	3.3%		
	absent	53	561		
		100.0%	96.7%		
Anxiety	present	2	1	13.352 <sup>a</sup>	< 0.0001*
·	•	3.8%	0.2%		
	absent	51	579		
		96.2%	99.8%		
Memory and Thinking Problems	present	0	4	$0.368^{a}$	0.544
	-	0.0%	0.7%		
	absent	53	576		
		100.0%	99.3%		
Increased Sensitivity of the Heat	present	0	1	$0.092^{a}$	0.762
	_	0.0%	0.2%		
	absent	53	579		
		100.0%	99.8%		
Palpitation	present	0	1	0.092 <sup>a</sup>	0.762
*	•	0.0%	0.2%		
	absent	53	579		
		100.0%	99.8%		
Breathing Difficulties	present	0	2	0.183 <sup>a</sup>	0.669
Č	Î	0.0%	0.3%		
	absent	53	578		
		100.0%	99.7%		

Table (20) shows the following:

- There are statistically significant differences at the level of significance (P <0.05), in the suspicious symptoms of MS among the patients with and without MS according to the presence or absent of the symptom of
  - "Weakness in arm or leg" (  $X^2 = 13.682$ , sig<0.0001). Indicating a Divergence in the symptom of "Weakness in arm or leg" of MS among the patients with and without MS in favor those who don't have the symptom of "Weakness in arm or leg".
- There are no statistically significant differences at the level of significance (P <0.05), with and without MS according to the presence or absent of the symptom of "Numbness in the extremities" ( $X^2 = 1.959$ , sig<0.162). Indicating a convergence in the symptom of "Numbness in the extremities" of MS among the national with and
  - Indicating a convergence in the symptom of "Numbress in the extremities" of MS among the patients with and without MS.
- There are statistically significant differences at the level of significance (P < 0.05), in the suspicious symptoms of MS among the patients with and without MS according to the presence or absent of the symptom of "Loss of

Balance" ( $X^2 = 13.682$ ,sig<0.0001). Indicating a Divergence in the symptom of "Loss of Balance" of MS of the patients with and without MS in favor those who don't have the symptom of "Loss of Balance".

- There are no statistically significant differences at the level of significance (P <0.05), with and without MS according to the presence or absent of the symptom of "Muscles Cramps" ( $X^2 = 0.368$ ,sig<0.544). Indicating

a convergence in the symptom of "Muscles Cramps" of MS among the patients with and without MS. There are no statistically significant differences at the level of significance (P <0.05), with and without MS

- according to the presence or absent of the symptom of "Walking Difficulty" ( $X^2 = 0.368$ ,sig<0.544). Indicating a convergence in the symptom of "Walking Difficulty" of MS among the patients with and without MS.
- There are no statistically significant differences at the level of significance (P <0.05), with and without MS

according to the presence or absent of the symptom of "Fatigue Exhaustion" ( $X^2 = 0.117$ , sig<0.732). Indicating a convergence in the symptom of "Fatigue Exhaustion" of MS among the patients with and without MS.

- There are no statistically significant differences at the level of significance (P <0.05), with and without MS according to the presence or absent of the symptom of "Vertigo" ( $X^2 = 1.790$ , sig<0.181). Indicating a convergence in the symptom of "Vertige" of MS among the national without MS
- convergence in the symptom of "Vertigo" of MS among the patients with and without MS. - There are no statistically significant differences at the level of significance (P <0.05), with and without MS

according to the presence or absent of the symptom of "Headache" ( $X^2 = 0.961$ ,sig<0.327). Indicating a convergence in the symptom of "Headache" of MS among the patients with and without MS.

- There are no statistically significant differences at the level of significance (P <0.05), with and without MS according to the presence or absent of the symptom of "Convulsion(Epilepsy)" ( $X^2 = 0.092$ ,sig<0.762). Indicating a convergence in the symptom of "Convulsion(Epilepsy)" of MS among the patients with and without MS.
- There are no statistically significant differences at the level of significance (P <0.05), with and without MS according to the presence or absent of the symptom of "Vision Problems" ( $\chi^2 = 0.028$ , sig <0.867). Indicating

a convergence in the symptom of "Vision Problems" of MS among the patients with and without MS. - There are no statistically significant differences at the level of significance (P <0.05), with and without MS

- according to the presence or absent of the symptom of "Bladder Problems" ( $X^2 = 368, \text{sig} < 0.544$ ). Indicating a convergence in the symptom of "Bladder Problems" of MS among the patients with and without MS.
- There are no statistically significant differences at the level of significance (P <0.05), with and without MS according to the presence or absent of the symptom of "Intestinal Problems" ( $X^2 = 0.461$ ,sig<0.497).
  - Indicating a convergence in the symptom of "Intestinal Problems" of MS among the patients with and without MS.
- There are no statistically significant differences at the level of significance (P <0.05), with and without MS according to the presence or absent of the symptom of "Sexual Problems" ( $X^2 = 0.368$ , sig<0.544). Indicating a convergence in the symptom of "Sexual Problems" of MS among the patients with and without MS.

- There are no statistically significant differences at the level of significance (P <0.05), with and without MS according to the presence or absent of the symptom of "Depression" ( $X^2 = 1.790$ ,sig<0.181). Indicating a convergence in the symptom of "Depression" of MS among the patients with and without MS.
- There are statistically significant differences at the level of significance (P < 0.05), in the suspicious symptoms of MS among the patients with and without MS according to the presence or absent of the symptom of

"Anxiety" ( $X^2 = 13.352$ ,sig<0.0001). Indicating a Divergence in the symptom of "Anxiety" of MS among the patients with and without MS in favor those who don't have the symptom of "Anxiety".

- There are no statistically significant differences at the level of significance (P <0.05), with and without MS according to the presence or absent of the symptom of "Memory and Thinking Problems" ( $X^2 = 0.220$  km/s<sup>2</sup> = 0.220 km/s<sup>2</sup> = 0.210 km/s<sup>2</sup>
  - 0.368,sig<0.544). Indicating a convergence in the symptom of "Memory and Thinking Problems" of MS among the patients with and without MS.
- There are no statistically significant differences at the level of significance (P <0.05), with and without MS
  - according to the presence or absent of the symptom of "Increased Sensitivity of the Heat" ( $X^2 = 0.092$ ,sig<0.762). Indicating a convergence in the symptom of "Increased Sensitivity of the Heat" of MS among the patients with and without MS.
- There are no statistically significant differences at the level of significance (P <0.05), with and without MS according to the presence or absent of the symptom of "Palpitation" ( $X^2 = 0.092$ ,sig<0.762). Indicating a convergence in the symptom of "Palpitation" of MS among the patients with and without MS.
- There are no statistically significant differences at the level of significance (P <0.05), with and without MS
  - according to the presence or absent of the symptom of "Breathing Difficulties" ( $X^2 = 0.183$ ,sig<0.669). Indicating a convergence in the symptom of "Breathing Difficulties" of MS among the patients with and without MS.

Table	(21):	presence of	autoimmune	and genet	ic diseases	in the	natients	with and	without	MS
Labic	(21).	presence of	autommune	and gener	ic unscases	in the	patients	with and	without	1410

		ms			
		have ms	donnot have MS	X2	P-value
		n=53	or donnot know		
			n=580		
	yes	9	14	29.431 <sup>a</sup>	< 0.0001*
		17.0%	2.4%		
Are you suffering from immune	no	44	566		
diseases?		83.0%	97.6%		
Are you suffering from Genetics	yes	2	86	4.958 <sup>a</sup>	0.026*
diseases		3.8%	14.8%		
	no	51	494		
		96.2%	85.2%		



Figure no. (7) presence of autoimmune and genetic diseases in the patients with and without MS

Table (21) shows the following:

- There are statistically significant differences at the level of significance (P <0.05), in the presence of autoimmune and genetic diseases in the patients with and without MS ( $X^2 = 29.431$ ,sig<0.0001). Indicating a Divergence of suffering from immune diseases in the patients with and without MS in favor of no suffering from immune diseases in the patients with and without MS.
- There are statistically significant differences at the level of significance (P <0.05), in the presence of autoimmune and genetic diseases in the patients with and without MS ( $X^2 = 4.958$ ,sig<0.026). Indicating a Divergence of suffering from Genetics diseases in the patients with and without MS in favor of no suffering from Genetics diseases in the patients with and without MS.

# **Discussion:**

The prevalence of MS as reported in our study was 11% and this is much higher than expected for a middle eastern population. The findings in our study were 28.3% of males as compared to 71.6% females had MS as picked up in this online survey. Prevalence in our study is astonishingly high. The incidence of 8.5/100 000 inhabitants during 2003–2007 was reported on MS frequency in the southern<sup>2</sup> and eastern<sup>8</sup> parts of Norway which is considered as a high risk area of MS. Similarly an Iranin study reports MS incidence as 0.68 to 9.1/100,000 per year in the Iranian population and Prevalence was reported in all studies and ranged from 5.3 to 74.28/100,000 with the higher prevalence among females (female/male ratio ranged from 1.8 to 3.6).

While in Kuwait during 2013, POMS incidence rate and prevalence(per 100,000) were 2.1 and 6.0 respectively. increased 10-fold from 20/100 000 in 1963 to 211 (95% CI 198.3 to 224.2) per 100 000 in 2013. The prevalence rate of 211/100 000 inhabitants was higher than a recent prevalence report of 186/100 000 in Western Norway.<sup>9</sup> These diverging results are most likely a result of the limitation of using data from the National Patients Registry included in this recent nationwide study.<sup>9</sup> Previous Norwegian studies using hospital records (as in our study) have reported MS prevalence rates of 170/100 000 in the south-eastern county of Oslo,<sup>10</sup> 180/100 000 in the southern county of Vest-Agder<sup>2</sup> and 185.6/100 000 in the eastern county of Oppland.<sup>8</sup> The prevalence rate in Hordaland was, thus, similar to the latest report from the UK,<sup>11</sup> but higher than reported in Denmark,<sup>12</sup> Sweden<sup>13</sup> and South East Wales,<sup>14</sup> and lower than reports from Orkney, Shetland and Aberdeen City,<sup>15</sup> all geographical areas close to Hordaland County.

Comparing MS prevalence in Hordaland County on prevalence day 1 January 2003 calculated in  $2003^{16}$  at 150/100 000 with the present study including follow-up until 2013 giving 191/100 000, highlights the importance of the

sample collection termination day, in order to calculate the valid prevalence. Thus, the follow-up identified undiagnosed patients who had symptom onset prior to 1 January 2003 and illustrates that the prevalence is rising and most interestingly, that the date for study termination has a major impact on prevalence. The rise in prevalence is a consequence of the underestimated prevalence reported previously <sup>16</sup>/<sub>4</sub> due to the time delay between onset and diagnosis. However, the time delay between onset and diagnosis is decreasing and consequently, the methodological issue of underestimated prevalence will probably be reduced in future studies.

The incidence of MS in Hordaland County has in previous studies increased from  $0.2/100\ 000\ in\ 1935$ ,<sup>17</sup> to  $0.67/100\ 000\ in\ 1951^{18}$  and to  $4.7/100\ 000\ in\ 1978-1982$ .<sup>19</sup> However, in the present long-term follow-up study, we also identified patients with disease onset years prior and thus higher incidence rates of  $1.8/100\ 000\ during\ 1953-1957$ ,  $6.9/100\ 000\ during\ 1978-1982$  followed by a stable high level of approximately 7–8/100\ 000\ during\ later years. Thus, this tendency towards increase in incidence rates and prevalence rates of MS, presented in the repeated studies we provide in this paper, demonstrates the necessity of repeated surveillance to study valid time trends of MS incidence rates.<sup>20.9</sup>

We showed relatively stable incidence rates during the past three decades. However, since we reported the year-ofonset incidence, we observed a drop in rate probably due to delayed diagnosed cases for the latest 5-year period. The stable incidence rate was consistent with reports from Olmstead County, Minnesota, USA,<sup>21</sup>andCanada,<sup>22</sup> but was in contrast to a downward incidence trend in the Orkney Islands,<sup>23</sup> the Faroe Islands<sup>24</sup> and in Gothenburg,<sup>25</sup> and the increased incidence trends in Denmark,  $\frac{20}{20}$  South East-Wales,  $\frac{14}{10}$  NortheastIreland  $\frac{25}{20}$  and another Canadian population.  $\frac{27}{10}$ The rise in prevalence of MS could partly be explained by the historical large increase in incidence of the disease until 1978–1982. The early increase in prevalence might be explained by the increase in incidence the first 3-4 decades. Also, owing to the onset of disease approach to incidence and prevalence estimations, and the time delay between onset and diagnosis, the prevalence has a delay up to about mean 7-9 years until the 1990's and hence, increase in incidence is followed by a parallel increase in prevalence after almost a decade. Because of the retrospective year of onset approach to incidence, the prevalence is catching up later. However, the continued recent increase in prevalence was not associated with a parallel increase in incidence. Thus some of the increase in prevalence in recent years may be explained by improved diagnostics especially with the introduction of MRI in the 1990s and the ability to identify younger patients and more benign disease living longer with the disease. The diagnostic criteria which has evolved from the early clinically based criteria<sup>28</sup> to MRI-grounded criteria,<sup>29</sup> recently revised,<sup>30</sup> have improved case ascertainment throughout the study period. Systematic use of the revised diagnostic criteria of McDonald with frequent use of repeated MRIs may lead to an increased diagnosis of patients with vague symptoms due to a benign disease. However, the diagnosing of more benign cases had probably a limited impact on prevalence, leaving increased survival as the most likely explanation to our findings. Improved survival in MS, possible due to more frequent use of advanced disease-modifying therapies,<sup>31</sup> was probably the most important factor related to the observed increase in prevalence. The importance of improved survival on the observed increase in prevalence was also supported by the shift towards an older age distribution of the present 2013 prevalence cohort compared with the prevalence reported in the 2003 study.<sup>16</sup> A change in age distribution has also previously been reported from Canada and the  $UK.^{11 22}$ 

Given the stable incidence rate, the higher ages in the cohort probably relate to improved survival either due to disease-modifying therapies or attributed to a general increase in life expectancy during the last decades. To determine the impact of treatment on survival, standardized mortality ratio calculations comparing MS to the general population in Norway are needed.<sup>32</sup>

In contrast to several reports of increasing female to male ratios in  $MS^{14}$   $\frac{33}{24}$  the overall rate has been stable in Hordaland County throughout the past six decades. Our follow-up data showed a stable sex-ratio throughout the period and does not indicate gender-specific environmental risk factors which affect women more than men. Explaining the stable incidence rates by changes in environmental risk factors for MS seems challenging. Epstein-Barr virus<sup>35</sup> infections are stable, but cigarette smoking<sup>36</sup> has declined during the last decadesand may have reduced

the risk of MS. However, both consumption of dietary salt intake<sup>37</sup> through processed food and use of sun-protection products,<sup>38</sup> which may lead to reduced serum levels of vitamin  $D^{39}$  has increased in the past three decades. These may be two other factors associated with increased risk of MS.

Improved case ascertainment during the past six decades can probably explain some of the increased prevalence found in the present study. This was indicated by the steady decline in time delay between onset and diagnosis of MS. Revised diagnostic criteria,<sup>30</sup> focusing on active use of MRI to define disseminated disease in time and space,

combined with improved disease-modifying treatments has increased the diagnostic awareness among physicians and patients, and have therefore, important impact on this time-delay.

Our study provides comprehensive data on MS prevalence and incidence during 60 years and confirms Norway as a high risk area for MS. The steady increase in MS incidence from the 1950s followed by a stable high incidence during the past three decades, calls for further studies focusing on environmental factors to explain this pattern. The tendency to identify more MS cases at follow-up, demonstrated in this study, indicates that previous studies with data collection close to the prevalence day might have underestimated the prevalence of MS. Thus future studies on prevalence of MS should explore the occurrence of disease with a prolonged follow-up of several years after prevalence day in order to estimate the true prevalence of disease.

# Conclusion

As shown above that most of the respondents (68.1%) were female, Also most of them (47.1%) aged between (20-24), (94.5%) of them were Saudi national, the largest proportion of them (34.4%) live in the eastern region, (69.8%) of them hold a university degree, and (57.7%) of the respondents are single.

Also, we found out that (66.2%) of the respondents don't know if they have MS or not, while (64.1%) of them don't have relatives suffer from MS, as (24.3%) of the relatives who suffer from MS were cousins, and the most common suspicious symptom of MS was Fatigue Exhaustion as (6.8%) of the respondents have that symptom, also (96.4%) of the respondents don't suffer from immune diseases, and most of those who suffer from immune diseases (26.1%) suffer from eczema.

Also, (86.1%) of the respondents don't suffer from Genetics diseases, while(18.2%) of the respondents who suffer from Genetic disease suffer from diabetes, and (71.7) of the respondents who suffer MS are females, while 49.1%) of the respondents who suffer MS aged between 25-35, (84.9%) of the respondents who suffer MS are Saudi national, and (39.6%) of the respondents who suffer MS live in the central region, as (73.6%) of the respondents who suffer MS hold a university degree.

The analysis illustrated that (64.2%) of the respondents who suffer from MS don't have relatives suffer from MS, and (33.3%) of the respondents who suffer from MS who have relatives suffer from MS have a mother suffers from MS, also (5.7%) of the respondents who suffer from MS have a symptom of Weakness in arm or leg, Numbness in the extremities, Loss of Balance or Fatigue Exhaustion, while (83.0%) of the respondents who suffer from MS don't suffer from MS and (22.2%) of the respondents who suffer from MS and immune diseases suffer from rhumatic fever or erthymatosis, as (96.2%) of the respondents who suffer from MS don't suffer from Genetic disease, and (50%) of the respondents who suffer from MS and Genetics disease suffer from diabetes or hypertension.

The results of analysis illustrated that there were statistically significant differences between those with and without MS as regard to age, nationality and the region (P<0.05), while there were no statistically significant differences as regard to gender, education and marital status(P>0.05). Also, MS was more prevalent between 25 and 30 years (49.1%), in Saudi nation (84.9%) and the central region (39.6%).

Also, there were statistically significant differences at the level of significance (P < 0.05), in the prevalence of MS in the relatives of the patients with and without MS in favor of no prevalence of MS in the relatives of (64.1%) patients with and without of respondents,

We found that there were statistically significant differences between those with and without MS as regard to absence of suspicious symptoms of MS of Weakness in arm or leg, Loss of Balance and Anxiety (P<0.05), while there were no statistically significant differences as regard to Numbness in the extremities, Muscles Cramps, Walking Difficulty, Fatigue Exhaustion, Vertigo, Headache, Convulsion(Epilepsy), Vision Problems, Bladder Problems, Intestinal Problems, Sexual Problems, Depression and Memory and Thinking Problems (P>0.05).as most of the respondents stated the absence of Weakness in arm or leg (99.5%), Loss of Balance (99.5%) and Anxiety (99.8%).

Finally, we indicated that there were statistically significant differences between those with and without MS as regard to absence of immune diseases and Genetics diseases (P<0.05), as (97.6%) of the respondents reported absence of Genetics diseases.

#### **Recommendations:-**

#### **Recommendations for patients:**

Patients have to Learn as much as possible about their disease which in this case is MS, also they have to make sure that their diagnosis with MS is definitive, and to understand that the symptoms of MS can not be predicted, and they shouldn't delay treatment as well as avoiding triggers that relapses MS, finally, they have to never give up hope even if there are currently no cure of MS, but the future is promising of discovering a cure soon.

#### **Recommendations for physicians:**

Physicians should first make sure that the diagnosis with MS is definitive, and they have to guide patients with the best practices for the alleviation of MS, also Physicians should start with prescribing medicines to modify the course of MS, then Physicians should prescribe medicines to control the effects of MS, also during the trip of treating MS, Physicians should bring hope in the hearts of patients so as not to suffer despair and frustration.

#### **Recommendations for future research:**

We recommend that future studies focus on escalating secondary multiple sclerosis and escalating Relapser multiple sclerosis. Also, future research could state the best practices of managing multiple sclerosis by patients at home and by Physicians clinically. And future research could illustrate the recent alternative treatments of MS.

#### **References:-**

- Bargagli AM, Colais P, Agabiti N, et al. Prevalence of multiple sclerosis in the Lazio region, Italy: use of an algorithm based on health information systems. J Neurol. 2016;263(4):751-759. doi:10.1007/s00415-016-8049-8.
- Olek M. J., Narayan R.N., Frohman E.M. and Frohman T.C. (2016). Clinical features of multiple sclerosis in adults. In F.Gonzalez-Scarano, Howe J.P. and Dashe J.F (Eds.), UptoDate. Available from <u>http://www.uptodate.com/contents/clinical-features-of-multiple-sclerosis-in-</u> <u>adults?source=see link&sectionName=CLINICAL+SYMPTOMS+AND+SIGNS&anchor=H9#H9</u>
- 3. Bohlega S, Inshasi J, Al Tahan AR, Madani AB, Qahtani H, Rieckmann P. Multiple sclerosis in the Arabian Gulf countries: A consensus statement. J Neurol. 2013;260(12):2959-2963. doi:10.1007/s00415-013-6876-4.
- 4. Ford HL, Gerry E, Johnson M, Williams R. A prospective study of the incidence, prevalence and mortality of multiple sclerosis in Leeds. J Neurol. 2002;249(3):260-265. doi:10.1007/s004150200002.
- Kingwell E, Zhu F, Marrie RA, et al. High prevalenceand increasing prevalence of multiple sclerosis in British Columbia, Canada: findings from over two decades (1991–2010). J Neurol. 2015;262(10):2352-2363. doi:10.1007/s00415-015-7842-0.
- 6. Jick, S. S., Li, L., Falcone, G. J., Vassilev, Z. P., & Wallander, M. A. (2014). Mortality of patients with multiple sclerosis: a cohort study in UK primary care. Journal of neurology, 261(8), 1508-1517.
- 7. Vatne A, Mygland A, Ljostad U. Multiple sclerosis in Vest-Agder County, Norway. Acta Neurol Scand 2011;123:396–9. doi:10.1111/j.1600-0404.2010.01411.x [PubMed]
- 8. Risberg G, Aarseth JH, Nyland H, et al. Prevalence and incidence of multiple sclerosis in Oppland County: a cross-sectional population-based study in a landlocked county of Eastern Norway. Acta Neurol Scand 2011;124:250–7. doi:10.1111/j.1600-0404.2010.01465.x [PubMed]
- 9. Berg-Hansen P, Moen SM, Harbo HF, et al. High prevalence and no latitude gradient of multiple sclerosis in Norway. Mult Scler 2014;20:1780–2. doi:10.1177/1352458514525871 [PubMed]
- 10. Smestad C, Sandvik L, Holmoy T, et al. Marked differences in prevalence of multiple sclerosis between ethnic groups in Oslo, Norway. J Neurol 2008;255:49–55. doi:10.1007/s00415-007-0659-8 [PubMed]
- 11. Mackenzie IS, Morant SV, Bloomfield GA, et al. Incidence and prevalence of multiple sclerosis in the UK 1990–2010: a descriptive study in the General Practice Research Database. J Neurol Neurosurg Psychiatry 2014;85:76–84. doi:10.1136/jnnp-2013-305450 [PMC free article] [PubMed]
- 12. Bentzen J, Flachs EM, Stenager E, et al. Prevalence of multiple sclerosis in Denmark 1950–2005. Mult Scler 2010;16:520–5. doi:10.1177/1352458510364197 [PubMed]
- 13. Ahlgren C, Oden A, Lycke J. High nationwide prevalence of multiple sclerosis in Sweden. Mult Scler 2011;17:901–8. doi:10.1177/1352458511403794 [PubMed]

- 14. Hirst C, Ingram G, Pickersgill T, et al. Increasing prevalence and incidence of multiple sclerosis in South East Wales. J Neurol Neurosurg Psychiatry 2009;80:386–91. doi:10.1136/jnnp.2008.144667 [PubMed]
- 15. Visser EM, Wilde K, Wilson JF, et al. A new prevalence study of multiple sclerosis in orkney, Shetland and Aberdeen city. J Neurol Neurosurg Psychiatry 2012;83:719–24. [PubMed]
- Grytten N, Glad SB, Aarseth JH, et al. A 50-year follow-up of the incidence of multiple sclerosis in Hordaland County, Norway. Neurology 2006;66:182–6. doi:10.1212/01.wnl.0000195549.95448.b9 [PubMed]
- 17. Larsen JP, Kvaale G, Riise T, et al. An increase in the incidence of multiple sclerosis in western Norway. Acta Neurol Scand 1984;70:96–103. doi:10.1111/j.1600-0404.1984.tb00809.x [PubMed]
- 18. Larsen JP, Riise T, Nyland H, et al. Clustering of multiple sclerosis in the county of Hordaland, Western Norway. Acta Neurol Scand 1985;71:390–5. doi:10.1111/j.1600-0404.1985.tb03218.x [PubMed]
- 19. Larsen JP, Aarli JA, Nyland H, et al. Western Norway, a high-risk area for multiple sclerosis: a prevalence/incidence study in the county of Hordaland. Neurology 1984;34:1202-7. doi:10.1212/WNL.34.9.1202 [PubMed]
- Koch-Henriksen N, Sorensen PS. The changing demographic pattern of multiple sclerosis epidemiology. Lancet Neurol 2010;9:520–32. doi:10.1016/S1474-4422(10)70064-8 [PubMed]
- 21. Mayr WT, Pittock SJ, McClelland RL, et al. Incidence and prevalence of multiple sclerosis in Olmsted County, Minnesota, 1985–2000. Neurology 2003;61:1373–7. doi:10.1212/01.WNL.0000094316.90240.EB [PubMed]
- 22. Marrie RA, Yu N, Blanchard J, et al. The rising prevalence and changing age distribution of multiple sclerosis in Manitoba. Neurology 2010;74:465–71. doi:10.1212/WNL.0b013e3181cf6ec0 [PubMed]
- 23. Cook SD, Cromarty JI, Tapp W, et al. Declining incidence of multiple sclerosis in the Orkney Islands. Neurology 1985;35:545–51. doi:10.1212/WNL.35.4.545 [PubMed]
- 24. Joensen P. Multiple sclerosis: variation of incidence of onset over time in the Faroe Islands. Mult Scler 2011;17:241-4. doi:10.1177/1352458510386997 [PubMed]
- Svenningsson A, Runmarker B, Lycke J, et al. Incidence of MS during two fifteen-year periods in the Gothenburg region of Sweden. Acta Neurol Scand 1990;82:161–8. doi:10.1111/j.1600-0404.1990.tb04483.x [PubMed]
- 26. Gray OM, McDonnell GV, Hawkins SA. Factors in the rising prevalence of multiple sclerosis in the north-east of Ireland. Mult Scler 2008;14:880–6. doi:10.1177/1352458508090663 [PubMed]
- 27. Warren SA, Svenson LW, Warren KG. Contribution of incidence to increasing prevalence of multiple sclerosis in Alberta, Canada. Mult Scler 2008;14:872–9. doi:10.1177/1352458508089226 [PubMed]
- 28. Poser CM, Paty DW, Scheinberg L, et al. New diagnostic criteria for multiple sclerosis: guidelines for research protocols. Ann Neurol 1983;13:227–31. doi:10.1002/ana.410130302 [PubMed]
- 29. Polman CH, Reingold SC, Edan G, et al. Diagnostic criteria for multiple sclerosis: 2005 revisions to the "McDonald Criteria". Ann Neurol 2005;58:840–6. doi:10.1002/ana.20703 [PubMed]
- 30. Polman CH, Reingold SC, Banwell B, et al. Diagnostic criteria for multiple sclerosis: 2010 revisions to the McDonald criteria. Ann Neurol 2011;69:292–302. doi:10.1002/ana.22366 [PMC free article] [PubMed]
- 31. Goodin DS, Reder AT, Ebers GC, et al. Survival in MS: a randomized cohort study 21 years after the start of the pivotal IFNbeta-1b trial. Neurology 2012;78:1315–22. doi:10.1212/WNL.0b013e3182535cf6 [PMC free article] [PubMed]
- 32. Grytten Torkildsen N, Lie S, Aarseth J, et al. Survival and cause of death in multiple sclerosis: results from a 50-year follow-up in Western Norway. Mult Scler 2008;14:1191–8. doi:10.1177/1352458508093890 [PubMed]
- Orton SM, Wald L, Confavreux C, et al. Association of UV radiation with multiple sclerosis prevalence and sex ratio in France. Neurology 2011;76:425–31. doi:10.1212/WNL.0b013e31820a0a9f [PMC free article] [PubMed]
- 34. Debouverie M, Pittion-Vouyovitch S, Louis S, et al. Increasing incidence of multiple sclerosis among women in Lorraine, Eastern France. Mult Scler 2007;13:962–7. doi:10.1177/1352458507077938 [PubMed]
- 35. Ascherio A, Munger KL. Environmental risk factors for multiple sclerosis. Part I: the role of infection. Ann Neurol 2007;61:288–99. doi:10.1002/ana.21117 [PubMed]
- Ascherio A, Munger KL. Environmental risk factors for multiple sclerosis. Part II: Noninfectious factors. Ann Neurol 2007;61:504–13. doi:10.1002/ana.21141 [PubMed]
- 37. Kleinewietfeld M, Manzel A, Titze J, et al. Sodium chloride drives autoimmune disease by the induction of pathogenic TH17 cells. Nature 2013;496:518–22. doi:10.1038/nature11868 [PMC free article] [PubMed]
- 38. Bjørnevik K, Riise T, Casetta I, et al. Sun exposure and multiple sclerosis risk in Norway and Italy: the EnvIMS study. Mult Scler 2014;20:1042–9. doi:10.1177/1352458513513968 [PubMed]
- 39. Munger KL, Levin LI, Hollis BW, et al. Serum 25-hydroxyvitamin D levels and risk of multiple sclerosis. JAMA 2006;296:2832–8. doi:10.1001/jama.296.23.2832 [PubMed]