Burden of Illness

PATIENT BURDEN OF MIGRAINE

Impact of Migraine

Impact of Migraine

- Migraine accounts for 1.3% of years lost to disability[2]
- Burden on sufferers[2]
  - Personal suffering
  - Impaired quality of life
  - Financial cost
  - Constant fear of another headache
  - Damage family and social life and employment

Depression is three times more common in people who suffer migraines or severe headaches than in healthy individuals[2]

1. Smitherman TA *et al. Headache.* 2013;53(3):427-36.
2. WHO 2012. Headache disorders. Available at: http://www.who.int/mediacentre/factsheets/fs277/en/

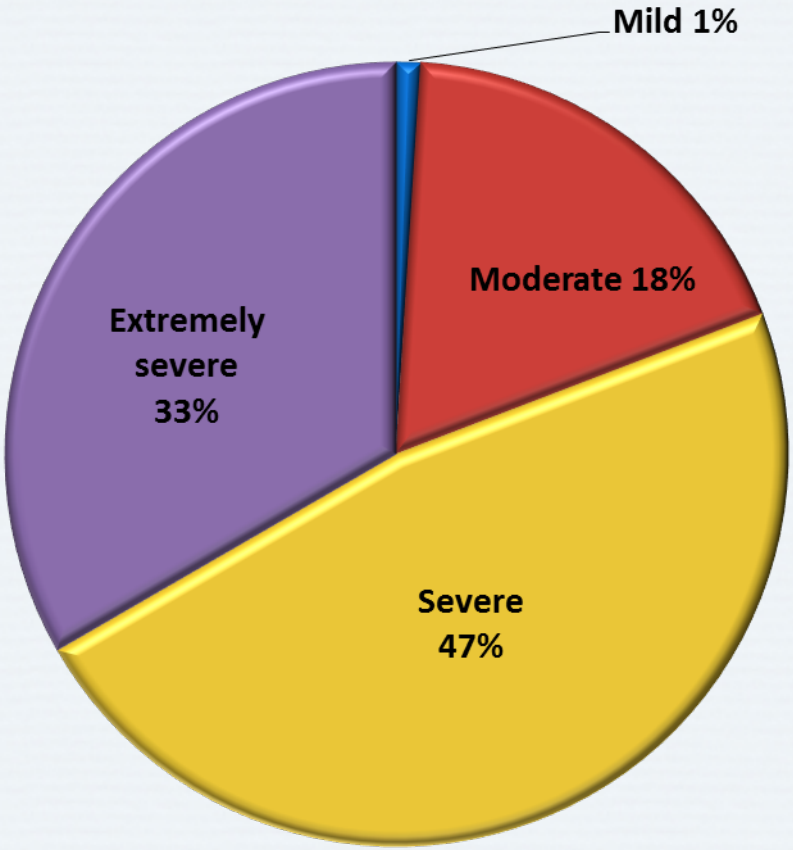
Impact of Migraine

- About 50% of migraine sufferers are severely disabled or require bed rest
- Some disability is due to comorbid conditions
- Financial cost of headache arises partly from direct treatment costs, but much more from loss of work time and productivity
- Annual U.S. direct medical costs attributable to migraine were estimated at $1 billion in 1999
- In 2004, the total cost of migraine in the EC (15 countries) was estimated at €25 billion per year, the next-highest after dementia among neurological disorders

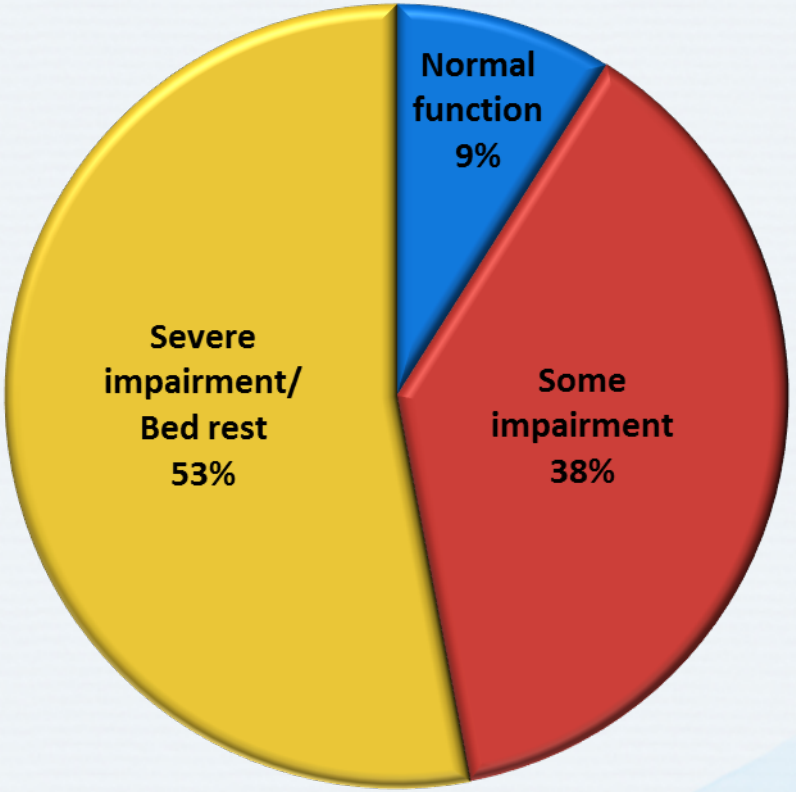
Migraine reduces health-related quality of life more than osteoarthritis or diabetes

IASP Fact Sheet – Epidemiology of Headache 2012

Migraine Patients Experience Severe Pain and Disability



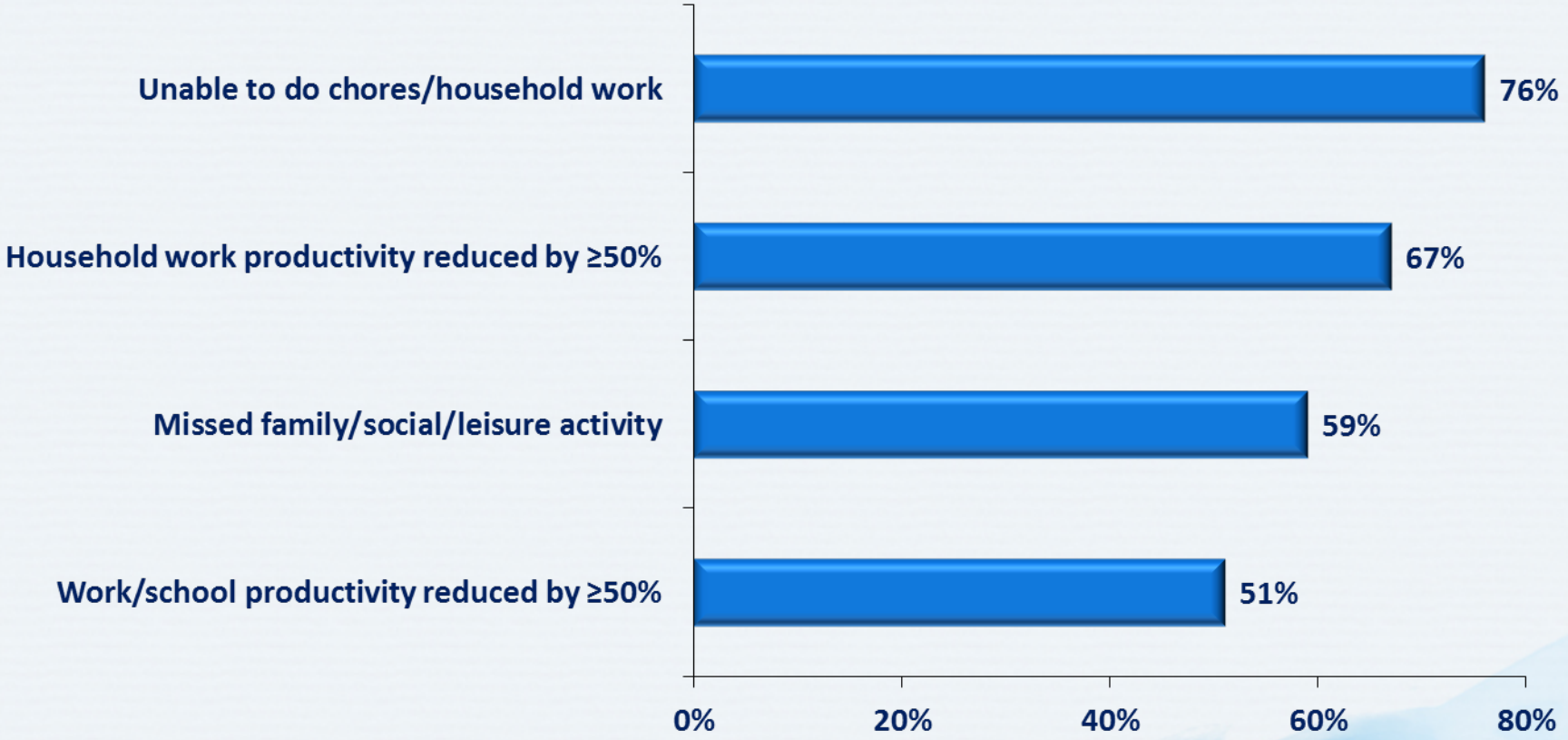
Pain



Disability

American Headache Society. Brainstorm. 2004. Available at: http://www.americanheadachesociety.org/assets/1/7/Book_-_Brainstorm_Syllabus.pdf. Accessed 04 December, 2014.

Impact of Migraine on Patient's Daily Lives



Lipton RB *et al*. Headache. 2001;41(7):646-57.

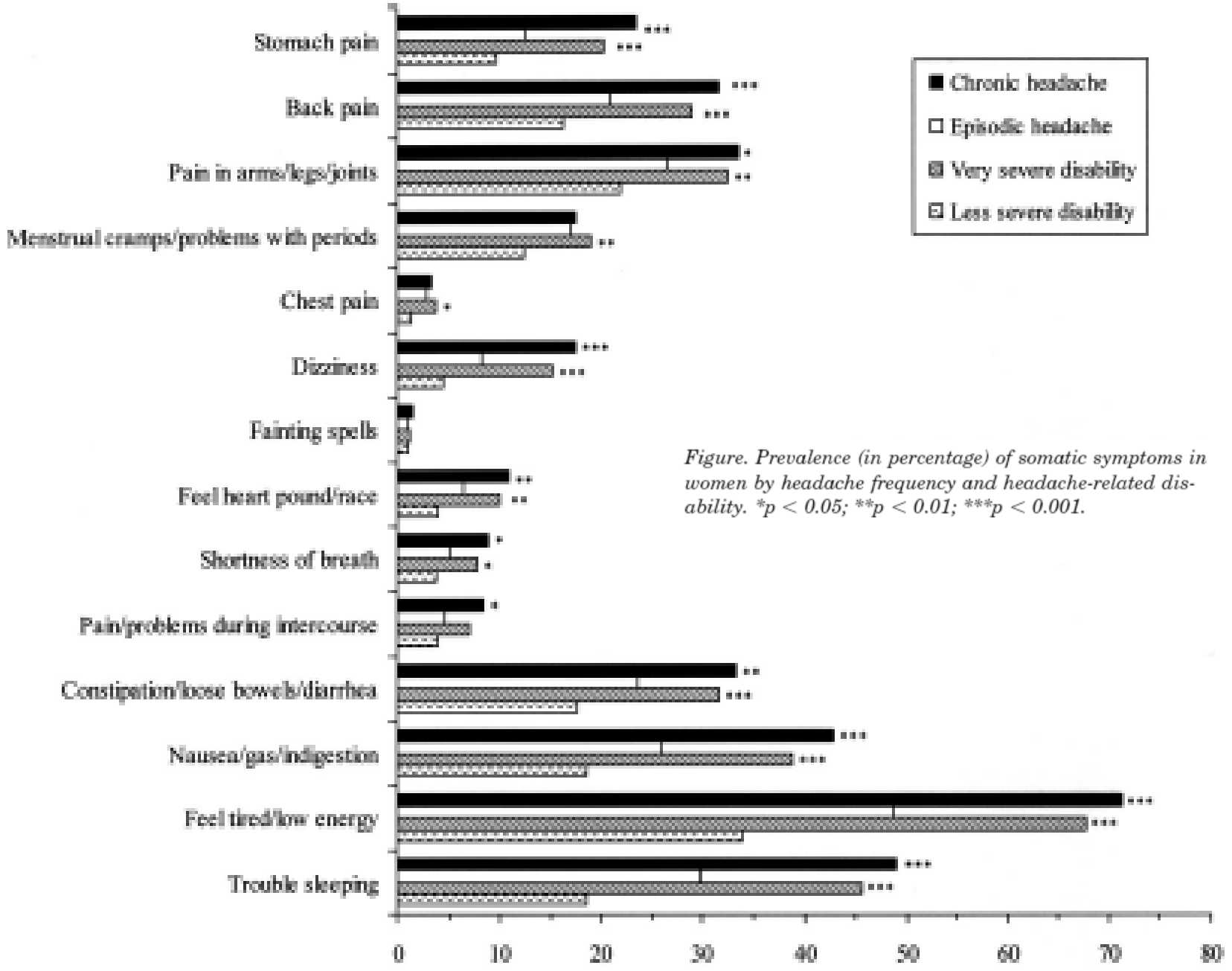


*Figure. Prevalence (in percentage) of somatic symptoms in women by headache frequency and headache-related disability. *$p < 0.05$; **$p < 0.01$; ***$p < 0.001$.*

Impact of Chronic Migraine on Daily Activities over a 3-Month Period

	CM N (%)	Migraine N (%)	
Days of missed work or school			
Complete responses	436	8768	$P = .0012$
None	329 (75.5)	6935 (79.1)	
1-4 days	65 (14.9)	1304 (14.9)	
5 or more	36 (8.2)	232 (2.2)	
Days with reduced productivity at work or school			
Complete responses	432	8542	$P < .001$
None	214 (49.5)	4495 (52.6)	
1-4 days	25 (5.8)	2158 (25.3)	
5 or more days	146 (33.8)	1051 (12.3)	
Household work			
Complete responses	493	9124	$P < .001$
No	98 (19.9)	2479 (27.2)	
1-4	47 (9.5)	3305 (36.2)	
5 or more	283 (57.4)	2219 (24.3)	
Days with reduced productivity at work			
Complete responses	482	8798	$P < .001$
No	99 (20.5)	3060 (34.8)	
1-4	27 (5.6)	2908 (33.1)	
5 or more	280 (58.1)	1602 (18.2)	
Days missed family activities			
Complete responses	490	9135	$P < .001$
No	139 (28.4)	4036 (44.2)	
1-4	87 (17.8)	2816 (30.8)	
5 or more	181 (36.9)	868 (9.5)	

Comparison with episodic migraine.[65]
CM = chronic migraine.

Bigal M *et al. Headache.* 2009;49(7):1028-41.

Social and Economic Burden of Headache Disorders

- Large amount of disability and financial costs to society
- Most troublesome during people's productive years
- 25 million working/school days lost annually in the UK due to migraine
  - Cost is matched by tension-type headache and chronic daily headache combined[1]
- Many do not receive effective care[1]
  - Only 50% of those with migraine consult a physician
    - Only two-thirds are correctly diagnosed[1]

1. WHO 2012. Headache disorders. Available at: http://www.who.int/mediacentre/factsheets/fs277/en/

Psychosocial Burden of Migraine

- Problems are commonly reported with:
  - Energy and drive function
  - Emotional functions
  - Sensation of pain
  - Remunerative employment
  - General evaluations of mental and physical health
  - Social function
  - Global disability evaluations

Symptomatic and prophylactic treatments can reduce patient difficulties and the associated burden of migraine

Raggi A, Giovannetti AM, Quintas R *et al. J Headache Pain.* 2012;13(8):595-606.

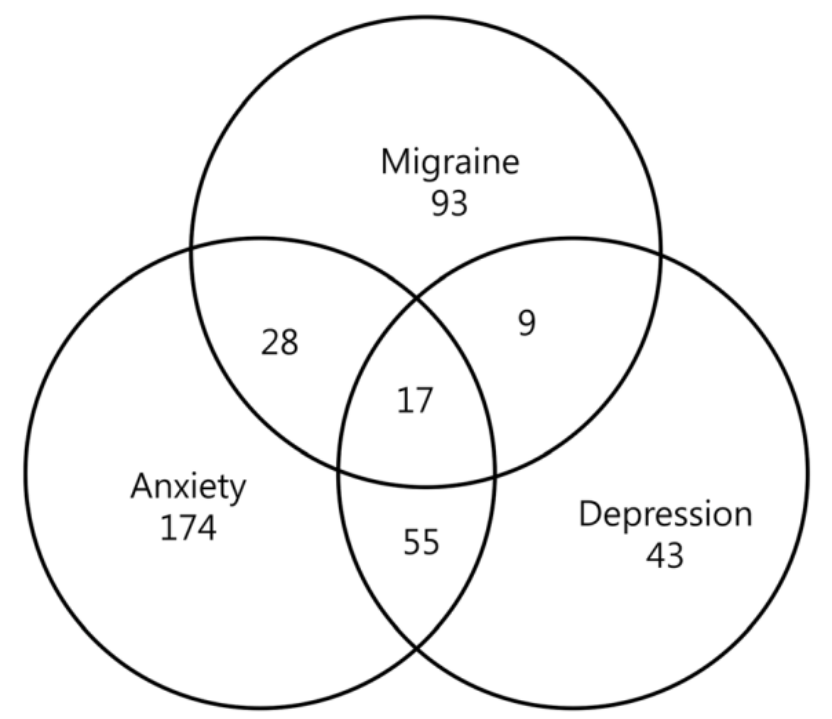
Comorbidities of Migraine

Comorbidities of Migraine

- Strong association with
  - Anxiety and mood disorders
  - Allergies
  - Chronic pain disorders
  - Epilepsy

- Migraine with aura is a risk factor for ischemic stroke and silent brain lesions on MRI, particularly in women with frequent attacks

Prevalence of Anxiety and Depression in Patients with Migraine*



Approximately 1/3 of migraine sufferers with anxiety had depression
Approximately 2/3 of migraine sufferers with depression had anxiety

*Numbers of patients

Oh K *et al. BMC Neurol.* 2014;14(1):238.

Anxiety and Depression Influence Frequency of Migraine Attacks

	Migraine subjects without anxiety or depression, N = 93 Median (25% -75%)	Migraine subjects with anxiety alone, N = 28 median (25% -75%)	Migraine subjects with depression alone, N = 9 median (25% -75%)	Migraine subjects with anxiety and depression, N = 17 median (25% -75%)
Frequency per month	1.0 (0.3-3.0)	2.0 (1.0-5.0)	1.0 (0.3-4.0)	8.0 (2.5-21.0)
VAS score for pain intensity	6.0 (5.0-7.0)	7.0 (6.0-8.0)	7.0 (6.0-8.0)	7.0 (5.0-9.0)
HIT-6 score	50.0 (46.0-58.0)	57.0 (49.0-60.8)	62.0 (52.0-70.5)	64.0 (61.0-67.0)

HIT-6: Headache Impact Test-6; VAS: Visual Analogue Scale.

Combination of anxiety and depression increases headache frequency
Anxiety increases headache intensity

Oh K *et al. BMC Neurol.* 2014;14(1):238.

Anxiety and Depression Influence Migraine-Induced Disability

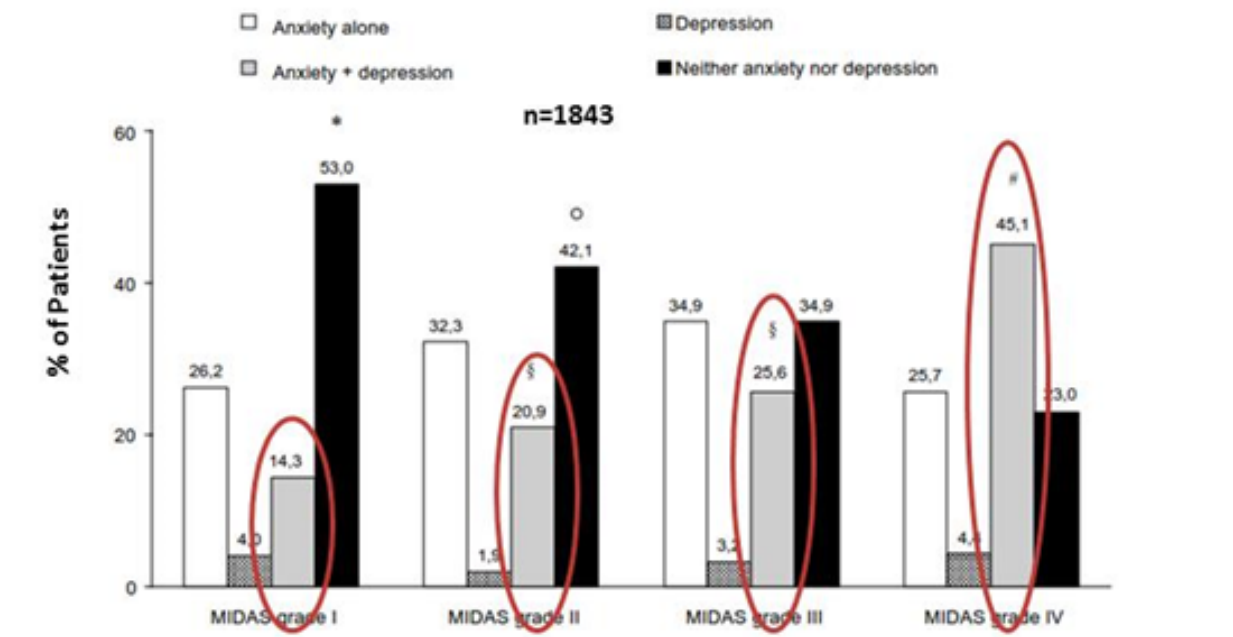


Fig. 1. Influence of anxiety alone, depression alone, and combined anxiety and depression on migraine-related disability as assessed by the MIDAS grade in subjects with assessable MIDAS grade ($n = 1843$). †, statistically significant versus the corresponding subjects in grade I; *, statistically significant ($P < 0.01$) versus the corresponding subjects in grades I, II and III; °, statistically significant ($P < 0.01$) versus the corresponding subjects in grades II, III and IV; ■, statistically significant ($P < 0.01$) versus the corresponding subjects in grade IV.

Anxiety and depression should be systematically looked for and cared for in patients with migraine

MIDAS = Migraine-related Disability

Lantéri-Minet M *et al. Pain*. 2005;118(3):319-26.

Migraine and Depression

- Migraine associated with depression, anxiety, phobias, and panic disorders
- Migraine with aura: higher lifetime prevalence of major depressive disorder than patients with migraine without aura
- Possible mechanisms:
  - Psychiatric disorders and migraine are associated as a result of chance
  - Migraine is a causal factor in the development of psychiatric conditions or vice versa – or both
  - Shared environmental risks for depression and migraine may exist
  - A common shared etiological factor may explain the coexistence of depression and migraine

Frediani F, Villani V. Migraine and depression. *Neurol Sci.* 2007;28 Suppl 2:S161-5.

Migraine and Depression: A Bidirectional Relationship with Common Neurobiology

- Monoamine and peptide transmitters may be involved in depression
- Endorphins and encephalins are involved in mood and pain control
- Serotonin has been implicated in **migraine**, and **tension-type headache**
  - Also implicated in mood disorders, anxiety disorders, sleep disorders, eating disorders, and obsessive-compulsive behavior
- Evidence suggests dopamine is involved in migraine
  - Migraine prodrome often characterised by dopaminergic symptoms
  - Anti-dopaminergic drugs can often be helpful in treating migraine

Severe headache, severe somatic symptoms, and major depression may be linked through dysfunction of the serotonergic and dopaminergic systems

Frediani F, Villani V. Migraine and depression. *Neurol Sci.* 2007;28 Suppl 2:S161-5.

Migraine, Depression, and Quality of Life

- Depression or anxiety are not determined by migraine intensity
  - Significant association between **migraine frequency** and depression
  - Significant association between depression and **duration of migraine attacks**
- Migraine and depression significantly decrease HRQoL
- Patients with migraine may have a lower HRQoL even after controlling for depression
  - More frequent attacks = poorer quality of life

HRQoL = health-related quality of life

Frediani F, Villani V. Migraine and depression. *Neurol Sci.* 2007;28 Suppl 2:S161-5.

Effect of Migraine on Sleep Quality

Table 1 Sleep quality assessed by means of the Pittsburgh Sleep Quality Index (PSQI) in patients with migraine and migraine-free controls

	Patients with								
	≥ 8 migraine days		5–7 migraine days		1–4 migraine days		Controls		
	Mean	S.D.	Mean	S.D.	Mean	S.D.	Mean	S.D.	*P*-value
PSQI total score	5.9	3.0	5.5	2.5	5.4	2.7	4.3	2.5	0.04
Sleep latency (min)	22.1	21.4	19.8	22.6	19.4	20.7	12.9	10.6	0.031
Hours asleep	7.1	1.3	7.0	1.1	7.2	5.0	7.1	1.0	0.902
Sleep disturbance									
Cannot get to sleep within 30 min	0.9	1.0	0.9	0.9	0.9	1.0	0.6	0.8	0.139
Wake up in the middle of the night or early morning	1.3	1.2	1.2	1.1	1.1	1.1	0.9	0.9	0.306
Get up to use bathroom	1.6	1.1	1.6	1.1	1.3	1.1	1.1	1.1	0.043
Cannot breathe comfortably	0.1	0.4	0.2	0.5	0.1	0.4	0.1	0.4	0.458
Cough or snore loudly	0.4	0.8	0.4	0.7	0.3	0.6	0.4	0.8	0.055
Feel too cold	0.3	0.6	0.4	0.6	0.3	0.6	0.2	0.5	0.215
Feel too warm	0.6	0.8	0.5	0.8	0.4	0.7	0.3	0.6	0.150
Bad dreams	0.5	0.8	0.5	0.7	0.3	0.6	0.3	0.6	0.371
Pain	1.2	1.0	1.1	0.9	0.8	0.9	0.3	0.8	<0.001
Other reasons	0.5	1.0	0.6	1.1	0.5	1.0	0.4	0.9	0.667
Quality of sleep	1.1	0.7	1.1	0.7	1.1	0.7	0.7	0.6	0.015
Sleep medication	0.3	0.8	0.2	0.7	0.1	0.4	0.2	0.6	0.130
Difficulties staying awake	0.5	0.8	0.5	0.8	0.4	0.7	0.4	0.8	0.875
Lack of enthusiasm for activities	1.3	0.8	1.3	0.7	1.1	0.7	0.8	0.7	0.125

- **PSQI score total score highest in patients with frequent migraine and lowest in controls**
- **↓ sleep quality is due to migraine; cannot be explained exclusively by comorbid depression or anxiety**

Seidel S *et al. Cephalalgia*. 2009;29(6):662-9.

Effect of Migraine on Fatigue

Table 2 Fatigue assessed by means of the Fatigue Severity Scale in patients with migraine and migraine-free controls

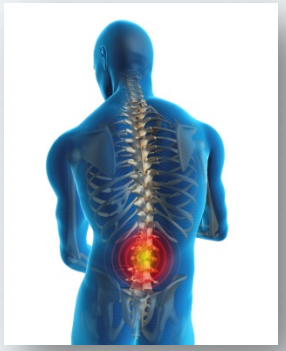
	Patients with								
	≥8 migraine days		5–7 migraine days		1–4 migraine days		Controls		
	Prevalence (%)		Prevalence (%)		Prevalence (%)		Prevalence (%)		*P*-value
SDS ≥ 40	40.2		32.0		24.4		16.3		< 0.001
SAS ≥ 40	30.9		30.7		24.9		6.7		< 0.001
SDS and/or SAS ≥ 40	46.4		44.2		33.3		16.3		< 0.001
	Mean	S.D.	Mean	S.D.	Mean	S.D.	Mean	S.D.	
SDS score	37.3	8.7	35.8	8.8	34.4	8.5	32.0	7.1	< 0.001
SAS score	36.5	7.6	36.8	7.6	34.8	7.4	28.4	6.1	< 0.001

SDS, Self-rating Depression Scale; SAS, Self-rating Anxiety Scale.

Prevalence of depression and/or anxiety and SDS and SAS scores decreased significantly from patients with ≥8 migraine days/month
Fatigue and daytime sleepiness did not differ between migraine suffers and control subjects

Seidel S *et al. Cephalalgia*. 2009;29(6):662-9.

Migraine and Other Comorbidities



Low back pain

Allergies

Irritable bowel syndrome

Fibromyalgia

Yoon MS, Manack A, Schramm S *et al. Pain*. 2013;154:484-92.

Migraine and Obesity

Body Weight	Risk of CM
Normal	3%
Overweight	9%
Obese	15%

Obesity increases migraine frequency

Tepper DE. *Headache: The Journal of Head and Face Pain.* 2013;53:71920.

Migraine and Vascular Disease

- Migraine associated with increased cardiovascular or cerebrovascular disease
- Migraine with aura increases risk of myocardial infarction and ischemic stroke
  - Migraine without aura raises both risks by approximately 25%
  - Migraines during pregnancy linked to stroke and vascular diseases
  - Migraine with aura for women in midlife associated with late-life vascular disease (infarcts) in the cerebellum
- Male and female migraine sufferers have a 2.5-fold increased risk of subclinical cerebellar stroke
  - Aura + increased headache frequency = highest risk
- Migraine associated with higher incidence of adverse cardiovascular profiles, including diabetes and hypertension

Chawla J. 2014. Available at http://emedicine.medscape.com/article/1142556-overview. Accessed 05 January 2014.

Medication Overuse Headache (MOH)

- New or worsening of existing headache develops in association with medication overuse
- Headache on ≥15 days/month for >3 months due to overuse of acute medications
  - About 50% of people have MOH
- Most patients improve after withdrawal of the overused medication

Headache Classification Committee of the International Headache Society (IHS). *Cephalalgia.* 2013;33(9):629-808.

If Migraine Is NOT Treated Effectively…

- It may cause severe suffering, loss of quality of life, loss of productivity, have economic considerations
- Patient may develop chronic migraine or medication overuse headache

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