

Fibromyalgia

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Overview: What Is Fibromyalgia?

- FM is a common chronic widespread pain condition
 - FM patients often have heightened sensitivity to pain (hyperalgesia); in addition, nonnoxious stimuli may result in pain (allodynia)
 - Patients may present with a wide range of additional symptoms including tenderness, sleep disturbances, fatigue, morning stiffness, cognitive complaints, and mood disorders

FM = fibromyalgia.

Wolfe et al. *Arthritis Rheum.* 1995;38:19-28; Staud and Rodriguez. *Nat Clin Pract Rheumatol.* 2006;2:90-98; Wolfe et al. *Arthritis Rheum.* 1990;33:160-172; Henriksson. *J Rehabil Med.* 2003;(suppl 41):89-94.

Case Study

- **A 45-year-old woman presents with diffuse muscle pain, weakness, and significant fatigue.**
- **Symptoms for over 3 years that have become slightly worse in past 6 months.**
- **Generalized pain and fatigue that limit her ability to work.**
- **Increasing sleep difficulty due to the pain**
- **Denies major depression or anxiety but increasingly frustrated by symptoms and lack of a diagnosis.**
- **Previously suffered from migraine but no**

Case Study (cont)

- **General physical examination is unremarkable**
- **Diffuse muscle tenderness is noted**
- **Some tenderness around the joints, but no synovitis**
- **No objective muscle weakness**
- **Normal neurologic examination**
- **CBC, ESR, and chemistry profile are normal**

Proposed Etiology of Fibromyalgia

- Emerging evidence of a genetic component of FM
 - Specific gene mutations may predispose individuals to FM
 - Polymorphisms in the COMT enzyme and the serotonin transporter are potentially associated with FM and other disorders
- Environmental factors that may trigger the onset of FM
 - Physical trauma or injury
 - Infections (hepatitis C, Lyme disease)
 - Psychological stressors
- FM may occur concurrently with arthritis (OA), autoimmune diseases (RA, SLE), and hypothyroidism

COMT = catechol-O-methyltransferase; RA = rheumatoid arthritis; OA = osteoarthritis; SLE = systemic lupus erythematosus. Zubieta et al. *Science*. 2003;299:1240-1243; Arnold et al. *Arthritis Rheum*. 2004;50:944-952; Clauw and Crofford. *Best Prac Res Clin Rheumatol*. 2003; 17:685-701; Burckhardt et al. APS Clinical Practice Guideline Series, No.4. Glenview, IL; 2005.

Fibromyalgia Controversies

- Is it real?
- Can it be reliably diagnosed?
- Is it physical or psychological?
- Is there any effective treatment?
- Is a diagnosis helpful or harmful?

Epidemiology of Fibromyalgia

- Prevalence

- FM is common worldwide and affects 2%-5% of US adult population
- Majority of patients between the ages of 35 and 60 years

- Gender differences

- Women are more likely to be diagnosed with FM than men

Determining FM Prevalence



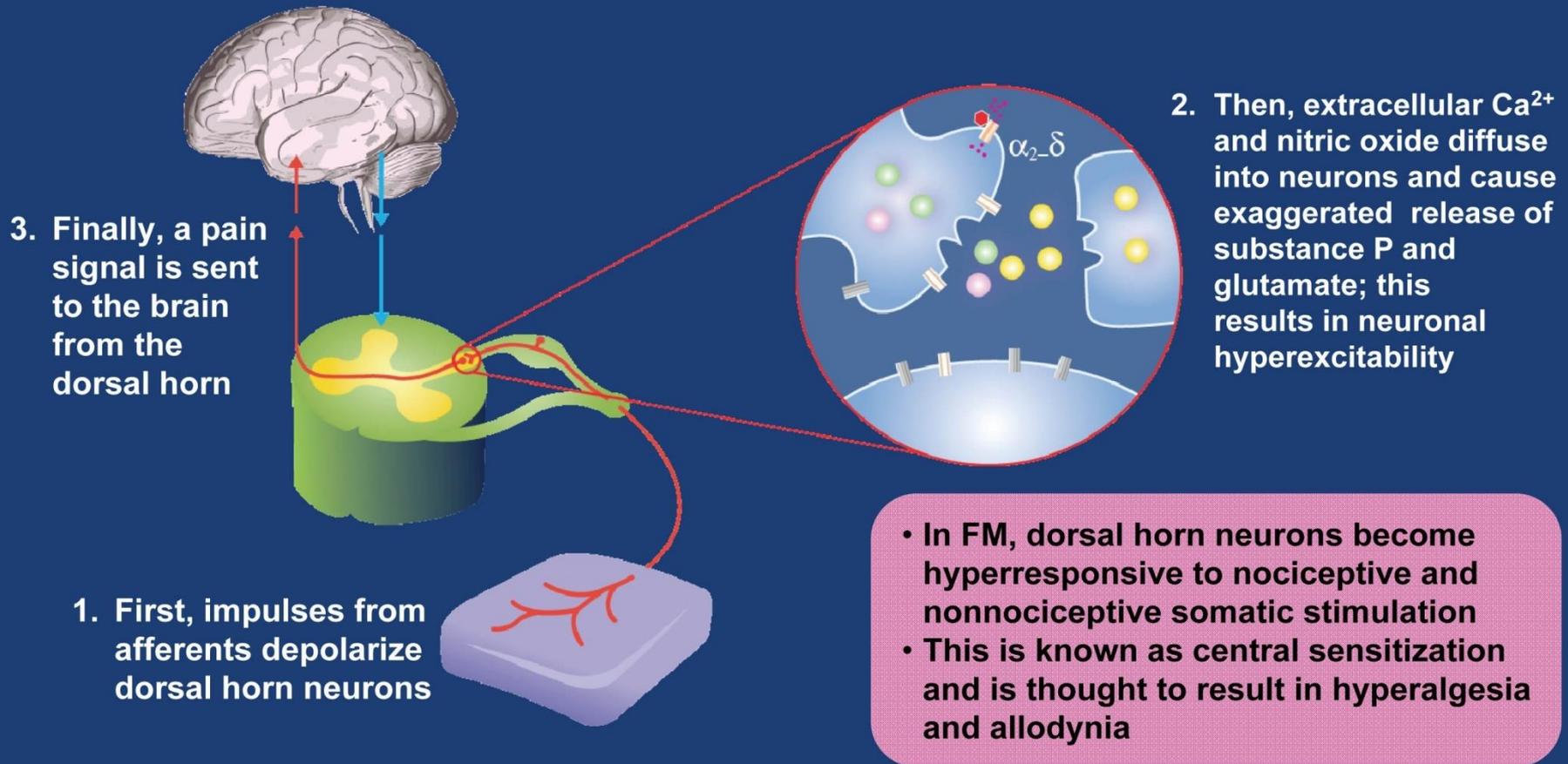
Pathophysiology of Fibromyalgia: Overview

- Central pain mechanisms in FM
 - CNS mechanisms (ie, central sensitization) may explain generalized heightened pain sensitivity of FM patients
 - Increased levels of excitatory neurotransmitters (glutamate and substance P) may contribute to neuronal hyperactivity and central sensitization
 - Compared with normal controls, CSF levels of substance P are 3-fold higher in patients with FM
- FM is believed to be a chronic, central pain state
 - fMRI data provide supporting evidence that FM involves altered central pain processing

Despite extensive research, the pathogenesis of pain in FM is not clearly understood. However, central sensitization has emerged as a leading theory of disease mechanism.

fMRI = functional magnetic resonance imaging; CNS = central nervous system; CSF = cerebrospinal fluid.
Staud and Rodriguez. *Nat Clin Pract Rheumatol*. 2006;2:90-98; Henriksson. *J Rehabil Med*. 2003;41(suppl 41):89-94; Gracely et al. *Arthritis Rheum*. 2002;46:1333-1343; Giesecke et al. *Arthritis Rheum*. 2004;50:613-623; Crofford and Clauw et al. *Arthritis Rheum*. 2002;46:1136-1138; Vaerøy et al. *Pain*. 1988;32:21-26; Russell et al. *Arthritis Rheum*. 1994;37:1593-1601.

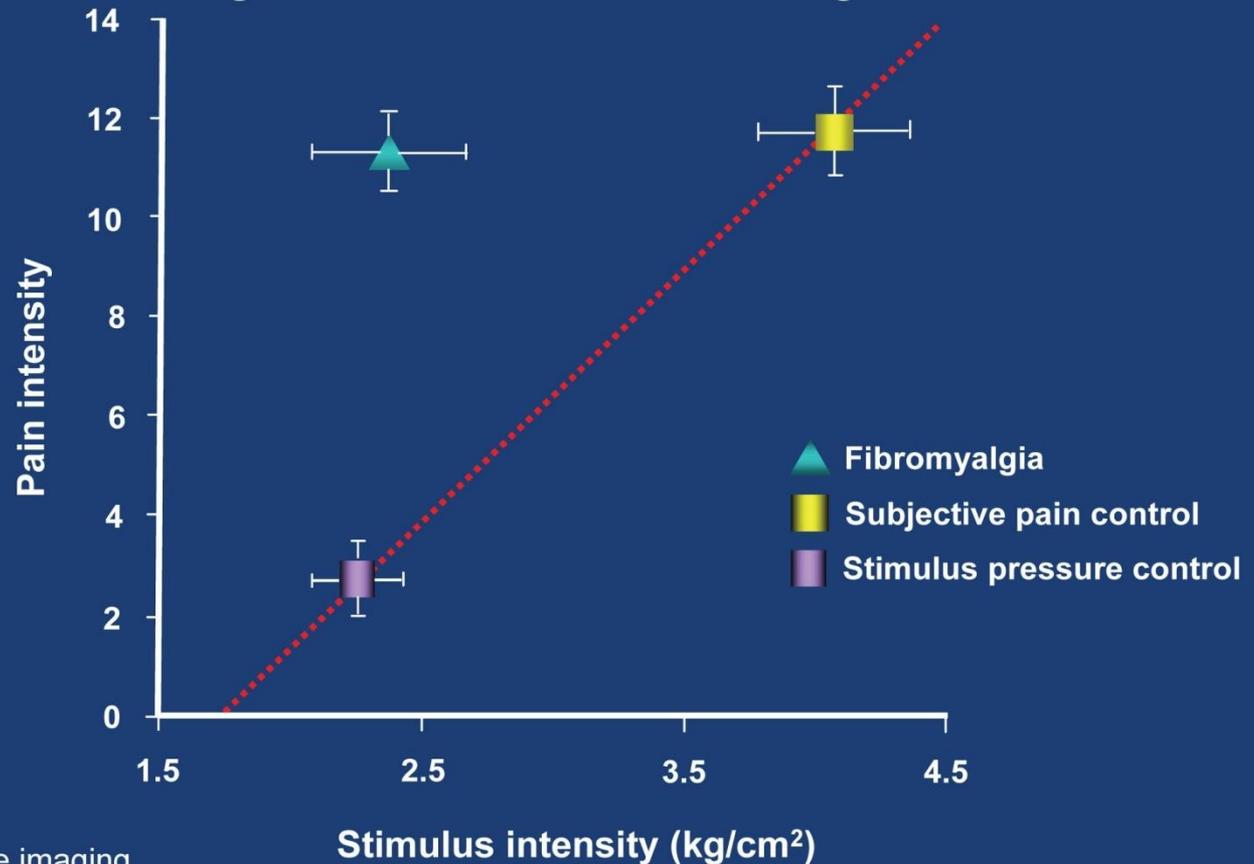
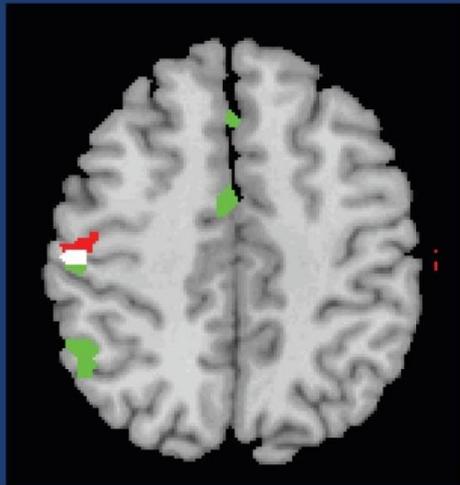
Pathophysiology of Fibromyalgia: The Role of Central Sensitization



Despite extensive research, the pathogenesis of pain in FM is not clearly understood. However, central sensitization has emerged as a leading theory of disease mechanism.

Fibromyalgia May Be a Central Pain Processing Disorder: fMRI Evidence

fMRI Studies Show Cortical/Subcortical Augmentation of Pain Processing in FM



fMRI = functional magnetic resonance imaging.
Gracely et al. *Arthritis Rheum.* 2002;46:1333-1343.

Fibromyalgia Pathophysiology: Summary

- Recent data suggest that alterations of the CNS may contribute to the chronic widespread pain of FM
- Central sensitization is emerging as a leading theory of FM pathophysiology
- fMRI data provide supporting evidence that FM is a central pain processing disorder
- Therapeutic agents that reduce neuronal hyperactivity by reducing the release of neurotransmitters may be one way to relieve the chronic pain of FM

Despite extensive research, the pathogenesis of pain in FM is not clearly understood. However, central sensitization has emerged as a leading theory of disease mechanism.

Staud and Rodriguez. *Nat Clin Pract Rheumatol*. 2006;2:90-98; Henriksson. *J Rehabil Med*. 2003;41(suppl 41):89-94; Gracely et al. *Arthritis Rheum*. 2002;46:1333-1343; Campbell and Meyer. *Neuron*. 2006;52:77-92; Rao. *Rheum Dis Clin N Am*. 2002;28:235-259; Maneuf and McKnight. *Br J Pharmacol*. 2001;134:237-240; Coderre et al. *J Neurochem*. 2005;94:1131-1139.

Clinical Features and Diagnosis of Fibromyalgia: Overview

- Clinically, FM presents with chronic widespread pain in addition to a wide range of symptoms, including tenderness, sleep disturbances, fatigue, and morning stiffness
- Patients with FM are more likely to have comorbidities such as painful neuropathies and circulatory disorders
- ACR and Canadian criteria may be used to diagnose FM
- Symptoms may overlap with other conditions (IBS, MDD, CFS, SLE, RA, OA, Lyme disease); differentiation is essential for optimal management

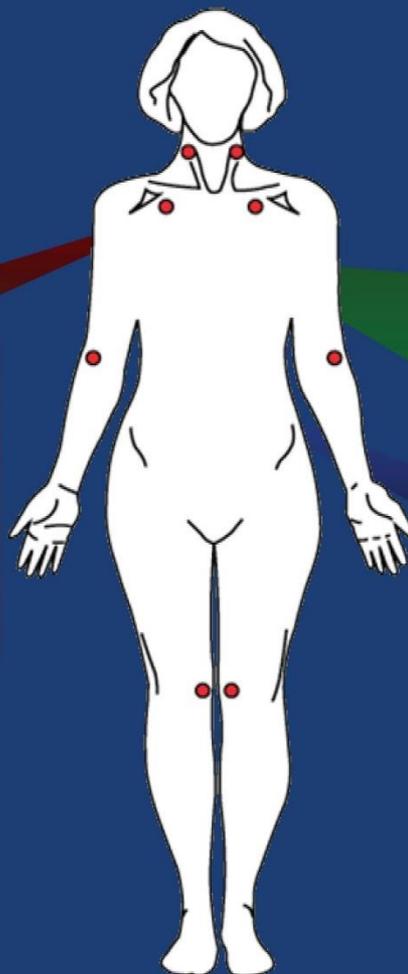
ACR = American College of Rheumatology; IBS = irritable bowel syndrome; MDD = major depressive disorder; CFS = chronic fatigue syndrome; SLE = systemic lupus erythematosus.

Wolfe et al. *Arthritis Rheum.* 1995;38:19-28; Wolfe et al. *Arthritis Rheum.* 1990;33:160-172; Berger et al. *Int J Clin Pract.* In press; Jain et al. *J Musculoskelet Pain.* 2003;11(4):3-107; Burckhardt et al. APS Clinical Practice Guideline Series, No.4.

Problems in Defining Fibromyalgia

- “Real” if no clear pathophysiologic basis?
- Gold standard is “expert opinion.”
- Tender points, symptoms are subjective.
- Fewer than 11 tender points?
- Symptoms are not dichotomous.
- Same diagnostic criteria and dilemma for any illness lacking objective biologic markers (depression, migraine, IBS, CFS).

Clinical Features of Fibromyalgia



WIDESPREAD PAIN

- Chronic, widespread pain is the defining feature of FM
- Patient descriptors of pain include: aching, exhausting, nagging, and hurting
- Presence of tender points

SLEEP DISTURBANCES

- Characterized by nonrestorative sleep and increased awakenings
- Abnormalities in the continuity of sleep and sleep architecture
- Reduced slow-wave sleep
- Abnormal alpha wave intrusion in non-REM sleep

FATIGUE/STIFFNESS

- Morning stiffness and fatigue are common characteristics of FM

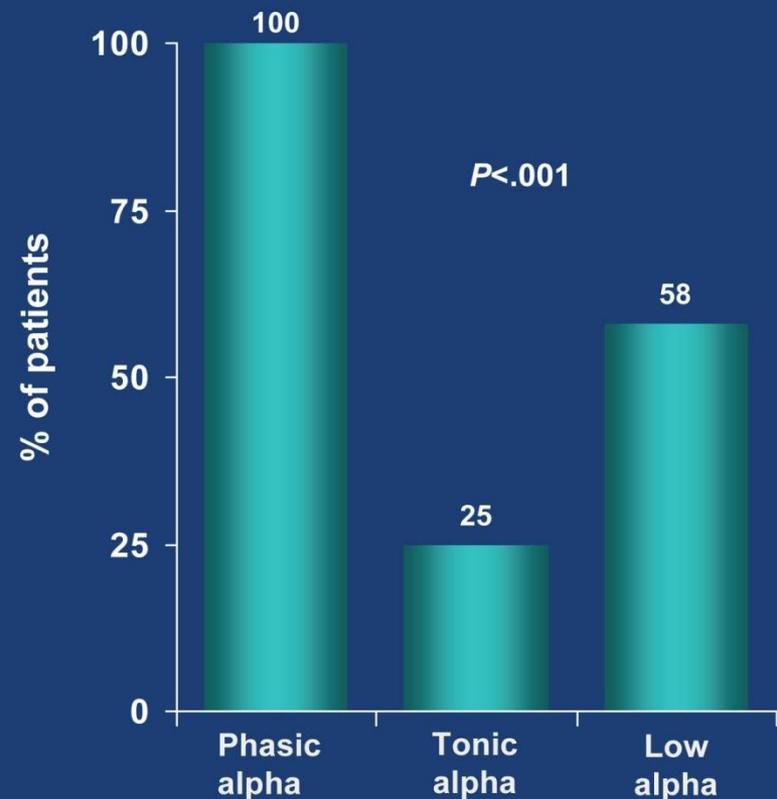
Functional Somatic Syndromes

Rheumatology	Fibromyalgia
Gastroenterology	Irritable bowel
Neurology	Tension headache
Infectious Disease	Chronic fatigue
Gynecology	Chronic pelvic pain
Cardiology	Non-cardiac chest pain
Urology	Irritable bladder (ICS)
Allergy	Multiple chemical sensitivity
ENT	TMJ

Fibromyalgia Is Often Associated With Sleep Disturbances

- Nonrestorative sleep is a prominent feature of FM
- FM patients report insomnia, early morning awakenings, and poor-quality sleep
- Alpha intrusion is a common but nonspecific EEG finding in FM patients
 - May interfere with sleep function and contribute to worsening of pain after sleep
 - Phasic, tonic, and low alpha are subtypes of alpha sleep intrusion observed in patients with FM

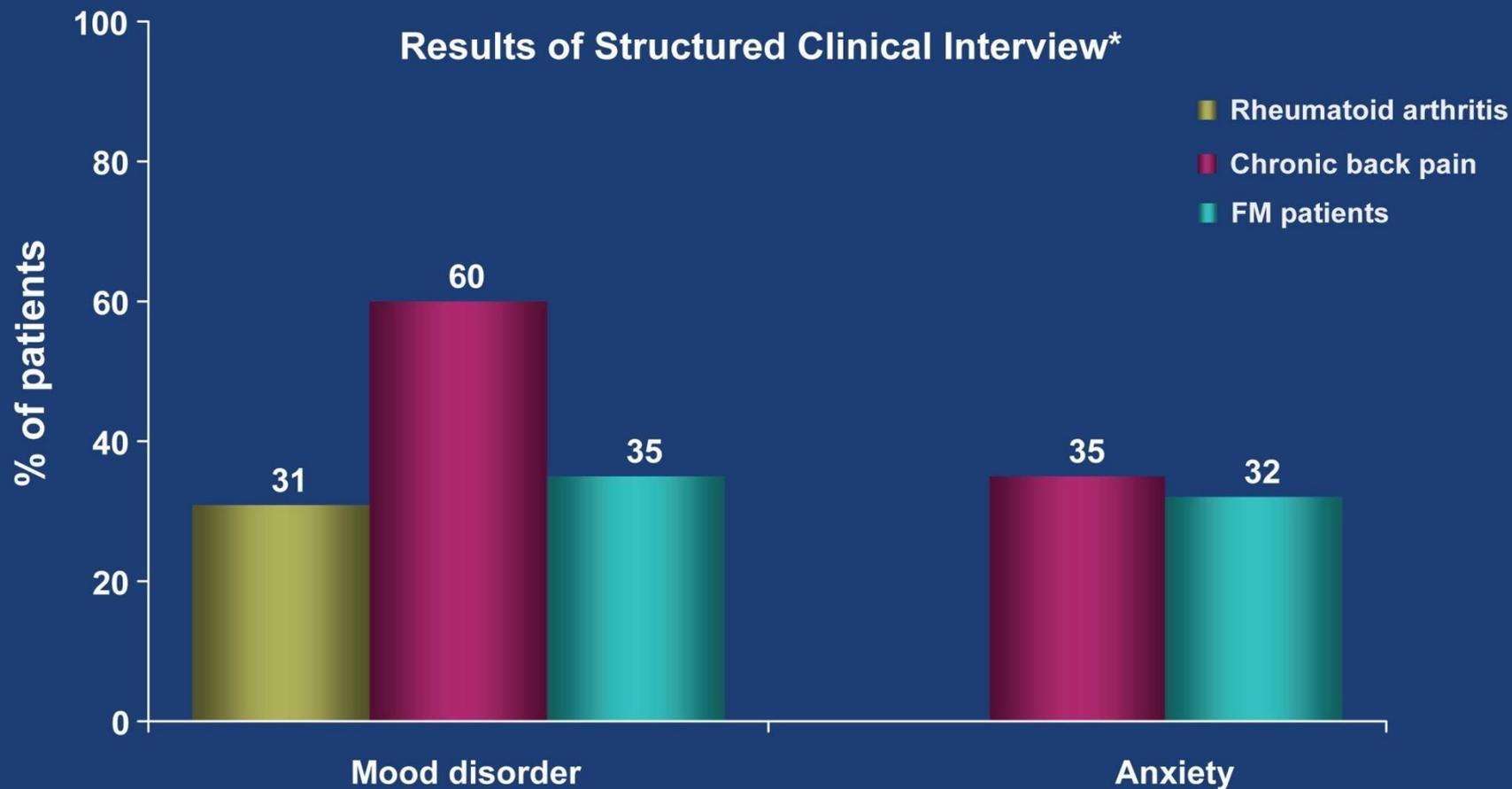
FM Patients Who Experienced Worsening of Pain After Sleep



EEG = electroencephalogram.

Roizenblatt et al. *Arthritis Rheum.* 2001;44:222-230; Harding. *Am J Med Sci.* 1998;315:367-376.

Rates of Mood Disorders in Fibromyalgia Are Similar to Other Rheumatologic Conditions



*Mood disorders included major depressive episode, major depressive disorder, and dysthymic disorder.

Thieme et al. *Psychosom Med.* 2004;66:837-844.

FMS and Mood Disorders

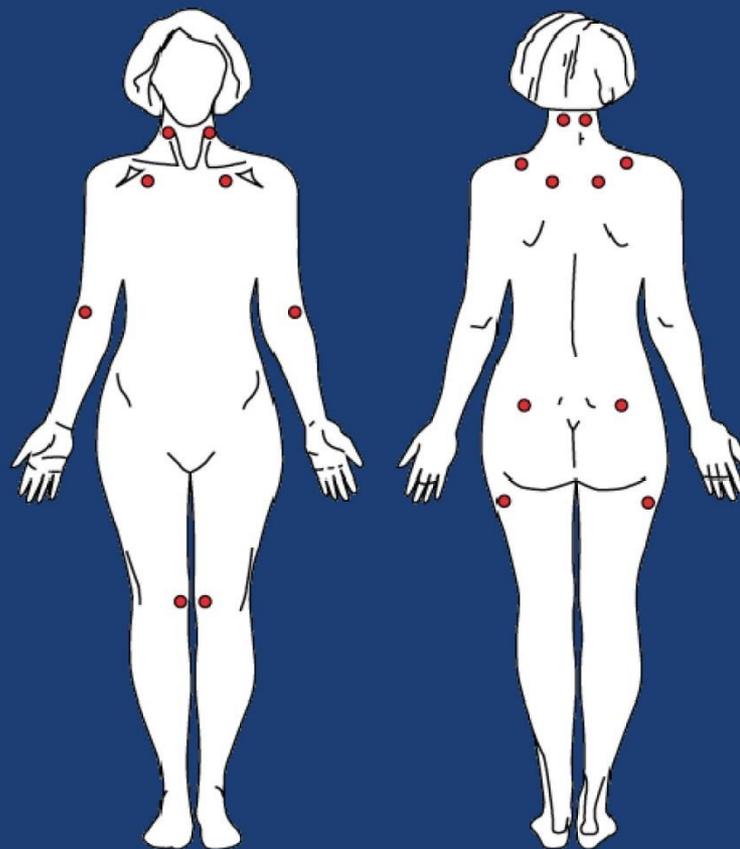
- At the time of FMS diagnosis, mood disorders are present in 30-50%, primarily depression.
- Increased prevalence of mood disorders is primarily in tertiary-referral patients.
- Increased lifetime and family history of mood disorders in FM vs RA (Odds = 2.0).
- FMS aggregates in families and co-aggregates with mood disorders. Odds of having FMS in relatives is 8.5 in FMS vs RA proband (Arnold, et al 2003).

Genetic Factors in Fibromyalgia

- Familial predisposition
 - Arnold¹ found that if an individual has fibromyalgia there is >8 odds ratio (OR) for first-degree relatives to develop fibromyalgia
- Candidate Genes
 - 5-HT_{2A} receptor polymorphism T/T phenotype²
 - Serotonin transporter³
 - Dopamine D4 receptor exon III repeat polymorphism⁴
 - COMT (catecholamine o-methyl transferase)⁵
 - Heterozygous beta-3 adrenergic receptor allele⁶

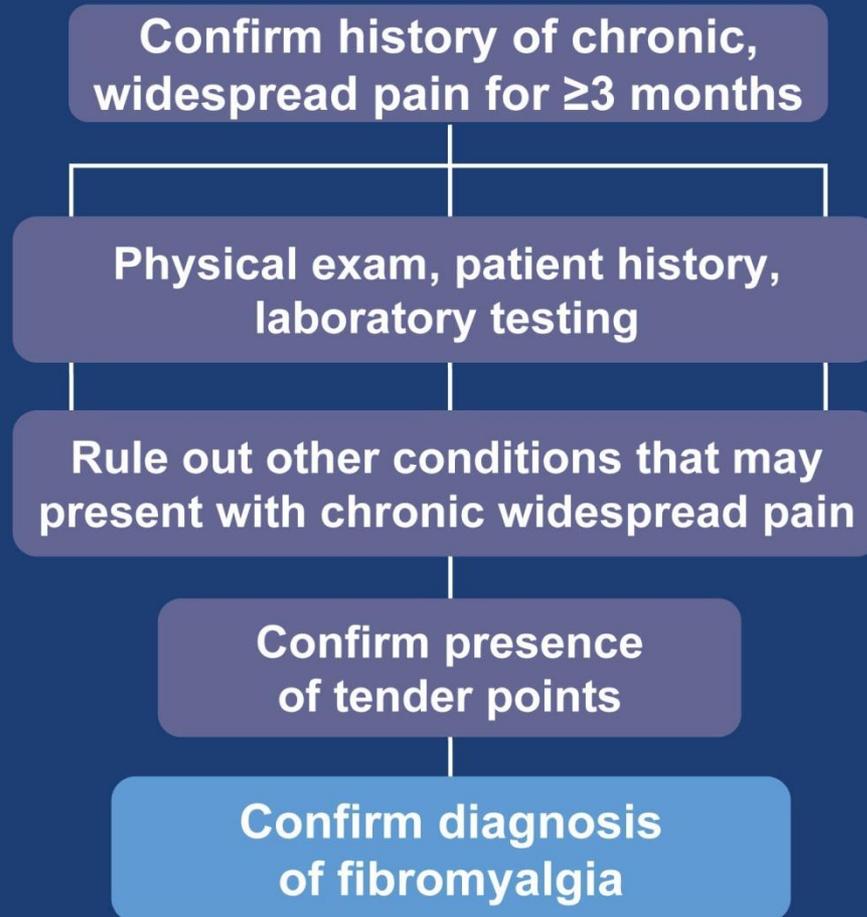
American College of Rheumatology (ACR) Criteria for FM

- ACR criteria
 - History of chronic widespread pain ≥ 3 months
 - Patients must exhibit ≥ 11 of 18 tender points
- Widespread pain was found in 97% of patients with FM, compared with 70% in controls
- FM can be identified from among other rheumatologic conditions with use of ACR criteria
 - Criteria need further refinement as knowledge about FM evolves

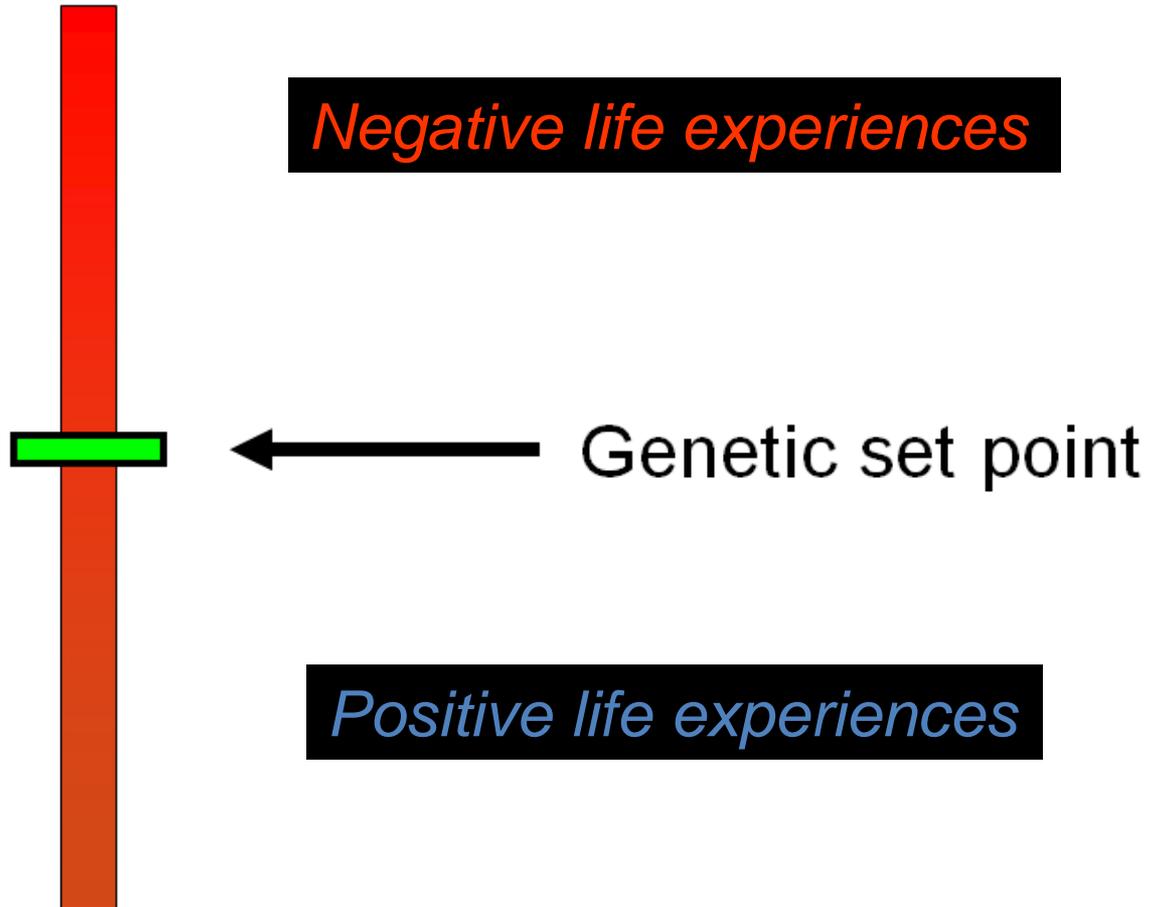


ACR criteria are both sensitive (88.4%) and specific (81.1%)

Example of Comprehensive Diagnostic Workup for Fibromyalgia



Stress Susceptibility



Management of Fibromyalgia (FM)

Nonpharmacologic

- Aerobic exercise
- Cognitive behavioral therapy
- Patient education
- Strength training
- Acupuncture
- Biofeedback
- Balneotherapy
- Hypnotherapy

Pharmacologic

- Antidepressants
- Analgesics
- Anticonvulsants

Until now there were no FDA-approved therapies for FM

Is there any effective management of fibromyalgia?

- **All patients**
 - **Reassurance re diagnosis**
 - **Give explanation, including, but not solely, psychological factors**
 - **Promote return to normal activity, exercise**
- **Most patients**
 - **Medication trial (esp antidepressants, anticonvulsants)**
 - **Cognitive behavior therapy, counseling**
 - **Physical rehabilitation**

Medications in FMS

- Strong evidence for efficacy:
 - Amitriptyline, 25-50 mg at bedtime
 - Cyclobenzaprine, 10-30 mgs at bedtime
 - Pregabalin, 300-450 mg/day
 - Gabapentin, 1600-2400 mg/day
 - Duloxetine, 60-120 mg/day
 - Milnacipran, 100-200 mg/day
- Modest evidence for efficacy:
 - Tramadol, 200-300 mg/day
 - SSRIc (fluoxetine, sertraline)

Medications in FMS (cont)

- Weak evidence for efficacy: pramipexole, gamma hydroxybutyrate, growth hormone, 5-hydroxytryptamine, tropisetron, s-adenosyl-methionine.
- No evidence: opioids, NSAIDS, benzodiazepene and nonbenzodiazepene hypnotics, melatonin, magnesium, DHEA, thyroid hormone, OTC including guaifenesin.

Modified from Goldenberg, et al: Management of fibromyalgia syndrome. JAMA 2004; 292:2388-95.

Tricyclic Antidepressants (TCAs)*: Published Trials ≥ 8 Weeks Duration

Study	Agent	N	Duration (weeks)	Primary End Point	Significant Improvement with TCA
Carette et al (1986)	AMI vs PBO	70	9	Morning stiffness, pain analog score	No
Carette et al (1994)	AMI vs CBP vs PBO	208	24	VAS (pain, sleep, stiffness, fatigue)	No
Ginsberg et al (1996)	AMI vs PBO	46	8	Pain VAS, TP score	Yes
Hannonen et al (1998)	AMI vs Moclobemide vs PBO	130	12	VAS (pain, sleep, fatigue) NHP, Sheehan disability	Yes
Heyman et al (2001)	AMI vs Nortriptyline vs PBO	118	8	NTP, FIQ, VSGI	No
Caruso et al (1987)	AMI vs Nortriptyline	60	8	Manual TP count	Yes
Bennett et al (1988)	CBP vs PBO	120	12	CGIC	Yes

***No TCAs are currently FDA approved for FM.**

AMI = amitriptyline; VAS = visual analog score; PBO = placebo; CBP = cyclobenzaprine; TP = tender points; NHP = Nottingham Health Profile; NTP = number of tender points; FIQ = Fibromyalgia Impact Questionnaire; VSGI = verbal scale global improvement; CGIC = clinician global impression of change; FDA = United States Food and Drug Administration.

Carette et al. *Arthritis Rheum.* 1986;29:655-659; Carette et al. *Arthritis Rheum.* 1994;37:32-40; Ginsberg et al. *J Musculoskelet Pain.* 1996;4(3):37-47; Hannonen et al. *Br J Rheumatol.* 1998;37:1279-1286; Heymann et al. *Clin Exp Rheumatol.* 2001;19:697-702; Caruso et al. *J Int Med Res.* 1987;15:154-159; Bennett et al. *Arthritis Rheum.* 1988;31:1535-1542; Arnold LM. In: Wallace & Clauw's *Fibromyalgia and Other Central Pain Syndromes.*

Serotonin Norepinephrine Reuptake Inhibitors (SNRIs)*: Published Trials

Study	Agent	N	Study Duration (weeks)	Primary End Point	Significant Improvement with SNRI
Vitton et al (2004)	Milnacipran vs PBO	125	12	Pain intensity (pain diary)	Yes
Gendreau et al (2005)	Milnacipran vs PBO	125	12	Average daily pain score	Yes
Arnold et al (2005)	Duloxetine vs PBO	354	12	BPI average pain severity	Yes
Arnold et al (2004)	Duloxetine vs PBO	207	12	FIQ (total and pain)	Yes
Dwight et al (1998)	Venlafaxine vs PBO	15	8	McGill Pain Questionnaire VAS	Yes
Sayar et al (2003)	Venlafaxine vs PBO	15	12	FIQ Pain score	Yes

*No SNRI is currently FDA approved for FM.

BPI = Brief Pain Inventory; VAS = Visual Analog Score.

Vitton et al. *Hum Psychopharmacol Clin Exp.* 2004;19:S27-S35; Gendreau et al. *J Rheumatol.* 2005;32:1975-1985; Arnold et al. *Pain.* 2005;119:5-15; Arnold et al. *Arthritis Rheum.* 2004;50:2974-2984; Dwight et al. *Psychosom.* 1998;39:14-17; Sayar et al. *Ann Pharmacother.* 2003; 37:1561-1565.

Analgesics*: Published Trials

Study	Agent	N	Study Duration (weeks)	Primary End Point	Significant Improvement with Tramadol
Bennett et al (2005)	Tramadol/acetaminophen vs PBO	313	13	SF-36, FIQ	Yes
Bennett et al (2003)	Tramadol/acetaminophen vs PBO	315	13	Time to discontinuation	Yes
Kemple et al (2003)	Opioid [†]	38	200	Improvement in pain	No
Russell et al (2000)	Tramadol vs PBO	100	9	Time to discontinuation	Yes
Biasi et al [‡] (1998)	Tramadol vs PBO	12	1	VAS	Yes
Sorensen et al (1995)	Morphine (IV) vs PBO	9	1	Reduction in pain intensity	No

*No analgesic is currently FDA approved for FM.

[†]Doses of morphine equivalent per 24 hour were determined; [‡]Single-dose cross-over trial with 1 week washout period.

SF-36 = short-form 36; IV = intravenous; VAS = visual analog score.

Bennett et al. *Arthritis Rheum.* 2005;53:519-527; Bennett et al. *Am J Med.* 2003;114:537-545; Kemple et al. *Arthritis Rheum.* 2003;48:S88; Russell et al. *J Clin Rheumatol.* 2000;6:250-257; Biasi et al. *Int J Clin Pharmacol Res.* 1998;18:13-19; Sorensen et al. *Scand J Rheumatol.* 1995;24:360-365.

Anticonvulsants*: Published Trials†

Study	Agent	N	Study Duration (weeks)	Primary End Point	Significant Improvement
Arnold et al (2007)	Pregabalin vs PBO	750	14	End point mean pain score	Yes
Crofford et al‡ (2007)	Pregabalin vs PBO	1051	32	Time to loss of therapeutic response	Yes
Crofford et al (2005)	Pregabalin vs PBO	529	8	End point mean pain score	Yes
Arnold et al (2007)	Gabapentin vs PBO	150	12	BPI average pain severity score	Yes

*Gabapentin is currently not FDA approved for FM.

†Published either in peer-reviewed journals or studies included in the Lyrica® package insert.

‡Includes open-label phase of trial.

Arnold et al. *APS*, 2007; Crofford et al. *APS*, 2007; Crofford et al. *Arthritis Rheum.* 2005;52:1264-1273; Arnold et al. *Arthritis Rheum.* 2007;56:1336-1344.

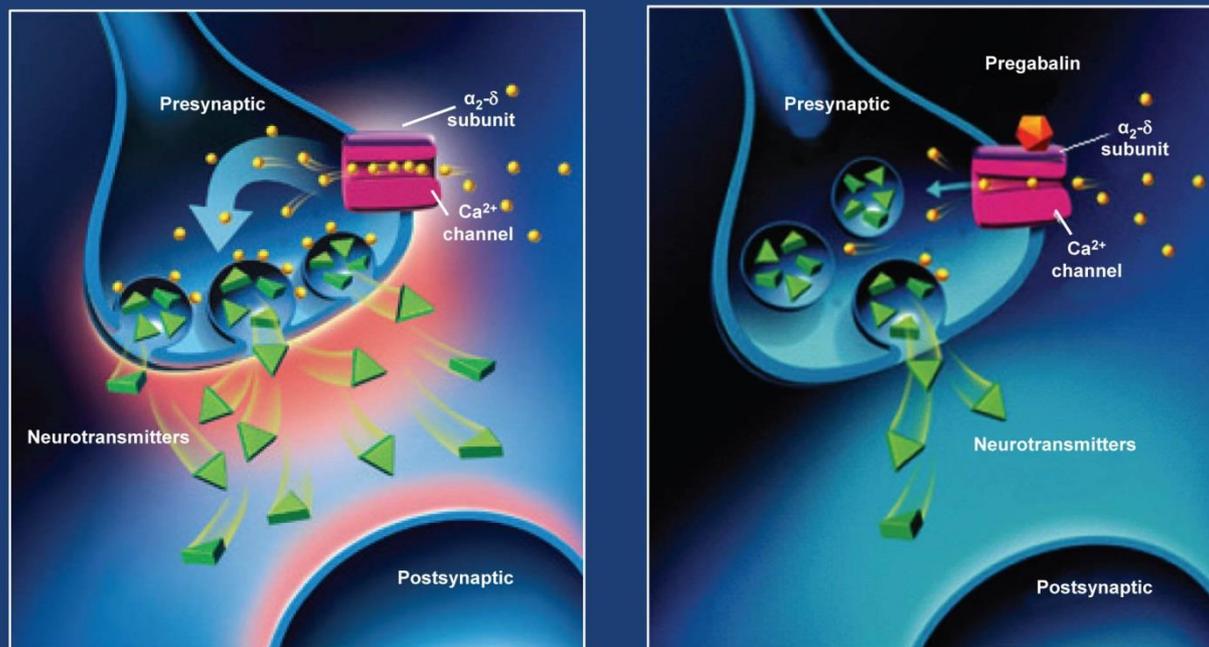
Nonpharmacologic Therapies*

- Patient education
 - Intensive patient education in FM has been shown to improve pain, sleep, fatigue, and quality of life in patients with FM
- Aerobic exercise
 - Exercise may increase aerobic performance and tender point pain pressure threshold, and improve pain
- Cognitive behavioral therapy (CBT)
 - Some evidence of improvements in pain, fatigue, mood, and physical function

***Only nonpharmacologic therapies with strong evidence are noted.**

Williams et al. *J Rheumatol*. 2002;29:1280-1286; Karper et al. *Rehabil Nurs*. 2006;31:193-198; Busch et al. *Cochrane Database Syst Rev*. 2002;CD003786; Goldenberg et al. *JAMA*. 2004;292:2388-2395.

Pregabalin Binds to the α_2 - δ Subunit of Voltage-Gated Ca^{2+} Channels in the Central Nervous System



Schematic representation of pregabalin's proposed mechanism of action

- Pregabalin selectively binds to α_2 - δ subunit of voltage-gated calcium channels
 - Modulates calcium influx in hyperexcited neurons
 - Reduces neurotransmitter release (glutamate, substance P, norepinephrine)
 - Pharmacologic effect requires binding at this site in animal models
 - The clinical significance of these observations in humans is currently unknown

Pregabalin 14-Week Fixed-Dose FM Trial: Overview of Efficacy End Points

Primary

End point Mean Pain Score Utilizing Pain Diary
(0=no pain to 10=worst possible pain)

Co-primary

Fibromyalgia Impact Questionnaire (FIQ)
Patient Global Impression of Change (PGIC)

Secondary*

Pain VAS (100 mm)
Medical Outcomes Study (MOS) sleep scale
Multidimensional Assessment of Fatigue (MAF)
Hospital Anxiety and Depression Scale (HADS)
Short-form-36 (SF-36) Health Survey

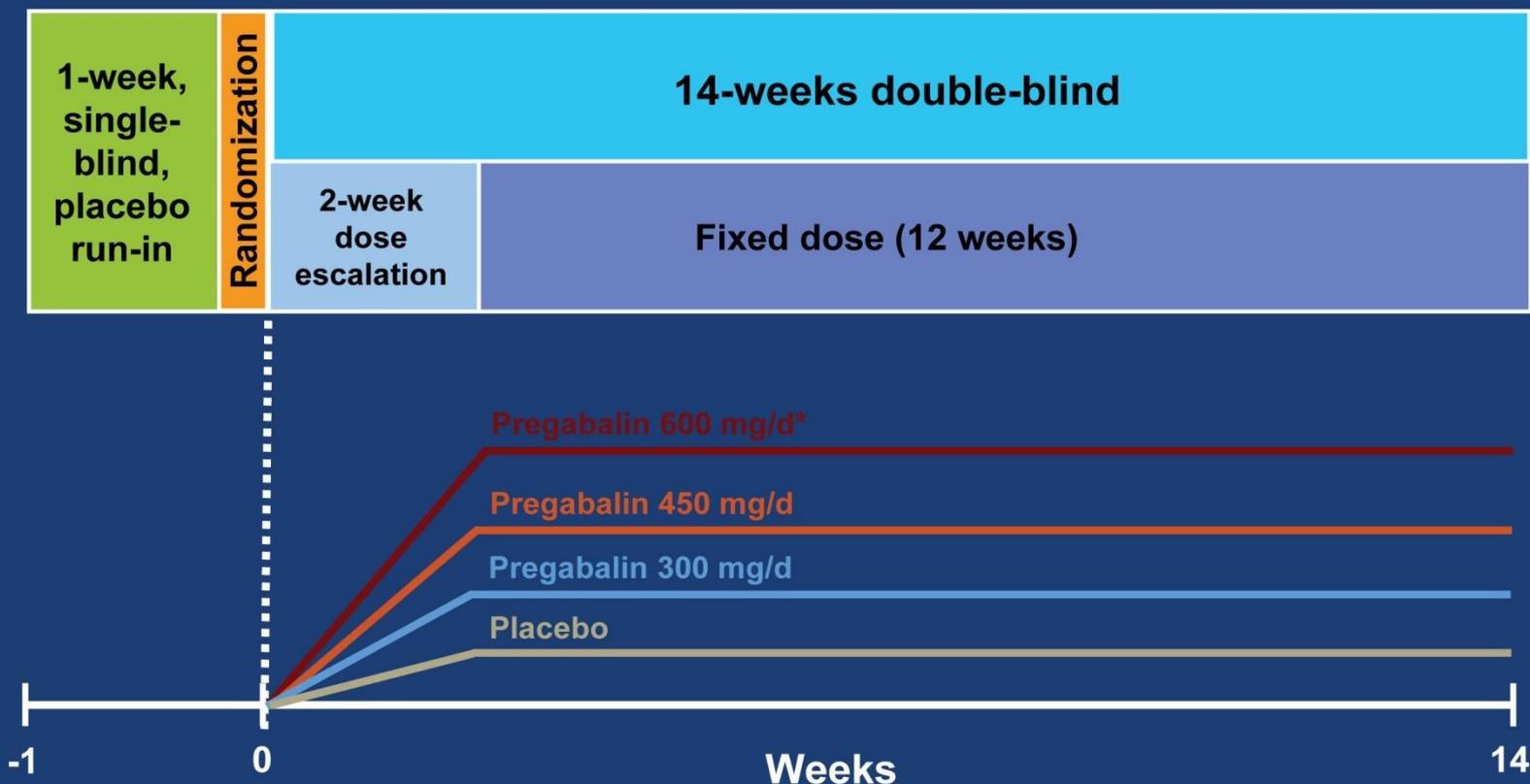
***Secondary end points were included in the study design. The results cannot be discussed as they were not included in the package insert.**

SF-MPQ = Short form McGill Pain Questionnaire.

Pain VAS derived from the SF-MPQ 13-week fixed-dose trial.

Arnold et al. APS, 2007; Data on file. Pfizer Inc, New York, NY.

Pregabalin 14-Week Fixed-Dose FM Trial: Design Overview



*600 mg/d pregabalin dose not approved for use in FM.

Pregabalin 14-Week Fixed-Dose FM Trial: Inclusion and Exclusion Criteria

● Inclusion

- Men or women aged ≥ 18 years
- Fibromyalgia as per ACR criteria
 - Widespread pain >3 months
 - Pain in at least 11/18 specific tender point sites
- Pain VAS ≥ 40 mm at screening and randomization
- Average score ≥ 4 on daily pain diary in week before treatment*

● Exclusion

- Evidence of inflammatory or rheumatologic disease
 - ANA ≥ 3 U, RF >80 IU/mL
- Severe medical illness
- Severe psychiatric illness (including MDD)

*Based on 4 completed out of 7 consecutive daily pain scores.

ACR = American College of Rheumatology; ANA = antinuclear antibody; RF = rheumatoid factor; MDD = major depressive disorder. Wolfe et al. *Arthritis Rheum.* 1990;33:160-172; Arnold et al. *APS*, 2007; Arnold et al. *EULAR*, 2007.

Pregabalin 14-Week Fixed-Dose FM Trial: Allowed and Prohibited Medications

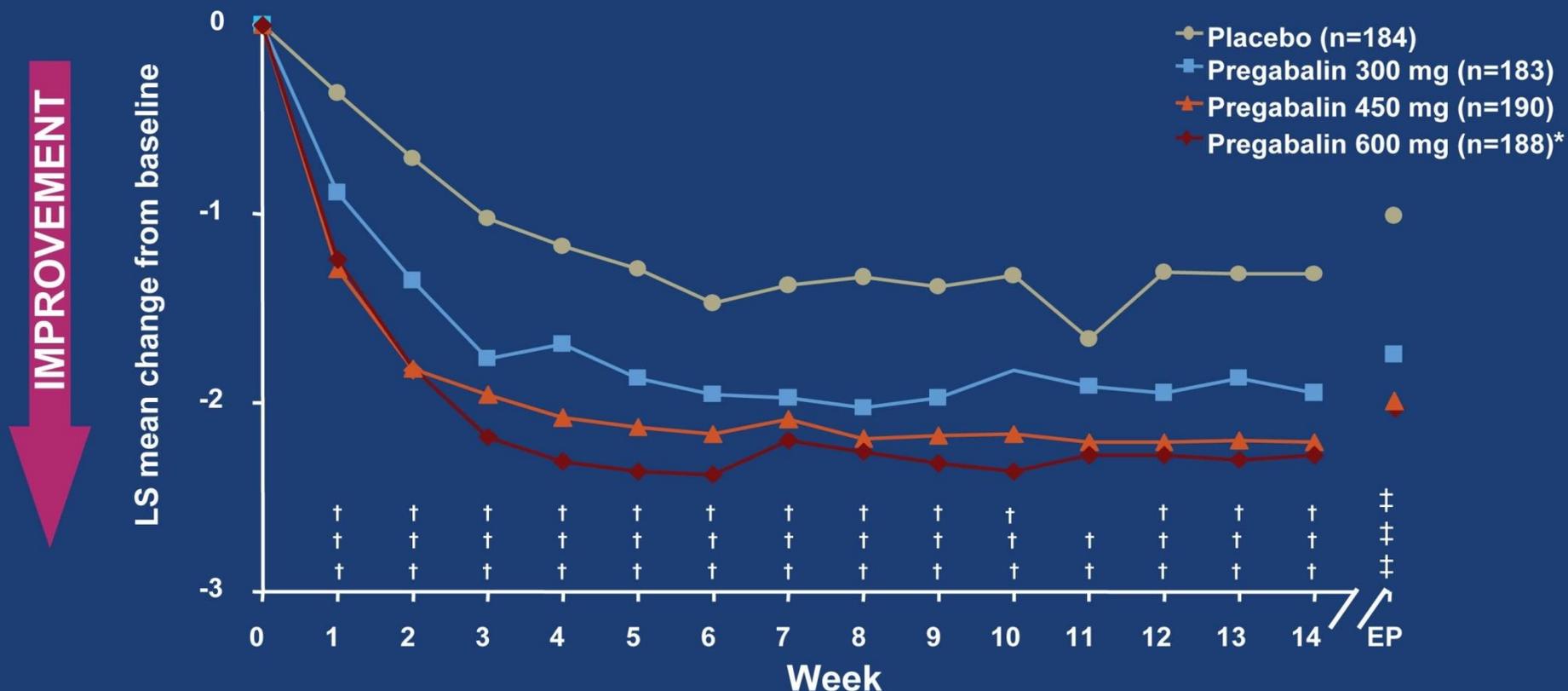
● Allowed medications

- Acetaminophen ≤ 4 g/d as needed for pain relief
- Aspirin ≤ 325 mg/d for MI and stroke prophylaxis

● Prohibited medications

- Skeletal muscle relaxants
- Antidepressants
- Anticonvulsants
- Anti-inflammatory agents (steroids and NSAIDs)
- Hypnotics
- Washout required for 7–30 days before the trial, based on drug half-life

Pregabalin 14-Week Fixed-Dose FM Trial: Significant Improvement in Pain



† $P < 0.01$; ‡ $P \leq 0.0125$.

***600 mg/day of pregabalin is not an approved dose for FM.**

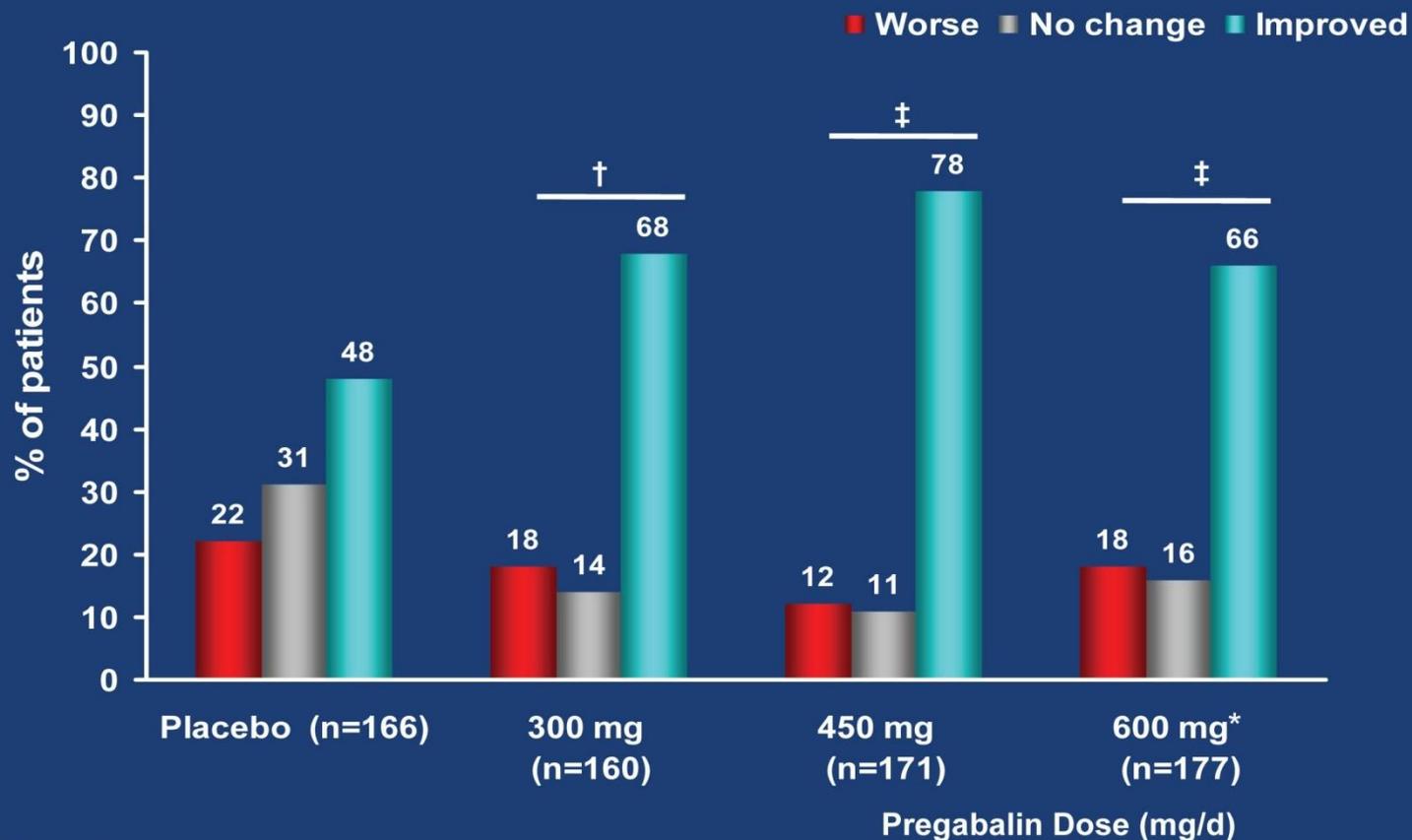
End point mean pain score based on modified baseline observation carried forward approach (BOCF).

Baseline mean = 6.7 (moderate to severe pain).

P value-based LS means using MMRM ANCOVA. Scored 0-10, lower score represents improvement.

Arnold et al. APS 2007; Data on file. Pfizer Inc, New York, NY.

Pregabalin 14-Week Fixed-Dose FM Trial: Patient Global Improvement (PGIC)



† $P < .01$, ‡ $P < .001$ vs placebo.

***600 mg/d of pregabalin is not an approved dose for FM.**

PGIC (Patient Global Impression of Change) is a patient-rated instrument with a scale that ranges from 1-7; scores are as follows: 1-3 = improvement; 4 = no change; 5-7 = worsening. PGIC was analyzed using a last observation carried forward (LOCF) approach. Arnold et al. APS, 2007; Data on file. Pfizer Inc, New York, NY.

Pregabalin 14-Week Fixed-Dose FM Trial: Efficacy Conclusions

- Pregabalin monotherapy is effective in reducing pain associated with FM
 - Some patients experienced a decrease in pain as early as week 1 which persisted throughout the duration of the trial
- Pregabalin demonstrated significant improvement in PGIC at all doses
- Pregabalin demonstrated significant improvement in FIQ at 450 and 600 mg/d
- 600 mg/d provided significant improvement in efficacy over placebo. However, there was no additional benefit over the 450 mg/d dose, but there was evidence of dose-related adverse events*

***600 mg/d of pregabalin is not an approved dose for FM.**

Arnold et al. APS, 2007; Lyrica® (pregabalin) Capsules Cv [package insert]. New York, NY: Pfizer Inc; 2007; Data on file. Pfizer Inc, New York, NY.

Onset and Resolution of Dizziness and Somnolence in Controlled Trials of Pregabalin in FM

	Dizziness	Somnolence
Incidence*	38%	20%
Discontinuation*	6%	3%
Median time to onset	2 days	3 days
Median time to resolution (completers)	17 days	34 days

*All pregabalin dose groups pooled (n=1,517)

85 patients withdrew due to dizziness; 52 patients withdrew due to somnolence.

Among those patients who reported dizziness or somnolence 38% and 58%, respectively continued to experience the reported adverse event for the duration of the trial.

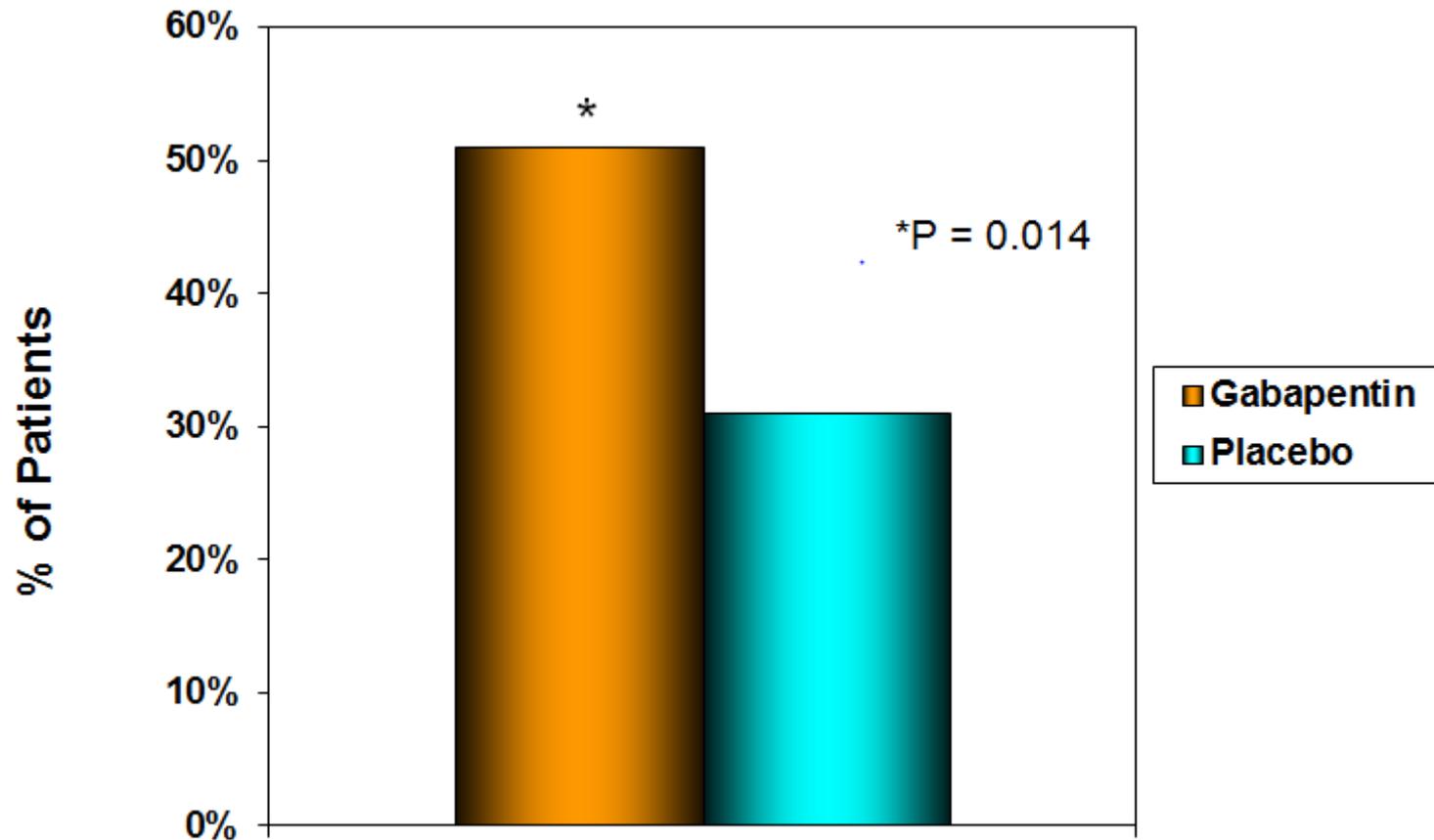
Assessment of safety and tolerability was based on the 3 fixed-dose trials in FM.

Data on file. Pfizer Inc, New York, NY.

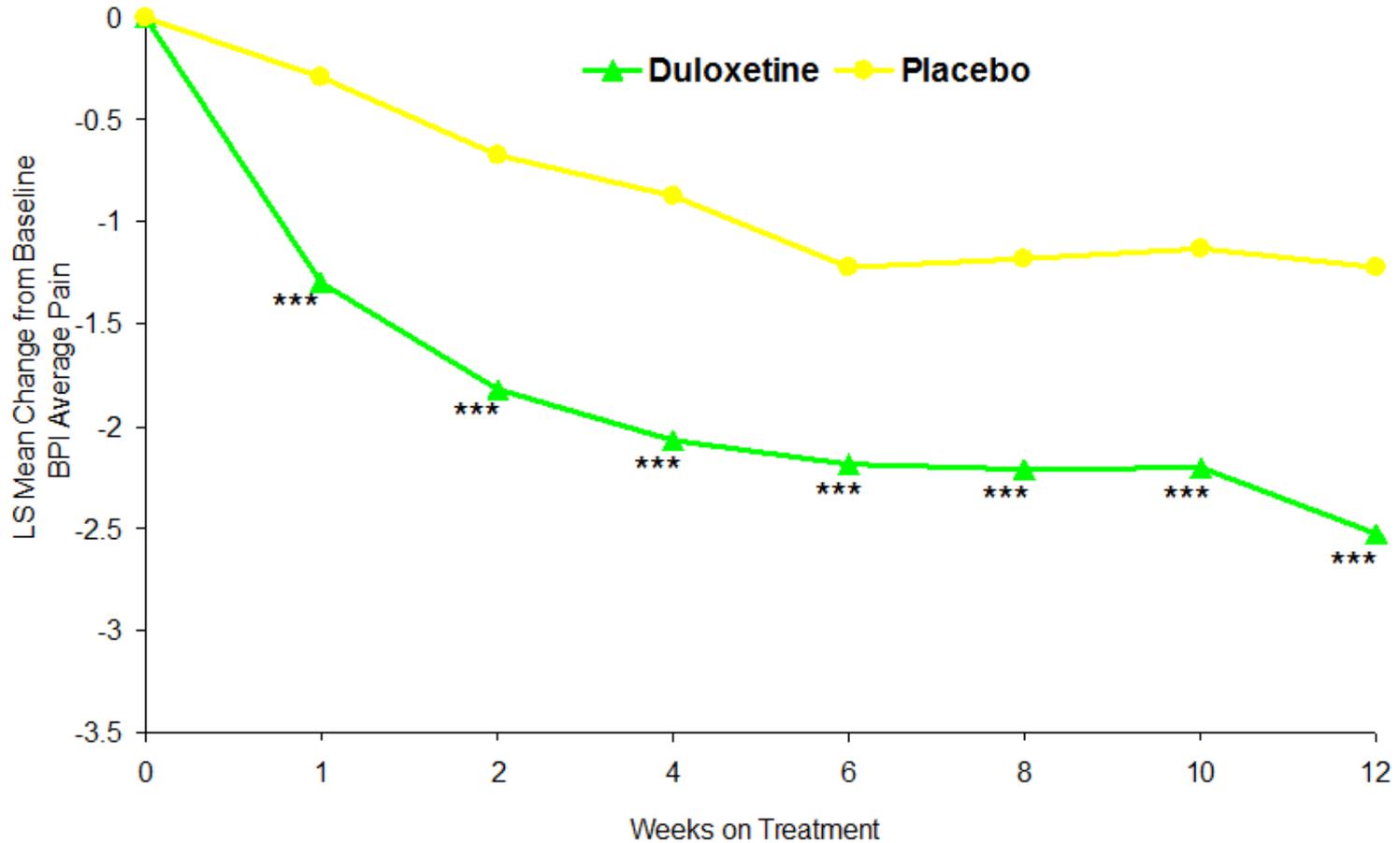
New Fibromyalgia Treatment Approaches

- Combination antidepressants (SSRI+TCA)
- Individualized dosing (fluoxetine)
- Dual reuptake inhibitors (venlafaxine, duloxetine, milnacipran)
- Antiepileptics (gabapentin, pregabalin)
- Patient subsets treated differently
- Combine non-medicinal with drug therapies
- Multi-disciplinary programs

Gabapentin in FM: 30% Reduction on BPI Pain Severity Score

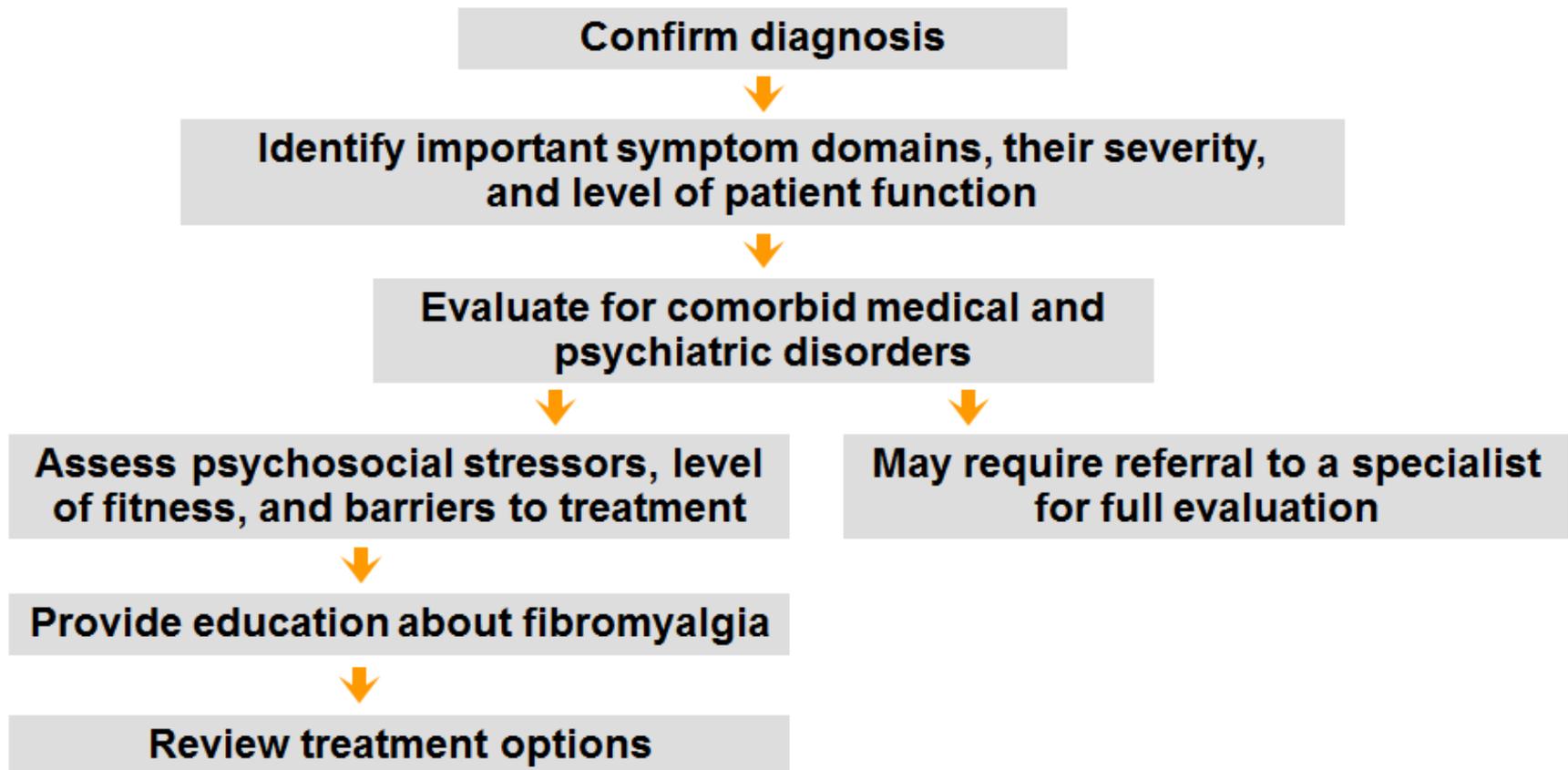


Changes in the Brief Pain Inventory Average Pain Severity Score: Duloxetine vs. Placebo



Arnold LM, et al. J Women's Health 2007;16:1145-1156

Stepwise Treatment of Fibromyalgia



Stepwise Treatment of Fibromyalgia (cont)

As a first-line approach for patients with moderate to severe pain, trial with evidence-based medications



Provide additional treatment for comorbid conditions



Adjunctive CBT for patients with prominent psychosocial stressors, and/or difficulty coping, and/or difficulty functioning



Encourage exercise according to fitness level

Therapies with No to Mixed Evidence in Fibromyalgia

No Evidence

- NSAIDs
- Corticosteroids
- Opiates
- Chiropractic
- Trigger or tender point injections
- TENS units

Mixed Evidence

- SSRIs
- Acupuncture
- Massage
- Strength exercises
- Hypnosis
- Biofeedback
- Balneotherapy

Why isn't FM outcome better with current medical care?

- Long delay in diagnosis, initial therapy.
- Patients are often led to believe they have an intractable disease for which treatment options are limited.
- Need Individual Rx plan with active patient participation.
- Patient subsets.
- Often best handled with multidisciplinary care.

Subgroups of FM Patients

Group 1 (n=50)

- Low depression/anxiety
- Not very tender
- Low catastrophizing
- Moderate control over pain

Psychological factors neutral

Group 2 (n=31)

- Tender
- High depression/anxiety
- Very high catastrophizing
- No control over pain

**Psychological factors
worsening symptoms**

Group 3 (n=16)

- Extremely tender
- Low depression/anxiety
- Very low catastrophizing
- High control over pain

**Psychological factors
improving symptoms**

Does the FM diagnostic label promote helplessness and disability?

- **Recent studies: Diagnostic label is helpful.**
- **Diagnosis should be reassuring and end doctor shopping.**
- **Only if diagnosis is coupled with education.**
- **Causation: issue is contentious.**