Walking the Tightrope: Pain, Addiction, and Suicide

Martin D. Cheatle, PhD
Associate Professor of Psychiatry
Director, Pain and Substance Use Disorder Program
Center for Studies of Addiction

Conflict of interest

- MDC has no conflict of interest related to the topic of this presentation

Learning Objectives

- **Describe the three major risk factors for suicidal behavior in patients with pain and a substance use disorder**
- **Explain the prevailing theory of suicidal ideation and behavior as it pertains to patients with pain and a substance use disorder.**
- **Contrast the pros and cons of the available pharmacologic agents used to treat substance use disorders**

- Suicide Overview
- Suicide and Unintentional Overdoses
- Pain, Mood and Substance Use Disorders
- Risk Factors, Mediators and Conceptual Models
- Risk Assessment and Mitigation
- Summary

CPS-Consequences

- **Untreated or mismanaged pain can lead to adverse effects such as delays in healing, changes in the central nervous system (neuroplasticity), chronic stress, depression, opioid addiction and suicide**

McCaffery & Pasero 1999

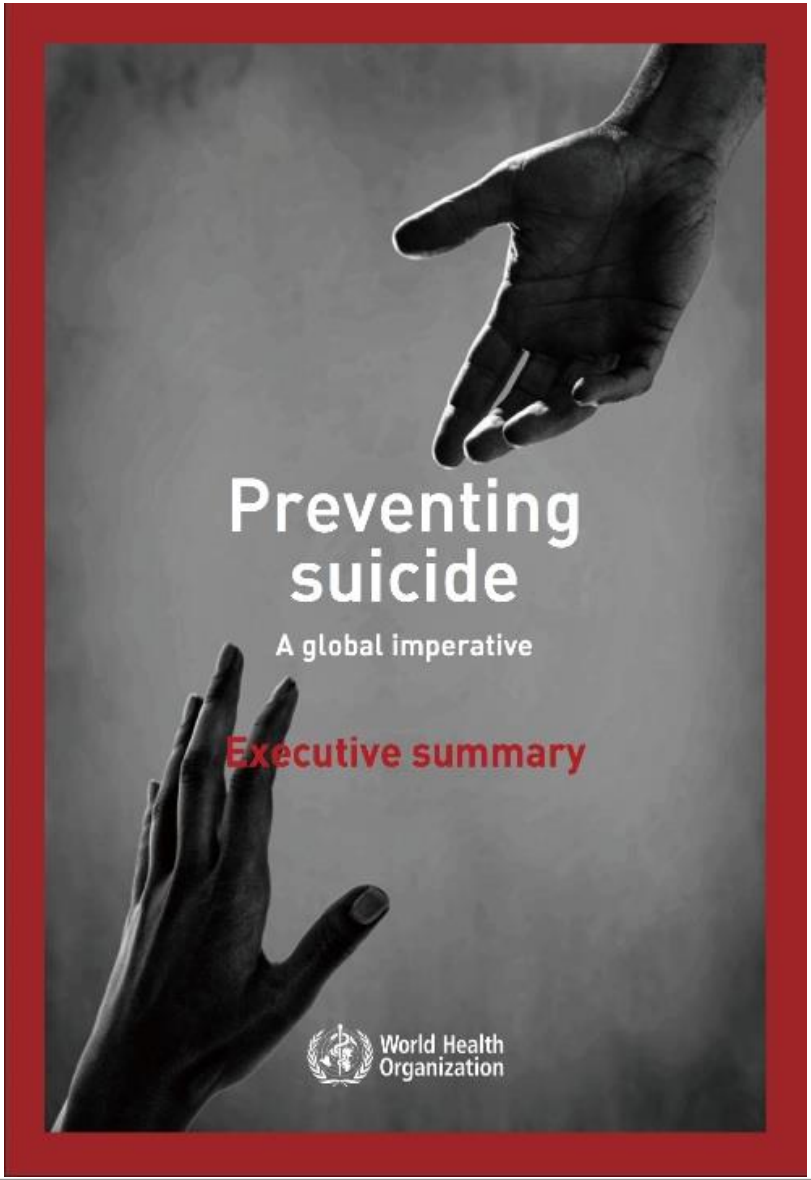
Fishbain 1999

Mendell & Sahenk 2003

“The suffering of the suicidal is private and inexpressible, leaving family members, friends and colleagues to deal with an almost unfathomable kind of loss, as well as guilt. Suicide carries in its aftermath a level of confusion and devastation that is, for the most part, beyond description”.

Kay Redfield Jamison

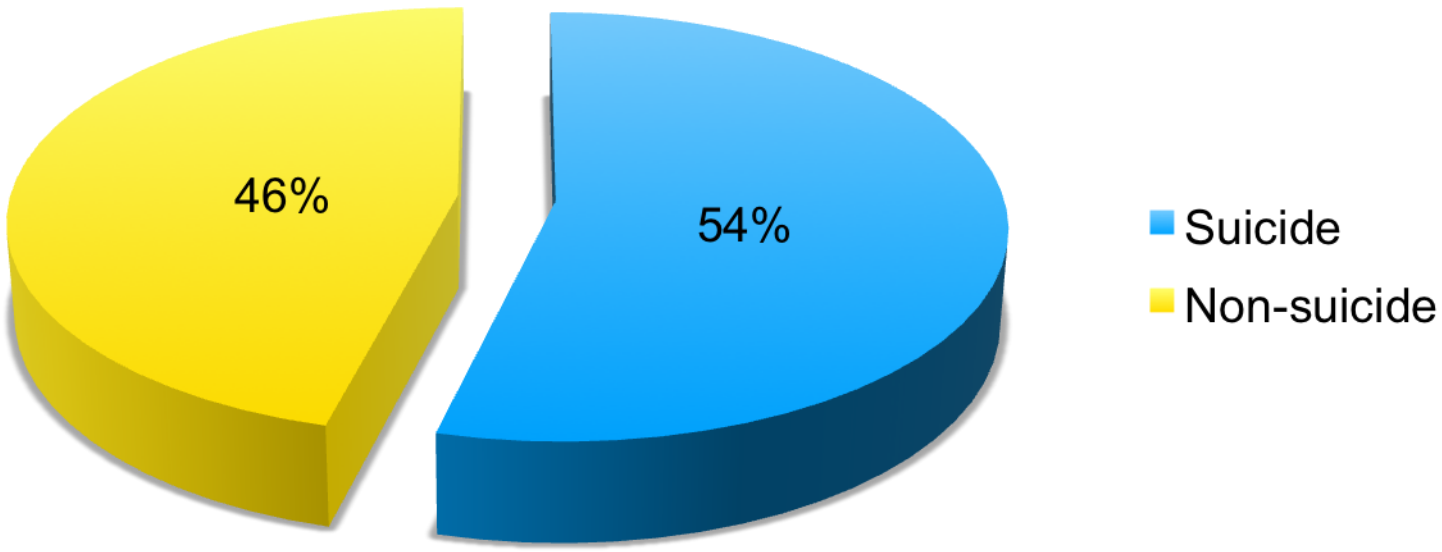
Epidemiology



- Every 40 seconds someone in the world dies of suicide
- An estimated 804,000 suicide deaths occurred worldwide in 2012
- The annual global suicide rate was 11.4 per 100,000 population (15.0 male, 8.0 female)
- In the 15-29 age group it is the second leading cause of death
- Suicide by ingestion of pesticides, hanging and firearms are the most common methods used globally

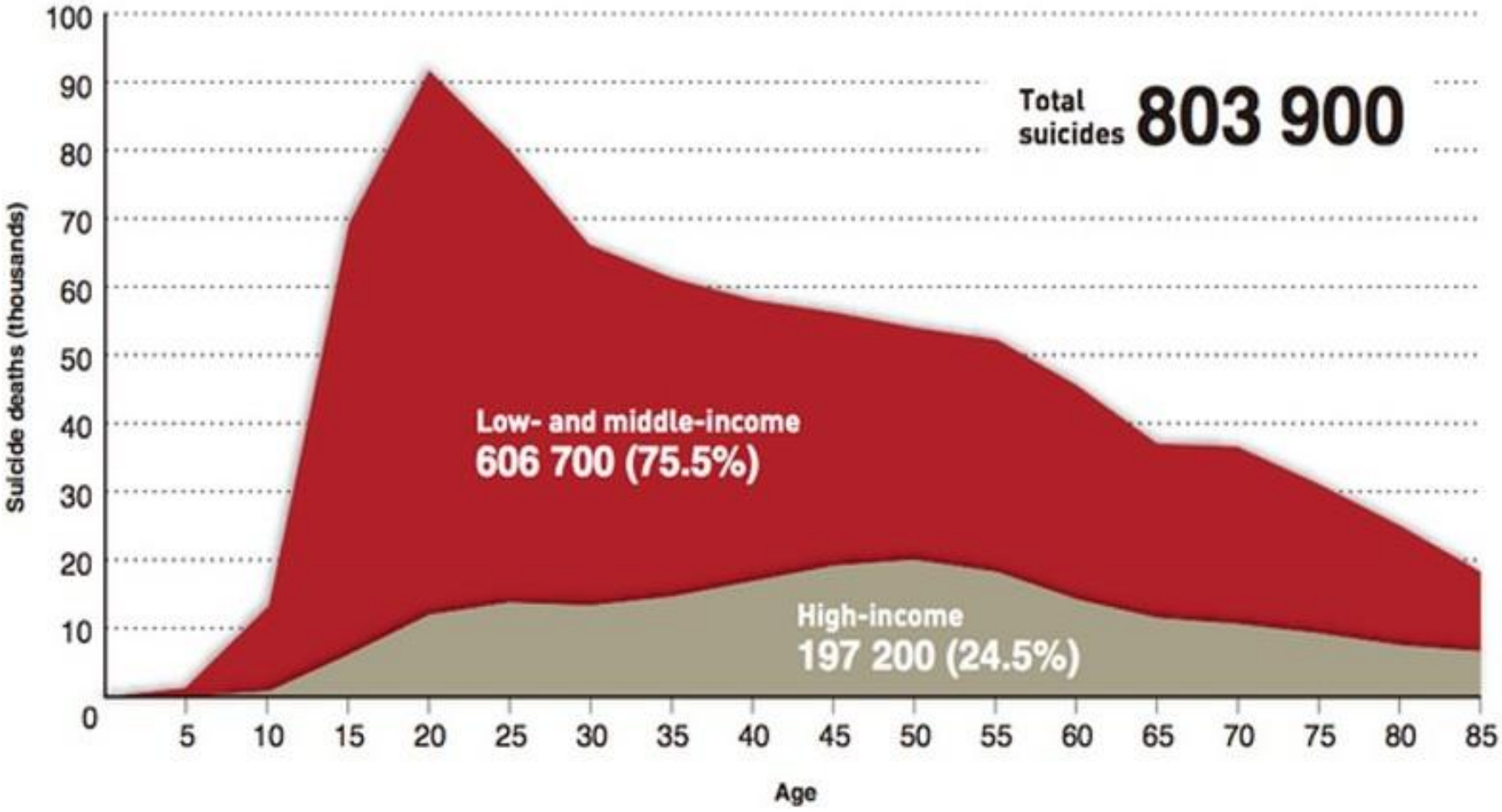
http://www.who.int/mentalhealth/suicide-prevention/exesummaryenglish.pdf

1.5 Million Violent Deaths Per Year



http://www.who.int/mentalhealth/suicide-prevention/exesummaryenglish.pdf

Suicide Rate by Income



Etiology – Biological Factors

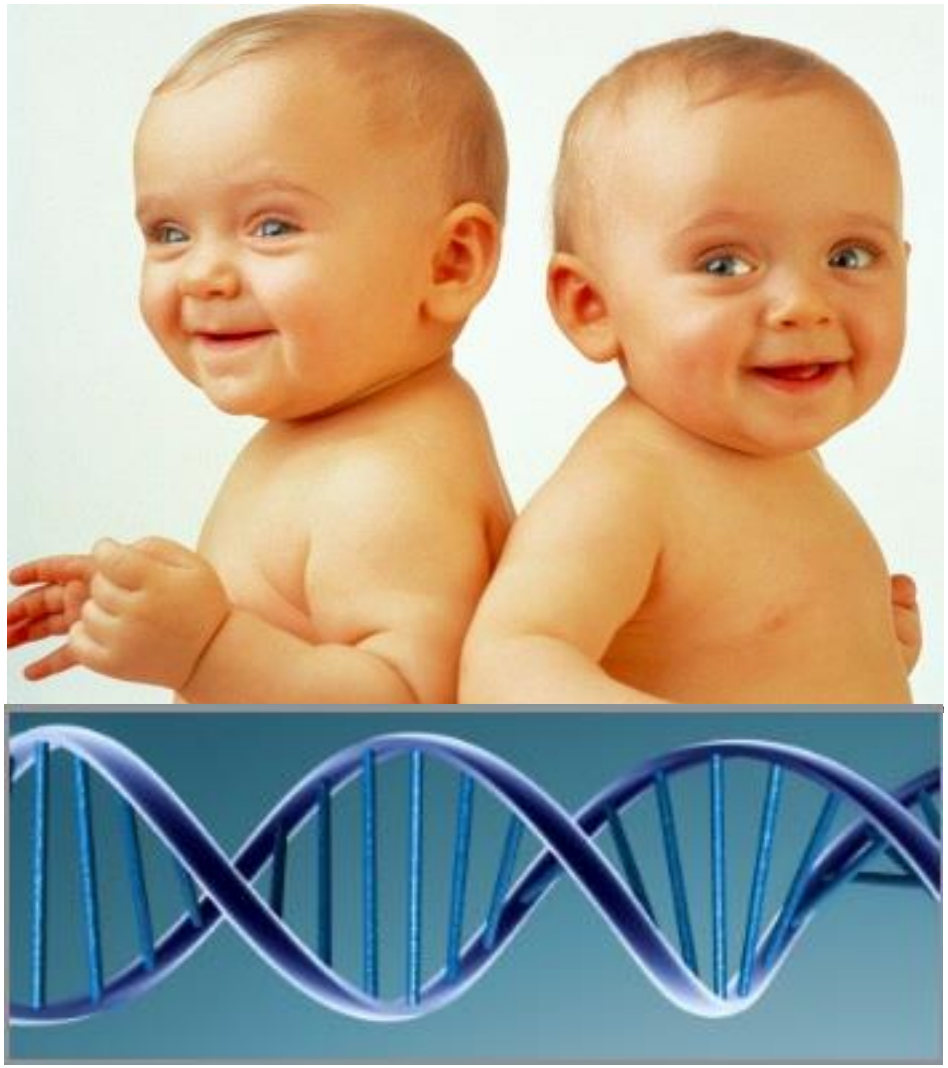
- **Diminished central serotonin plays a role in suicidal behavior**
- **Low concentration of 5-HIAA (5-hydroxyindoleacetic acid) in the CSF predicted future suicidal behavior and was discovered in depressed suicide attempters and in the brain stems of autopsied completed suicide victims**

Lester D (1995) The concentration of neurotransmitter metabolites in the cerebrospinal fluid of suicidal individuals: a meta-analysis. Pharmacopsychiatry. 1995, 28:45–50.

Placidi GP, Oquendo MA, Malone KM, Huang YY, Ellis SP, Mann JJ Aggressivity, suicide attempts, and depression: relationship to cerebrospinal fluid monoamine metabolite levels. Biol Psychiatry. 2001, 50:783–79

Boulougouris V, Malogiannis I, Lockwood G, Zervas I, Di Giovanni G. Serotonergic modulation of suicidal behaviour: integrating preclinical data with clinical practice and psychotherapy. Exp Brain Res. 2013 Oct;230(4):605-24.

Etiology – Genetic Factors



- Suicidal behavior, like other psychiatric disorders, tends to run in families
- In psychiatric patients, a family history of suicide increases the risk of attempted suicide and that of completed suicide in most diagnostic groups
- This has been substantiated with twin studies and adoption studies

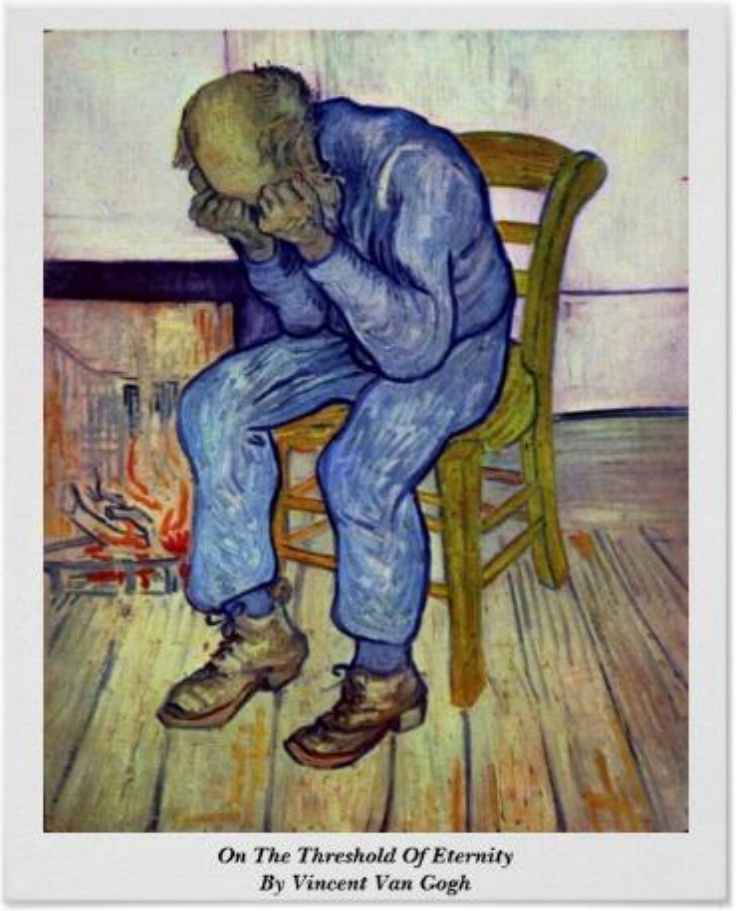
Voracek M, Loibl LM. Genetics of suicide: a systematic review of twin studies. Wien Klin Wochenschr 2007; 119: 463–475

Etiology – Genetic Factors-cont

- Clinical risk factors to date have low predictive value
- A number of potential biomarkers of suicide have been studied
- The most promising to date has been the serotoninergic system, particularly the polymorphism of the gene coding for the serotonin transporter (5-HTTLPR) and brain-derived neurotrophic factor

Costanza A, D'Orta I, Perroud N, Burkhardt S, Malafosse A, Mangin P, La Harpe R. Neurobiology of suicide: do biomarkers exist? Int J Legal Med. 2014 Jan;128(1):73-82.

Pain, Mood and Anxiety Disorders



On The Threshold Of Eternity
By Vincent Van Gogh

Pain 106 (2003) 127–133

PAIN

www.elsevier.com/locate/pain

Mood and anxiety disorders associated with chronic pain: an examination in a nationally representative sample

Lachlan A. McWilliams[a,b,*], Brian J. Cox[b], Murray W. Enns[b]

[a]*Department of Psychology, University of Manitoba, Winnipeg, Man., Canada*
[b]*Department of Psychiatry, PZ-430 PsycHealth Centre, University of Manitoba, 771 Bannatyne Avenue, Winnipeg, Man., Canada R3E 3N4*

Received 4 March 2003; received in revised form 10 July 2003; accepted 18 July 2003

- **National Comorbidity Survey to evaluate the association between chronic pain and common mood and anxiety disorders**
- **Participants (n= 5877) completed the Composite International Diagnostic Interview based on the DSM**

Diagnosis	Number of participants meeting diagnostic criteria (% in parentheses)		Inferential statistics	
	Chronic pain ($n = 382$)	General population ($n = 5495$)	χ^2	p
Any mood disorder	83(21.7)	551(10.0)	32.16	<0.0001
Depression	77(20.2)	510(9.3)	26.53	<0.0001
Dysthymia	20(5.2)	128(2.3)	5.48	<0.01
Any anxiety disorder	134(35.1)	992(18.1)	21.54	<0.0001
Generalized anxiety disorder	28(7.3)	144(2.6)	9.10	<0.005
Panic disorder with or without agoraphobia	25(6.5)	103(1.9)	7.84	<0.01
Simple phobia	60(15.7)	456(8.3)	8.70	<0.01
Social phobia	45(11.8)	428(7.8)	5.91	<0.05
Agoraphobia with or without panic	32(8.4)	182(3.3)	6.52	<0.05
Posttraumatic stress disorder	41(10.7)	182(3.3)	16.29	<0.001

Diagnoses were made using the *Composite International Diagnostic Interview*. Psychiatric diagnostic categories were not mutually exclusive.

Pain, SUD and Suicidal Ideation

- **There is robust literature that there is a high prevalence of SI in patients with pain ranging from18% to > 50%**

Hitchcock L, Ferrell B, McCaffery M. The experience of chronic nonmalignant pain. *J Pain Symptom Manage* 1994; 9: 312-318.

Stenager EN, Stenager E, Jensen K. Attempted suicide, depression and physical diseases: a 1-year follow-up study. *Psychother Psychosom* 1994; 61: 65-73.

Fishbain DA, Goldberg M, Rosomoff RS, Rosomoff H. Completed suicide in chronic pain. *Clin J Pain* 1991; 7: 29-36.

Fishbain DA. The association of chronic pain and suicide. *Semin Clin Neuropsychiatry* 1999; 4: 221–227.

Smith MT, Edwards RR, Robinson RC, Dworkin RH. Suicidal ideation, plans and attempts in chronic pain patients: Factors associated with increased risk. *Pain* 2004; 111: 201-208.

Braden JB, Sullivan MD. Suicidal thoughts and behavior among adults with self-reported pain conditions in the national comorbidity survey replication. *J Pain* 2008; 9:1106-1115.

Ilgen MA, Zivin K, McCammon RJ, Valenstein M. Pain and suicidal thoughts, plans and attempts in the United States. *Gen Hosp Psychiatry* 2008; 30: 521-527.

Ratcliffe GE, Enns MW, Belik SL, Sareen J. Chronic pain conditions and suicidal ideation and suicide attempts: an epidemiologic perspective. *Clin J Pain* 2008; 24 : 204-210.

Substance Abuse and Mental Health Services Administration Office of Applied Studies. *Drug Abuse Warning Network, 2007: Estimates of Drug-Related Emergency Department Visits*. Rockville, MD; 2010.

Racine M, Choinière M, Nielson WR. Predictors of Suicidal Ideation in Chronic Pain Patients: An Exploratory Study. *Clin J Pain*. 2013 Jul 24. [Epub ahead of print]

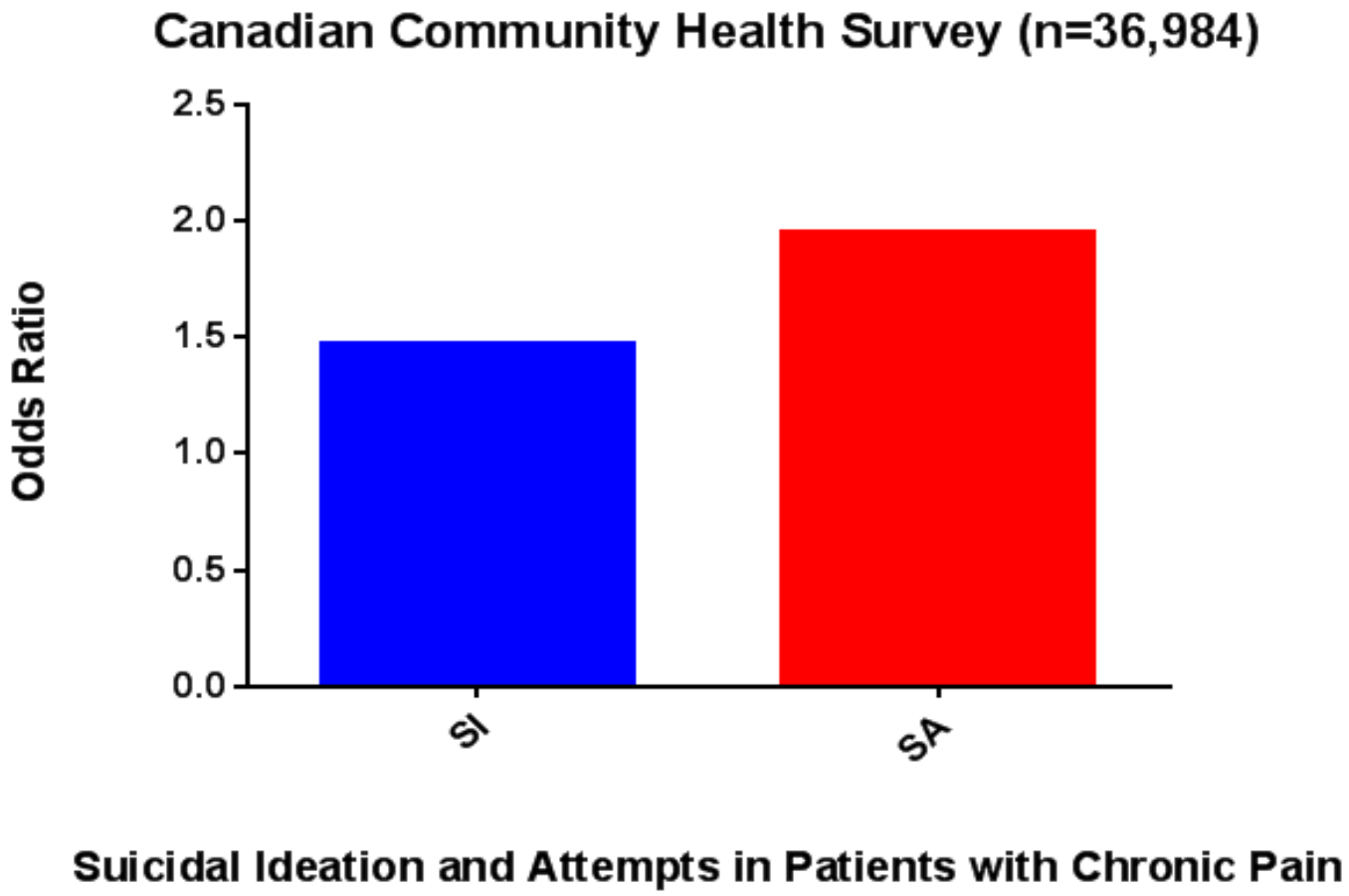
Cheatle M, Wasser T, Foster C, Olugbodi A, Bryan J. Prevalence of suicidal ideation in patients with chronic noncancer pain referred to a behaviorally based pain program. *Pain Phys*, in press.

Edwards RR, Smith MT, Kudel I, Haythornthwaite J. Pain-related catastrophizing as a risk factor for suicidal ideation in chronic pain. *Pain* 2006;126 : 272-279.

- **A systematic review by Tang and Crane revealed that the risk of successful suicide was doubled in patients with CP as compared to non-pain controls**

Tang NK, Crane C. Suicidality in chronic pain: A review of the prevalence, risk factors and psychological links. *Psychol Med* 2006; 36 :575-586.

Suicide and Chronic Pain



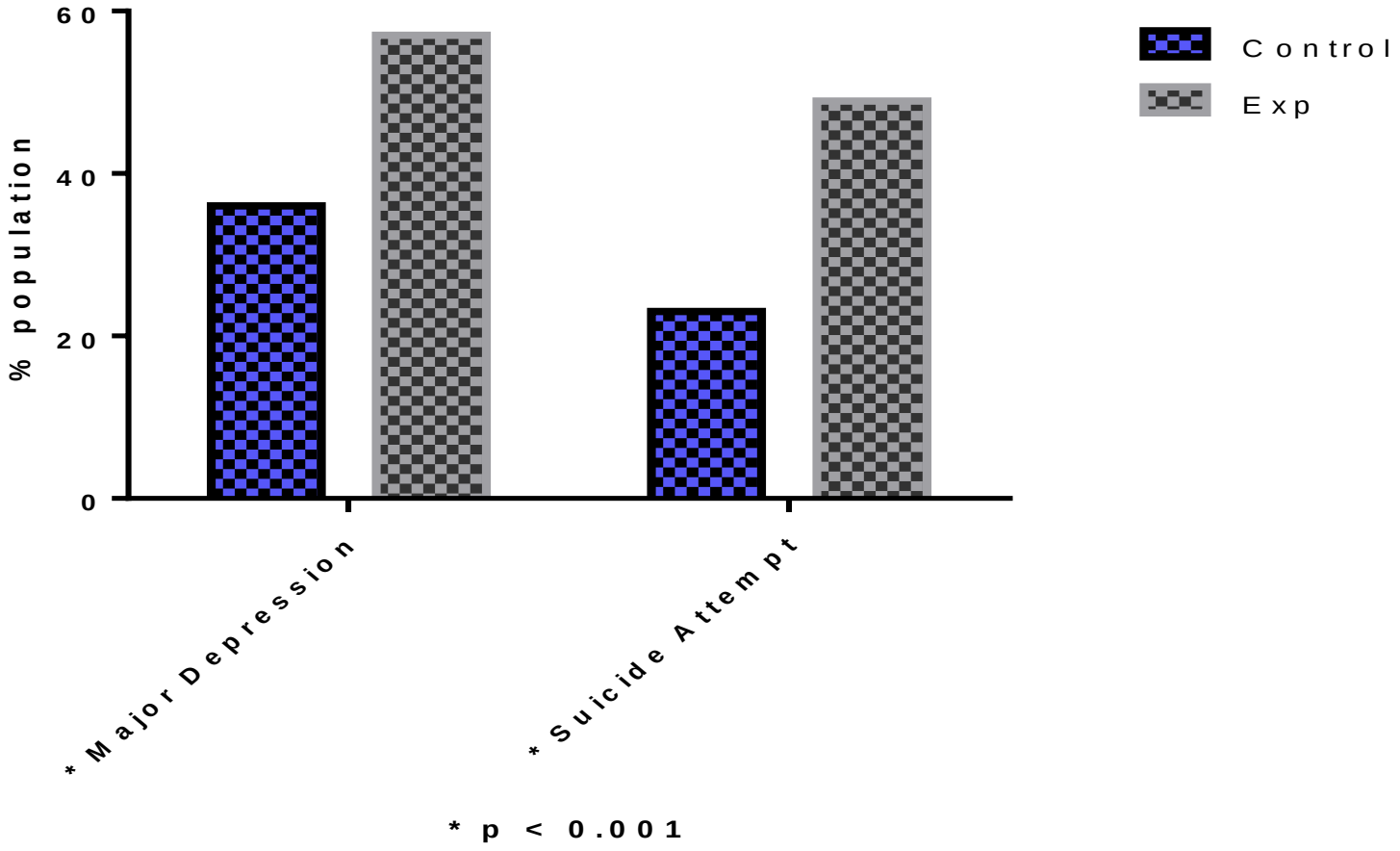
Ratcliffe GE, Enns MW, Belik SL, Sareen J. Chronic pain conditions and suicidal ideation and suicide attempts: an epidemiologic perspective. *Clin J Pain* 2008; 24 : 204-210.

Suicidal Ideation and Behavior and SUD

- **Approximately 40% of patients seeking treatment for substance use disorders report a history of suicide attempts [1-3]**
- **Compared to the general population, those with alcohol use disorders are almost 10 times more likely to die by suicide and those who inject drugs are about 14 times more likely to commit suicide.[4]**

1)Roy A, Janal MN. Risk factors for suicide among alcohol-dependent patients. Arch Suicide Res. 2007; 11:211–217; 2) Roy A. Characteristics of cocaine dependent patients who attempt suicide. Arch Suicide Res. 2009; 13:46–51;3). Roy A. Risk factors for attempting suicide in heroin addicts. Suicide Life Threat Behav. 2010; 40:416–420; 4) Wilcox HC, Conner KR, Caine ED. Association of alcohol and drug use disorders and completed suicide: an empirical review of cohort studies. Drug Alcohol Depend. 2004; 76:S11–S19.

% of Population



Cheatle et al Clinical and genetic characteristics of opioid addiction in patients with chronic pain 1R01DA032776-01 NIH/NIDA

SBQ-R

SBQ-R Suicide Behaviors Questionnaire-Revised

Patient Name _____ Date of Visit _____

Instructions: Please check the number beside the statement or phrase that best applies to you.

1. Have you ever thought about or attempted to kill yourself? (check one only)

- ☐ 1. Never
- ☐ 2. It was just a brief passing thought
- ☐ 3a. I have had a plan at least once to kill myself but did not try to do it
- ☐ 3b. I have had a plan at least once to kill myself and really wanted to die
- ☐ 4a. I have attempted to kill myself, but did not want to die
- ☐ 4b. I have attempted to kill myself, and really hoped to die

2. How often have you thought about killing yourself in the past year? (check one only)

- ☐ 1. Never
- ☐ 2. Rarely (1 time)
- ☐ 3. Sometimes (2 times)
- ☐ 4. Often (3-4 times)
- ☐ 5. Very Often (5 or more times)

3. Have you ever told someone that you were going to commit suicide, or that you might do it? (check one only)

- ☐ 1. No
- ☐ 2a. Yes, at one time, but did not really want to die
- ☐ 2b. Yes, at one time, and really wanted to die
- ☐ 3a. Yes, more than once, but did not want to do it
- ☐ 3b. Yes, more than once, and really wanted to do it

4. How likely is it that you will attempt suicide someday? (check one only)

- ☐ 0. Never
- ☐ 1. No chance at all
- ☐ 2. Rather unlikely
- ☐ 3. Unlikely
- ☐ 4. Likely
- ☐ 5. Rather likely
- ☐ 6. Very likely

SBQ-R

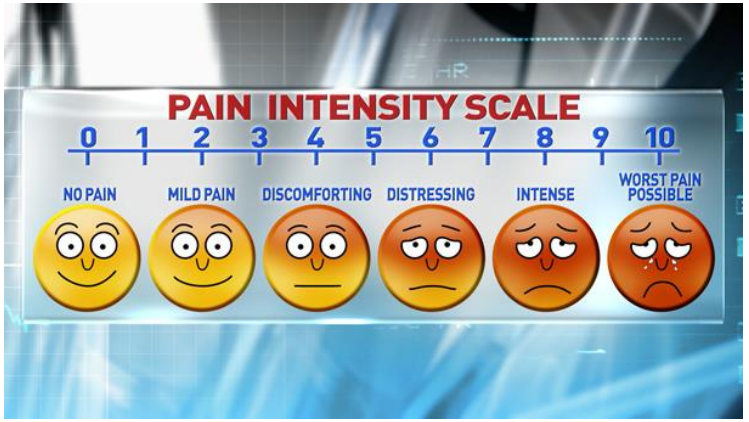
Control	Experimental	p value
Mean= 5.12	Mean= 8.48	0.002**
SD= 3.49	SD= 4.73	

For the SBQR the range of scores is from 3-18 where higher scores indicate more suicidal behavior. A cut point of =/> 7 is considered to indicate high risk for suicide with a sensitivity of 93% and specificity of 95%

Pain and Suicidal Ideation: Risk Factors and Mediators

Risk Factors

- Sleep
- Pain Intensity
- Pain Duration
- Pain Type
- Opioid Dosing

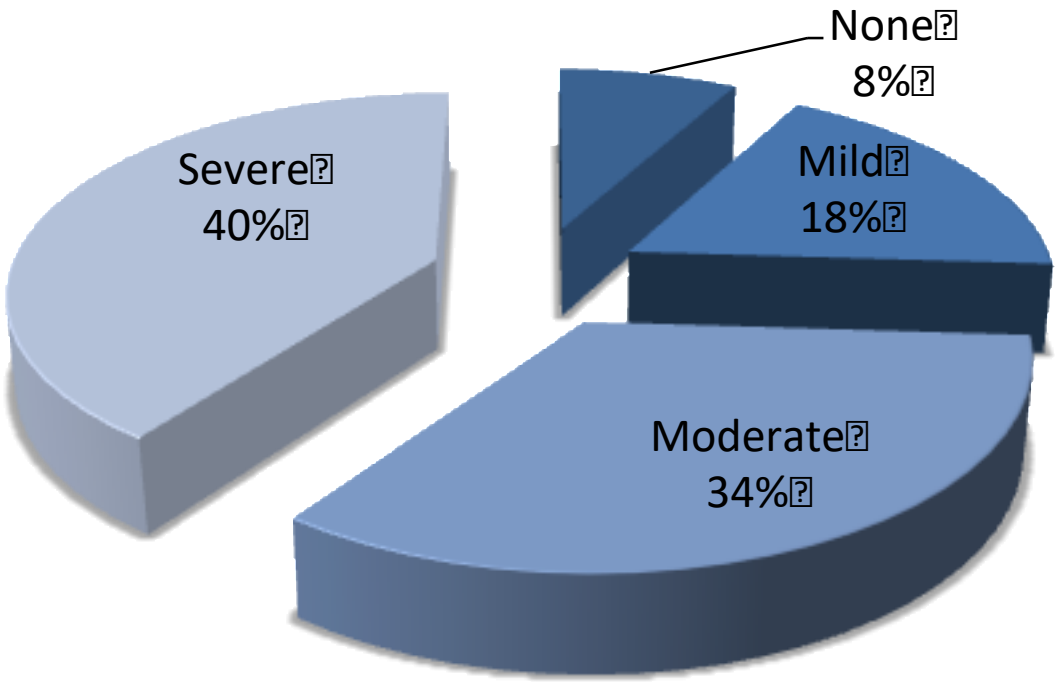


Pain and Sleep Disorders

- **Chronic pain is associated with multiple symptoms that may impair a patient's quality of life, including emotional distress, fatigue and sleep disturbance.**
- **Studies have demonstrated that 50% of patients with a number of different chronic pain conditions complain of sleep disturbance, with estimates as high as 70%-88%.**

Cheatle MD, Foster S, Pinkett A, Lesneski M, Qu D, Dhingra L. Assessing and Managing Sleep Disturbance in Patients with Chronic Pain. Anesthesiol Clin. 2016 Jun;34(2):379-93

% Population Sleep Disturbance (n= 1038)



Cheatle M et al "Clinical and Genetic Characteristics of Opioid Addiction in Chronic Pain" 1RO1DA032776-01 NIH/NIDA unpublished data

Suicidal Ideation in Outpatients With Chronic Musculoskeletal Pain

An Exploratory Study of the Role of Sleep Onset Insomnia and Pain Intensity

Michael T. Smith, PhD, Michael L. Perlis, PhD,†‡ and Jennifer A. Haythornthwaite, PhD**

- 51 outpatients with non-cancer chronic pain were recruited and completed the Pittsburgh Sleep Quality Index, the Beck Depression Inventory, and the Multi-Dimensional Pain Inventory. Subjects were classified as suicidal ideators or non-ideators, based on the BDI
- Results indicated that 24% reported suicidal ideation and endorsed higher levels of sleep-onset insomnia, pain intensity, medication usage, pain related interference, affective distress and depressive symptoms
- Step-wise, discriminate function analysis revealed that sleep onset insomnia severity and pain intensity predicted 84.3% of the cases
- *Authors concluded that chronic pain patients who self-report severe and frequent initial insomnia with concomitant daytime dysfunction and high pain intensity were more likely to report passive suicidal ideation, independent of the effects of depression severity*

Smith MT, et al Clin J Pain 2004; 20 (2):111-8

Pain Intensity

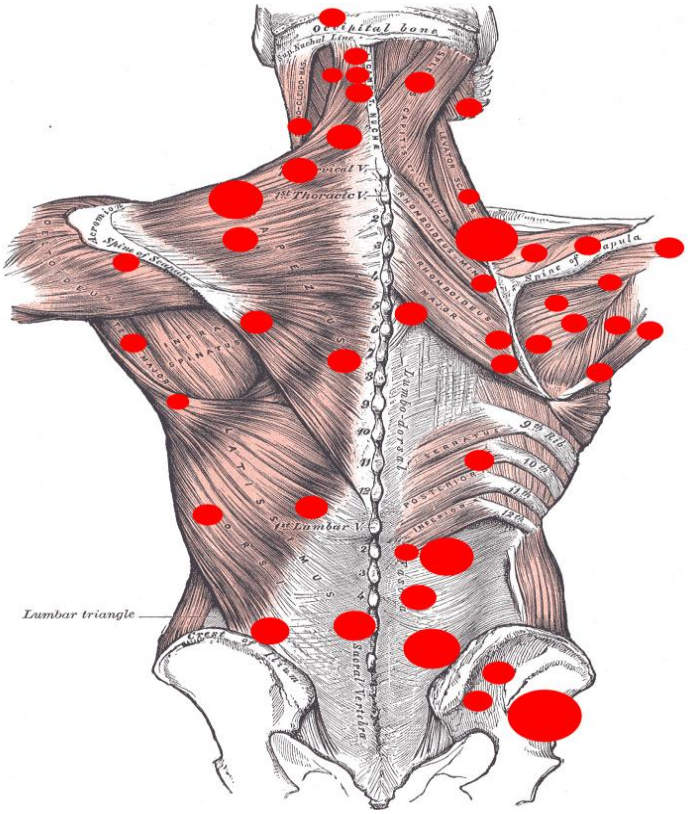
Suicide and Life-Threatening Behavior 40(6) December 2010

Severe Pain Predicts Greater Likelihood of Subsequent Suicide

Mark A. Ilgen, PhD, Kara Zivin, PhD, Karen L. Austin, MPH,
Amy S. B. Bohnert, PhD, Ewa K. Czyz, MA, Marcia Valenstein, MD, MS,
and Amy M. Kilbourne, PhD, MPH

- **Analyzed data Veteran's Affairs' medical records and the National Death Index (n=260,254) evaluating the association between self-assessed pain severity and SB in veterans.**
- **They discovered after controlling for demographic and psychiatric factors that veterans with severe pain were more likely to die by suicide than ones with mild or moderate pain (HR:1.33; 95% CI: 1.15-1.54).**

Potentially Vulnerable Pain Populations



Neuropsychiatric Disease and Treatment

Dovepress
open access to scientific and medical research

Open Access Full Text Article

ORIGINAL RESEARCH

Suicidal ideation and the risk of suicide in patients with fibromyalgia: a comparison with non-pain controls and patients suffering from low-back pain

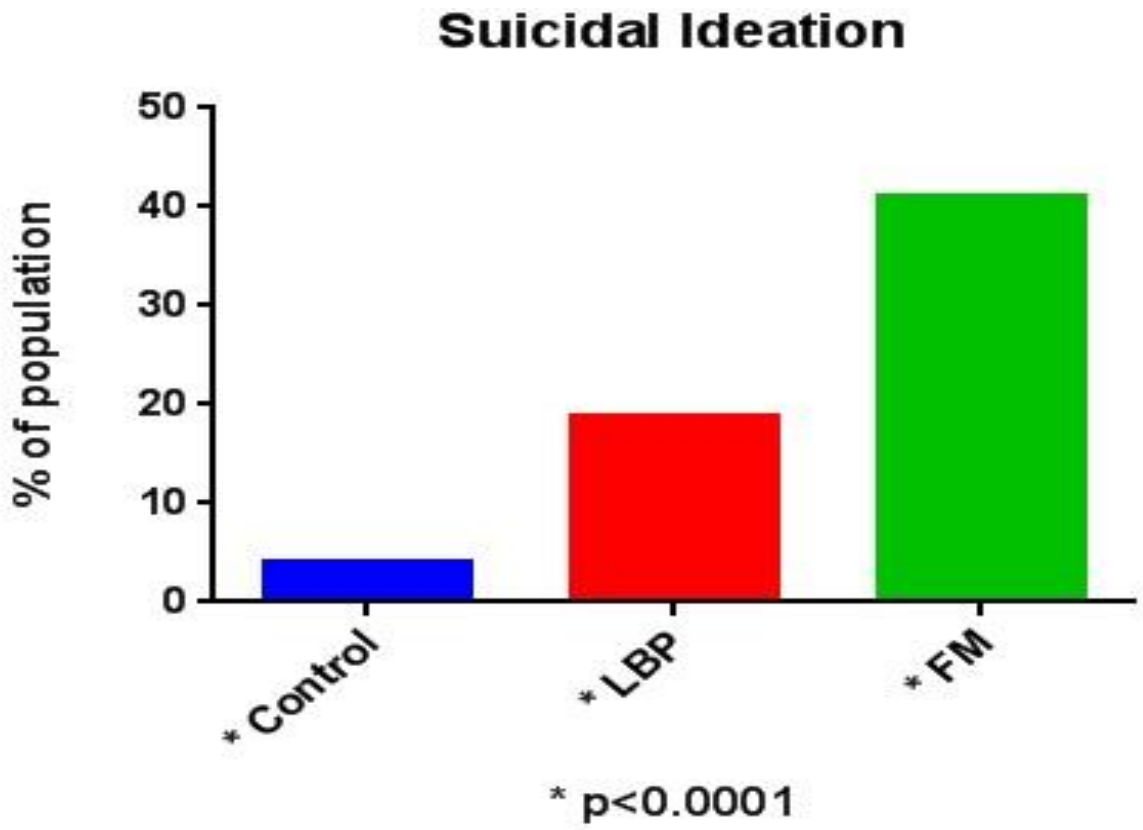
This article was published in the following Dove Press journal:
Neuropsychiatric Disease and Treatment
16 April 2014
Number of times this article has been viewed

Irene Jimenez-Rodríguez[1]
Juan Miguel Garcia-Leiva[1]
Beatriz M Jimenez-Rodriguez[2]
Emilia Condés-Moreno[3]
Fernando Rico-Villademoros[1]
Elena P Calandre[1]

[1]Instituto de Neurociencias, Universidad de Granada, Granada, Spain; [2]Servicio de Neumología, Hospital Universitario Virgen de las Nieves, Granada, Spain; [3]Departamento de Especialidades Biomédicas, Universidad Europea de Madrid, Villaviciosa de Odón, Spain

Abstract: Fibromyalgia is associated with an increased rate of mortality from suicide. In fact, this disease is associated with several characteristics that are linked to an increased risk of suicidal behaviors, such as being female and experiencing chronic pain, psychological distress, and sleep disturbances. However, the literature concerning suicidal behaviors and their risk factors in fibromyalgia is sparse. The objectives of the present study were to evaluate the prevalence of suicidal ideation and the risk of suicide in a sample of patients with fibromyalgia compared with a sample of healthy subjects and a sample of patients with chronic low-back pain. We also aimed to evaluate the relevance of pain intensity, depression, and sleep quality as variables related to suicidal ideation and risks. Logistic regression was applied to estimate the likelihood of suicidal ideation and the risk of suicide adjusted by age and sex. We also used two logistic regression models using age, sex, pain severity score, depression severity, sleep quality, and disease state as independent variables and using the control group as a reference. Forty-four patients with fibromyalgia, 32 patients with low-back pain, and 50 controls were included. Suicidal ideation, measured with item 9 of the Beck Depression Inventory, was almost absent among the controls and was low among patients with low-back pain; however, suicidal ideation was prominent among patients with fibromyalgia ($P<0.0001$). The risk of suicide, measured with the Plutchik Suicide Risk Scale, was also higher among patients with fibromyalgia than in patients with low-back pain or in controls ($P<0.0001$). The likelihood for suicidal ideation and the risk of suicide were higher among patients with fibromyalgia (odds ratios of 26.9 and 48.0, respectively) than in patients with low-back pain (odds ratios 4.6 and 4.7, respectively). Depression was the only factor associated with suicidal ideation or the risk of suicide.

Keywords: chronic low-back pain, suicidal risk, depression


Suicidal Ideation
% of population
50
40
30
20
10
0
* Control
* LBP
* FM
* p<0.0001

	OR	95% CI	*P*-value
Suicidal ideation			
Fibromyalgia	26.889	5.72–126.42	<0.0001
Low-back pain	4.583	0.826–25.432	0.082
Risk of suicide			
Fibromyalgia	48.000	12.929–178.206	<0.0001
Low-back pain	4.725	1.297–17.209	0.019

Risk Factors for Suicidal Ideation among Patients with Complex Regional Pain Syndrome

Do-Hyeong Lee[1], Eun Chung Noh[2], Yong Chul Kim[3], Jae Yeon Hwang[5], Sung Nyun Kim[1], Joon Hwan Jang[1], Min Soo Byun[1], and Do-Hyung Kang[1,4] ✉

[1]Department of Neuropsychiatry, Seoul National University Hospital, Seoul, Republic of Korea
[2]Interdisciplinary Program of Neuroscience, Seoul National University, Seoul, Republic of Korea
[3]Department of Anesthesiology and Pain Medicine, Seoul National University Hospital, Seoul, Republic of Korea
[4]Department of Psychiatry, Seoul National University College of Medicine, Seoul, Republic of Korea
[5]Department of Psychiatry, SMG-SNU Boramae Medical Center, Seoul, Republic of Korea

Objective Chronic pain frequently coexists with psychiatric symptoms in patients diagnosed with complex regional pain syndrome (CRPS). Previous studies have shown a relationship between CRPS and the risk of suicide. The purpose of this study was to assess risk factors for suicidal ideation in patients with CRPS.

Methods Based on criteria established by the International Association for the Study of Pain, 39 patients diagnosed with CRPS Type 1 or Type 2 were enrolled in this study. Suicidal ideation was assessed using item 3 of the Hamilton Depression Rating Scale (HAMD), and symptoms of pain were evaluated using the short form of the McGill Pain Questionnaire (SF-MPQ). Psychiatric symptoms were assessed in using the Structured Clinical Interview for DSM-IV Disorders (SCID-I, SCID-II), the HAMD, the Hamilton Anxiety Rating Scale (HAMA), the Global Assessment of Functioning Scale (GAF), and the Pittsburgh Sleep Quality Index (PSQI).

Results Twenty-nine patients (74.4%) were at high risk and 10 (25.6%) were at low risk for suicidal ideation. Risk factors significantly associated with suicidal ideation included depression ($p=0.002$), severity of pain ($p=0.024$), and low scores on the GAF ($p=0.027$). No significant correlations were found between suicidal ideation and anxiety or quality of sleep.

Conclusion Significant risk factors for suicidal ideation in patients with CRPS include severity of pain, depressive symptoms, and decreased functioning. These results suggest that psychiatric evaluation and intervention should be included in the treatment of CRPS.

Psychiatry Investig 2014;11:32-38

Opioid Dosing

Pain. 2016 May ; 157(5): 1079–1084. doi:10.1097/j.pain.0000000000000484.

Opioid dose and risk of suicide

Mark A. Ilgen, PhD[1,2], Amy S. B. Bohnert, PhD[1,2], Dara Ganoczy, MPH[1], Matthew J. Bair, MD[3,4], John F. McCarthy, PhD[1,2], and Frederic C. Blow, PhD[1,2]

- **Retrospective data analysis on the risk of suicide by different opioid doses in Veterans with CNMP.**
- **After controlling for demographic and other clinical features (depression, PTSD etc) the results indicated that higher opioid doses were associated with increased risk of suicide mortality**
- **Compared with individuals that received </= 20 mg morphine equivalent daily dose (MEDD), those prescribed 20 to 50 MEDD had a hazard ratio (HR) of 1.48 (95% CI: 1.25-1.75); 50 to ,100 MEDD HR of 1.69 (95% CI: 1.33-2.14); and 100 + a HR of 2.15 (95% CI: 1.64-2.81).**

Possible Mediators

Catastrophizing

Burdensomeness

Social Isolation

Mental Defeat

Pain 126 (2006) 272–279

PAIN

www.elsevier.com/locate/pain

Pain-related catastrophizing as a risk factor for suicidal ideation in chronic pain

Robert R. Edwards [a,*], Michael T. Smith [a], Ian Kudel [b], Jennifer Haythornthwaite [a]

[a] Department of Psychiatry and Behavioral Sciences, Johns Hopkins University School of Medicine, 600 N. Wolfe Street, Meyer 1-108, Baltimore, MD 21287, USA

[b] Health Services Research and Development, Cincinnati VA Medical Center, USA

Received 16 January 2006; received in revised form 13 June 2006; accepted 6 July 2006

- 1,512 patients seeking treatment for chronic pain completed a variety of questionnaires assessing pain, coping and psychosocial functioning
- Approximately 32% of this population reported some form of recent suicidal ideation
- Results indicated that the 2 predictors of the presence and degree of suicidal ideation were the magnitude of depressive symptoms and the degree of pain-related catastrophizing
- *Authors concluded that independent of pain severity or depressive symptomatology there is a strong association between pain-coping strategies and suicide related cognitions*

Suicidal Ideation and Perceived Burdensomeness in Patients with Chronic Pain

Kathryn E. Kanzler, PsyD*; Craig J. Bryan, PsyD, ABPP†; Donald D. McGeary, PhD, ABPP‡; Chad E. Morrow, PsyD, ABPP§

*Department of Behavioral Medicine, Wilford Hall Medical Center, Lackland AFB, San Antonio, Texas; †National Center for Veterans Studies, University of Utah, Salt Lake City, Utah; ‡Department of Psychiatry, University of Texas Health Science Center at San Antonio, San Antonio, Texas; §Mental Health Clinic, Maxwell Air Force Base, Montgomery, Alabama, U.S.A.

- 113 patients referred for pain related health complaints to a Clinical Health Psychology clinic
- Intake interview included BDI-II, MPQ and one question on burdensomeness "It would be better for everyone involved if I were to die'' on a 5-point Likert scale measuring frequency of having the thought (1 = ''Never or none of the time'' to 5 = ''Always or a great many times'')
- Results revealed that perceived *burdensomeness* was the sole significant predictor of SI (b = 3.068, P = 0.004, OR = 21.503 [2.680 to 172.547]).

Pain Pract. 2012 Nov;12(8):602-9

Pain Physician 2014; 17:E359-E367 • ISSN 2150-1149

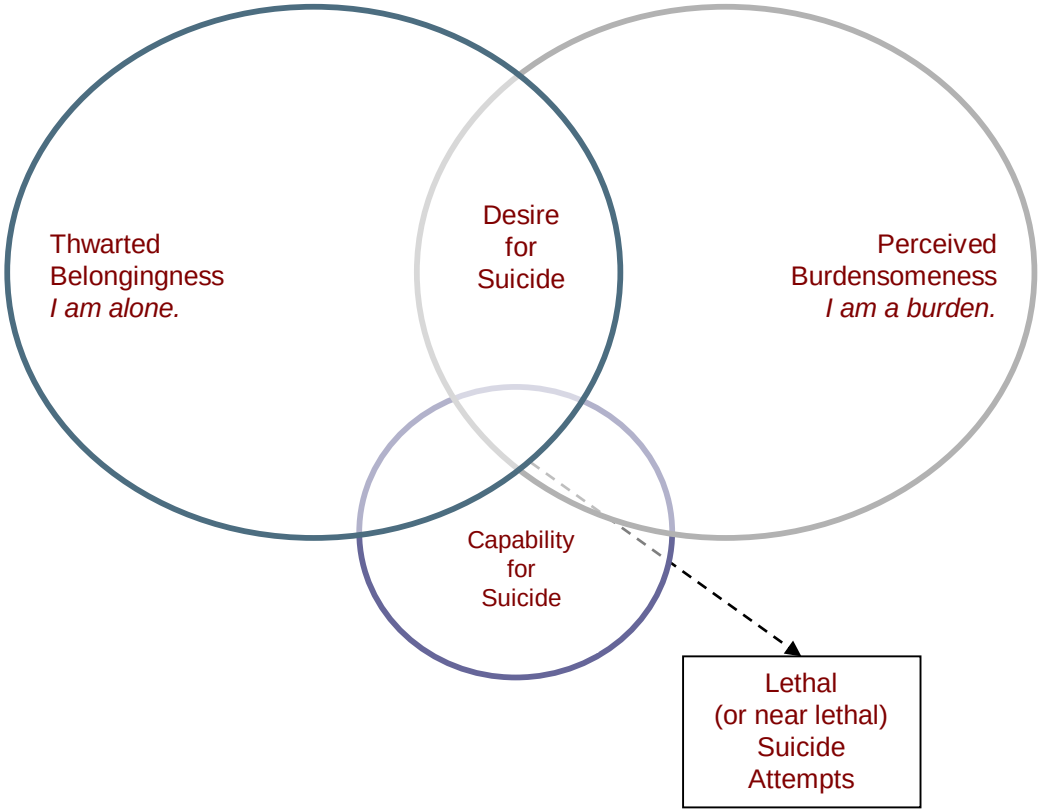
Retrospective Review

Prevalence of Suicidal Ideation in Patients with Chronic Non-Cancer Pain Referred to a Behaviorally Based Pain Program

Martin D. Cheatle, PhD[1,2], Thomas Wasser, PhD[3], Carolyn Foster, MSN[1], Akintomi Olugbodi, MD[2], and Jessica Bryan, BA[1]

- A retrospective chart review of 466 patients with CNCP treated in a behaviorally based pain program
- Results revealed a high rate of SI (26%).
- Logistic regression revealed that history of sexual/ physical abuse (Beta=0.825; p<0.020; OR=2.657 [95% CI=1.447-4.877]), family history of depression (Beta=0.471; p<0.006; OR= 1.985 [95% CI= 1.234-3.070]) and being ***socially withdrawn*** (Beta=0.482; p< 0.001; OR= 2.226 [95% CI= 1/413-3.505]) were predictive of SI

Interpersonal Theory of Suicide



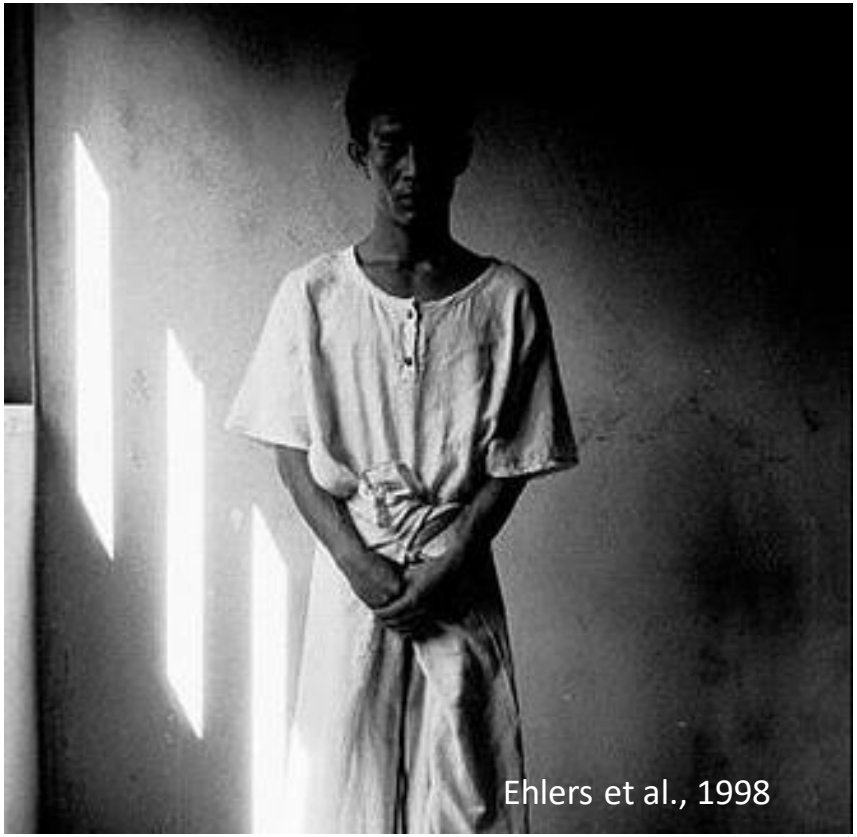
Joiner TE, Pettit JW, Walker RL, et al. Perceived burdensomeness and suicidality: two studies on the suicide notes of those attempting and those completing suicide. J Soc Clin Psychol. 2002;21:531–545.

Mental defeat

Depression - Social Rank Theory

Gilbert & Allan, 1998

PTSD – CBT & Exposure therapy



Ehlers et al., 1998

Mental defeat in chronic pain

- A concept to characterise the deeper impact of pain on self-concept
- A state of mind marked by a sense of a loss of autonomy, agency and human integrity
- A type of self-processing, where persistent pain results in negative beliefs about the self in relation to pain

Tang et al, 2007 CJP; Tang et al., 2010; PAIN

Mental defeat

- **“Defeat of the mind”**
- **“The pain is taking over and you cannot cope with what you are supposed to do”**
- **“I just felt everything had beaten me and there’s nothing I could do. I couldn’t fight anymore.”**
- **“The pain belittles you as a person”**
- **“It’s like you’re not a human being”**

Tang, Salkovskis et al., 2009; BJCP, 48; 1-20

Mental Defeat Is Associated With Suicide Intent in Patients With Chronic Pain

Nicole K.Y. Tang, DPhil, Philippa Beckwith, DClinPsych,† and Polly Ashworth, DClinPsych‡*

- **N=62 chronic pain pts (42F; 20M)**
- **Past suicide attempts**
  - 12.9% once
  - 9.7% twice or more
- **Current and worst ever suicidal ideation**
  - Beck Scale of Suicide Ideation – to measure intent
- **Other psychological predictors of suicidality**
  - Depression, Anxiety, Hopelessness and Pain self-efficacy

Tang NK, Beckwith P, Ashworth P. Mental Defeat Is Associated With Suicide Intent in Patients With Chronic Pain. Clin J Pain. 2016 May;32(5):411-9.

Correlations with suicide intent

	Suicidal ideation (Worst ever)	Suicidal Ideation (In the past week including today)
Anxiety	0.33*	0.002
Depression	0.32*	0.19
Pain Self-Efficacy	-0.20	0.005
Hopelessness	0.19	-0.12
Mental defeat	0.45**	0.13

Correlation between worst ever & current SI = 0.33**

Risk Mitigation

- Risk Assessment
- Intervention

Cheatle MD. Depression, Chronic Pain, and Suicide by Overdose: On the Edge. Pain Medicine. 2011;12(s2):S43-S48.

Risk Assessment

- Age >45
- Gender (female)
- Alcohol dependence
- Past suicide attempts
- History of psychological hospitalization
- Poor social support
- Unemployed
- Divorced
- Mental disorders

Centers for Disease Control and Prevention (CDC), National center for Injury Prevention and Control. 2010. Suicide: Risk and protective factors. Available at: http://www.cdc.gov/ViolencePrevention/suicide/riskprotectivefactors.html (accessed June 2015).

Assessment

- Mental Health Screening
- Suicide Risk
- SUD Screening
- UDS

Mental Health Screening Tools

Tool	# of Items	Time to Complete
Beck Depression Inventory II (Beck et al, 1996)	21	5 - 10 minutes
Beck Depression Inventory – Fast Screen for Medical Patients (Beck et al, 2000)	7	< 5 minutes
Profile of Mood States II: Full	65	10 - 15 minutes
Short (McNair et al, 1971)	35	5 - 10 minutes
Zung Self-Rating Depression Scale (Zung 1965)	20	10 minutes
Center for Epidemiologic Studies Depression Scale: Full	20	5 - 10 minutes
Short (Radloff, 1977)	10	5 minutes
Patient Health Questionnaire: PHQ-9	9	5 minutes
PHQ-4 (Kroenke et al19990	4	< 5minutes

Opioid Abuse and SUD Screening Tools

Patients considered for long-term opioid therapy:	Items	Administered
ORT Opioid Risk Tool	5	By patient
SOAPP® Screener & Opioid Assessment for Patients w/ Pain	24, 14, & 5	By patient
DIRE Diagnosis, Intractability, Risk, & Efficacy Score	7	By clinician
Characterize misuse once opioid treatments begins:		
PMQ Pain Medication Questionnaire	26	By patient
COMM Current Opioid Misuse Measure	17	By patient
PDUQ Prescription Drug Use Questionnaire	40	By clinician
Not specific to pain populations:		
CAGE-AID Cut Down, Annoyed, Guilty, Eye-Opener Tool, Adjusted to Include Drugs	4	By clinician
RAFFT Relax, Alone, Friends, Family, Trouble	5	By patient
DAST Drug Abuse Screening Test	28	By patient
SBIRT Screening, Brief Intervention, & Referral to Treatment	Varies	By clinician
AUDIT-C Alcohol Use Disorders Identification Test Consumption	3	By patient

Urine Drug Monitoring

- **Recent guidelines (Chou et al, 2009) recommend periodic UTS for CNCP patients on COT**
- **Assess only the presence of a particular drug and/or metabolite in a specific concentration at a specific moment in time**
- **A positive result does *not* diagnose**
  - Drug addiction
  - Physical dependence
  - Impairment
- **Absence of Rx opioid may reflect diversion, but also hoarding**

The P4: A Brief Measure

Past suicide attempts

Suicide **P**lan

Probability of completing suicide

Preventative factors

Slide courtesy of Lynn Webster, MD

P4 Suicidality Screener

Have you had thoughts of actually hurting yourself?

NO **YES**

1. **Have you ever attempted to harm yourself in the past?**

   NO **YES**

2. **Have you thought about how you might actually hurt yourself?**

   NO **YES**

3. **There's a big difference between having a thought and acting on a thought. How likely do you think it is that you will act on these thoughts about hurting yourself or ending your life some time over the next month?**

   a) Not at all likely _____
   b) **Somewhat likely** _____
   c) **Very likely** _____

4. **Is there anything that would prevent you from harming yourself?**

NO **YES → [What? _____]**

Risk Category	Shared ("Risk" Response	
	Items 1 and 2	**Items 3 and 4**
Minimal	Neither is shaded	Neither is shaded
Lower	At least one item is shaded	Neither is shaded
Higher		At least one item is shaded

Dube P, et al. *Prim Care Companion J Clin Psychiatry*. 2010;12(6):PCC. 10m00978.

Perelman School of Medicine University of Pennsylvania

Slide courtesy of Lynn Webster, MD

SBQ-R

SBQ-R Suicide Behaviors Questionnaire-Revised

Patient Name _____ Date of Visit _____

Instructions: Please check the number beside the statement or phrase that best applies to you.

1. Have you ever thought about or attempted to kill yourself? (check one only)

- ☐ 1. Never
- ☐ 2. It was just a brief passing thought
- ☐ 3a. I have had a plan at least once to kill myself but did not try to do it
- ☐ 3b. I have had a plan at least once to kill myself and really wanted to die
- ☐ 4a. I have attempted to kill myself, but did not want to die
- ☐ 4b. I have attempted to kill myself, and really hoped to die

2. How often have you thought about killing yourself in the past year? (check one only)

- ☐ 1. Never
- ☐ 2. Rarely (1 time)
- ☐ 3. Sometimes (2 times)
- ☐ 4. Often (3-4 times)
- ☐ 5. Very Often (5 or more times)

3. Have you ever told someone that you were going to commit suicide, or that you might do it? (check one only)

- ☐ 1. No
- ☐ 2a. Yes, at one time, but did not really want to die
- ☐ 2b. Yes, at one time, and really wanted to die
- ☐ 3a. Yes, more than once, but did not want to do it
- ☐ 3b. Yes, more than once, and really wanted to do it

4. How likely is it that you will attempt suicide someday? (check one only)

- ☐ 0. Never
- ☐ 1. No chance at all
- ☐ 2. Rather unlikely
- ☐ 3. Unlikely
- ☐ 4. Likely
- ☐ 5. Rather likely
- ☐ 6. Very likely

Columbia–Suicide Severity Rating Scale (C-SSRS)

Ideation			
	Yes	No	NA
1. Wish to be dead or not wake up			
2. Nonspecific thoughts			
3. Specific thoughts of method			
4. Some intent to act, no plan			
5. Specific plan and intent			

	Intensity						
Most Severe Ideation:	0	1	2	3	4	5	NA
a. Frequency of thought							
b. Duration of thoughts							
c. Controllability of thoughts							
d. Deterrents							
e. Reasons							

Behaviors				
	Yes	No	#	NA
Actual suicide attempts				
Interrupted attempts				
Aborted attempts				
Preparatory actions				
Non-suicidal self-injurious behaviors				

	Severity of Injury					
Lethality of Suicide Attempts	0	1	2	3	4	NA
Most serious attempt						

Potential Lethality of Suicide Attempts	0	1	2	NA
Most serious attempt				

Posner et al. Am J Psychiatry. Dec 2011; 168(12): 1266–1277.

Perelman School of Medicine University of Pennsylvania

Intervention

Risk Stratification

	LOW	HIGH
Plans	Vague	Specific
Means	No	Yes (lethal supply Rx opioids)
H/O Suicide Attempts	No	Yes
Level of Support	High	Low
Coping Abilities	Good	Poor
Relationship with HCP	Good	Poor
Willingness to Contract	Yes	No

Acute Suicidal Phase

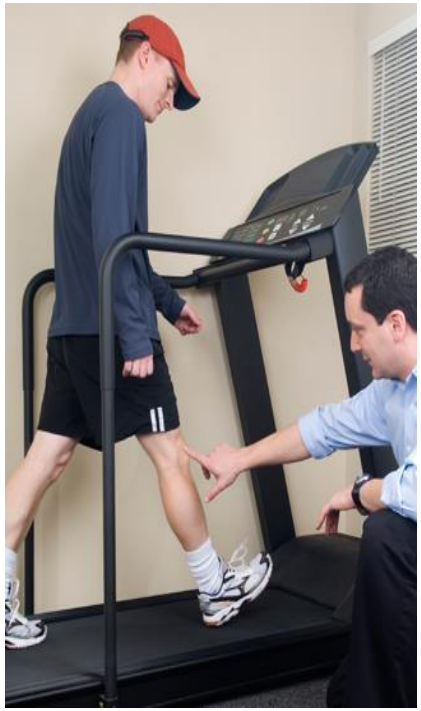
- IP treatment depending on severity of depression and SI/plans
- Pharmacotherapy targeting depression and sleep
- If opioids Rx do so in small amounts with family member dispensing
- Frequent UDS to ensure adherence

Chronic Depression/SI

- Require ongoing psychiatric/psychological care as part of overall pain management program
- Frequent UDS if opiods Rx until mood stabilizes
- Regular mental health screening

Risk Mitigation

Biopsychosocial Approach to Pain and Addiction Care



Biopsychosocial Approach to CPS

Comprehensive pain management programs based on the biopsychosocial model of pain, typically emphasizing *cognitive behavioral therapy*, a graded *exercise program* and appropriate *medication management* have been shown to significantly improve treatment outcomes (return to work, pain reduction and increase in activity).

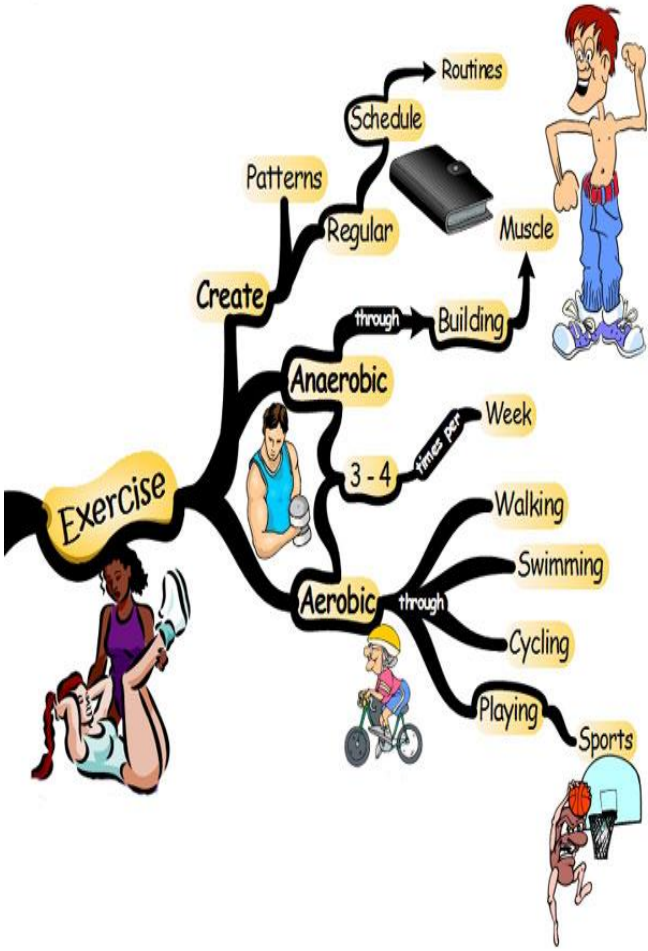
Gallagher, 1999
Loeser & Turk, 2000
McCraken & Turk, 2002
Cheatle & Gallagher, 2006

Biopsychosocial Treatment Program

- CBT
- Exercise
- Nutrition
- Evidence-based rational pharmacotherapy
- Social Support

Exercise, Pain and Opioid Sparing

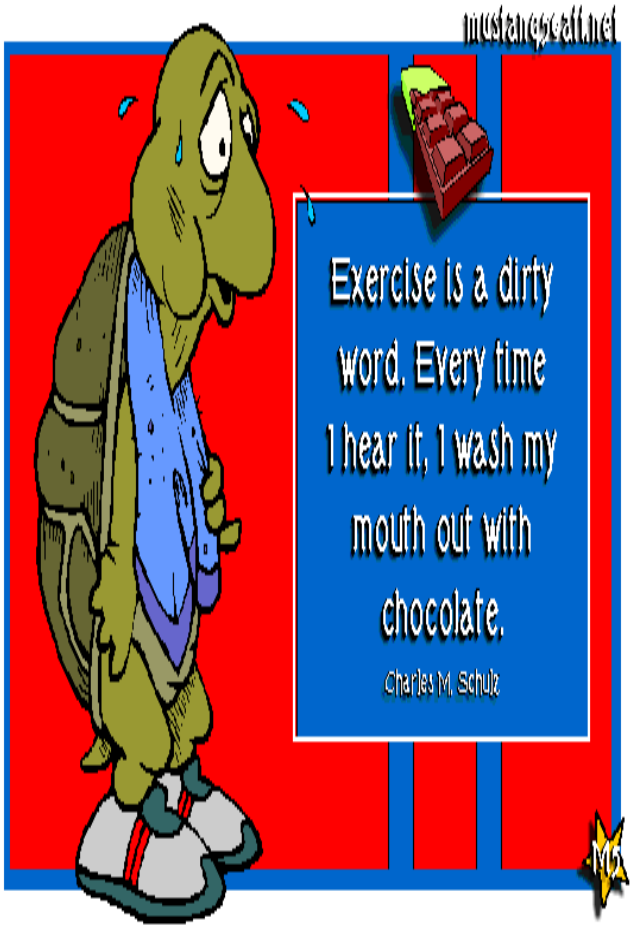
- Exercise not only can enhance the release of endogenous opioids (endorphins) thus reducing the use of prescription opioids, but can also reduce the mortality and morbidity related to major health conditions.
- Recent data from randomized studies suggest that aerobic exercise also significantly improves function and quality of life in patients with chronic low back pain.
- Exercise has proven to be a potent anxiolytic as it both blunts the body's response to cortisol and increases brain serotonin levels; epidemiological studies have shown that exercise both prevents anxiety disorders and effectively treats them



Heldt, S.A., et al., *Hippocampus-specific deletion of BDNF in adult mice impairs spatial memory and extinction of aversive memories.* Mol Psychiatry, 2007. 12(7): p. 656-70. Wipfli, B.M., C.D. Rethorst, and D.M. Landers, *The anxiolytic effects of exercise: a meta-analysis of randomized trials and dose-response analysis.* J Sport Exerc Psychol, 2008. 30(4): p. 392-410.

Physical Therapy

- **Most patients with chronic noncancer pain have had multiple trials of physical therapy, many of which have been not efficacious and, in some cases, exacerbated the pain**
- **Physical therapy program for patients with chronic noncancer pain should include:**
  - Acquiring first-aid techniques for pain relief at home
  - Establish a well-balanced independent exercise program. This should include establishing weekly goals that can be achievable that will not lead to an increase in pain or discouragement



CBT

Cognitive Behavioral Therapy

- CBT focuses on maladaptive thought patterns (catastrophizing) and behaviors (kinesiophobia) that occur frequently in patients with CNCP
- The objective of CBT is to guide the patient in recognizing and reconceptualizing his/her personal view of pain, identifying their role in the process of healing and promoting the patient being proactive rather than passive, and competent rather than incompetent
- CBT include specific skill acquisition (relaxation therapy, stress management, cognitive restructuring) followed by skill consolidation and rehearsal, and relapse training (Turk, Flor, 2006)

CBT cont'd

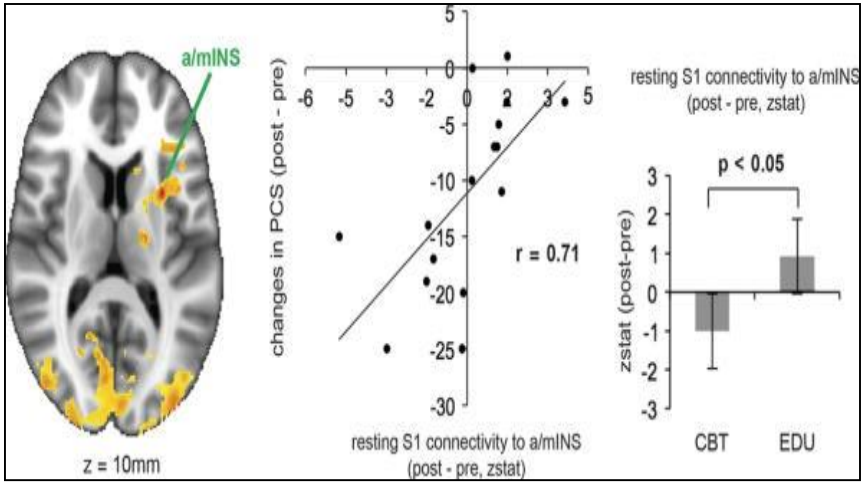
- **CBT has been found to be efficacious for a number of chronic pain disorders including:**
  - Arthritis (Keefe & Caldwell, 1997)
  - Sickle Cell disease (Chen et al, 2004)
  - Chronic low back pain (Lamb et al, 2010; Glombiewski et al, 2010)
  - TMJ (Turner et al, 2006)
  - Lupus (Greco et al, 2004)
  - Pain in breast cancer patients (Tatrow et al, 2006)

Biological Substrates of CBT on Pain

- **16 high catastrophizing patients with fibromyalgia were randomized into a group that received a 4 week course of CBT or a control group that received only fibromyalgia education material.**
- **Resting state fMRI evaluated functional connectivity between key pain processing brain regions at baseline and post-treatment.**

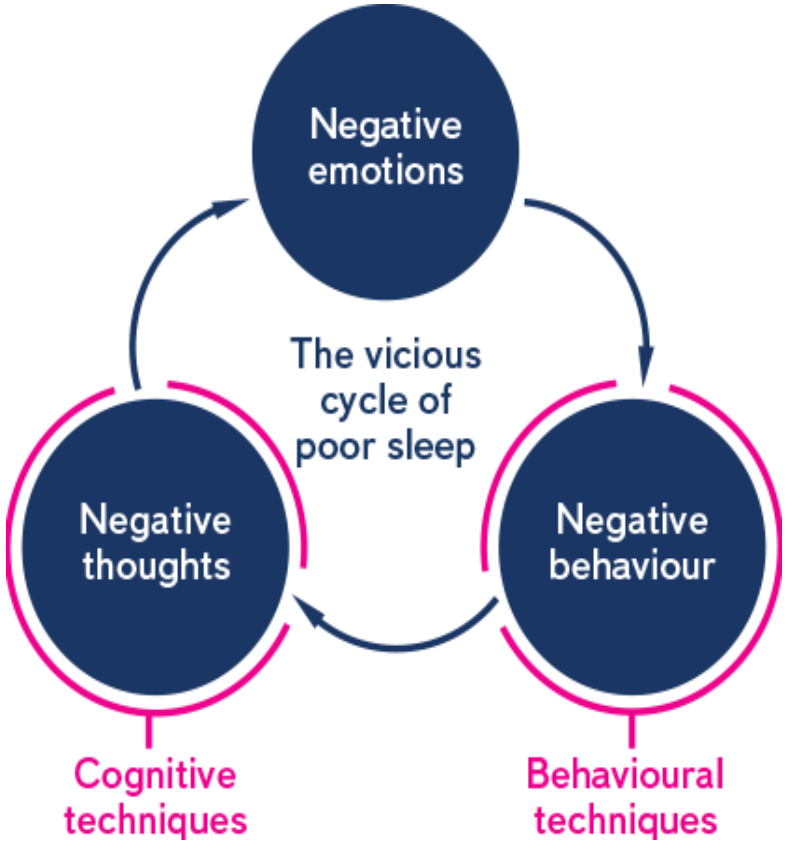
Lazaridou, A., et al., *Effects of Cognitive-Behavioral Therapy (CBT) on Brain Connectivity Supporting Catastrophizing in Fibromyalgia.* Clin J Pain, 2017. **33**(3): p. 215-221.

- **Results revealed that catastrophizing correlated with increased resting state functional connectivity between S1 and anterior insula.**
- **The CBT group demonstrated a larger reduction in both pain and catastrophizing as compared to the control group at the 6-month follow-up and reduced resting state connectivity between S1 and anterior/medial insula at post-treatment and these changes were associated with concurrent treatment-related reduction in catastrophizing.**
- ***The authors concluded that CBT via reducing catastrophizing helps normalize pain-related brain responses***



Cognitive Behavioral Therapy for Insomnia

- **CBT-I has been demonstrated to be equally effective or even superior to pharmacotherapy in patients with chronic primary insomnia.**



CBT-I cont'd

- **CBT-I consists of:**
  - Psychoeducation about sleep and insomnia
  - Stimulus control
  - Sleep restriction
  - Sleep hygiene
  - Relaxation training
  - Cognitive restructuring

Research Article

The Durability of Cognitive Behavioral Therapy for Insomnia in Patients with Chronic Pain

Carla R. Jungquist,[1,2] Yolande Tra,[3] Michael T. Smith,[4] Wilfred R. Pigeon,[2,5] Sara Matteson-Rusby,[2] Yinglin Xia,[6] and Michael L. Perlis[7]

[1] *School of Nursing, University at Buffalo, Wende Hall 304, Buffalo, NY 14214, USA*
[2] *Sleep & Neurophysiology Research Lab, University of Rochester Medical Center, Rochester, NY 14642, USA*
[3] *Maryland Poison Center, School of Pharmacy, University of Maryland Baltimore, Baltimore, MD 21201, USA*
[4] *Department of Psychiatry and Behavioral Sciences, John Hopkins University, Baltimore, MD 21287, USA*
[5] *VA Center of Excellence for Suicide Prevention, Washington, DC 20420, USA*
[6] *Department of Biostatistics and Computational Biology, University of Rochester School of Medicine, Rochester, NY 14642, USA*
[7] *Department of Psychiatry, University of Pennsylvania, Philadelphia, PA 19104, USA*

- **This was a parallel-group, randomized, single blind trial of CBT-I with a contact/measurement control condition**
- **Twenty-eight subjects with chronic neck and back pain were randomized into the 2 groups.**
- **Results revealed that patients who received CBT-I had significantly improved sleep and these patients maintained a statistically and clinically improved total sleep time even 6 months after treatment ended, despite the persistence of moderate to severe pain**

Sleep Disord. 2012;2012:679648.

Pharmacotherapy

- **Pharmacotherapy should target 4 domains:**

  - **Pain**
  - **Sleep**
  - **Mood**
  - **Substance Use Disorders**

Pharmacologic Approaches to Sleep Disorders

- Benzodiazepine and Receptor Agonists (BzRAS)
- Non-benzodiazepine receptor agonists
- Melatonin receptor agonists
- Sedative antidepressants
- Atypical antipsychotic medications,
- Antiepileptic Drugs

Benzodiazepine and Receptor Agonists (BzRAS)

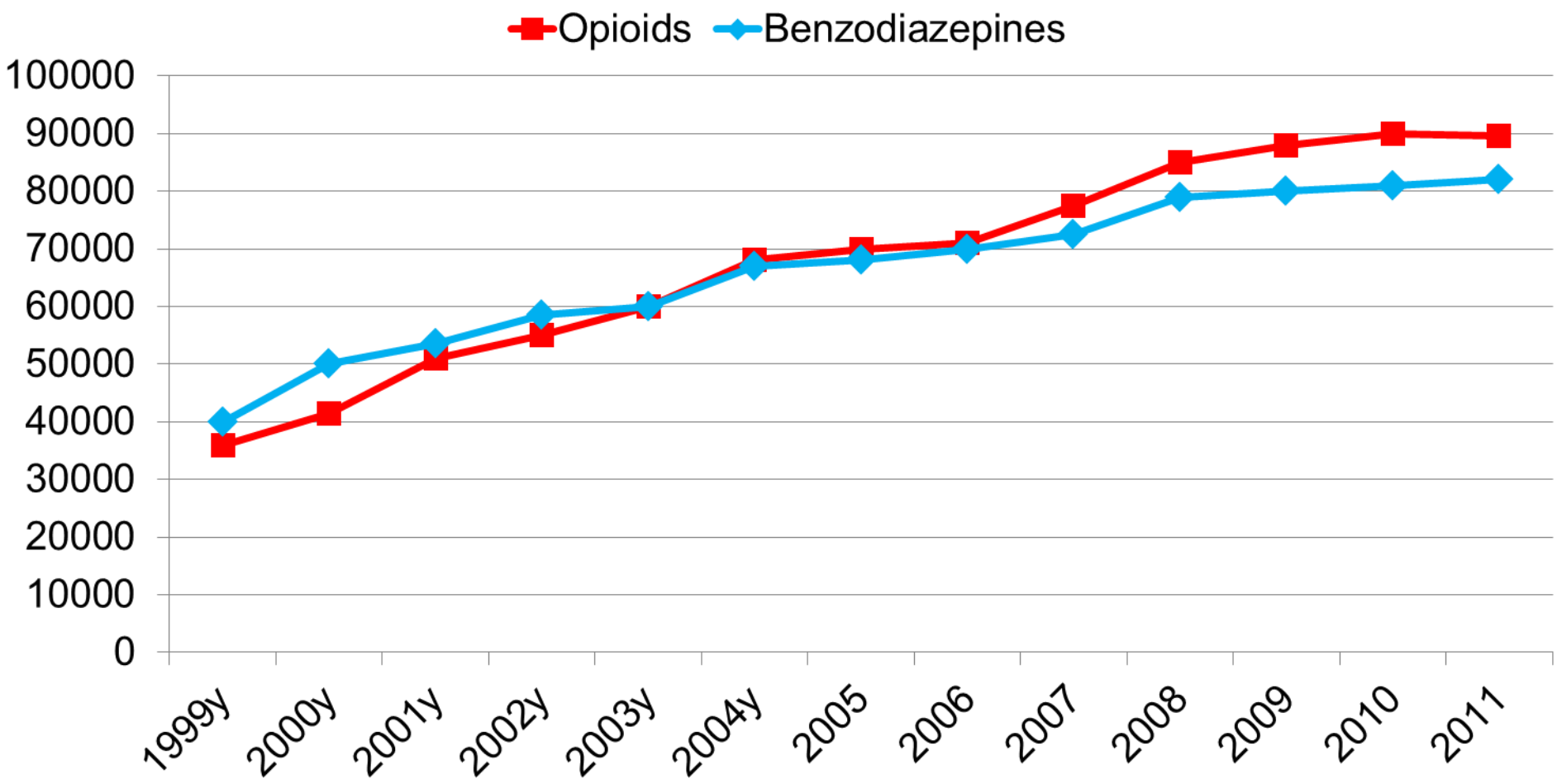
- **BzRAS include benzodiazepines (example Temazepam, Triazolam) and a newer class of non-benzodiazepine drugs (for example, Zolpidem).**
- **This class of drugs binds to GABA-A receptors and induces sedative/hypnotic, amnestic, anxiolytic and anticonvulsant effects.**
- **Many short term clinical trials show that BzRAS improve sleep quality, sleep latency, wakefulness after sleep onset and total sleep time.**
- **Most benzodiazepines (excluding Triazolam) have intermediate to long half-life, helping patients fall asleep and stay asleep longer.**

- **Benzodiazepines may work well in short-term efficacy trials, but there is a paucity of data on long-term use and there are many documented adverse effects:**

  - **Cognitive impairment**
  - **Decreased attention**
  - **Anterograde amnesia**
  - **Depressive symptomatology with cognitive and psychomotor slowing**
  - **Abruptly discontinuing benzodiazepines may lead to rebound insomnia, seizure activity**

- ***Given these multiple safety concerns, benzodiazepines have fallen out of favor as a class of drugs for use in sleep disorders.***

Drug Misuse and Abuse



Spiller HA. What every clinician needs to know about overdoses - poison center surveillance. Presented at: The 2012 National Rx Abuse Summit. April 10 – 12, 2012; Orlando, FL. http://www.slideshare.net/OPUNITE/henry-spiller-edited

Non-Benzodiazepine Receptor Agonists (NBzRAS)

- **Non-benzodiazepine receptor agonists include Ambien (Zolpidem), Sonata (Zalepon), and Lunesta (eszopiclone) are the newest class of FDA approved hypnotics used for insomnia.**
- **These class of drugs improve sleep latency and have potential for fewer daytime side effects, given their short half-life and receptor binding profile.**

Antidepressants

Antidepressants

- **Sedative antidepressants, such as tricyclic antidepressants mirtazapine and Trazodone, are useful in treating chronic pain patients with insomnia.**

- **These classes of drugs help to relieve:**
  1. Insomnia
  2. Any associated depression that negatively influences pain perception
  3. The pain condition itself

- **Tricyclic antidepressants have pro-serotonergic, noradrenergic, dopaminergic and sodium channel blocking effects that may account for their efficacy in pain and depression, along with anticholinergic and antihistaminic effects that lead to sedation.**

Antidepressant medication

- The role of antidepressant medication may relate, in part, to the high prevalence of co-occurring depression in chronic pain
- There is evidence of the analgesic properties of tricyclics and certain SNRIs
- TCAs, SNRIs like opioids are used to modulate descending inhibitory pain pathways

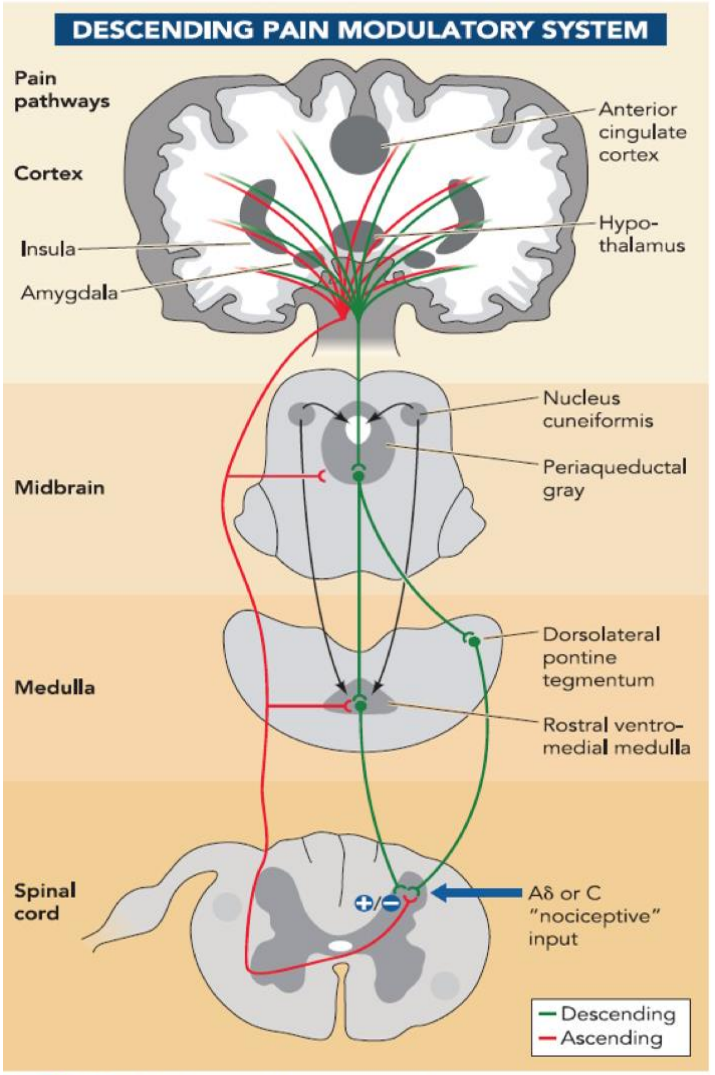


FIGURE 3. The descending pain modulatory system
+/- indicates both pro- and anti-nociceptive influences, respectively.

AEDs

- Gabapentin and pregabalin often used to treat chronic pain conditions with comorbid insomnia.
- In multiple studies of patients with neuropathic pain and fibromyalgia, self-reported sleep outcomes suggest positive effects on sleep latency and wakefulness after sleep onset, as well as increased deep sleep.
- Both have adjunctive effects on depression and anxiety.
- Pregabalin showed increased efficacy in promoting sleep in patients with diabetic neuropathy, compared to amitriptyline in a recent study.
- Adverse effects include dizziness, next day sedation, GI symptoms and peripheral edema.

Medication-Assisted Therapy

Medication Assisted Treatment

- Methadone
- Buprenorphine
- Extended Release and Oral Naltrexone

Methadone

- Methadone is a full mu opioid agonist
- Blocks NMDA and monoamine reuptake
- Pharmacokinetic and pharmacodynamic effects of methadone have advantage over other opioids in that methadone is long-acting, development of tolerance is low, thus potentially leading to lower dosing long-term
- Methadone has NMDA receptor blocking activity and this may be the reason for efficacy in treating neuropathic pain
- Patients on MMT for OUD who do experience CNCP require higher dosing

Buprenorphine Formulations

- **Buprenorphine is a partial agonist at the mu-opioid receptors and an antagonist at the kappa receptors.**

- **Mu-opioid receptor activity produces the analgesic effects of buprenorphine, while a strong affinity for the kappa receptors render them inactive.**

Ultra-Low-Dose Buprenorphine as a Time-Limited Treatment for Severe Suicidal Ideation: A Randomized Controlled Trial

Yoram Yovell, M.D., Ph.D., Gali Bar, Ph.D., Moti Mashiah, M.D., Yehuda Baruch, M.D., Irina Briskman, M.D., Jack Asherov, M.D., Amit Lotan, M.D., Amihai Rigbi, Ph.D., Jaak Panksepp, Ph.D.

- **A randomized double-blind placebo-controlled trial of ultra-low-dose sublingual buprenorphine as an adjunctive treatment.**
- **Severely suicidal patients without substance abuse were randomly assigned to receive either buprenorphine or placebo (in a 2:1 ratio), in addition to their ongoing individual treatments**
- **Patients who received ultra-low-dose buprenorphine had a greater reduction in Beck Suicide Ideation Scale scores than patients who received placebo, both after 2 weeks (mean difference -4.3, 95% CI=-8.5, -0.2) and after 4 weeks (mean difference=-7.1, 95% CI=-12.0, -2.3)**

Am J Psychiatry. 2016 Oct 1;173(10):1043

Extended Release and Oral Naltrexone

- Naltrexone for extended-release injectable suspension
- Effective for treatment of opioid and alcohol dependence
- Low dose naltrexone now being used off label to treat fibromyalgia

Access Issues

Interventions

- **Office-based interventions**
  - Training non-BH staff on CBT etc
  - Antidepressant therapy/pain self-management program

    Kroenke et al 2009
- **E-health**
  - Computer-assisted CBT
  - Telemedicine
  - Smartphone Apps

Summary

- Pain and SUD are potentially independent risk factors for suicide
- Patients suffering from both pain and SUD are particularly vulnerable
- Possible mediators of the relationship between pain,SUD and suicidal risk include insomnia, sense of burdensomeness, social isolation and poor stress-coping abilities, in particular, catastrophizing
- Given the high co-occurrence of pain, SUD and suicidal ideation, patients with chronic pain should be routinely screened for depression and suicide
- A clinic should have an action plan for intervention in cases of patients identified as being actively suicidal or at high-risk for suicide (contracting, referral to behavioral health, close monitoring of potentially lethal medications, etc)
- ***Globally poor access to mental health services needs to be addressed***

Future Directions

- Develop and test novel delivery systems for CBT/CAM and other non-pharmacologic interventions
- Healthcare economics research to support improved access to interdisciplinary pain care, behavioral health and SUD treatment
- Pharmacogenomics research supporting decision making for non-opioid pharmacotherapeutics (precision medicine)
- Research on biological substrates of non-pharmacologic interventions
- Investigate phenotypic and genotypic characteristics of suicidal ideation and behavior in patients with pain and pain and SUD

From: mother of pain sufferer

Date: Fri 3 Feb 2012

To: cheatle@upenn.edu

Subject: daughter's suicide from unrelieved pain

"My 45 yo daughter suffered for 4 ½ years of constant back pain-unrelieved by narcotics and mostly ignored by all of the MD's I took her to….on Jan 9th 2012, she killed herself by jumping off a high bridge to end her agony. It was HER RELENTLESS AGONIZING PAIN which eventually killed her. When she recognized the only narcotic she could tolerate no longer worked, there was no hope left…she knew her old age would be a nightmare…it is then that she made the decision to get out of her inferno. "

Acknowledgements

- **Grant 1RO1DA032776-01 from the National Institute on Drug Abuse, National Institutes of Health**
- **University of Pennsylvania**
  - Charles P. O'Brien, MD, PhD
  - Wade Berrettini, MD, PhD
  - Kelly Farraday, BA, MSOD
  - Aaron Pinkett, BS
- **University of Washington**
  - Dennis C. Turk, PhD
  - Dana Divens
  - Ann Bradshaw
- **Lifetree Clinical Research Salt Lake City**
  - Lynn Webster, MD
- **Harvard University**
  - Mohammed Issa, MD
  - Robert Jamison, PhD

THANK YOU !!

Martin D. Cheatle, Ph.D.

cheatle@upenn.edu