

The Natural History of Chronic Opioid Therapy in a Population of Patients with Chronic Non-Cancer Pain



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Introduction

The medical management of chronic pain is a global health problem complicated by rising rates of non-medical prescription opioid use, addiction, questionable efficacy of long-term chronic opioid treatment (COT), and a paucity of extended duration studies. This study involved outpatients seen in a highly regulated practice, over the past 20 years, to determine longitudinal outcomes in pain, mood, and function, as well as clarify the effects of COT over time, both in terms of benefits and harms.

Study Design & Methods

Design: An IRB-approved archival study that was retrospective in nature.

Subjects: All individuals treated for chronic pain from 1995-2013 at the Cleveland Clinic Neurological Institute's Center for Pain with any opioid for greater than twelve consecutive months were included (n=91).

Data Collection: Patient information was abstracted from the medical record at COT initiation; months 1,3,6; every six months through year seven; and yearly thereafter. Data for each individual was averaged across each year past month one.

Measures: Longitudinal measures included pain (0-10 Likert scale), function (Pain disability index, PDI), mood (Beck Depression Inventory, BDI); Personal Health Questionnaire-9, (PHQ9); or Depression Anxiety Stress Scale, (DASS); collapsed with parallel depression levels into single variable), & morphine equivalent dosages (MED).

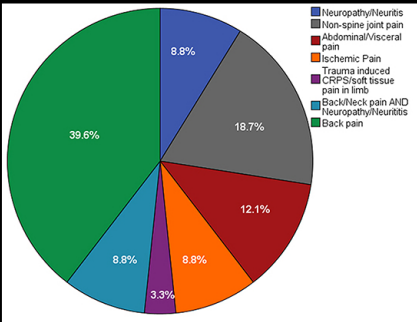
Statistics: One-way ANOVA, Chi Square, Cox regression analyses, binary/multinomial logistic regression, and a series of hierarchical longitudinal linear mixed models were constructed. Unconditional null, quadratic, and repeated models were analyzed and optimal individual growth curves with predictors were selected in SPSS v.19.0.

Results

Table 1. Characteristics of COT Subjects

Demographics:		Number (%)	Medical History:		Number (%)	
Gender	Male	53 (58.2%)	Number of distinct Pain Conditions	One	51 (56.0%)	
	Female	38 (41.8%)		Two	33 (36.3%)	
Race	Caucasian	76 (83.5%)	Age of Pain Onset	Three	7 (7.7%)	
	African American	12 (13.2%)		(years old)	Mean ± SD	
	Hispanic	1 (1.1%)			(years)	37 ± 17
Highest Education Achieved			Duration Pain		12.1 ± 11.3	
Missing: n=2 or 2.2%	Didn't finish HS	15 (16.5%)	Chronic Comorbidities	Hypertension	25 (27.5%)	
	Graduated HS/GED	18 (19.8%)		Dyslipidemia	24 (26.4%)	
	Some College	29 (31.9%)		Asthma, CAD, VitD defic. each	11 (12.1%)	
	Earned Bachelor's degree	7 (7.7%)		Diabetes	10 (11.0%)	
	Some Graduate School	5 (5.5%)		Prior Depression	55 (60.4%)	
Main Employment Status	Graduate/Professional Degree	12 (13.2%)	Mean Number Comorbidities		2 ± 1.7 (0-7)	
	Unemployed	16 (17.6%)	Past Substance Abuse	Any	60 (65.9%)	
	Receiving Disability/Worker's Compensation/Retired	34 (37.8%)		Any EXCLUDING Tobacco	39 (42.9%)	
Part or Full Time Employed	40 (44.0%)	Alcohol Abuse		19 (20.9%)		
Marital Status	Single/Never Married	17 (18.7%)		Cocaine Use	9 (9.9%)	
	Married	52 (57.1%)		Marijuana Use	14 (15.4%)	
	Divorced/Separated/Widowed	17 (18.7%)	Opioid Abuse	21 (23.1%)		
Engaged/Living with Partner	5 (5.5%)	Mean ± SD	Street Opioid Use	13 (14.3%)		
			Prescription Opioid Abuse	9 (9.9%)		
Age at COT start	(years old)	48.1 ± 12.6	Poly-Substance Abuse	19 (20.9%)		
			EXCLUDING Tobacco			

Figure 1. Primary Pain Diagnosis for COT



Results

Table 2. The Course of COT

Duration of Treatment		Primary Opioid Prescribed		Adjuncts Utilized	
Mean: 60.6 ± 44.3 months		Methadone (18.7%)		Ever an antiepileptic: 31.9% Yes	
Range: 12-206 months		Oxycodone (25.3%)		Ever an antidepressant: 36.3% Yes	
52.7% discontinued care		Hydrocodone (14.3%)		41.8% NSAIDs	
		Buprenorphine (n= 23.1%)			
		Tramadol, Fentanyl, Morphine or Darvocet (18.6%)			

Figure 2.. All-cause Survival Time in COT Predicted by Poly-drug use and Lack of Antidepressant Treatment

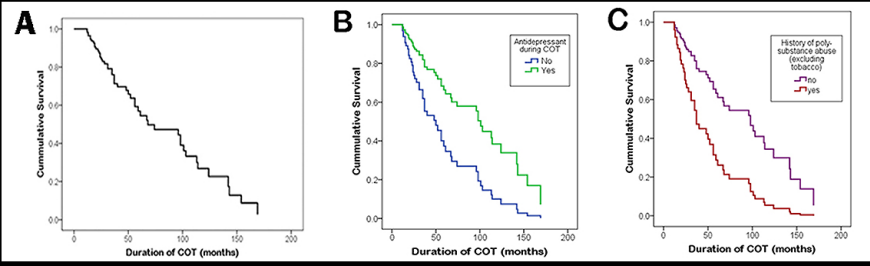
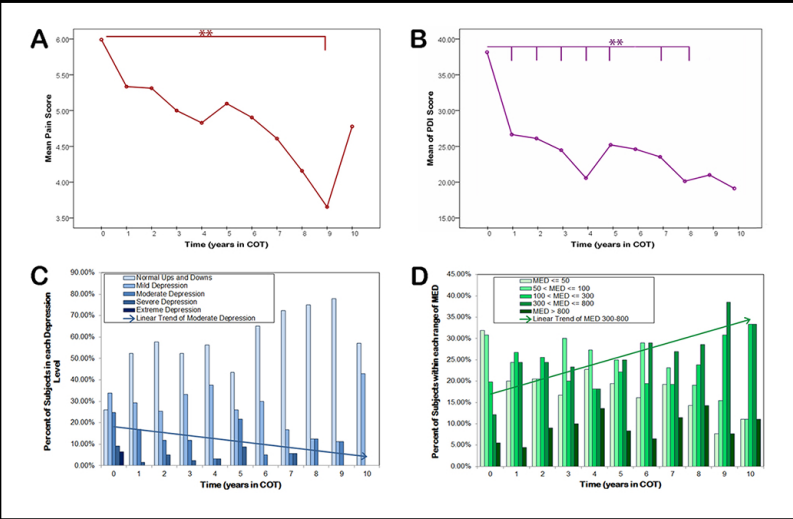


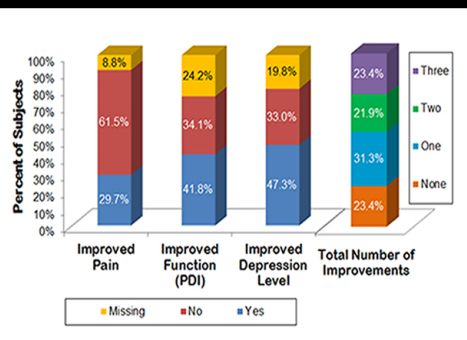
Figure 3. Trends in Pain, Mood, Function, & MED over COT



Trends were assessed by collapsing data across individual subjects and ANOVA was used to compare across time points over the first ten years of COT. A) Pain decreased slowly but steadily over time; $F(10)=3.08$, $p=0.001$. Post-hoc Tukey test showed the Average initial pain score at admission \pm one month (6.0 ± 1.6) was significantly different than those surveyed across the eighth ($p=0.023$) and ninth ($p=0.008$) years in COT. B) Function, as measured by PDI, improved dramatically from admission (38.2 ± 14.9); $F(10)=4.84$, $p<0.001$. Mean function was significantly better compared to admission for all time points except years six, nine, and ten without showing any statistical difference between pairs of any other time points. C) Percent of subjects that reported scores within each composite level of depression showed a trend towards improved depression over time; $X^2(40)=63.2$, $p=0.011$. D) The average categorical level of MED each year never significantly changed but trended towards increased opioid doses.

Results

Figure 4. Improvements in Pain, Mood, & Function over COT



Improved Pain ($\Delta \geq 2$ pts):
+ Full-time work (odds 18.5) vs. Unemployed
+ Antidepressant use (odds 7.65) vs. None
Improved PDI ($\Delta \geq 10$ pts):
- For each increase in number of chronic comorbidities the probability of improved PDI is decreased to a little over half.
+ Improved pain (odds 14.5) vs. No change in pain

Improved Depression ($\Delta \geq 1$ level):

+ Primary buprenorphine (odds 18) vs. Morphine

Number of Improvements:

+ More pain conditions increased the likelihood of improvement.

-- More chronic comorbidities resulted in an individual being half as likely per additional condition to show improvements over COT, regardless of how many categories of improvements are considered.

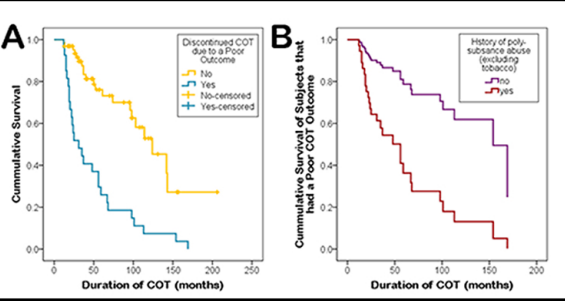
Linear Mixed Model Longitudinal Data Analysis

MED: 1) \uparrow over COT but acceleration slows over time. 2) Initial MED is predicted to be highest in unemployed individuals with higher pain, earlier age of chronic pain onset, who were mainly on buprenorphine and were treated between 2001 and 2005. 3) Past opioid abuse increases earlier rates of linear growth but slows more quickly 4) Overall pain marginally increases the rate of dose escalation.

Pain: 1) Initial pain is 6.67 for individuals in the highest dose range of MED with the most severe depression level. 2) Linear decline of pain by a mean of 0.3 points per year is further decreased by the presence of abdominal pain (suggesting beneficial impact of COT in this population) and a longer duration of chronic pain marginally impairs and slows this improvement in pain score.

PDI: 1) Admission score 25.365 on average for employed individuals with back pain on morphine in the highest dose range of MED with the most severe depression level. 2) For every increased point of reported average pain the disability level is increased by 2.88 ± 1.54 points. 3) Linear decline of PDI by a mean of 2.869 points per year is less substantial for individuals with a history of illicit drug use. Quadratic time component suggests that there is a slight acceleration (8.6% of linear growth rate) in the rate of PDI score improvement.

Figure 5. Discontinuation of COT due to Poor Outcomes



A) Poor outcome of death related to opioids, removal by clinician, or AWOL; n=29
B) Cox analysis with forward likelihood predictor inclusion of variables without missing values (n=91 for all) showed poly (non-tobacco) drug use predicted 4.236x higher likelihood of poor outcome ($p<0.001$).

Conclusions

** Compared with admission, pain, mood, and function statistically improved initially and stably over the first 5-7 years of COT without further significant changes in trends.

** Clinically significant improvements in at least one dimension were found in 76.6% of subjects, however, ~32% ended COT with a poor outcome.

** Reciprocal changes in pain, depression (mood or antidepressant use), and function (PDI or employment) were observed. Illicit or poly-drug use, which is prevalent in this population, as well as number of chronic comorbidities are poor prognostic factors in COT.

These results confirm the usefulness of COT but suggest that clinical improvement plateaus after >5 years, in high-risk individuals, and may not provide optimal safe management of chronic pain.