

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).

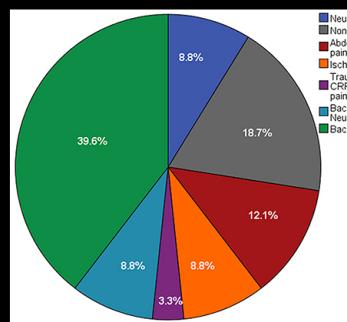
Statistics: One-way ANOVA, Chi Square, Cox regression analyses, binary/multinomial logistic regression, and a series of hierarchical longitudinal linear mixed models were constructed. Unconditional null, quadratic, and repeated models were analyzed and optimal individual growth curves with predictors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

Results

Table 1. Characteristics of COT Subjects

Demographics:	Number (%)		Medical History:	Number (%)	
	Male	Female		One	Two
Gender	53 (58.2%)	38 (41.8%)	Number of distinct Pain Conditions	51 (56.0%)	33 (36.3%)
Race	76 (83.5%)	12 (13.2%)	Mean ± SD (Range)	7 (7.7%)	7 (7.7%)
Missing: n=2 or 2.2%			(years old)	37 ± 17	12 ± 11.3
Highest Education Achieved	Didnt finish HS	15 (16.9%)	Duration Pain	25 (27.5%)	24 (26.4%)
Missing: n=5 or 5.5%	Graduated HS/GED	18 (19.8%)	Hypertension	11 (12.1%)	10 (11.0%)
Earned Bachelor's degree	29 (31.9%)	Chronic Comorbidities	Dyslipidemia	55 (60.4%)	
Some College	7 (7.7%)	Asthma, CAD, VitD defic.	25 (27.5%)		
Some Graduate School	5 (5.5%)	each	24 (26.4%)		
Graduate/Professional Degree	12 (13.2%)	Diabetes	11 (12.1%)		
Main Employment Status	Unemployed	Prior Depression	10 (11.0%)		
Missing: n=1 or 1.1%	Receiving Disability/Worker's Compensation/Retired	Mean Number Comorbidities	55 (60.4%)		
Part or Full Time Employed	34 (37.8%)	2.2 ± 1.7 (0.7)			
Marital Status	Single/Never Married	Any			
Divorced/Separated/Widowed	17 (18.7%)	Any EXCLUDING TOBACCO	60 (65.9%)		
Engaged/Living with Partner	52 (57.1%)	Alcohol Abuse	39 (42.9%)		
Age at COT start	Mean ± SD (years old)	Cocaine Use	19 (20.9%)		
	48.1 ± 12.6	Marijuana Use	9 (9.9%)		
		Opioid Abuse	14 (15.4%)		
		Street Opioid Use	21 (22.1%)		
		Prescription Opioid Abuse	13 (14.3%)		
		Poly-Substance Abuse	9 (9.9%)		
		EXCLUDING TOBACCO	19 (20.9%)		

Figure 1. Primary Pain Diagnosis for COT



Results

Table 2. The Course of COT

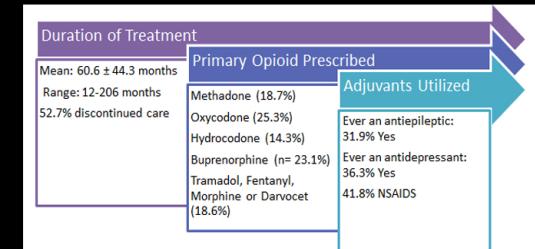


Figure 2.. All-cause Survival Time in COT Predicted by Poly-drug use and Lack of Antidepressant Treatment

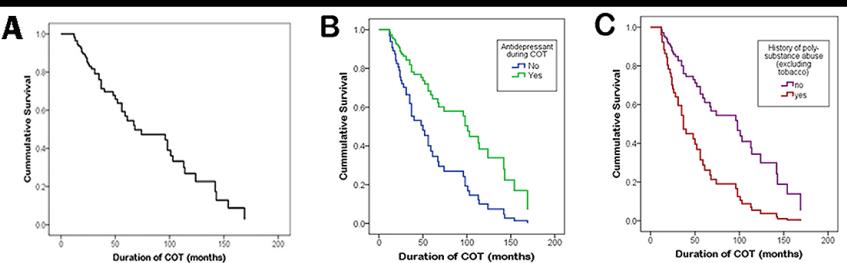
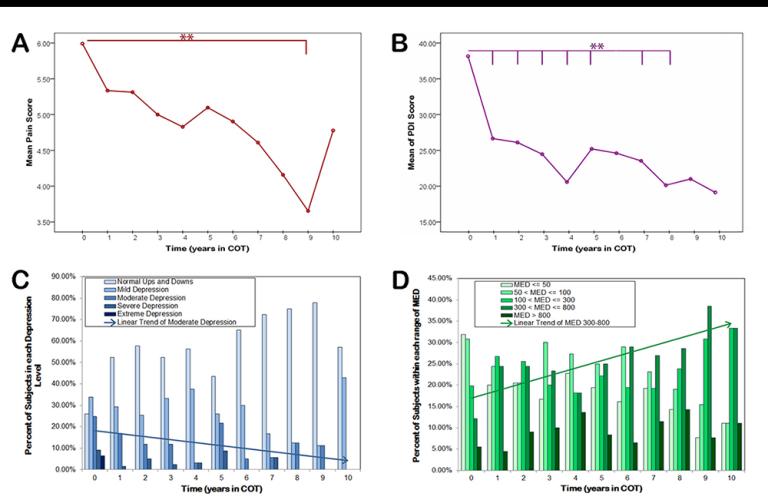


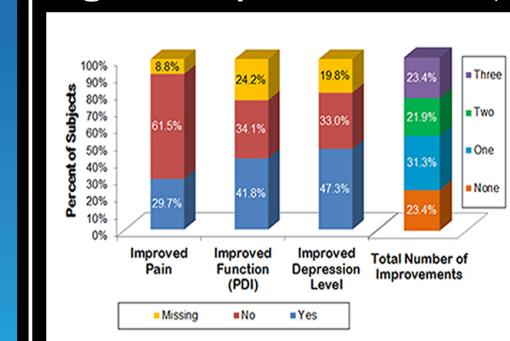
Figure 3. Trends in Pain, Mood, Function, & MED over COT



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 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.

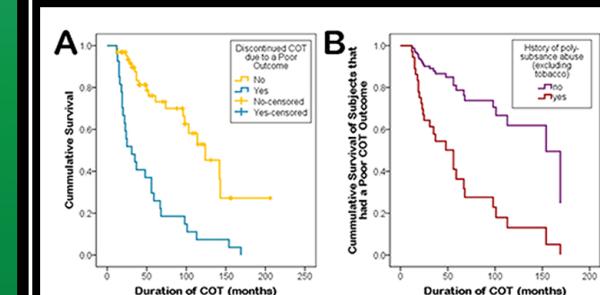
Linear Mixed Model Longitudinal Data Analysis

MED: 1) ↑ 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



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.