

## Abstract

Patient prescriber agreements (PPAs) also known as opioid contracts or opioid treatment agreements, have been recommended as a strategy to mitigate non-medical opioid use (NMOU). The purpose of our study was to characterize the proportion of patients with PPAs, the rate of non-adherence, and clinical predictors for PPA completion.

This retrospective study covered consecutive cancer patients seen at a palliative care clinic at a safety net hospital between 09/01/2015 and 12/31/2019. We included patients 18 years or older with cancer diagnoses receiving opioids. We collected patient characteristics at consultation and information regarding PPA. Descriptive statistics and multivariable logistic regression models were used for the analysis.

In summary, we found that PPA non-adherence occurred in a substantial minority of patients, 10%, and was more likely in patients with known NMOU risk factors. These findings underscore the potential role of universal PPAs and systematic screening of NMOU risk factors to streamline care.



## Introduction

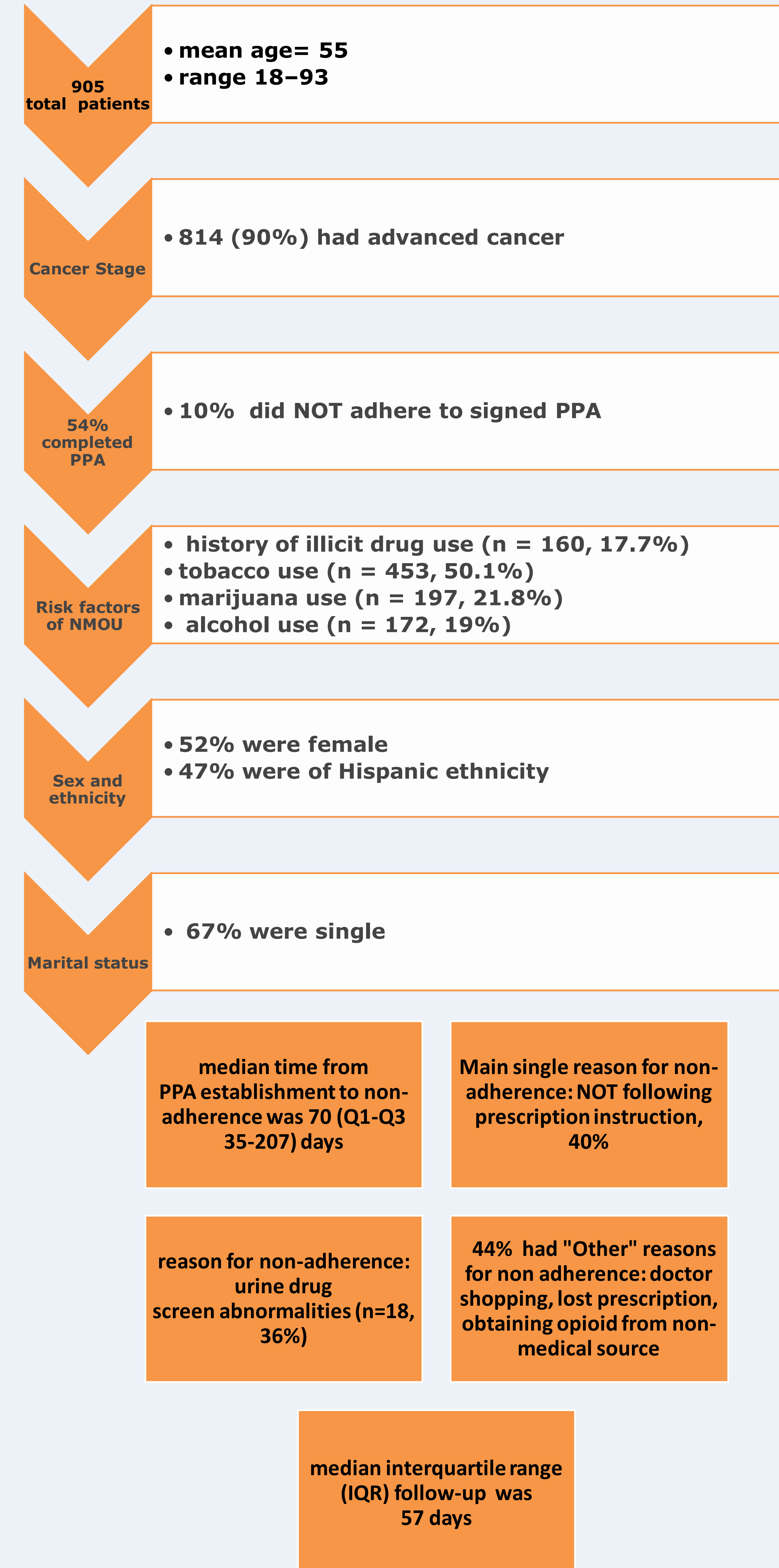
Although PPAs are recommended in guidelines as a risk-mitigation strategy for NMOU, few studies have examined their outcomes in the real-world, particularly in the cancer palliative care setting. NMOU is defined as use without a prescription or in greater amounts, more often, or longer than prescribed, or for a reason other than a doctor's instruction.

In the palliative care clinic, we have implemented a safe opioid use program in which patients starting on opioids were asked to sign a PPA as a risk mitigation strategy.

## Methods

This is a retrospective study of consecutive cancer patients seen at a palliative care clinic at a safety-net hospital between 09/01/2015 and 12/31/2019. We collected patient demographics, symptom burden using the Edmonton Symptom Assessment Scale (ESAS), PPA information (date of establishment, documentation of non-adherence, reason for non-adherence) Patients were followed until December 2021 for non-adherence. Descriptive statistics and multivariable logistic regression models were used for analysis.

**Results:** In multivariable analysis, non-adherence to PPA was associated with being male, single, smoker, history of alcohol use, contact with persons involved in criminal activity, use for non-malignant pain and higher pain expression at consultation (Table 1).



**Table 1. Association between non-adherence to a Patient Prescriber Agreement and patient characteristics**

	Univariate analysis		Multivariable analysis	
	Unadjusted Odds Ratio (95% Confidence Interval)	P-value	Adjusted Odds Ratio (95% Confidence Interval)	P-value
<b>Age</b>				
< 60 years	0.92 (0.49-1.72)	0.79	0.93 (0.38-2.26)	0.87
≥ 60 years	Ref		-	
<b>Sex</b>				
Male	2.44 (1.30-4.60)	0.006	3.66 (1.43-9.32)	0.007
Female	Ref		Ref	
<b>Race-ethnicity</b>				
White, Non-Hispanic	1.99 (0.82-4.85)	0.13	0.61 (0.19-1.96)	0.41
Black, Non-Hispanic	4.38 (2.06-9.33)	<0.001	1.74 (0.65-4.72)	0.27
Other race, Non-Hispanic	2.16 (0.25-18.72)	0.49	-	-
Hispanic, any race	Ref		Ref	
<b>Marital status</b>				
Single	6.07 (2.15-17.20)		12.23 (2.29-65.45)	0.003
Married	Ref		Ref	
<b>Cancer stage</b>				
Locally advanced	1.91 (1.00-3.67)	0.05	-	-
Localized	1.31 (0.48-3.59)	0.60	-	-
Recurrent	-	-	-	-
Advanced	-	-	-	-
Metastasis	Ref		-	-
<b>Risk factors of NMOU</b>				
History of Illicit drug use	6.30 (3.42-11.63)	<0.001	1.81 (0.66-4.96)	0.25
History of Marijuana use	3.23 (1.78-5.86)	<0.001	1.98 (0.76-5.12)	0.16
History of Tobacco use	5.45 (2.40-12.38)	<0.001	3.34 (1.12-9.99)	0.03
History of Alcohol use	1.85 (1.00-3.44)	0.05	0.29 (0.10-0.79)	0.02
History of Depression	1.42 (0.71-2.84)	0.32	-	-
History of Bipolar disorder	3.01 (0.79-11.52)	0.11	-	-
History of Schizophrenia	9.17 (1.80-46.73)	0.008	7.72 (0.94-63.17)	0.06
Family history of illicit drug use	3.89 (0.97-15.56)	0.06	-	-
Personal History of criminal activity	8.69 (4.52-16.71)	<0.001	0.86 (0.27-2.76)	0.80
Contact with persons involved in criminal activity	13.8 (6.70-28.41)	<0.001	9.86 (2.75-35.38)	<0.001
Inconsistent pain presentation	82.48 (10.07-675.43)	<0.001	-	-
Use for Non-malignant pain	6.90 (2.50-19.06)	<0.001	7.45 (1.80-30.90)	0.006
Others **	27.64 (2.82-271.50)	0.004	-	-
<b>MEDD at consultation</b>	1.00 (0.99-1.00)	0.70	-	-
<b>ESAS at consult only</b>				
Pain	1.15 (1.03-1.28)	0.01	1.20 (1.04-1.38)	0.01
Tiredness	1.05 (0.95-1.16)	0.32	-	-
Nausea	1.07 (0.97-1.18)	0.15	-	-
Depression	1.11 (1.02-1.22)	0.02	-	-
Anxiety	1.11 (1.02-1.21)	0.02	-	-
Drowsiness	0.99 (0.90-1.10)	0.92	-	-
Appetite	1.12 (1.02-1.22)	0.02	-	-
Well-being	1.05 (0.95-1.15)	0.35	-	-
Shortness of breath	1.09 (1.00-1.20)	0.06	-	-
Family distress	1.11 (1.02-1.22)	0.02	-	-
Spiritual distress	1.07 (0.95-1.20)	0.30	-	-
Constipation	1.02 (0.94-1.12)	0.59	-	-
Sleep	1.05 (0.96-1.15)	0.25	-	-

\*\*Others: homelessness, history of sexual abuse.  
Abbreviations: ESAS, Edmonton Symptom Assessment System; MEDD, morphine equivalent daily dose; NMOU, non-medical opioid use; Patient Prescriber Agreement, PPA.

## Conclusions

To our knowledge, this is the largest series to date to examine non-adherence to PPAs in the cancer palliative care setting. Our results underscore that PPAs can be easily done in large sample size, even in resource limited settings. The retrospective study design did NOT allow us to capture important predictors, such as patients' attitudes and beliefs regarding PPAs. Among the patients who did not complete PPAs, we could not tell from the chart if it was because PPAs were not offered or patient refused to sign. Thus, we could not evaluate the effectiveness of PPAs in this study.

A prospective study may improve data collection, but having to obtain patient consent may result in selection bias. Future research, such as randomized controlled trials, is needed to assess the benefit of universal PPAs in reducing NMOU. In this era of the opioid epidemic, the management of patients on opioids is highly complex, and PPAs may potentially represent a low-cost and simple intervention among other risk-mitigation strategies to support safe opioid use.

## References:

Pacheco, S.; Nguyen, L.M.T.; Halphen, J.M.; Samy, N.N.; Wilson, N.R.; Sattler, G.; Wing, S.E.; Feng, C.; Paulino, R.A.D.; Shah, P.; et al. Adherence to Opioid Patient Prescriber Agreements at a Safety Net Hospital. *Cancers* 2023, 15, 2943. <https://doi.org/10.3390/cancers15112943>