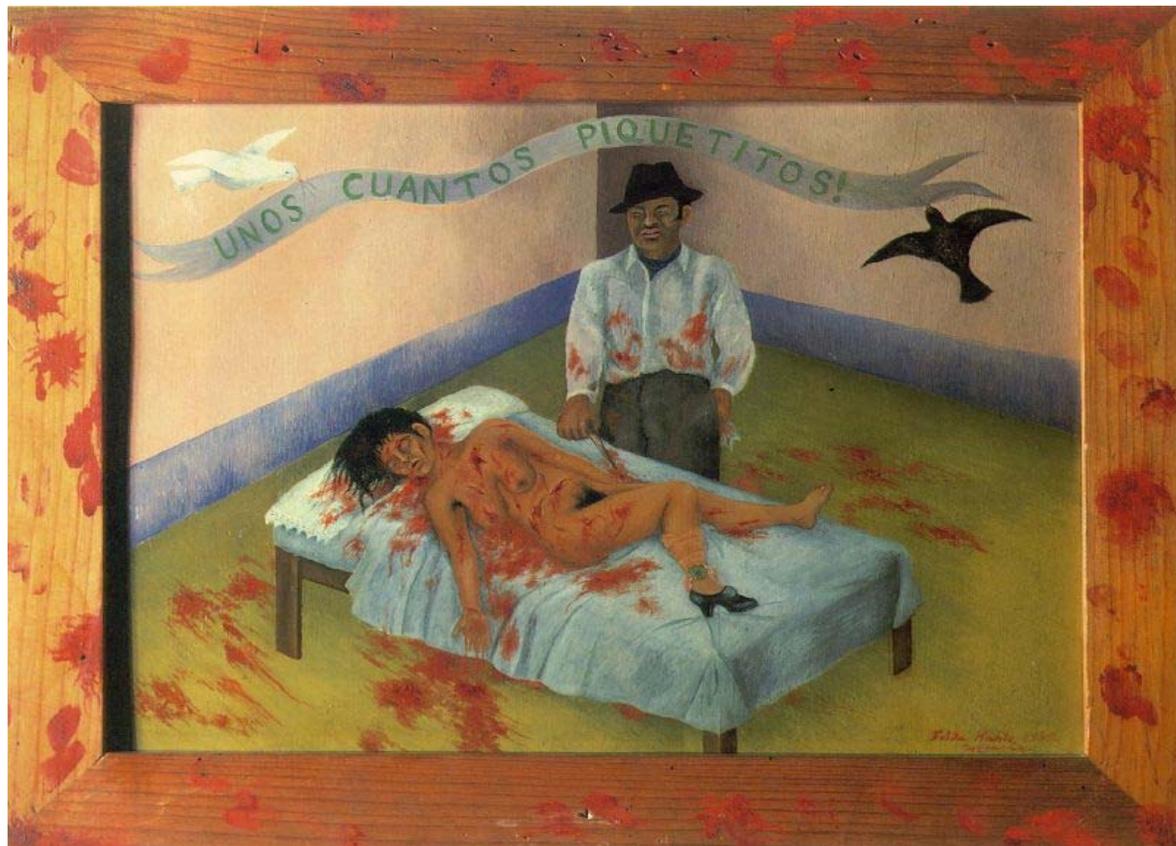
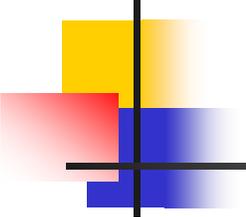


Epidemiology of Chronic Non-Cancer Pain and its Treatment with Opioids

Mark Sullivan, MD, PhD
University of Washington





“We are threatened with suffering from three directions:

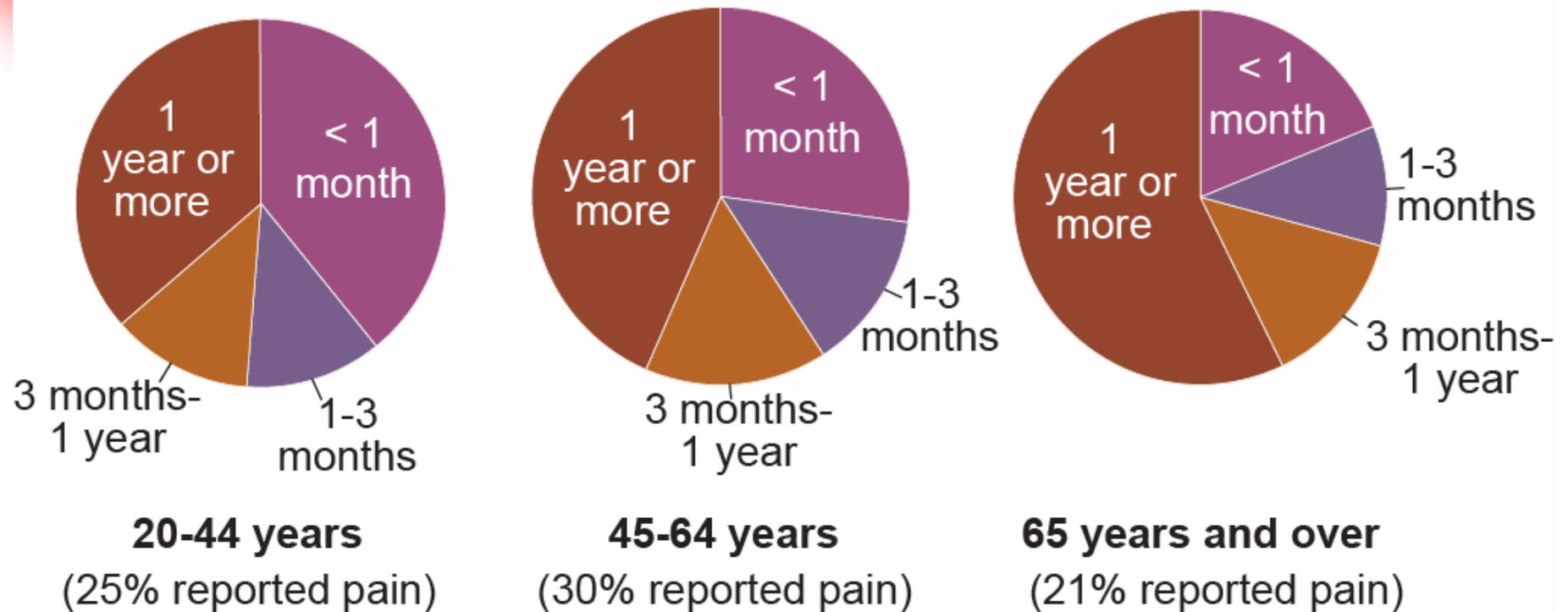
from our own body, which is doomed to decay and dissolution and which cannot do without pain and anxiety as warning signals;

from the external world, which may rage at us with overwhelming and merciless forces of destruction;

and finally from our relations to other men. The suffering which comes from this last source is perhaps more painful than any other.”

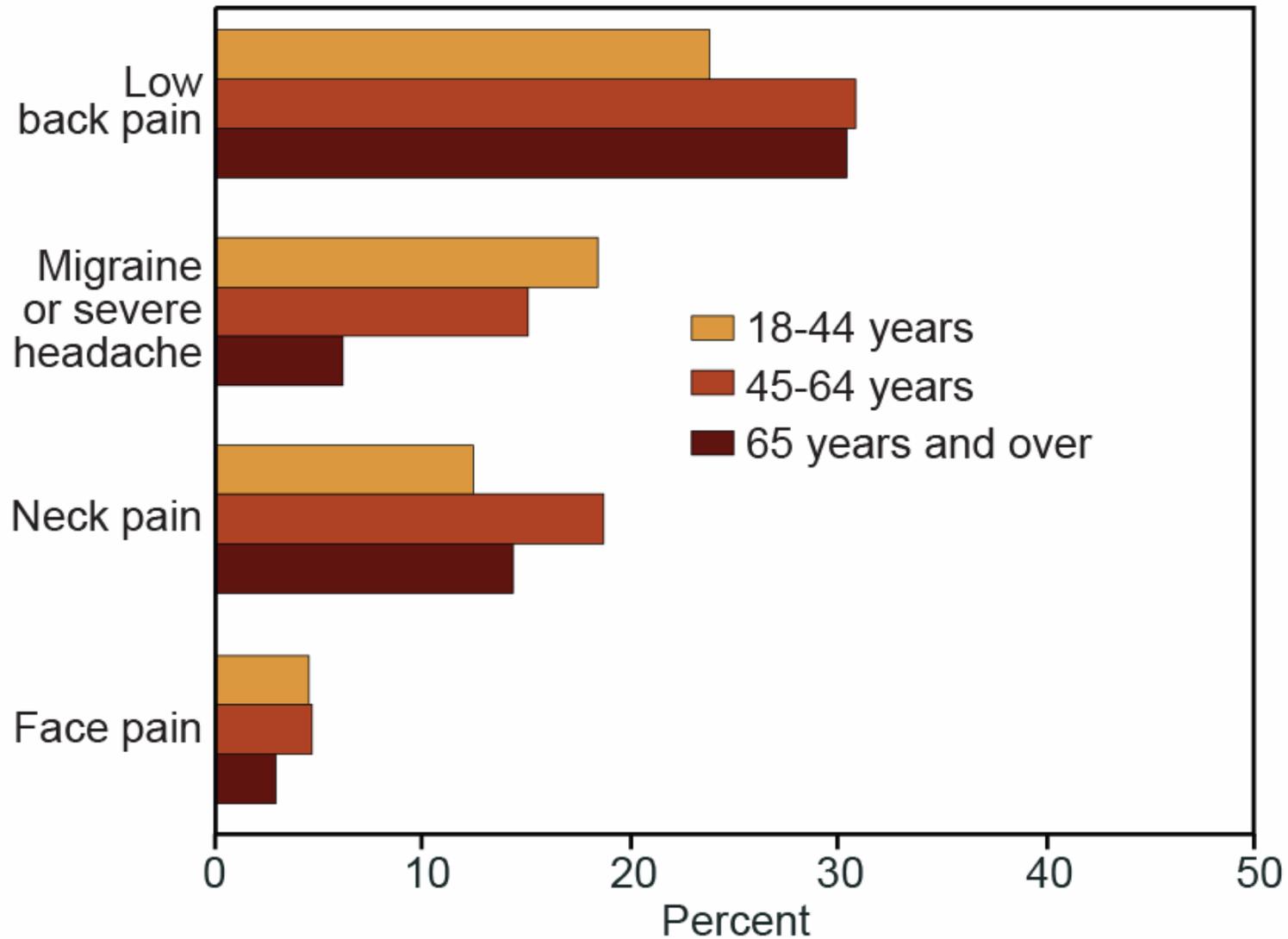
--Sigmund Freud, *Civilization and its Discontents*

Pain duration, 1999-2002



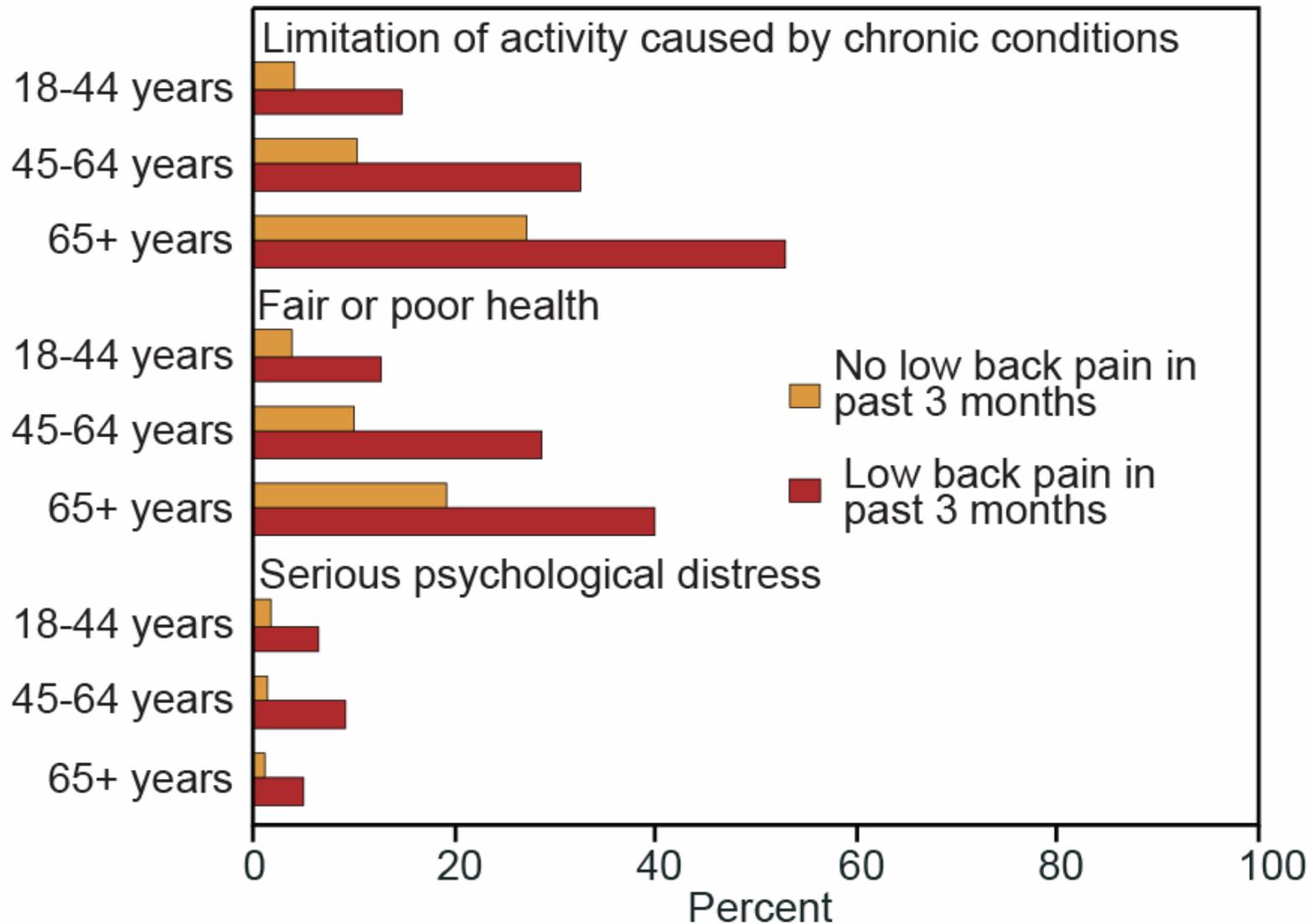
SOURCES: Centers for Disease Control and Prevention, National Center for Health Statistics, *Health, United States, 2006*, Figure 29. Data from the National Health and Nutrition Examination Survey.

Low back, neck, migraine, face pain in past 3 months, 2004



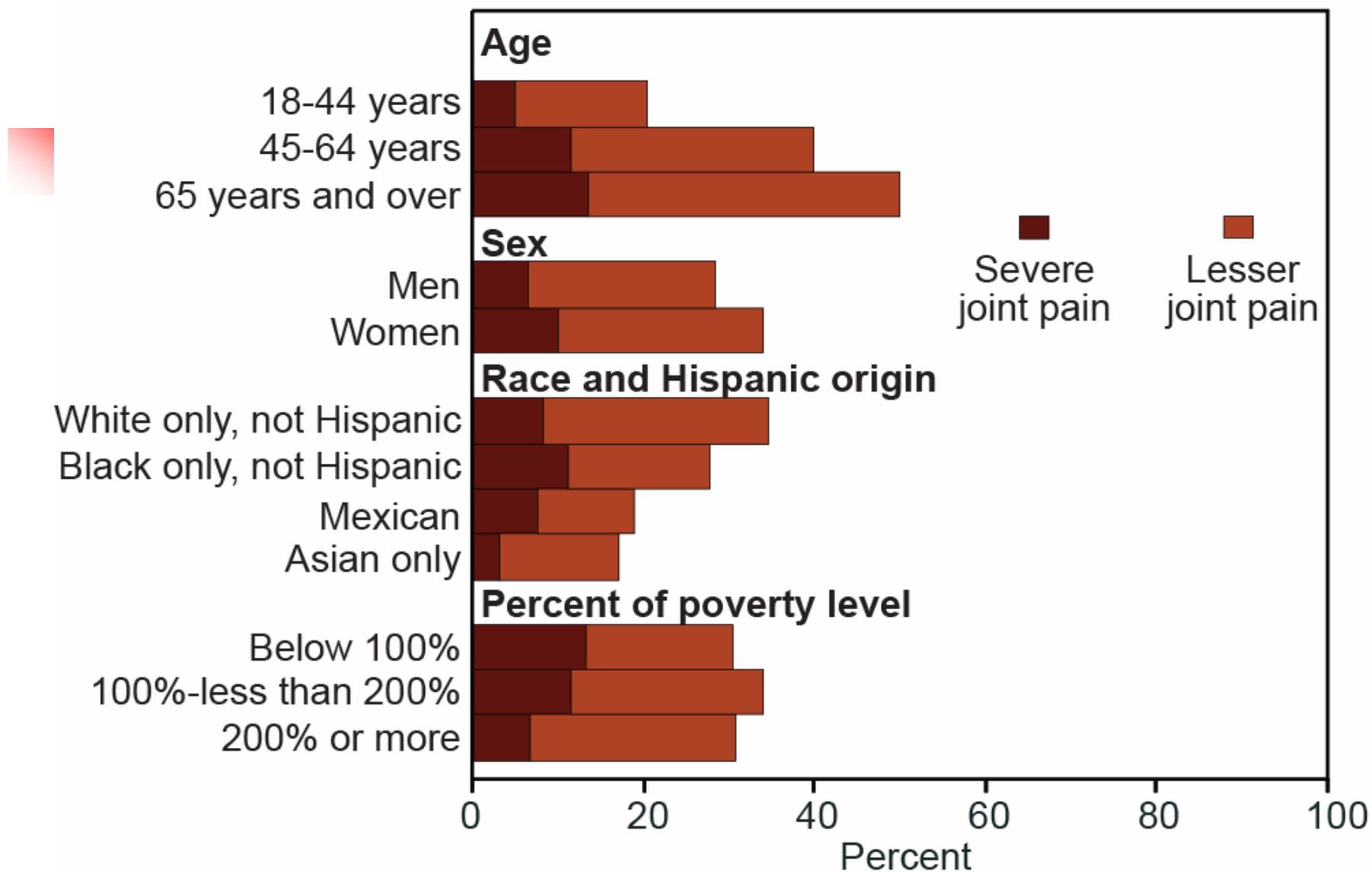
SOURCES: Centers for Disease Control and Prevention, National Center for Health Statistics, Health, United States, 2006, Figure 30. Data from the National Health Interview Survey.

Health status measures for adults with/without recent low back pain, 2004

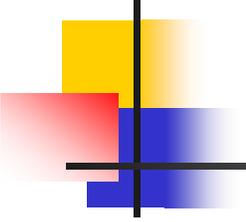


SOURCES: Centers for Disease Control and Prevention, National Center for Health Statistics, *Health, United States, 2006*, Figure 37. Data from the National Health Interview Survey.

Joint pain in past 30 days, 2003

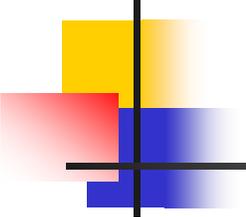


SOURCES: Centers for Disease Control and Prevention, National Center for Health Statistics, *Health, United States, 2006*, Figure 32. Data from the National Health Interview Survey.



Epidemiology of chronic pain in the community (UK)

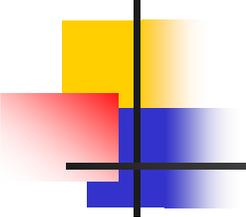
- Postal survey of random sample of 5035, 3605 returned
- 1817 (50%) of patients reported chronic pain (>3 mo), 576 back pain and 570 arthritis
- 49% had low intensity/ low disability pain, 16% had high intensity/ high disability pain
- 17% reported no treatment need
28% reported highest treatment need



Persistent pain in primary care: World Health Organization (WHO) Study

- 5438 patients from 15 sites in 14 countries were assessed by interview and questionnaires
- 22% of primary care patients had persistent pain (>6 months + care or disability)
 - More likely to have anxiety or depressive disorder (OR* =4.14)
- Pain-distress relationships were more consistent across cultures than pain-disability

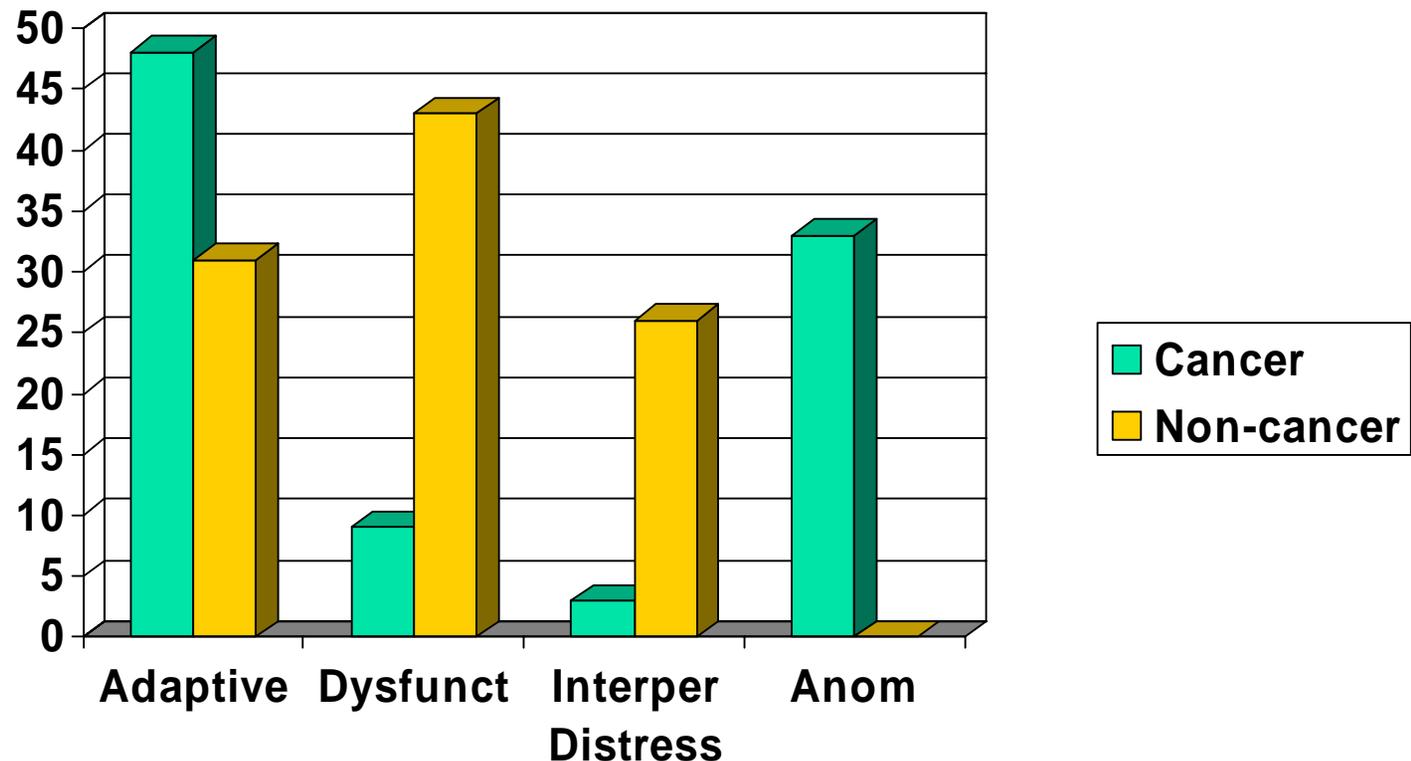
Gureje et al, *JAMA* 1998;280:147-151



Persistent pain in primary care: WHO Study

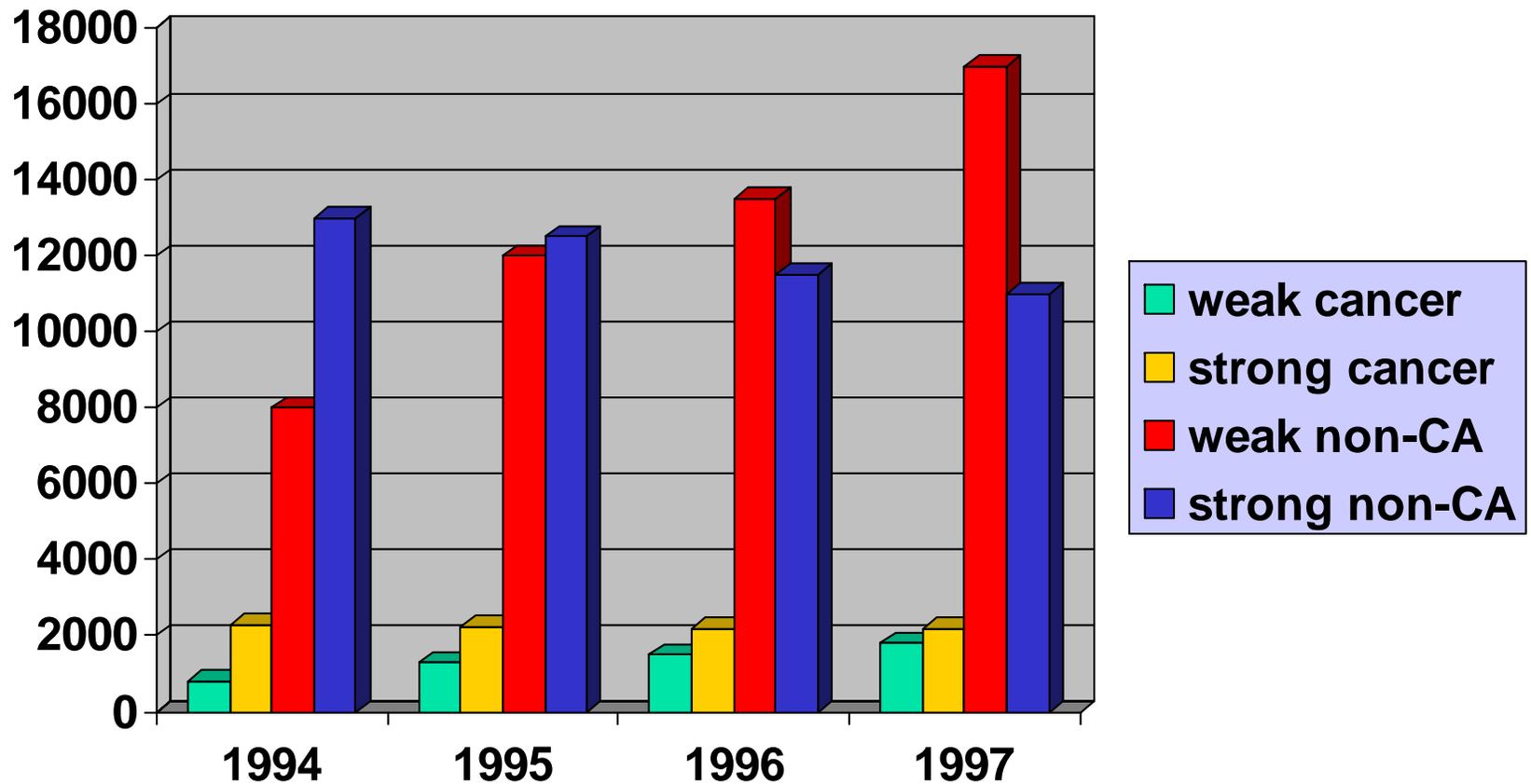
- 3197 patients from 15 sites in 14 countries were assessed at baseline and 12 months
- 50% with persistent pain at baseline still had pain at 12 months
 - Predicted by number of pain sites at baseline
- 8.8% had new-onset persistent pain
 - Predicted by psychiatric disorder, perceived poor health, and occupational role disability

Cancer vs. non-cancer pain: intensity, distress, interference



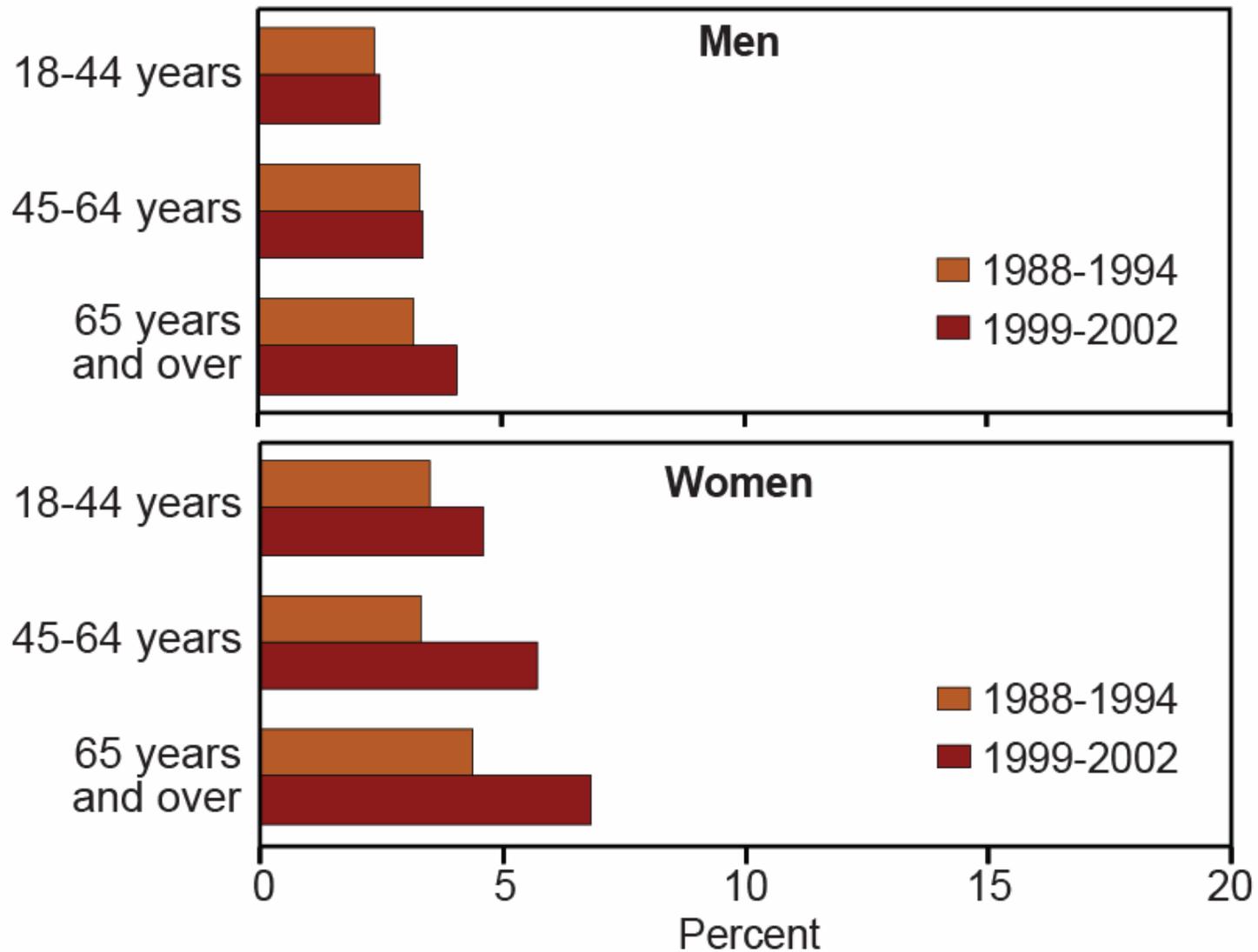
Zaza C et al. *Pain* 2000;87:75-82

Opioid users for cancer pain and non-cancer pain (in Denmark)



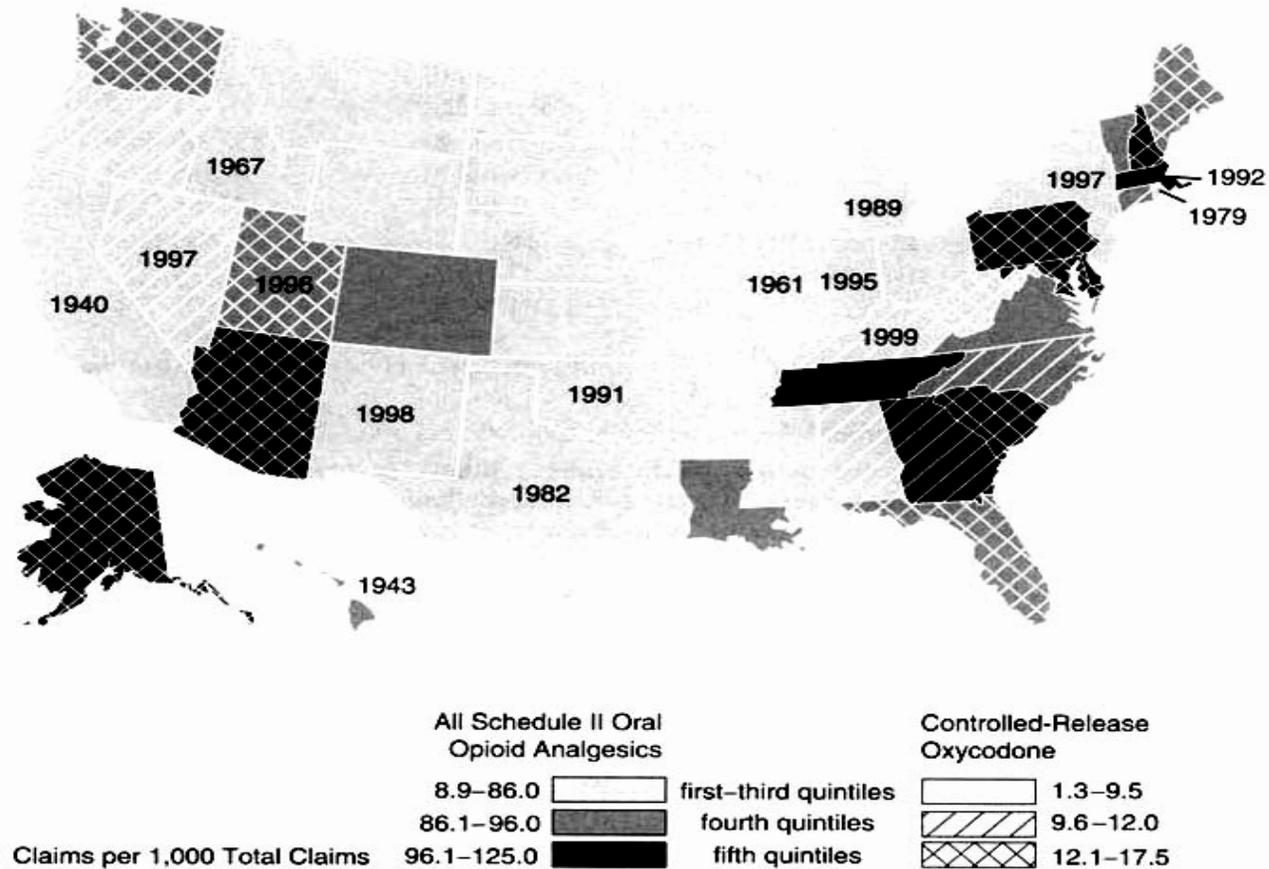
Jarlbaek L et al. *J Pain Sympt Mgmt* 1994;27:36-43

Narcotic analgesic drug use in past month



SOURCES: Centers for Disease Control and Prevention, National Center for Health Statistics, *Health, United States, 2006*, Figure 34. Data from the National Health and Nutrition Examination Survey.

Geographic variation in opioid prescription claims in 2000

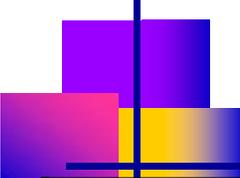


Curtis LH et al. *Health Serv Res* 2006;41:837-55

Provisional Results

Profile of Opioid Use Episodes in Group Health Cooperative

Years: 1997-2005, 457,095 episodes of opioid use in adults



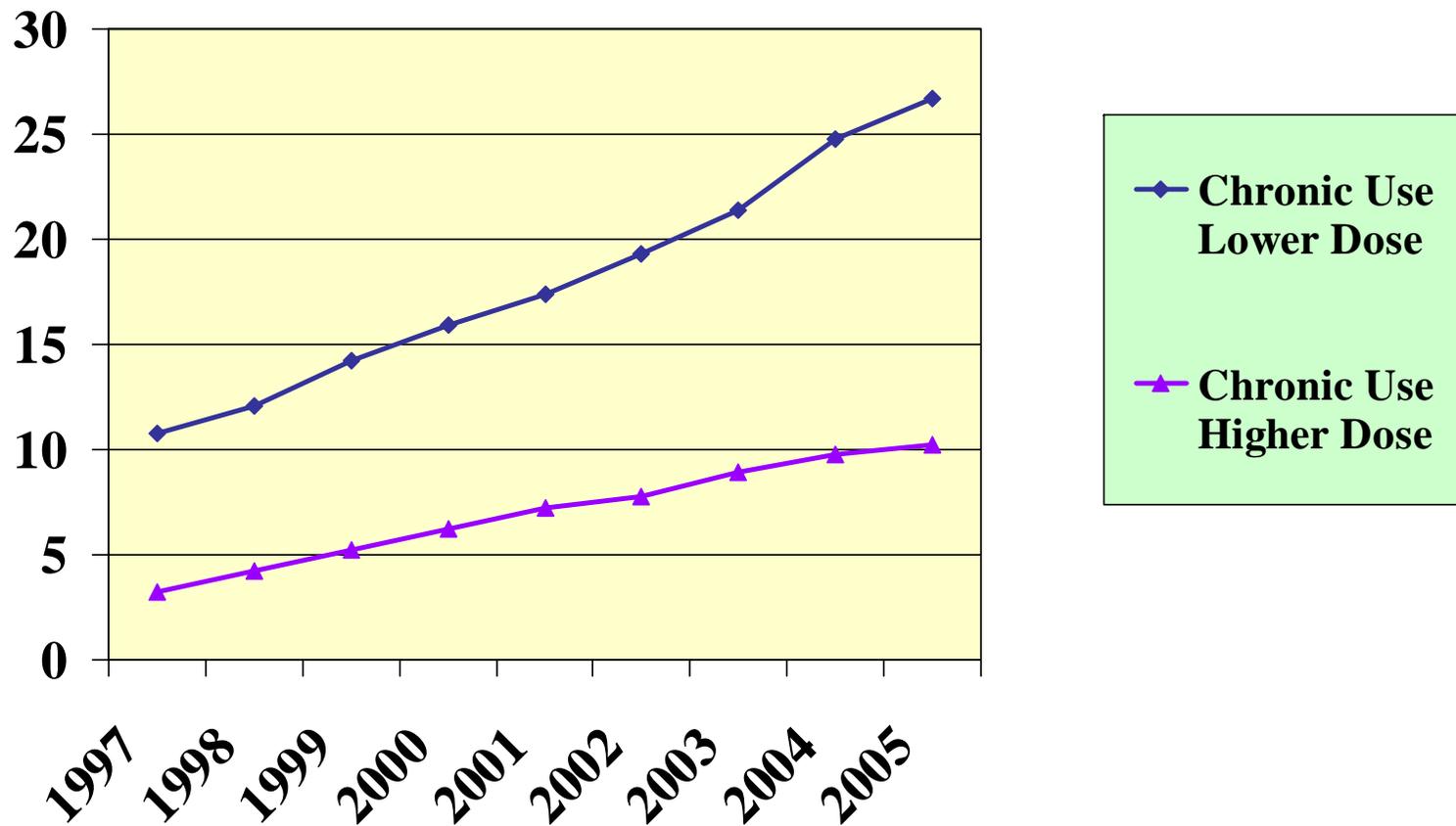
Episode Type	Mean Days Duration	Mean Days Supply	Average Daily Dose (mg morphine equiv)
Acute (<90 days duration) N=369,649 episodes	14	9.4	24.4 mg
Episodic (<10 fills & 120 days supply) N=63,392 episodes	103	29.4	4.5 mg
Chronic-Lower Dose (10+ fills OR 120+ days supply AND <20 mg) N=17,777 episodes	800	338.4	8.1 mg
Chronic-Higher Dose (10+ fills OR 120+ days supply AND >20 mg) N=6,277 episodes	906	834.8	53.7 mg

Supported by NIDA grant DA-022557 (PIs: Michael Von Korff and Connie Weisner)

Provisional Results

Prevalence of opioid use episodes per 1,000 adults:
chronic non-cancer pain at Group Health Cooperative*

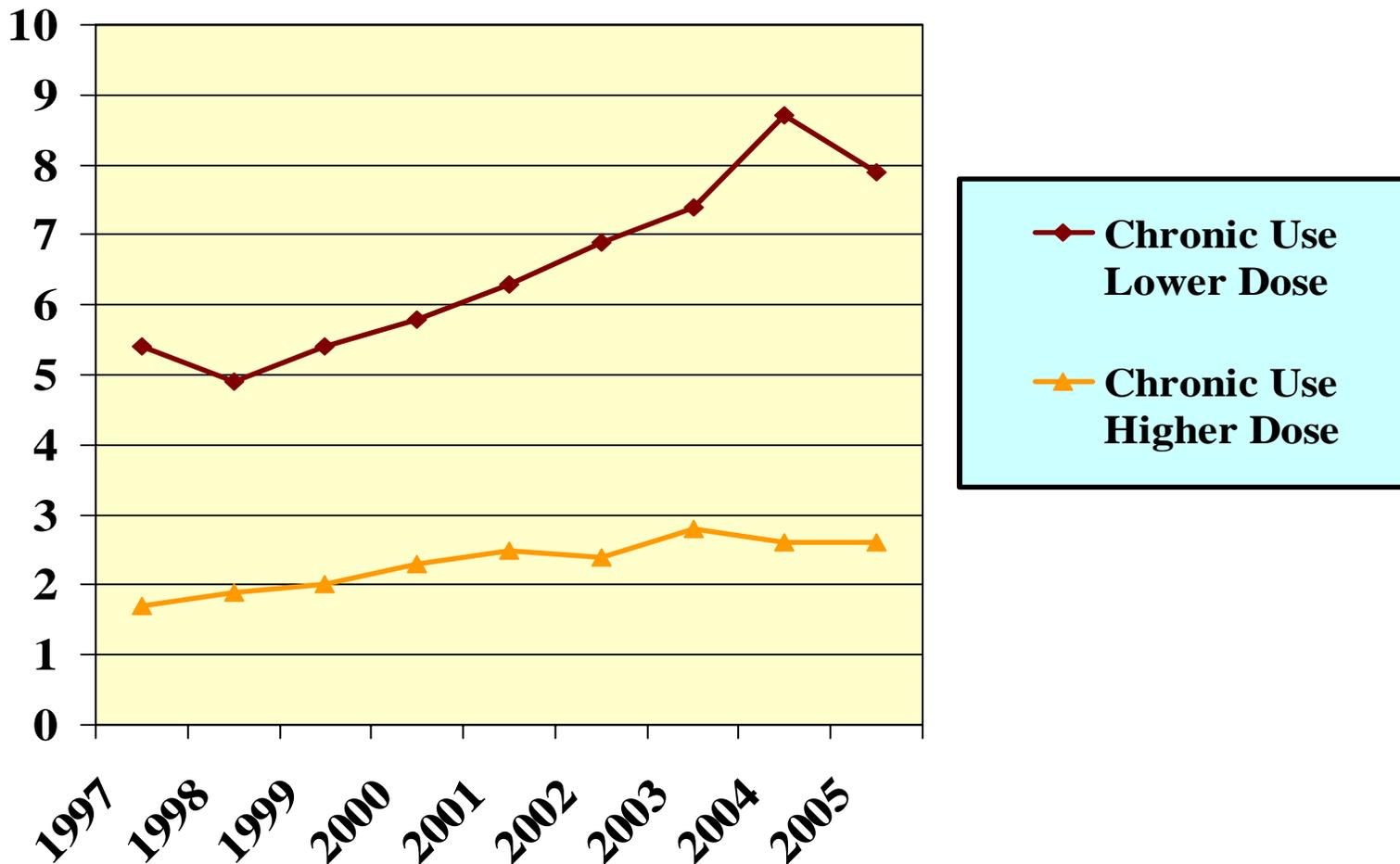
* population of approximately 300,000 adults



Supported by NIDA grant DA-022557 (PIs: Michael Von Korff and Connie Weisner)

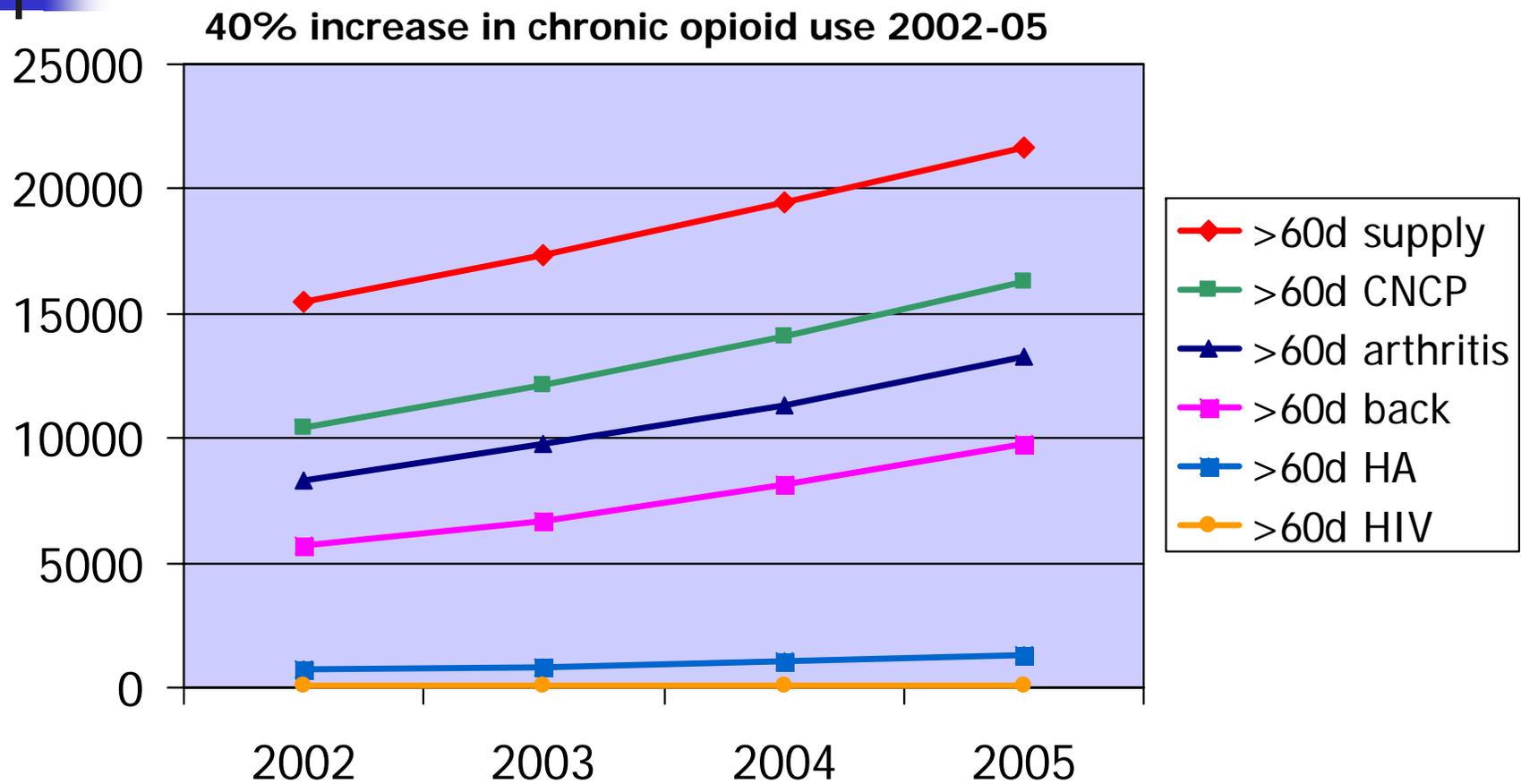
Provisional Results

Incidence of Opioid Use Episodes per 1,000 Adults:
Chronic Non-Cancer Pain at Group Health Cooperative*
** population of approximately 300,000 adults*

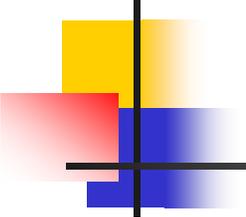


Supported by NIDA grant DA-022557 (PIs: Michael Von Korff and Connie Weisner)

Trends in opioid use (>60d supply) Arkansas Medicaid population 2002-05

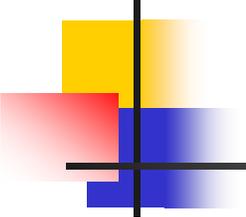


Supported by NIDA grant DA022560 (PI: Mark Sullivan)



Who regularly uses prescribed opioids for chronic non-cancer pain?

- Health Care for Communities (HCC)
 - Nationally representative household phone survey, 2 waves: 1997-1998, 2000-2001
 - DV: ≥ 1 mo regular use of prescribed opioids in 2000-2001
 - Asked about all prescribed medications they had taken “at least several times a week for a month or more” in the past 12 months



Independent Variables

- WHO-CIDI mental health and substance use disorders in 1997-1998
- Sociodemographics
- Physical Health (PCS from SF-12)
- Pain Interference (from SF-12)
- Self-Report General Health
- Chronic Conditions
 - (4 painful conditions: arthritis, back pain, headaches, other pain)
 - (13 non-painful conditions: hypertension, diabetes, heart disease...)

Sullivan MD et al. *Arch Intern Med* 2006

Characteristics of Users and Non-Users of Opioids for CNCP (continued)

	Total Sample (n=7,909)	Rx Opioid Users (n=262)	Non-Users Opioids (n=7,647)	χ^2 test: p- value
	Percent	Percent	Percent	
Demographic Characteristics				
Age				
18-30	15.7%	10.4%	15.9%	0.350
30-45	35.1%	37.1%	35.1%	0.771
46-60	23.9%	30.3%	23.8%	0.147
61 and older	25.3%	22.2%	25.3%	0.539
Female	52.6%	60.9%	52.4%	0.413
Race				
White	73.9%	87.8%	73.6%	0.001
Black	11.9%	4.2%	12.1%	<0.001
Hispanic	11.1%	4.7%	11.2%	0.005
Other	3.1%	3.4%	3.1%	0.869

Characteristics of Users and Non-Users of Opioids for CNCP (continued)

	Total Sample (n=7,909)	Rx Opioid Users (n=262)	Non-Users Opioids (n=7,647)	χ^2 test: p- value
	Percent	Percent	Percent	
Marital Status				
Married	60.2%	66.9%	60.1%	0.196
Single	33.9%	29.7%	34.0%	0.380
Unmarried partner	5.6%	3.3%	5.6%	0.236
Education				
Less than high school	13.4%	15.1%	13.3%	0.415
High school	61.6%	67.3%	61.4%	0.366
More than high school	25.1%	17.6%	25.3%	0.219
Household Income				
<= \$19,000	23.6%	29.7%	23.4%	0.082
\$19,001-\$40,000	25.8%	26.1%	25.8%	0.942
\$40,001-70,000	26.9%	28.6%	26.9%	0.813
\$70,001 or higher	23.7%	15.6%	23.9%	0.227

Sullivan MD et al. *Arch Intern Med* 2006

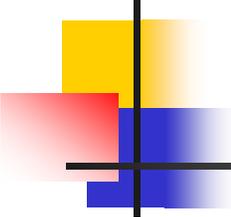
Characteristics of Users and Non-Users of Opioids for CNCP (continued)

	Total Sample (n=7,909)	Rx Opioid Users (n=262)	Non-Users of Opioids (n=7,647)	χ^2 test: p- value
	Percent	Percent	Percent	
Health Status				
Level of Pain Interference				
High pain	10.3%	57.2%	9.2%	<0.001
Moderate pain	36.3%	35.1%	36.3%	0.820
No pain	53.4%	7.7%	54.4%	<0.001
Self-rated Health				
Excellent	16.2%	8.7%	16.4%	0.091
Very Good	37.2%	9.0%	37.8%	<0.001
Good	28.7%	29.2%	28.7%	0.950
Fair	13.6%	28.4%	13.2%	0.001
Poor	4.4%	24.8%	3.9%	<0.001
BMI				
Under 20	5.5%	6.1%	5.5%	0.632
20 to 25	32.8%	38.9%	32.7%	0.243
25 to 30	36.7%	28.4%	36.9%	0.045

Characteristics of Users and Non-Users of Opioids for CNCP (continued)

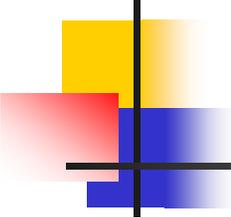
	Total Sample (n=7,909)	Rx Opioid Users (n=262)	Non-Users of Opioids (n=7,647)	χ^2 test: p- value
	Percent	Percent	Percent	
Painful Conditions				
Arthritis or rheumatism	25.9%	62.9%	25.0%	<0.001
Chronic back problems	16.5%	59.3%	15.5%	<0.001
Migraine/chronic headaches	11.6%	38.3%	11.0%	<0.001
Other chronic pain condition	8.8%	35.2%	8.3%	<0.001
Any of 4 pain conditions above	42.5%	89.6%	41.4%	<0.001
Any of 3 pain conditions (not other)	39.3%	87.5%	38.3%	<0.001

Sullivan MD et al. *Arch Intern Med* 2006



Characteristics of Users and Non-Users of Opioids for CNCP (continued)

	Total Sample (n=7,909)	Rx Opioid Users (n=262)	Non-Users of Opioids (n=7,647)	χ^2 test: p- value
	Percent	Percent	Percent	
Mental Health and Substance Abuse				
Major Depression (MDD)	9.8%	37.1%	9.2%	<0.001
Dysthymia	4.3%	13.6%	4.1%	<0.001
Generalized Anxiety (GAD)	4.0%	12.0%	3.8%	<0.001
Panic Disorder	3.2%	13.1%	3.0%	<0.001
At least one of 4 disorders above	13.7%	44.2%	13.0%	<0.001
Any illicit substance use	5.8%	8.8%	5.7%	0.065
Problem drug use	2.0%	4.1%	2.0%	0.029
Problem alcohol use	5.1%	2.6%	5.2%	0.089

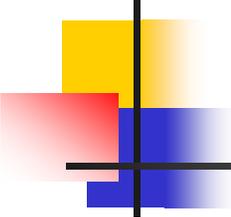


Predicting 2001 opioid use from 1998 demographic and clinical variables

OR (95% CI)

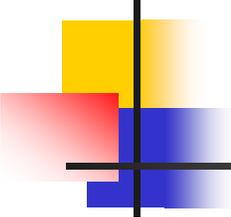
Common mental health disorders and problem alcohol and drug use

Any common mental health disorders	1.96 (1.47, 2.62)
Any problem alcohol use	0.63 (0.35, 1.15)
Any problem drug use	2.98 (1.68, 5.30)



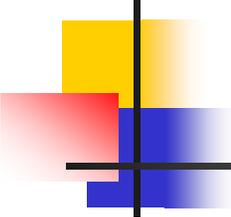
Predicting 2001 opioid use from 1998 demographic and clinical variables

	OR (95% CI)
Sociodemographics	
Gender	0.88 (0.49, 1.58)
Age	
<30	1.62 (0.46, 5.69)
30 – 45	1.27 (0.79, 2.03)
46 – 60	1.01 (0.61, 1.66)
>60	--
Race	
White	--
Black/African American	0.78 (0.53, 1.16)
Hispanic	0.76 (0.40, 1.41)
Other race	0.56 (0.38, 0.81)



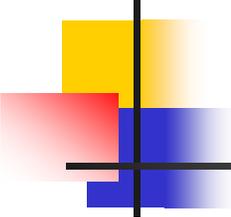
Predicting 2001 opioid use from 1998 demographic and clinical variables

	OR (95% CI)
Marital Status	
Married	--
Single	0.99 (0.68, 1.43)
Living with Partner	0.87 (0.37, 2.04)
Education	
Less than high school	1.61 (1.07, 2.43)
High school graduate	--
College or higher	1.38 (1.00, 1.91)



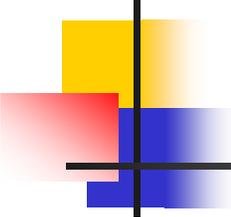
Predicting 2001 opioid use from 1998 demographic and clinical variables

	OR (95% CI)
Currently Insured	1.23 (0.83, 1.82)
Region of the Country	
West	--
South	1.70 (1.10, 2.65)
Midwest	1.04 (0.77, 1.40)
Northeast	0.97 (0.64, 1.47)



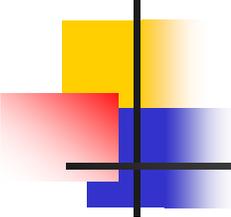
Predicting 2001 opioid use from 1998 demographic and clinical variables

	OR (95% CI)
Family income	
≤19,000	1.07 (0.5, 2.28)
\$19,001 - \$40,000	1.17 (0.73, 1.89)
\$40,001 - \$70,000	0.97 (0.58, 1.60)
>\$70,000	--
Reporting work disabled as employment status	1.36 (0.89, 2.07)



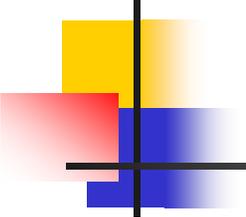
Predicting 2001 opioid use from 1998 demographic and clinical variables

	OR (95% CI)
Clinical Variables	
SF-12 Physical Component Score	0.96 (0.91, 1.00)
Self-Reported Health	
Excellent	--
Very good	0.84 (0.49, 1.45)
Good	0.70 (0.35, 1.38)
Fair	0.85 (0.35, 2.07)
Poor	0.59 (0.16, 2.12)



Predicting 2001 opioid use from 1998 demographic and clinical variables

	OR (95% CI)
Number of Self-Reported Chronic Conditions	1.06 (0.99, 1.14)
Chronic Pain Conditions	
Arthritis	1.47 (1.14, 1.88)
Chronic back pain	2.39 (1.80, 3.17)
Chronic severe headaches	0.76 (0.52, 1.12)
Other chronic pain conditions	1.06 (0.63, 1.81)
High Pain Interference (extremely/a lot)	2.37 (1.51, 3.71)



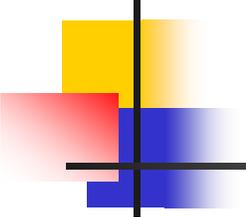
Who develops opioid abuse/dependence among those receiving opioid therapy for chronic non-cancer pain?

Using pharmacy and diagnostic codes from VA VISN-16 data warehouse for 2000-2005 to identify individuals with at least 91+ days of opioid use in 2002. [N= 15,162; ~5% of all pts]

Excluded individuals with opioid abuse diagnosis in 2000-2002, to ensure that predictors preceded the outcome.

Dependent Variable:

Diagnosis of Opioid Abuse or Dependence in Years 2003-2005. [N=298; ~2% chronic users]



Independent variables from 2002

- Mental Health and Substance Use Disorders
- Common Painful conditions (back pain, arthritis, migraines, headaches)
- Sociodemographic factors
- Number of days of opioid supply
- Health care utilization (proxy for medical comorbidity)

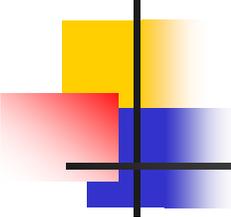
Used multiple logistic regression to investigate diagnosis of opioid abuse/dependence in 2003 to 2005, using covariates from 2002.

Predictors of opioid abuse/dependence diagnoses (2003-05) among individuals with >90d use of opioids in 2002

	OR	95% CI		p-value
Age				
< 40	1.22	0.77	1.90	.40
40-49	1.00	reference group		--
50-59	0.61	0.46	0.80	<.001
60 +	0.21	0.14	0.31	<.001
Marital Status				
Married	1.00	reference group		--
Divorced	1.58	1.22	2.06	.001
Single	1.60	1.02	2.51	.04
Separated	1.84	1.12	3.02	.02
Widowed	1.21	0.64	2.30	.56
Race				
White	1.00	reference group		--
Black	0.60	0.41	0.88	.01
Other	1.49	0.77	2.91	.24
Unknown	0.47	0.30	0.72	.001
Gender				
Male	1.00	reference group		--
Female	0.59	0.35	1.00	.05

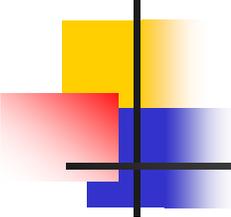
Predictors of opioid abuse/dependence diagnoses (2003-05) among individuals with >90d use of opioids in 2002 (continued)

	OR	95% CI		p-value
Days with Physical Health Care Visits				
0-6	1.00	reference group		--
7-11	1.07	0.71	1.60	.75
12-19	1.24	0.85	1.82	.27
20+	1.52	1.03	2.25	.03
Physical Inpatient Stay	1.27	0.95	1.71	.11
Non-Opioid Substance Abuse/Dependence	2.34	1.75	3.14	<.001
Mental Health Diagnosis	1.46	1.12	1.91	.005
Back Pain	1.27	0.98	1.64	.07
Arthritis	0.86	0.67	1.10	.23
Headache/Migraine,	1.13	0.79	1.62	.49
Days Opioid Supply				
91-150	1.00	reference group		--
151-210	1.08	0.72	1.61	.71
211+	1.84	1.35	2.51	<.001
New User	0.88	0.67	1.15	.34



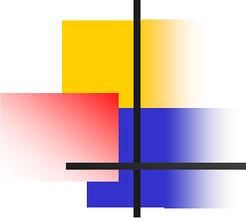
Collaborators

- Mark Edlund, MD, PhD
Diane Steffick, PhD
Teresa Hudson, PharmD
 - University of Arkansas for Medical Sciences
- Kenneth Wells, MD, MPH
Lily Zhang, MS
 - University of California, Los Angeles
- Jurgen Unutzer, MD, MPH
 - University of Washington



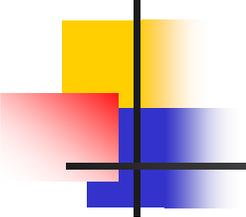
Summary of results

- Individuals who regularly use of opioids for CNCP have high rates of medical (painful and non-painful) and psychiatric comorbidity.
- Psychiatric disorders (MH and SA) are associated with use of opioids for CNCP.
- Among individuals with opioid use for CNCP, psychiatric disorders are risk factors for development of opioid abuse/dependence.



Discussion of results

- Though individuals with psychiatric disorders are more likely to receive opioids for CNCP and to abuse opioids, they have been excluded as 'high risk' from almost all opioid clinical trials.
- Thus there is a serious mismatch between the evidence base for opioid use and current clinical practice



Discussion of results

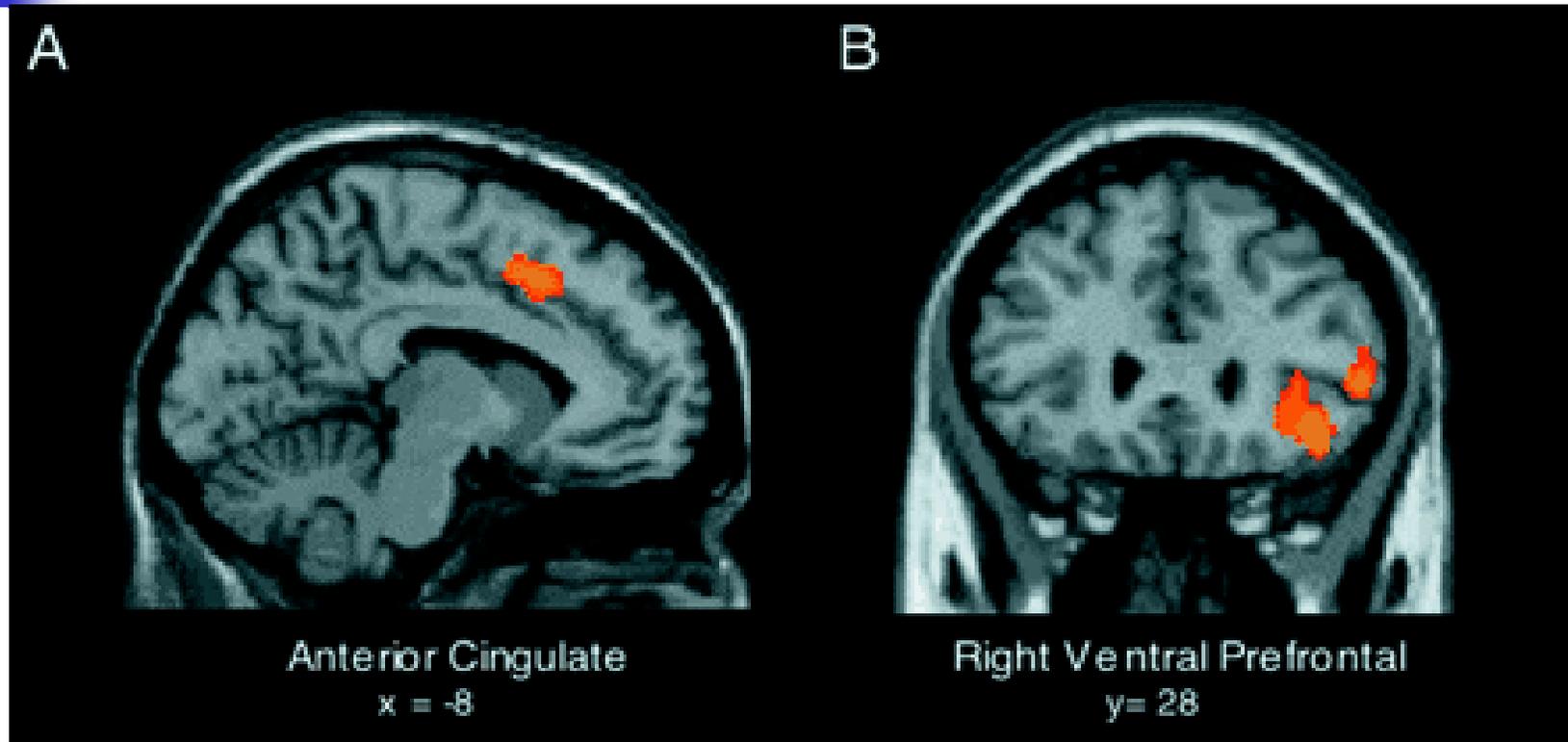
- Substance abuse has received the most attention as a risk factor for misuse of prescribed opioids.
- But the population attributable risk for opioid abuse from mental health disorders (OR=1.46, prevalence=45%) is likely greater than the population attributable risk from non-opioid substance disorders (OR=2.43, prevalence=7.6%).

Does rejection hurt?

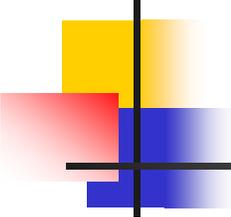
An fMRI study of social exclusion

- Participants underwent fMRI:
excluded from virtual ball tossing game,
mimicking social rejection.
- Increased activity in anterior cingulate cortex
correlated positively with distress.
Increased activity in right ventral prefrontal
cortex correlated negatively with distress.
- Parallel to findings of physical pain studies.

The brain in pain: physical or social?



In mammals, the social-attachment system borrowed computations of the pain system to prevent the harmful consequences of social separation.



Clinical implications

- Diagnosis and treatment of psychiatric disorders (MH and SA) are important when considering patients for chronic opioid therapy.
- However, which psychiatric services would actually help these individuals is not well defined.

May I never see in the patient anything
but a fellow creature in pain.

--Oath of Maimonides

