


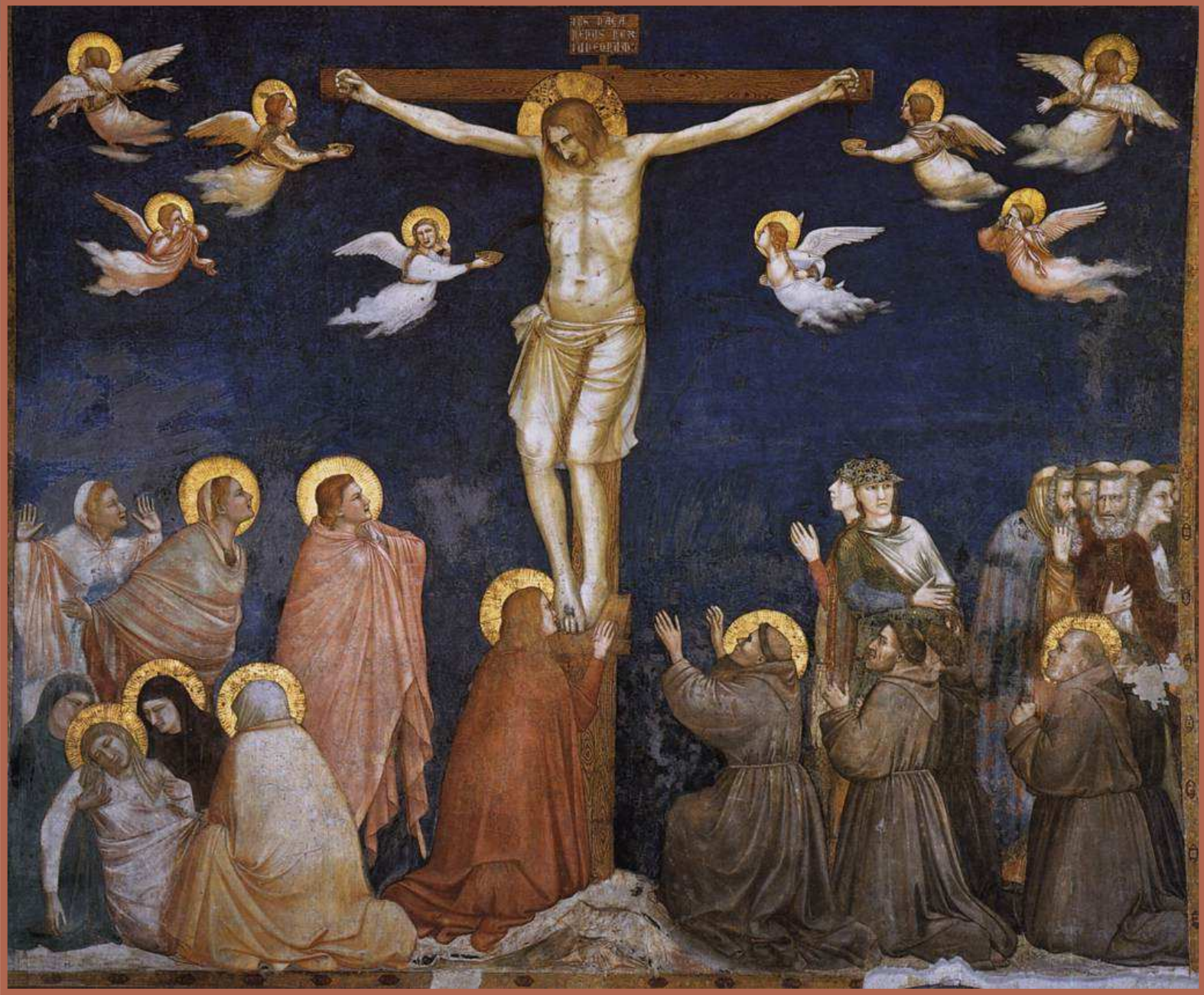


Journal Club  
**Venerdì Santo**  
**25 marzo 2016**  
*Aggiornamenti in geriatria*

# Il dolore e la sofferenza

**Marco Trabucchi**

- 
- **Il medico “Signore del sabato”**
  - **Divinum opus est sedare dolorem**
  - **Una medicina inadeguata**
  - **Le contraddizioni nella prescrizione degli oppiacei**
  - **Cannabinoidi e dolore**
  - **Rispetto della complessità e non semplificazioni nella cura del dolore**
  - **Il senso della sofferenza**




## **“Misericordia io voglio e non sacrifici”**

Mt 12, 1-8


*Gesù passò, in giorno di sabato, fra campi di grano e i suoi discepoli ebbero fame e cominciarono a cogliere delle spighe e a mangiarle.*

*Vedendo ciò, i farisei gli dissero: «Ecco, i tuoi discepoli stanno facendo quello che non è lecito fare di sabato».*

*Ma egli rispose loro: «Non avete letto quello che fece Davide, quando lui e i suoi compagni ebbero fame? Egli entrò nella casa di Dio e mangiarono i pani dell’offerta, che né a lui né ai suoi compagni era lecito mangiare, ma ai soli sacerdoti. O non avete letto nella Legge che nei giorni di sabato i sacerdoti nel tempio violano il sabato e tuttavia sono senza colpa? Ora io vi dico che qui vi è uno più grande del tempio. Se aveste compreso che cosa significhi: “Misericordia io voglio e non sacrifici”, non avreste condannato persone senza colpa. Perché il Figlio dell’uomo è signore del sabato».*



**... il medico deve imparare -per quanto sia molto difficile- a diventare “Signore del sabato”, cioè capace di misericordia non condizionata da fattori economico-organizzativi.**



**Una visione della cura del dolore che  
comprenda la presa in carico  
dell'ammalato e di tutte le sue difficoltà.  
Alcuni esempi ...**

Invito alla  
**LITURGIA**

pensata in modo particolare per persone con disturbi cognitivi e demenza,  
loro famigliari, operatori professionali e volontari.



**Giovedì, 17 marzo 2016 - ore 15**

presso la chiesa parrocchiale S. Maria Assunta di Merano

*Le persone con deterioramento cognitivo e demenza  
saranno al centro di questa particolare funzione religiosa,  
insieme ai loro famigliari e a chi presta loro assistenza.*

Accoglieremo l'invito di Dio ad avvicinarci a Lui  
grazie ad una celebrazione che ci coinvolgerà attraverso i vari sensi,  
con un vocabolario e con parole semplici, canti tradizionali ed immagini  
che ci guideranno nella preghiera, risvegliando ciò che potrebbe essere sbiadito.

**Chiediamo di voler allargare l'invito a tutti gli interessati!**

Possibilità di parcheggio davanti alla chiesa.

Vi aspettiamo!

**Promotori:**  
Can. Johannes Noisternigg, incaricato per la Pastorale degli anziani presso la  
Diocesi Bolzano-Bressanone  
Associazione A.S.A.A. - Alzheimer Südtirol Alto Adige



Istituto per l'Analisi dello Stato Sociale

primavera 2015



# L'Arco di Giano

83

RIVISTA DI MEDICAL HUMANITIES

83 primavera 2015

Chi soffre per l'Alzheimer



## Chi soffre per l'Alzheimer


A CURA DI ANGELO BIANCHETTI E MARCO TRABUCCHI



Poste Italiane SPA - Spedizione in Abbonamento Postale - DL 353/2003 (conv. in L. 27/2/2004 n. 46) art. 1 comma 1 DCB - Roma







**Un dolore è sempre nuovo per chi non ha memoria: è una sensazione senza storia, che certamente induce paura nella mente di chi non ricorda di esserne stato colpito in altre occasioni.**

**Nessuna persona “normale” sarà mai in grado di descrivere questa sensazione; non per questo si deve rinunciare a collocarsi nella vita di chi ha perso la mente... per esprimere un sentimento di dolente comprensione, volta ad un impegno perché il dolore possa rapidamente essere cancellato.**

(Bianchetti e Trabucchi, L'Arco di Giano “Chi soffre per l'Alzheimer”, (83):3-14, 2015)

# Psicogeriatría

ANNO X - SUPPLEMENTO - NUMERO 2 - MAGGIO-AGOSTO 2015

## La depressione nella persona che invecchia



Documento dell'Associazione Italiana di Psicogeriatría



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# Le depressioni nell'esperienza clinica

- **La depressione sotto soglia**
- **La depressione dei depressi**
- **La depressione maschile; la depressione delle donne**
- **La depressione associata alla malattia grave (i.e. il cancro)**  
La domanda di verità
- **La depressione dell'ammalato cronico, della persona disabile**
- **La depressione nel lutto: del coniuge, del figlio, degli amici**
- **La depressione di chi sta perdendo la memoria, di chi l'ha persa (i.e. AD)**
- **La depressione legata della decrepitezza senile**  
Ogni cosa è un problema, difficili le cose normali; viene meno ciò che dava piacere e non si può più fare
- **La depressione in ospedale e quella in casa di riposo. La depressione nell'hospice**
- **La depressione della solitudine, dell'abbandono (si può morire di solitudine)**  
Imposta da un destino di malattia  
Imposta dalla perdita di umane relazioni  
Imposta dall'indigenza (che si accompagna alla perdita del lavoro o della casa)  
La depressione dei vecchi preti
- **La depressione di chi ha perso la patente (e non il desiderio di guidare)**  
La guida e l'autonomia
- **La depressione (la vergogna) per la separazione dei figli; dell'anziano che è lasciato; dell'anziano che si separa**
- **La depressione causata dalla malvagità umana**  
Crudeltà raccapriccianti che gli uomini sono capaci di commettere ai danni di altri esseri umani
- **La depressione caratterologica**  
La "lamentosità poco dignitosa" verso la quale è difficile provare compassione
- **La depressione del caregiver**  
(e di chi non lo è, ma vorrebbe esserlo)
- **La depressione narrata (il dolore raccontato)**





**... dalla religiosità, alla cultura, alla clinica:  
le molte diverse espressioni della cura del dolore.**



La medicina e il dolore: *“Divinum opus est sedare dolorem”*.

Dopo secoli di storia, l’analgesia farmacologica presenta ancora incertezze, contraddizioni, errori.



**La medicina contemporanea è in grado  
tecnicamente e culturalmente di curare  
il dolore?**

**Over the course of a given year, approximately 100 million people in the United States suffer from pain.**

**Some 9 million to 12 million of them have chronic or persistent pain, while the remainder have short-term pain from injuries, illnesses, or medical procedures.**

**All of them should benefit from skillful and appropriate pain management, which may include the judicious use of opioid medicines in conjunction with other methods of treatment or in circumstances in which nonaddictive therapies are insufficient to control pain.**

(Califf RM, et al. New Engl J Med, February 4, 2016)

# Zero Pain Is Not the Goal

Thomas H. Lee, MD, MSc

**What should health care be trying to accomplish? This question becomes increasingly important as research advances, the population ages, and financial pressures intensify. Simple measures for which 100% is the target cannot define performance for the complex work of health care. Quality does not mean the elimination of death or perfect compliance with guidelines. Efficiency does not mean the elimination of all spending or even 100% elimination of all wasteful spending. And compassion for patients does not mean the elimination of all pain.**

JAMA Published online March 15, 2016






**Una medicina non solo inadeguata,  
ma anche pericolosa ...**

# Rising morbidity and mortality in midlife among white non-Hispanic Americans in the 21st century


Anne Case<sup>1</sup> and Angus Deaton<sup>1</sup>

This paper documents a marked increase in the all-cause mortality of middle-aged white non-Hispanic men and women in the United States between 1999 and 2013. This change reversed decades of progress in mortality and was unique to the United States; no other rich country saw a similar turnaround. The midlife mortality reversal was confined to white non-Hispanics; black non-Hispanics and Hispanics at midlife, and those aged 65 and above in every racial and ethnic group, continued to see mortality rates fall. This increase for whites was largely accounted for by increasing death rates from drug and alcohol poisonings, suicide, and chronic liver diseases and cirrhosis. Although all education groups saw increases in mortality from suicide and poisonings, and an overall increase in external cause mortality, those with less education saw the most marked increases. Rising midlife mortality rates of white non-Hispanics were paralleled by increases in midlife morbidity. Self-reported declines in health, mental health, and ability to conduct activities of daily living, and increases in chronic pain and inability to work, as well as clinically measured deteriorations in liver function, all point to growing distress in this population. We comment on potential economic causes and consequences of this deterioration.



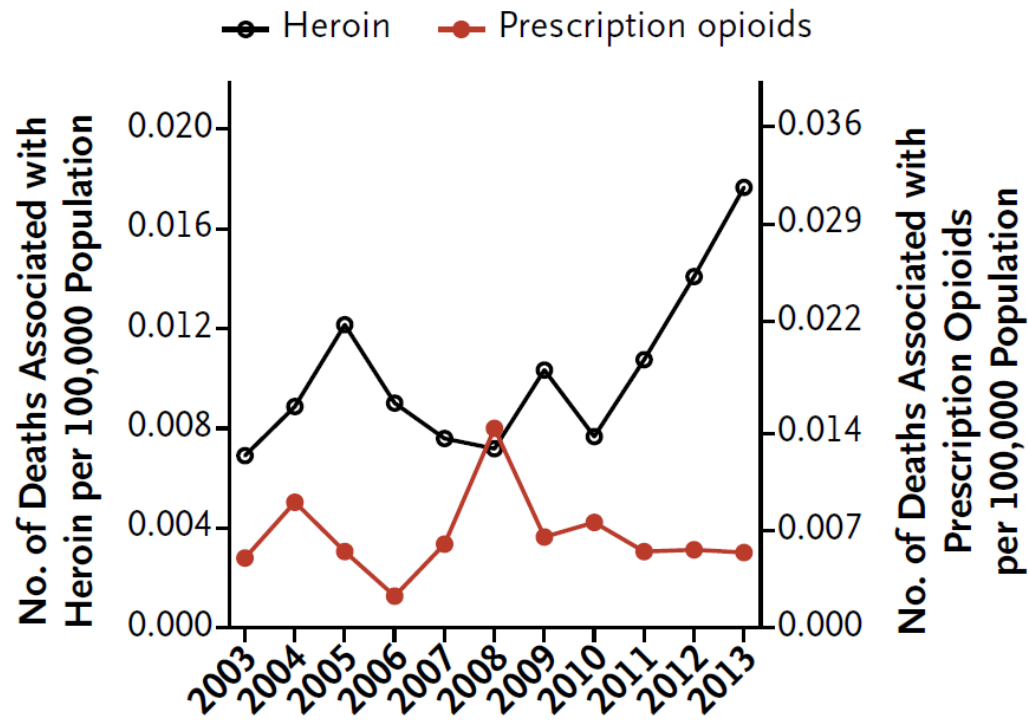
**But while universal health care, higher minimum wages, aid to education, and so on would do a lot to help Americans in trouble, I'm not sure whether they're enough to cure existential despair.**

**(Paul Krugman, 2015)**



**Many Americans are now addicted to prescription opioids, and the number of deaths due to prescription opioid overdose is unacceptable. This past month, the Centers for Disease Control and Prevention (CDC), estimated that in 2014 there were almost 19,000 overdose deaths in the United States associated with prescription opioids.**

(Califf RM, et al. New Engl J Med, February 4, 2016)

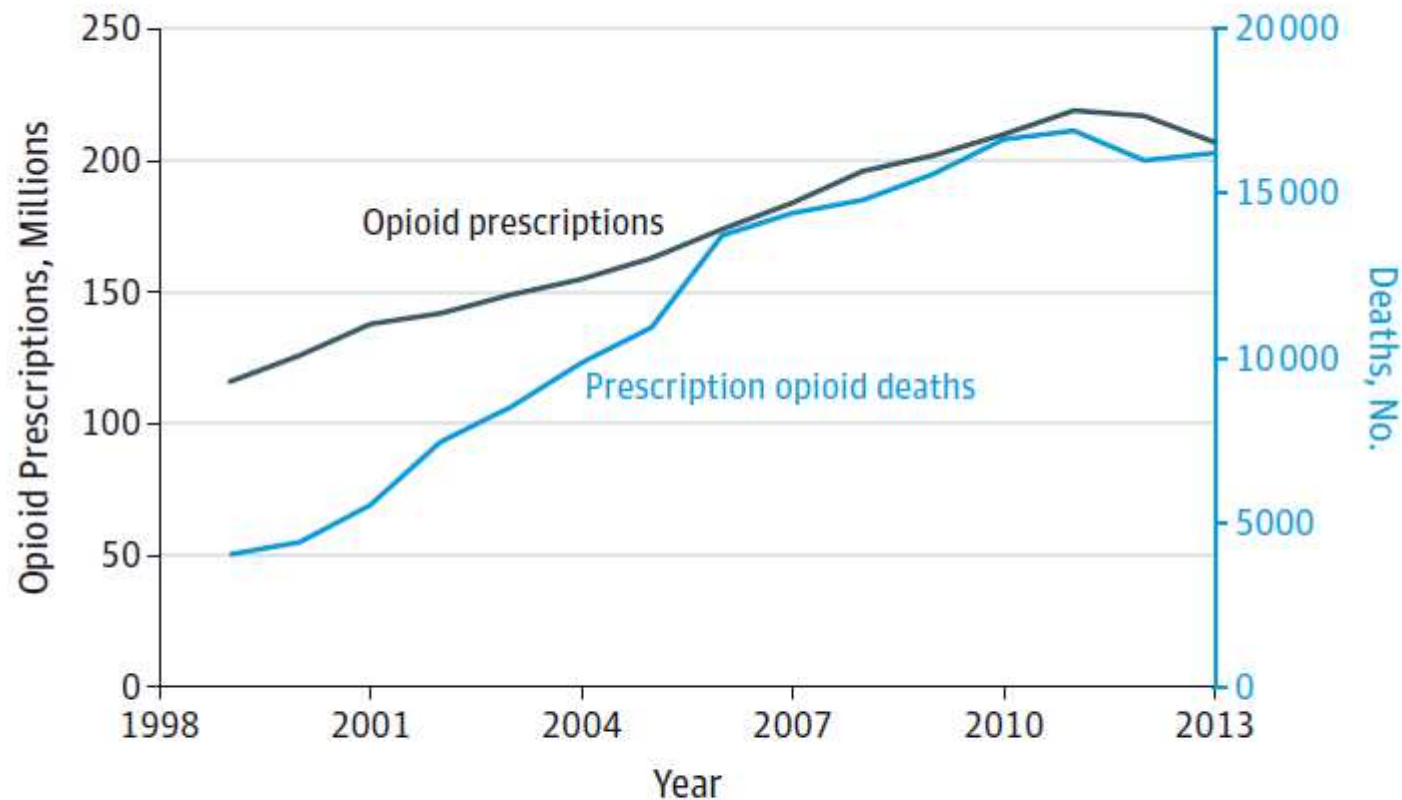


**Figure 3. Rates of Death Associated with Heroin and Prescription Opioids, 2002–2013.**


Shown is the rate of death associated with prescription opioid drugs (RADARS Poison Center Program) and with heroin (National Poison Data System, American Association of Poison Control Centers), with adjustment for population.

**(Dart RC, et al. New Engl J Med 372:241-8, 2015)**

Figure. Opioid Prescriptions and Opioid-Related Deaths From 1999-2013



Data compiled from National Institute on Drug Abuse, 2014,<sup>3</sup> and National Prescription Audit, 1997-2013.<sup>4</sup>



**Un fallimento drammatico, di enormi dimensioni,  
che mina a fondo la storia della medicina  
contemporanea, così orgogliosa dei suoi successi ...**

Using data from nearly half a million respondents to the annual National Survey on Drug Use and Health (NSDUH), the authors found that overall trends in self-reported nonmedical use of prescription opioids decreased from 5.4% to 4.9% over an 11-year period, including a decline in new users of opioids, from 1% in 2003 to 0.6% in 2013. Although this overall finding of a reduction in nonmedical use of prescription opioids is encouraging, the study also reported increases in the prevalence of prescription opioid use disorders (abuse and addiction) and increases in the prevalence of opioid-associated mortality, using data from the National Vital Statistics System's Multiple Cause of Death Files. The authors also reported an increased prevalence of frequent opioid use (>100 days/year) and highly frequent use (>200 days/year), as well as a greater prevalence of prescription opioid use disorders in patients with major depressive episodes (MDEs) than in patients without them. The findings of Han et al suggest that more patients are experiencing an inexorable progression from initial opioid use to frequent use, highly frequent use, or an opioid use disorder.

(Nelson LS et al, JAMA 314(14):1453-4, 2015)



**Prescribing of opioid analgesics, particularly for chronic pain, appears to be a main factor in the majority of nonmedical use. Based on other data available in the NSDUH, prescribers are, directly or indirectly, the source of most misused opioids. An estimated 53% of nonmedical users reported obtaining prescription opioids from a friend or relative, 81% of whom received their drug from a physician. It is unclear whether these prescriptions were issued for therapeutic purposes or originated from unscrupulous prescribers (ie, “pill mills”); regardless, the source of opioid use and misuse is often a seemingly legitimate prescription.**

(Nelson LS et al, JAMA 314(14):1453-4, 2015)

**There is little evidence for long-term benefit from opioid therapy for most types of chronic pain. It remains unclear why this practice of opioid prescribing continues despite recommendations to the contrary. New opioid medications, many of them with tamper-resistant formulations, continue to be marketed despite the lack of evidence that these preparations reduce the risk of addiction. More than 10% of patients who initiate treatment with opioids will likely progress to chronic use, defined as ongoing treatment for more than 3 months. Nearly all patients treated with long-term opioid therapy develop tolerance and dependence to varying degrees, about 25% become nonmedical users, and 10% develop features suggestive of addiction. These are sobering percentages in light of the millions of patients prescribed these drugs every year. Consequently, for the many patients who need treatment for addiction or complications of substance misuse, there are often significant barriers to obtaining care.**

(Nelson LS et al, JAMA 314(14):1453-4, 2015)

**In 2014, the death toll from overdoses involving prescription painkillers or heroin reached 28,647, a 14 percent increase from the previous year, according to federal data. Many recent heroin deaths involve the use of illicitly produced fentanyl, a prescription opioid often mixed with heroin.**

**It is unclear what effect the laws about prescription painkillers are having on death rates, which in some ways are the ultimate measure for any public policy aimed at reducing substance abuse. Some experts argue that measures to reduce prescribing painkillers may be having the unintended consequence of driving people to try heroin and other illicit drugs. Others dispute that, pointing out that the shift toward heroin use happened before the recent policy focus on opioids took hold.**

(Meier B, Tavernise S. The New York Times, March 11, 2016)



## **Le persistenti pesanti contraddizioni**

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## Increasing worldwide access to medical opioids



*\*James F Cleary, Asra Husain, Martha Maurer*

www.thelancet.com Published online February 3, 2016 [http://dx.doi.org/10.1016/S0140-6736\(16\)00234-8](http://dx.doi.org/10.1016/S0140-6736(16)00234-8)



**Una drammatica perdita di controllo da parte dei medici: gli oppiacei in odontoiatria e in altre procedure a basso rischio.**

**Table 1. Proportion of Medicaid Patients Dispensed Opioids Following Surgical Extraction of Teeth, 2000-2010<sup>a</sup>**

	No. of Patients	Dispensed Opioid, No. (%)
Overall cohort	2 757 273	1 161 747 (42)
Age group, y		
≤13	367 219	52 528 (14)
14-17	657 535	400 549 (61)
18-24	646 370	339 386 (52)
25-34	492 104	196 051 (40)
35-44	302 048	97 703 (32)
45-54	184 500	51 557 (28)
≥55	107 497	23 973 (22)
Sex		
Men	979 352	405 120 (41)
Women	1 777 921	756 627 (43)
Procedure type		
Surgical extraction of nonimpacted tooth	1 718 053	544 971 (32)
Removal of impacted tooth		
Soft tissue	245 505	140 514 (57)
Partially bony	475 053	301 706 (64)
Completely bony	669 199	466 616 (70)
Completely bony with unusual surgical complications	60 478	41 280 (68)
Surgical removal of residual tooth roots	169 613	53 853 (32)

<sup>a</sup> Data were from the Medicaid Analytic eXtract.

## Opioid Prescribing After Surgical Extraction of Teeth in Medicaid Patients, 2000-2010

James A. Baker, BS  
 Jerry Avorn, MD  
 Raisa Levin, MS  
 Brian T. Bateman, MD, MS

**JAMA** Published online March 15, 2016

# Opioids Prescribed After Low-Risk Surgical Procedures in the United States, 2004-2012

Hannah Wunsch, MD, MSc  
 Duminda N. Wijeyesundera, MD, PhD  
 Molly A. Passarella, MS  
 Mark D. Neuman, MD, MSc

JAMA Published online March 15, 2016

Table 2. Total Opioids Prescribed, Mean Daily Dose, and Duration of Prescription for Opioid-Naive Patients Who Filled an Opioid Prescription for Hydrocodone/Acetaminophen or Oxycodone/Acetaminophen Within 7 Days After Surgery (Outpatients) or Hospital Discharge (Inpatients), 2004-2012

Surgery Type	Total Morphine Equivalents Prescribed			Mean Daily Dose Prescribed, mg			Duration of Prescription, d		
	Mean (95% CI)	Absolute Change (95% CI)	P Value <sup>a</sup>	Mean (95% CI)	Absolute Change (95% CI)	P Value <sup>a</sup>	Mean (95% CI)	Absolute Change (95% CI)	P Value <sup>a</sup>
All 4 surgical procedures <sup>b</sup>									
All years	235.1 (234.4 to 235.8)			51.6 (51.4 to 51.7)			5.0 (5.0 to 5.1)		
2004	219.2 (218.1 to 220.2)	Reference		48.7 (48.5 to 49.0)	Reference		5.1 (5.0 to 5.1)	Reference	
2008	237.4 (236.3 to 238.5)	17.83 (16.23 to 19.44)	<.001	51.0 (50.7 to 51.2)	2.19 (1.84 to 2.54)	<.001	5.1 (5.1 to 5.1)	0.03 (-0.01 to 0.07)	.10
2012	247.4 (246.1 to 248.8)	29.71 (28.08 to 31.35)	<.001	54.8 (54.6 to 55.1)	6.29 (5.93 to 6.65)	<.001	4.9 (4.9 to 5.0)	-0.12 (-0.17 to 0.08)	<.001
Carpal tunnel release <sup>c</sup>									
All years	213.1 (211.1 to 215.1)			47.0 (46.7 to 47.4)			5.0 (4.9 to 5.0)		
2004	201.6 (198.7 to 204.5)	Reference		44.4 (43.8 to 45.1)	Reference		5.1 (5.0 to 5.2)	Reference	
2008	216.4 (213.1 to 219.8)	13.21 (8.34 to 18.08)	<.001	46.6 (45.9 to 47.2)	2.03 (1.06 to 2.99)	<.001	5.1 (5.0 to 5.1)	-0.05 (-0.17 to 0.07)	.39
2012	220.5 (216.6 to 224.4)	17.58 (12.74 to 22.43)	<.001	50.0 (49.3 to 50.7)	5.38 (4.42 to 6.34)	<.001	4.8 (4.7 to 4.9)	-0.30 (-0.41 to -0.18)	<.001

<sup>a</sup> Linear regression adjusting for patient characteristics assessing trends over time.

<sup>b</sup> Adjusted for age, sex, inpatient/outpatient procedure, region, and surgical procedure.

<sup>c</sup> Adjusted for age, sex, inpatient/outpatient procedure, and region.

(continued...)



**Table 2. Total Opioids Prescribed, Mean Daily Dose, and Duration of Prescription for Opioid-Naive Patients Who Filled an Opioid Prescription for Hydrocodone/Acetaminophen or Oxycodone/Acetaminophen Within 7 Days After Surgery (Outpatients) or Hospital Discharge (Inpatients), 2004-2012**

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<b>Laparoscopic cholecystectomy<sup>c</sup></b>									
All years	203.0 (202.1 to 204.0)			49.2 (49.0 to 49.5)			4.6 (4.5 to 4.6)		
2004	190.1 (188.4 to 191.8)	Reference		47.0 (46.6 to 47.5)	Reference		4.6 (4.5 to 4.6)	Reference	
2008	203.8 (202.2 to 205.4)	12.47 (10.07 to 14.86)	<.001	48.9 (48.5 to 49.3)	1.75 (1.12 to 2.37)	<.001	4.6 (4.5 to 4.6)	-0.02 (-0.08 to 0.05)	.58
2012	211.9 (210.2 to 213.5)	20.39 (17.99 to 22.79)	<.001	51.3 (50.9 to 51.7)	4.15 (3.52 to 4.78)	<.001	4.6 (4.5 to 4.6)	-0.05 (-0.12 to 0.01)	.13
<b>Inguinal hernia repair<sup>b</sup></b>									
All years	221.5 (220.1 to 222.9)			51.9 (51.6 to 52.3)			4.7 (4.7 to 4.7)		
2004	212.1 (209.9 to 214.3)	Reference		50.4 (49.8 to 50.9)	Reference		4.7 (4.7 to 4.8)	Reference	
2008	224.6 (222.2 to 226.9)	11.84 (8.57 to 15.10)	<.001	51.7 (51.1 to 52.2)	1.29 (0.47 to 2.11)	.002	4.8 (4.7 to 4.8)	0.03 (-0.05 to 0.11)	.51
2012	229.3 (226.7 to 232.0)	16.57 (13.09 to 20.05)	<.001	54.2 (53.6 to 54.9)	3.82 (2.95 to 4.69)	<.001	4.6 (4.6 to 4.7)	-0.10 (-0.18 to -0.01)	.03
<b>Knee arthroscopy<sup>b</sup></b>									
All years	268.8 (267.6 to 270.0)			54.3 (54.0 to 54.5)			5.5 (5.5 to 5.5)		
2004	244.8 (243.1 to 246.6)	Reference		50.3 (49.9 to 50.7)	Reference		5.5 (5.5 to 5.6)	Reference	
2008	271.1 (269.1 to 273.0)	25.30 (22.47 to 28.12)	<.001	53.3 (52.9 to 53.6)	2.90 (2.33 to 3.47)	<.001	5.6 (5.6 to 5.7)	0.10 (0.03 to 0.16)	.005
2012	289.2 (286.8 to 291.6)	45.16 (42.26 to 48.07)	<.001	59.2 (58.7 to 59.6)	9.11 (8.53 to 9.70)	<.001	5.4 (5.3 to 5.4)	-0.14 (-0.21 to -0.08)	<.001

<sup>a</sup> Linear regression adjusting for patient characteristics assessing trends over time.

<sup>b</sup> Adjusted for age, sex, inpatient/outpatient procedure, region, and surgical procedure.

<sup>c</sup> Adjusted for age, sex, inpatient/outpatient procedure, and region.

Hannah Wunsch, MD, MSc  
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Molly A. Passarella, MS  
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**JAMA** Published online March 15, 2016

## Original Investigation

# Prescription Opioid Duration of Action and the Risk of Unintentional Overdose Among Patients Receiving Opioid Therapy

Matthew Miller, MD, ScD; Catherine W. Barber, MPA; Sarah Leatherman, PhD; Jennifer Fonda, BS; John A. Hermos, MD; Kelly Cho, PhD; David R. Gagnon, MD

**IMPORTANCE** The unprecedented increase in unintentional overdose events that has occurred in tandem with escalating sales of prescription opioids over the past 2 decades has raised concerns about whether the therapeutic use of opioids has contributed to increases in overdose injury. Few controlled studies have examined the extent to which ecologic measures of increases in opioid prescribing and overdose injuries reflect risk among patients prescribed opioids, let alone whether some opioid regimens are safer than others.

**OBJECTIVE** To examine whether the risk of unintentional overdose injury is associated with the duration of opioid action (ie, long-acting vs short-acting formulations).

**DESIGN, SETTING, AND PARTICIPANTS** A propensity score–adjusted cohort study was conducted using population-based health care utilization data from the Veterans Administration Healthcare System. The patients were veterans with chronic painful conditions who began therapy with opioid analgesics between January 1, 2000, and December 31, 2009.

**MAIN OUTCOMES AND MEASURES** Unintentional overdoses that are explicitly coded using *International Classification of Disease, Ninth Revision* codes as drug or medication poisonings of accidental intent (E850.x-860.x) or undetermined intent (E980.x or drug poisoning [960.x-980.x] without an accompanying external cause of injury code).

**RESULTS** A total of 319 unintentional overdose events were observed. Patients initiating therapy with long-acting opioids were more than twice as likely to overdose compared with persons initiating therapy with short-acting opioids. After adjustment for age, sex, opioid dose, and other clinical characteristics, patients receiving long-acting opioids had a significantly higher rate of overdose injury than did those receiving short-acting opioids (hazard ratio [HR], 2.33; 95% CI, 1.26-4.32). The risk associated with long-acting agents was particularly marked during the first 2 weeks after initiation of treatment (HR, 5.25; 1.88-14.72).

**CONCLUSIONS AND RELEVANCE** To our knowledge, the findings of the present study provide the first evidence that the risk of unintentional overdose injury is related to the prescribed opioid's duration of action. If replicated in other cohorts, our findings suggest that clinicians weighing the benefits and risks of initiating different opioid regimens should consider not only the daily dose prescribed but also the duration of opioid action, favoring short-acting agents whenever possible, especially during the first 2 weeks of therapy.

*JAMA Intern Med.* 2015;175(4):608-615.

**Table 2. Incidence Rate and HR for Unintentional Overdose Comparing Long-Acting With Short-Acting Opioids<sup>a</sup>**

Characteristic	No. of Events	No. of Person-years	Crude Rate (95% CI) <sup>b</sup>	Crude HR (95% CI)	Adjusted HR (95% CI)	
					Age, Sex, Index Dose <sup>c</sup>	sIPWT
<b>Overall</b>						
Short-acting	282	194 683	14.49 (12.79-16.18)	1 [Reference]	1 [Reference]	1 [Reference]
Long-acting	37	10 623	34.83 (23.61-46.05)	2.84 (2.01-4.02)	2.56 (1.67-3.93)	2.33 (1.26-4.32)
<b>Strata of Opioid Duration</b>						
<b>≤14 d</b>						
Short-acting	70	27 762	25.21 (19.31-31.12)	1 [Reference]	1 [Reference]	1 [Reference]
Long-acting	10	697	143.4 (54.51-232.20)	5.70 (2.94-11.06)	5.25 (2.61-10.54)	5.25 (1.88-14.72)
<b>15-60 d</b>						
Short-acting	79	49 266	16.04 (12.50-19.57)	1 [Reference]	1 [Reference]	1 [Reference]
Long-acting	6	1666	36.00 (7.19-64.81)	2.42 (1.05-5.56)	2.19 (0.92-5.19)	2.30 (0.67-7.90)
<b>&gt;60 d</b>						
Short-acting	133	115 398	11.53 (9.57-13.48)	1 [Reference]	1 [Reference]	1 [Reference]
Long-acting	21	8188	25.65 (14.68-36.62)	2.39 (1.50-3.78)	2.14 (1.25-3.65)	1.50 (0.68-3.33)

Abbreviations: HR, hazard ratio; sIPWT, stabilized inverse probability weight.

<sup>a</sup> Seventy-five of the 319 unintentional overdose events were noted to be opioid overdoses. Stabilized inverse probability weights were used to balance potential confounding of the relationship between opioid use and overdose. All baseline characteristics from Table 1 were included in the propensity score model for receipt of a long-acting opioid. In addition, all significant 2-way interactions of characteristics from Table 1 were included when modeling the probability of receiving a long-acting opioid. These included, among many

other baseline factors, interactions of benzodiazepines, pain clinic visits, and antidepressant use. Other recurring factors with significant interactions were the use of cyclooxygenase 2 inhibitors, baseline hyperlipidemia, and baseline liver disease. These propensity scores were then used to adjust the association between opioid use and overdose for all included covariates and interactions.

<sup>b</sup> Per 10 000 person-years.

<sup>c</sup> Morphine-equivalent mean daily dose.

Matthew Miller, MD, ScD; Catherine W. Barber, MPA; Sarah Leatherman, PhD; Jennifer Fonda, BS; John A. Hermos, MD; Kelly Cho, PhD; David R. Gagnon, MD

*JAMA Intern Med.* 2015;175(4):608-615.

## List of Extended Release and Long Acting Opioid Products Required to Have an Opioid REMS

### Brand Name Products

	Trade Name	Generic Name	Sponsor
1	Avinza	Morphine sulfate extended-release capsules	Pfizer
2	Butrans	Buprenorphine transdermal system	Purdue Pharma
3	Dolophine	Methadone hydrochloride tablets	Roxane
4	Duragesic	Fentanyl transdermal system	Janssen Pharmaceuticals
5	**Embeda	Morphine sulfate and naltrexone extended-release capsules	Pfizer
6	Exalgo	Hydromorphone hydrochloride extended-release tablets	Mallinckrodt
7	Kadian	Morphine sulfate extended-release capsules	Actavis
8	MS Contin	Morphine sulfate controlled-release tablets	Purdue Pharma
9	Nucynta ER	Tapentadol extended-release oral tablets	Janssen Pharmaceuticals
10	Opana ER	Oxymorphone hydrochloride extended-release tablets	Endo Pharmaceuticals
11	OxyContin	Oxycodone hydrochloride controlled-release tablets	Purdue Pharma
12	*Palladone	Hydromorphone hydrochloride extended-release capsules	Purdue Pharma

\*No longer being marketed, but is still approved.

\*\*Not currently available or marketed due to a voluntary recall, but is still approved.

HEALTH

## F.D.A. Toughens Warning Labels for Some Opioid Painkillers

By SABRINA TAVERNISE

WASHINGTON — The Food and Drug Administration said Tuesday March 22, 2016 that it was requiring new warning labels for certain types of opioid painkillers, a step that it said would help ease an epidemic of abuse in the United States. The agency said the changes would mostly apply to immediate-release opioids — usually intended for use every four to six hours — and would include new boxed warnings, the agency's strongest type, about the risks of abuse and death.

**IMPORTANCE** Primary care clinicians find managing chronic pain challenging. Evidence of long-term efficacy of opioids for chronic pain is limited. Opioid use is associated with serious risks, including opioid use disorder and overdose.

**OBJECTIVE** To provide recommendations about opioid prescribing for primary care clinicians treating adult patients with chronic pain outside of active cancer treatment, palliative care, and end-of-life care.

**PROCESS** The Centers for Disease Control and Prevention (CDC) updated a 2014 systematic review on effectiveness and risks of opioids and conducted a supplemental review on benefits and harms, values and preferences, and costs. CDC used the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) framework to assess evidence type and determine the recommendation category.

**EVIDENCE SYNTHESIS** Evidence consisted of observational studies or randomized clinical trials with notable limitations, characterized as low quality using GRADE methodology. Meta-analysis was not attempted due to the limited number of studies, variability in study designs and clinical heterogeneity, and methodological shortcomings of studies. No study evaluated long-term ( $\geq 1$  year) benefit of opioids for chronic pain. Opioids were associated with increased risks, including opioid use disorder, overdose, and death, with dose-dependent effects.

**RECOMMENDATIONS** There are 12 recommendations. Of primary importance, nonopioid therapy is preferred for treatment of chronic pain. Opioids should be used only when benefits for pain and function are expected to outweigh risks. Before starting opioids, clinicians should establish treatment goals with patients and consider how opioids will be discontinued if benefits do not outweigh risks. When opioids are used, clinicians should prescribe the lowest effective dosage, carefully reassess benefits and risks when considering increasing dosage to 50 morphine milligram equivalents or more per day, and avoid concurrent opioids and benzodiazepines whenever possible. Clinicians should evaluate benefits and harms of continued opioid therapy with patients every 3 months or more frequently and review prescription drug monitoring program data, when available, for high-risk combinations or dosages. For patients with opioid use disorder, clinicians should offer or arrange evidence-based treatment, such as medication-assisted treatment with buprenorphine or methadone.

**CONCLUSIONS AND RELEVANCE** The guideline is intended to improve communication about benefits and risks of opioids for chronic pain, improve safety and effectiveness of pain treatment, and reduce risks associated with long-term opioid therapy.

Special Communication

## CDC Guideline for Prescribing Opioids for Chronic Pain—United States, 2016

Deborah Dowell, MD, MPH; Tamara M. Haegerich, PhD; Roger Chou, MD

*JAMA*. doi:10.1001/jama.2016.1464  
Published online March 15, 2016.

## CDC Guideline for Prescribing Opioids for Chronic Pain—United States, 2016

Deborah Dowell, MD, MPH; Tamara M. Haegerich, PhD; Roger Chou, MD

JAMA. doi:10.1001/jama.2016.1464  
Published online March 15, 2016.

**Table 4. Morphine Milligram Equivalent Doses for Commonly Prescribed Opioids<sup>a</sup>**

Opioid <sup>b</sup>	Conversion Factor
Codeine	0.15
Fentanyl transdermal, µg/h	2.4
Hydrocodone	1
Hydromorphone	4
Methadone, mg/d	
1-20	4
21-40	8
41-60	10
≥61-80	12
Morphine	1
Oxycodone	1.5
Oxymorphone	3
Tapentadol <sup>c</sup>	0.4

<sup>a</sup> Adapted from Von Korff M, Saunders K, Ray GT, et al. *Clin J Pain*. 2008;24:521-527, and Interagency Guideline on Prescribing Opioids for Pain. Washington State Agency Medical Directors' Group. <http://www.agencymeddirectors.wa.gov/Files/2015AMDGOpioidGuideline.pdf>. Accessed February 19, 2016.

<sup>b</sup> All doses are in mg/d except for fentanyl, which is µg/h. Multiply the daily dosage for each opioid by the conversion factor to determine the dose in morphine milligram equivalents (MME). For example, tablets containing hydrocodone, 5 mg, and acetaminophen, 300 mg, taken 4 times a day would contain a total of 20 mg of hydrocodone daily, equivalent to 20 MME daily; extended-release tablets containing oxycodone, 10 mg, and taken twice a day would contain a total of 20 mg of oxycodone daily, equivalent to 30 MME daily.

<sup>c</sup> Tapentadol is a µ-receptor agonist and norepinephrine reuptake inhibitor. Morphine milligram equivalents are based on degree of µ-receptor agonist activity, but it is unknown if this drug is associated with overdose in the same dose-dependent manner as observed with medications that are solely µ-receptor agonists.


# The CDC Guideline on Opioid Prescribing Rising to the Challenge

Yngvild Olsen, MD, MPH

**The CDC guideline for prescribing opioids for chronic pain is an important and essential step forward.**

**With support from physicians across the country, as well as from policy makers at all levels, implementation of the recommendations in this guideline has the potential to improve and save many, many lives.**





**A key lesson learned during the development of the CDC guideline is that there is very little research on the long-term benefits of opioids for treating chronic pain.**


**There is, however, growing evidence of harms associated with such use, and of the benefits of other nonopioid treatment alternatives.**

(Califf RM, et al. New Engl J Med, February 4, 2016)

**What is really needed is a sea change within the medical profession itself. We should be educating and training our medical students and residents about the risks and limited benefits of opioids in treating pain. All medical professional organizations should back mandated education about safe opioid treatment as a prerequisite for licensure and prescribing. At present, the American Academy of Family Physicians opposes such a measure because it could limit patient access to pain treatment with opioids, which I think is misguided. Don't we want family doctors, who are significant prescribers of opioids, to learn about their limitations and dangers?**

**It is physicians who, in large part, unleashed the current opioid epidemic with their promiscuous use of these drugs; we have a large responsibility to end it.**

(Friedman RA, New York Times, November 7, 2015)



**La prescrizione di oppiacei e l'attenzione  
agli effetti indesiderati ... solo una piccola  
parte dei problemi.**

## Costipazione indotta da oppioidi. La naldemedina

E' un antagonista del recettore oppioide mu, ad assunzione orale, che in uno studio di fase III si è mostrato superiore al placebo nel trattamento della Cio, senza ridurre gli effetti analgesici degli oppioidi. La naldemedina non attraversa la barriera emato-encefalica ma agisce a livello periferico. Il profilo di tollerabilità del nuovo farmaco è migliore rispetto a quelli già esistenti.

Lo studio è stato condotto su 545 pazienti con dolore cronico non oncologico in cura con oppioidi da almeno tre mesi e soffrivano di costipazione. Suddivisi in due gruppi con un algoritmo di randomizzazione, i 273 pazienti che hanno ricevuto il farmaco hanno risposto positivamente nel 47,6% dei casi, rispetto al 34,6% rilevato nel gruppo placebo.

Gli effetti avversi più comuni associati alla naldemedina sono stati a carico del tratto gastrointestinale: dolore, diarrea e nausea, dovuti al meccanismo d'azione del farmaco. Il dolore addominale è stato riportato dal 6,3% dei pazienti trattati rispetto all'1,8% dei soggetti inseriti nel gruppo di controllo; per la diarrea le percentuali sono state rispettivamente del 6,6% e del 2,9% e per la nausea del 4,8% e del 2,6%; c'è però da rilevare che nella maggior parte dei casi si è trattato di effetti collaterali transitori, sperimentati solo nel periodo iniziale di assunzione della naldemedina.

## A Startling Injustice: Pain, Opioids, and Addiction

Jessica Gregg, MD, PhD

**L**ike other residents and medical students in the late 1990s, I was taught to assess the “5th vital sign”—pain—and address it, usually with opioids. My colleagues and I were taught that the medical community had long ignored the treatment of pain and it was now time to redress that wrong. Our teachers, medical boards, and professional associations (and always in the background, the pharmaceutical companies) urged us to assess and treat pain aggressively (1).

Thus, with no training in pain management, and no training in addiction, I was soon prescribing large doses of opioids to treat pain in patients who were clearly not improving and who were marginally functional at best. They crowded the examination room with physical complaints and stories of unemployment, fractured households, and deepening depression. According to their Global Assessment of Functioning, they were drowning in dysfunction. According to my 15-minute clinical assessment, this meant I should raise their methadone dose.

Fast-forward 15 years. Since 1999, the United States has seen a 300% increase in sales of prescription opioids and a similar increase in deaths from overdosing on pain pills. More Americans now die of overdose of prescription pain pills than of heroin or cocaine. In some states, opioid-related deaths exceed deaths from motor vehicle accidents (2, 3). If they survive overdose, many individuals addicted to prescription pain killers will eventually turn to heroin, which is cheaper and often easier to obtain (4).

Through good intentions and bad medicine, the medical community helped create a deadly epidemic. Now, in an act of startling injustice, we are abandoning its victims.

*Ann Intern Med.* 2015;162:651-652.



**... ma dopo tanti anni di retorica pro-opioidi non è facile convincere il medico a cambiare atteggiamento.**

**Sarà mai raggiunto un equilibrio?**

**Attenzione ad evitare che in Italia arrivi in ritardo l'onda lunga dell'eccesso prescrittivo.**


## OPPIOIDI



- Azione a livello somatico, viscerale e nervoso
- Adatto per il dolore oncologico
- Azione tempestiva

Infine, numerose evidenze in letteratura dimostrano che gli oppioidi **non sono farmaci pericolosi o in grado di indurre dipendenza**: quando si prova dolore, infatti, si attivano nell'organismo dei meccanismi recettoriali del tutto diversi rispetto a quelli che entrano in gioco nei soggetti tossicodipendenti, che ricorrono agli oppiacei per provare sensazioni di piacere.

Ciononostante, **in Italia gli oppioidi sono ancora ampiamente sottoutilizzati.**



**The FDA has approved nonopioid medications for treatment of various chronic-pain syndromes, including gabapentin (Neurontin), pregabalin (Lyrica), milnacipran (Savella), duloxetine (Cymbalta), and others, and a number of promising development programs are in the pipeline. But we need more. The FDA will use all the tools at its disposal to move these alternatives along as expeditiously as possible, while remaining mindful that all medicines have risks.**

**For example, although nonsteroidal antiinflammatory drugs do not carry a risk of addiction, we now know that they carry increased risks of myocardial infarction, stroke, and serious gastrointestinal bleeding.**

(Califf RM, et al. New Engl J Med, February 4, 2016)



# Effectiveness of non-steroidal anti-inflammatory drugs for the treatment of pain in knee and hip osteoarthritis: a network meta-analysis

Bruno R da Costa\*, Stephan Reichenbach\*, Noah Keller, Linda Nartey, Simon Wandel, Peter Jüni, Sven Trelle

## Summary

**Background** Non-steroidal anti-inflammatory drugs (NSAIDs) are the backbone of osteoarthritis pain management. We aimed to assess the effectiveness of different preparations and doses of NSAIDs on osteoarthritis pain in a network meta-analysis.

**Methods** For this network meta-analysis, we considered randomised trials comparing any of the following interventions: NSAIDs, paracetamol, or placebo, for the treatment of osteoarthritis pain. We searched the Cochrane Central Register of Controlled Trials (CENTRAL) and the reference lists of relevant articles for trials published between Jan 1, 1980, and Feb 24, 2015, with at least 100 patients per group. The prespecified primary and secondary outcomes were pain and physical function, and were extracted in duplicate for up to seven timepoints after the start of treatment. We used an extension of multivariable Bayesian random effects models for mixed multiple treatment comparisons with a random effect at the level of trials. For the primary analysis, a random walk of first order was used to account for multiple follow-up outcome data within a trial. Preparations that used different total daily dose were considered separately in the analysis. To assess a potential dose-response relation, we used preparation-specific covariates assuming linearity on log relative dose.

**Findings** We identified 8973 manuscripts from our search, of which 74 randomised trials with a total of 58 556 patients were included in this analysis. 23 nodes concerning seven different NSAIDs or paracetamol with specific daily dose of administration or placebo were considered. All preparations, irrespective of dose, improved point estimates of pain symptoms when compared with placebo. For six interventions (diclofenac 150 mg/day, etoricoxib 30 mg/day, 60 mg/day, and 90 mg/day, and rofecoxib 25 mg/day and 50 mg/day), the probability that the difference to placebo is at or below a prespecified minimum clinically important effect for pain reduction (effect size [ES]  $-0.37$ ) was at least 95%. Among maximally approved daily doses, diclofenac 150 mg/day (ES  $-0.57$ , 95% credibility interval [CrI]  $-0.69$  to  $-0.46$ ) and etoricoxib 60 mg/day (ES  $-0.58$ ,  $-0.73$  to  $-0.43$ ) had the highest probability to be the best intervention, both with 100% probability to reach the minimum clinically important difference. Treatment effects increased as drug dose increased, but corresponding tests for a linear dose effect were significant only for celecoxib ( $p=0.030$ ), diclofenac ( $p=0.031$ ), and naproxen ( $p=0.026$ ). We found no evidence that treatment effects varied over the duration of treatment. Model fit was good, and between-trial heterogeneity and inconsistency were low in all analyses. All trials were deemed to have a low risk of bias for blinding of patients. Effect estimates did not change in sensitivity analyses with two additional statistical models and accounting for methodological quality criteria in meta-regression analysis.

**Interpretation** On the basis of the available data, we see no role for single-agent paracetamol for the treatment of patients with osteoarthritis irrespective of dose. We provide sound evidence that diclofenac 150 mg/day is the most effective NSAID available at present, in terms of improving both pain and function. Nevertheless, in view of the safety profile of these drugs, physicians need to consider our results together with all known safety information when selecting the preparation and dose for individual patients.

# Does paracetamol still have a future in osteoarthritis?

*\*Nicholas Moore, Francesco Salvo, Mai Duong,  
Sinem Ezgi Gulmez*

A crucial need remains to find new painkillers for osteoarthritis. Have any new analgesics been released since ibuprofen and diclofenac came out in the early 1970s, apart from the clinically minor COX-2 selective NSAIDs? All existing painkillers are merely minor variations on those early NSAIDs or opioids. Can't we do better?

www.thelancet.com Published online March 17, 2016 [http://dx.doi.org/10.1016/S0140-6736\(15\)01170-8](http://dx.doi.org/10.1016/S0140-6736(15)01170-8)



**Il dolore sembra prevalere sulla possibilità di cura...  
una “maledizione” invincibile?**



## **Il (mezzo) imbroglio dei cannabinoidi per il dolore.**

Original Investigation

# Cannabinoids for Medical Use A Systematic Review and Meta-analysis

Penny F. Whiting, PhD; Robert F. Wolff, MD; Sohan Deshpande, MSc; Marcello Di Nisio, PhD; Steven Duffy, PgD; Adrian V. Hernandez, MD, PhD; J. Christiaan Keurentjes, MD, PhD; Shona Lang, PhD; Kate Misso, MSc; Steve Ryder, MSc; Simone Schmidtkofer, MSc; Marie Westwood, PhD; Jos Kleijnen, MD, PhD

**IMPORTANCE** Cannabis and cannabinoid drugs are widely used to treat disease or alleviate symptoms, but their efficacy for specific indications is not clear.

**OBJECTIVE** To conduct a systematic review of the benefits and adverse events (AEs) of cannabinoids.

**DATA SOURCES** Twenty-eight databases from inception to April 2015.

**STUDY SELECTION** Randomized clinical trials of cannabinoids for the following indications: nausea and vomiting due to chemotherapy, appetite stimulation in HIV/AIDS, chronic pain, spasticity due to multiple sclerosis or paraplegia, depression, anxiety disorder, sleep disorder, psychosis, glaucoma, or Tourette syndrome.

**DATA EXTRACTION AND SYNTHESIS** Study quality was assessed using the Cochrane risk of bias tool. All review stages were conducted independently by 2 reviewers. Where possible, data were pooled using random-effects meta-analysis.

**MAIN OUTCOMES AND MEASURES** Patient-relevant/disease-specific outcomes, activities of daily living, quality of life, global impression of change, and AEs.

**RESULTS** A total of 79 trials (6462 participants) were included; 4 were judged at low risk of bias. Most trials showed improvement in symptoms associated with cannabinoids but these associations did not reach statistical significance in all trials. Compared with placebo, cannabinoids were associated with a greater average number of patients showing a complete nausea and vomiting response (47% vs 20%; odds ratio [OR], 3.82 [95% CI, 1.55-9.42]; 3 trials), reduction in pain (37% vs 31%; OR, 1.41 [95% CI, 0.99-2.00]; 8 trials), a greater average reduction in numerical rating scale pain assessment (on a 0-10-point scale; weighted mean difference [WMD], -0.46 [95% CI, -0.80 to -0.11]; 6 trials), and average reduction in the Ashworth spasticity scale (WMD, -0.12 [95% CI, -0.24 to 0.01]; 5 trials). There was an increased risk of short-term AEs with cannabinoids, including serious AEs. Common AEs included dizziness, dry mouth, nausea, fatigue, somnolence, euphoria, vomiting, disorientation, drowsiness, confusion, loss of balance, and hallucination.

**CONCLUSIONS AND RELEVANCE** There was moderate-quality evidence to support the use of cannabinoids for the treatment of chronic pain and spasticity. There was low-quality evidence suggesting that cannabinoids were associated with improvements in nausea and vomiting due to chemotherapy, weight gain in HIV infection, sleep disorders, and Tourette syndrome. Cannabinoids were associated with an increased risk of short-term AEs.

JAMA. 2015;313(24):2456-2473.

# Medical Marijuana for Treatment of Chronic Pain and Other Medical and Psychiatric Problems

## A Clinical Review

Kevin P. Hill, MD, MHS

**IMPORTANCE** As of March 2015, 23 states and the District of Columbia had medical marijuana laws in place. Physicians should know both the scientific rationale and the practical implications for medical marijuana laws.

**OBJECTIVE** To review the pharmacology, indications, and laws related to medical marijuana use.

**EVIDENCE REVIEW** The medical literature on medical marijuana was reviewed from 1948 to March 2015 via MEDLINE with an emphasis on 28 randomized clinical trials of cannabinoids as pharmacotherapy for indications other than those for which there are 2 US Food and Drug Administration–approved cannabinoids (dronabinol and nabilone), which include nausea and vomiting associated with chemotherapy and appetite stimulation in wasting illnesses.

**FINDINGS** Use of marijuana for chronic pain, neuropathic pain, and spasticity due to multiple sclerosis is supported by high-quality evidence. Six trials that included 325 patients examined chronic pain, 6 trials that included 396 patients investigated neuropathic pain, and 12 trials that included 1600 patients focused on multiple sclerosis. Several of these trials had positive results, suggesting that marijuana or cannabinoids may be efficacious for these indications.

**CONCLUSIONS AND RELEVANCE** Medical marijuana is used to treat a host of indications, a few of which have evidence to support treatment with marijuana and many that do not. Physicians should educate patients about medical marijuana to ensure that it is used appropriately and that patients will benefit from its use.

Medical marijuana use is now common in clinical practice, and it is critical for physicians to understand both the scientific rationale and the practical implications of medical marijuana laws. Medical marijuana and cannabinoids have significant health risks as well as many potential medical benefits. While medical marijuana has been at times a controversial and contentious issue, physicians have a responsibility to provide evidence-based guidance on this important issue.

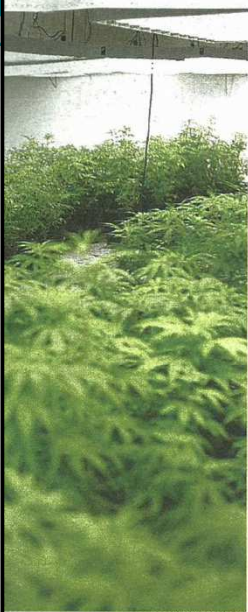
- With more states enacting medical marijuana laws, it is imperative for physicians to understand both the scientific rationale and the practical implications of medical marijuana laws.
- Aside from nausea and appetite stimulation, indications for which there are 2 FDA-approved cannabinoids (dronabinol and nabilone), chronic pain, neuropathic pain, and spasticity associated with multiple sclerosis are the indications for medical marijuana supported by high-quality evidence.
- Medical marijuana and cannabinoids have significant potential health risks, such as addiction and worsening of psychiatric illnesses such as some anxiety disorders, mood disorders, psychotic disorders, and substance use disorders, as well as many potential medical benefits.
- Evaluations to determine the appropriateness of medical marijuana for a patient should be comprehensive assessments that revolve around risk-benefit discussions.

(Hill KP, JAMA 313(24):2474-83, 2015)

**Marijuana use has been associated with substantial adverse effects, some of which have been determined with a high level of confidence. Marijuana, like other drugs of abuse, can result in addiction. During intoxication, marijuana can interfere with cognitive function (e.g., memory and perception of time) and motor function (e.g., coordination), and these effects can have detrimental consequences (e.g., motor-vehicle accidents). Repeated marijuana use during adolescence may result in long-lasting changes in brain function that can jeopardize educational, professional, and social achievements. However, the effects of a drug (legal or illegal) on individual health are determined not only by its pharmacologic properties but also by its availability and social acceptability. In this respect, legal drugs (alcohol and tobacco) offer a sobering perspective, accounting for the greatest burden of disease associated with drugs not because they are more dangerous than illegal drugs but because their legal status allows for more widespread exposure. As policy shifts toward legalization of marijuana, it is reasonable and probably prudent to hypothesize that its use will increase and that, by extension, so will the number of persons for whom there will be negative health consequences.**

(Volkow ND et al, N Engl J Med 370(23):2219-27, 2014)





BILAL GABLER/REUTERS

**In cura dal 2004**  
Andrea Triscioglio, ex agente immobiliare colpito dieci anni da sclerosi multipla: «Mi umiliava pagare gli spacciatori per potermi curare»



GAETANO LO PORTO/AGF

**il caso**  
GIACOMO GALEAZZI  
ROMA

«Sai qual è il colmo per un ragazzo che a 24 si ammala di sclerosi multipla e di epilessia? Subire perquisizioni in casa e dover spiegare ai carabinieri che la cannabis è un medicinale». Andrea Triscioglio era un rampante agente immobiliare quando i suoi polsi cominciarono ad irrigidirsi. Spasmodia, sminuirono i medici. Purtroppo era ben altro. «Dal 2004 al 2009 ho fatto uso illegale di marijuana, da cinque ricevo il Bedrocan attraverso l'ospedale», racconta Andrea. Ho dovuto affrontare un percorso ad ostacoli, una trafila surreale. Un vero e proprio calvario di carte bollate da affiancare a quello provocato da una malattia inesorabile. Con momenti da

# “Per la mia terapia non dovrò più pagare gli spacciatori”

L'odissea di Andrea, malato di sclerosi e epilessia: “Per anni ho subito le perquisizioni dei carabinieri”

teatro dell'assurdo. Come il giorno in cui Andrea comprò su Internet «semi di canapa» e rischiò di finire nei guai con le forze dell'ordine per una pianta «ad uso personale». Eppure nel quadro clinico i vantaggi sono stati immediatamente evidenti. E così è da un decennio. «I dolori si attenuano e ho benefici su sonno, umore, appetito», spiega. E soprattutto «diminuiscono gli spasmi, i sintomi della neuropatia, i tremo-

ri», aggiunge. «Mi pesava dovermi rifornire al mercato nero, scendere in strada a comprare la dose come un tossicodipendente. Mi umiliava pagare gli spacciatori per acquistare una terapia». Da lì l'idea di coltivare da sé quella marijuana che rende più sopportabile le sue sofferenze fisiche. «La fumo solo raramente perché la combustione spreca il 40% dei principi attivi, ma la assumo in preva-

lenza come olio oppure tramite vaporizzatore», precisa Andrea. Qui in Puglia dal 2009 basta una firma e un timbro su una prescrizione medica per avere la continuità terapeutica. Guai a paragonarlo a chi fuma per diletto. «Io con la canapa mi curo in modo sistematico», replica. In maniera metodica elenca la sua «tabella di marcia». Per il tremore affianca ai cannabinoidi i farmaci antiepilettici, però non gli va

**Ha detto**

**I benefici**  
I dolori si attenuano, diminuiscono gli spasmi e migliorano sonno, umore e appetito

**Gli effetti collaterali**  
L'incidenza è bassissima, e poi non si può criminalizzare un malato che vuole stare meglio

giù di sentirsi un «privilegiato» anche se sa che «per tanta gente bisognosa quanto me il diritto alla salute è ancora una lotta atroce contro la burocrazia e l'ignoranza». Troppi i tabù da abbattere. Adesso perciò Andrea aiuta pazienti come lui attraverso «Laplantiamo», un'associazione per la libertà di cura. «L'incidenza di effetti collaterali è bassissima, eppure si incontrano una sequela infinita di difficoltà a curarsi se la terapia è con farmaci che contengano la parola cannabis», sottolinea Andrea. Infatti «la legge Fini-Giovanardi regola l'accesso alla canapa con pesanti pene per chi coltiva canapa».

Il risultato è che «molti malati, persone oneste e integerrime, vengono trattati come criminali». Andrea ai carabinieri che lo perquisivano ha chiesto: «Vi sembra il tipo che usa la cannabis per sballarsi?». La risposta è stato uno sguardo abbassato. «Cercavano ovunque piante di canapa, addirittura nelle federe del cuscino di mio figlio neonato che piangeva mentre mi portavano via in caserma per il verbale».

E la voce si incrina: «Aveva otto mesi, ho ancora il suo pianto nella testa». La malattia gli ha creato gravi disabilità. L'utilizzo dei farmaci tradizionali (chemioterapici, immunosoppressori, miorilassanti) e trecento punture di interferone sono un incubo dai mille effetti negativi: febbre alta, continui tremori e incontinenza. «Non si può criminalizzare un malato che ha bisogno della canapa per soffrire meno», scuote la testa. E non «si può dirgli che questa terapia provoca buchi nel cervello ed è l'anticamera delle droghe pesanti». Del suo corpo malato Andrea ha fatto un «campo di battaglia». Il sorriso non lo abbandona, come la convinzione di «fare qualcosa di buono per me e per gli altri». La libertà di cura «non deve soccombere ai luoghi comuni e ai pregiudizi». Una parola d'ordine per una giusta causa: «Non darsi per vinti è un passo avanti di civiltà: mai arrendersi».

# LA REPUBBLICA

## GIOVEDÌ 12 FEBBRAIO 2015



Per la prima volta nella storia dei cartelli messicani **cala il traffico della marijuana: grazie alla legalizzazione.** L'effetto: meno reati, maggiori entrate nelle casse dello Stato, meno flussi di denaro criminale. **È la sconfitta dei proibizionisti**

ROBERTO SAVIANO

**P**er la prima volta nella loro storia i cartelli messicani hanno visto precipitare la richiesta di marijuana. Entra in crisi un business miliardario che sino ad ora non aveva mai subito flessioni. I dotti diffusi dalla polizia frontaliere americana (l'Us Border Patrol) non lasciano spazi a dubbi: la riduzione del traffico di erba nel 2014 è stata del 24% rispetto al 2011. Che è successo? Nessuno fuma più spinelli? Una stagione di arresti particolarmente efficace? La risposta è più semplice: ed è la legalizzazione delle droghe leggere in Colorado e nello Stato di Washington.

La vendita legale di marijuana non ha solo creato una rivoluzione economica che ha portato oltre 800 milioni di dollari di nuovi introiti fiscali, ma ha anche iniziato a trasformare il tessuto criminale. La crisi delle organizzazioni a sud del Rio Grande che hanno sempre

inondato gli Usa di erba è paragonabile alla crisi dei titoli del Nasdaq. I cartelli messicani non hanno mai abbandonato il business dell'erba, tutte le organizzazioni storiche che oggi sono egemoni nel traffico di coca e di metanfetamina hanno sempre coltivato la "mota" (come chia-

### LE NUOVE REGOLE

*In Colorado e nello Stato di Washington la marijuana può essere acquistata solo a 21 anni. Si possono possedere circa 28 grammi. Vietato il consumo in pubblico e alla guida*

### I GUADAGNI FUTURI

*Il Colorado prevede un incremento di cassa di 175 milioni di dollari in due anni. Lo Stato di Washington prevede un'entrata di 600 milioni di dollari in cinque anni*

### LA SVOLTA IN CORSO

*Le entrate fiscali sono fra gli argomenti che hanno convinto altri Stati: il tragitto verso la legalizzazione è in corso in Alaska, Oregon, Florida, Washington D.C.*

mano la marijuana), che è al contempo fonte di una liquidità economica gigantesca ed ha una crescita di mercato esponenziale grazie alla tolleranza culturale diffusa in tutti gli Stati Uniti.

Un esempio tra i molti che dimostra lo storico legame tra l'erba messicana e gli Usa: Kiki Camarena era un poliziotto della DEA che riuscì a infiltrarsi ai vertici dei narcos negli anni '80: fu così che scoprì El Bufalo, un ranch che nascondeva la più grande piantagione di marijuana del mondo. Oltre mille ettari di terra e diecimila contadini a lavorarci. Per averla fatta sequestrare Kiki fu barbaramente torturato e ucciso.

L'erba messicana ha riempito gli Stati Uniti e metà pianeta per più di cinquant'anni. Ora, finalmente, la tendenza di crescita si sta invertendo. Dopo tanti dibattiti ideologici c'è la prova che la legalizzazione è uno strumento reale di contrasto al narcocapitalismo. In Colorado e a Washington ci sono diversi vincoli per il consumo: la marijuana può essere acquistata solo se si è maggiori di 21 anni, si può possedere sino a poco più di 28 grammi. In pubblico è vietato consumarla (come l'alcol del re-

sto) e guidare sotto effetto di erba è vietato (sospensione di patente per un anno o arresto serale).

Le grandi obiezioni mosse dai proibizionisti contro l'esperimento di legalizzazione in Usa sono le medesime da sempre sostenute dal proibizionismo europeo: aumento del mercato dei consumatori, aumento degli incidenti stradali, aumento della criminalità. Allarmi tutti smontati dall'esperienza reale. Non c'è stata nessuna catastrofe. La polizia di Denver in Colorado ha registrato una diminuzione del 4% dei reati, nessun aumento di incidenti stradali (la maggior parte continuano ad essere provocati dall'alcol). Non solo: sottrarre una massa di capitali enormi alle organizzazioni criminali ha portato il Colorado a prevedere la possibilità di incrementare la propria cassa con

Le prime liberalizzazioni hanno messo in crisi le organizzazioni a sud del Rio Grande

circa 175 milioni di dollari nei prossimi due anni, mentre lo Stato di Washington prevede un'entrata di oltre 600 milioni di dollari nei prossimi cinque anni. Come se non bastasse, sembra che lo Stato potrà addirittura restituire ai cittadini parte delle tasse. Tutto è dovuto da una legge del Colorado che impone allo Stato una quota limite sui soldi che può ricevere dalle tasse superata la quale deve ridistribuire il denaro ai contribuenti. Grazie alle entrate per l'acquisto di marijuana, il Colorado rimborserà i 30 milioni di dollari in eccedenza ricevuti. Mai successo a memoria d'uomo che la quota fosse superata, la legalizzazione l'ha permesso. Soldi che prima finivano nella tasca dei narcos messicani e delle banche complicità orso-

# L'erba contro i Narcos

Scienze terapie palliative

## **Una cura di nome Maria**

**Sclerosi multipla, lesioni neurologiche, cancro e Aids. Si moltiplicano le applicazioni cliniche della cannabis.**

**Un esperto spiega che è efficace e sicura**

*Maurizio Bifulco*

Per ridurre i costi legati all'importazione dei farmaci cannabinoidi è stato approvato un progetto pilota di produzione in Italia, presso lo Stabilimento farmaceutico militare toscano. I medicinali a base di cannabis come il Bedrocan, Bediol, Bedrobinol e Bedica, caratterizzati da differenti percentuali dei due principali principi farmacologicamente attivi della cannabis - il tetraidrocannabinolo (Thc) e il cannabidiolo (Cbd) - somministrabili mediante vaporizzazione o tisane, vengono al momento prodotti esclusivamente dall'olandese Bedrocan Bv, unica autorizzata alla produzione dal ministero della Salute olandese, che li esporta in altri paesi europei. Dai Paesi Bassi, dove il possesso e l'uso personale di cannabis, catalogata come droga leggera, è decriminalizzato, proviene anche la più lunga esperienza nel suo utilizzo medico.

## Gli effetti della liberalizzazione



**24%**  
il calo del traffico di marijuana rispetto all'anno scorso



**680 000 kg**  
di marijuana sequestrati nell'ultimo anno

l'anno precedente erano più di **1,3 milioni**



**800 milioni**  
di dollari di nuovi introiti fiscali grazie alla legalizzazione della marijuana

la Repubblica

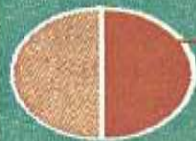
12 febbraio 2015

## La liberalizzazione e i dubbi sull'efficacia della repressione



diminuzione del **4%** dei reati in Colorado

**30 milioni**  
di dollari di tasse che il Colorado ridistribuirà ai contribuenti



In Usa il **50%** dei detenuti è in carcere per reati legati alla droga

The fact is that we are all walking around with a random and totally unfair assortment of genetic variants that make us more or less content, anxious, depressed or prone to use drugs. Some people might find it a relief to discover that they had a genetic variant that made them naturally more anxious — that they were wired for anxiety, not weak — even if right now there is no exact fix. My patient benefited greatly from antidepressant medication and meditation. But psychotropic medications, therapy and relaxation techniques don't help everyone, so what's wrong with using marijuana to treat anxiety?

The problem is that cannabis swamps and overpowers the brain's cannabinoid system, and there is evidence that chronic use may not just relieve anxiety but interfere with learning and memory. What we really need is a drug that can boost anandamide — our bliss molecule — for those who are genetically disadvantaged. Stay tuned.

(Richard A. Friedman is a professor of clinical psychiatry at Weill Cornell Medical College)

## Review


# Effects of Cannabis Use on Human Behavior, Including Cognition, Motivation, and Psychosis: A Review

Nora D. Volkow, MD; James M. Swanson, PhD; A. Eden Evins, MD; Lynn E. DeLisi, MD; Madeline H. Meier, PhD; Raul Gonzalez, PhD; Michael A. P. Bloomfield, MRCPsych; H. Valerie Curran, PhD; Ruben Baler, PhD

With a political debate about the potential risks and benefits of cannabis use as a backdrop, the wave of legalization and liberalization initiatives continues to spread. Four states (Colorado, Washington, Oregon, and Alaska) and the District of Columbia have passed laws that legalized cannabis for recreational use by adults, and 23 others plus the District of Columbia now regulate cannabis use for medical purposes. These policy changes could trigger a broad range of unintended consequences, with profound and lasting implications for the health and social systems in our country. Cannabis use is emerging as one among many interacting factors that can affect brain development and mental function. To inform the political discourse with scientific evidence, the literature was reviewed to identify what is known and not known about the effects of cannabis use on human behavior, including cognition, motivation, and psychosis.

*JAMA Psychiatry*. 2016;73(3):292-297. doi:10.1001/jamapsychiatry.2015.3278

Published online February 3, 2016.



**... ancora grandi incertezze.  
Ma la problematica merita questa  
attenzione diffusa?**

**If the states' initiative to legalize medical marijuana is merely a veiled step toward allowing access to recreational marijuana, then the medical community should be left out of the process, and instead marijuana should be decriminalized.**

**Conversely, if the goal is to make marijuana available for medical purposes, then it is unclear why the approval process should be different from that used for other medications.**


**Evidence justifying marijuana use for various medical conditions will require the conduct of adequately powered, double-blind, randomized, placebo/active controlled clinical trials to test its short- and long-term efficacy and safety.**

**The federal government and states should support medical marijuana research.**

**Since medical marijuana is not a life-saving intervention, it may be prudent to wait before widely adopting its use until high-quality evidence is available to guide the development of a rational approval process.**


**Perhaps it is time to place the horse back in front of the cart.**






**Il trattamento con marijuana per il dolore cronico resta ancora un aspetto incerto; certamente non riveste un ruolo centrale, ma di supporto.**

**Resta da chiarire il rapporto tra analgesia ed azione euforizzante ed alcuni effetti indesiderati.**



**La medicina contemporanea è in grado  
di curare il dolore?  
Ritorna la domanda drammatica posta  
all'inizio del seminario.**



**L'attuale modificazione dell'organizzazione della medicina tende verso la semplificazione, che non induce processi per migliorare la qualità delle cure.**

**Il dolore somatico e della psiche non potrà mai essere inquadrato in schemi semplificati di diagnosi e terapia.**

# The McDonaldization of Medicine

**E. Ray Dorsey, MD,  
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Table. Dimensions of McDonaldization of Medicine

Dimension	Description	Example	
		Fast Food	Medicine
Efficiency	Choosing the optimal means to achieve a given end	Drive-through window, limited menu, self-ordering register, finger foods, customers clear their table	Minute clinics, broader use of medical assistants, robotic surgery, brief visits with physicians, patients complete questionnaires
Calculability	Calculating, counting, and quantifying means and ends, with quantity serving as a surrogate for quality	Big Mac, supersize options, No. of hamburgers sold, precise measurement of hamburger size (9.843 cm)	"Big Med," medical school rankings, RVUs to measure productivity, ICD-10, length of stay, 30-d readmission rates
Predictability	Services and products being very similar from one time and place to another time and place	Extensive use of logos, standardized appearance of stores, use of frozen products, assembly-line food production, scripted interaction with customers	Extensive use of logos, standardized order sets, checklists and templates, clinical pathways, scripted histories and physicals
Control	Increased control of humans through use of nonhuman technology	Factory farms of chicken and cattle, hormone-treated animals, precut and preprepared food, automated soft-drink dispenser, uncomfortable chairs	Billing codes, electronic medical record, debt burden, formularies, utilization review

Abbreviations: ICD-10, *International Statistical Classification of Diseases and Related Health Problems, Tenth Revision*; RVUs, relative value units.

**Such work could be caring for those with limited means, helping ensure the neurological well-being of young athletes, or preparing families for the increasing burden of Alzheimer disease. If we are going to count in medicine, let it not be the number of medical records reviewed but rather the number of lives touched, minds stimulated, and hearts moved. The struggle against the McDonaldization of medicine will be both increasingly necessary and ennobling.**

# Medical Taylorism

Pamela Hartzband, M.D., and Jerome Groopman, M.D.

We need to recognize where efficiency and standardization efforts are appropriate and where they are not.

Good medical care takes time, and there is no one best way to treat many disorders.

When it comes to medicine, Taylor was wrong: “man” must be first, not the system.

N ENGL J MED 374;2 NEJM.ORG JANUARY 14, 2016

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# “CLICK HERE TO SEE A DOCTOR”

Technology is bringing consultations back into the home. **Nigel Hawkes** reports below on a global trend for app happy doctors to adopt the Uber model to market services via a smartphone. **Ingrid Torjesen** looks at the rise of private companies offering virtual access to GPs for a fee, a model that finds no favour with the profession's leaders

## Uber for healthcare

**I**s it time to reinvent the home visit? In the NHS they have been in steady decline for decades and now account for fewer than one in 25 general practitioner consultations. In the US the rate of house calls is even lower—around one in every 100 consultations—but app happy entrepreneurs backed by venture capitalists believe that they can turn back the clock.

Nigel Hawkes, freelance journalist, London, UK


Cite this as: *BMJ* 2016;352:i771

Find this at: <http://dx.doi.org/10.1136/bmj.i771>

20 February 2016 | **thebmj**



**Questi modelli rappresentano la fine della  
medicina o indicano un travaglio che potrebbe  
essere positivo?**



**Uno spunto di Gawande (Essere mortale, Einaudi, 2016) sulla complessità della cura del dolore. *“Non credo che la generazione dei baby boomer, in ogni parte del mondo, sia disposta ad accettare il genere di esperienza vissuta dai loro vecchi negli ultimi stadi della vita. Alla fine quello che vogliono è un’esistenza che conservi il suo valore”.***

**Cosa significa nella prospettiva delle tecniche per la cura del dolore “conservare il valore della vita”? E’ ancora una domanda senza risposta.**



# Zero Pain Is Not the Goal

Thomas H. Lee, MD, MSc

**The data will never be perfect.  
The measures will never be perfect.  
The guidelines will never be perfect.  
And neither will clinicians and their performance.  
But by acknowledging these imperfections and  
trying to get better with the tools available,  
physicians can more effectively reduce the suffering  
of patients.**

**JAMA** Published online March 15, 2016

**Questo è il nostro modo per esercitare la misericordia**

***«Dio attende con pazienza che io voglia infine acconsentire a amarlo. Dio attende come un mendicante che se ne sta in piedi, immobile e silenzioso, davanti a qualcuno che forse gli darà un pezzo di pane. Il tempo è questa attesa. Il tempo è l'attesa di Dio che mendica il nostro amore» (Simone Weil)***

**La parola spesso oggi più sfuggita e censurata, “dolore”, è piena di significati nella prospettiva religiosa. Perchè l'ombra più oscura può indurre nostalgia di Dio, e il sentiero più desertico non porta al nulla ma a colui che, fedele, mendicante, aspetta.**