[Docket No. FDA–2012–N–1172]

Implications of Opioid Relabeling on Chronic Non-Cancer patients

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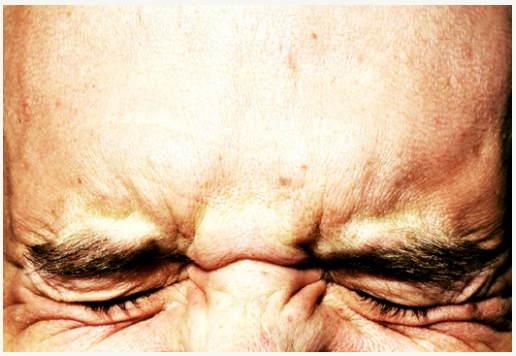


INTRODUCTION

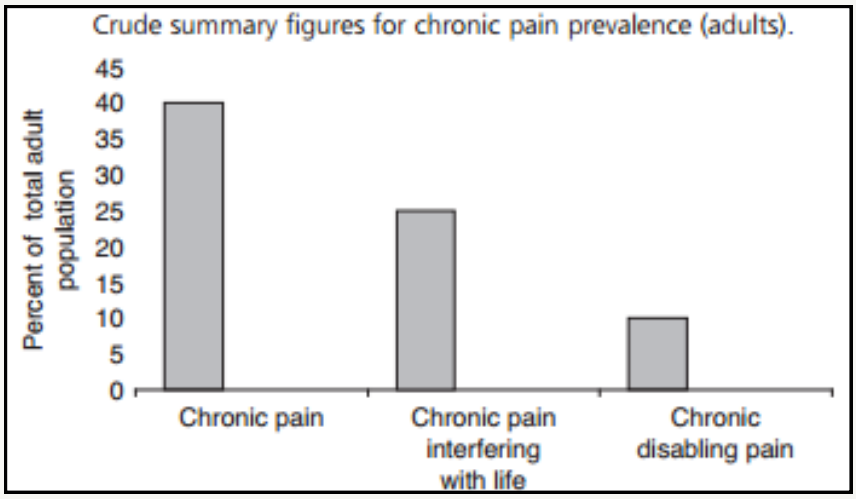
Treating chronic pain is unlike treating many other chronic medical conditions. The diagnosis of hypertension and type II diabetes can easily be quantified using objective information such as blood pressure and hemoglobin A1c%. Health care professionals can use laboratory data such as these to reach clearly defined goals which are supported by strong clinical evidence. Pain is different in that there is no measured laboratory value to gauge the severity or, at times, the existence of pain. Practitioners rely on the patient's own subjective information, which can be one of the greatest obstacles in opioid prescribing. Practitioners have to adequately treat pain in a manner that is both safe and appropriate for the patient. When inadequately treated, chronic pain has significant morbidity on the patient's quality of life. It not only affects one's social life, but also their work and school life. There are many different components of pain that could be improved other than for physical reasons, including economic and emotional. With this in mind, it also makes sense to help ease pain not only medically, but also with non-pharmacological therapies. These should be used in combination to achieve better results than with either treatments alone.

BACKGROUND

Chronic pain is defined as being both:

- Persistent beyond the usual course of an acute disease or a reasonable time for any injury to heal
- Not amenable to routine pain control methods[1]

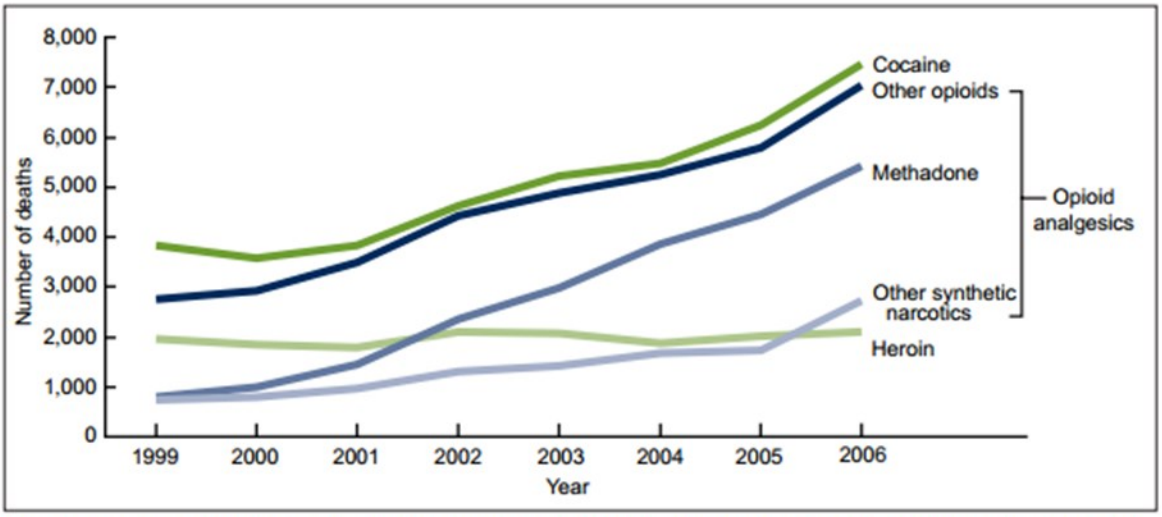
The prevalence of moderate to severe non-cancer pain ranged widely from 2% to 40% of the United States adult population[2,3].



Main opinions made in this comment:

- For opioid use in chronic non-cancer pain, there should be no rigidly defined:
  - ◊ Maximum daily dose
  - ◊ Duration
- Treatment should be given at the lowest effective dose as long as it is needed to treat pain.
- Complimentary and alternative medicine should always be considered in combination with opioid therapy in chronic non-cancer pain.
- Health care professionals including pharmacists should play an active role in patient education to deter improper use.

From 1999 through 2006, poisoning deaths involving methadone rose more rapidly than those involving other opioid analgesics, cocaine, or heroin.



NOTES: Drug categories are not mutually exclusive. Deaths involving more than one drug category shown in this figure are counted multiple times. Access data table for Figure 2 at ftp://ftp.cdc.gov/pub/Health_Statistics/NCHS/Publications/Data_Briefs/db022/fig02.xls.
SOURCE: CDC/NCHS, National Vital Statistics System.

INCREASING TRENDS IN DEATH AND SALES

There are some issues when analyzing the sheer number of deaths due to opioid overdose. While it is undisputable that the number of overdoses due to opioids is increasing, the US population has effectively doubled in 60 years. The number of retail sales of opioid medications have also increased from 1997 to 2006, but that fact in itself is no reason to cause alarm. The problem with considering the number of deaths is that it may lead to untrue and distorted conclusions. An increase in sales is expected with the increasing population. It would be more bizarre if there was a constant or declining trend. This is because the actual cause of pain (due to injury, genetics, comorbidities) often times cannot be prevented or curbed appreciably. Even if extreme restrictions were applied to opioid prescribing, sales and deaths will eventually fall back into the same increasing pattern overtime. That is not to say there is nothing to be done to help prevent some of these deaths due to improper use or diversion.

United States Population from 1910-2010

Year	US population
1910	92,228,531
1920	106,021,568
1930	123,202,660
1940	132,165,129
1950	151,325,798
1960	179,323,175
1970	203,211,926
1980	226,545,805
1990	248,709,873
2000	281,421,906
2010	308,745,538

Resident Population Data. "Resident Population Data – 2010 Census". www.census.gov. Retrieved February 22, 2013.

Retail sales of opioid medications (grams of medication), 1997–2006.

Drug	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	% of change from 1997
Total	50,713,010	56,273,194 (11%)	59,445,465 (6%)	35,962,089.84 (15%)	75,294,939 (11%)	82,874,845 (10%)	92,987,076 (12%)	98,456,163 (6%)	101,251,950 (6%)	115,272,706 (14%)	127%

Numbers in parenthesis are percentage of change from previous year. * For year 2000, data is not available; the average of 1999 and 2001 was taken. Source: www.deadiversion.usdoj.gov/arcos/retail_drug_summary/index.html
Adapted from Manchikanti and Singh (5). Therapeutic opioids: A ten-year perspective on the complexities and complications of the escalating use, abuse, and nonmedical use of opioids. *Pain Physician* 2008; 11: S63-S88.

Prevalence of Antihypertensive Medication Use Among Hypertensive Adults Over Time by Drug Classes: United States 2001 to 2010

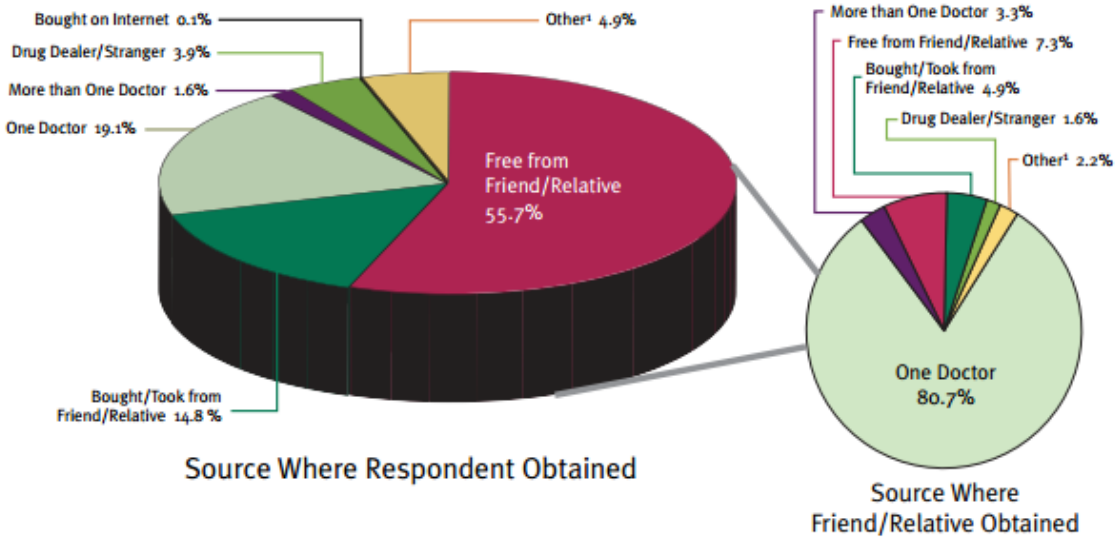
Drug Classes and Therapy	2001–2002 % (SE)	2003–2004 % (SE)	2005–2006 % (SE)	2007–2008 % (SE)	2009–2010 % (SE)	P_{trend}
Diuretics						
Overall	30.0 (2.2)	32.1 (1.7)	34.0 (2.2)	34.7 (2.0)	35.8 (1.2)	0.01
Calcium channel blockers						
Overall	19.2 (1.7)	20.7 (1.4)	21.7 (1.7)	19.4 (1.3)	20.9 (1.4)	0.65
Angiotensin–converting enzyme inhibitors						
Overall	25.5 (1.2)	29.8 (2.0)	29.4 (1.7)	29.3 (1.7)	33.3 (1.1)	<0.01
Angiotensin receptor blockers						
Overall	10.5 (1.0)	14.5 (1.2)	14.5 (1.3)	20.3 (1.3)	22.2 (1.6)	<0.01

Hypertension medication use have also increased over the years. Gu Q, Burt VL, Dillon CF, Yoon S. Trends in Antihypertensive Medication Use and Blood Pressure Control Among United States Adults With Hypertension. Circulation. 2012. Vol 126 no 17. 2105-2114.

MAXIMUM DAILY DOSES

Established maximum daily doses give health care professionals a guideline to help avoid serious adverse effects in patients. There are proposed maximum daily doses for opioids, however these will not target the cause of overdose. Patients who are prescribed <100 mg/day morphine equivalent account for an estimated 20% of all prescription drug overdoses[4]. The real issue that needs attention is diversion and training health care professionals to be actively educating their patients on the severe consequences of misusing opioids.

Illegal drug dealing is commonly what comes to mind when drug diversion is mentioned. However, the results of the SAMHSA survey found that 55.7% of nonmedical users of prescription pain relievers, tranquilizers, stimulants, and sedatives obtained them from a friend or relative. This indicates the lack of patient understanding about the life-threatening properties of opioids. They are not regular pain killers like ibuprofen and acetaminophen - one tablet at a high dose may be enough to be the last tablet that person will ever take. On two separate occasions, I witnessed a free opioid offer from one friend to another in case they experienced future pain. The prescriptions were originally for short-term legitimate reasons for pain (dental), however they had some left over once they did not need them anymore. The nonchalant attitude of the offer from one friend to another was startling. Upon further questioning, I was further surprised to find that they had not been counseled by either the doctor or pharmacist of their potentially addictive and life-threatening capacity. The role of the pharmacist as being the last professional contact in dispensing these medications is incredibly important. As health care professionals, we should all take a hard look at ourselves and what we can do to help our patients live well and safe. Being an active educator to our patients is one of the best ways we can help prevent opioids from being diverted from one person to another.



Note: Totals may not total to 100% because of rounding or because suppressed estimates are not shown.
[1]The Other category includes the sources: "Wrote Fake Prescription," "Stole from Doctor's Office/Clinic/Hospital/Pharmacy," and "Some Other Way."

Where pain relievers were obtained for most recent nonmedical use among past year users aged 12 or older: 2006 (1).
Source: Abuse and Mental Health Services Administration (2007) (190). Results from the 2006 National Survey on Drug Use and Health: National Findings.

MAXIMUM LENGTH OF TREATMENT

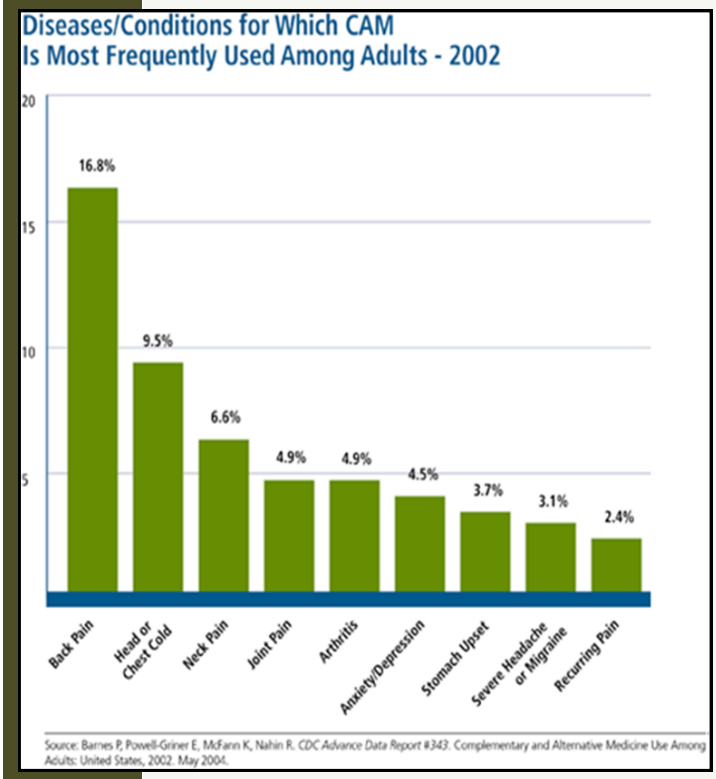
There is a debate about establishing a maximum length of treatment concerning opioids in treating non-cancer pain. A reason that is made for establishing a rigidly defined maximum length is that over 60% of patients who were taking daily opioids for at least 90 days were also taking opioids 5 years later[5]. Having an extended length of therapy to help alleviate pain should not be a negative argument. Medications are prescribed for as long as it takes to treat, prevent, or mitigate conditions. For example, post-MI patients take daily aspirin for decades despite possessing serious adverse effects such as GI bleeding. There are many different causes of chronic back pain. Therefore, establishing a rigidly defined maximum length of therapy does not make much sense. It is akin to having a fixed maximum length of SSRI/SNRI therapy for depression, generalized anxiety disorder, panic disorder, social anxiety disorder, post-traumatic stress disorder, and obsessive compulsive disorder. Despite arising from diverse causes, they are all mood disorders treated pharmacologically with SSRI/SNRIs. The diagnosis of these mood disorders are also largely based on the patient's subjective information. Why not determine a maximum treatment length of 6 months for these conditions? Some answers may suggest that mood disorders deserve a more patient-centered approach to treatment than pain.

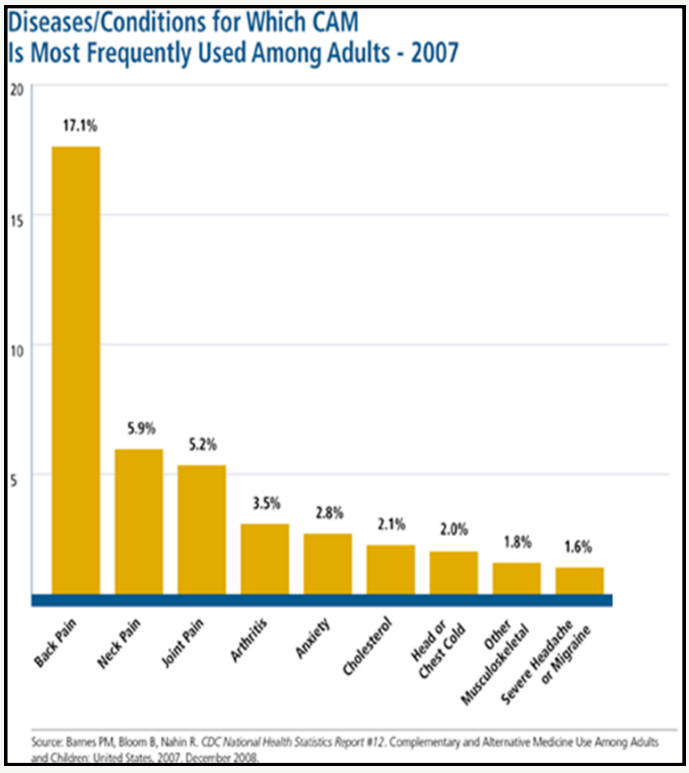
Common Sources of Back Pain[6]

- Slipped or bulging discs
- Spinal stenosis
- Compression fractures
- Soft tissue damage
- Traumatic fractures

COMPLIMENTARY AND ALTERNATIVE MEDICINE

Patients seeking relief from chronic pain should not only be treated with opioids. Complimentary and alternative medicine (CAM) is used in combination to what people consider conventional medical treatments. CAM includes natural products such as herbs and other plant-derived products, deep breathing exercises, meditation, and movement therapies. Most patients that used CAM sought relief for back, neck, or joint pain[7]. Eisenberg et al conducted a survey that adding on CAM to conventional therapy was better than either treatment alone in back and neck pain[8].





Relative Helpfulness of Complementary and Alternative Medical Therapies Compared with Conventional Medical Care among Respondents Who Used Both for Specific Medical Conditions*

Medical Condition	Total Weighted Sample, n†	Respondents' Perception, %‡		P Value§
		Conventional Care Was Better	CAM Therapy Was Better	
Back conditions	158.3	12.4	46.1	<0.001
Arthritis	72.1	25.9	44.8	0.06
Neck conditions	87.9	6.4	61.0	<0.001

* CAM = complementary and alternative medical.
† Values represent the sum of standardized sampling weights for the respondents with the condition.
‡ The remainder of respondents found their physician's care and CAM therapy to be equally helpful.
§ Based on a two-sided McNemar test.

Eisenberg, et al. 2001. Annals of Internal Med. 135:344

There are certain situations where just talking about pain and performing stretches cannot help. This is where medication, including opioids, come in. The additive benefit of utilizing both pharmacologic and CAM should always be considered when treating patients with chronic pain.

CONCLUSION

There should be an individualized patient-centered approach to treating chronic pain, as it is with many other conditions. Treatment with opioids should be given at the lowest effective dose as long as they are needed for pain. Patient understanding of the differences and risks between regular OTC pain relievers is paramount when prescribing and dispensing opioids. Complimentary and alternative medicine, as indicated by its name, should be considered in conjunction with opioids.

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