

# **Appropriate Opioid Dosing for Activities of Daily Living**

**BY**

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## INTRODUCTION

Recent years have witnessed the widespread acceptance of opioid treatment of non-malignant, chronic pain. As many as 10 million Americans now use opioids for chronic pain on a regular basis.<sup>1</sup> Although there is now recognized acceptance of opioid treatment, the debate has shifted to correct dosage and "excessive prescribing". The vast majority of pain practitioners and observers have stated that there is no ceiling dosage for opioids or excessive prescribing in a legitimate pain patient who simply requires a high dosage and who isn't an addict or diverts drugs. The prevailing view is clearly that the proper dosage, regardless of daily amount, should be whatever allows the patient to achieve pain relief while performing normal physiologic, mental, and social functions of daily living. Unfortunately, some individuals and institutions are trying to arbitrarily establish a maximal ceiling dosage for opioids. Their basis for this desire appears to be the erroneous belief that opioids are either not effective above a certain dosage or that a pain patient never reaches a plateau or maintenance dosage and eternally desires to continually raise his/her opioid dosage. Another misconception is that withdrawal from opioids is a difficult and dangerous procedure once chronic pain is reduced or cured. The high cost of opioids and other financial motives also likely underlie a desire to limit opioid dosages and make false claims of excessive prescribing.

This paper compiles and reviews the objective physical signs and symptoms that must be present before a diagnosis of excess opioid dosage or prescribing can be made. A diagnosis of excessive opioid dosage or prescribing can only be made by physical examination done by a qualified person and not by simply "counting pills", the number of different opioids prescribed, or by comparing one patient group to another, such as a severe intractable group compared to the usual chronic pain population.

BASIC OPIOID PHYSIOLOGY

There are legendary controlled studies on the physiologic effects of opioids that date back to the 1930's.<sup>2-5</sup> At the Lexington, Kentucky United States Public Health Service Hospital, Himmisbach, Eddy, Fraser, and Seevers clearly documented the physiologic signs of opioid excess and withdrawal following abrupt cessation of opioids.<sup>2-5</sup> Others have confirmed their findings.<sup>6-7</sup> Severe pain produces great stimulation of the autonomic, sympathetic nervous system and simultaneously activates the hypothalamic-pituitary axis to elevate serum catecholamines and cortisol.<sup>8-10</sup> These concomitant effects produce obvious and easily observed physical signs of sympathetic nervous system stimulation. The physiologic signs of severe pain are essentially identical to those of opioid withdrawal. These include mydriasis (pupil dilation), hypertension, tachycardia, hyperreflexia, and elevated respiratory rate and temperature. (See Table One) Opioid blood levels above an individual's tolerance level will produce the physiologic signs of sympathetic nervous system suppression which include miosis (pupil constriction), bradycardia, hypotension, hyporeflexia, and decreased temperature and respiratory rate among others.

<u>TABLE ONE</u>	
<u>Physical Signs of Excess Opioids*</u>	<u>Physical Signs of Uncontrolled Pain or Opioid Withdrawal</u>
Hypotension	Hypertension
Bradycardia	Tachycardia
Respiratory Depression	Elevated Respiratory Rate
Dry Skin	Diaphoresis/Gooseflesh
Hypothermia	Hyperthermia
Hyporeflexia	Hyperreflexia
Pupil Constriction (Miosis)	Pupil Dilation (Mydriasis)
Slow Reactive Pupil	Rapid Pupil Reaction
Droopy Eyelid	Normal Speech
Slurred /Slow Speech	Normal Gait
Shuffling /Wide Gait	Cold Extremities (Vasoconstriction)
<i>* These signs are visible and prominent in an overdose case and also present to a lesser degree in cases of excessive prescribing.</i>	

The classic, physiologic signs of opioid excess and uncontrolled pain as outlined here, in addition to patient and family reports of analgesic effectiveness and physical functioning should routinely be used by practitioners to assess and determine the need for an appropriate opioid dosage regardless of the number of pills or number of different opioids required to produce sympathetic homeostasis and tolerable pain control. (Table Two)

Before any party can make a determination of under or excessive prescribing, a physical examination of the patient has to be done by a practitioner qualified and licensed to perform the examination, and the classic physiologic signs of opioid excess or deficiency have to be assessed and recorded. It is grossly unscientific to make any statement that a given oral dosage or number of opioids simultaneously administered is excessive or deficient without a physical examination on the day and time that opioid excess or deficiency is claimed to be present.

<b><u>TABLE TWO</u></b>		
<b><u>RECOMMENDED PHYSICAL, OBJECTIVE MEASURES TO HELP DETERMINE EXCESS OPIOID PRESCRIBING AND UNCONTROLLED PAIN</u></b>		
<b><u>UNCONTROLLED PAIN</u></b>	<b><u>GOOD PAIN CONTROL</u></b>	<b><u>EXCESS OPIOIDS</u></b>
Pulse rate > 88 per minute	Pulse between 64 and 88 per minute	Pulse rate < 64 per minute
Blood pressure > 130/90mmHg	Blood pressure between 110/70 and 130/90mmHg	Blood pressure < 110/70mmHg
Pupil diameter > 5.0	Pupil diameter between 3.0 and 5.0mm	Pupil diameter < 3.0mm
Cold hands/feet	Normal temperature	Very warm hands/feet

## GOALS OF OPIOID TREATMENT

While a variety of outcome measures have been reported with opioid treatment, all generally speak of a variety of improved mental, physical, social, vocational functions, and activities of daily living. One broad goal category is "quality of life". A basic recommendation is that opioid treatment should provide enough pain relief to allow a patient to escape a bed or house bound state, carry on activities of daily living such as eating and dressing, and do so without demonstrating physical evidence of opioid excess or impairment.

<p style="text-align: center;"><u>TABLE THREE</u></p> <p style="text-align: center;"><u>GENERAL GOALS OF OPIOID</u> <u>TREATMENT</u></p> <p style="text-align: center;">Improved Mental Functioning</p> <p style="text-align: center;">Improved Activities of Daily Living</p> <p style="text-align: center;">Decrease of a Bed or Couch Bound State</p> <p style="text-align: center;">Improved Quality of Life</p> <p style="text-align: center;">No Physical Sign of Opioid Excess</p>
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## WIDE VARIATIONS IN INDIVIDUAL DOSAGES

Opioid dosages exhibit an extremely wide range as do their blood levels. (See Table Four) The reasons for this wide variation are multiple. Naturally the severity of pain, age, weight, and sex may play a role as these factors do with any other pharmaceutical agent. Opioids, however, have additional factors which may require an effective dosage to be high. There may be gastrointestinal malabsorption, overactive liver enzyme activity, defects at the blood brain barrier, or genetic opioid receptor abnormalities.<sup>11</sup> These

factors which are primarily genetic must be considered in determining opioid dosage since one or more may be responsible for high opioid dosage requirements.

Every disease and class of pharmaceutical agents has what are classified as outliers. Diabetics, hypertensives, schizophrenics, asthmatics, depressives, epileptics, and Parkinsonians and chronic pain patients have a severity spectrum that may range from a single drug given on an "as needed" basis to those whose severity is such that multiple drugs in the same pharmaceutical class must be used. The notion that there should be a ceiling or restricted dose of opioids is non-sensical, unscientific and inhumane. A glance at Table Four shows the wide spectrum of some opioid dosages and blood levels.

## TABLE EIGHT

### EXAMPLES OF HIGH DOSE OPIOID THERAPY THAT ARE NOT OVERPRESCRIBING

1. A 60 year old female has porphyria and requires a very high opioid dose to physically function, suppress acute pain episodes, and remain out of a hospital. She takes daily liquid morphine 50 to 70mg, oxycodone short-acting 5 to 20mg every 4 to 6 hours for a total of 50 to 60mg a day, and fentanyl transdermal 100mcg every third day.
2. A 43 year old male who is president and chief operations officer of a \$15-20 million company developed neuropathies following successful chemotherapy and surgery for malignant melanoma. He takes each day the following: Morphine 400mg extended release, fentanyl transmucosal 6400mcg, and Propoxyphene 400mg.
3. A 57 year old male has severe Lyme Disease arthropathy and neuropathy. He also has coronary heart disease and has angina without good opioid pain control. He requires each day: Morphine sustained release 300mg, hydromorphone 24 to 32mg, and Propoxyphene 300mg. He is able to work full-time as a prison guard.
4. A 44 year old male stands 6' 3", and weighs 230 lbs. He has inoperable spine disease and has had a hip replacement. He now works full-time as a community college instructor. Daily dosage is: Fentanyl transdermal 100mcg every 2nd day; methadone 200mg per day, and fentanyl transmucosal 6400mcg per day.
5. A 66 year old female has severe degenerative spine disease. She has had 3 spine surgeries including cervical fusion and lumbar laminectomy. She was bed and house bound until her opioid dosage was titrated upward to oxycodone extended release about 1000mg a day and liquid morphine about 650mg a day. She now can leave her home, visit grandchildren and she claims a high quality of life.
6. A 56 year old female, registered nurse has abdominal neuropathies and rheumatoid arthritis. She works full-time. Her only opioid is Propoxyphene 400mg per day which she has taken daily for over 20 years.
7. A 46 year old diabetic weighs between 350 and 400 pounds. She requires liquid methadone 180mg a day, 400mg of extended release morphine and 600mg of short-acting morphine to control her severe pain. She has severe neuropathies and inoperable degenerative spinal disease. She is known to malabsorb a number of medications.
8. A 47 year old civil engineer works full-time with an amputated leg and phantom pain. He takes 5, 100mcg fentanyl patches a day, and has done so for 14 years.
9. A 39 year old, full-time contractor takes 320mg of methadone a day. This dose was arrived at by titration over several months. This dose has remained stable for over 5 years. His basic cause of pain is degenerative spine disease.
10. A 45 year old male teacher takes 190mg of methadone 3 times a day (570mg total). He was able to work only after titrating his dose upward over about a year's time.
11. A 55 year old physician takes oxycodone, short-acting, 15mg for a total of 300mg a day. His pain was caused by an arm fracture that became infected and required a metal plate. His dosage has remained stable for about 5 years.
12. A 37 year old, full-time sheriff's deputy sustained a severe back injury in the line of duty which left him in severe pain unresponsive to paraspinal interventions. After a long titration he was able to function with long-acting oxymorphone 560mg a day plus compounded hydrocodone, 300 to 350mg a day.

*ALTHOUGH OPIOID DOSAGES ARE HIGH AND THESE PATIENTS ARE OUTLIERS, THEIR OPIOID REGIMEN IS NOT EXCESSIVE, SINCE THE PATIENT FUNCTIONS WELL WITHOUT SIGNS OF EXCESS OPIOID USE.*

Opioid	No.	% Females / Males	Age Range	Weight Range - Lbs.	% Full Function	% Drive	% Work/Volunteer	Years On Opioid	Daily Dosage Range	Mean Dosage	Range of Serum Concentration ng/ml	Mean Concentration
Codeine	1	100/0	55	135	100%	100%	100.00%	10	120mg	NA	408	NA
Fentanyl Transdermal	8	63/37	28-64	128-375	100%	100%	50.00%	3-20	100-300*	181.3 ± SD 69	1.2-8.9	4.8 ± 2.65 SD
Fentanyl Transmucosal	18	61/39	35-64	112-250	100%	94%	50.00%	1.5-25	1200-48,000mc	14588.9 ± 131.5 SD	0.9-9.5	5.0 ± 2.4 SD
Hydrocodone	11	64/36	25-74	120-225	100%	100%	73.00%	1-10	30-300mg	101.4 ± 79.0	18-396	94.7 ± 109.7
Hydromorphone	11	55/45	37-71	115-207	100%	100%	45.00%	2-50	20-540mg	186.2 ± 171.1	9.4-230	59.4 ± 69.9
Methadone	32	34/66	35-63	105-285	97%	88%	44.00%	3-20	40-600mg	218.8 ± 161.0	60-2580	497.0 ± 553.6
Morphine IR	10	60/40	37-59	108-430	100%	90%	50.00%	6-25	100-1800mg	798.0 ± 552.2	22-828	250.6 ± 273.2
Morphine SR	18	61/39	28-73	112-285	94%	83%	39.00%	2-18	60-2000mg	570.9 ± 519.9	16-2837	515.4 ± 789.4
Oxycodone IR	14	64/36	31-71	108-245	100%	79%	43.00%	1-50	15-2700mg	525.7 ± 741.2	5-3077	360.7 ± 776.5
Oxycodone SR	33	42/58	26-87	108-270	94%	82%	25.00%	1.5-13	40-880mg	382.7 ± 232.0	10-650	200.6 ± 148.5
Propoxyphene	2	50/50	36-50	190	100%	100%	100.00%	8-20	400-1300mg	NA	227-240	NA

\* Fentanyl transdermal is the dosage applied by patch every 72 hours. All other dosages are oral, daily dosages. This chart previously published in Practical Pain Management (Tennant Blood Study). Please note the wide variation in dosages and serum concentrations.

## SIMULTANEOUS USE OF MULTIPLE OPIOIDS

The mu opioid receptor, which is the primary endorphin receptor responsible for analgesia, is a complex structure with several subunits. It has been studied extensively, and found to have wide variability in its structure between individuals. This can be expected to lead to a wide range of sensitivity between individuals, and also to explain why one person may respond much more effectively than another to a particular opioid.

Due primarily to genetic receptor sensitivity in addition to metabolic factors, such as serum half life, multiple opioids, simultaneously administered, may be necessary to adequately control severe pain. The most common example is an intractable pain patient who requires a long acting opioid for persistent or baseline pain and one or more short-acting opioids for breakthrough or flare pain throughout a 24 hour

period. There are some severe pain patients who may require as many as 3 to 4 different opioids to adequately control baseline and flare pain. Criticism of the use of the simultaneous use of multiple opioids in severe pain cases is misplaced, since this same situation may exist in severe diabetics, hypertensives, schizophrenics, depressives, epileptics, and Parkinsonians and asthmatics that may require the simultaneous administration of as many as 3 to 4 agents. Fortunately, these individuals represent a small segment of the chronic pain population, and their opioid treatment should only be done by physicians who are experienced and structure their practice to accommodate the severe, pain patient who requires multiple opioids.

### TITRATION TO CORRECT DOSAGE

Proper opioid dosage in a bonafide chronic pain patient is determined by titration. In a new patient the initial opioid dosage is low and then titrated upward as the patient is followed. As the dosage is titrated upward, by incremental increases, the patient should achieve the goals of treatment without demonstrating opioid excess, impairment, or hyperalgesia. It is our collective experience that upward titration reaches a dosage plateau at which time the patient will remain in a fairly narrow dosage range which may last for several years. Opioid dosage changes, up or down, in the chronic pain patient should be done on patient self report of therapeutic effectiveness plus some objective physical signs, such as pulse rate, blood pressure, and pupil size.

Tolerance to opioids begins with the first dosage and is quite significant within one week of daily use. Consequently, a long-term opioid-managed pain patient who is educated about proper dosing seldom demonstrates opioid excess. Severe pain also puts the endogenous-opioid system in a hyper state which allows a high dose of exogenous opioids to be taken without evidence of excess or overdose.

Proper opioid titration of a chronic pain patient is done in incremental dosages over a time period that may take several months. Titration may require the addition of opioids to produce an effective combination of opioids. There is no one opioid, dosage, or combination. One size does not fit all.

<p style="text-align: center;"><u>TABLE FIVE</u></p> <p style="text-align: center;"><u>SOME REASONS FOR HIGH OPIOID DOSAGES</u></p> <p style="text-align: center;">Pain Severity</p> <p style="text-align: center;">Weight, Sex, Age</p> <p style="text-align: center;">Receptor Sensitivity</p> <p style="text-align: center;">Metabolic Abnormalities</p> <p style="text-align: center;">Gastrointestinal Malabsorption</p> <p style="text-align: center;">Rapid Liver Metabolism</p>
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#### BLOOD AND URINE LEVELS OF OPIOIDS

Although every pain patient must have a minimal or floor opioid blood level to achieve pain control, a high blood level of opioids does not, per se, provide a diagnosis of "too high an opioid dose" or represent excessive prescribing. Opioid-tolerance is the reason that a high urine or blood opioid level does not diagnose opioid excess. Some opioid tolerance develops with only 7 to 10 days of repeated opioid administration, high blood or urine level simply indicate the presence of tolerance and regular opioid administration. It is not evidence of opioid excessive or excess prescribing. A high opioid level, accompanied by normal physiologic signs of blood pressure, pulse rate, and pupil size also suggests, but is not completely diagnostic, of good pain control. On the contrary a low opioid or urine blood level in

the face of documented, high oral intake suggests either gastrointestinal malabsorption or rapid liver metabolism of opioids. A high urinary opioid level is often indicative of oral regimen compliance, while a low level may suggest otherwise. Neither high nor low urine or blood levels can be completely diagnostic of excess or deficient opioid dosage or evidence of non-compliance or diversion. Blood and urine opioid levels in a chronic pain patient are clinical aides but are not, per se, diagnostic of diversion, non-compliance, or excessive prescribing.

### ANCILLARY DRUGS: THE REAL PROBLEM

The usual impairment problem with opioid-managed, chronic pain patients is the use of benzodiazepines, muscle-relaxants and other sedatives. These drugs and opioids tend to potentiate each other.

Consequently, most opioid-managed patients who appear sedated use excessive amounts of sedative-producing drugs. Pain patients often require drugs such as muscle relaxants and sleep aides which can produce sedation. The presence of over-use and interaction with opioids must be continually monitored, and the patient educated as to the dangers of combined use. Pain patients may sometimes appear sleepy, exhausted, and require a long-period of sleep after a severe pain flare. A sleepy patient can be easily differentiated from an opioid excess patient, however, since the opioid excess patient will demonstrate sympathetic nervous system suppression of such signs as pupil constriction and bradycardia.

### SIGNALS OF EXCESS PRESCRIBING: THIRD PARTY REPORTS

A high dose of opioids is only appropriate for the legitimate chronic pain patient and not the addict, recreational abuser, diverter, or non-pain patient. The only indicator that a physician will know of diversion, abuse, or sedative impairment is likely a third party report. Physicians may receive reports

form a 3rd party such as a family member, visiting nurse, pharmacist, or law enforcement official that indicates impairment, diversion, or misuse of opioids. Third party reports of sedation or impairment almost always represent non-compliance with prescribing instructions and/or use of sedatives since chronic pain patients become tolerant to opioids after about 7 to 10 days of administration. A credible report that a patient is illegally, diverting opioids, calls for immediate cessation of prescribing by the physician. A family member or friend may report that a patient is intentionally taking too many opioids due to depression or other psychiatric condition. Fundamentally, prescription opioids can be episodically used in binges for no-pain purposes just as alcohol may be used. Other reports may inform the physician that his opioid prescriptions are being shared, used at parties, or stolen by teenagers for abuse purposes. Obviously opioid prescriptions must be curtailed in these circumstances.

#### WHEN SHOULD AN OPIOID DOSAGE BE REDUCED?

Physicians who prescribe opioids should educate patients as to a specific time that opioid dosages can be reduced. When the patient's pain abates, physical signs of opioid excess or strong desire on the part of the patient are the usual indicators for dosage reduction. As long as the patient claims severe pain and there are no physical signs of excess opioids, there is no need to reduce opioid dosage. In fact, a too rapid a withdrawal schedule may precipitate a pain flare that could cause enough sympathetic over activity to pose a cardiovascular risk.

#### ARE HIGHWAY PATROLMEN MORE SCIENTIFIC?

Claims of excess opioid dosage and prescribing by physicians seems estranged from law enforcement personnel who arrest opioid users. The unscientific and inappropriate use of "pill counting" or

comparison of disparate patient groups (i.e. intractable pain patients versus usual chronic patient) is simply wrong. The courts require law enforcement officers to provide scientific, physical evidence before a diagnosis of opioid excess can be made, For example, a highway patrolman who arrests a "drugged driver" must arrange to have the person who is arrested to undergo a physical examination by a trained observer commonly known as a "Drug Recognition Expert". This examiner will examine the eyes for a droopy eye lid, pupil size, and light reactivity. Blood pressure and pulse rate will be taken. Some chronic physical signs of opioid excess must be present along with a qualitative, confirming opioid urine test before a diagnosis of "opioid excess or influence" can be made. Given this common and accepted practice, it is difficult to understand that some physicians are accused of "overprescribing" when the accuser hasn't even examined the patient.

#### WHEN DOES EXCESSIVE OPIOID PRESCRIBING OCCUR?

This paper does not contend that opioid overprescribing or too high a dosage does not exist. It does. Practical Pain Management maintains a regular dialogue with physicians accused of overprescribing by regulatory agencies and insurance companies as well as some anti-opioid physicians. A topical subject today is "hyperalgesia" which is oversensitivity to opioids and diminished effectiveness of opioids. This situation can clinically exist if a physician overprescribes opioids to a mild pain patient or a person who doesn't have pain. This situation almost always exists because the physician is unfamiliar with the Controlled Substance Act Schedules. These schedules are in place for a purpose in that a legitimate chronic pain patient must be started on a weak (Schedule 3 or 4) opioid rather than a stronger (Schedule 2) opioid. Ambulatory, chronic pain patients must be initially treated with a short-acting, Schedule 3 or 4 opioid used on an as-needed (prn) basis. Short-acting opioids initially need to be used since they maintain an effective blood level for only 2 to 4 hours which allows blood clearance and receptor adjustment. If

potent, (Schedule 2) or long-acting opioids are used in a new or opioid naïve patient, physical signs of opioid excess and/or hyperalgesia will likely occur. Table Six lists the common, opioids which are the first line treatment in chronic pain. The more potent and long-acting opioids (Schedule 2) are used only if the weaker, short-acting opioids in Schedule 3 or 4 fail to control pain. (See Table Seven)

Physicians who fail to heed third party reports of abuse, misuse, impairment, or diversion and continue to prescribe must be declared to "excessively prescribe". Since opioids are abusable and can be dangerous, patients who take them must be educated and regularly monitored. A monthly check-up is rather standard for opioid treatment until the patient is quite stable. Patients who legitimately require Schedule 2 or multiple opioids are severe pain patients who have an obvious underlying basis or cause of pain and demonstrate some sympathetic discharge signs such as tachycardia, hypertension, vasoconstriction, hyperreflexia, diaphoresis, or mydriasis. In these cases, family involvement in the opioid treatment process is recommended. It is clearly excessive to prescribe to a patient who openly tells the doctor that they intend to use the opioid at parties or for other than pain purposes. Opioid addicts should be treated in licensed methadone or certified buprenorphine (Suboxone®) programs. The profiles of addicts are widely published and they generally identify most addicts who prey upon physicians as some one who is under age 30 years, a smoker, and has no real documentation of legitimate pain by virtue of physical examination, x-ray, past records, or family verification. Naturally, prescribing to a patient who doesn't demonstrate a physical examination and history compatible with bonafide pain is clearly excessive.

TABLE SEVEN

EXAMPLES OF EXCESSIVE OPIOID PRESCRIBING

Physicians who prescribe opioids to:

- A patient without a bonafide, cause or basis of pain
- A patient reported to divert, misuse, or exhibit impairment
- A patient not monitored and followed on a regular basis
- A patient who has never taken opioids and is given a Schedule 2 opioid
- A patient without an initial history and physical examination
- A patient who exhibits physical signs of opioid excess

TABLE SIX

Weak 1st Line Opioids  
(Schedules 3 and 4)

Tramadol\*

Codeine

Hydrocodone

Propoxyphene

Stronger 2nd Line Opioids  
(Schedule 2)

Morphine

Oxycodone

Hydromorphone

Oxymorphone

Methadone

\* Is the weakest opioid, so it is unscheduled.

DISCUSSION

Medical practice is sometimes influenced as much by societal prejudices as by science. It is clear that there are prejudicial societal attitudes towards opioids. Pharmaceutical agents for other major indolent diseases such as diabetes, hypertension, depressives, epileptics, Parkinsonians, schizophrenia, and asthma require a wide range of dosages. Such is the case with opioids. The proverbial mild, moderate, and severe profile is often called the "bell-shaped curve". This curve plainly exists with chronic pain. There

are no scientific reasons, rationally, to an upper limit on opioid dosage. If so, they have, as yet, not been elucidated.

It has been said that there is little evidence that opioids above a certain dosage range increase function. This begs yet another question, borrowed straight from the philosophy of science. Is the absence of evidence equivalent to the evidence of absence?

It is certainly the case that many physicians practicing pain medicine could give numerous examples anecdotally as to patients functioning at a much higher level when the effective dose of opioids was reached for them. Table Eight shows several real life examples. It is not difficult, in practically any pain practice, to come up with examples of physicians, attorneys, business executives, nurses, as well as people in the trades, all with severe chronic pain, who are back to work because their pain is adequately controlled on what many would consider to be high-dose opioids. (Table Eight)

## CONCLUSION

In a bonafide, chronic pain patient there is no dosage or number of opioids that, per se, can be labeled too high or excessive. Excess opioid dosage and prescribing can only be diagnosed by a physical examination that documents the presence of the classic signs of opioid excess including hypotension, bradycardia, and miosis among others. A high intake of opioids may be required to achieve a blood level that will control pain due to any number of metabolic abnormalities including gastrointestinal malabsorption, rapid liver metabolism, blood brain barrier defects, and opioid receptor resistance. Regardless of dosage or the number of opioids prescribed, the goal of opioid therapy is to provide pain control without physical signs of opioid excess and which improves the physical, mental, and social functions of the patient being treated.

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