Pain Management and Practice

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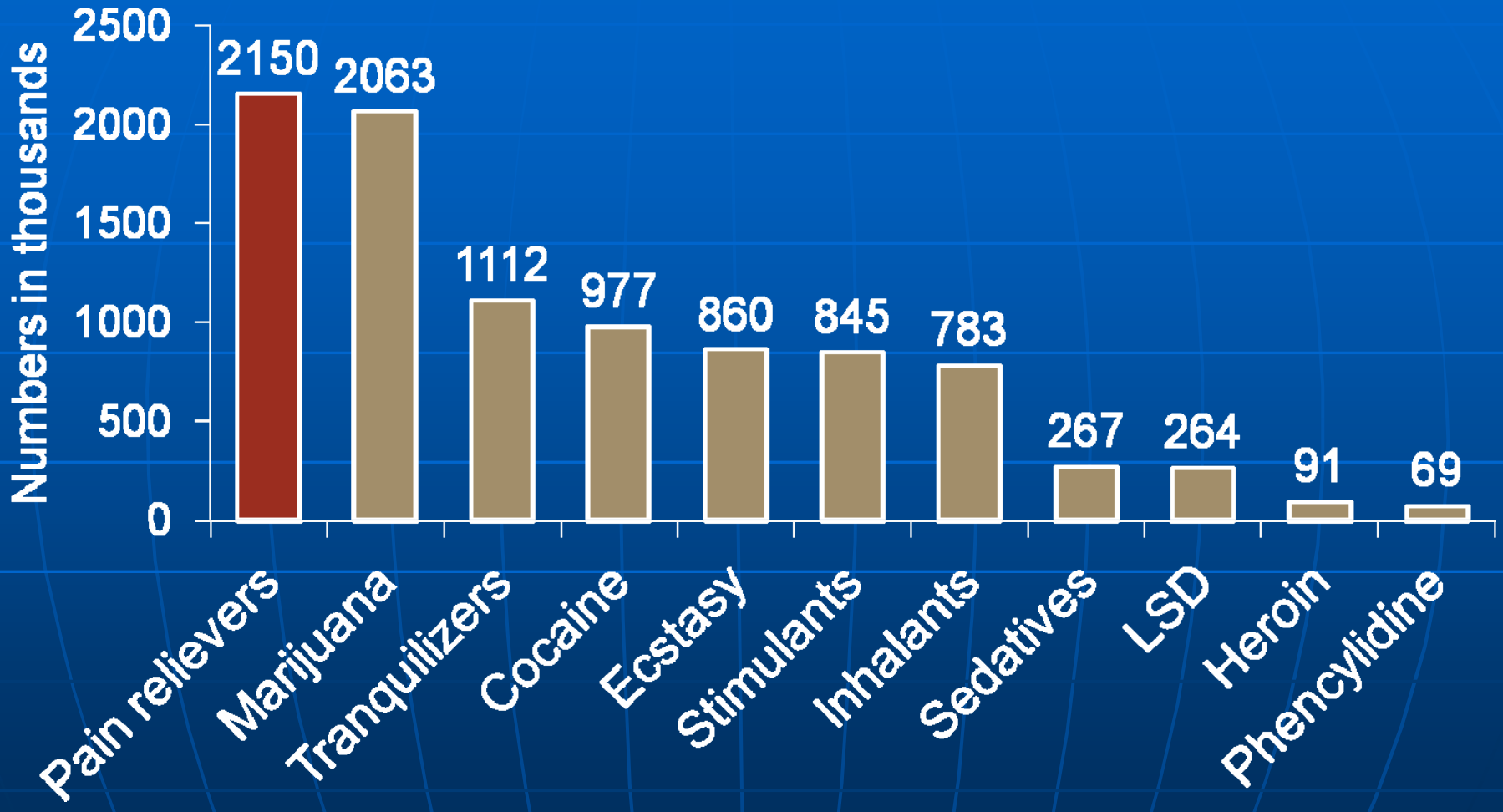
Pain Treatment Today

- Wherever pain is treated, a market can be expected to grow vying for access to controlled substances for misuse
- All pain management in our society goes on against a backdrop of addiction, diversion and misuse
- All stakeholders (practitioners, patients, regulators, insurance companies, pharmaceutical companies) need to develop realistic strategies for the use of pain medicines in a drug abusing world

New* Illicit Drug Use in the US: 2006



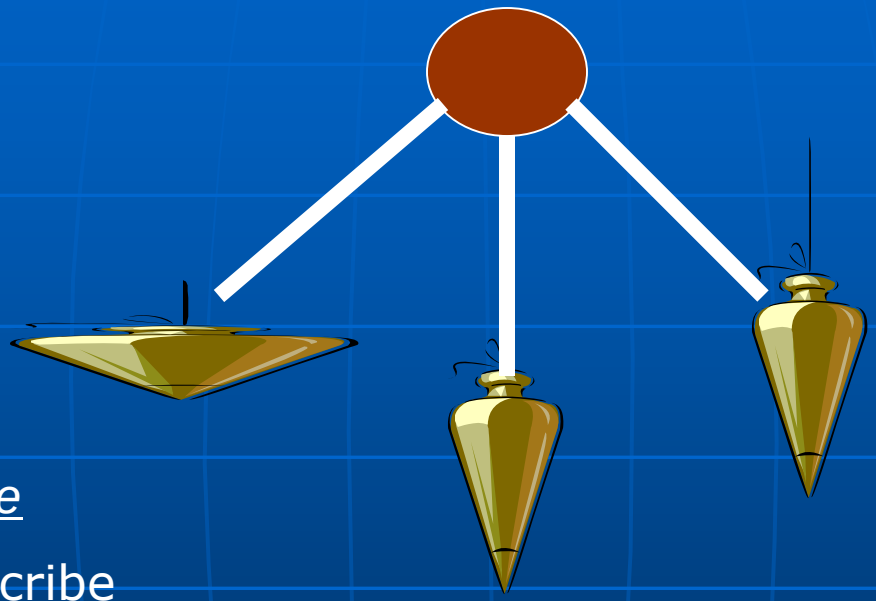
*Past-yr initiates for specific illicit drugs among persons aged ≥12 yrs

SAMHSA. (2007). *Results from the 2006 National Survey on Drug Use and Health: National Findings* (Office of Applied Studies, NSDUH Series: H-32, DHHS Publication No. SMA 07-4293). Rockville, MD

Responsibility of Healthcare Providers

- Acknowledge: Rx drug abuse is real – not isolated or purely media hype
- Evaluate: Conduct medical evaluation + risk hx before starting opioids
- Recognize limitations: Available time, psychiatric expertise, setting, resources, etc.
- Obtain: Consultations as needed
- Employ: Rational pharmacotherapy
- Comply: with state/federal guidelines

The Pendulum Rarely Stops in the Middle



Avoidance

- "Will not prescribe opioids for any reason"
- Driven by fear of regulatory action or being "burned"

Balance

- Rational pharmacology
- Driven by continued prescribing with close monitoring

Widespread Use

- "Less than 1% will ever become addicted"
- Prescribing without recognition of dangers

Embracing Common Definitions

- Tolerance
- Physical Dependence
- Pseudoaddiction
- Substance Abuse
- Addiction

Identifying Addiction – The 4 C's

- **C**ontinued use of drug despite harm
- Loss of **C**ontrol re: taking the drug
- **C**ompulsive use of the drug
- **C**ravings for the drug

Note: Tolerance and physical dependence do not play a defining role

Protecting Medical Practice

document, document, document

Documentation

- Poor documentation is a stumbling block to good pain management:
  - Review of 520 randomly selected visits at an outpatient oncology practice:
    - quantitative assessment of pain scores was virtually absent (<1%)
    - qualitative assessment of pain occurred in only 60% of cases (Rhodes, et al, 2001)
  - Review of medical records of 111 randomly selected patients who underwent urine toxicology screens in a cancer center:
    - documentation was infrequent: 37.8% of physicians failed to list a reason for the test
    - 89% of the charts did not include the results of the test (Passik et al, 2000)

Screening Tools

A Rational First Step for Safety

Assessment of Addiction Risk

- Measures for Screening for Addiction Risk
  - STAR/SISAP
  - CAGE AID
  - Opioid Risk Tool (Emerging Solutions in Pain)
  - SOAPP (see painedu.org)
- Psychiatric Interview Assessment of Risk
  - Chemical
  - Psychiatric
  - Social/Familial
  - Genetic
  - Spiritual

Screening Instruments

- Several clinical tools are available that estimate risk of noncompliant opioid use[1,2,3]

- The results determine how closely a patient should be monitored during the course of opioid therapy[3]
  - *Scores implying a high risk of abuse are not reasons to deny pain relief*[3]

[1]Webster & Webster. *Pain Med.* 2005;6:432.
[2]Coambs et al. *Pain Res Manage.* 1996;1:155.
[3]Butler et al. *Pain.* 2004;112:65.

Opioid Risk Tool (ORT)

Mark each box that applies:		Female	Male
1.	Family history of substance abuse		
	Alcohol	☐ 1	☐ 3
	Illegal drugs	☐ 2	☐ 3
	Prescription drugs	☐ 4	☐ 4
2.	Personal history of substance abuse		
	Alcohol	☐ 3	☐ 3
	Illegal drugs	☐ 4	☐ 4
	Prescription drugs	☐ 5	☐ 5
3.	Age (mark box if between 16-45 years)	☐ 1	☐ 1
4.	History of preadolescent sexual abuse	☐ 3	☐ 0
5.	Psychological disease		
	ADO, OCD, bipolar, schizophrenia	☐ 2	☐ 2
	Depression	☐ 1	☐ 1
	Scoring totals:	_____	_____

Administration

- On initial visit
- Prior to opioid therapy

Scoring

- 0-3: low risk (6%)
- 4-7: moderate risk (28%)
- ≥ 8: high risk (> 90%)

Webster & Webster. *Pain Med.* 2005;6:432.

Screening Instrument for Substance Abuse Potential (SISAP)

Question	Caution
1) How many alcoholic drinks/day? 2) How many alcoholic drinks/week? 3) Use of marijuana/hashish in last year?	Men: ≥ 5 drinks/day or ≥ 17/wk Women: ≥ 4 drinks/day or ≥ 13/wk
4) Have you ever smoked cigarettes? 5) What is your age?	Admission of recent use Persons who are younger than 40 years and smoke

Coambs et al. *Pain Res Manage.* 1996;1:155.

Screener and Opioid Assessment for Patients in Pain (SOAPP)

- 14-item, self-administered form, capturing the primary determinants of aberrant drug-related behavior
  - Validated over a 6-month period in 175 chronic pain patients
  - Adequate sensitivity and selectivity
  - May not be representative of all patient groups
- A score of ≥ 7 identifies 91% of patients who are high risk

Butler et al. *Pain.* 2004;112:65.

Ongoing Assessment Tool

Or: What Elements Should Be Documented on a Consistent Basis?

Documentation: The 4 A's

- Analgesia (pain relief)
- Activities of Daily Living (psychosocial functioning)
- Adverse effects (side effects)
- Aberrant drug taking (addiction related outcomes)

Passik and Weinreb, 1998; Passik, Kirsh et al, 2004; 2005

Analgesia

If zero indicates "no pain" and ten indicates "pain as bad as it can be," on a scale of 0 to 10, what is your level of pain for the following questions?

1. What was your pain level on average during the past week? (Please circle the appropriate number)

No Pain 0 1 2 3 4 5 6 7 8 9 10 **Pain as bad as it can be**

2. What was your pain level at its worst during the past week?

No Pain 0 1 2 3 4 5 6 7 8 9 10 **Pain as bad as it can be**

3. What percentage of your pain has been relieved during the past week? (Write in a percentage between 0% and 100%.) _____

4. Is the amount of pain relief you are now obtaining from your current pain relievers enough to make a real difference in your life?

❑ Yes ❑ No

5. **Query to clinician**: Is the patient's pain relief clinically significant?

❑ Yes ❑ No ❑ Unsure

Activities of Daily Living

Please indicate whether the patient's functioning with the current pain reliever(s) is Better, the Same, or Worse since the patient's last assessment with the PADT.* (Please check the box for Better, Same, or Worse for each item below.)

	Better	Same	Worse
1. Physical functioning	❑	❑	❑
2. Family relationships	❑	❑	❑
3. Social relationships	❑	❑	❑
4. Mood	❑	❑	❑
5. Sleep patterns	❑	❑	❑
6. Overall functioning	❑	❑	❑

* If the patient is receiving his or her first PADT assessment, the clinician should compare the patient's functional status with other reports from the last office visit.

Adverse Events

1. Is patient experiencing any side effects from current pain relievers? ❑ Yes ❑ No

Ask patient about potential side effects:

	None	Mild	Moderate	Severe
a. Nausea	❑	❑	❑	❑
b. Vomiting	❑	❑	❑	❑
c. Constipation	❑	❑	❑	❑
d. Itching	❑	❑	❑	❑
e. Mental cloudiness	❑	❑	❑	❑
f. Sweating	❑	❑	❑	❑
g. Fatigue	❑	❑	❑	❑
h. Drowsiness	❑	❑	❑	❑
i. Other _____		❑	❑	❑
j. Other _____		❑	❑	❑

2. Patient's overall severity of side effects?
❑ None ❑ Mild ❑ Moderate ❑ Severe

Potential Aberrant Drug-Related Behavior

*Please **check** any of the following items that you discovered during your interactions with the patient.*
Please note that some of these are directly observable (eg, appears intoxicated), while others may require more active listening and/or probing. Use the "Assessment" section below to note additional details.

- ❑ Purposeful over-sedation
- ❑ Negative mood change
- ❑ Appears intoxicated
- ❑ Increasingly unkempt or impaired
- ❑ Involvement in car or other accident
- ❑ Requests frequent early renewals
- ❑ Increased dose without authorization
- ❑ Reports lost or stolen prescriptions
- ❑ Attempts to obtain prescriptions from other doctors
- ❑ Changes route of administration
- ❑ Uses pain medication in response to situational stressor
- ❑ Insists on certain medications by name
- ❑ Contact with street drug culture
- ❑ Abusing alcohol or illicit drugs
- ❑ Hoarding (ie, stockpiling) of medication
- ❑ Arrested by police
- ❑ Victim of abuse

Other: _____

_____

_____

Classifying Assessment Findings

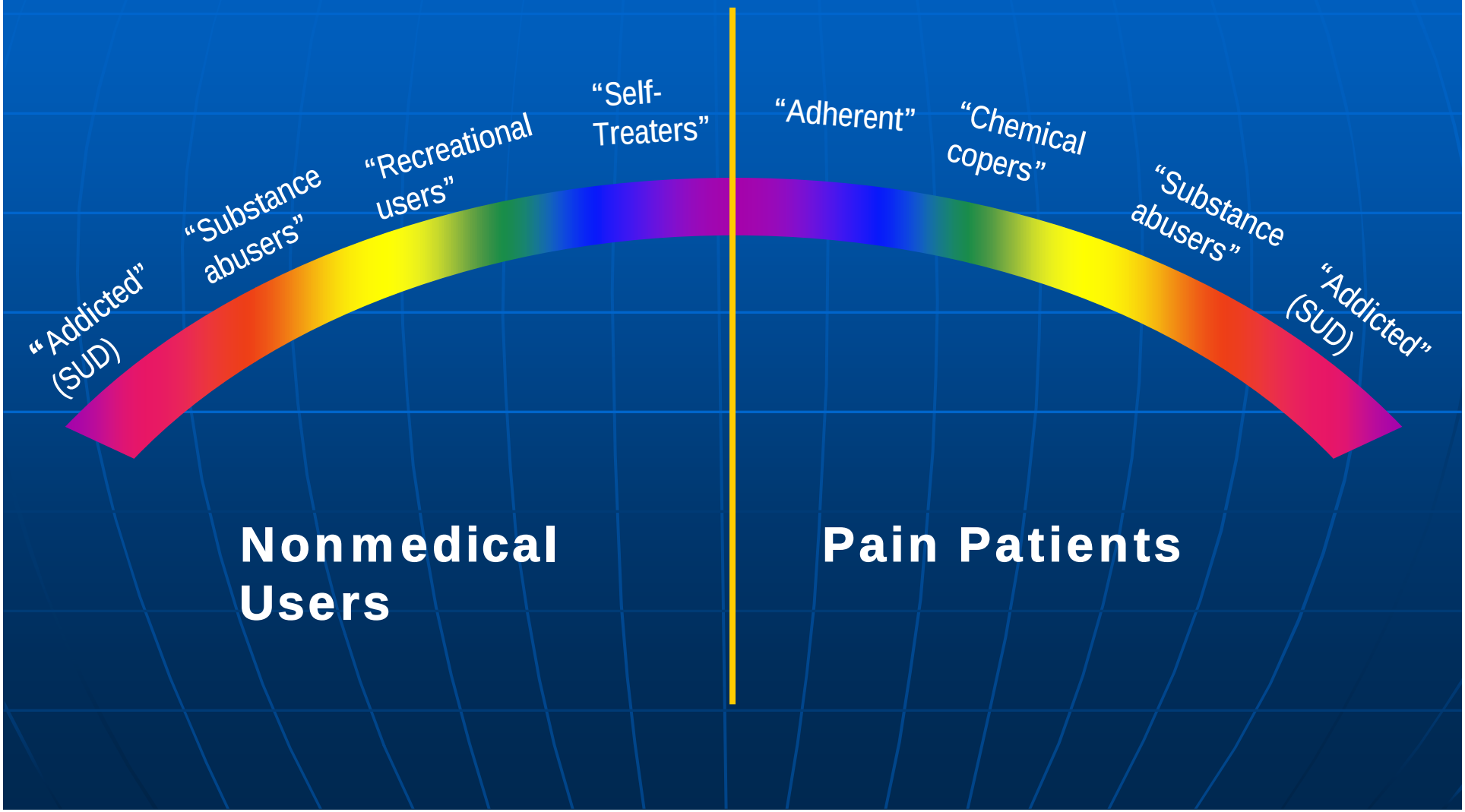
Or: Does Every Problem Indicate Addiction?

Addiction or Something Else?

- Most research on addiction has focused on:
  - Prediction,
  - Assessment,
  - Treatment of substance use disorders
- A vast grey area exists between extremes of compliance (beneficial opioid therapy) and addiction (harmful opioid therapy)
- Patients in this grey area are
  - Not likely to display aberrant behaviors that rise to the level of compulsivity or loss of control
  - Not likely to be driven by cravings in a fashion that would make a clinician concerned about addiction.

Bottlender & Soyka, 2005; Comfort et al, 2003; Dekel et al, 2004; Schuckit et al, 2005

Population of Rx Opioid Users Is Heterogeneous



Differential Diagnosis of Aberrant Drug-Taking Attitudes and Behavior

- Addiction
- Pseudoaddiction (inadequate analgesia)
- Chemical Copers
- Other psychiatric diagnosis
  - Encephalopathy
  - Borderline personality disorder
  - Depression
  - Anxiety
- Criminal Intent

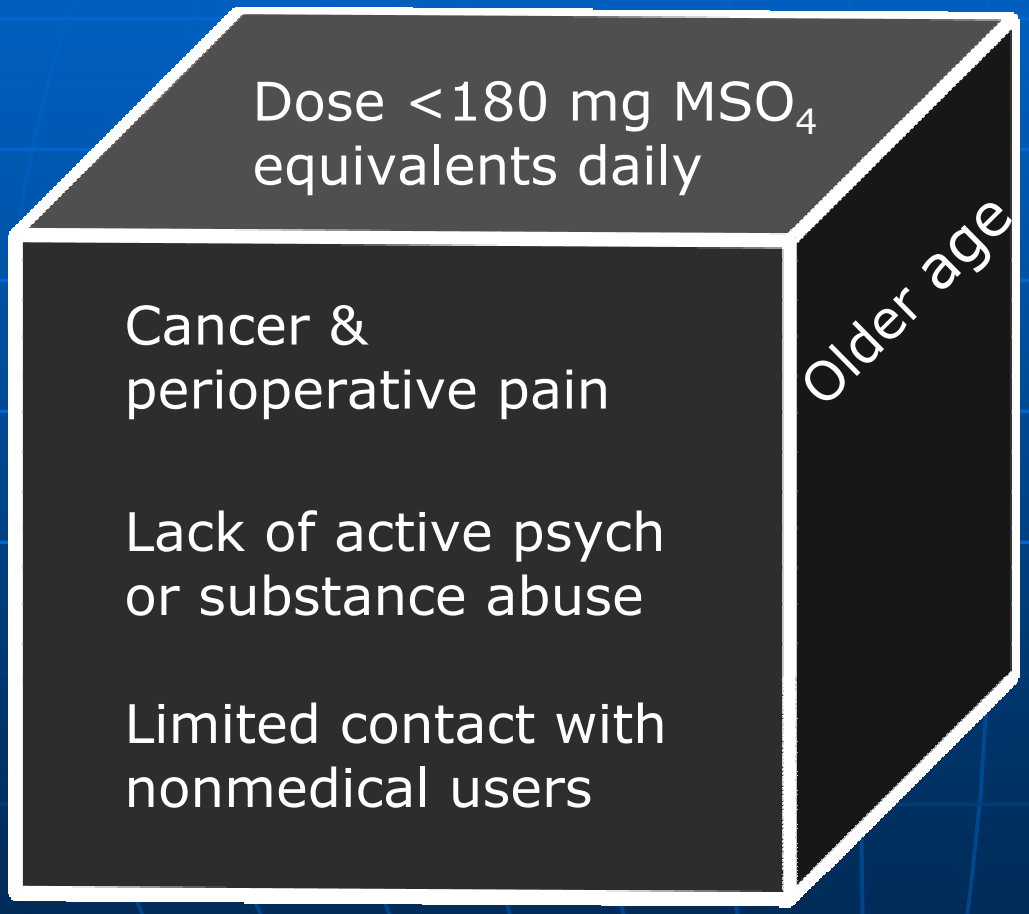
(Passik & Portenoy 1996)

Management Issues Past Screening

Management of Risk Is a "Package Deal"

- Screening & risk stratification
- Use of PMP data
- Compliance monitoring
  - Urine screening
  - Pill/patch counts
- Education regarding drug storage & sharing
- Psychotherapy & highly "structured" approaches
- Abuse-deterrent formulations

Opioid Prescribing: In & Out of the Box



Pain syndrome in which opioid use controversial

Dose >180 mg MSO_4 equivalents daily

Active psych disorder or substance abuse

Contact with nonmedical users

Younger age

Methadone Focus

- History:
  - Discovered 1938 Hoechst-Am-Main in Germany
    - Question if developed as anti-spasm or analgesic medication
    - Patent 1942
  - Developed after WWII during occupation
    - Eli-Lilly produced Dolophine®
      - "Dolor" for pain, "fin" for end
    - Name derivation:
      - 6-Dimethylamino-4, 4-diphenyl-3-heptanone

Original German patent application

DEUTSCHES REICH

AUSGEGEBEN AM 25. SEPTEMBER 1941

REICHSPATENTAMT

PATENTSCHRIFT

№ 711069

KLASSE **12p** GRUPPE **1 01**

Hoechst Werke

Dr. Max Bockmühl und Dr. Gustav Ehrhart in Frankfurt, Main-Höchst
sind als Erfinder genannt worden.

I. G. Farbenindustrie Akt.-Ges. in Frankfurt, Main

Verfahren zur Darstellung von basischen Estern

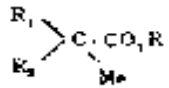
Patentiert im Deutschen Reich vom 15. September 1938 ab

Patenterteilung bekanntgemacht am 21. August 1941

Gemäß § 2 Abs. 1 der Verordnung vom 20. Juli 1936 ist die Erklärung abgegeben worden, daß sich der Schutz auf das Protektorat Böhmen und Mähren erstrecken soll

Gegenstand des Patents ist ein Verfahren zur Darstellung von basischen Estern durch Umsetzung von Diarylessigsäurenitrilen mit basisch substituierten Halogenalkylen und Überführung der erhaltenen tertiären Nitrile in die zugehörigen Ester.

Es wurde nun gefunden, daß man zu diesen basischen Estern auch dadurch gelangen kann, daß man Metallverbindungen der allgemeinen Formel



worin R_1 und R_2 Arylreste, die auch unter sich gebunden sein können, Me ein Alkalimetall und R einen Alkyl- oder Aralkylrest bedeuten, mit basisch substituierten Halogenalkylen, wie z. B. Piperidinoäthylchlorid, Diäthylaminoäthylchlorid, Morpholinoäthylchlorid u. dgl., umsetzt. Man stellt zweckmäßig zunächst die Natriumverbindung des Diarylessigsäureesters her, z. B. durch Einwirkung von Diäthylaminoisopropylnatrium auf den Diarylessigsäureester, wobei gleichzeitig Diäthylaminoisopropylacetat zurückgebildet wird. Auf die Natriumverbindung des Diarylessigsäureesters läßt man dann ein basisch substituiertes Halogenalkyl einwirken. Man kann aber auch z. B. die Kaliumverbindung des Phenyl-p-tolylessigsäureäthylesters durch Einwirkung von Kaliumalkoholat auf Phenyl-p-tolylessigsäureäthylester darstellen und dann das basisch substituierte Halogenalkyl einwirken lassen. Die neuen Verbindungen sind hervorragende Spasmolytica und Analgetica.

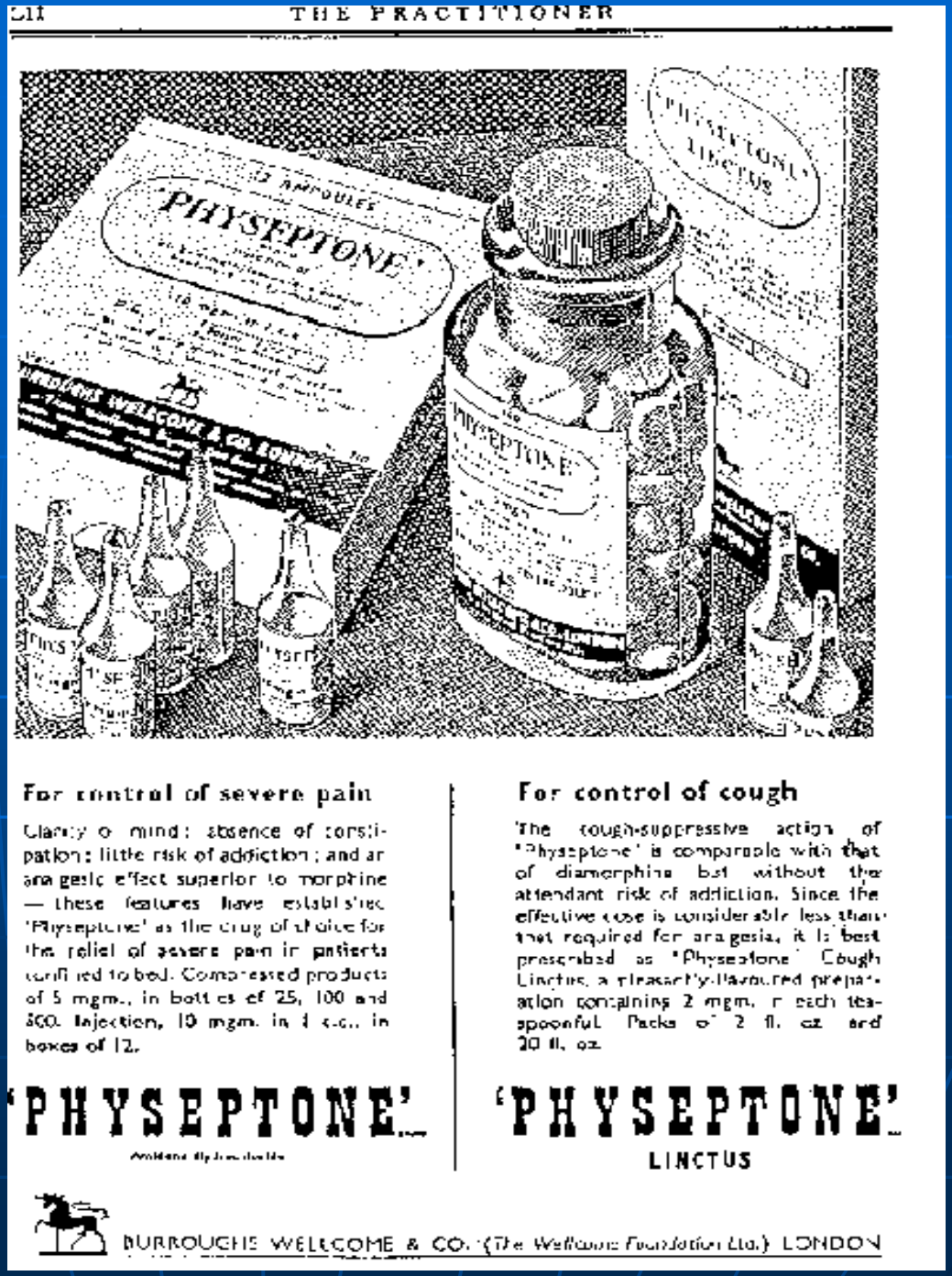
Beispiele

1. Zu 4,6 g Natrium, das mit 50 ccm Benzol überschichtet ist, läßt man unter Rühren eine Mischung von 9,7 g Diäthylaminonitril und 11,3 g Chlorbenzol einfließen. Die Temperatur wird durch Kühlen zweckmäßig

- Trade name "Physeptone" for methadone branded under Wellcome company in United Kingdom

- Rec'd for pain and cough, even studied in infants (studies stopped due to respiratory depression in babies)

- Believed to have no addiction risk



Methadone

- Pharmacokinetics:
  - Extensive peripheral tissue distribution
  - Racine mixture: RS-methadone
    - R enantiomer opioid activity
    - S enantiomer, NMDA antagonist (weak to moderate), potent inhibitor of 5-hydroxytryptamine and norepinephrine uptake
  - Half life = 17-128 hours, average 36 hours
    - Analgesic half-life is much less

Methadone

- Conversion:
  - "No universally safe or effective conversion ration or method currently exists, and because of the large variability in opioid ratios, it is not possible to derive a simple conversion method for rotating to or from methadone" (Weschules, 2008)
- Not good for immediate release usage
- Cheap, effective analgesic
  - Must know drug well to use it!

Opioid Preference and Cost

Number of Instances of Abuse of Specific Drugs Preferred by Addicts, Where the Drug was Obtained, and Cost per Opioid.

Opioid:*	# of Instances of Abuse (of n = 109):	Purchased from street dealer?**	Amount of $ per mg/mcg (mean/range):
OxyContin	65 (60%)	62 (95%)	$1.01/mg (.50-1.50/mg)
Lortab	40 (37%)	37 (93 %)	$0.82/mg (.50-1.20/mg)
Percocet	15 (14%)	15 (100%)	$1.11/mg (.20-1.60/mg)
Methadone	7 (6%)	6 (86%)	$1.05/mg (.80-1.50/mg)
Morphine	4 (4%)	3 (75%)	$0.73/mg (.25-1.50/mg)
Lorcet	3 (3%)	2 (67%)	$0.77/mg (.60-.90/mg)
Duragesic	3 (3%)	2 (67%)	$0.90/mcg (.80-1.00/mg)
Dilaudid	2 (2%)	2 (100%)	$10.00/mg (7.50-12.50/mg)
Vicodin	1 (1%)	1 (%)	$0.06/mg
Tylenol #3	1 (1%)	1 (%)	$0.03/mg

* Drug listed as reported by patients (trade names reported when they were specified)
** At least once

Passik, Hays, Eisner, Kirsh. J Pain Pall Care Pharmacotherapy, 2006; 20(2):5-13.

Future Horizons

Can Pain Management Be Made ‘Safer’?

Abuse Deterrent Formulation: Questions

- Requirements for "reduced abuse liability" label claim
  - Bioequivalence to existing product?
  - Short-term evaluation of therapeutic efficacy?
  - Long-term studies in susceptible populations?
  - Acceptable risk?
- How much does the barrier approach deter the determined?
- How much do agonist/antagonist compounds retain efficacy & pose serious adversity?
- Will it be possible to retain titratable or rapid onset properties required for some analgesic needs?

Conclusion

- Pain management is under intense scrutiny
- However, chronic pain is still under-treated in this country
- We must use standards of good practice
  - documentation, rational prescribing, opioid agreements, urine screens, etc. to protect ourselves and our patients
  - A growing number of screening tools are becoming available, but more work needs to be done
  - We must not be afraid to ask the difficult questions of our patients about their lives, loved ones, and social circles.