



Responsible Use of Opioids: Principles, Practices, and Paradigms

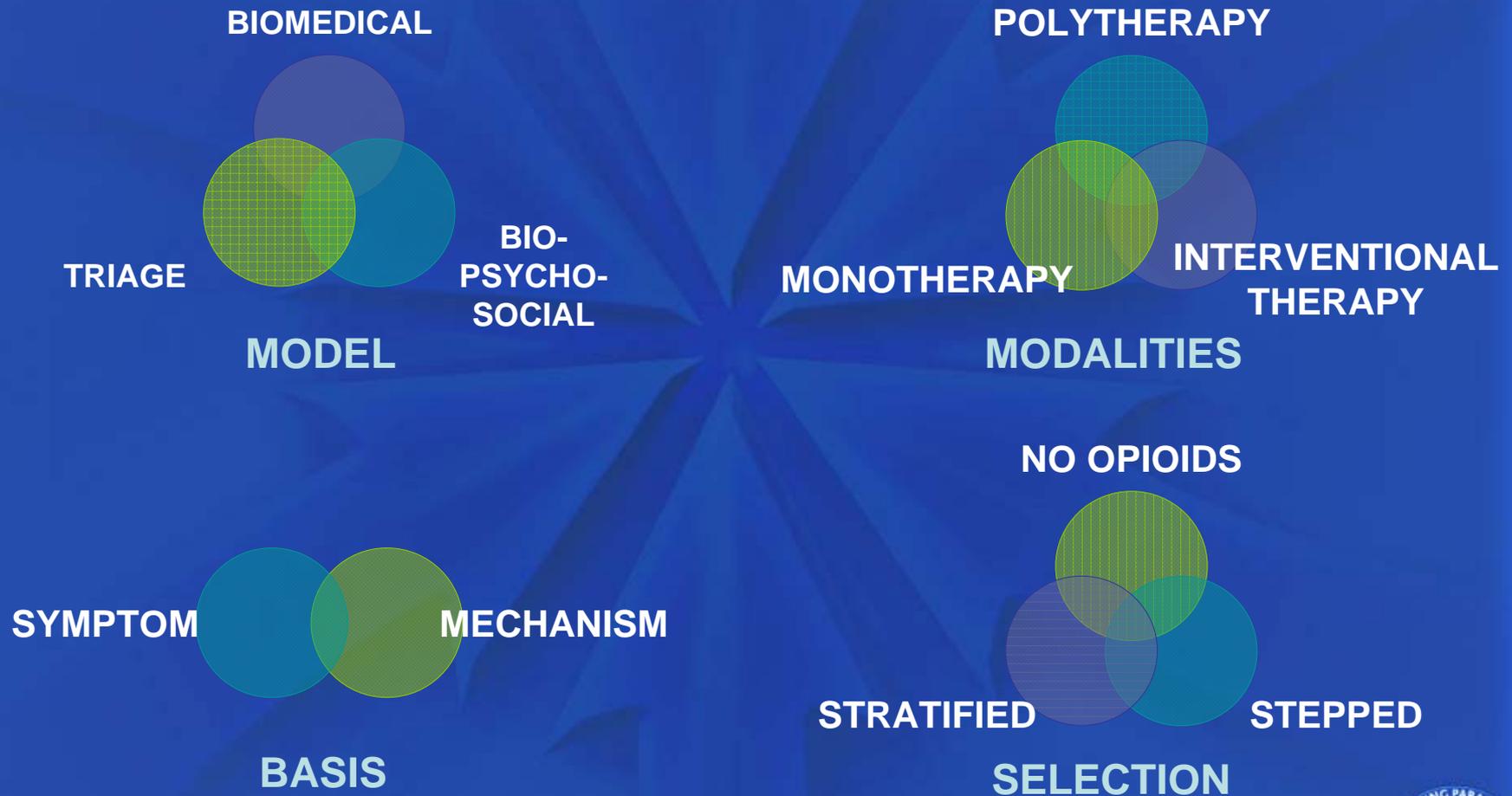
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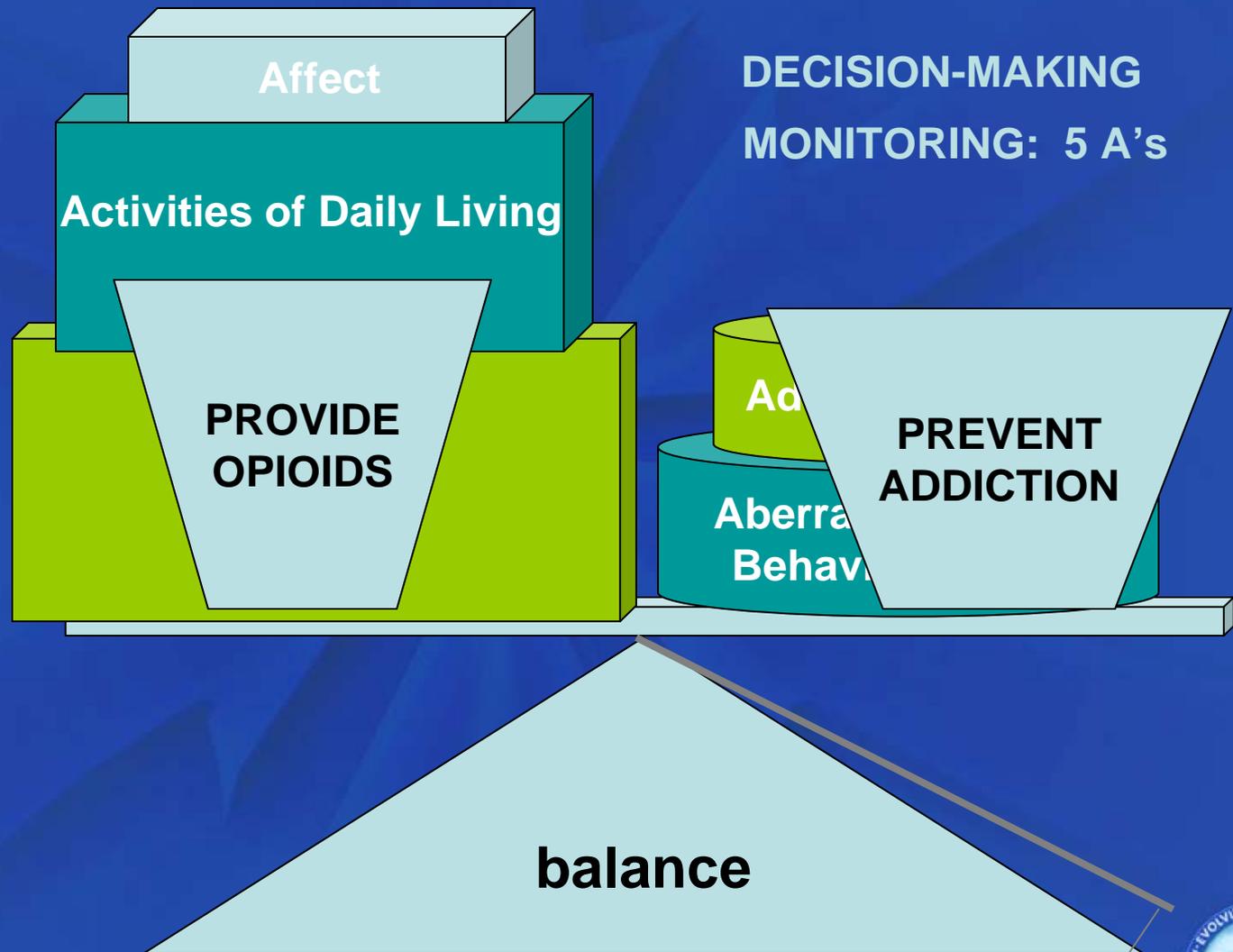
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Opioid therapy in pain management: an epitome of evolving paradigms



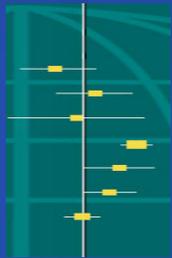
Balanced opioid therapy is possible



Gourlay. Pain Medicine 2005;6(2):107-112



Consider using these approaches to optimize opioid therapy



Evidence-based Approach:

Principles of Opioid Use



Universal Approach:

Risk Management

Frameworks for managing opioid therapy



Opioids are broad-spectrum



**Show
efficacy**

Neuropathic pain

Nociceptive pain

- **Musculoskeletal**

- **Osteoarthritis**

Mixed pain

Fibromyalgia

**Inconsistent
results**

Back pain

**Lack of
evidence**

Central pain



All tested opioids shown to be efficacious

- **Analgesia outcomes: consistent results**
- **Functional capacity: inconsistent results**
 - Only 3 of 8 trials showed improved function
 - Only 1 of 3 trials showed improved QoL
- **Global improvement: insufficient evidence**

Martell 2007; Chou 2006; Moore 2005; Rowbotham 2003; Bouhassira 2002; Moulin 1996; Kalso 2004



Opioids are not the panacea for all pain

- **30%-60% mean decrease in pain**
- **42%-44% achieve $\geq 50\%$ pain reduction**
- **36%-63% respond on global assessment**

Martell 2007; Chou 2006; Moore 2005; Rowbotham 2003; Bouhassira 2002; Moulin 1996



Lack of evidence that one agent is better

- **Insufficient evidence to support that one long-acting opioid is better than another[†]**
- **Insufficient evidence to support that long-acting opioids are better than short-acting opioids (at equivalent doses)[†]**
- **No RCTs have evaluated efficacy and safety of switching opioids[‡]**

† Chou R, Carson S. Drug class review on long-acting opioid analgesics. 2008.

<http://www.ohsu.edu/drugeffectiveness/reports/final.cfm>

‡ Quigley, C. (2008). Cochrane Database of Systematic Reviews 1



Only strong opioids shown to be better than nonopioids, but evidence is limited

- **Opioids ~ NSAIDs (pain, function)**
 - Strong opioid > NSAIDs (pain only)
 - Weak opioids = NSAIDs (pain, function)
- **Opioids ~ TCADs (pain, function)**
 - Strong opioid > TCADs (pain only)
 - Weak opioids = TCADs (pain, function)
- **Strong Opioid = AED** (1 RCT)
- **Strong Opioid + AED > Monotherapy** (1 RCT)

Weak opioids: tramadol, propoxyphene, codeine

Strong opioids: morphine, oxycodone

Furlan, et al. CMAJ 2006;174(11):1589-94.

Gilron, et al. NEJM 2005; 352(13):1324-34



Study patients received relatively low doses of strong opioids for short periods

DRUG	MEAN mg/d (# RCTs)	RANGE mg/d (# RCTs)	DURATION wk	REF/ Dx
Morphine LA	91-120 (3)	15-300 (8)	1-6	Furlan, 2006
Oxycodone CR	37-45 (3)	20-120 (5)	2-6	CNCP
Methadone	15	---	6	
Opioids (MOR equiv)	73 (6)	30-232 (6)	1-16	Martell, 2007 CLBP



Adverse events and withdrawals due to adverse events are common

Systematic review: WHO Step 3 Opioids in CNCP

- **15 PCTs (N=1145); 11 PCTs (N=1025) oral**
- **6 of 15 PCTs had open-label follow-up**
- **80%** of patients experienced 1 or more AEs
- **Only 44%** of 388 patients still on opioids after 7-24 mo

Systematic review: All oral opioids in CNCP

- **34 RCTs (N=5546), 16 PCTs (N=2293), < 8 wk**
- **51%** of patients (95% CI: 49-53) experienced any AE
- **22%** (95% CI: 21-23) withdrew due to AE
- **6.5%** (95% CI: 5.6-7.4) withdrew due to inefficacy

Kalso, et al. Pain. 2004 Dec;112(3):372-80

Moore and McQuay. Arthritis Res Ther. 2005; 7(5): R1046–R1051



Opioid-induced Hyperalgesia

- **Mechanism is unclear**
 - Hormone regulation
 - M3G antagonism of morphine
- **Pain improves when opioid is decreased**
- **Is opioid analgesia really dose-related?**
- **Should there be a maximal dosage limit?**
- **Dilemma of high dosage requirements**
 - Tolerance
 - Opioid-insensitive pain
 - Aberrant drug-use behavior or addiction
 - Opioid-induced hyperalgesia



Hypogonadism: not just a laboratory phenomenon

- **Decreases in sex hormones, gonadotropins, and GnRH**
- **Oral, transdermal, or intrathecal**
- **Sexual dysfunction, fatigue, depression, weakness, QoL**
- **High prevalence rates reported (~70%)**

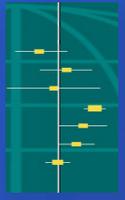
Smith 2006; Daniell 2006; Rajagopal 2004; Finch 2000; Roberts 2002; Daniell 2006a; Daniell 2006b



ADUB and addiction definitions vary, inadequately measure addiction diagnosis

Ref	N	Measure	Results
Mahowald, 2005	230 (VA)	Abuse behaviors	5%
Adams, 2006	11,352	Abuse Index	2.5% NSAIDs 2.7% Tramadol 4.9% Hydrocodone
Ives, 2006	196	Opioid Misuse	32%
Martell, 2007	634 (5 CO/CS)	Aberrant medication-use behaviors	5%-24%





Develop a framework for consistent principles and rational decision-making: The Evidence-based Approach

Principles of Opioid Therapy

Supporting Evidence / Rationale

Establish failure of nonopioid therapies

At least similar efficacy, lower risk than opioids overall; establish responsible use of nonopioid drugs

Set realistic expectations

Most patients achieve only partial relief

Set limits and goals; establish criteria for success and failure

Individuals vary in response to opioids; individualize therapy

Taper and discontinue opioids if treatment goals are not met

Many patients do not respond to or do not tolerate opioids





Why use a Universal Approach? ADUBs create diagnostic problems

Aberrant Drug-taking Behaviors

Probably more predictive of addiction

- Selling prescription drugs
- Prescription forgery
- Stealing or borrowing another patient's drugs
- Injecting oral formulation
- Obtaining prescription drugs from non-medical sources
- Concurrent abuse of related illicit drugs
- Multiple unsanctioned dose escalations
- Recurrent prescription losses

Probably less predictive of addiction

- Aggressive complaining about need for higher doses
- Drug hoarding during periods of reduced symptoms
- Requesting specific drugs
- Acquisition of similar drugs from other medical sources
- Unsanctioned dose escalation 1 – 2 times
- Unapproved use of the drug to treat another symptom
- Reporting psychic effects not intended by the clinician

Passik and Portenoy, 1998

Passik, Kirsh, Portenoy, 2002



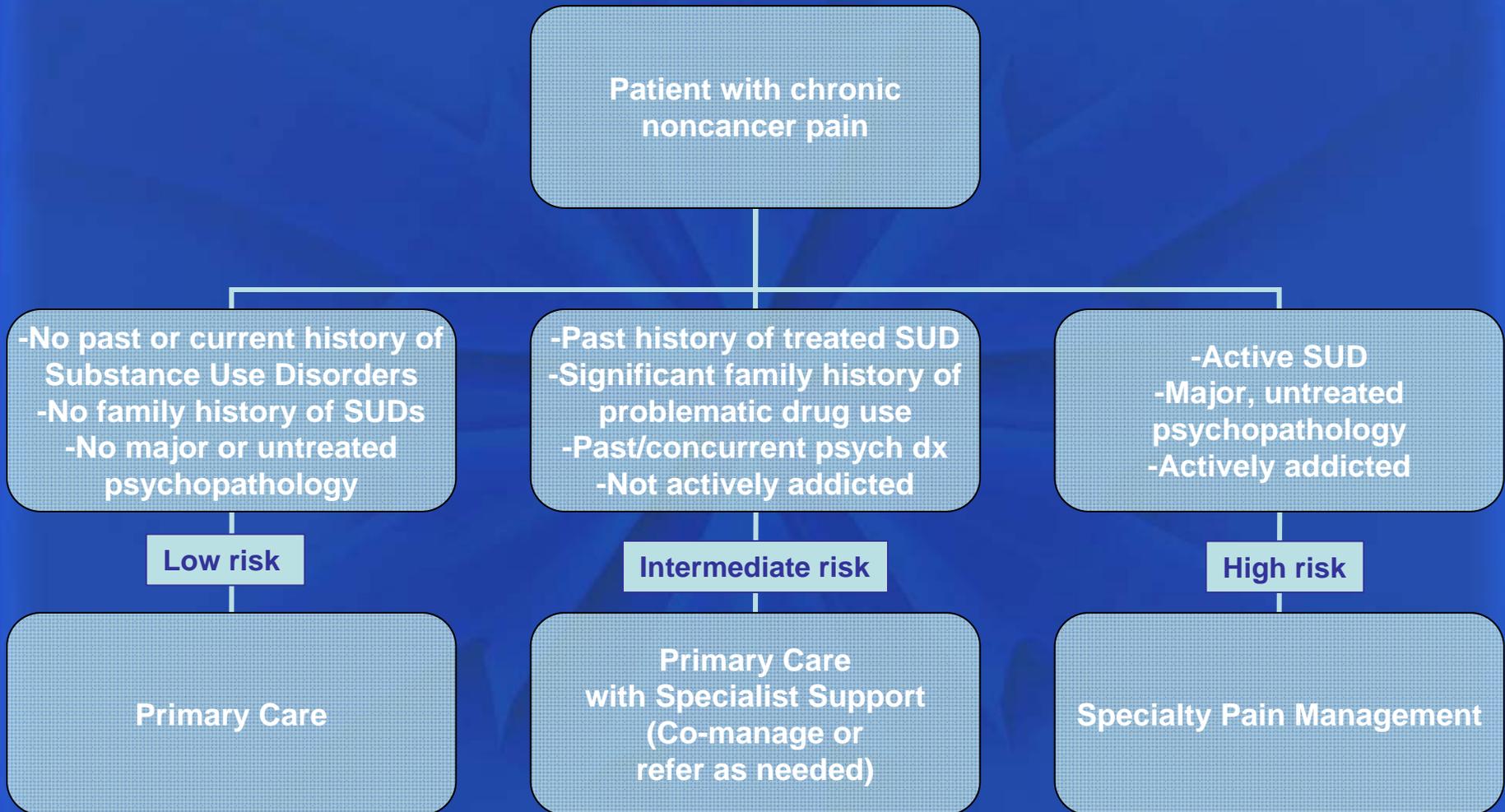
Use a structured strategy to manage opioid use

- C** Compliance is monitored and aberrant behaviors are addressed
- O** Often assess pain intensity and functional status
- M** Medical Records are accurate, complete, and accessible
- P** Plan of treatment has objectives and goals to gauge success
- L** Legitimate diagnosis of a chronic painful condition exists
- I** Informed consent and/or treatment agreement exists
- A** Addiction risk assessment is ongoing
- N** Nonaddictive medications have proven inadequate or unacceptable
- C** Consultation(s) obtained p.r.n.; other health concerns addressed
- E** Evaluation (history and physical) is adequately thorough

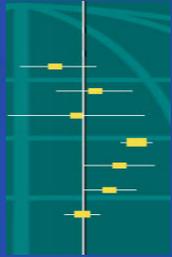
Modified from Murphy. Pain Medicine
2005;6(4):329-330



Consider triaging according to risk



Conclusion



**Evidence-based
Approach:**

**Assess benefits and risks
Use opioids selectively
Individualize therapy**



**Universal
Approach:**

**Use a structured program
Triage by risk**
