A Framework for Successful Intrathecal Pain Management

New Insights from the 2017 Polyanalgesic Consensus Conference (PACC) Guidelines

March 18, 2017 - Loews Sapphire Falls Resort, Orlando, FL - Grand Caribbean Ballroom 6

An official independent commercially supported satellite symposium held in conjunction with the American Academy of Pain Medicine's 33rd Annual Meeting and Pre-meeting Activities.

CME Outfitters

Supported by an educational grant from Jazz Pharmaceuticals, Inc.

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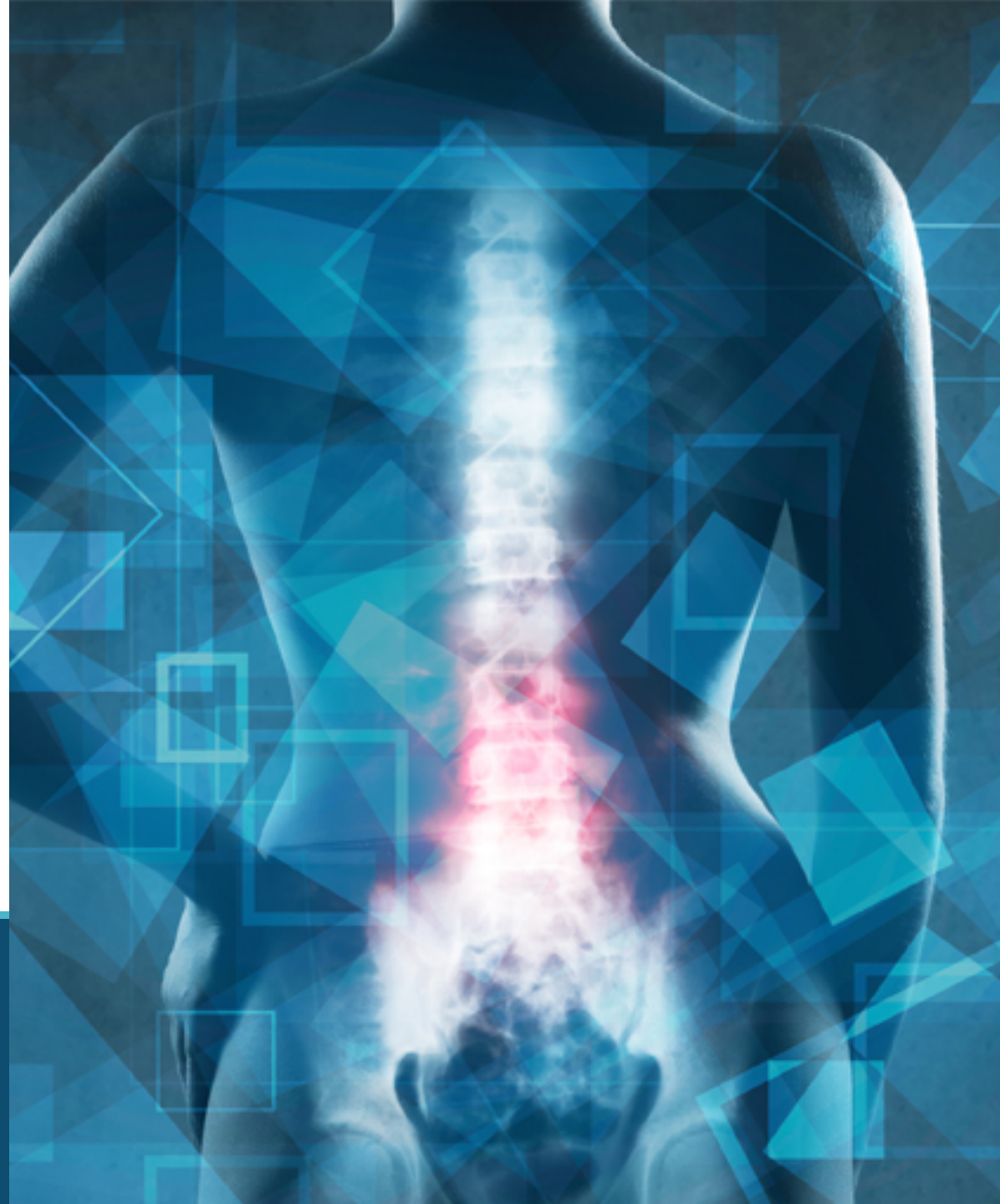

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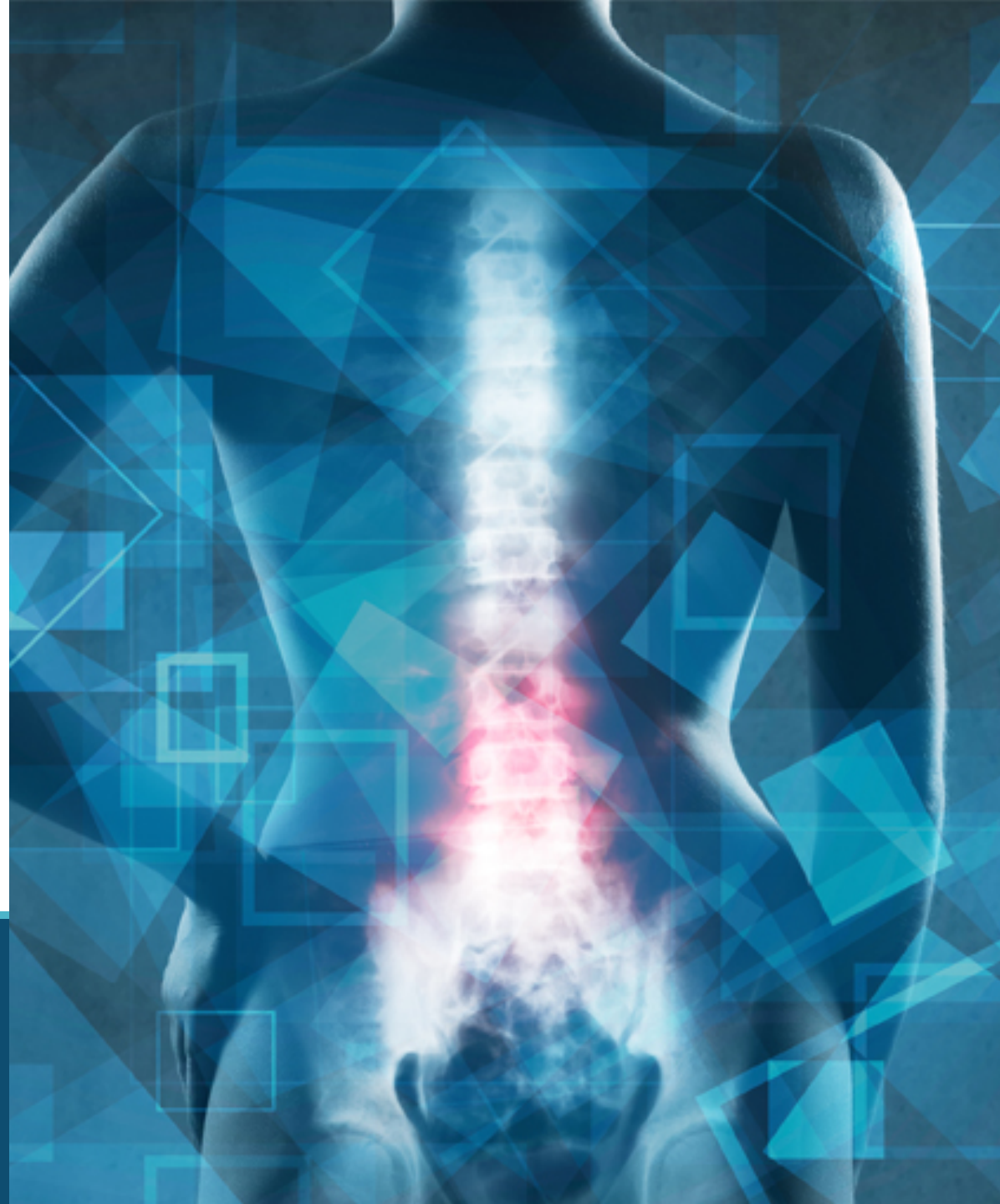

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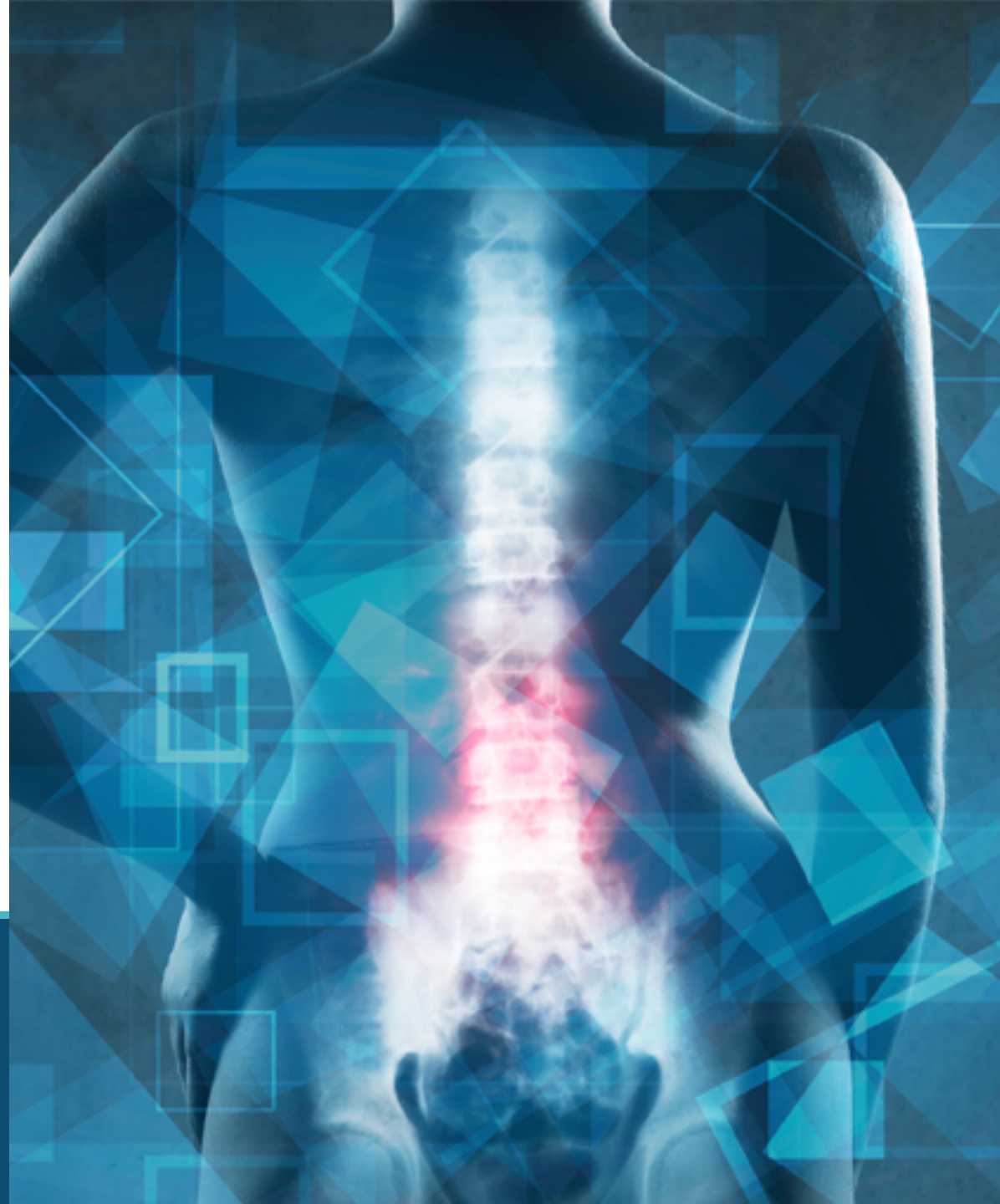
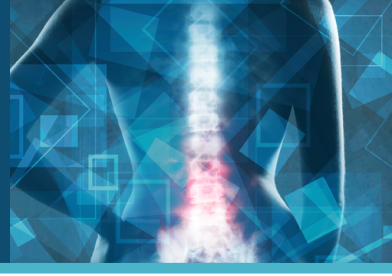


Agenda



Introductions

What's New in the 2017 PACC Guidelines? Translating Recommendations and Best Practices to Clinical Practice

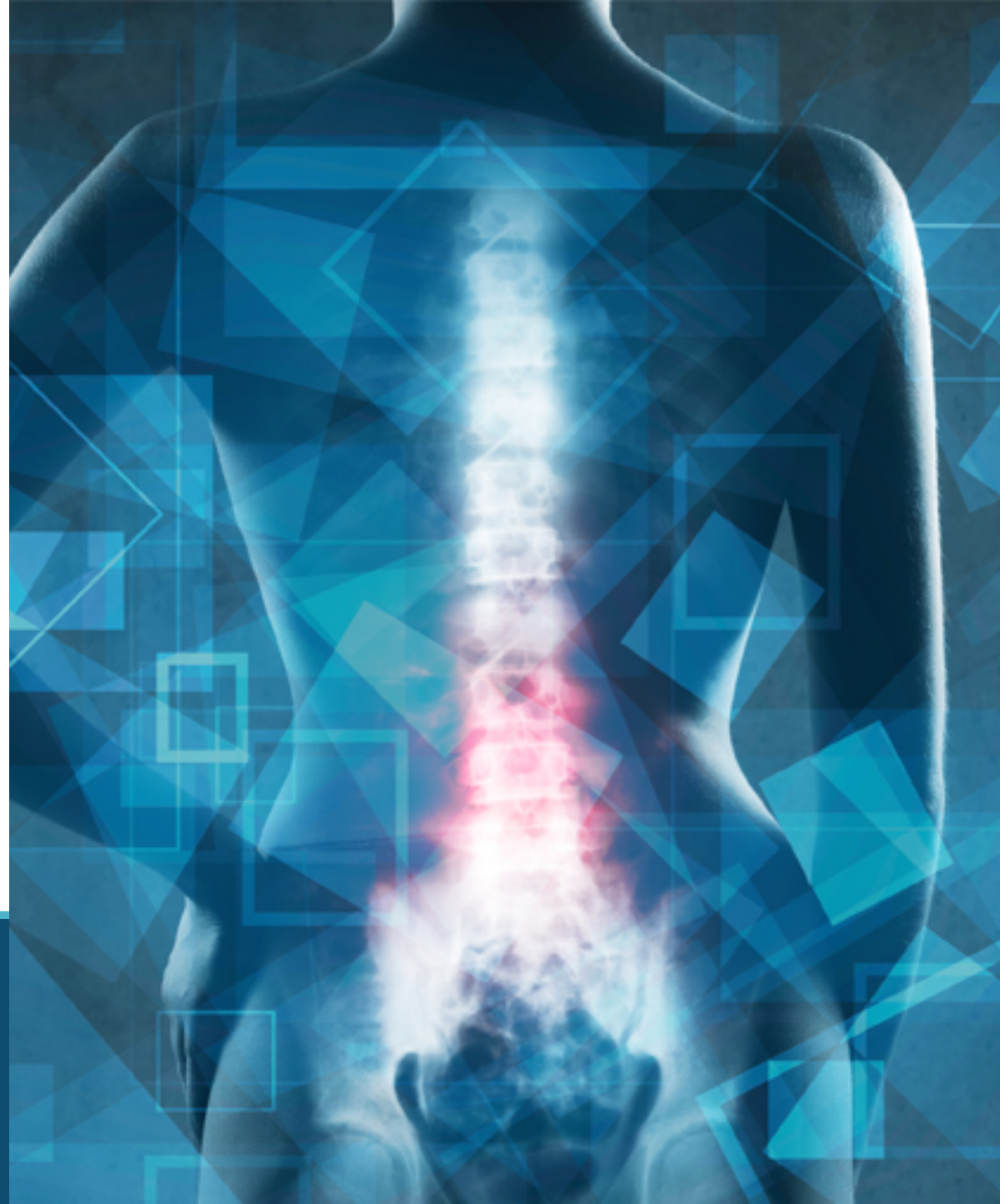
Individualizing IT Trialing Strategies

Dosing and Titration Strategies to Maximize Efficacy and Mitigate Risk

Questions

Learning Objective 1

Translate updates and recommendations in the 2017 PACC guidelines to clinical decision-making for patients with refractory chronic pain who are candidates for intrathecal (IT) therapy.



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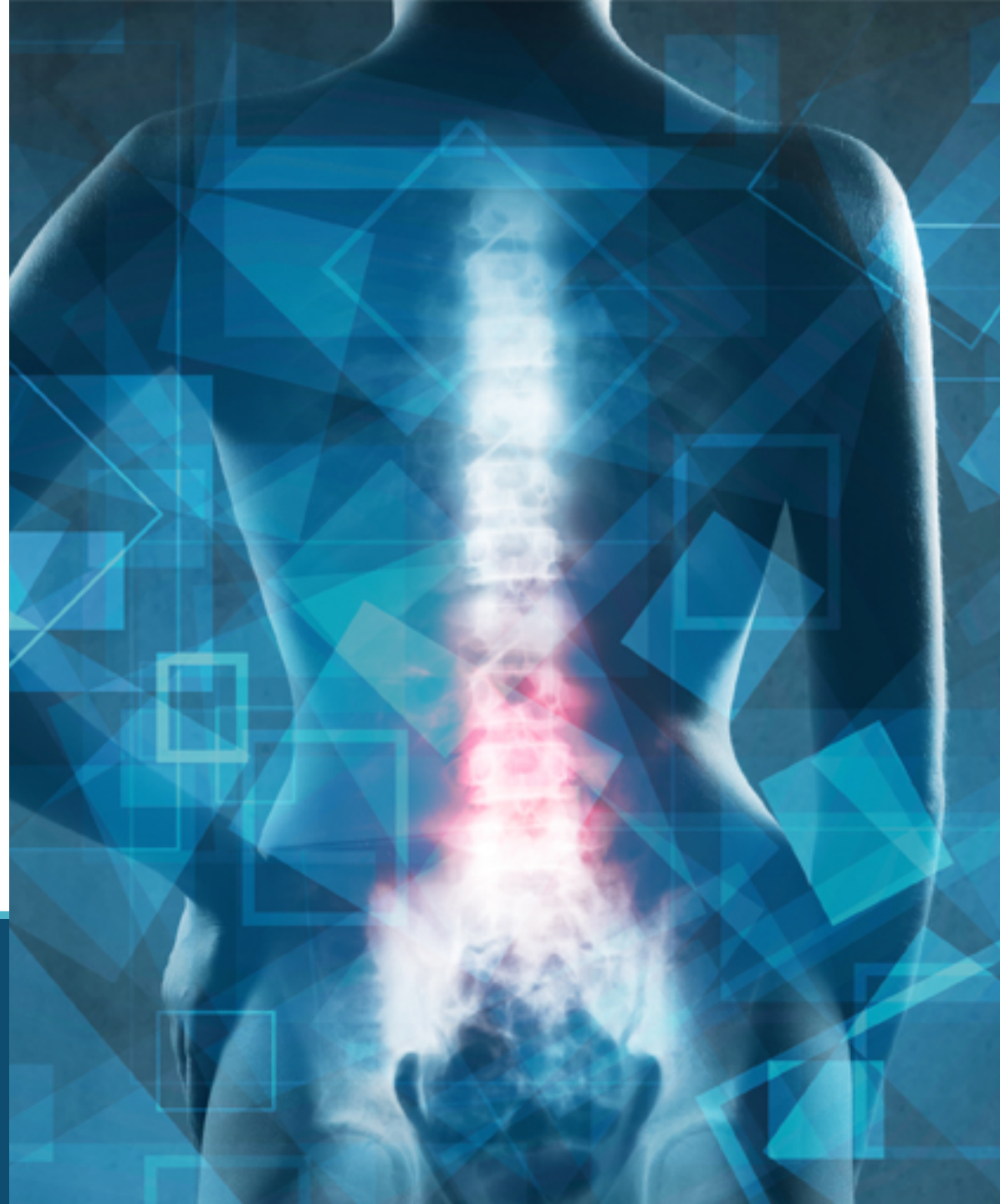
Learning Objective 2

Apply PACC recommendations for trialing of appropriate patients who are candidates for IT therapy.



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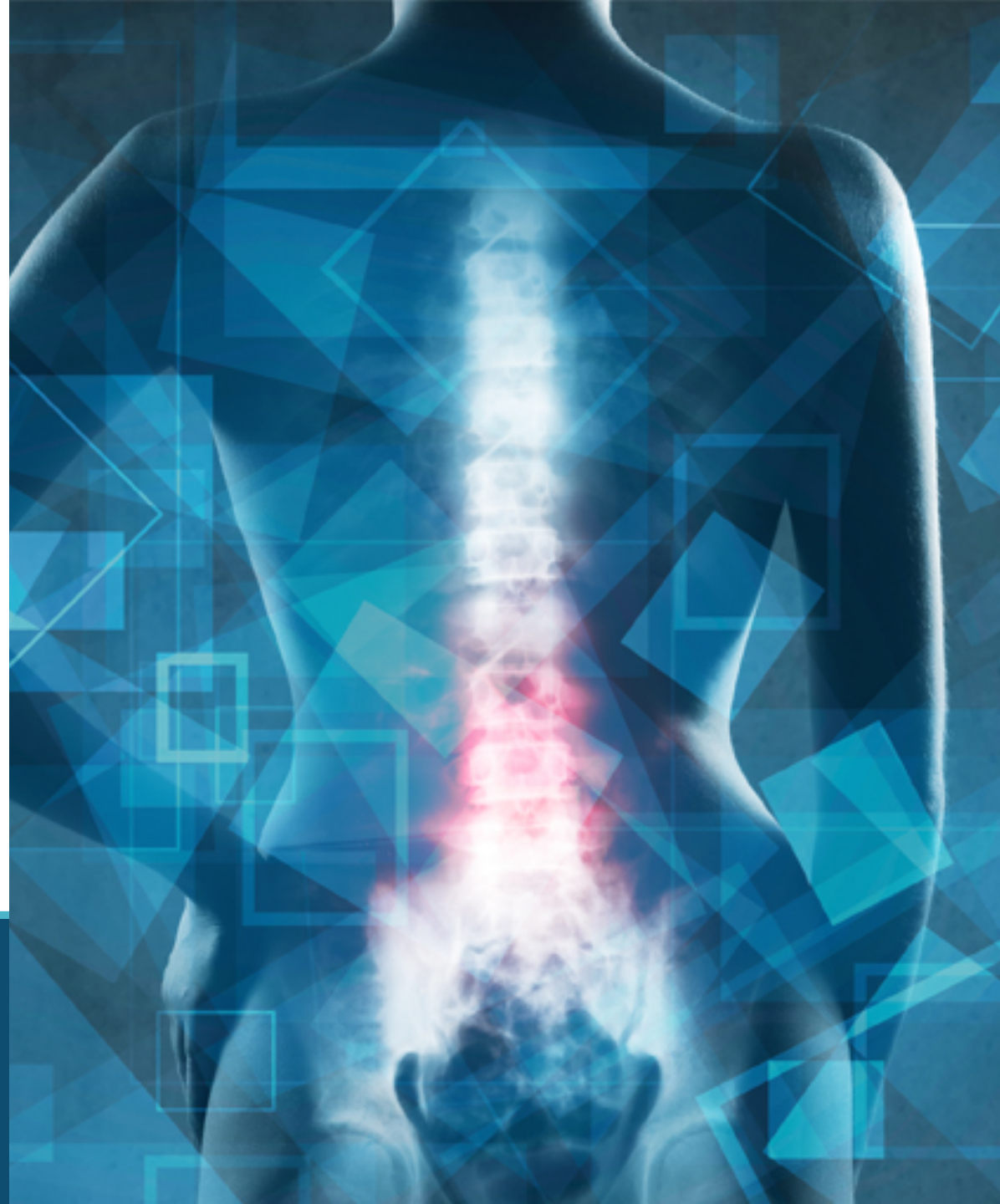
Learning Objective 3

Implement dosing and titration strategies in patients utilizing IDD to maximize results while mitigating risks.



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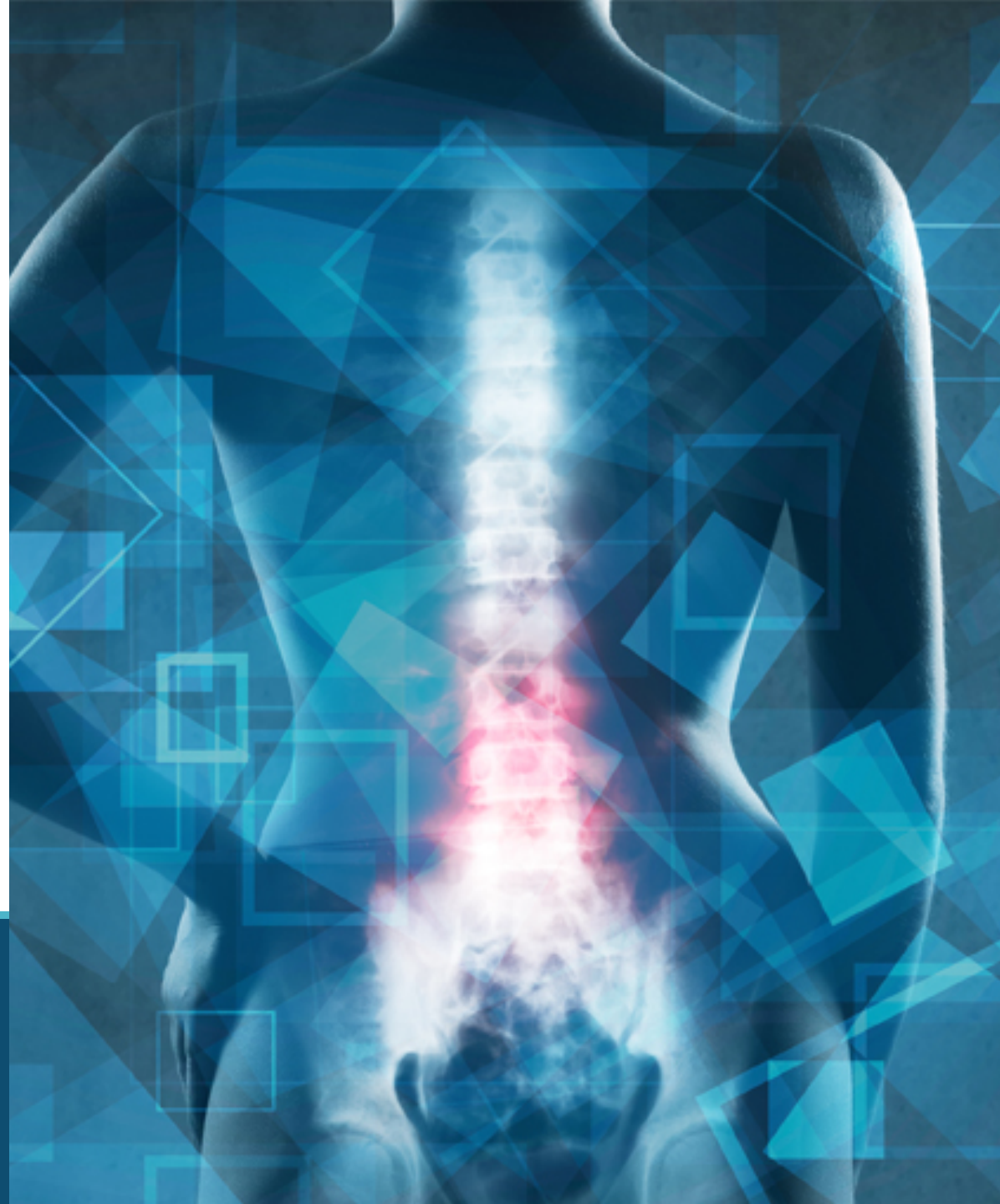
Why Were the 2012 PACC Guidelines Updated?



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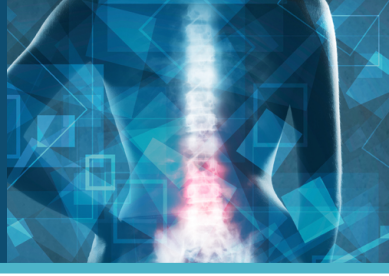
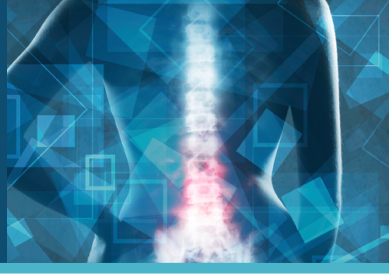
Basics of Patient Safety



- **Patient Safety:** Actions undertaken by individuals and organizations to protect health care recipients from being harmed by the effects of health care services.

People Are Set Up to Make Mistakes

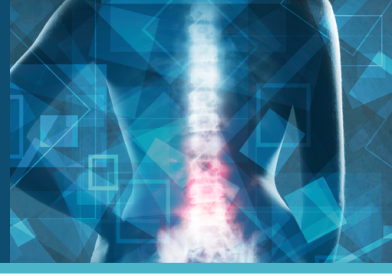


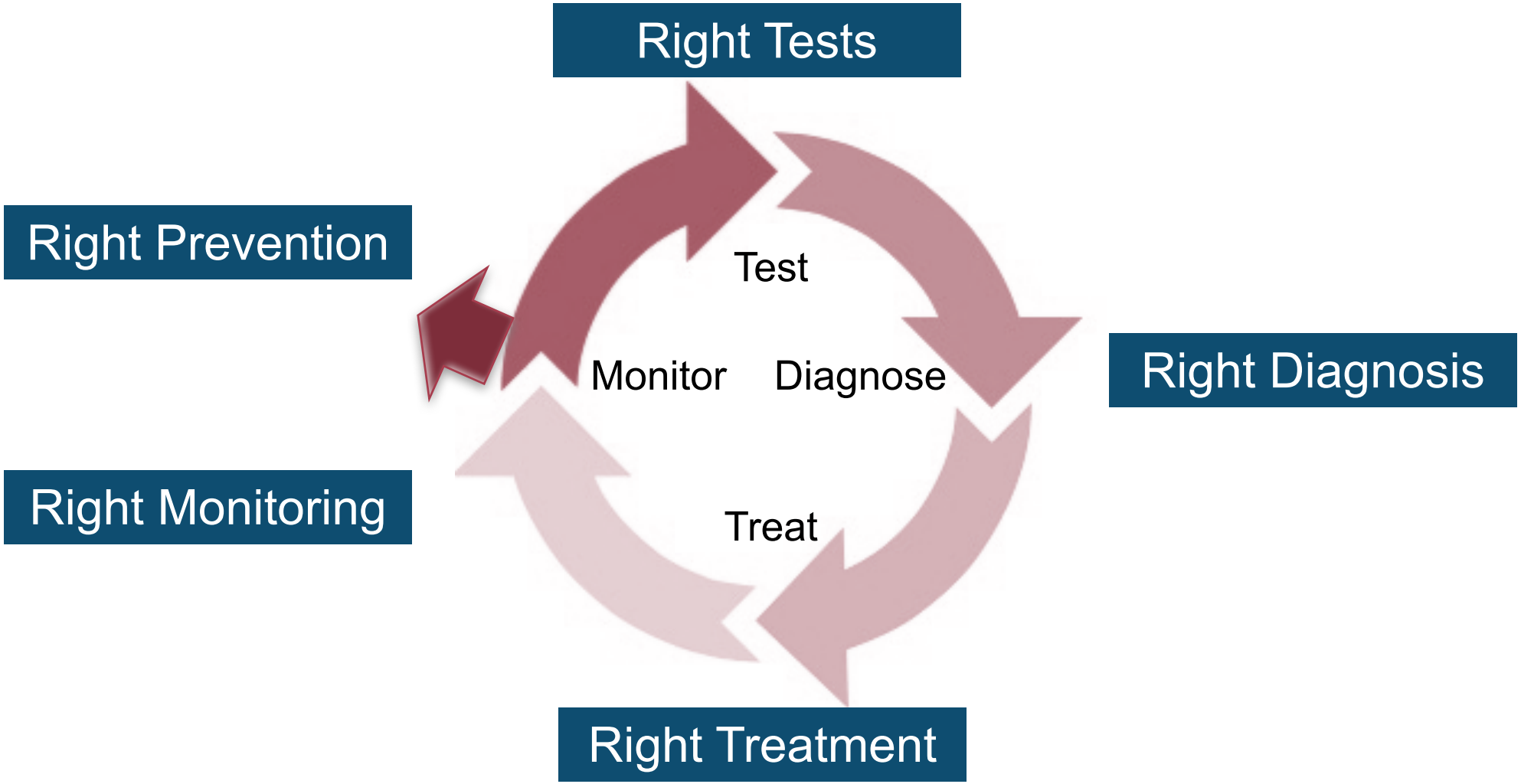
- Institute of Medicine report *To Err is Human: Building a Safe Health System*
  - Errors cause between 44,000 and 98,000 deaths per year in American hospitals and over 1 million injuries[1]
- Incompetent people are, at most, 1% of the problem. The other 99% are good people trying to do a good job who make very simple mistakes and it's the processes that set them up to make these mistakes.

-Dr. Lucian Leape, Harvard School of Public Health

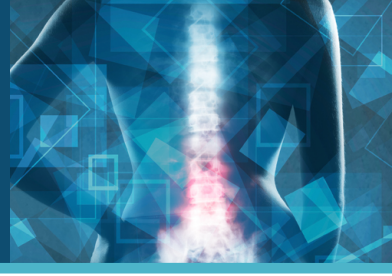
Kohn LT, Corrigan JM, Donaldson MD (Institute of Medicine). Washington, DC: National Academy Press, 2000.

5 Rights of Pain Care™



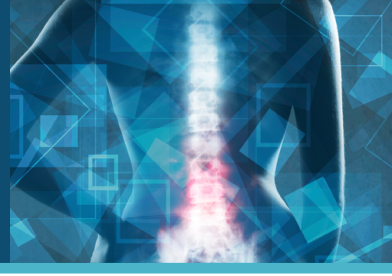


Traditional Methods of Protecting Patients From Harm



- Well-structured systems
- Explicit processes
- Professional standards of practice
- Individual competence reviews

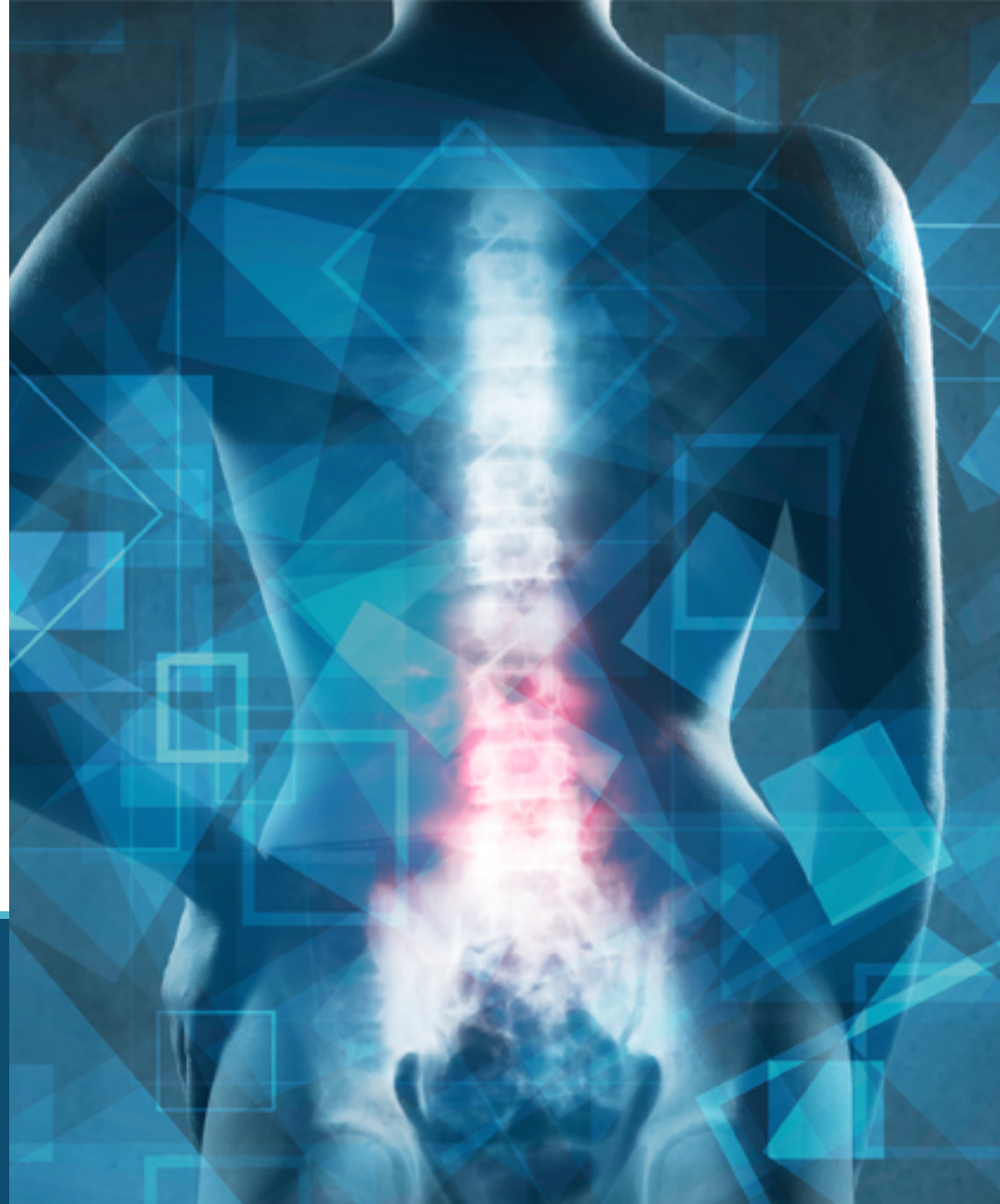
Process Redesign Solutions



- Redesign of processes to minimize and avoid harm to patients
  - Eliminate opportunities for errors
  - Consider safeguards to catch and correct errors before they reach the patient
- Reduce harm caused by mistakes
  - People must be able to quickly recognize the adverse event and take action
    - Human interventions
    - Response plans
    - Backups
    - Algorithms

Learning Objective 1

Translate updates and recommendations in the 2017 PACC guidelines to clinical decision-making for patients with refractory chronic pain who are candidates for intrathecal (IT) therapy.



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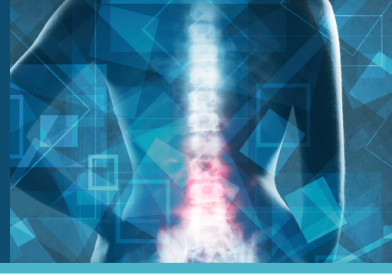
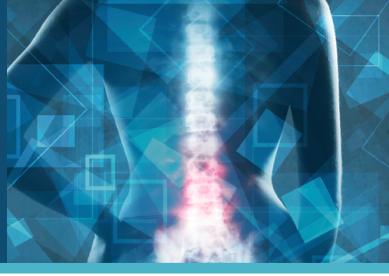
PACC of 2012: Challenges



- Evidence has improved since 2012
- Evolving understanding of the intrathecal space and pharmacokinetics
- PACC of 2012 did not address some of the identified factors associated with medication selection
- Adoption of PACC is certainly not universal and some deviate significantly from the Tiered suggested approach
  - Survey data indicate poor adoption of previous algorithms
- No transparent critical method for Evidence Assessment, Recommendation Grade, and Consensus Strength

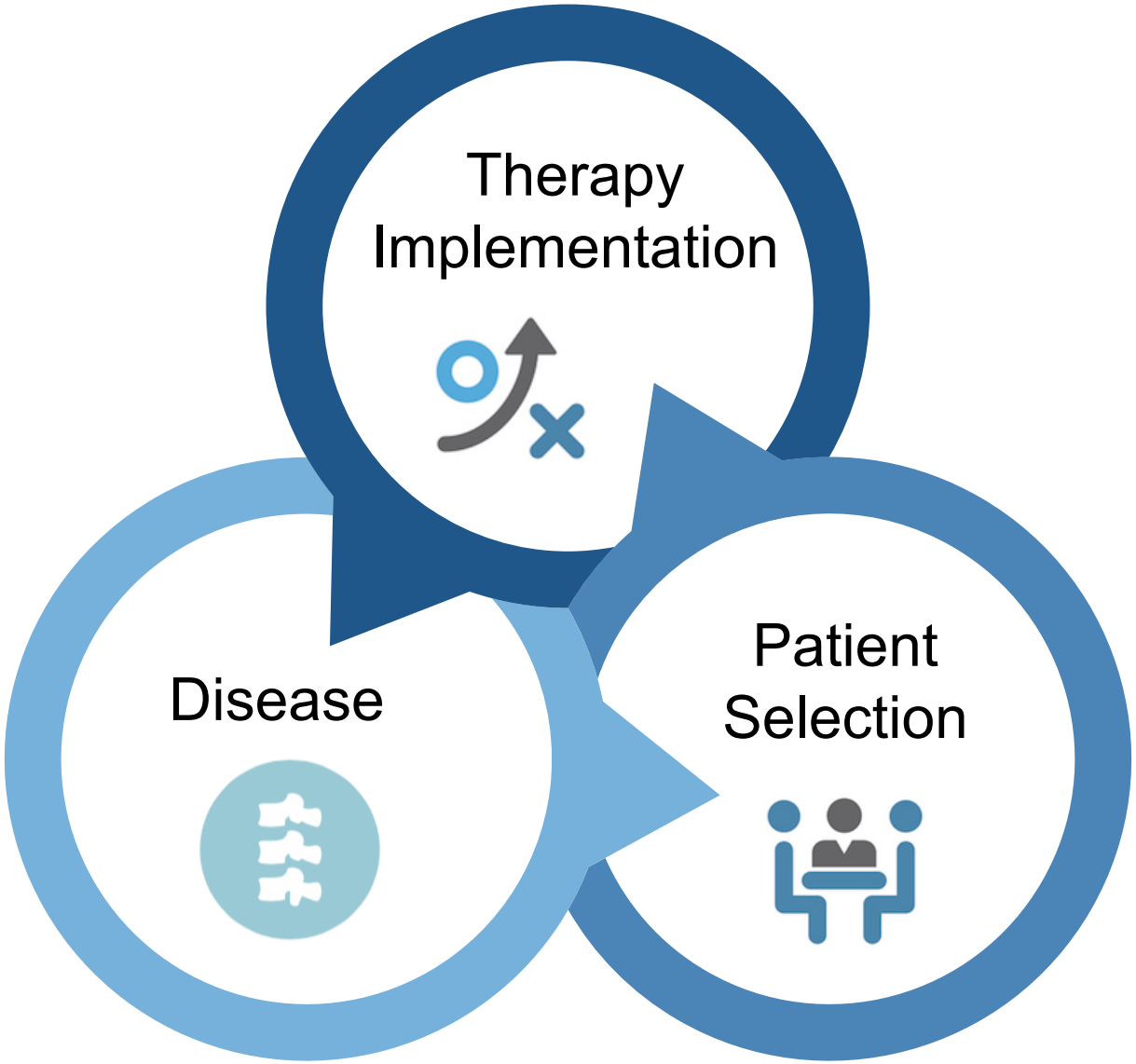
Goals of New PACC



- Published in 2017
- Provide an evidence driven, consensus based recommendations on
  - The need for IT therapy
  - Disease specific indications
  - Patient selection considerations
  - Risk stratification
  - Implementation of the therapy and maintenance
- Evidence assessment, regardless of strength, needs interpretation for clinical application whenever used[1]

Deer TR, Pope JE, Hayek S, et al. *Neuromodulation*. 2017;20(2):96-132.

Goals of New PACC



Hierarchy of Studies by Type of Design

Evidence Level	Study Type
I	At least one controlled and randomized clinical trial, properly designed
II-1	Well-designed, controlled, nonrandomized clinical trials
II-2	Cohort or case studies and well-designed controls, preferably multicenter
II-3	Multiple series compared over time, with or without intervention, and surprising results in noncontrolled experiences
III	Clinical experience-based opinions, descriptive studies, clinical observations or reports of expert committees

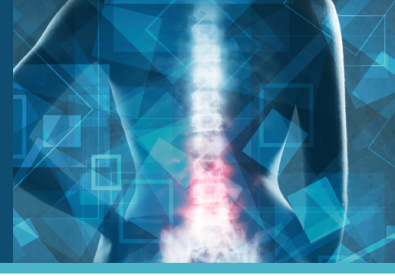
Harris RP, et al. for the Methods Work Group, Third US. Prevention Service Task Force. *Am J Prev Med* 2001;20:21-35.

Meaning of Recommendation Degrees

Degree of Recommendation	Meaning
	Extremely recommendable (good evidence that the measure is effective and benefits outweigh the harms)
	Recommendable (at least, moderate evidence that the measure is effective and benefits exceed harms)
	Neither recommendable nor inadvisable (at least moderate evidence that the measure is effective, but benefits are similar to harms and a general recommendation cannot be justified)
	Inadvisable (at least moderate evidence that the measure is ineffective or that the harms exceed the benefits)
	Insufficient, low quality or contradictory evidence; the balance between benefit and harms cannot be determined

Harris RP, et al. for the Methods Work Group, Third US. Prevention Service Task Force. *Am J Prev Med* 2001;20:21-35.

Strength of Consensus

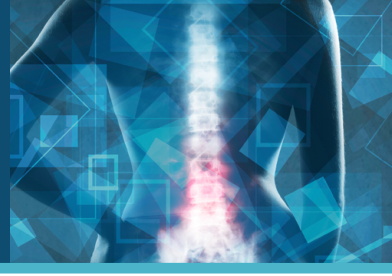


Strength of Consensus	Definition*
Strong	> 80% Consensus
Moderate	50% - 79% Consensus
Weak	< 49% Consensus

*Quorum defined as 80% of participants available for vote.

Deer TR, Pope JE, Hayek S, et al. *Neuromodulation.* 2017;20(2):96-132.

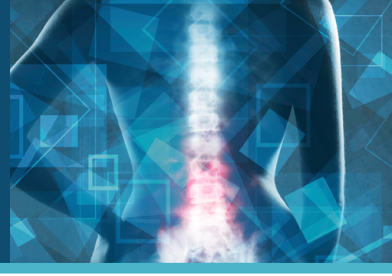
Clinical Factors That Shape IT Interventions and Medication Choice



- Patient diagnoses and expected survival time[1]
- Sustainability of the IT regimen
- Previous exposure to opioids[2-4]
- Location of pain (diffuse vs. localized)
- Type of pain (nociceptive, neuropathic or mixed)
- Physiochemical properties of lipid solubility of the IT agents[5,6]
- Cerebrospinal fluid flow dynamics and pharmacokinetics[7,8]
- IT catheter location[9]
- Pump and catheter characteristics[9]
- Kinetics of the intrathecal infusate[9]
- Psychological status of the patient with chronic pain[10-12]

Deer TR, Pope JE, Hayek S, et al. *Neuromodulation.* 2017;20(2):96-132. See supplemental reference 1-12.

Recommendations for Evidence Assessment of IT Therapy by the PACC Using USPSTF Criteria



Statement	Evidence Level	Rec Grade	Consensus Level
IT therapy should be utilized for active cancer-related pain with opioids	I	A	Strong
IT therapy should be utilized for active cancer-related pain with ziconotide	I	A	Strong
IT therapy should be utilized for active noncancer-related pain with opioids	III	B	Strong
IT therapy should be utilized for active noncancer-related pain with ziconotide	I	A	Strong

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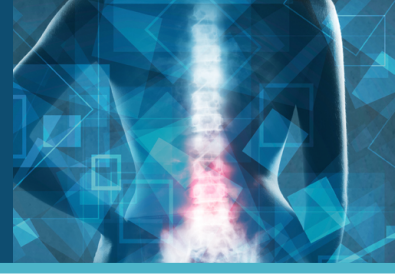
Recommendations for Application of IT Therapy vs. Neurostimulation by the NACC Using USPSTF Criteria



Statement	Evidence Level	Rec Grade	Consensus Level
IT therapy should be considered within the same line as neurostimulation strategies to treat noncancer-related pain	III	C	Moderate
IT therapy should be considered after neurostimulation strategies to treat noncancer-related pain if the pain is isolated and unlikely to spread	III	I	Strong
IT therapy should be considered before neurostimulation therapy for active cancer-related pain that is mechanical and likely to spread	III	C	Strong

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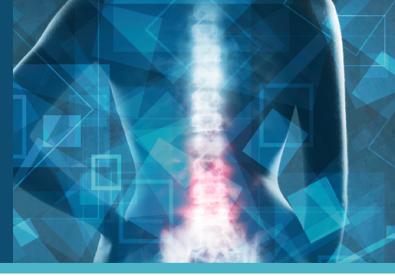
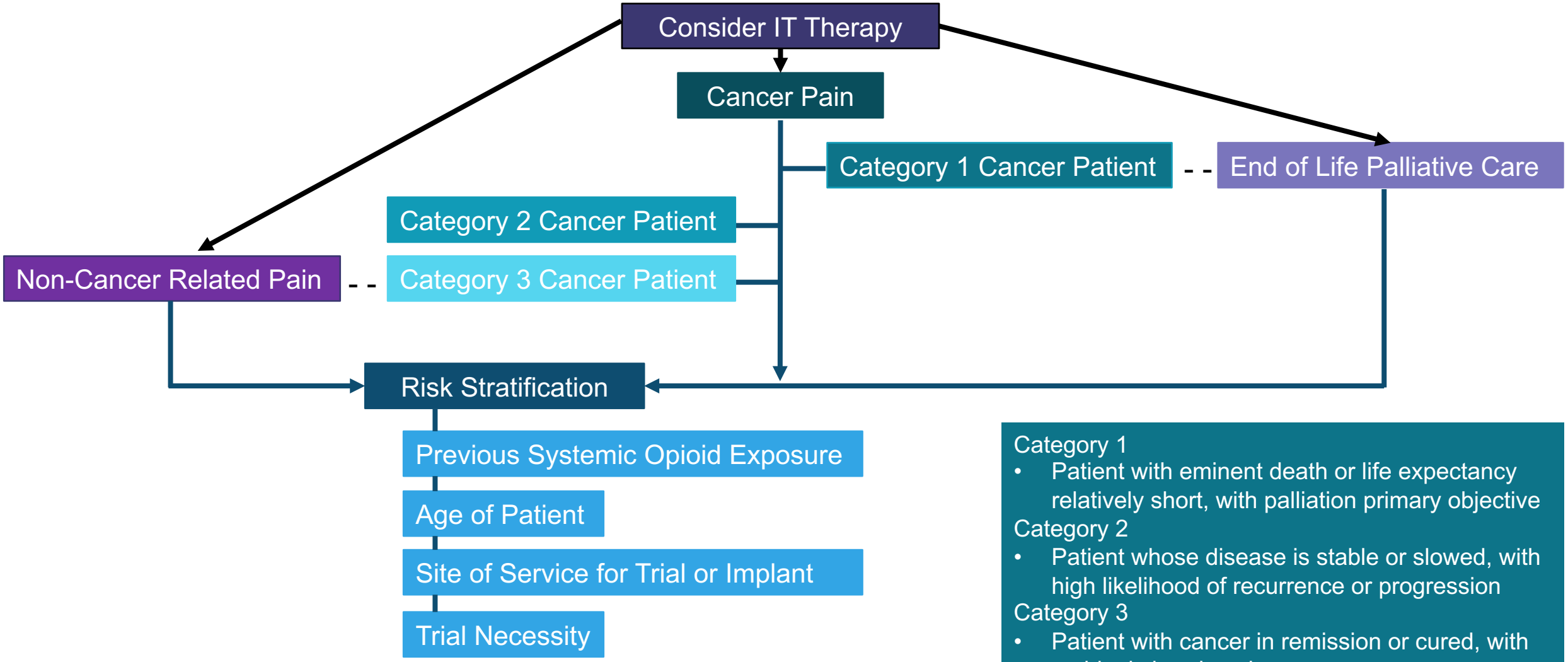
Disease Indications for IT Drug Delivery



- Axial neck or back pain; not a surgical candidate
  - Multiple compression fractures
  - Discogenic pain
  - Spinal stenosis
  - Diffuse multiple-level spondylosis
- Failed back surgery syndrome
- Abdominal/pelvic pain
  - Visceral
  - Somatic
- Extremity pain
  - Radicular pain
  - Joint pain
- Complex regional pain syndrome (CRPS)
- Trunk pain
  - Postherpetic neuralgia
  - Post-thoracotomy syndromes
- Cancer pain, direct invasion and chemotherapy related
- Analgesic efficacy with systemic opioid delivery complicated by intolerable side effects

Algorithm of Patient Selection Characteristics



Category 1
- Patient with eminent death or life expectancy relatively short, with palliation primary objective

Category 2
- Patient whose disease is stable or slowed, with high likelihood of recurrence or progression

Category 3
- Patient with cancer in remission or cured, with residual chronic pain

Deer TR, Pope JE, Hayek S, et al. *Neuromodulation.* 2017;20(2):96-132.

Recommendations for Patient Selection Criteria for IT Therapy by the PACC Using USPSTF Criteria

Statement	Evidence Level	Recommendation Grade	Consensus Level
Patients with comorbidities that negatively affect cardiopulmonary function need increased vigilance when instituting IT opioid therapy	III	C	High
Localized pain can be adequately covered with intrathecal therapy	II	B	Strong
Diffuse pain can be adequately treated with IT therapy	III	C	Moderate
Global pain can be adequately treated with IT therapy	III	D	Moderate
IT therapy should not be used as salvage therapy for failing systemic opioids	II	B	Moderate

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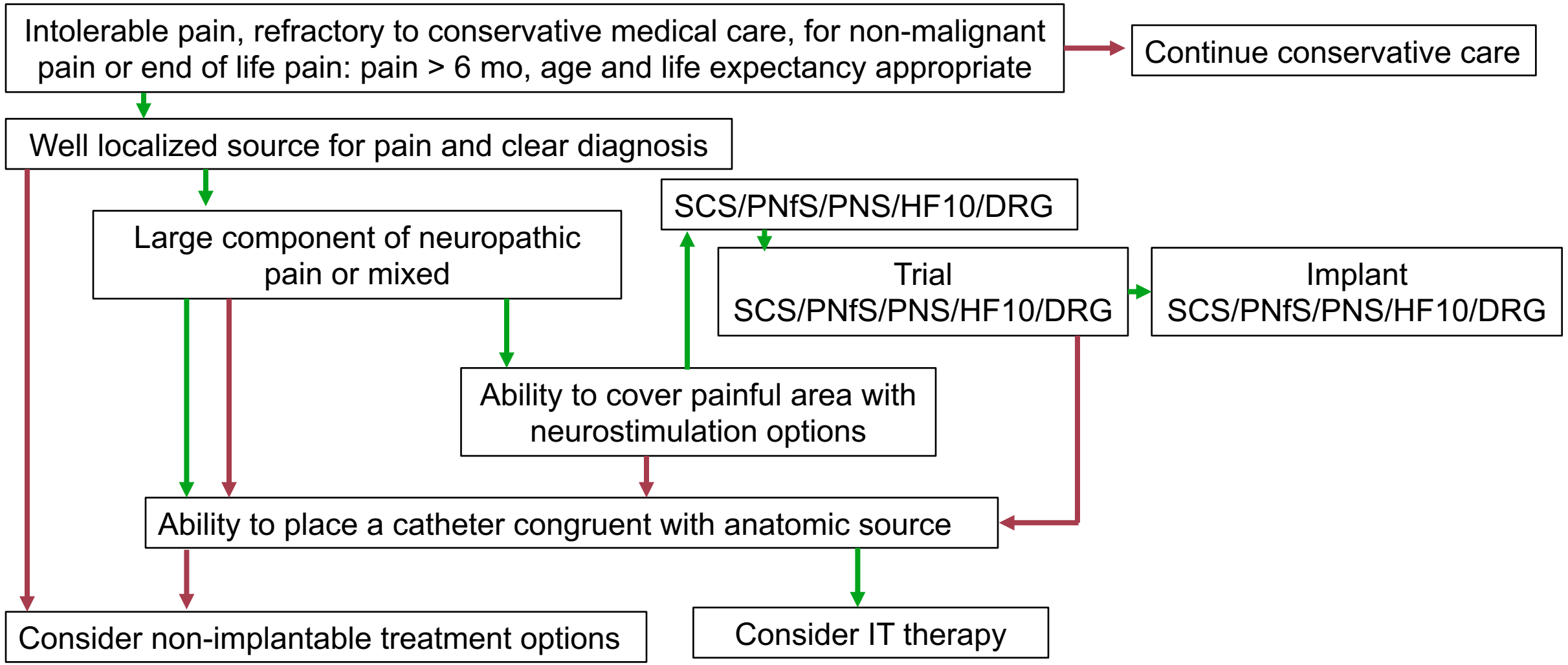
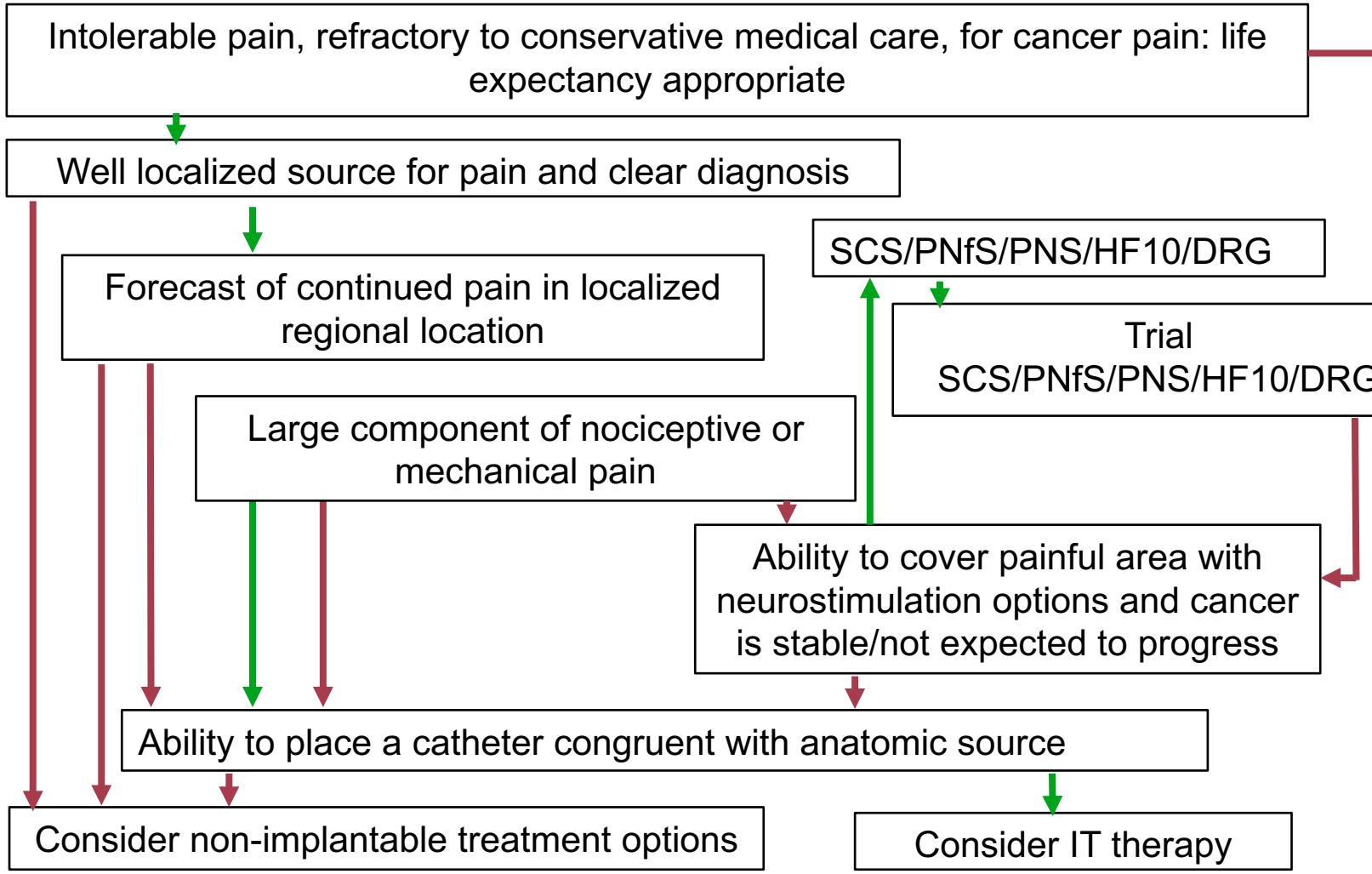
Algorithm for Placement within the Pain Care Algorithm for Noncancer or Non-End of Life Pain



SCS = Spinal cord stimulation; PNfS = Peripheral field nerve stimulation; PNS = Peripheral nerve stimulation; DRG = Dorsal root ganglion

Deer TR, Pope JE, Hayek S, et al. *Neuromodulation.* 2017;20(2):96-132.

Algorithm for Placement within the Pain Care Algorithm for Cancer-Related Pain



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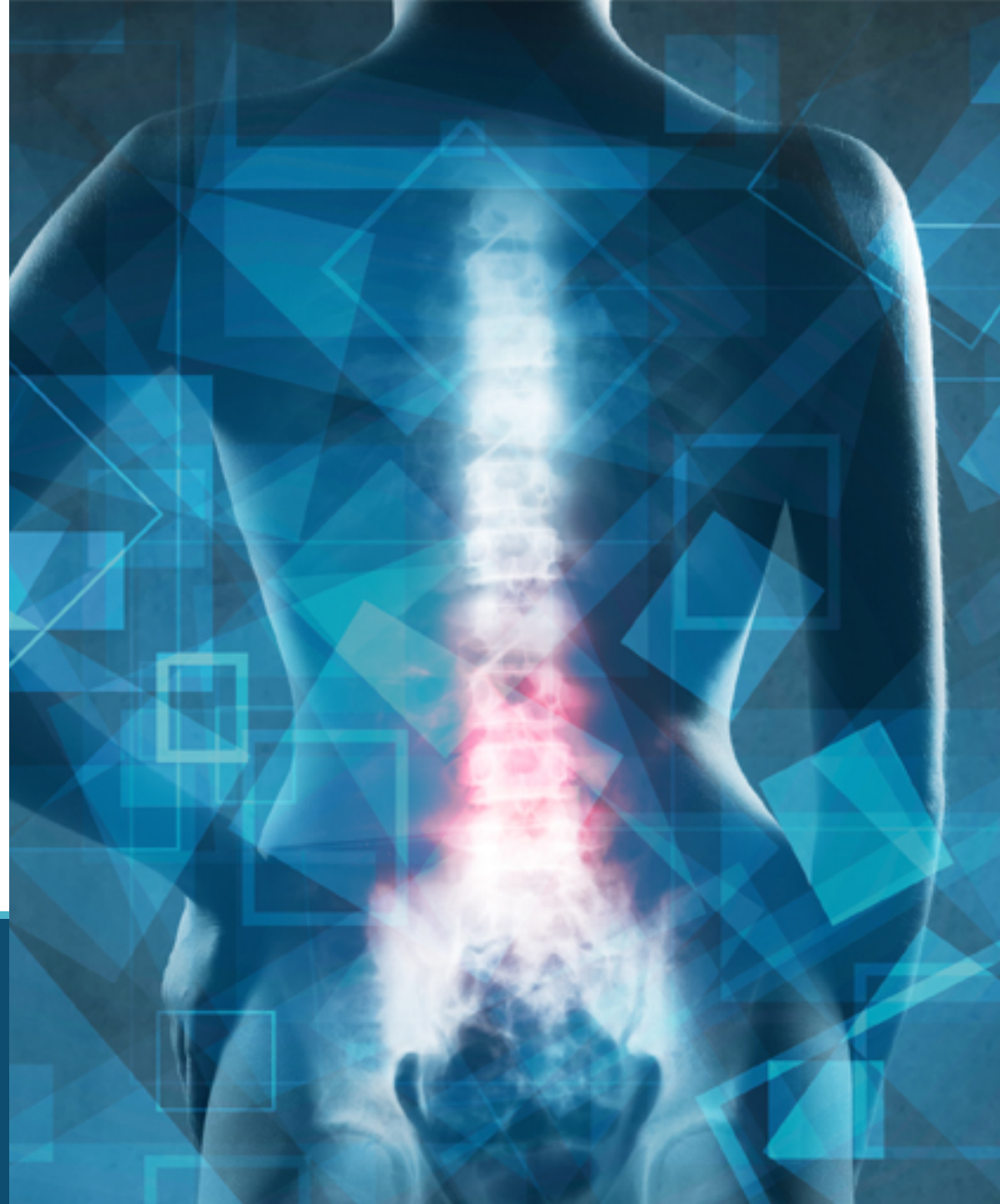
Medication Selection



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Cancer or Other Terminal Condition-Related Pain with Localized Nociceptive or Neuropathic Pain

Tier	Medication					Evidence Level	Rec Grade	Consensus Level
Line 1A	Ziconotide		Morphine			I	A	Strong
Line 1B	Fentanyl		Morphine or fentanyl + bupivacaine			II-1	B	Strong
Line 2	Hydromorphone	Hydromorphone + bupivacaine	Hydromorphone or morphine or fentanyl + clonidine	Morphine or hydromorphone or fentanyl + ziconotide		II-3	B	Strong
Line 3	Hydromorphone or morphine or fentanyl + bupivacaine + clonidine	Ziconotide + bupivacaine	Ziconotide + clonidine	Hydromorphone or morphine or fentanyl + bupivacaine + ziconotide	Sufentanil	III	C	Moderate

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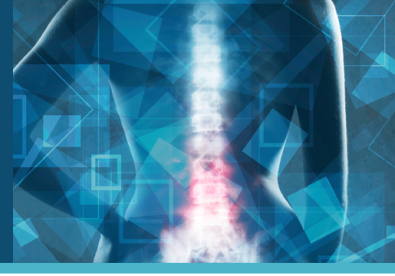
Cancer or Other Terminal Condition-Related Pain with Localized Nociceptive or Neuropathic Pain



Tier	Medication						Evidence Level	Rec Grade	Consensus Level
Line 4	Sufentanil + ziconotide	Sufentanil + bupivacaine	Baclofen	Sufentanil + clonidine	Bupivacaine + clonidine + ziconotide	Bupivacaine + clonidine	III	I	Weak
Line 5	Sufentanil + bupivacaine + clonidine						III	I	Weak
Line 6	Opioid* + bupivacaine + clonidine+ adjuvants**						III	I	Weak

*Opioid (all known intrathecal opioids); **Adjuvants include midazolam, ketamine, octreotide

Deer TR, Pope JE, Hayek S, et al. *Neuromodulation.* 2017;20(2):96-132.

Cancer or Other Terminal Condition-Related Pain with Diffuse Nociceptive or Neuropathic Pain

Tier	Medication					Evidence Level	Rec Grade	Consensus Level
Line 1A	Ziconotide			Morphine		I	B	Strong
Line 1B	Hydromorphone			Morphine or hydromorphone + bupivacaine		II	B	Moderate
Line 2	Hydromorphone or morphine + clonidine			Morphine or hydromorphone + ziconotide		II-3	B	Strong
Line 3	Hydromorphone or morphine or fentanyl + bupivacaine + clonidine	Ziconotide + bupivacaine	Ziconotide + clonidine	Hydromorphone or morphine or fentanyl + bupivacaine + ziconotide	Sufentanil	III	C	Moderate

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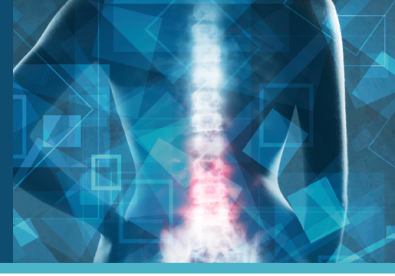

Tier	Medication						Evidence Level	Rec Grade	Consensus Level
Line 4	Sufentanil + ziconotide	Baclofen	Sufentanil + bupivacaine	Sufentanil + clonidine	Bupivacaine + clonidine + ziconotide	Bupivacaine + clonidine	III	I	Weak
Line 5	Sufentanil + bupivacaine + clonidine		Sufentanil + bupivacaine + ziconotide		Sufentanil + clonidine + ziconotide		III	I	Weak
Line 6	Opioid* + bupivacaine + clonidine+ adjuvants**						III	I	Weak

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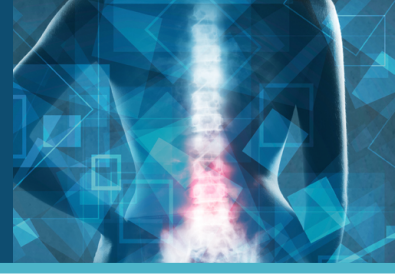
Noncancer-Related Pain with Localized Nociceptive or Neuropathic Pain

Tier	Medication				Evidence Level	Rec Grade	Consensus Level
Line 1A	Ziconotide		Morphine		I	A	Strong
Line 1B	Fentanyl		Fentanyl + bupivacaine		II-3	B	Strong
Line 2	Fentanyl + clonidine	Hydromorphone or morphine + bupivacaine	Fentanyl + bupivacaine + clonidine	Bupivacaine	II-3	B	Strong
Line 3	Fentanyl + ziconotide + bupivacaine	Morphine or hydromorphone + clonidine	Ziconotide + clonidine or bupivacaine or both	Bupivacaine + clonidine	III	C	Moderate

Deer TR, Pope JE, Hayek S, et al. *Neuromodulation.* 2017;20(2):96-132.

Noncancer-Related Pain with Localized Nociceptive or Neuropathic Pain



Tier	Medication			Evidence Level	Rec Grade	Consensus Level
Line 4	Sufentanil + bupivacaine or clonidine	Baclofen	Bupivacaine+ clonidine + ziconotide	III	I	Weak
Line 5	Sufentanil + bupivacaine + clonidine	Sufentanil + ziconotide		III	I	Weak

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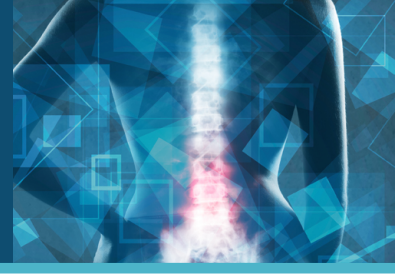
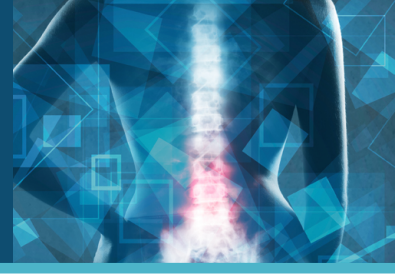


Tier	Medication			Evidence Level	Rec Grade	Consensus Level
Line 1A	Morphine	Ziconotide*		I	A	Strong
Line 1B	Hydromorphone	Morphine or hydomorphone + bupivacaine		II	B	Strong
Line 2	Hydromorphone or morphine + clonidine	Fentanyl + bupivacaine	Ziconotide + Morphine or hydomorphone	III	C	Strong
Line 3	Hydromorphone or morphine + bupivacaine + clonidine	Fentanyl + ziconotide	Sufentanil + bupivacaine or clonidine	Ziconotide + clonidine or bupivacaine or both	III	I	Moderate

*Ziconotide should be first choice in patients with > 120 morphine equivalents or fast systemic dose escalation, in the absence of history of psychosis

Deer TR, Pope JE, Hayek S, et al. *Neuromodulation.* 2017;20(2):96-132.

Noncancer-Related Pain with Diffuse Nociceptive or Neuropathic Pain

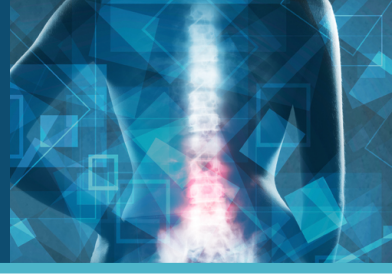


Tier	Medication			Evidence Level	Rec Grade	Consensus Level
Line 5	Fentanyl or sufentanil + bupivacaine + clonidine	Sufentanil + ziconotide	Baclofen	III	I	Weak
Line 6	Opioid + ziconotide + bupivacaine or clonidine			III	I	Weak

*Ziconotide should be first choice in patients with > 120 morphine equivalents or fast systemic dose escalation, in the absence of history of psychosis

Deer TR, Pope JE, Hayek S, et al. *Neuromodulation.* 2017;20(2):96-132.

PACC Update Takeaways: Consensus Points

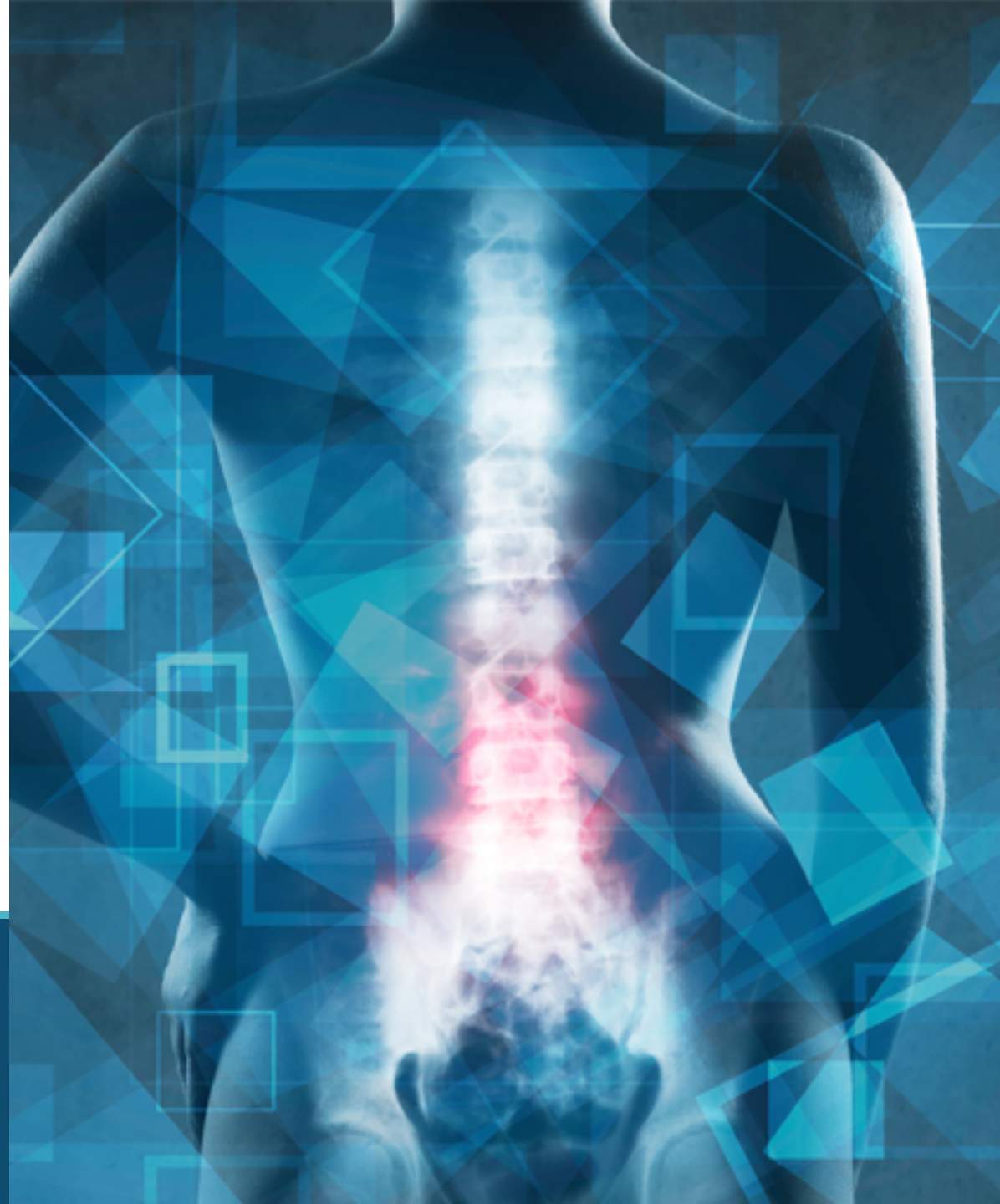


- An update of the best practices of IT drug delivery is needed due to many changes in patient care since the last version of this working document
- Localized, diffuse and global pain can be adequately treated with intrathecal therapy
- Intrathecal therapies should be used at an appropriate time in the algorithm and not as salvage treatment
- Algorithms are based on evidence and consensus on safety. The patient's physician and good clinical judgement should guide individual patient care
- Unless contraindicated, ziconotide should be the first drug selected in the population of noncancer patients discussed in this consensus

Deer TR, Pope JE, Hayek S, et al. *Neuromodulation.* 2017;20(2):96-132.

Learning Objective 2

Apply PACC recommendations for trialing of appropriate patients who are candidates for IT therapy.



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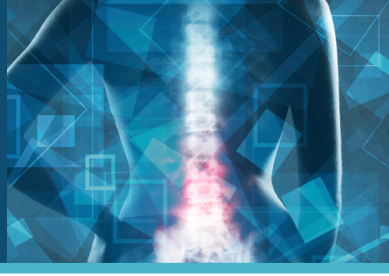
Screening Trial



- Rationale is to offer clinician and patients preview of response to intrathecal therapy
- Preimplantation trial considered standard of care and often required by insurers, but predictive value has been under increased scrutiny[1]
- PACC concludes that there are equal levels of evidence for trialing methods[2]
  - Single shot trialing
  - Bolus trialing
  - Continuous infusion

1. Deer TR, et al. *Pain Physician* 2010;13:E175-E213.; 2. Deer TR, Pope JE, Hayek S, et al. *Neuromodulation*. 2017;20(2):133-154.

Psychological Screening

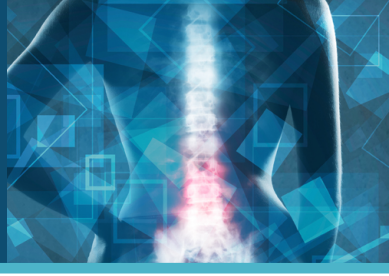
Patients with a psychological profile deemed appropriate for implantable therapy have better outcomes than those deemed inappropriate.

Several studies state that depression, hysteria, and hypochondriasis are so common in pain patients and do not constitute a contraindication to implants.

PACC recommends a psychological assessment prior to any implant for noncancer pain.

Deer TR, et al. *Pain Physician*. 2010;13(3):E175-213.; Deer TR, Pope JE, Hayek S, et al. *Neuromodulation.* 2017;20(2):133-154.

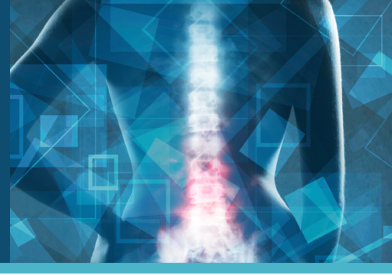
Psychologic Exclusion Criteria



- Active psychosis
- Active suicidality or homicidality
- Major uncontrolled depression or other mood disorders
- Somatization or other somatoform disorders
- Alcohol or illicit drug dependency
- Lack of appropriate social support
- Neurobehavioral or cognitive deficits that preclude sound decision making

Deer TR, et al. *Neuromodulation*. 2012;15(5):436-464.

Define the Goals of the Trial: Measuring Success



- Acceptable pain relief should be achieved during a trial
  - Acceptable pain relief varies between 30% - 70%[1]
- Goals of pain relief should be discussed with patient/caregivers before trial
  - Assessment of decrease in pain based on visual analog scale (VAS) compared to baseline measurement
  - If functional improvement is goal, pretrial benchmarks should be set
- If side effects occur at lowest reasonable dose, trial is a failure and medication switch should be considered

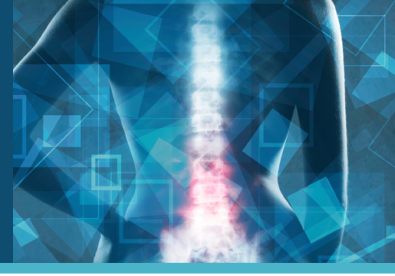
Pope JE, Deer TR. *Neuromodulation*. 2015;18:414-420.
Deer TR, Pope JE, Hayek S, et al. *Neuromodulation*. 2017;20(2):133-154.

Does Trialing Predict Therapy Outcome?

PACC Recommendation	Evidence Level	Recommendation Strength	Consensus Level
A trial should be considered before initiating IT drug delivery for noncancer pain.	II-3	B	Moderate
A trial is not a necessity before initiating IT drug delivery for cancer pain.	III	I	Moderate
If a trial is performed, delivery of the medication within the IT space is an acceptable method	II	C	Strong
IT trials should be monitored in a safe setting, with due vigilance, appropriate monitoring of the patient and appreciation for patient comorbidities	II-3	B	Strong
IT ziconotide trials should be monitored in a safe setting, with due vigilance, and appropriate monitoring of the patient.	II-3	B	Strong

Deer TR, Pope JE, Hayek S, et al. *Neuromodulation.* 2017;20(2):133-154.

Recommending Doses for Intrathecal Bolus Trialing

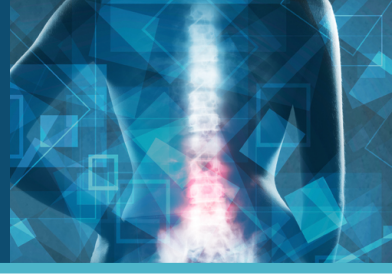


Drug	Recommendation of Dose*
Morphine	0.1 – 0.5 mg
Hydromorphone	0.025 – 0.1 mg
Ziconotide	1 – 5 mcg
Fentanyl	15 – 75 mcg
Bupivacaine	0.5 – 2.5 mcg
Clonidine	5 – 20 mcg
Sufentanil	5 – 20 mcg

*Starting doses of medication in the opioid-naïve patient for outpatient bolus delivery do not exceed -.15 mg morphine, 0.04 mg hydromorphone, or 25 mcg fentanyl.

Deer TR, Pope JE, Hayek S, et al. *Neuromodulation*. 2017;20(2):133-154.

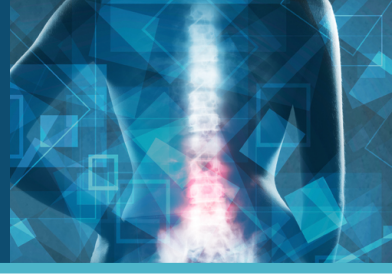
Possible Outcome of Bolus IT Trials



Outcomes	Consideration
Relief without side effects	Successful trial, medication and dose considered for chronic therapy
Relief with side effects	May be appropriate IT medication; consider reduction in medication dose for retrial or medication switch
No relief, side effects noted	Medication switch recommended for retrial
No relief, no side effects	Consider retrial with higher dose or medication switch

Deer TR, Pope JE, Hayek S, et al. *Neuromodulation.* 2017;20(2):133-154.
McDowell G, Pope JE. *Neuromodulation.* 2016;19:522-532.

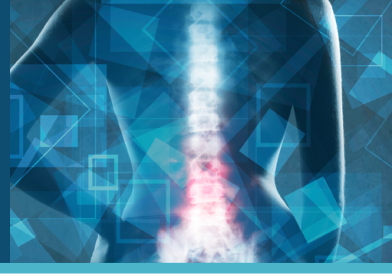
PACC Recommendations: When is a Trial Required?



- Patient is being trialed with ziconotide as the first-line chronic infusion choice to assess response and side effects
- Patient is being trialed with opioid and has increased risk of respiratory depression
- Patient is being trials with baclofen to assess response and side effects
- Patient is being trialed with an infusion of a drug combination
- Patient is being assessed for functional improvement or behavior during an extended period of time

Deer TR, Pope JE, Hayek S, et al. *Neuromodulation*. 2017;20(2):133-154.

PACC Recommendations: When is a Trial Not Required?



- Patient has advanced disease with limited survival time and is a high risk for procedures
- Patient has risk of bleeding or has an infection that makes the trial high risk
- Patient demographics suggest a high likelihood of success
  - Older person
  - Localized pain
  - On no- or low-dose systemic opioids pretrial

Deer TR, Pope JE, Hayek S, et al. *Neuromodulation.* 2017;20(2):133-154.

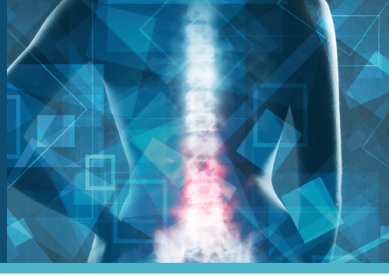
Risk Assessment: Site of Service for Trialing and Dosing of IT Therapy

Recommendation has been modified from PACC 2012

- **Opioids**
  - No data to suggest safety or danger of IT opioid initiation in the outpatient setting
  - Suggest that the 24-hr initiating IT dose be half of efficacious/successful trialed IT opioid dose
- **Ziconotide**
  - Previous recommendation of 12-hr observation period after initiation has been revised, by consensus, to 6-hrs as long as there is no neurologic dysfunction prior to initiation
- **Morphine**
  - In settings where the initial drug concentrations create the need for a starting dose outside PACC recommendations, an overnight admission is advised

Deer TR, Pope JE, Hayek S, et al. *Neuromodulation.* 2017;20(2):96-132.

Trialing Takeaways: Consensus Points

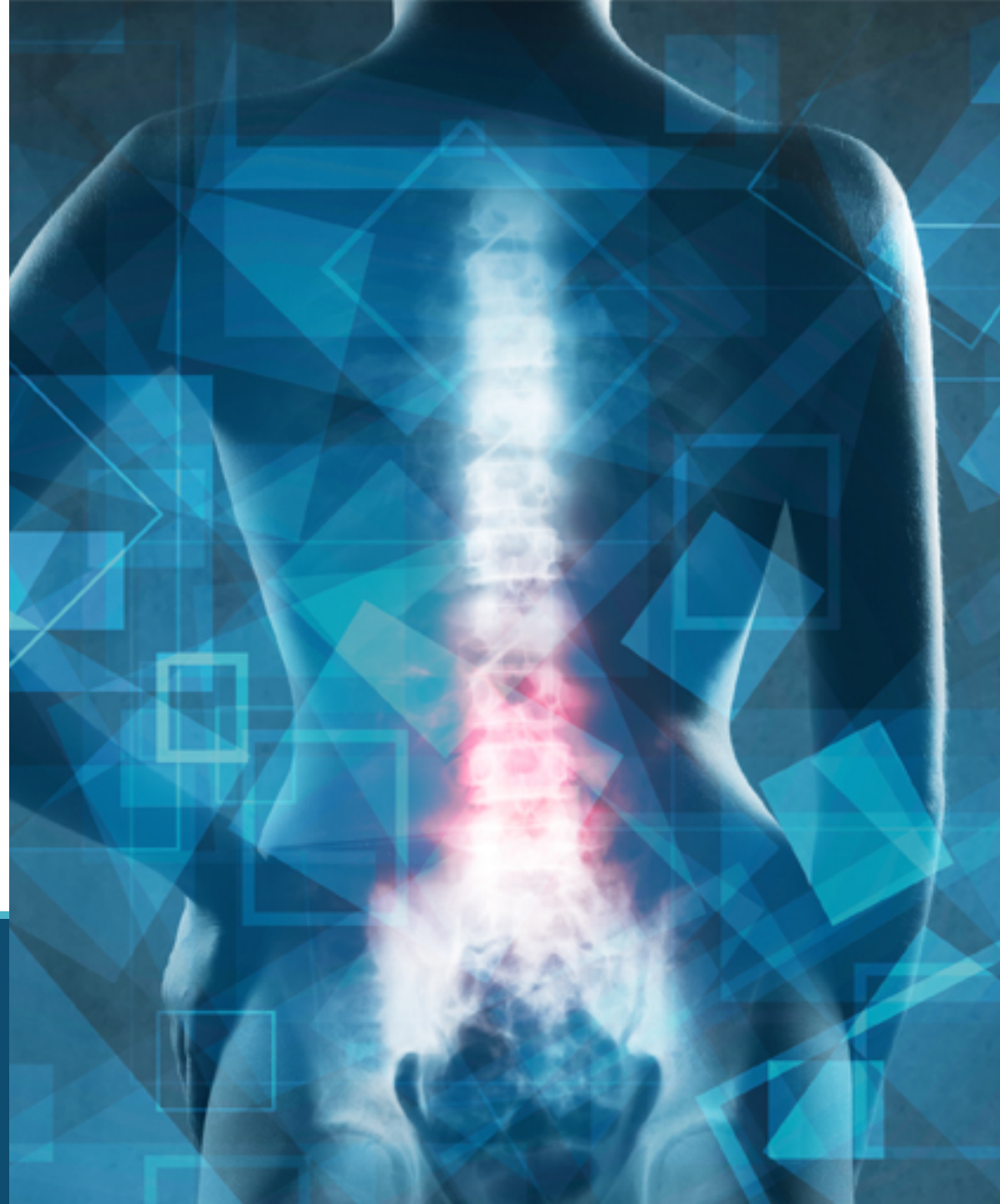


- Initial dose of intrathecal opioids and ziconotide should be as low as reasonable expected to provide analgesia
- Initiating dose of intrathecal opioids and ziconotide delivered continuously should be 50% or less of the dose used in bolus trialing
- Abrupt stopping of an opioid is not recommended
- Ziconotide and bupivacaine do not have risk of withdrawal and weaning is not needed
- Pay careful attention to side effects when adding any adjuvant drug to a primary drug

Deer TR, Pope JE, Hayek S, et al. *Neuromodulation.* 2017;20(2):96-132.

Learning Objective 3

Implement dosing and titration strategies in patients utilizing IDD to maximize results while mitigating risks.



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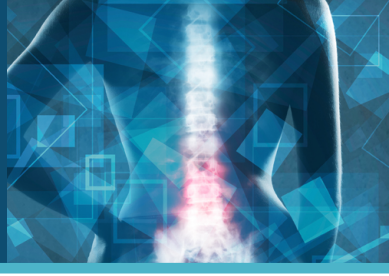
A Patient-Centric Approach to Pain



- Economic data demonstrate that costs associated with IT therapy and safety are markedly better compared with systemic opioids[1,2]
- In defined patient groups, IT may provide improved longevity and treatment flexibility vs. spinal cord stimulations (SCS)[3]
- **Consensus Point:** The risk to benefit ratio of IDD makes it relatively safe therapy for both cancer- and noncancer-related pain[2]
- **Consensus Point:** Compared to chronic, long-lasting opioid therapy, IDD is markedly more safe and has less associated morbidity and mortality[2]

1. Pope J. Presentation at the 9th Annual Scientific Meeting of the Canadian Neuromodulation Society. Septemer 30-October 2, 2016; Regina, Saskatchewan, Canada.; 2. Deer TR, Pope JE, Hayek S, et al. *Neuromodulation.* 2017;20(2):155-176.; 3. Pope JE, et al. *Neuromodulation*. 2015;18:414-420.

PACC Evidence and Recommendations for IT Therapy

Statement	Drug	Evidence Level	Rec Grade	Consensus Level
Intrathecal therapy should be utilized for active cancer-related pain	Opioids	I	A	Strong
	Ziconotide	I	A	
Intrathecal therapy should be utilized for noncancer-related pain	Opioids	II-2	B	Strong
	Opioids in combo with bupivacaine	II-3	B	
	Ziconotide	I	B	

Deer TR, Pope JE, Hayek S, et al. *Neuromodulation.* 2017;20(2):155-176.

Safety of FDA Approved Intrathecal Agents for Pain Relief

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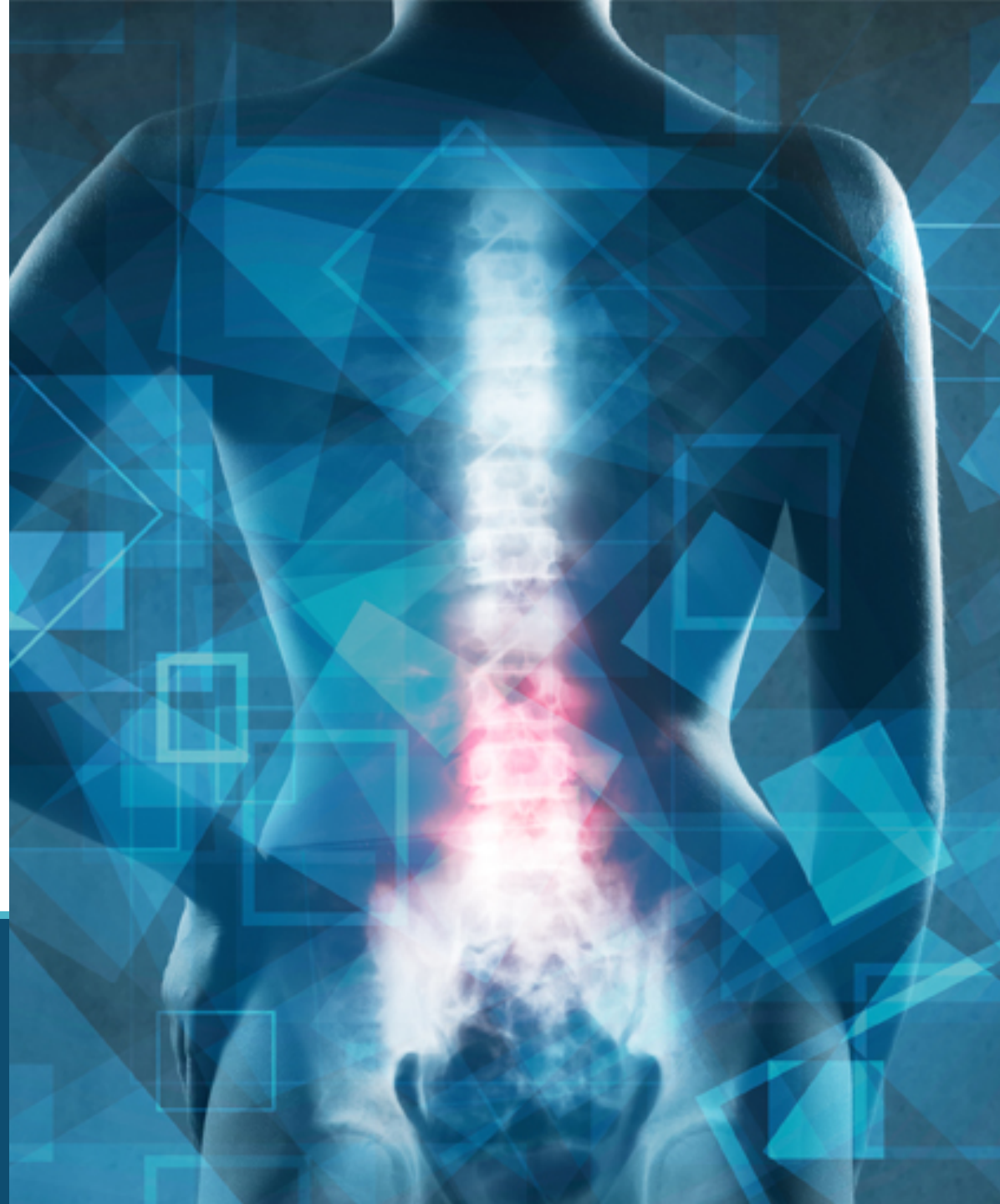
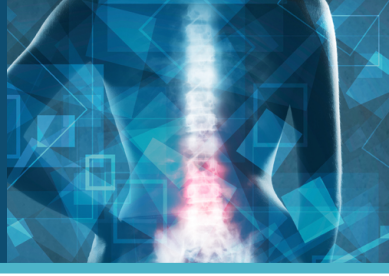


Morphine

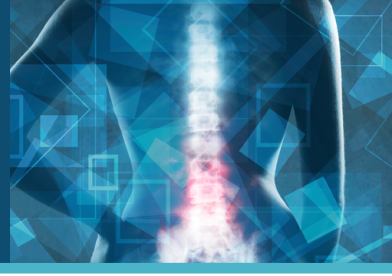


- Considerable side effects, but morbidity and mortality of IT opioids is markedly less vs. long-acting systemic opioid delivery
- Analysis of 6,398 patients demonstrated no opioid-related deaths attributed to IT infusion delivery over a 10-year period
- Risk of intrathecal catheter tip granuloma
- Potentially a safer patient option to offer refractory, chronic pain patients

Medtronic. 2015 Product Performance Report. Targeted Drug Delivery Systems. http://professional.medtronic.com/ppr/intrathecal-drug-delivery-systems/index.htm#.WAY_sySkyzw.

Deer TR, Pope JE, Hayek S, et al. Neuromodulation. 2017;20(2):155-176.

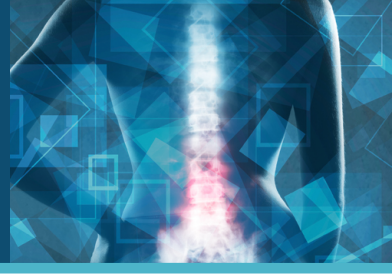
Ziconotide



- Should be considered as a first choice in the treatment of cancer- or noncancer-related pain, in the absence of psychiatric comorbidities or significant baseline renal disease[1]
- Suggested that ziconotide long-term efficacy is greater if first in pump than if introduced later in IT therapy[2]
- Narrow therapeutic window requires careful and strategic dosing for efficacy and reduction of side effects[1]
  - Rapid titration has been associated with cognitive and neuropsychiatric adverse events
- Ziconotide is not associated with the formulation of granulomas to date

1. Deer TR, Pope JE, Hayek S, et al. *Neuromodulation.* 2017;20(2):155-176.
2. McDowell G, et al. Presented at the North American Neuromodulation Society, 20th Annual Meeting. January 19-22, 2017, Las Vegas, NV.

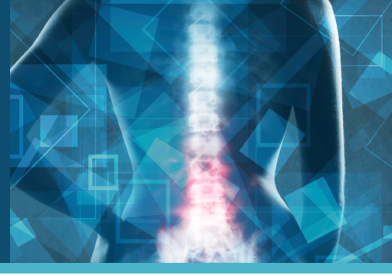
Recommended Starting Dosage Ranges of Intrathecal Medications for Long-term Therapy Delivery



Drug	Recommendation of Starting Dose
Morphine	0.1 – 0.5 mg/day
Hydromorphone	0.01 – 0.15 mg/day
Ziconotide	0.5 – 1.2 mcg/day (to 2.4 mcg/day per product labeling)
Fentanyl	25 – 75 mcg/day
Bupivacaine	0.01 – 4 mcg/day
Clonidine	20 – 100 mcg/day
Sufentanil	10 – 20 mcg/day

Deer TR, Pope JE, Hayek S, et al. *Neuromodulation.* 2017;20(2):96-132.

Maximum Concentrations and Daily Doses of Intrathecal Agents as Recommended by PACC

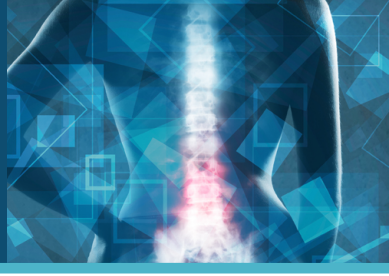


Drug	Maximum Concentration	Maximum Dose Per Day
Morphine	20 mg/mL	25 mg
Hydromorphone	15 mg/mL	10 mg
Fentanyl	10 mg/mL	1000 mcg
Sufentanil	5 mg/mL	500 mcg
Bupivacaine	30 mg/mL	15 – 20 mg*
Clonidine	1000 mcg/mL	600 mcg
Ziconotide	100 mcg/mL	19.2 mcg

*May be exceeded in end-of-life care and complicated cases as determined by medical necessity.

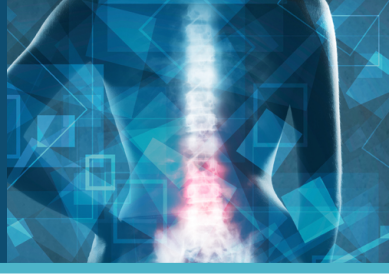
Deer TR, Pope JE, Hayek S, et al. *Neuromodulation.* 2017;20(2):96-132.

First Responders



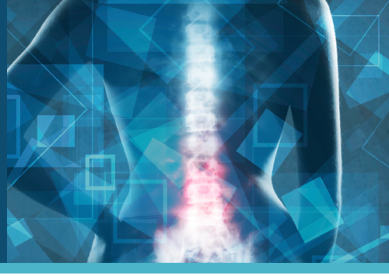
- First responders should be trained to identify patients with implantable systems
- Should be able to distinguish between pacemakers, SCS, and implantable pumps
- When an implantable pump is suspected, first responder should have the info available and ability to contact a pump manager or representative of pump manufacturer

Dosing Takeaways: Consensus Points



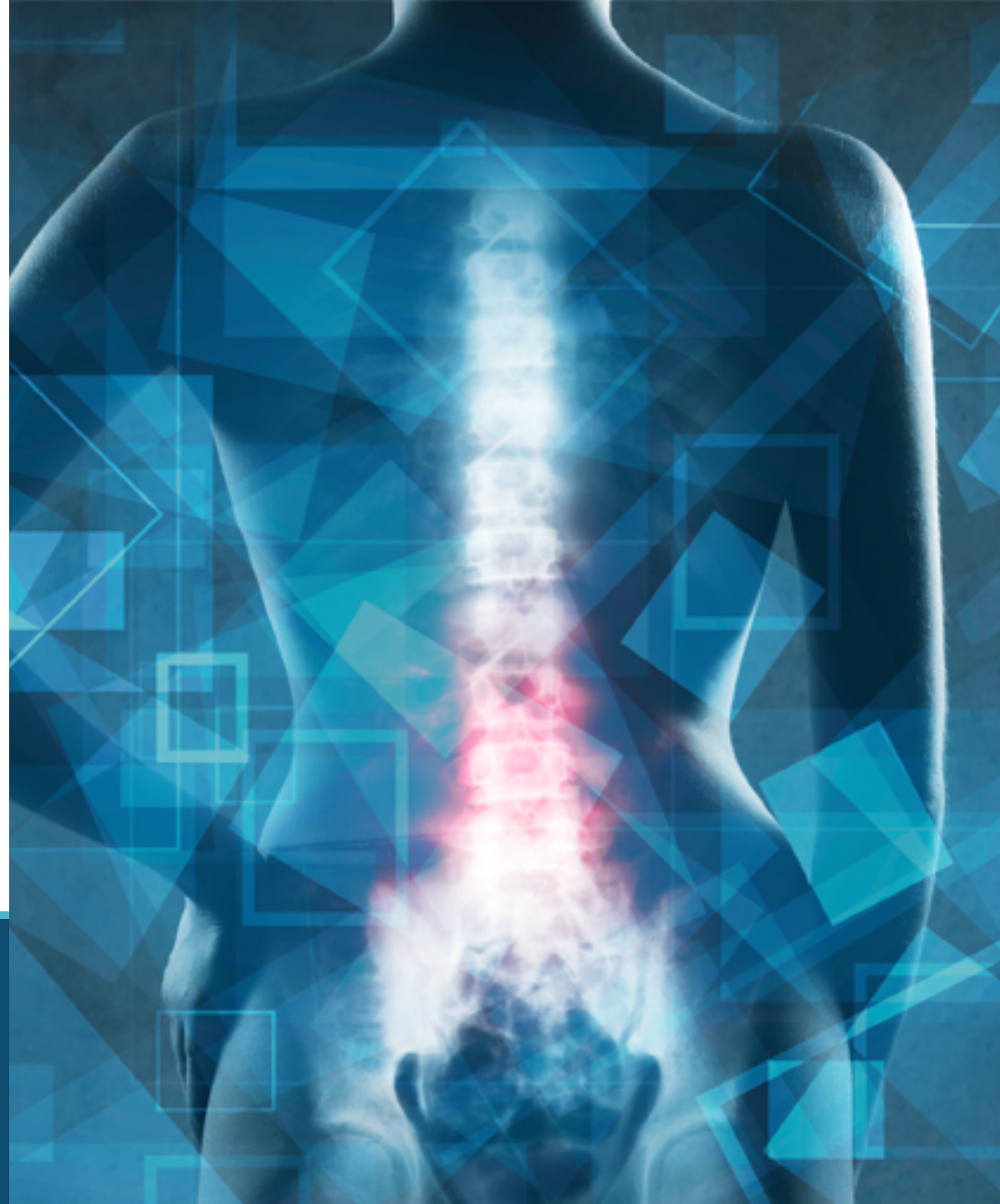
- The initiating dose of intrathecal opioids and ziconotide should be as low as reasonably expected to provide relief
- The initiating dose of intrathecal opioids and ziconotide delivered continuously should be 50% or less of the dose used during bolus trialing
- PACC recommends careful attention to side effects when adding an adjuvant drug to a primary drug

SMART Goals



- Consider IT therapy early rather than high dose opioids
  - There is evidence of an ongoing role for IT therapy for cancer and certain noncancer conditions
- Review and integrate key concepts of the PACC guidelines into clinical practice

Questions?



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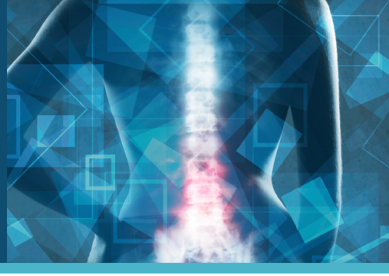

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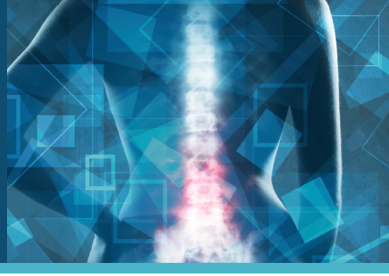

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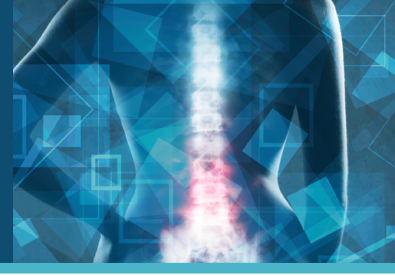

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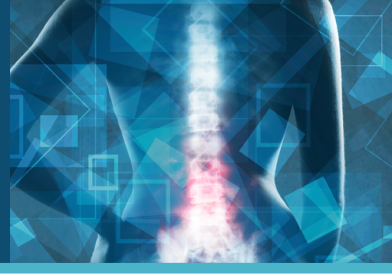

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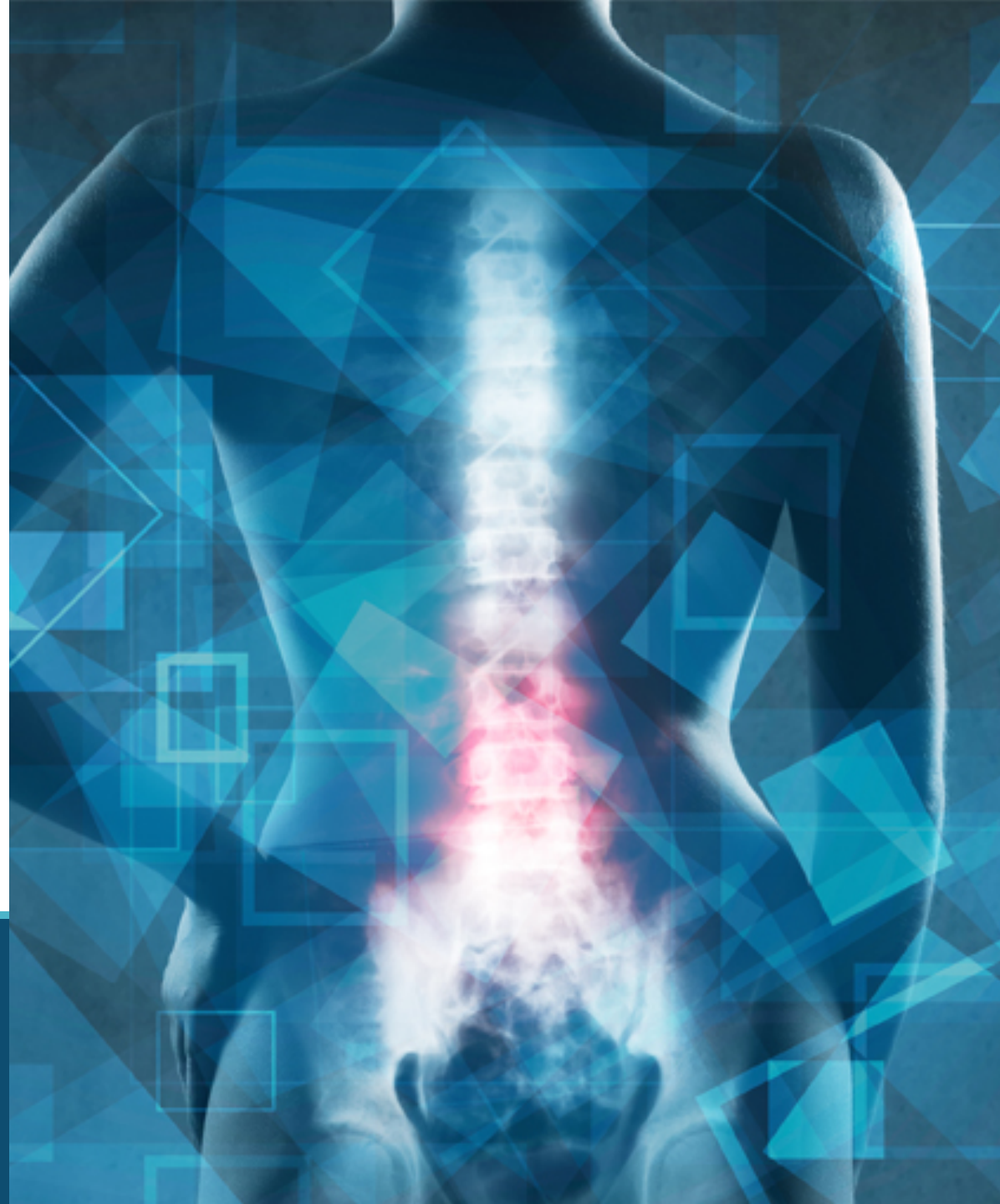
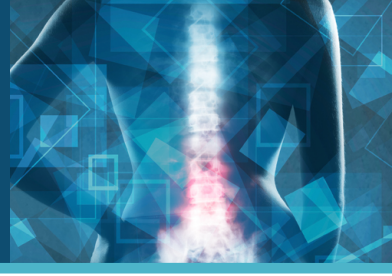


Supplemental References



1. Smith TJ, et al. *J Clin Oncol* 2002;20:4040-40.49.
2. Dominguez E, et al. *Pain Pract* 2002;2:315-325.
3. Grider JS, et al. *Pain Physician* 2011;14:343-351.
4. Hamza M, et al. *Pain Med* 2012;13:1304-1313.
5. Bernards CM. *Curr Opin Anaesthesiol* 2004;17:441-447.
6. Krames ES. *J Pain Symptom Manage* 1993;8:36-46.
7. Friese S, et al. *Investigat Radiol* 2004;39:120-130.
8. Henry-Feugeas MC, et al. *Magn Reson Imaging*. 2000;18:387-395.
9. Bernards CM. *Anesthesiology* 2006;105:169-178.
10. Doleys DM. *Neurosurg Clin North Am* 2003;14:409-417.
11. Doleys DM. *Neuromodulation* 2001;4:93-97.
12. Doleys DM. *Neuromodulation* 2006;9:270-283.