Opiates…What do we do know

Evidence Based Information Alternatives And Appropriate Use Of Opiates

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OUTLINE

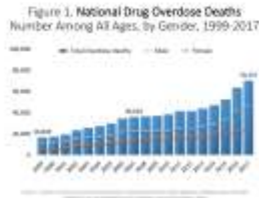
- INTRODUCTION
- What is Pain?
- Repel effects of chronic pain
- Assessment of Acute and Chronic Non-Cancer Pain:
  - low back,
  - headaches,
  - neuropathic,
  - fibromyalgia
- Treatment of Acute Pain and Chronic Non-Cancer Pain
  - Medication
  - Interventional Procedures
  - Alternative Treatments
  - Special Populations: pregnant, nursing, treatment of acute pain in patients on chronic opioid therapy, treatment of acute pain in patients who are actively addicted to opioids
  - CHOICE OF PAIN MEDICATIONS: NON OPIOID and OPIOID
- Pain Medications Indications, Limitation, side effects:
- Non opioid Pain Medications
- OPIOID PAIN MEDICATIONS
  - Choice of drug
  - Short versus long acting opioid
  - Dose of opioid
  - Morphine equivalents
  - DURATION OF OPIOID THERAPY
  - RISK OF LONG-TERM OPIOID USE
  - EXCESSIVE PRESCRIPTION
  - EXISTING GUIDELINES AND STATE RECOMMENDATIONS
- PATIENT INSTRUCTION
  - Expectation for pain relief
  - Risks of opioid therapy
  - How to take medication
  - Safe storage and disposal
  - Written information for patients
- STRATEGY FOR PAIN CONTROL at Integrated Pain Management
- PRESCRIPTION DRUG MONITORING PROGRAMS
- SUMMARY AND RECOMMENDATIONS
- REFERENCES

Objectives

At the conclusion of this presentation attendees will be able to:

- Assess and treat pain: Low back, headaches, neuropathic, fibromyalgia
- Apply evidence based methods in the treatment of pain: Opiates and Alternatives
- Describe goals of pain management: Clearly define expectations to patients

Where we are today?



Current Drug Overdose Epidemic in USA

- 1999 to 2016: >630,000 people died from a drug overdose.
- 1990s: Began - **driven by dramatic increases in prescribing of opioids for "chronic pain".**
- In 2010: **Second wave -** rapid increases - **Heroin**.
- 2013: **Third wave** - increased significantly - **Illicit synthetic opioids, Fentanyl.**
- Increased ED visits and hospital admissions - **Fatal and non fatal.**

2018 ANNUAL SURVEILLANCE REPORT OF DRUG-RELATED RISKS AND OUTCOMES. https://www.cdc.gov/drugoverdose/pdf/pubs/2018-cdc-drug-surveillance-report.pdf

How did we get here?
A brief history on journey of opioids.

- 1600s, many European doctors gave their patients Opium to relieve pain.
- 1800s, Ether and Chloroform were introduced as anesthetics for surgery.
- 1900s, Morphine and Heroin use as pain medications.

Some of the Debates

Before 1900s

- Concern: **Managing pain in Acute Care** (surgery, injury) & painful cancer death
- the ethics of operating on unconscious patients
- Considered **Anesthesia a Divine Blessing.**
- Chronic pain without obvious pathology => " **deluded or malingers or drug abusers**." => Drug, psychotherapy or neurosurgery.

After 1900s

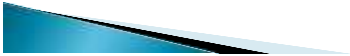
- Debate to improve the **quality of patients' lives** vs patient become vulnerable to **addictions** vs risk of **overdose & death.**
- Pain can be **without Stimulus** - Sensory and Emotional experience.
- **Chronic Pain Syndrome:** Pain + Psychological + Social problem.

INTRODUCTION

Chronic Non Cancer Pain

Chronic non cancer pain – Why it's important?

- Among the **most frequent** reasons - seeking medical attention in the US. 20 to 50% PCP visits.[1]
- >100 million people affected in US.[1,2]
- >100 billion dollars in direct and indirect expenses [3].(direct costs and lost wages)
- Pain-related expenditures exceed those for cancer, heart disease, and diabetes combined [4]. +



What is Pain?

- **Current Definition of Pain: "***An unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage."*
- **Notes: "Pain is always subjective."** This definition avoids tying pain to the stimulus. Activity induced in the nociceptor and nociceptive pathways by a noxious stimulus is not pain, which is **always a psychological state,** even though we may well appreciate that pain most often has a proximate physical cause.

(**International Association for the Study of Pain)**

Pain related other terms

- **Pain threshold:** The minimum intensity of a stimulus that is perceived as painful.
- **Pain tolerance level:** The maximum intensity of a pain-producing stimulus that a subject is willing to accept in a given situation.
- **Chronic Pain:** Pain persists for ≥12 weeks

Repel Effect of Chronic pain

Pain impact — Activities of daily living (ADLs), on function (social and physical) and overall quality of life:

●Social and recreational functioning

●Mood, affect, and anxiety

●Relationships

●Occupation

●Sleep

●Exercise

Repel Effects of Chronic pain

- **"Chronic Pain Syndrome."** Behavioral Change due to Persistent pain+Psychological+Social problems
- Persisting pain that may have arisen from organic causes
  - compounded by psychological
  - social problems
  - leads to behavioral changes.

COMMON CAUSES OF CHRONIC PAIN

●**Neuropathic pain** (either peripheral, including post-herpetic neuralgia, diabetic neuropathy; or central, including post-stroke pain or multiple sclerosis)

●**Musculoskeletal pain** (eg, back pain, myofascial pain syndrome, ankle pain)

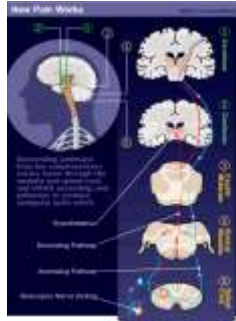
●**Inflammatory pain** (eg, inflammatory arthropathies, infection)

●**Mechanical/compressive pain** (eg, renal calculi, visceral pain from expanding tumor masses) [6]

Note: Most pain are multifactorial

Nociception

- Nociceptive pain, is caused by stimuli that threaten or provoke actual tissue damage.



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Neuropathic Pain

- Neuropathic pain - caused by damage/pathology within central or peripheral nervous system.
- Causes **are multiple, some are**
  - Diabetes mellitus,
  - Postherpetic neuralgia, and
  - Stroke.
- Quality of pain: Burning, Tingling, Electric shock, Weakness

Assessment of Acute and Chronic Non Cancer pain

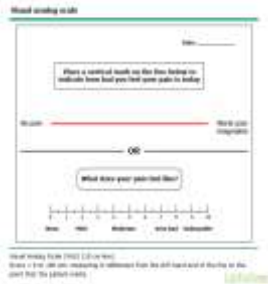
Brief Pain Inventory (BPI)

The BPI assesses

- Pain location,
- Intensity
- Pattern
- Patient beliefs
- Impact of pain on the patient's quality of life.

Pain Intensity Scale

- Sale from 0 to 10 is the most commonly used pain intensity rating tool. (NRS-11)
- Pain intensity increasing or decreasing



Physical Examination

- A baseline evaluation complete physical examination, including **a detailed neurologic assessment**, should be performed, regardless of the patient's area of complaint.
- Help to assess patient's progress in terms of
  - Functional capacity,
  - Range of motion,
  - Endurance,
  - Strength, and other
  - Pain-related clinical manifestations.

Diagnostic testing

Blood test, Imaging, other test: NCS, EMG

- Appropriate laboratory, imaging, and other testing can be helpful to evaluate or follow certain painful conditions.
- Diagnostic abnormal findings may not be source of the patient's pain syndrome.

Assessment of Acute and Chronic Pain

- **Low back pain**
- **Fibromyalgia**
- **Neuropathic pain**
- **Headaches**

Low Back Pain

- 84% of adults have low back pain at some time in their lives [1,2]
- For many individuals, episodes of back pain are self-limited.
- Acute period (four weeks)
- "Advice to stay active; Activity and exercise as tolerated (bed rest no more than 2-3 days." (Kaiser Guidelines)
- Subacute back pain (lasting between 4 and 12 weeks)
- **Chronic back pain (persists for ≥12 weeks)** [3]
- Rarely, back pain is a harbinger of serious medical illness.

ETIOLOGIES

ASSESSMENT OF LOWER BACK PAIN: PHYSICAL EXAM

Sign	Condition
Paravertebral muscle spasm	• Mechanical disease
Asymmetric range of motion of the lumbar spine	• Mechanical disc disease • Unstable lumbar spine
Spinal tenderness	• Vertebral compression fracture • Infection
Weakness of the L4-L5 and L5-S1 muscles	• Mechanical disc disease • Lumbar spinal stenosis
Normal exam of the lumbar spine	• Osteoporotic sacral fracture • Hip disease • Tumor • Referred visceral pain

Slide 10

https://slideplayer.com/slide/11883172/

Complete Back Care: Red Flags

Taken from KP Referral Tapestry for Pain Management

Diagnostic Testing and Imaging for Low Back Pain

When to do diagnostic imaging and testing:

- Severe or progressive neurologic deficits are present
- Serious underlying conditions are suspected on the basis of history and physical examination
- When pain persists and failed initial treatment (use clinical judgement).[23]

Fibromyalgia

- Etiology: Unknown
- Pathophysiology: Unclear
- Genetic - NO clear association with **any single candidate gene**
- Studies suggested: 1 relatives with FM Vs 1 relatives with RA, it is 8.5 times more likely to have FM
- Physical or emotional trauma may trigger
- 2 to 4 percent of the population, (American College of Rheumatology (ACR)).
- Mostly women, in early to middle adulthood.

Fibromyalgia Cont.

Hypothesis:

- A disorder of pain regulation
- Due to neuro endocrinological changes in the central and peripheral nervous systems,
- In genetically susceptible individuals,
- Possibly in response to environmental triggers.
- This results in heightened pain perception and hypersensitivity to numerous stimuli.

Other overlapping diagnoses,

- Migraine
- Tension headaches
- TMJ (Temporomandibular joint disorder)
- IBS (Irritable bowel syndrome)

(The ACTTION-American Pain Society Pain Taxonomy (AAPT): an evidence-based and multidimensional approach to classifying chronic pain conditions.)

Studies Proved Fibromyalgia Is a Real Medical Condition

- October 1, 2015, Fibromyalgia official diagnostic ICD-10-CM codes given.
- In June 2007, Lyrica (pregabalin) became the first FDA-approved drug for specifically treating fibromyalgia;
- June 2008, Cymbalta (duloxetine hydrochloride) became the second;
- January 2009, Savella (milnacipran HCl) became the third.

- https://www.fda.gov/consumers/consumer-updates/living-fibromyalgia-drugs-approved-manage-pain
- https://www.fibrocenter.com/fibromyalgia-disease

Year	Event
1981	The first scientific study confirmed that symptoms and tender points could be found in the body.
1990	The American College of Rheumatology wrote the first set of guidelines to help diagnose fibromyalgia.
2005	The first guidelines for treating fibromyalgia pain were published by the American Pain Society.
2007	The first prescription medication was FDA-approved to manage fibromyalgia.

Characteristic features and diagnostic evaluation for fibromyalgia

History
Widespread (multisite) pain
Present for at least 3 months
Fatigue, sleep disturbances
Other symptoms, such as cognitive disturbances, headaches, bowel irritability
Physical examination
Widespread (multisite) tenderness
Absence of joint swelling, inflammation
Laboratory testing
Normal acute phase reactants (ESR/CRP)
Normal CBC
In selected cases, muscle enzymes, thyroid testing

ESR: erythrocyte sedimentation rate; CRP: C-reactive protein; CBC: complete blood count.

UpToDate

Stepwise fibromyalgia therapy

Initial approach in every patient
Confirm the diagnosis
Education: explain the condition
Evaluate and treat comorbidities, such as mood and sleep disturbances
Most patients
Trial with low-dose tricyclic antidepressants or selected antidepressants or anticonvulsants proven effective in fibromyalgia
Exercise program
Patients not responding to above
Specialty referral (eg, rheumatologist, physiatrist, psychiatrist, pain management)
Combinations of drug therapies
Physical therapy sessions
Psychological interventions, such as cognitive behavioral therapy
Multidisciplinary programs

Adapted from: Goldenberg DL, Burckhardt C, Crofford L. Management of fibromyalgia syndrome. JAMA 2004; 292:2388.

UpToDate

Treatment options for chronic pain

6 major categories

- Pharmacologic
- Physical medicine
- Behavioral medicine
- Neuromodulation
- Interventional
- Surgical approaches

Overview of the treatment of chronic non-cancer pain

Topic Outline

- APPROACH TO THE PATIENT
- PHARMACOLOGIC OPTIONS
- CHOICE OF THERAPY BY TYPE OF PAIN
  - Neuropathic pain
  - Nociceptive pain
- NONOPIOID ANALGESICS
  - Acetaminophen
  - Nonsteroidal anti-inflammatory drugs
    - - Side effects
- ANTICONVULSANTS
  - Gabapentin and pregabalin
  - Other antiepileptics
- ANTIDEPRESSANTS
  - Tricyclic antidepressants
  - Serotonin norepinephrine reuptake inhibitors
    - - Venlafaxine
    - - Duloxetine
  - Concurrent depression
- ADJUVANT MEDICATIONS
  - Topical agents
  - Antispasmodics
  - Botulinum toxin
  - Benzodiazepines
  - Cannabis and cannabinoids
- OPIOIDS
- NONPHARMACOLOGIC THERAPIES
  - Behavioral medicine approaches
    - - Cognitive-behavioral therapy
    - - Biofeedback
  - Physical medicine approaches
    - - Spinal manipulation
  - Neuromodulation approaches
    - - Transcutaneous electrical stimulation
    - - Spinal cord stimulation
    - - Deep brain stimulation
  - Interventional approaches
  - Surgical approaches

Opioid for chronic non-cancer pain management 1

- Mechanism of action
- Opioid formulations
    - \- Short-acting
    - \- Long-acting
    - \- Abuse deterrent

INDICATIONS FOR OPIOID THERAPY

EVALUATION OF RISK PRIOR TO INITIATING THERAPY

- Risk assessment
    - \- Risk assessment tools
- Risk stratification
    - \- Low risk
    - \- Moderate risk
    - \- High risk

INITIATING A TRIAL OF OPIOID THERAPY

- Setting patient responsibilities, expectations, and treatment goals
    - \- Opioid agreement/consent form
- Choice of agent and dose
- Monitoring for adverse effects
- Risks of misuse and overdose
    - \- Drug interactions
- Follow-up during trial
- Monitoring and risk management strategies during trial

Opioid for chronic non-cancer pain management 2

CHRONIC OPIOID THERAPY

- Choice of agent and dosing for chronic therapy
    - \- Converting from IR/SA to ER/LA
    - \- Buprenorphine for chronic pain
    - \- Methadone and fentanyl
- Follow-up and monitoring during chronic opioid therapy
    - \- Ongoing risk assessment tools
    - \- Other issues

PATIENTS WITH ABERRANT BEHAVIORS

DISCONTINUING THERAPY

REFRACTORY PAIN

SPECIAL POPULATIONS

- Older patients
- Kidney disease
- Liver failure

SUMMARY AND RECOMMENDATIONS

NONOPIOID ANALGESICS

NONOPIOID ANALGESICS

- Acetaminophen
- Nonsteroidal anti-inflammatory drugs
    - \- Side effects
- ANTICONVULSANTS
    - Gabapentin and pregabalin
    - Other antiepileptics
- ANTIDEPRESSANTS
    - Tricyclic antidepressants
    - Serotonin norepinephrine reuptake inhibitors
        - \- Venlafaxine
        - \- Duloxetine
- ADJUVANT MEDICATIONS
    - Topical agents
    - Antispasmodics
    - Botulinum toxin
    - Benzodiazepines
    - Cannabis and cannabinoids

Treatment Approach for Patients with Chronic Pain 1

- **Medication - Not the sole focus to treatment goals :**
  - Used when needed with other treatment modalities [6].
- **Setting reasonable expectations for response.**
  - Ongoing **evaluation, education and reassurance**.
- A**ddress** when deciding between different treatment modalities:
  - **patient expectations**
  - **patient preferences**
  - Patient should be **informed of the rationale**
    - **Expected benefits of therapy**
    - **Duration of treatment**
    - **Possible and likely side effects**

Treatment Approach for Patients with Chronic Pain 2

- Currently available treatment modalities can provide **about 30% decrease in pain**, which is clinically significant and improve the patient's quality of life [7] [8].
- **Collaborative care models** in primary care is recommended to improve pain management and patient satisfaction [4,5].
- **A multidisciplinary team** approach often results in **optimal patient outcomes** [3].

Choice Of Therapy By Type Of Pain

Choice of an initial pharmacologic agent will be guided by individual patient: Nociceptive vs Neuropathic

- Pathophysiology of the pain.
- Other symptoms and comorbidities,
- Other medications being taken,
- Organ reserves,
- Pharmacokinetics/pharmacodynamics,
- Likelihood of adverse effects.

5 FDA Approved Neuropathic Pain Medication:
- Gabapentin
- Pregabalin
- Duloxetine5% Lidocaine patch
- Carbamazepine (1st line for Trigeminal Neuralgia)

Primarily involves non narcotic and opioid analgesia (algorithm 2).

Nociceptive pain: Pharmacologic Therapy

Medication is used in conjunction with

- **Nonpharmacologic** therapies and
- Approaches to relieve the **source of the pain.**

- 1st Line Therapy: acetaminophen or NSAIDs is typically recommended for Osteoarthritis (OA) [21,22] & chronic low back pain [23], however studies have proven **NSAIDs are superior in reducing pain for OA.** [24,25]
  - Daily recommended dose of Acetaminophen: Generally recommended upto **4 gram a day** - however advised to use Clinical judgement, for studies showed ALT elevation when used daily 4 gram of Acetaminophen by healthy individual. [26].

List of NSAIDs

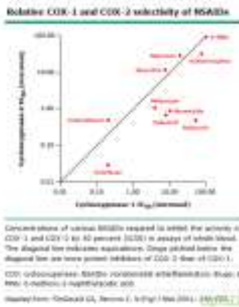
List of Prescription NSAIDs

- Celecoxib (Celebrex)
- Diclofenac (Voltaren)
- Etodolac (Lodine)
- Ibuprofen (Motrin)
- Indomethacin (Indocin)
- Ketoprofen (Orudis)
- Ketorolac tromethamine (Toradol)
- Mefenamic acid meloxicam (Mobic)
- Nabumetone (Relafen)
- Naproxen sodium (Anaprox)
- Piroxicam (Feldene)
- Sulindac (Clinoril)

OTC NSAIDs

- Ibuprofen (Motrin, Advil, Nuprin, Medipren)
- Aspirin (Bayer, Excedrin, Bufferin)
- Naproxen sodium (Aleve)

NSAIDs Medication Guide approved by FDA:
"https://www.fda.gov/media/73092/download"



NSAIDs Adverse Effects

Serious side effects:

MI, Risk of Heart Failure, Stroke
Hypertension
Gastric Ulcer/Bleeding
Risk of Renal Failure
Serious Allergic reaction

Other side effects:

Dizziness/Drowsiness

Headache

Leg swelling

Liver problems

Nausea/Vomiting/Diarrhea/

Heartburn/Stomach pain

Ringing in the ears

Treatment of acute low back pain

- INTRODUCTION
- GENERAL APPROACH TO CARE
- NONPHARMACOLOGIC THERAPIES
  - Heat
  - Massage
  - Acupuncture
  - Spinal manipulation
  - Exercise and physical therapy
  - Other
- PHARMACOTHERAPY
  - Initial therapy
    - Nonsteroidal antiinflammatory drugs
    - Limited benefit of acetaminophen
  - Second-line therapy
    - Combination with muscle relaxants
  - Refractory or severe pain
    - Opioids
    - Tramadol
  - Other medications
- PHARMACOTHERAPY
  - Initial therapy
    - Nonsteroidal antiinflammatory drugs
    - Limited benefit of acetaminophen
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    - Combination with muscle relaxants
  - Refractory or severe pain
    - Opioids
    - Tramadol
  - Other medications
- PATIENT EDUCATION
- PROGNOSIS
- PREVENTION
- INFORMATION FOR PATIENTS
- SUMMARY AND RECOMMENDATIONS

Non Pharmacologic Treatment of acute low back pain

Evidence of the effectiveness of these therapies **low to moderate:**[7]

- Heat
- Massage
- Acupuncture
- Spinal manipulation
- Exercise and physical therapy

With **little or no evidence to:**

- Cold
- Traction
- Lumbar supports
- Mattress recommendations
- Yoga
- Paraspinal injections - epidural spinal, trigger point, or facet joint injections

Opioid and Steroid for Acute Low back pain

- **OPIOIDS and Tramadol have limited evidence to support their use.**
- If other drugs failed or contraindicated, consider **limited use of opioid for 3-7 days.**
- **Tramadol should not be prescribed for more than 2 weeks.** (See 'Refractory or severe pain' above.)

- **Drugs with limited or no evidence of effectiveness, are reserved when initial therapy failed, include**
  - **Systemic glucocorticoids**
  - **Antidepressants**
  - **Antiepileptics**
  - **Topical agents**
  - **Herbal therapies** (See 'Other medications')

- If no improvement **after four weeks** of pharmacotherapy, the patient should be reassessed. (See 'Prognosis')

Fibromyalgia Pharmacology Treatment

Headache

Headache (HA) is among the most common medical complaints.

Types of Headache

- Migraine
- Tension-type headache
- Cluster headache
- Secondary headache 'Danger signs'

Imaging Not Required: Low-Risk Features

Patients who are **unlikely** to have serious underlying cause for headache [3,4]:

●Age ≤50 year

●Features typical of primary headaches (table 1)

●History of similar headache

●No abnormal neurologic findings

●No concerning change in usual headache pattern

●No high-risk comorbid conditions

●No new or concerning findings on history or examination

Further Evaluation (CT and MRI) Danger Signs

Red Flag: "SNOOP" is a reminder - can cause acute or subacute headache [14,15]:

●**Systemic symptoms,** illness, or condition (eg. fever, weight loss, cancer, pregnancy, immunocompromised state, including HIV)

●**Neurologic symptoms** or abnormal signs (eg. confusion, impaired alertness or consciousness, papilledema, focal neurologic symptoms or signs, meningismus, or seizures)

●**Onset is new** (particularly for age >50 years) or sudden (eg, "thunderclap")

●**Other** associated conditions or features (eg, head trauma, illicit drug use, or toxic exposure; headache awakens from sleep, is worse with Valsalva maneuvers, or is precipitated by cough, exertion, or sexual activity)

●**Previous headache history:** change from usually HA presentation/frequency/severity.

Need for emergency evaluation

Laboratory tests, imaging, and LP for CSF analysis may be included:

●**Sudden onset "thunderclap" headache.**" subarachnoid hemorrhage (table 5).

●**Acute or subacute neck pain or headache with Horner syndrome and/or neurologic deficit** – ischemic stroke or transient ischemic attack. [17,18].

●**Headache with suspected meningitis or encephalitis** – Fever, altered mental status, with or without nuchal rigidity.

●**Headache with global or focal neurologic deficit or papilledema** – increased ICP,

●**Headache with orbital or periorbital symptoms** – visual impairment, periorbital pain, acute angle closure glaucoma, infection, inflammation, or tumor involving the orbits.

●Headache and possible carbon monoxide exposure.

(See "Overview of thunderclap headache".)

(See "Evaluation of the adult with nontraumatic headache in the emergency department".)

Treatment of TTH 1

Identifying and eliminating the triggering or exacerbating factors.

Acute therapies: TTH who have up to 10 headache days per month

- acetaminophen
- nonsteroidal anti-inflammatory drugs.

- Chronic tension-type headache: (>10 days/month)
  - daily prophylactic medications (eg, tricyclic antidepressants), behavioral therapies and physical therapy or the combined use of these interventions is often optimal. (See "Tension-type headache in adults: Preventive treatment")

Treatment of TTH 2

Frequent episodic TTH or chronic TTH.

- amitriptyline has the strongest date - Avoid patient with obesity, bipolar disease, or cardiac conduction defects.)
- may consider:
  - antidepressants mirtazapine and venlafaxine
  - anticonvulsants: topiramate and gabapentin, [19-22].
  - muscle relaxant tizanidine.

- **Selective serotonin reuptake inhibitors** are **NOT effective** for TTH prophylaxis.
- Trigger point injection; possibly effective
- botulinum toxin: uncertain
- **Behavioral and tricyclic therapy** — A combination of the two therapies may be **superior to either alone.** ('Combined behavioral and tricyclic therapy')
- heat, ice, acupuncture, massage

Acute Migraine Management

Mild/Mod with no n/v:

Acetaminophen, NSAIDS, combination analgesics (acetaminophen-asa-caffeine)

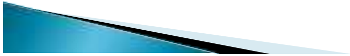
N/V? give antiemetic (po/pr) first : metoclopramide, chlorpromazine, prochlorperazine

Moderate to Severe Attacks

No n/v: oral triptans, sumatriptan-naproxen

N/V:: non-po route triptans- subcutaneous or nasal sumatriptan, zolmitriptan non-oral antiemetics, IV DHE

pts with variable attacks may need multiple options for self-management!



Which Triptan?

Formulary (few trials comparing head to head)

Naratriptan/frovatriptan slower in onset/lower efficacy, less SEs

Patients who don't respond to one triptan may respond well to another

50mg of Imitrex is usually suboptimal dose for adults

Consider analgesic response and SE's in determining efficacy

Propranolol increases rizatriptan levels by 70%

Triptan Limitations

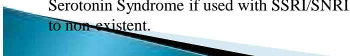
Take early on- may not work if CA develops it

May contribute to analgesic overuse HA if taken >10 days per month

Avoid with: hemiplegic migraine, basilar migraine, ischemic stroke, ischemic heart disease, pregnancy, Prinzmetal's angina, uncontrolled HTN (albeit limited evidence)

CI; use with MAOIs (exceptions are eletriptan, frovatriptan, naratriptan)

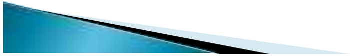
Serotonin Syndrome if used with SSRI/SNRI? risk appears to be very low to non-existent.



Migraines and the ED

Account for 1.2 million ED visits annually

IV opioids (hydromorphone most commonly) used first line to treat migraine in more than 50% of all ED visits



Friedman and colleagues study

127 pts with migraine (no opioid in the past month)

Almost DOUBLE the number of participants receiving IV prochlorperazine + diphenhydramine achieved sustained HA relief (60%) after 48 hours than those receiving **IV hydromorphone** (31%)

Hydromorphone arm: 31% requested a second dose compared to prochlorperazine/diphenhydramine arm (8%)

36% of pts in hydromorphone arm requested other pain relievers compared to 6% for prochlorperazine/diphenhydramine arm.

Non Opioid treatment superior to opioids for migraine. Friedman BW, et al. Neurology. 2017

ED Management of Acute Migraine

1) Sumatriptan 6mg sc

2) Antiemetic/Dopamine receptor blocker:

Metoclopramide 10mg IV

Prochlorperazine 10 mg IV IM

Chlorpromazine 0.1mg/kg IV to a total dose of 25 mg IV

3) DHE 1mg IV + Metoclopramide 10mg IV

4) Ketorolac 30 mg IV or 60 mg IM

consider IV diphenhydramine 12.5-25 mg IV q hour up to 2 doses- to prevent akathisia/dystonic reactions to IV antiemetics

ED Management Cont.

Alternate options (more aggressive):

*High-dose metoclopramide (20mg IV q 30 minutes up to 4 doses) + diphenhydramine

*DHE 45 1mg IV + metoclopramide 10mg IV (use if metoclopramide monotherapy is ineffective)

- DHE 45 - do not use as monotherapy
- CI'd in pt's with hx of ischemic vascular dz, HTN, do not use W/I 24 hours of triptan/ergot-like agent. Do not use in combo with potent CYP3A4 inhibitors (PIs, azole antifungals, some macrolides) or with peripheral/central vasoconstrictors. Do not use if pregnant/nursing

DEXAMETHASONE

Reduce the risk of early HA recurrence (not shown to reduce pain)

10-25 mg IV or IM as a single dose (frequent use not recommended d/t cumulative toxicity)

Take-Home Point

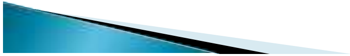
Do not use opioids in the acute management of migraine headache!

(significantly more likely to return to the ED with a HA w/i 7 days of the original visit)

Risk of Opioid outweigh the benefit

Studies show the risk of opioids are likely greater than their benefits when used for non-cancer chronic conditions including back pain, HEADACHES, and fibromyalgia

Franklin, G.M (2014). "Opioids for chronic non-cancer pain: A position paper of the American Academy of Neurology 83 (14): 1277-1284



AMPP Study

Opioid use for migraines was associated with

More severe HA related disability (MIDIAS scores)

More severe symptomatology

More comorbidities (depression, anxiety, cardiovascular diseases and events)

Greater health care resource utilization (ED, UC)

Buse, D et al

Headache (2012) 52: 18-36

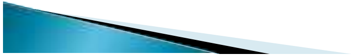
AMPP study

8 days or more/month use of opioids was a risk factor to progress to medication overuse headaches (MOH)

Bigal et al (2008) Headache, 48: 1157-1168

Choosing Wisely

This campaign advocates for avoidance of the use of opioid or butalbital treatment for migraine; except as a last resort.



Chronic Daily Headaches and Opioids

<u>Saper and Colleagues 5 yr study:</u>

Increasing # pts violated contractual agreements, used meds inappropriately, multi-sourced rxs, tried to fill rx early, or claimed to lose them and request more

Many pts who reported improvements in pain control with opioids did NOT return to work or demonstrate improvements in measures of disability (MIDAS)

More than half required escalating doses during the 5 yr study

Saper et al (2004) Neurology 62: 1687-1694

Acute Migraine in Pregnancy/Postpartum

Acetaminophen 1000 mg

If above ineffective, consider: metoclopramide 10 mg

codeine 30mg

Butalbital-acetaminophen-caffeine

(caffeine thought to be safe up to total daily amount of <200mg)

avoid prolonged use of butalbital or codeine near term d/c risk of NAS

Pregnancy Cont.

second line:

ASA, NSAID (naproxen, ibuprofen, ketorolac)- safest in the 2nd trimester

in the 3rd trimester, limit use to less than 48 hours (serious concerns including necrotizing enterocolitis, pulmonary hypertension, oligohydramnios..)

Third-line: Opioids , triptans

N/V: if needed, meclizine, diphenhydramine, promethazine preferred

Migraine Prevention

Reasonable to start if > 4 HA's per month or HA that lasts >12 hours

Short term therapy for menstrual migraine

Helps prevent progression from episodic to chronic

Avoid overuse of acute HA meds (analgesics, triptans, ergots)

Efficacy often first noted at 4 weeks and can increase for months

Migraine Prevention

First line: Amitriptyline, venlafaxine, propranolol, topiramate

Novel: Calcitonin gene-related peptides (CGRP) antagonists (erenumab..) not first line d/t high cost, absence of long-term safety data, lack of head to head trials with other first line agents

Topiramate

Anticonvulsant

Starting dose 25mg, increase weekly to max of 100 mg bid for migraine prevention

Doses of 100mg or less well tolerated (paresthesia most common SE)

Weight loss is a unique SE and dose dependent

Possible residual benefit for migraine for up to 6 months after it is d/c'd

Doses >100 mg/day may induce estrogen metabolism and impact the efficacy of OCPs- (risk of oral clefts and SGA in pregnancy- likely dose dependent)

Special Considerations

Child-bearing potential: verapamil. Avoid VPA! Caution with topiramate)

HTN + smoker or >60- do not use bb first line (may have higher rate of stroke

Consider co-morbid conditions- "two birds with one stone"

Chronic migraine treatment

First-line : Amitriptyline, propranolol, topiramate, venlafaxine

Second-line agents:
- Botulinum toxin type A (onabotulinumtoxinA)
- CGRP antagonists (erenumab, fremanezumab, and galcanezumab)
- Verapamil
- Other beta blockers (atenolol, metoprolol)
- Gabapentin
- Magnesium
- Riboflavin
- Candesartan
- Other tricyclic antidepressants (nortriptyline)

Third-line agents
- Tizanidine [33]
- Memantine
- Pregabalin
- Cyproheptadine
- Zonisamide

Antidepressants function - Mechanism of analgesic effect

- **Analgesia is not dependent on mood elevation,** and pain can be improved in euthymic patients.
- **Inhibition of norepinephrine reuptake appears to be the most important mode of action,** but serotonergic and dopaminergic effects also may play a role in analgesia [19].
- TCA > SNRI analgesic effective

Side Effects of Antidepressant Medications

Side effects of tricyclic antidepressants

Anticonvulsant Pain Medication

Used since 1960s.

Gabapentin and pregabalin - (Common side effects: Somnolence, dizziness, ataxia)

- Gabapentin is primarily found effective for the treatment of
  - postherpetic neuralgia and
  - painful diabetic neuropathy [55,56].
- Initiate treatment at a low dose with gradual increases until pain relief, dose limiting adverse effects, or 3600 mg per day in three divided doses is achieved. An adequate trial require 2 months or more.
- Pregabalin may provide analgesia more quickly than gabapentin,
  - effective at lower initial dose (150 mg/day)
  - a shorter time required to titrate to a full dose [58].

Other Antiepileptics drugs used for chronic pain and Headache: topiramate, lamotrigine, levetiracetam phenytoin, sodium valproate, zonisamide, tiagabine,

Common Side Effects of Antiseizure Drugs

Antispasmodic Drugs

- Treating muscle spasm
- Mechanism of action is sedation
- Can cause CNS depression cautiously with opioids or with sleep aids. Benzodiazepine and Barbituates
- Avoid for 65 years or older

Muscle relaxants for chronic pain

Drug	Dose
Cyclobenzaprine	10 mg three times daily (10 to 40 mg/day)
Carisoprodol (Soma)	350 mg three times daily
Baclofen (Lioresal)	5 mg once a day, titrated gradually to 5 to 20 mg three times daily
Methocarbamol (Robaxin)	1500 mg four times daily

UpToDate

ADJUVANT MEDICATIONS - Topical agents

Topical lidocaine - Gel , Cream, Ointment, Patch

5% Lidoderm Patch - efficacy and excellent tolerability - with postherpetic neuralgia and allodynia.

Capsaicin cream - A systematic review- moderate to poor efficacy for relief of chronic musculoskeletal or neuropathic pain.The major adverse effects of capsaicin are burning, stinging, and erythema at the site of application, leading to intolerance in up to one-third of patients

Topical nonsteroidal anti-inflammatory drugs - gel, spray, or cream, provide modest relief for acute than chronic musculoskeletal pain.

Special Population

- Pregnant
- Nursing: Gabapentin
- Treatment of acute pain in patients on chronic opioid therapy.
- Treatment of acute pain in patients who are actively addicted to opioids.

Pain Management during Pregnancy

- Use conservative and multi-modal ways to manage pain
  - Physical therapy,
  - Complementary therapies
  - Acupuncture and acupressure, and
  - Exercise.
- If drugs are needed to relieve pain during pregnancy,
  - acetaminophen is the preferred medication.
  - Nonsteroidal anti-inflammatory drugs can be used weeks 12 to 30 of pregnancy.
  - Opioids should be avoided
- **Opioid use disorder during pregnancy** or Pregnancy during chronic opioid use - Consider High Risk Pregnancy - Refer to Perinatologist - If needed doctors advice from Pain Management and/or Addiction Medicine can be sought for patient specific plan to avoid miscarriage and fetal withdrawal.

(See "Prenatal care: Patient education, health promotion, and safety of commonly used drugs", section on 'Pain and fever medications'.)

Pain Management for Breastfeeding Mothers

Safety of common analgesics in breastfeeding women — Most analgesics are considered safe during breastfeeding with some exceptions. Detailed information on specific drugs can be found in LactMed.

- Acetaminophen **(paracetamol)** [56]
- **NSAIDs** – Ibuprofen and diclofenac suppositories, which have a short half-life (<6 hours),56].
- Avoid Naproxen - for its long acting
- **Opioids** – Risks and benefits should be evaluated,
  - Including newborn signs of toxicity [54].
  - Limit it to the lowest effective dose and shortest duration to control acute pain.

Preferred opioid choices – The Committee on Drugs of the American Academy of Pediatrics prefers use of butorphanol, morphine, or hydromorphone over other opiates [57].

Treatment of acute pain in patients on chronic opioid therapy or history of opioids or substance use disorder

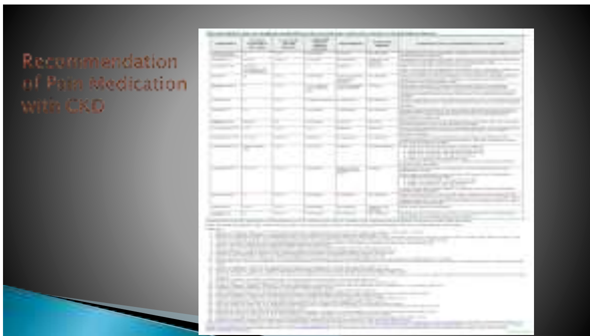
The goals of treating acute pain in patients chronically using opioids are

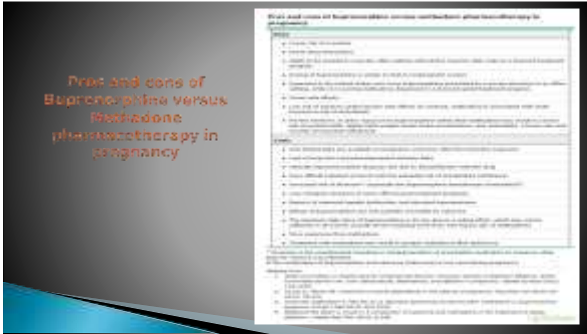
- To prevent withdrawal
- To provide adequate analgesia

Patients with a history of opioid or substance use disorder,

- To avoid triggering a relapse or worsening of the addiction disorder.

General approach: Combination therapy - Smallest dose - Shortest duration - Short acting opioid.





Cannabis and cannabinoids

- The use of cannabis and cannabinoids (plant base) for **chronic pain is controversial.**
  - **cannabis might alleviate neuropathic pain in some patients,** but
  - **insufficient evidence for other types of chronic pain** [108].

Referral to pain specialist

When to refer remains a controversial question. Many patients can be managed without specialty referral. Some of several reasons:

- Symptoms that are debilitating
- Symptoms located at multiple sites
- Symptoms that do not respond to initial therapies
- Escalating need for pain medication - (Maladaptive coping strategies have begun to emerge.)
- Drug aberrant behaviour.

Referral to Specialist

Low Back, Neck pain - Spine Center or Physical Medicine

Joint Pain due to OA - Orthopedic - See KP Referral Tapestry for guidelines.

Multiple Joints and Myofascial pain syndrome - Rheumatologist

https://cl.kp.org/scal/cpg/referral/neurology.html#headache_migraine

Prognosis of Acute Low back pain

- The prognosis for acute low back pain is excellent.
- Only 1/3 of patients seek medical care at all [56].
- Of those **70 to 90%** improve **within 7** weeks [57,58].
- Recurrences: **50%** of patients within **6 months** and **70%** within **12 months** [59,60].
- Only **5 to 10%** develop chronic low back pain [60-62].

REFERRAL TO PHYSICAL MEDICINE FOR MUSCULOSKELETAL PAIN

Condition	Action
[illegible]	[illegible]

REFERRAL PHYSICAL THERAPY / OCCUPATIONAL THERAPY

Accept

KP - Pain Management Referral Guide

Chronic Pain for 3 – 6 months:

Refer to Pain Management for:

- **Chronic pain lasting 3–6 months**

Fibromyalgia should be referred to Physical Medicine or Rheumatology

*****Headaches should be referred to Neurology***

******Evaluations for medication abuse should be referred to Addiction Medicine***

Chronic Pain for greater than 6 months

**** Patients must have completed a diagnostic workup from appropriate specialty (Physical Medicine, Neurology, Orthopedics, Rheumatology)***

Chronic Low Back Pain

Refer to Pain Management for:

- **Chronic pain has lasted more than 3 months and continues despite all medical and/or surgical interventions**
- **Patient is not currently a surgical candidate, is not pending surgery in the next 3 months or is declining surgical intervention**
- **Diagnostic workup has been completed**

KP Fibromyalgia Referral to Rheumatologist

- Consider **managing** these patients **in Primary Care.**
- Encourage patient to attend **chronic pain and/or sleep classes.**
- If assistance is needed **to confirm an uncertain diagnosis** and/or **ruling out alternate/additional causes** of the patient's pain (polymyalgia rheumatica, rheumatoid arthritis, myositis, etc.), refer to Rheumatology.

Much of what is practiced in the management of chronic pain comes from experience with cancer pain. The World Health Organization's (WHO) "analgesic ladder" approach to cancer pain management, which was originally published in the mid-1980s, outlines an approach to pain control that is based upon the severity of pain (figure 1) [10]. The WHO analgesic ladder should **NOT** be viewed as evidence-based or a best practice guideline, but it has widely influenced cancer pain management, and many of the strategies are used in nonmalignant pain.

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Have we become a pill culture?

- Nearly 70% of Americans are prescribed at least one medication, with Antibiotics, Antidepressant, and Opioid topping the list. (A Mayo Clinic study)
- "We are in **this culture** now where too many people see **drugs** as the answer not only to pain, but to **improving their lives**," said Meldrum.

A short history of pain management: http://www.cmaj.ca/content/190/1/e26

NONPHARMACOLOGIC THERAPIES

- NONPHARMACOLOGIC THERAPIES
  - Behavioral medicine approaches
    - - Cognitive-behavioral therapy
    - - Biofeedback
  - Physical medicine approaches
    - - Spinal manipulation
  - Neuromodulation approaches
    - - Transcutaneous electrical stimulation
    - - Spinal cord stimulation
    - - Deep brain stimulation
  - Interventional approaches
  - Surgical approaches

Behavioral Medicine Approaches

Cognitive-behavioral therapy (CBT):

- Is the most commonly used behavioral medicine approach for pain patients. [115]
- CBT for pain incorporates three components:
  - patient education,
  - behavioral skill training,
  - cognitive-skill training [116].
- Randomized trial- chronic widespread pain, after **six months** - symptom improvement:
  - 8 % - usual care,
  - 35 % - telephone CBT
  - 37 % - telephone CBT & Exercise [117].

- Biofeedback : A systematic review - effective for Migraine and tension-type headaches, has the greatest impact on
  - headache frequency, and
  - anxiety
  - medication consumption [118].

Physical medicine approaches

Physical/Occupational therapy program:

- Exercise regimen specifically tailored to the
  - Range of Motion
  - Muscle conditioning
  - Improve stability, function, & pain.
- Muscle conditioning focuses on three areas:
  - Strength,
  - Endurance,
  - Re-education [119].

Spinal manipulation:

- Chiropractors, Physical therapists, and Osteopathic clinicians use mainly to relief for musculoskeletal neck and back.

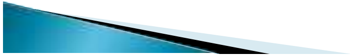
Interventional approaches

- Play a complementary role to other strategies and typically attempt to target the presumed "pain generators." - includes:
  - Intercostal nerve blockade,
  - Spinal injections (epidural steroid injections,
  - Selective nerve root injections, and
  - Medial branch nerve injections of the facet or zygapophyseal joint),
  - Occipital nerve injections, and
  - Multiple other peripheral nerve injections.

Surgery

If all conservative treatments fails – refer for surgical evaluation. (Usually less than 3-5% of population.)

(KP Guideline)



Neuromodulation approaches

Transcutaneous electrical stimulation (TENS):

- Systematic reviews - inconclusive results on its efficacy in chronic pain management [121].
- Lacking rigorous randomized controlled trials (RCTs).

Spinal cord stimulation (SCS)

- Chronic neuropathic pain.
- Chronic low back pain - failed back surgery syndrome.
- Complex regional pain syndrome,
- Intractable angina
- Painful peripheral vascular disease.

Deep brain stimulation

To achieve analgesia is in its infancy.

Alternative Medicine

Is not a part of mainstream medicine to treat a health problem.

Other related terms include:

- "Complementary Medicine."
- "Holistic care" – whole person - including spiritual and emotional state -
- "Integrative Medicine"

Examples of alternative medicine include

- **Acupuncture**
- **Homeopathy**
- **Herbal remedies** – Even though herbal remedies are "natural," they are not always safe.
- **Mind-body techniques** – hypnosis and guided imagery => supposed to calm & change the way we think.
- **Massage therapy**
- **Reiki and other "energy therapies"**
- **Special diets -** Turmeric, Ginger, Garlic

Integrated Pain Management

- Provide Multimodal pain control methods through multidisciplinary approach includes:
  - Pharmacologic Therapy by Pain providers
  - Individual or Group Classes Counseling (CBT) by Pain Psychologist
  - Pain Psychiatrist to treat psychological disorders
  - Physical Therapy and Exercises by Physical Therapist

Expectation from Chronic Pain Management should be clearly communicated to patients

- A reasonable goal should be set after discussing the treatment approach and making a plan.
- The goal should be tolerable pain that allows the patient to function.
- Medications should not be the sole focus of treatment.
- Patients willing to utilize multimodal pain control methods through multidisciplinary approach at Integrated Pain Management Program and should not expect decrease in pain over 30%.

INFORMATION FOR PATIENTS

Patient education is an important aspect of care. Use UpToDate patient educational materials, "The Basics" and "Beyond the Basics."

- Educate patients about
  - Causes of pain
  - Favorable prognosis,
  - Diagnostic testing provide minimal value
  - Activity as tolerated
  - Work recommendations
  - Emergency precautions (See Patient education)

PATIENT INSTRUCTION

Patient education: Opioids for short-term treatment of pain (The Basics)
Patient education: Chronic pain (The Basics)
Patient education: Alternative medicine (The Basics)
Patient education: Fibromyalgia (The Basics)
Patient education: Low back pain in adults (Beyond the Basics)
Patient education: Low back pain in adults (The Basics)
Patient education: Managing pain when you have cancer (The Basics)
Patient education: Neuropathic pain (The Basics)
Patient education: Neuropathic pain (The Basics)
View in Spanish
Patient education: Chronic pain (The Basics)
Patient education: Nerve damage caused by diabetes (The Basics)
Patient education: Shingles (The Basics)
Patient education: Stroke (The Basics)

Patient education: Depression (The Basics)

Patient education: Migraines in adults (The Basics)

Patient education: Headache causes and diagnosis in adults (Beyond the Basics)

Patient education: Headache treatment in

Patient education: Side effects from medicines (The Basics)

Patient education: When you have multiple health problems (The Basics)

Patient education: Opioids for short-term treatment of pain (The Basics)
Patient education: Brand versus generic medicines (The Basics)
Patient education: Chronic pain (The Basics)
Patient education: Coping with high drug prices (Beyond the Basics)
Patient education: Managing pain after surgery (The Basics)
Patient education: Managing pain when you have cancer (The Basics)
Patient education: Nonsteroidal antiinflammatory drugs (NSAIDs) (Beyond the Basics)
Patient education: Nonsteroidal antiinflammatory drugs (NSAIDs) (The Basics)
Patient education: Opioid use disorder (The Basics)
Patient education: Prescription drug misuse (The Basics)
Patient education: Side effects from medicines (The Basics)
Patient education: Opioids for short-term treatment of pain (The Basics)

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Prescription Drug Monitoring Program

PRESCRIPTION DRUG MONITORING PROGRAMS (will be covered in next ppt)

Summary and Recommendations

SUMMARY AND RECOMMENDATIONS

Opiates and the law
CURES, State and Kaiser guidelines

Outline for Presentation (for ACNM CE only)

- Understanding epidemic of prescription opioids
- Chronic Pain and Iatrogenic Drug Dependance
- Is opioids safe and an ideal treatment for acute and chronic non cancer pain?
- Opioids Interactions with sedatives and hypnotics
- Review CDC Guideline for Prescribing Opioids for Chronic Pain
  - CURES
  - California Law: AB 2760 - Naloxone Prescribing Law
  - Check Urine Drug Screen
  - Consequences of not following the CDC guidelines
- Medical Board of California Guideline
- Review Kaiser Permanente April 2019 Update to Opioid Escalation Practice Recommendation (OEPR)
  - Understanding the Role of Prescribing Clinician and Pharmacist

- Understanding epidemic of prescription opioid
- Pain Treatment History or How we got where we are now :
- Chronic Pain and Iatrogenic Drug Dependance : Aberrant Behaviour
- Understanding the impact of opioid on acute and chronic pain. Is opioid safe and ideal treatment for acute and chronic pain?
- Is opioid the right choice for acute and chronic pain
- Benzodiazepines and Opioids

- Review CDC guidelines for opioid prescription.
  - CURES
  - California Law: AB 2760 - Naloxone Prescribing Law
  - Check Urine Drug Screen
  - Consequences of not following the CDC guidelines
- Medical Board of California Guideline
- Review Kaiser Permanente April 2019 Update to Opioid Escalation Practice Recommendation (OEPR)
  - Understanding the Role of Prescribing Clinician and Pharmacist

Questions

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