Prescribing Opioid Medications in the Outpatient Setting: Risks and Guidelines

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Faculty Disclosure

- I have no financial disclosures.

Educational Need/Practice Gap

Gap = Willingness and approach to managing opioid medications in the outpatient setting is variable.

Need = Having a uniform, simple approach to opioid prescribing could ease concerns and fears for providers and patients.

Objectives

Upon completion of this educational activity, you will be able to:

- Describe best practices for when and how to initiate opioid prescribing
- Review opioid dosing and tapering strategies
- Identify at risk populations
- Recommend strategies for managing risk and maintaining patient safety

Expected Outcome

- What is the desired change/result in practice resulting from this educational intervention?
  - The desired result is improved comfort level with opioid prescribing by presenting a safe and simple approach that is advantageous to the patient and the practitioner.

Basis for Opioid Prescribing…

Centers for Disease Control and Prevention
MMWR
Morbidity and Mortality Weekly Report
Recommendations and Reports / Vol. 71 / No. 3
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CDC Clinical Practice Guideline for Prescribing Opioids for Pain — United States, 2022

Evidence-based guidelines for clinicians providing outpatient pain care:

- Patients 18 yrs and older
- Acute (<30 days); Subacute (1-3 months); chronic (>3 months)

Not applicable for the following patient groups:

- Sickle Cell Anemia
- Cancer-related Pain
- Palliative Care/End-of-Life Care
- Inpatients (while inpatient or at discharge); ER settings

To Start Opioids or Not…

Recommendation 1: Nonopioid therapies are at least as effective as opioids for many common types of acute pain. Clinicians should maximize use of non-pharmacologic and nonopioid pharmacologic therapies … and only consider opioid therapy for acute pain if benefits are anticipated to outweigh risk… [and] discuss with patients the realistic benefits and known risks of opioid therapy. (Recommendation B; Evidence 3)

Recommendation 2: Nonopioid therapies are preferred for subacute or chronic pain. Clinicians should maximize use of nonpharmacologic and nonopioid pharmacologic therapies … and only consider initiating therapy if expected benefits for pain and function are anticipated to outweigh risks … [and] establish treatment goals for pain and function [and] consider how opioid therapy will be discontinued if benefits do not outweigh risks. (Recommendation A; Evidence 2)

To Start Opioids or Not…

Prior to starting opioid medications for acute, subacute, or chronic pain…

- maximize non-pharmacologic treatment where able:
  - superficial heat, massage, acupuncture, spinal manipulation for acute low back pain[1]
  - acupressure, TENS for acute musculoskeletal injury[2]
  - exercise therapy, aquatic/resistance exercise, CBT, manual therapy, massage, mind/body practices, acupuncture, myofascial release for chronic low back and neck pain, fibromyalgia, hip/knee OA[3]
  - Some non-opioid, non-pharmacologic options may not be covered by insurance and may be cost-prohibitive for some patients
  - directed medication delivery – injections, interventions
- maximize non-opioid pharmacology where able:
  - Acetaminophen, NSAIDs, selected antidepressants, selected anticonvulsants
  - Greatest benefit-harm ratio for acute MSK injury: topical NSAIDs > PO NSAIDs, acetaminophen[4]
  - Some non-opioid pain medications may pose risks to some patients – older adults, pregnant patients, patients with cardiovascular, renal, gastrointestinal, and liver disease

How to Select Opioids and Dosage…

Recommendation 3: When starting opioid therapy for acute, subacute, or chronic pain, clinicians should prescribe immediate-release opioids instead of extended-release (ER) and long-acting (LA) opioids. (Recommendation A; Evidence 4)

Common Short-Acting Opioids:

- Morphine Immediate-Release (MSIR)
- Hydrocodone (Vicodin®, Lortab®, Norco®)
- Oxycodone (Roxicodone®, Percocet®)
- Tramadol (Ultram®, Ultracet®)
- Hydromorphone (Dilaudid®)
- Codeine (Tylenol with Codeine #3, #4)

Common Long-Acting or Extended-Release Opioids:

- Morphine Extended-Release (MS Contin)
- Oxycodone Extended-Release (OxyContin®)
- Tramadol (Ultram ER®)
- Transdermal Fentanyl
- Methadone

- Higher risk of overdose among patients treated with ER/LA opioids than IR opioids, especially within the first two weeks[5], and they should be reserved for those already on
- Limited evidence suggesting that continuous, time-schedule use of ER/LA opioids is more effective or safe than intermittent use of IR opioids[5]
- “Abuse-deterrent” labelling of many ER opioids can be misleading as there is no evidence that they prevent opioid misuse or overdose through oral intake

How to Select Opioids and Dosage…

Special Considerations…

- Methadone (long acting)
  - Long and variable half-life; peak respiratory depressant effect tends to occur after and last longer than peak analgesic effect
  - Associated with disproportionate numbers of overdose deaths relative to the frequency with which it is prescribed[6]
  - Associated with cardiac arrhythmias and QT prolongation
- Transdermal Fentanyl (long acting)
  - Complex absorption and pharmacodynamic profile
    - serum concentration gradually increases during the first part of the 72-hour patch interval
  - External heat can increase adsorption rates
  - mcg/hour dosing could be confusing for some patients and lead to accidental overdose

How to Select Opioids and Dosage…

Recommendation 4: When opioids are initiated for opioid-naïve patients, prescribe the lowest effective dosage. Carefully evaluate individual benefits and risks when considering increasing dosage. Avoid increasing dosage above levels likely to yield diminishing returns in benefits relative to risks. (Recommendation A; Evidence 3)

Recommendation 5: For patients already established on opioid therapies, carefully weigh risks and benefits prior to changing opioid dosage. Continue to optimize non-opioid therapies. If benefits do not outweigh risks, work closely with the patient to gradually taper or lower dosage. Opioid therapy should not be discontinued abruptly and higher dosages should not be rapidly reduced unless there are indications of life-threatening issues (confusion, sedation, etc.). (Recommendation B; Evidence 4)

How to Select Opioids and Dosage…

TABLE. Morphine milligram equivalent doses for commonly prescribed opioids for pain management

Opioid	Conversion factor*
Codeine	0.15
Fentanyl transdermal (in mcg/hr)	2.4
Hydrocodone	1.0
Hydromorphone	5.0
Methadone	4.7
Morphine	1.0
Oxycodone	1.5
Oxymorphone	3.0
Tapentadol†	0.4
Tramadol§	0.2

Sources: Adapted from Von Korff M, Saunders K, Ray GT, et al. Clin J Pain 2008;24:521–7 and Nielsen S, Degenhardt L, Hoban B, Gisev N. Pharmacoepidemiol Drug Saf 2016;25:733–7.
Abbreviations: mcg/hr = microgram per hour; mg = milligram; MME = morphine milligram equivalent.

Calculating MME…

- For hydrocodone 5mg q6h:
  - 4 doses/day x 5mg/dose = 20 mg/day
  - Convert to MME:
    20 mg/day x 1 MME/mg HC = **20 MME/day**

- For oxycodone 10mg q8h:
  - 3 doses/day x 10mg/dose = 30mg/day
  - Convert to MME:
    30mg/day x 1.5 MMD/mg Oxy = **45 MME/day**

- For transdermal fentanyl 25 mcg/hr:
  - 25 mcg/hr patch x 2.4 MME/mcg/hr = **60 MME/day**

  OR
  - use 10 mcg fentanyl to 1 mg morphine
  - 25 mcg/hr patch = 600 mcg/day
  - 600 mcg fentanyl / 10 = **60 MME/day**

Opioid Dosing Learning Point

Of the following opioid regimens, which carries the highest daily morphine milliequivalents (MME)?

- Percocet 10mg q8h + tramadol 100mg BID
- Morphine ER 30mg BID + Norco 5mg q6h
- Fentanyl Patch 25 mcg/hr + morphine IR 10mg TID

Opioid	Conversion factor*
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Oxycodone	1.5
Oxymorphone	3.0
Tapentadol†	0.4
Tramadol§	0.2

Percocet 10mg q8h = 30mg/day
Tramadol 100mg BID = 200mg/day
Convert to MME
30mg oxycodone x 1.5 = 45 MME
200mg tramadol x 0.2 = 40 MME

Total 95 MME

Morphine ER 30mg BID = 60mg/day
Hydrocodone 5mg q6h = 20mg/day
Convert to MME
60mg morphine x 1.5 = 60 MME
20mg hydrocodone x 1 = 20 MME

Total 80 MME

Fentanyl Patch 25 mcg/hr =
Morphine IR 10mg TID = 30mg/day
Convert to MME
25mcg/hr x 2.4 MME/mcg/hr = 60 MME
30mg morphine x 1 = 30 MME

Total 90 MME

How to Select Opioids and Dosage…

- Dosages of 50-90 MME/day showed minimal improvements in mean pain intensity and no mean improvement in function when compared with dosages <50 MME/day[5]
- Risk for opioid misuse, overdose, death increased at higher opioid dosage[7-10]
    - In acute pain, when compared to dosages 1-20 MME/day:
        - Dosages of 50-100 MME/day were associated with 4.73 times the risk of overdose
        - Dosages of >100 MME/day were associated with 6.64 times the risk of overdose
    - In chronic pain, when compared to dosages 1-20 MME/day:
        - Dosages of 50-100 MME/day were associated with 1.9-4.6 times the risk of overdose
        - Dosages of >100 MME/day were associated with 2.0-8.9 times the risk of overdose

While not a set limit or rigid guideline, evidence suggests that **50 MME/day** is a good target ceiling dosage.

How to Select Opioids and Dosage…

Decreasing or discontinuing opioid therapy…

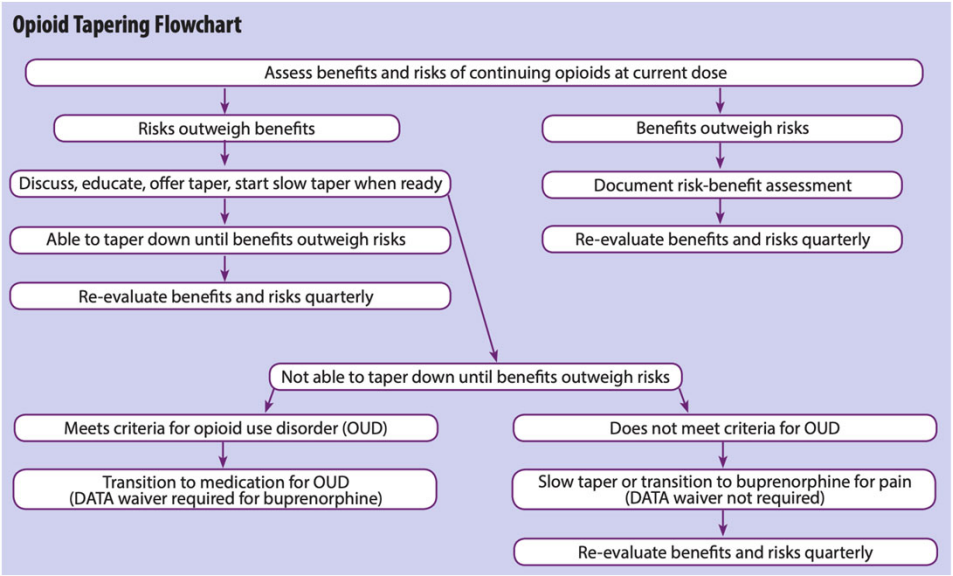
Discontinuation of long-term, high-dosage opioid therapy is associated with adverse events including mental health crisis, overdose events, overdose death[11-15]

- Abrupt stoppage of opioids in patients with physical dependence can induce acute withdrawal and should only be considered in life—threatening situation
  - *Clonidine, lofexidine, tizanidine can mitigate symptoms*

- General rule of thumb: *high doses over longer periods of time require slower, drawn-out tapers*
  - Opioid use weeks-months: decrease by 10% per week
  - Opioid use for longer: decrease by 10% per month

- Special Case: for **pregnant patients** exhibiting signs of opioid use disorder or physical dependence, transitioning to a medication for OUD (suboxone, methadone) is preferred over withdrawal management[16-17]

HHS Guide for Clinicians on the Appropriate Dosage Reduction or Discontinuation of Long-Term Opioid Analgesics



How to Select Opioids and Dosage…

Feature	Opioid Tolerance	Opioid-Induced Hyperalgesia (OIH)
Definition	Decreased responsiveness to opioids	Increased sensitivity to pain stimuli induced by opioids
Mechanism	Receptor desensitization, changes in signaling	Central nervous system sensitization
Clinical Effect	Reduced pain relief, increased dose needed	Increased pain, paradoxically worsening with higher doses

•OIH and opioid tolerance can sometimes coexist, making diagnosis and management challenging.

•Clinicians should be vigilant in recognizing and differentiating between these phenomena to optimize pain management strategies and minimize the risks associated with opioid therapy.

•Treatment approaches may involve opioid rotation, dose reduction, or adjunctive pain management techniques, as appropriate.

Tapering – Case Example

Patient with a history of colorectal cancer s/p surgery and chemotherapy treatment is now in remission. Their cancer-related pain was successfully treated with 90mg morphine SR q8h for 1 year. They would now like to stop their opioid medications. What strategy is implemented to successfully taper/wean?

90mg morphine SR x 3 doses/day = 270 MME (target is <50 MME)

- Month 1: reduce to 75mg morphine SR x 3 doses/day (225 MME; 16.7% reduction)
- Month 2: reduce to 60mg morphine SR x 3 doses/day (180 MME; 20% reduction)
- Month 3: reduce to 45mg morphine SR x 3 doses/day (135 MME; 25% reduction)
- Month 4: reduce to 30mg morphine SR x 3 doses/day (90 MME; 33.3% reduction)
- Month 5: reduce to 15mg morphine SR x 3 doses/day (45 MME; 50% reduction)
- Month 6: reduce to 15mg morphine SR x 2 doses/day (30 MME; 33.3% reduction)
- Month 6: reduce to 15mg morphine SR x nightly (15 MME; 50% reduction)

How to Select Duration and Follow Up…

Recommendation 6: When opioids are needed for acute pain, clinicians should prescribe no greater quantity than needed for the expected duration of pain severe enough to require opioids. (Recommendation A; Evidence 4)

- Consider 2-week or less follow up intervals for patients with acute pain requiring opioid therapy, at which time all reversible causes of pain should be re-addressed and non-opioid therapies maximized

Recommendation 7: Clinicians should evaluate benefits and risks with patients within 1-4 weeks of starting opioid therapy for subacute or chronic pain or of dosage escalation. Clinicians should regularly reevaluate benefits and risks of continued opioid therapy with patients. (Recommendation A; Evidence 4)

- Given the elevated risk for overdose within the first 2 weeks of starting ER/LA opioids or changing to higher dosages (>50 MME), consider following up with the patient an increased intervals early on in treatment
- For IR opioids at <50 MME/day, a 4-week follow up is appropriate

Assessing Risk and Addressing Potential Harms…

Recommendation 8: Before starting and periodically during continuation of opioid therapy, clinicians should evaluate risk for opioid-related harms and discuss risk with patients. Clinicians should work with patients to incorporate into the management plan strategies to mitigate risk, including offering naloxone. (Recommendation A; Evidence 4)

Offer naloxone and re-evalute patients more frequently when factors are present that increase risk:

- sleep apnea
- history of overdose
- history or substance use disorder
- higher dosages of opioids (>50 MME/day)
- concurrent use of benzodiazepines.

Consider prescribing naloxone when starting opioid therapy. At each visit, ensure the patient has naloxone in an accessible location and review the risks of accidental overdose, not only for the patient but for others that may inadvertently or purposely ingest their medication. Refill annually.

Assessing Risk and Addressing Potential Harms…

- Patients with sleep-disordered breathing/apnea
  - Avoid prescribing opioids to patients with moderate to severe sleep-disordered breathing, when possible
- Pregnant patients
  - Associations with stillbirth, poor fetal growth, preterm delivery, neonatal abstinence syndrome[19-22]
  - Risks require frank discussions with patients that are pregnant or may become pregnant
- Renal or hepatic insufficiency
  - Increased risk for adverse events due to the susceptibility of accumulating opioids
- Patients over 65
  - Include functional assessment to better evaluate the efficacy of opioid therapy
  - Increased risk of medication errors, polypharmacy, drug-drug interactions
- Patients with a history of overdose
  - Substantial risk for future opioid overdose[26]
  - Repeat overdose <2 yrs: 17% for MME >100; 15% for MME 50-100; 9% for MME <50[26]

Assessing Risk and Addressing Potential Harms…

- Patients in safety critical jobs (i.e. driving, working at heights, operating machinery)
  - Opioid therapy may be incompatible
- Patients with co-morbid mental health conditions
  - Generalized Anxiety Disorder (GAD-7), Patient Health Questionnaire (PHQ-9) can be helpful to identify underlying confounding factors
  - This population may be at an elevated risk for OUD and overdose[24-25]
  - Optimize any underlying conditions (TCAs; SNRIs)
- Patients with Substance Use Disorder
  - Screening tools (SOAPP; SOAPP-R; Opioid Risk Tool) have limited and variable accuracy on their own
  - Ask about illicit drug use and alcohol use (Drug Abuse Screening Test; TAPS; AUDIT-C)
  - Always have a plan to mitigate risk (frequency of visits; naloxone prescribing)

Assessing Risk and Addressing Potential Harms…

Recommendation 9: When prescribing initial opioid therapy for acute, subacute, or chronic pain, and periodically during opioid therapy for chronic pain, clinicians should review the patient's history of controlled substance prescriptions using state prescription drug monitoring program (PDMP) data to determine whether the patient is receiving opioid dosages or combinations that put the patient at high risk for overdose. (Recommendation B; Evidence 4)

KASPER – review prior to writing/re-writing any controlled substance

- Methadone for OUD will not show up on a KASPER
- Not all prescriptions filled within a few days of obtaining the KASPER will present on the report
- Includes the capability of to request information from the Kentucky Health Information Exchange (KHIE) to determine if a patient has had an ED visit or hospital admission related to a non-fatal or suspected non-fatal drug overdose

Assessing Risk and Addressing Potential Harms…

Recommendation 10: When prescribing opioids for subacute or chronic pain, clinicians should consider the benefits and risks of toxicology testing to assess for prescribed medications as well as other prescribed and nonprescribed controlled substances. (Recommendation B; Evidence 4)

Limited toxicology screening with presumptive immunoassay panel (UDS) with confirmation from liquid chromatography-mass spectrometry (LCMS)

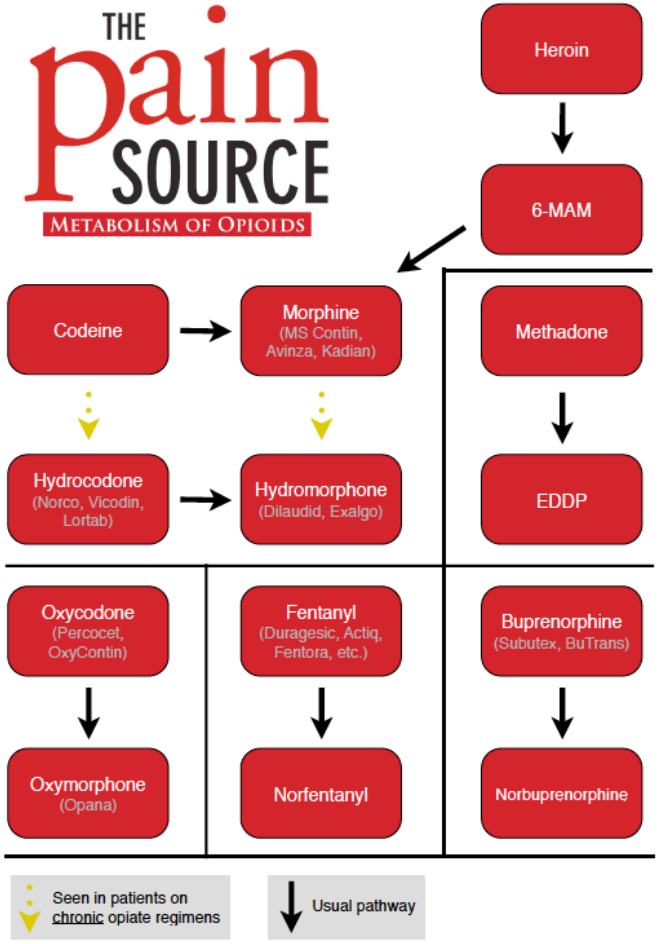
- Open, honest, nonjudgemental communication with the patient is a must
- Not to be used as a "gotcha" moment, but rather for safety
- Clinical judgements should not be made based on UDS alone; however, the plan must be known and understood before the test is ordered

Assessing Risk and Addressing Potential Harms…

New patients under consideration for opioid prescribing…

- provide a urine drug screen for LCMS analysis
- undergo a KASPER review
- undergo an in-depth chart review, including any outside information from pain management groups or prescribers
- are provided a Pain Contract for review

The process usually takes 2-3 weeks. Nobody is prescribed controlled substances on the first visit.



Assessing Risk and Addressing Potential Harms…

Recommendation 11: Clinicians should use caution when prescribing opioid pain medication and benzodiazepines concurrently and consider whether benefits outweigh risks of concurrent prescribing of opioids and other central nervous system depressants. (Recommendation B; Evidence 3)

Studies find concurrent benzodiazepine use in large populations of opioid-related overdose deaths[27-28]

- One study found concurrent benzo use to be associated with nearly 4x's risk for overdose death[29]

Communication between prescribing physicians is critical for monitoring patient safety and minimizing risk

Assessing Risk and Addressing Potential Harms…

Recommendation 12: Clinicians should offer or arrange treatment with evidence-based medications to treat patients with opioid use disorder. Detoxification on its own, without medications of opioid use disorder, is not recommended for opioid use disorder because of increased risks for resuming drug use, overdose, and overdose death. (Recommendation A; Evidence 1)

Among patients with chronic pain:

- Rate of opioid addiction: 8%-12%[30]
- Any prescription opioid use disorder: 23.9%-26.5%[31-32]

Recent 2024 data[33], showed that MOUD therapy (buprenorphine, methadone, naltrexone) over 18 months…

- Increased opioid abstinence from 55% to 77%
- Decreased opioid-related overdose from 7% to 2%
- ED visits declined from 9% to 4%
- Arrest rates decreased from 15% to 7%

Assessing Risk and Addressing Potential Harms…

According to DSM-5, opioid use disorder is defined as a problematic pattern of opioid use leading to clinically significant impairment or distress.

(2 of the diagnostic criteria within 12 months)

- Mild: 2-3 criteria
- Moderate: 4-5 criteria
- Severe: ≥6 criteria

OUD should not used as grounds for dismissal from clinic. Clinicians unable to provider treatment themselves should arrange for patients with OUD to see a substance use disorder treatment specialist.

Diagnostic Criteria
1. Opioids are often taken in larger amounts or over a longer period than was intended.
2. There is a persistent desire or unsuccessful efforts to cut down or control opioid use.
3. A great deal of time is spent in activities necessary to obtain the opioid, use the opioid, or recover from its effects.
4. Craving, or a strong desire or urge to use opioids.
5. Recurrent opioid use resulting in a failure to fulfill major role obligations at work, school, or home.
6. Continued opioid use, despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of opioids.
7. Important social, occupational, or recreational activities are given up or reduced because of opioid use.
8. Recurrent opioid use in situations in which it is physically hazardous.
9. Continued opioid use, despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by the substance.
10. Tolerance,* as defined by *either* of the following:
A. A need for markedly increased amounts of opioids to achieve intoxication or desired effect.
B. A markedly diminished effect with continued use of the same amount of an opioid.

In a nutshell…

- Maximize conservative measures and non-opioid medications for acute and chronic pain prior to starting opioid medications.
- Start with the lowest effective dose and amount of immediate release opioids. Avoid starting opioid therapy with long-acting or extended release opioids.
- Give special consideration to patient populations that are at risk of developing adverse effects or are at risk of opioid use disorder and/or overdose
- MME <50 is safe ceiling dose for most patients
- Taper high dose opioids slowly to avoid precipitating withdrawal
- Coordinate a plan with your patient to mitigate risk, including prescribing naloxone.
- Establish a regular and frequent plan for ongoing evaluation.
- Utilize point of care drug testing and LCMS confirmation when needed
- Review KASPER regularly
- Use caution when co-prescribing with benzodiazepines
- Monitor for opioid use disorder and be ready to offer solutions (MOUDs vs addiction medicine)

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