Managing Opioid Complexity in Individuals with Serious Illness

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In this session, we discuss the complexity of opioid prescribing in patients with serious illness. We will review the available evidence on chronic pain, long-term opioid therapy, and opioid misuse/use disorders in the general population. We will then apply the relevant and emerging evidence in palliative care populations to generate best practices that can inform future quality metrics.

QMC Quality Matters Conference
December 8-9, 2022

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Learning Outcomes

At the end of this session:

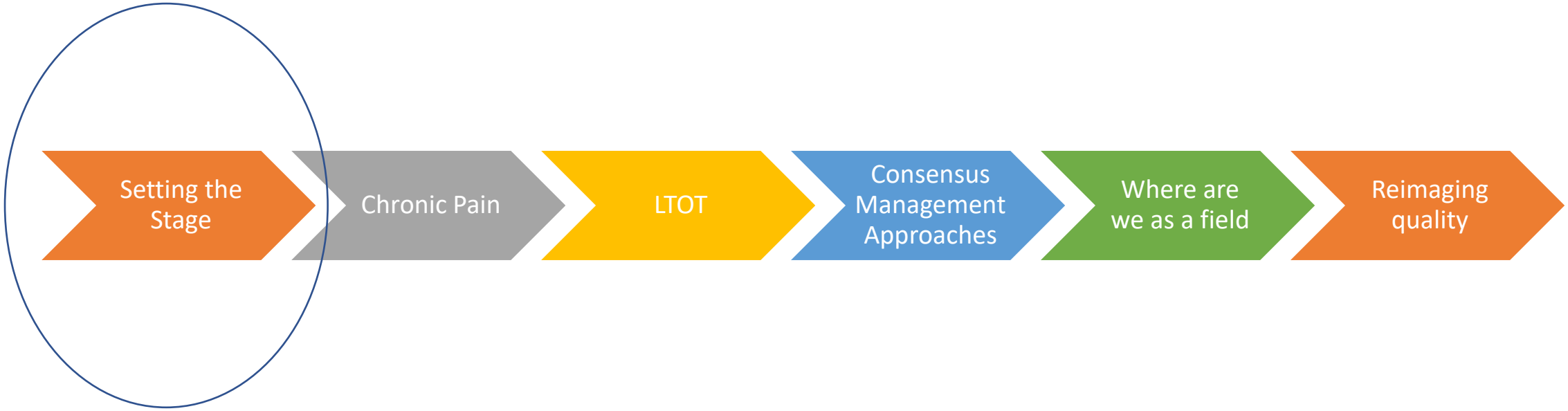
Understand the complexities of managing pain and opioid misuse/use disorder in patients with serious illness.

Apply the available evidence on chronic pain, long-term opioid therapy (LTOT), and opioid misuse/use disorder to your patients.

Plan at least 3 things you will do to improve quality pain and opioid management.

Get your X waiver or, if you are already waivered, recruit a colleague!

Road Map


Setting the Stage
Chronic Pain
LTOT
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Where are we as a field
Reimaging quality

We are in a different place now…

Journal of Pain Research

Dovepress

open access to scientific and medical research

Open Access Full Text Article

COMMENTARY

Terminology of chronic pain: the need to "level the playing field"

This article was published in the following Dove Press journal:
Journal of Pain Research
27 January 2016
Number of times this article has been viewed

Opinion

VIEWPOINT

Bridging the Critical Divide in Pain Management Guidelines From the CDC, NCCN, and ASCO for Cancer Survivors

Chronic pain as a symptom or a disease Classification of Chronic Pain for the *In Classification of Diseases (ICD-11)*

Rolf-Detlef Treede[a,*], Winfried Rief[b], Antonia Barke[b], Qasim Aziz[c], Michael I. Bennett[d], Milton Cohen[f], Stefan Evers[g], Nanna B. Finnerup[h,i], Michael B. First[j], Maria Adele Giamb Beatrice Korwisi[b], Eva Kosek[o], Patricia Lavand'homme[p], Michael Nicholas[q], Serge Per Stephan Schug[t,u], Blair H. Smith[v], Peter Svensson[w,x], Johan W.S. Vlaeyen[y,z,aa], Shuu-

VIEWPOINT

Use of Palliative Care Earlier in the Disease Course in the Context of the Opioid Epidemic
Educational, Research, and Policy Issues

Opinion

Long-term Risk of Overdose or Mental is After Opioid Dose Tapering

AND JOURNAL of MEDICINE

VOLUME 35 · NUMBER 36 · DECEMBER 20, 2017

JOURNAL OF CLINICAL ONCOLOGY | ORIGINAL REPORT

New Persistent Opioid Use Among Patients With Cancer After Curative-Intent Surgery

Jay Soong-Jin Lee, Hsou Mei Hu, Anthony L. Edelman, Chad M. Brummett, Michael J. Englesbe, Jennifer F. Waljee, Jeffrey B. Smerage, Jennifer J. Griggs, Hari Nathan, Jacqueline S. Jeruss, and Lesly A. Dossett

Perspective

DECEMBER 27, 2018

Harder to Treat Than Leukemia — Opioid Use Disorder in Survivors of Cancer

Alison Wakoff Loren, M.D., M.S.C.E.

Treating Addiction as a Terminal Disease

Why do we care about pain in people with opioid complexity?

- Substance use is common
  - Including 1.7 million Americans with prescription opioid use disorder (OUD) and 691,000 with heroin use disorder[1]
- Chronic pain is common
  - 20% of Americans (50 million people); 40% with high impact chronic pain[2]
- Substance use and chronic pain often co-occur and are interrelated[3]

1. NSDUH 2021. 2. Dahlhamer J et al, MMWR, 2018. 3. Ditre J et al, 2019

Key Take Away:
If you care for patients with serious illness

- These are our patients
- We have the power to make a difference
- As a leader, you can make this a priority

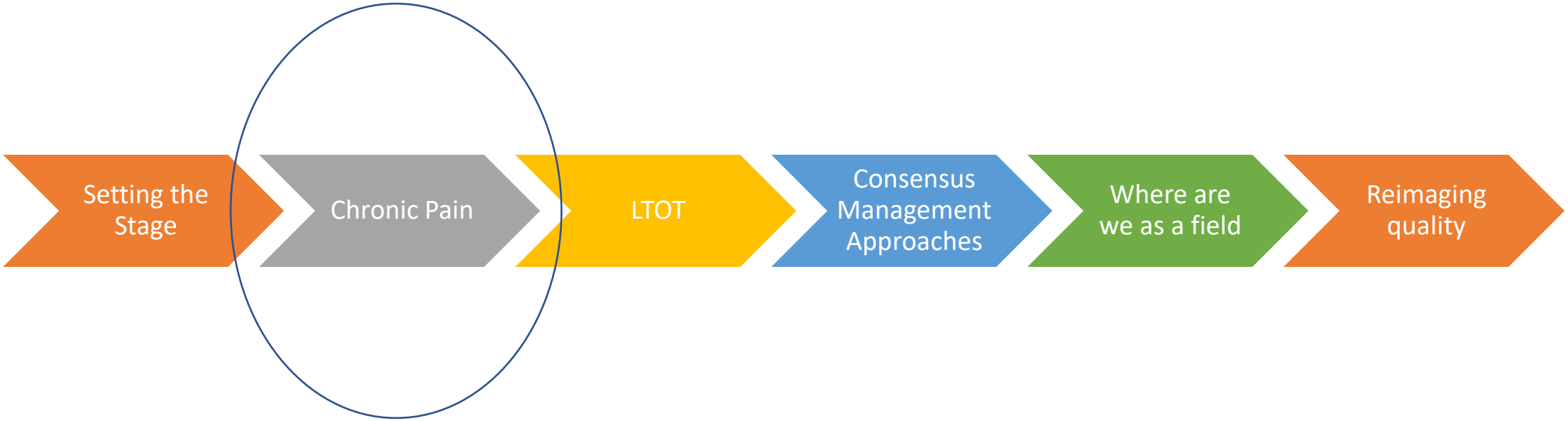
Stigma

- Definition: "Stigma is a social process that occurs in the context of power, characterized by labeling, stereotyping, and discrimination based on real or perceived attributes."

- Includes people who experience:
  - Pain
  - Opioid receipt
  - Opioid use disorder
  - Minoritization (i.e., Black, LatinX, individuals with disabilities)

1. Bulls, Merlin et al, 2021
2. Wakeman et al., Substance Abuse, 2018

Road Map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Key Term: Chronic pain

- An unpleasant sensory and emotional experience associated with or resembling that associated with actual or potential tissue damage.
- Pain lasting > 3 months[1]
- Common[2]
- Unique neurobiologic basis influenced by biological, psychological, and social factors[3,4]

1. International Association for the Study of Pain Classification, 2020. 2. CDC MMWR 2018.
3. DHHS National Pain Strategy, 2016. 4. Von Korff M, 2016

Key Term: Chronic pain cont'd

- A chronic disease
- Optimal treatment: multimodal (pharmacologic and non-pharmacologic), multidisciplinary

1. DHHS National Pain Strategy, 2016. 2. Von Korff M, 2016

Pain and Serious Illness

- How someone with serious illness might have chronic pain:
  - Pre-existing chronic pain
  - Acute → chronic pain, from:
    - Serious illness itself
    - Serious illness-related treatment
  - Sometimes patients don't distinguish between these – hence "chronic pain in cancer"
    - Sometimes it is indistinguishable

What is challenging for patients?

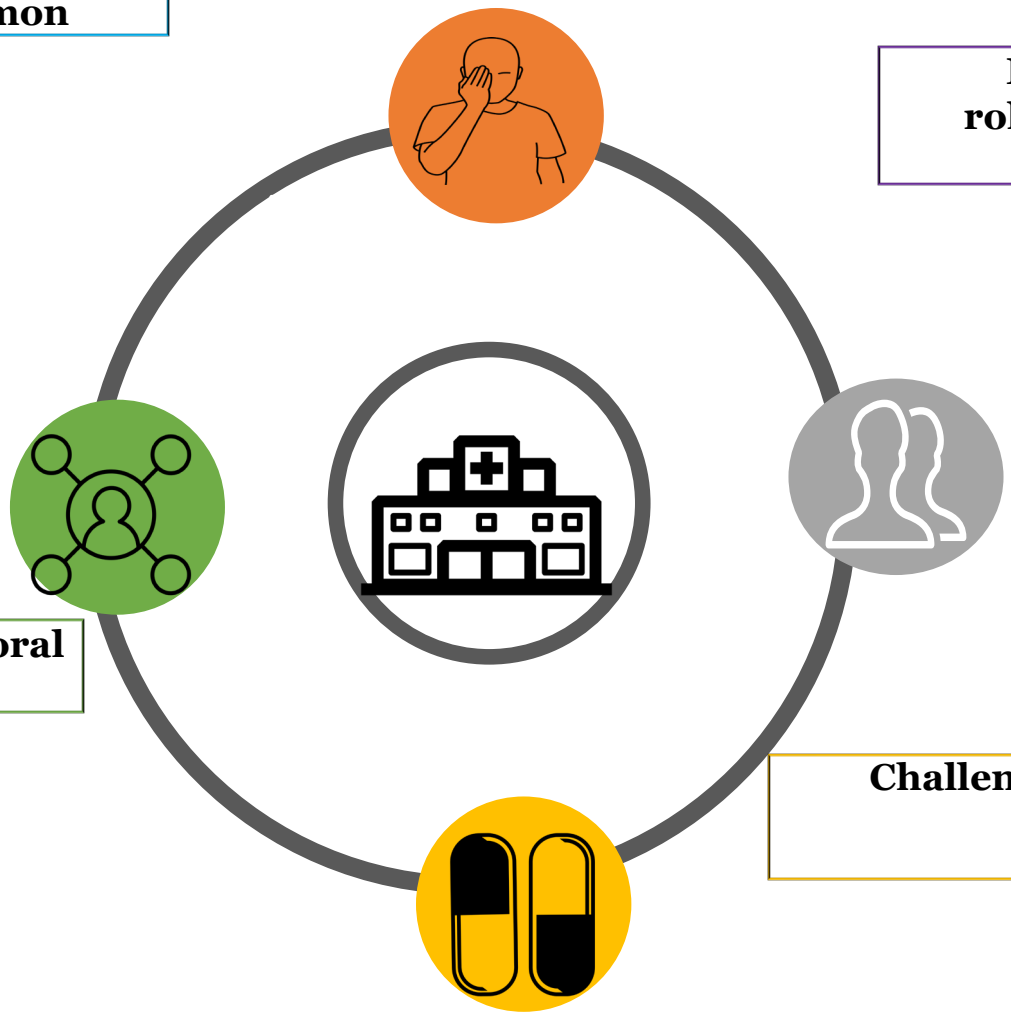
- Their suffering is invisible, and they are dismissed by clinicians
- Clinical encounters do not facilitate adequate discussion of pain
- Pain is the cost of survival and causing patients to minimize their suffering
- Management requires self-advocacy and resources
- Troubleshooting is the most common approach with evidence and non-evidence resources.
- Management is characterized by an opioid paradox

Jones, Merlin, et., under review
O'Regan, Jones, Merlin, Check et al., under review

What is challenging for clinicians?

Chronic pain perceived as uncommon

Lack of clarity around clinician roles/responsibilities; difficult care transitions



Inaccessibility of psychological & behavioral pain management expertise

Challenges with long-term opioid management

Check, Jones, Merlin, et al., in press

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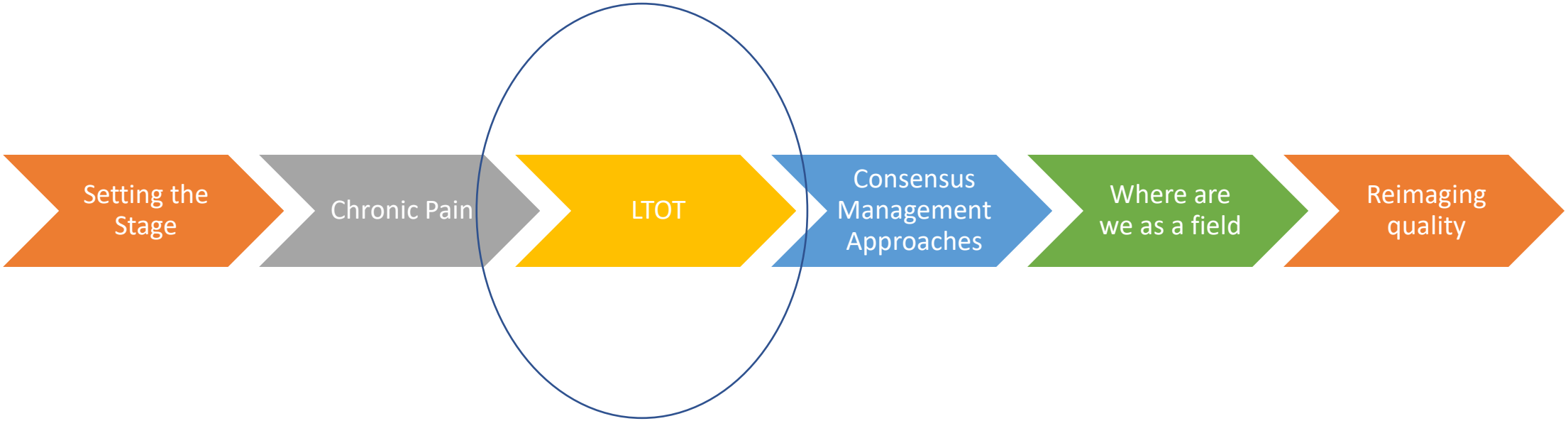
What are we missing?

- Behavioral interventions
  - Modifiable psychosocial factors are associated with worsening and prolonged pain, opioid use, and ED admission in people with cancer
- Integrative Medicine
  - There is moderate evidence for complementary and integrated health therapies, but many are not covered by insurance or integrated into palliative care practice
- Opioid Prescribing
  - Our patients are excluded from prominent opioids guidelines, like the CDC
  - But not necessarily state laws or insurance barriers
  - There is little guidance

Flowers et al, 2022; Azizoddin et al, 2021; Jones, Merlin et al. under review; Jones, Merlin, Bulls et al, 2021

Road Map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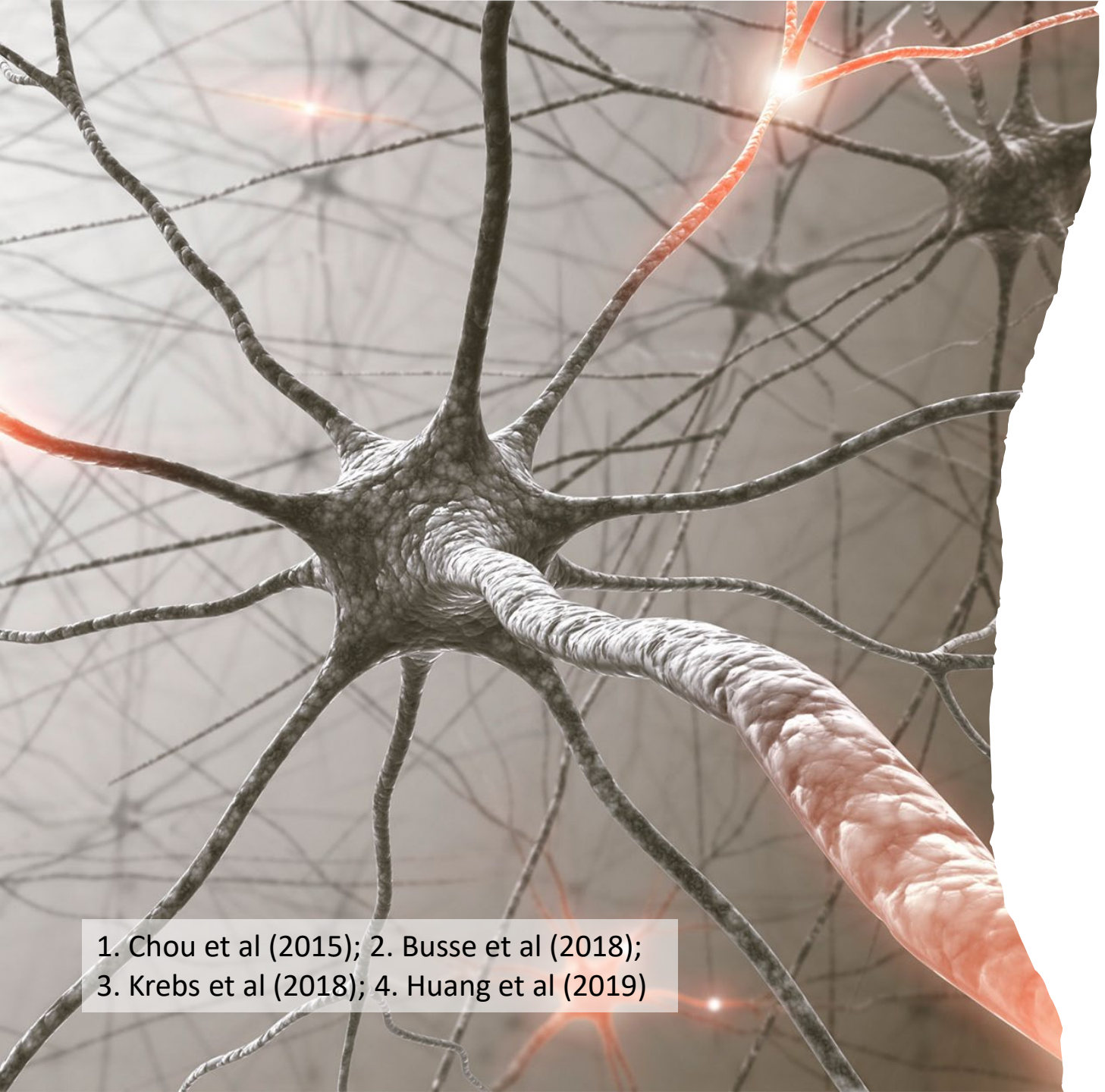
Key concept: Long-term Opioid Therapy (LTOT)

- Definition: opioids prescribed for at least 3 consecutive months
- How does this happen in serious illness?
  - Chronic pain on LTOT prior to serious illness
  - Chronic pain not on LTOT but serious illness fuels opioid prescribing
  - Pain associated with serious illness treated with opioids
  - Combination of these

Karmali RN, Bush C, Raman SR, Campbell CI, Skinner AC, Roberts AW. (2020)



LTOT: Benefits

- General population:[1-3]
  - Few high quality and no long-term trials
  - Small improvements in pain intensity/function, uncertain clinical significance
- Chronic cancer pain: what works? [4]
- Global change: class efficacy non-opioid analgesics > NSAIDS > opioids; only lido and codine+ asa > placebo
- Pain: opioids (class or single drug) not better than placebo

1. Chou et al (2015); 2. Busse et al (2018);
3. Krebs et al (2018); 4. Huang et al (2019)

LTOT: Harms in general population[1]

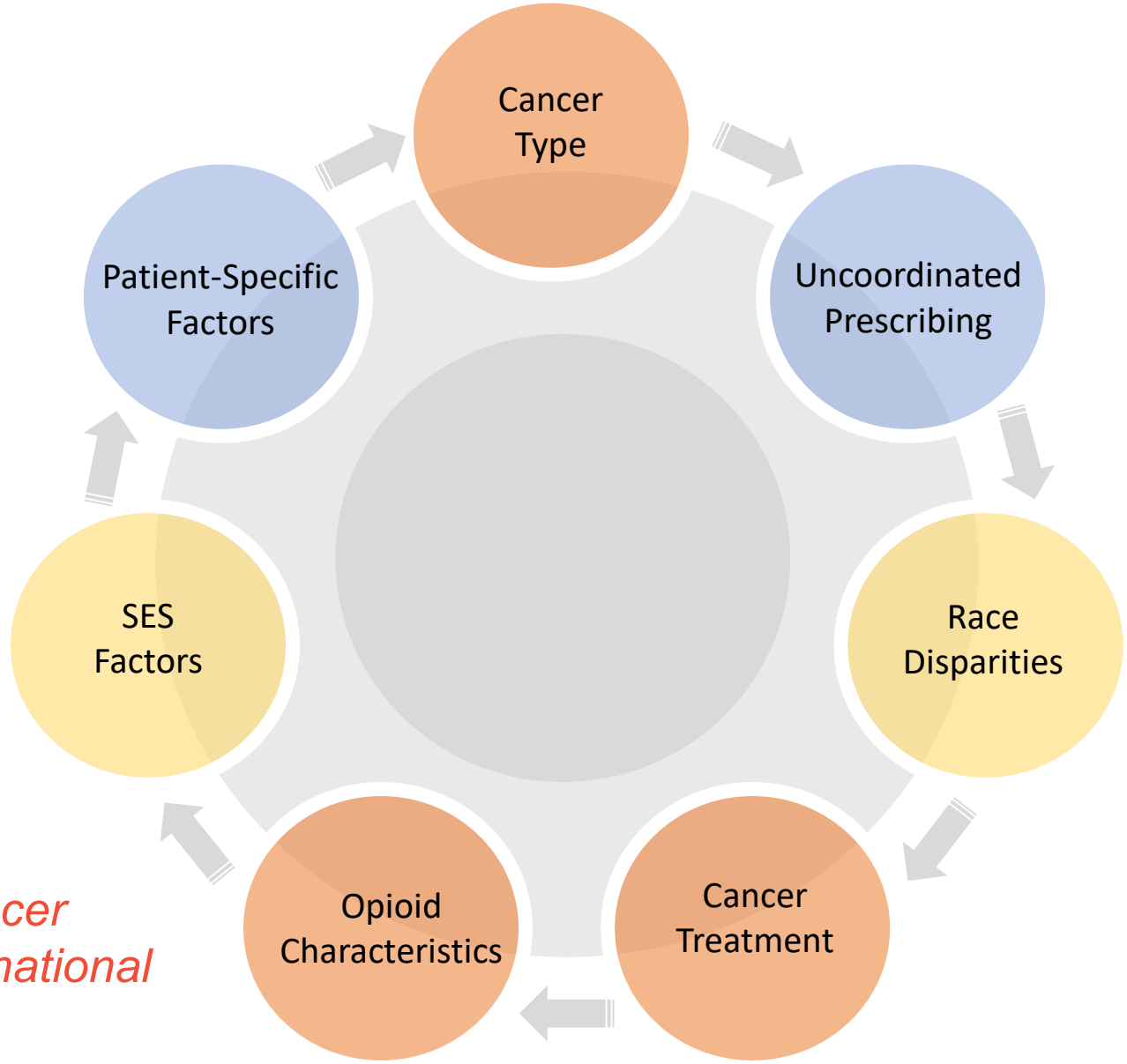
- Decreased function/return to work[1-6]
- Induced depression (more of a duration than a dose effect)[7]
- Motor vehicle accidents (OR 1.2-1.4 @ 20 MME vs. < 20)[8]
- Falls (especially soon after initiation)[9]
- OUD (primary care 3-26%, pain clinic 2-14% on LTOT)[10]
- Overdose/mortality[11] (worse with > 100MME, co-prescription of benzodiazepines[12-13], gabapentenoids[12-13]; includes Tramadol[14])

1. Chou (2015); 2. Webster et al (2007); 3. White et al (2009); 4. Volinn et al (2009); 5. Franklin et al (2008); 6. Brede et al (2012); 7. Scherrer (2016); 8. Gomes (2013); 9. Soderberg (2013); 10. CDC, MMWR (March 2016). 11. Dunn (2010); 12. Gomes (2011); 13. Bohnert (2011); 14. Zedler (2014)

Dose Related Harms

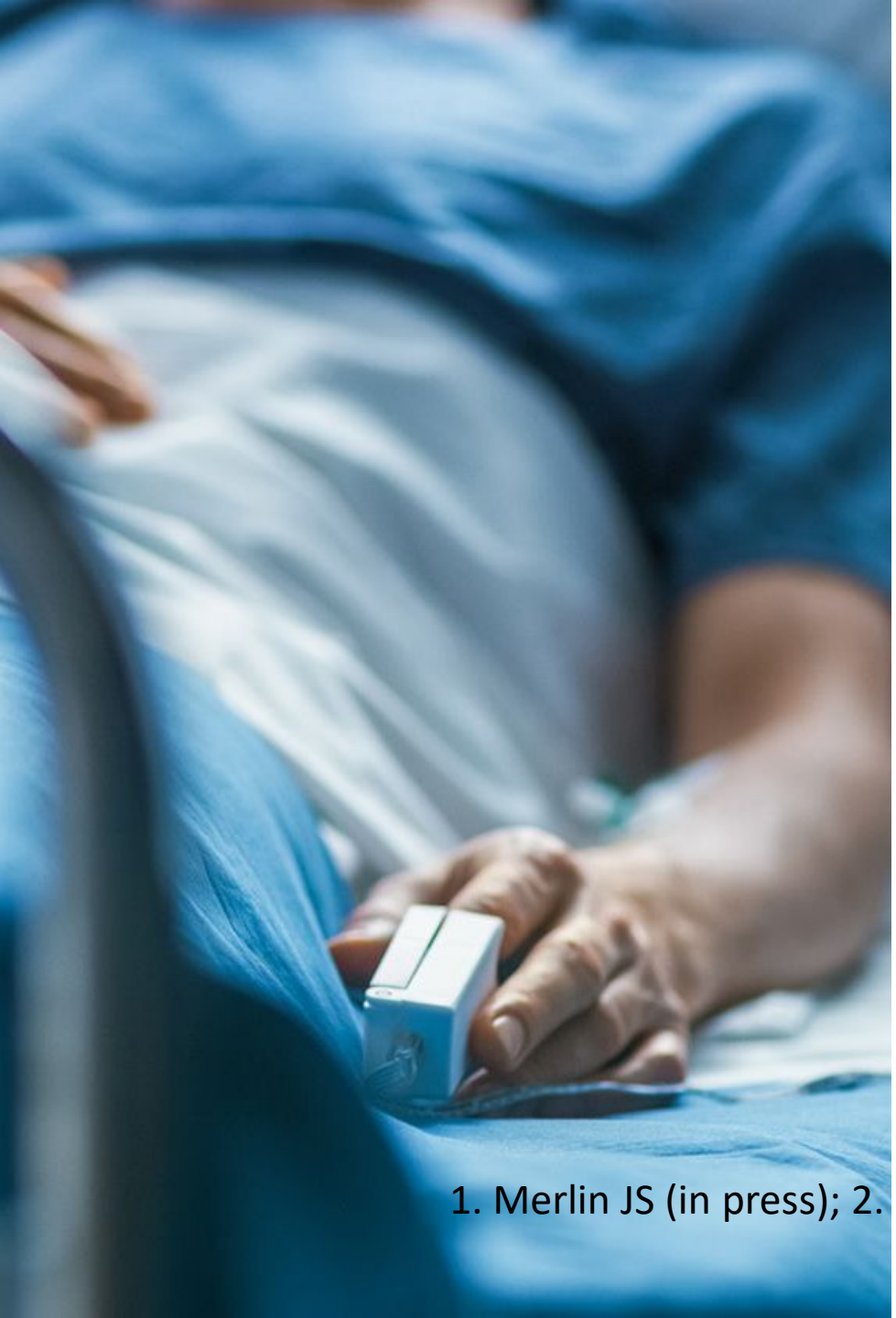
Total Daily Dose (oral morphine equivalence mg/day)	Dunn et al., 2010 Hazard Ratio (95% CI)	Gomes et al.,2011 Odds Ratio (95% CI)	Bohnert et al., 2011 Hazard Ratio (95% CI)
< 20 mg/day	1.00 reference value	1.00 reference value	1.00 reference value
20-50 mg/day	1.2 (0.4-3.6)	1.3 (0.9-1.8)	1.9 (1.3-2.7)
50-100 mg/day	3.1 (1.0-9.5)	1.9 (1.3-2.9)	4.6 (3.2-6.7)
>100mg/day	11.2 (4.8-26.0)	2.0 (1.3-3.2)	7.2 (4.9-10.7)

Factors associated with LTOT in Cancer Survivors



Average prevalence rate of LTOT in cancer survivors was 24% -5X higher than the national average.

Jones, Fu, Merlin et al (2021)



LTOT in serious illness: Why does it matter?

- No reason why serious illness or cancer would be ”protective” [1, 2]
- Some of our most complex patients end up on LTOT[3,4]
- Evidence of LTOT benefit in general and in serious illness is not strong
- Risks of LTOT in the general population are well-known and recent data showing risk of serious adverse events in patients with cancer

1. Merlin JS (in press); 2. Chino et al (2020); 3. Merlin et al (2021) 4. Jones, Merlin et al. (2021)

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What are we seeing in our practice?

- Condition X or complex persistent opioid dependence [1]
- “The gray area between opioid dependence and addiction” [2]
- Many on LTOT report poor pain and function
- Tapers worsen psychiatric and medical instability [3]
- Increased risk if you continue or stop [3]
- LTOT conundrum: A new clinical entity or just OUD? [4]

1. Edmond et al. Journal of Pain (2022)
2. Ballantyne et al. Archives of Internal Medicine (2012)
2. Agnoli et al. JAMA (2021)
3. Manhapra, A., Arias, A. J., & Ballantyne, J. C. (2018)

What are some experts saying

- Condition “X” is a new diagnostic entity needed?
  - 3/4 Yes
  - 1/4 No
  - Many argued for both sides of the debate

  Themes
  - Current implementation of the DSM criteria of OUD is not meeting the clinical needs of patients or clinicians
  - There are shared biological underpinnings of pain and OUD
  - Stigma plays a role in both sides of the debate

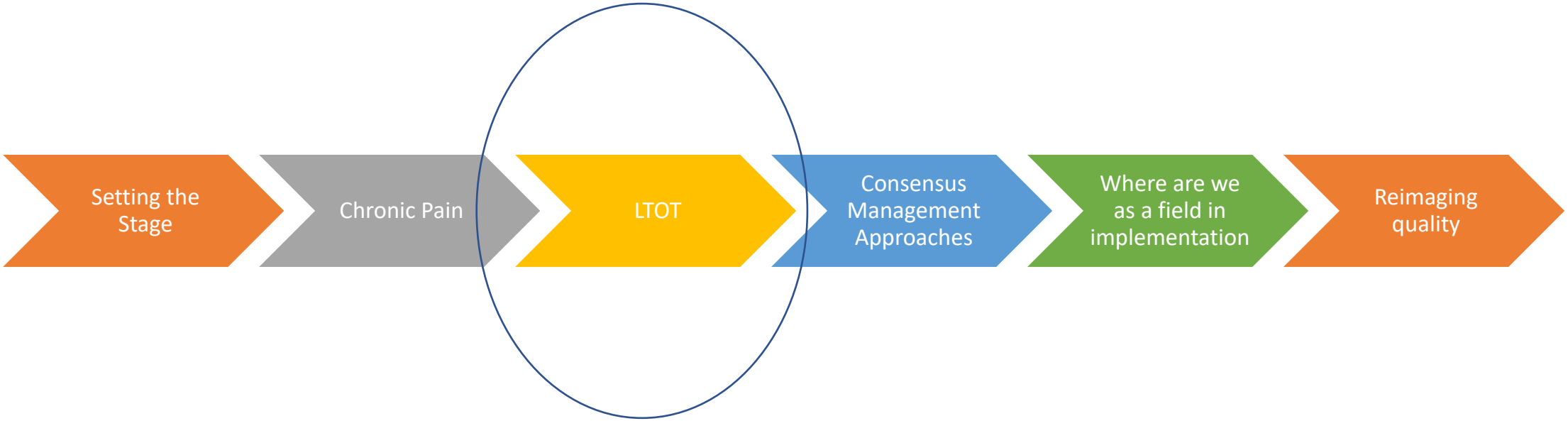
Edmond et al. (2022)

Our thoughts

- We know from our work in serious illness that patients have varying levels of acceptance of their illness
- We often use language that resonates with the patient and their lived experience
- We are also honest, unafraid of hard conversations, and transparent in a way that is patient-centered and goal-oriented
- Name the behaviors then call it what you and the patient want but don't ignore something that is causing suffering
- No matter what you call it treatment is the same
  - Psychosocial support +/-
  - Opioid tapering
  - Buprenorphine

Jones and Merlin (2022)

Road Map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Key Term: Opioid Misuse

Behaviors potentially associated with increased risk of opioid-related serious harms such as:

1) Missing appointments
2) Taking opioids for symptoms other than pain
3) Using more opioid than prescribed
4) Repeatedly asking for an increase in opioid dose
5) Aggressive behavior related to the opioid
6) Concurrent alcohol and other substance use

Synonyms: “~~red flag~~”, “~~aberrant~~”, “~~chemical coping~~”, concerning behaviors

How common is opioid misuse in individuals with serious illness?

- Studies in oncology palliative care settings have found:
  - Opioid misuse: 20-40%[1-3]
  - Abnormal drug screens: 30-50% of patients tested[4]
- A survey of ambulatory palliative care clinicians found that 53% spent > 30 min/day managing opioid misuse[5]

1. Yennurajalingam et al (2018); 2. Ma (2014); 3. Koyyalagunta et al (2013); 4. Rauenzahn (2017); 5. Merlin (2018)

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Predicting risk of opioid misuse

Traditional approach

- Tools to predict opioid misuse risk, which are widely available but low quality.
- Example: Opioid Risk Tool (ORT): low quality studies, poor sensitivity and specificity, no studies evaluating effectiveness for misuse, OUD, overdose

More recent approach

- Factors predictive of high OUD risk: hx of OUD, non-opioid SUD, certain mental health dx, certain psych meds. If one or more of these factors are present, use caution.
- No symptoms, signs, or tools can identify low-risk individuals.

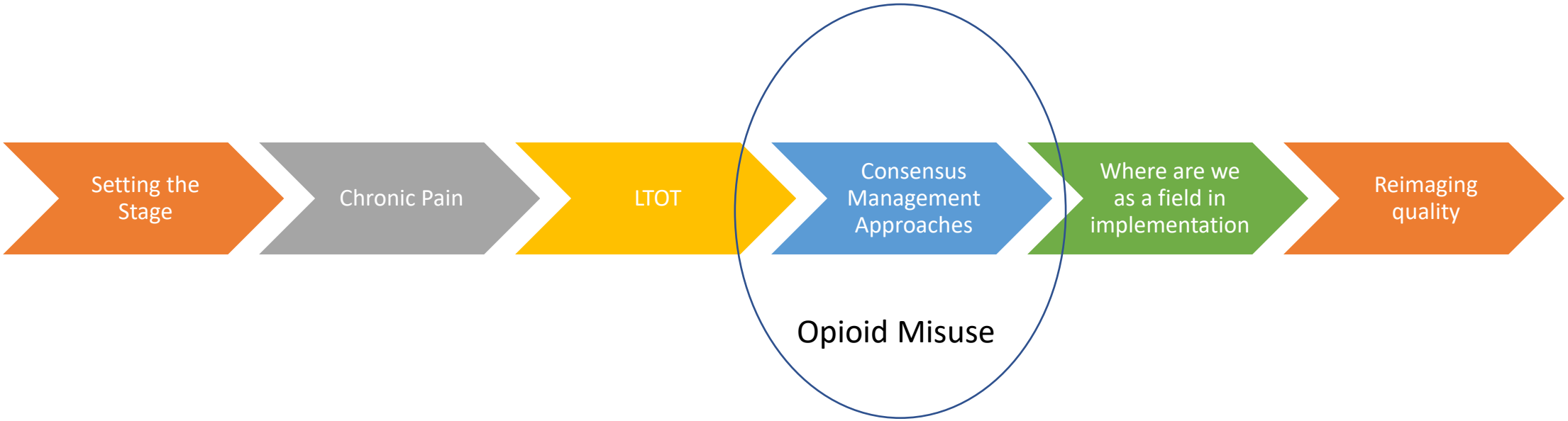
Chou et al (2015); Klimas et al (2019); Wood, Simel, & Klimas (2019)

Stop asking is this pain or addiction?

- False Dichotomy
  - The patient has pain
  - The patient may also have an opioid misuse or an opioid use disorder
  - High prevalence of pain in OUD
    - 42% of patients with OUD report chronic pain
    - 10-30% of patients on LTOT develop an OUD
- What is the optimal treatment plan for pain if opioid use disorder is co-occurring?

Vowles (2015)
Boscarino, et al (2015)
Jones and Mason (2022

Road Map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Opioid Misuse

Case 1: Opioid Misuse: other substance use

Ms. H is a 60 y/o woman with breast cancer with metastases to the spine and low back pain. She has been getting regular prescriptions for oxycodone 10mg QID to treat her back pain. She has a urine drug test that is positive for cocaine.

The patient does not have a history of OUD, has no other opioid misuse behaviors, and her urine is positive for prescribed oxycodone.

She reports good pain control and requests that her current regimen be continued.

A review of oncologist notes suggests that her prognosis is likely years.

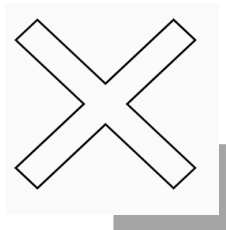
Which management strategies would you use?

a. Continue patient's opioids
b. Increase monitoring
c. Taper opioids
d. Transition the patient to buprenorphine/naloxone

Delphi Results: intermittent stimulant use

Appropriate

- Continue opioids
- Increase monitoring



Inappropriate

- Taper opioids

Uncertain

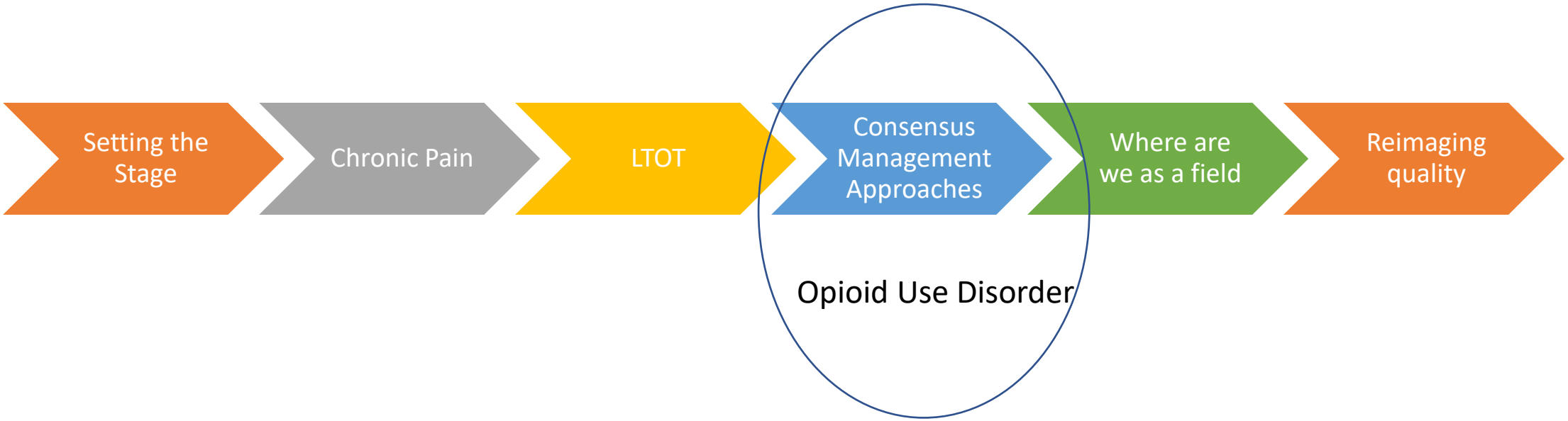
- Transition to buprenorphine

Disclaimer

- High-quality evidence on opioid tapering is limited
  - Some evidence supports improved pain and quality of life
  - But for some tapering leads to adverse effects opioid withdrawal, psychological distress, and increased pain.
  - Buprenorphine can help
- Harm reduction
  - Frequent check-ins
  - Short prescriptions
  - Naloxone
  - Interdisciplinary multimodal care.
- An OUD may emerge as an aspect of opioid tapering
- This is an area where new research is emerging.
- Policies make it challenging to provide individualized care.

Frank 2017 Larochelle et al (2021); Agnoli et al (2021)

Road Map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Opioid Use Disorder

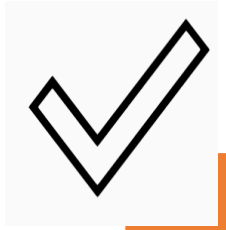
Case 2: Opioid use disorder on treatment

Mr. R is a 50 y/o male with early-stage laryngeal cancer undergoing **curative** intent XRT. He also has OUD on buprenorphine/naloxone (suboxone) at a stable dose of 16mg daily x many years. He has pain related to his XRT. How would you best address his pain?

Which management strategies would you use?

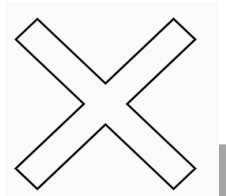
a. Continue buprenorphine/naloxone and divide the original dose into two or three times a day dosing
b. Continue buprenorphine/naloxone and add a full agonist opioid (e.g. oxycodone, morphine, hydromorphone, fentanyl).
c. Discontinue the buprenorphine/naloxone and start methadone three times per a day
d. Discontinue the buprenorphine/naloxone and start full opioid agonist other than methadone
e. Refer to a methadone treatment program

Delphi Results: OUD on treatment



Appropriate

- Continue buprenorphine and divide dose
- Stop buprenorphine and add methadone TID



Inappropriate

- Discontinue buprenorphine add another full agonist
- Refer to a methadone program

Uncertain

- Continue buprenorphine and add another full agonist

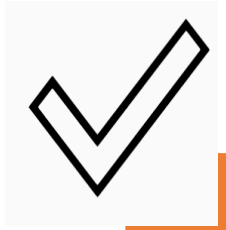
Case 3: OUD on methadone

- 60-year-old with advanced cancer who is in remission from OUD on methadone obtain through a methadone treatment program who develops cancer-related pain. Prognosis is > 1 year.

Which management strategies would you use?

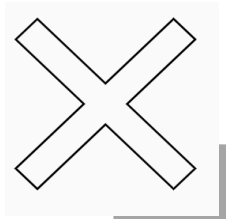
a. Split methadone dosing to BID-TID
b. Discontinue methadone and start a full agonist
c. Transition from methadone to buprenorphine
d. Continue methadone and add a full agonist
e. Ask the methadone clinic to split the dose

Delphi Results: Methadone treatment



Appropriate

- Split methadone into BID or TID dosing and take over prescribing



Inappropriate

- Discontinue methadone and start a full agonist
- Transition from methadone to buprenorphine

Uncertain

- Asking methadone clinic to split the doses
- Adding a full agonist (although appropriate if prognosis was short)

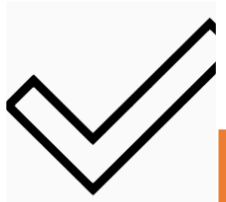
Case 4: OUD not on treatment

- 59-year-old with advanced cancer who has a recent history of OUD not on treatment and who develops cancer-related pain. The prognosis is > 1 year.

Which management strategies would you use?

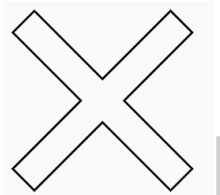
a. Begin bup/nx with twice or three times a day dosing
b. Send patient to a methadone clinic for daily dosing
c. Prescribe a full agonist
d. Prescribe methadone BID or TID

Delphi Results: History of OUD experiencing pain and not on treatment for OUD: Longer prognosis



Appropriate

- Begin bup/nx with twice or three times/day dosing.



Inappropriate

- Send patient to a methadone clinic for daily dosing

Uncertain

- Prescribe a full agonist
- Prescribe methadone BID or TID

Jones and Merlin et al. 2022 JAMA Onc

Curveball: What if the patient has a recurrence and now the prognosis is weeks? Would your management change?

Delphi Results: History of OUD experiencing pain and not on treatment for OUD

With a *shorter prognosis*

Prescribe methadone dosed two to three times/day

Jones and Merlin et al. 2022 JAMA Onc

Which is better to treat comorbid OUD and pain, bup/nx or methadone?

- Choice dependent on patient preference, availability
- For OUD comparative effectiveness same
- Retention slightly better for methadone, but ?feasibility
- No head-to-head trial of bup/nx vs. methadone for pain or pain/OUD
  - Bup/nx ± full agonist is very effective

SAMHSA (2018) Medications for Opioid Use Disorder TIP 63; Wakeman et al., 2020, Jones & Merlin et al. under review; Weimer et al. 2022

Buprenorphine is a unique opioid

- Its strong affinity for the μ opioid receptor and slow dissociation may provide sustained analgesia at relatively low doses.
  - Doses of buprenorphine can be divided in patients with pain
  - OK to add full agonists to buprenorphine if more analgesia needed, may need higher doses
  - NOT OK to add buprenorphine to full agonists, may precipitate withdrawal
  - Co-formulated with naloxone, which has minimal absorption
- Partial μ agonist ≠ partial analgesic
- Unique Receptor activity may improve mood instability
- Despite being a saferoption it is highly regulated

Jones (2019); Webster et al (2020); Gudin & Fudin (2020)

Where does buprenorphine come in?

Patients without serious illness

- Always: patient with OUD (reduces opioid use[1,3], HIV[3-5], mortality[6])
- Very often: patients with opioid misuse that does not resolve, and for whom you have a high suspicion for "subclinical OUD"
- Newer approach: in patients without misuse/OUD but for whom you are tapering (e.g., due to lack of functional benefit, patient preference)
- Sometimes: pain in individuals who are high risk for opioid side effects (e.g., frail older adults)
- Uncharted territory but makes sense: complex persistent dependence (or is this just OUD?); patients for whom opioids are being considered who are at high risk (e.g., due to SUD history)

1. Mattick (2009); 2. Mattick (2014); 3. Karki (2016). 4. Woody (2014); 5. Edelman (2014); 6. Gibson (2008); 7. Fitzgerald Jones & Merlin (2021)

Where does buprenorphine come in?

Patients with serious illness

- Little literature, approach likely moderated by expected course of serious illness, functional expectations, prognosis

1. Mattick (2009); 2. Mattick (2014); 3. Karki (2016). 4. Woody (2014); 5. Edelman (2014); 6. Gibson (2008); 7. Fitzgerald Jones & Merlin (2021)

Philosophical note

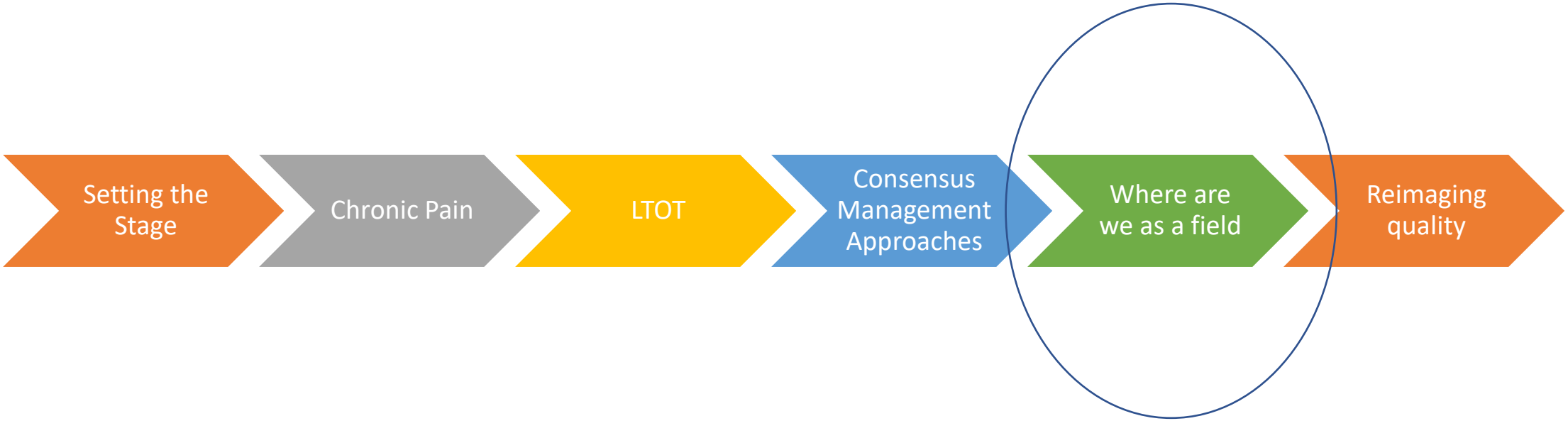
- These are already our patients
- Now there is no excuse for not having an X waiver

New X waiver legislation

- As of April 27, 2021, the waiver became more accessible, with the of new Buprenorphine Practice Guidelines
  - Allows DEA licensed clinicians to apply for an X waiver to treat up to 30 patients, without completing the additional educational training or attesting to the ability to refer for counseling.
- You must submit a Notice of Intent
- Early data indicates the new legislation has not slowed the pandemic growth of X waivered clinicians

SAMSHA (2021); Spetz et al (2022)

Road Map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How are we doing?

- Only 13% of palliative care clinicians are X waivered
- A national study of 100 clinicians who expressed interest in OUD
  - 1/3 did not have a X waiver
  - 1/3 had a X waiver but did not prescribe
  - The X waiver is only one of many implementation barriers
- NP/PAs are the most rapidly growing waivered clinicians, but in approximately half of states they require their collaborating physician to be X waivered
- Stigma is a significant barrier

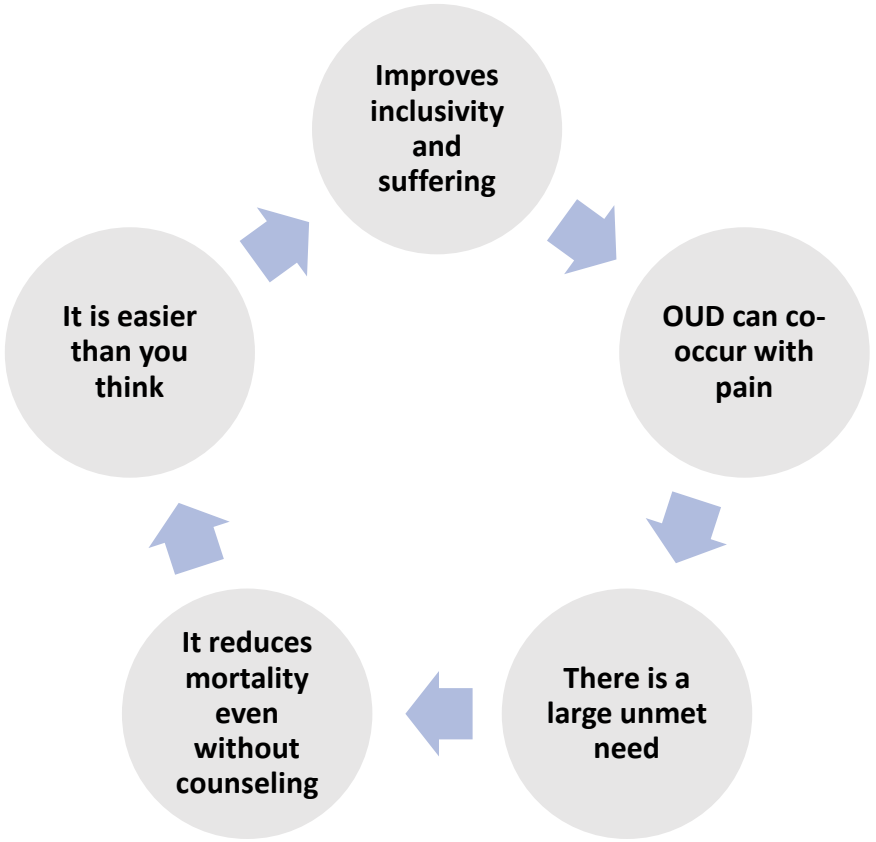
Merlin et al (2019); Jones, Merlin et al (2022); Ho, Jones, Merlin et al. (2022)

The X waiver to prescribe buprenorphine

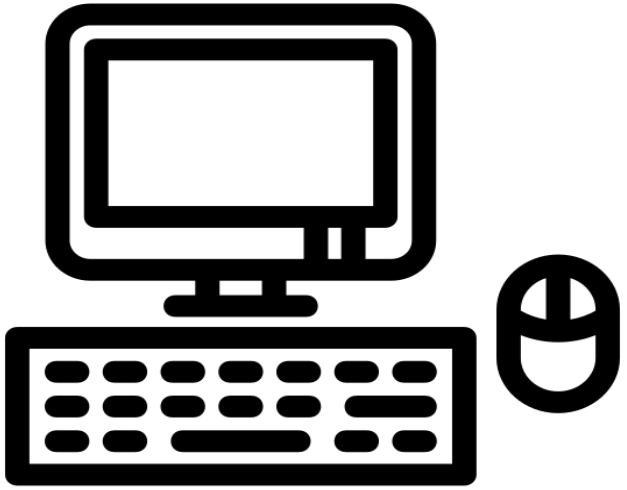
What?

Every palliative care prescriber should have a DEA X waiver

Why?



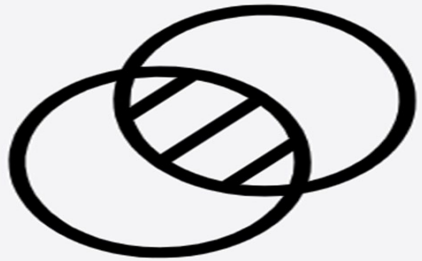
How?



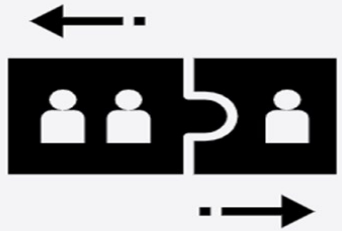
Complete a notice of intent at https://buprenorphine.samhsa.gov

Jones, Merlin et al., 2022

Why do I need an X waiver if I am treating *pain*?



- Improves transparency

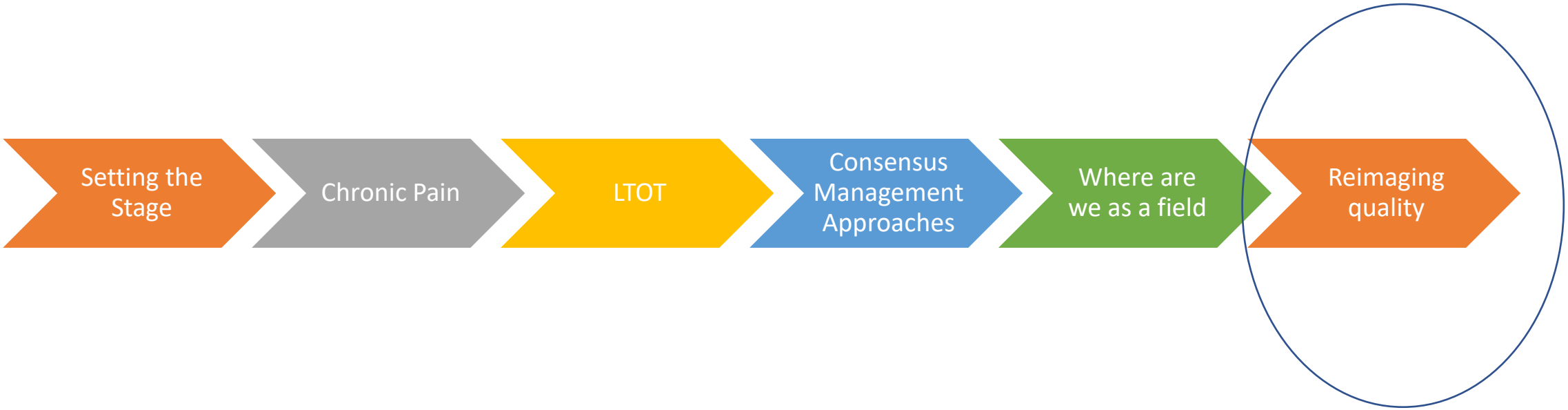


- Combats Stigma

- Makes you a better clinician

Jones, Merlin et al., 2022

Road Map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Our Quality Wish List

- Move beyond the biomedical model and opioid-centric approach to pain management
- Re-imagine an approach drawing from our strengths as a field

And

- State-of-the-art evidence from various fields:
  - pain
  - behavioral science
  - nursing science
  - addiction
- Prioritize training these skills using existing resources
- We can lead the way to a new model of pain care that is a force for the greater good.

Thank you!

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