Complex challenges in pain and opioid management: relevance to de-prescribing

Jessica Merlin MD, PhD, MBA
Professor of Medicine with Tenure
@JessicaMerlinMD

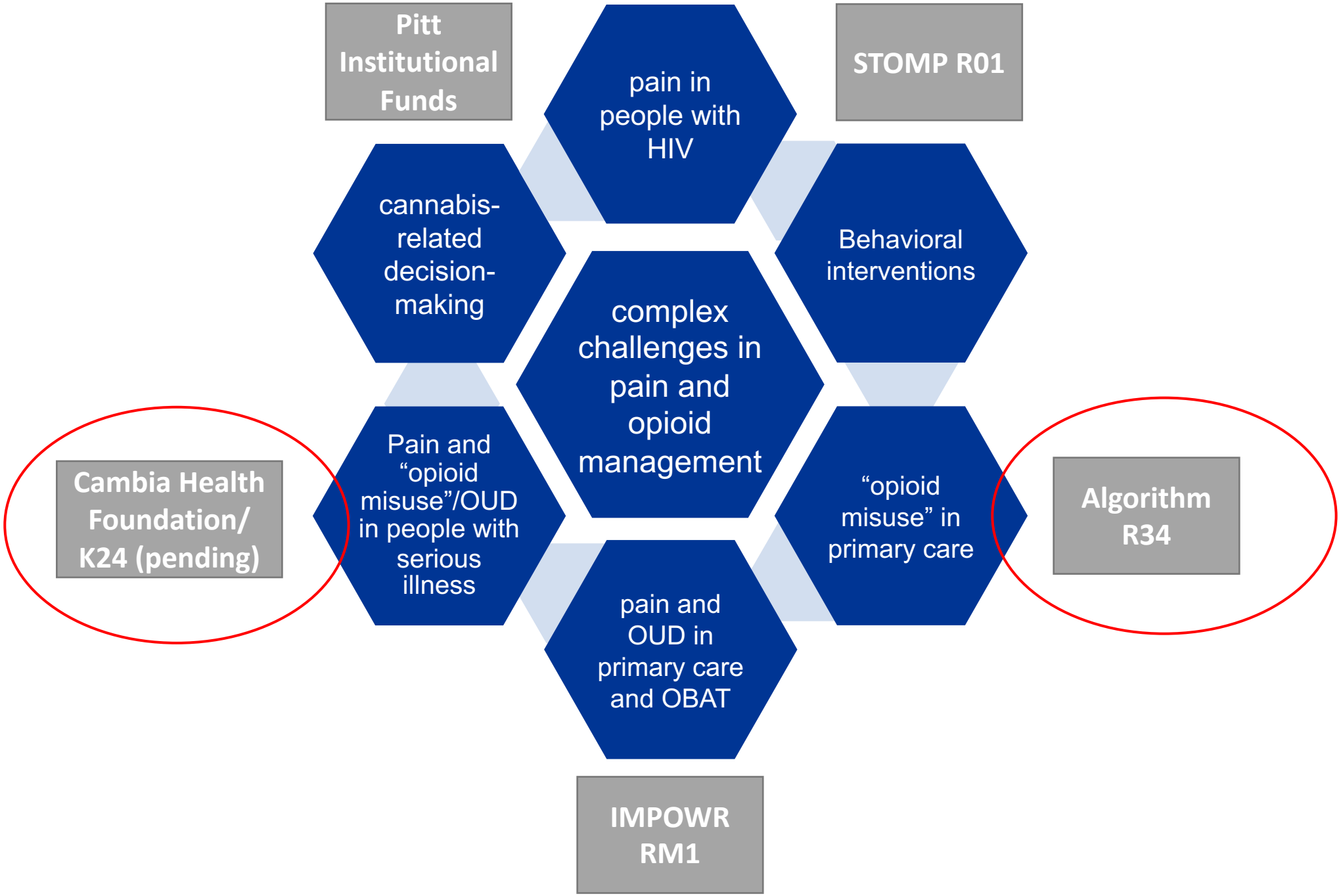
University of Pittsburgh

CHAMPP
CHALLENGES IN MANAGING AND PREVENTING PAIN

TREETOP

Conflicts of Interest

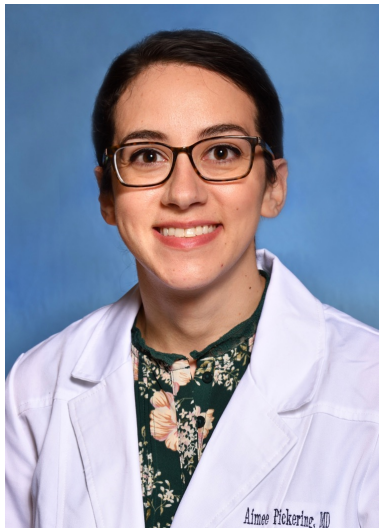
- My research is funded in part by a grant to Pitt from the Cambia Health Foundation.


Pitt Institutional Funds
pain in people with HIV
STOMP R01
cannabis-related decision-making
Behavioral interventions
complex challenges in pain and opioid management
Cambia Health Foundation/ K24 (pending)
Pain and "opioid misuse"/OUD in people with serious illness
"opioid misuse" in primary care
Algorithm R34
pain and OUD in primary care and OBAT
IMPOWR RM1

How I learned about de-prescribing

Older Patient and Caregiver Perspectives on Medication Value and Deprescribing: A Qualitative Study

*Aimee N. Pickering, MD,** *Megan E. Hamm, PhD,†* *Alicia Dawdani, BS,†*
Joseph T. Hanlon, PharmD,‡§¶‖ *Carolyn T. Thorpe, PhD, MPH,¶*** *Walid F. Gellad, MD,†§¶* *and*
Thomas R. Radomski, MD†§¶



Dr. Aimee Pickering

Dr. Tom Radomski

Themes: Medication features that add value

- Perceived effectiveness

Aimee Pickering,

Themes: Medication features that add value

- Perceived effectiveness
  - **Subjective improvement in symptoms**

"I've always looked at it not… whether or not I needed it (the medication) beforehand, but whether or not it made me feel better afterward."

Themes: Medication features that add value

- Perceived effectiveness
  - Subjective improvement in symptoms
  - **Objective improvement in clinical values**

"I know mine's (medication) working [because] I'm diabetic, because there's one point my A1C was 9.1… and now it's down to 6.1"

Themes: Medication features that add value

- Perceived effectiveness
  - Subjective improvement in symptoms
  - Objective improvement in clinical values
  - **Disease prevention**

"I wasn't really following up on all those medications… and then I ended up having another heart attack and then the reality set it and started taking my medications like I was supposed to…"

Aimee Pickering,

Themes: Medication features that detract value

- Adverse effects on quality-of-life

Aimee Pickering,

Themes: Medication features that detract value

- Adverse effects on quality-of-life
  - **Severity of side effects**

"I think if it's debilitating in any form like nausea, vomiting… diarrhea… [and the side effects] are going to impact your life… and your ability to do even basic things like leaving the house… that's when it's not worth it anymore…."

Themes: Medication features that detract value

- Adverse effects on quality-of-life
  - Severity of side effects
  - **Inconvenience associated with administration**

"I hate testing myself for my sugar every morning, and I don't do it every day… so I don't take insulin, like after my meals…."

Aimee Pickering,

Themes: Medication features that detract value

- Adverse effects on quality-of-life
  - Severity of side effects
  - Inconvenience associated with administration
  - **Discomfort associated with administration**

"They put me on an injection which I did not like, and I tried that for a while and went back to the doctor and said I can't do this… I can't give myself injections…."

Aimee Pickering,

How these insights relate to opioid prescribing

- Patient perception of symptom improvement
- Many formulations and medications to address side effects
- Fairly convenient/comfortable to administer

Among patients (with or without HIV) in primary care prescribed opioids, what is the best way to manage misuse behaviors?

Opioid misuse in primary care

- Opioids are commonly prescribed for chronic pain[1]
- Safe opioid prescribing requires careful attention to patient behavior
- "Misuse behaviors" are common in clinical practice[2]

1. Bohnert AS, *Ann Int Med*, 2018. 2. Vowles KE, *Pain*, 2015.

Opioid misuse in primary care

- May signal serious underlying (e.g., opioid use disorder)[1]
- Unclear course of action
- Leads clinician dissatisfaction/ burnout[3,4]
- Focus on identification of behaviors, ***limited evidence*** on how to respond when they arise

1. Fishbain DA et al, *Pain Med*, 2008. 2. Meltzer EC et al, *Pain Med,* 2012.
3. Dobscha SK et al, *Pain Med*, 2008. 4. Merlin JS et al, *Pain Med,* 2014.

Study: opioid misuse in primary care

Delphi approach

- Developed by RAND during the cold war[1]
- Used when there is a lack of evidence but an urgent need for guidance[2]
- Systematic approach to explore whether consensus exists, and if it does, to identify consensus beliefs among a diverse group of experts[3,4]
- Widely accepted as a level of evidence that can drive policy and practice[5]

1. https://en.wikipedia.org/wiki/Delphi_method. 2. Keeney S, Wiley-Blackwell, 2011.
3. Barber CE, *Arthritis Res Ther,* 2015. 4. Khodyakov D, *J Eval Clin Pract,* 2017.
5. Khodyakov D, *BMC Med Res Methodol,* 2011.

Study: opioid misuse in primary care

- Participants recruited from expert groups who prescribe opioids and are self-reported experts
- Four online rounds:
  1. Brainstorm behaviors, pick 2 most common & 2 most challenging
  2. Asked about management of most important Round 1 behaviors

Merlin JS, *BMJ Open*, 2016.

Study: opioid misuse in primary care

3. Rate importance of Round 2 strategies on 1-9 scale. A priori rules:
   - 1-3 “not important,” 4-6 “uncertain,” 7-9 “very important”
   - Disagreement: ≥1/3 “not important” AND ≥1/3 “very important”
   - Consensus: absence of disagreement
     - If consensus: median ≥ 7 management strategy important, ≤ 3 not important, 4-6 uncertain importance
   - Free-text clarification encouraged

Merlin JS, *BMJ Open*, 2016.

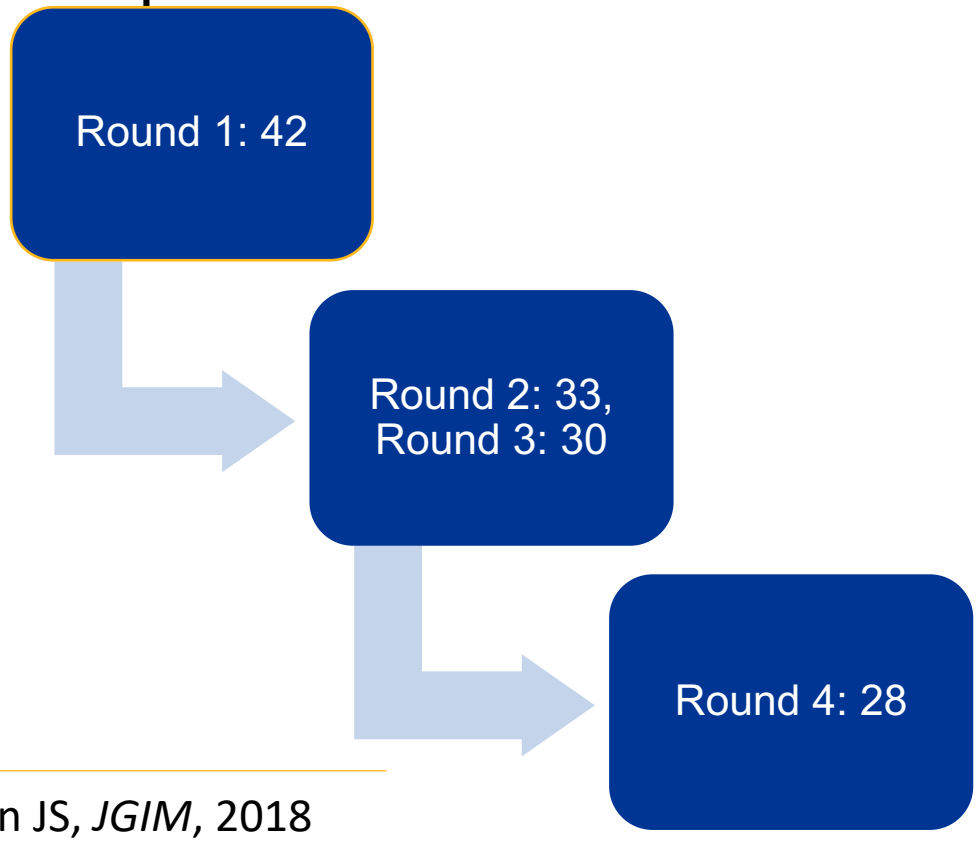
Study: opioid misuse in primary care

4. Developed cases:
   - Told participants all consensus approaches had been utilized
   - Highlighted branch points based on comments
   - If there was disagreement, provided prior round response and re-asked question

Merlin JS, *BMJ Open*, 2016.

Study: opioid misuse in primary care

Participants:



Merlin JS, *JGIM*, 2018

Round 1 participants:

- Female: 52%
- White: 83%
- Physicians: 71% (90% internists)
- Academic primary (40%) or specialty care (19%); 48% VA
- All US regions represented

Study: opioid misuse in primary care

The 6 most frequently cited common and challenging behaviors

- missing appointments
- taking opioids for symptoms other than pain
- using more opioid medication than prescribed
- asking for an increase in opioid dose
- and alcohol and other substance use

Merlin JS, *JGIM*, 2018.

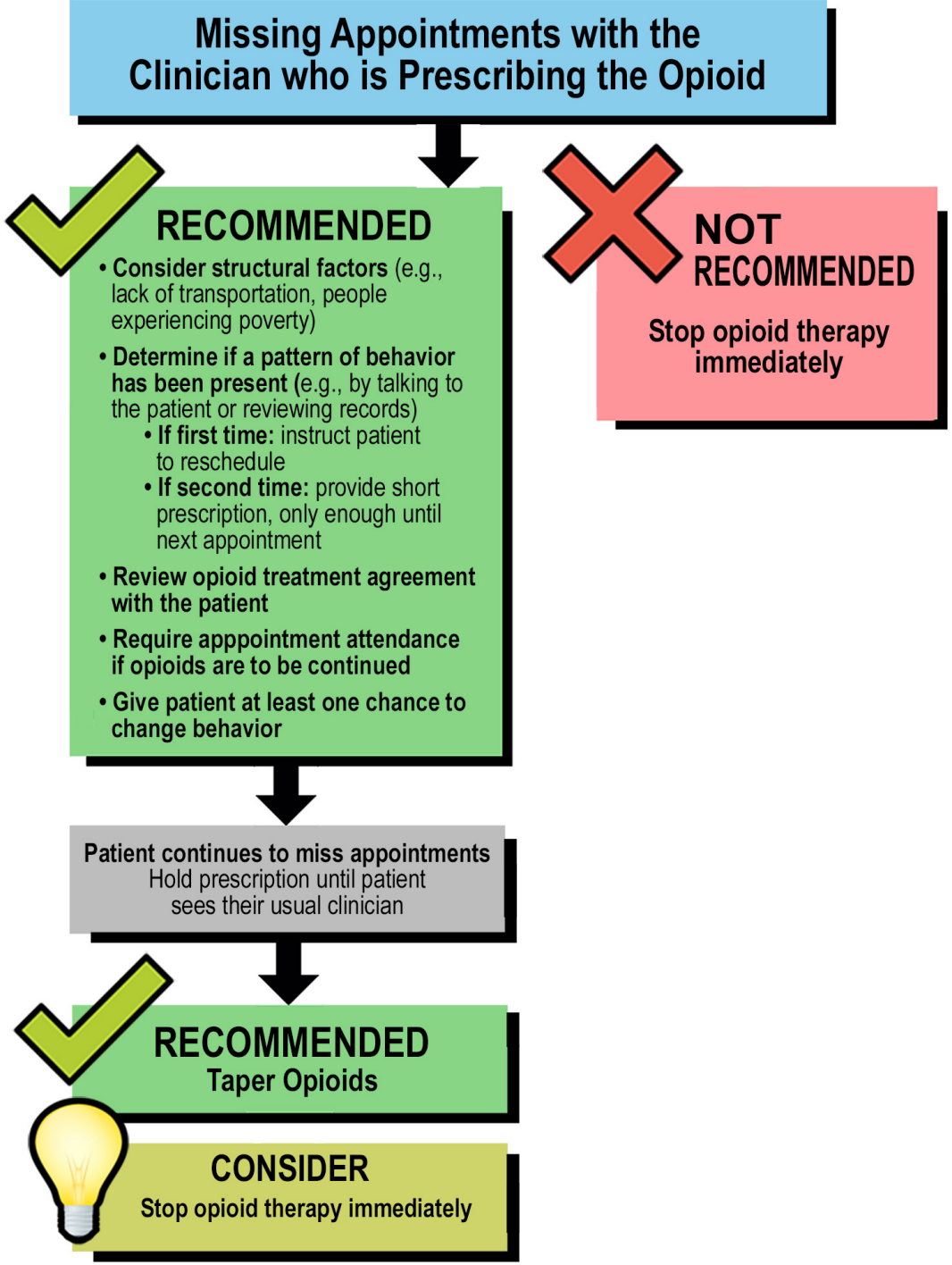
Young S, Merlin JS, *Pain Med*, 2019.

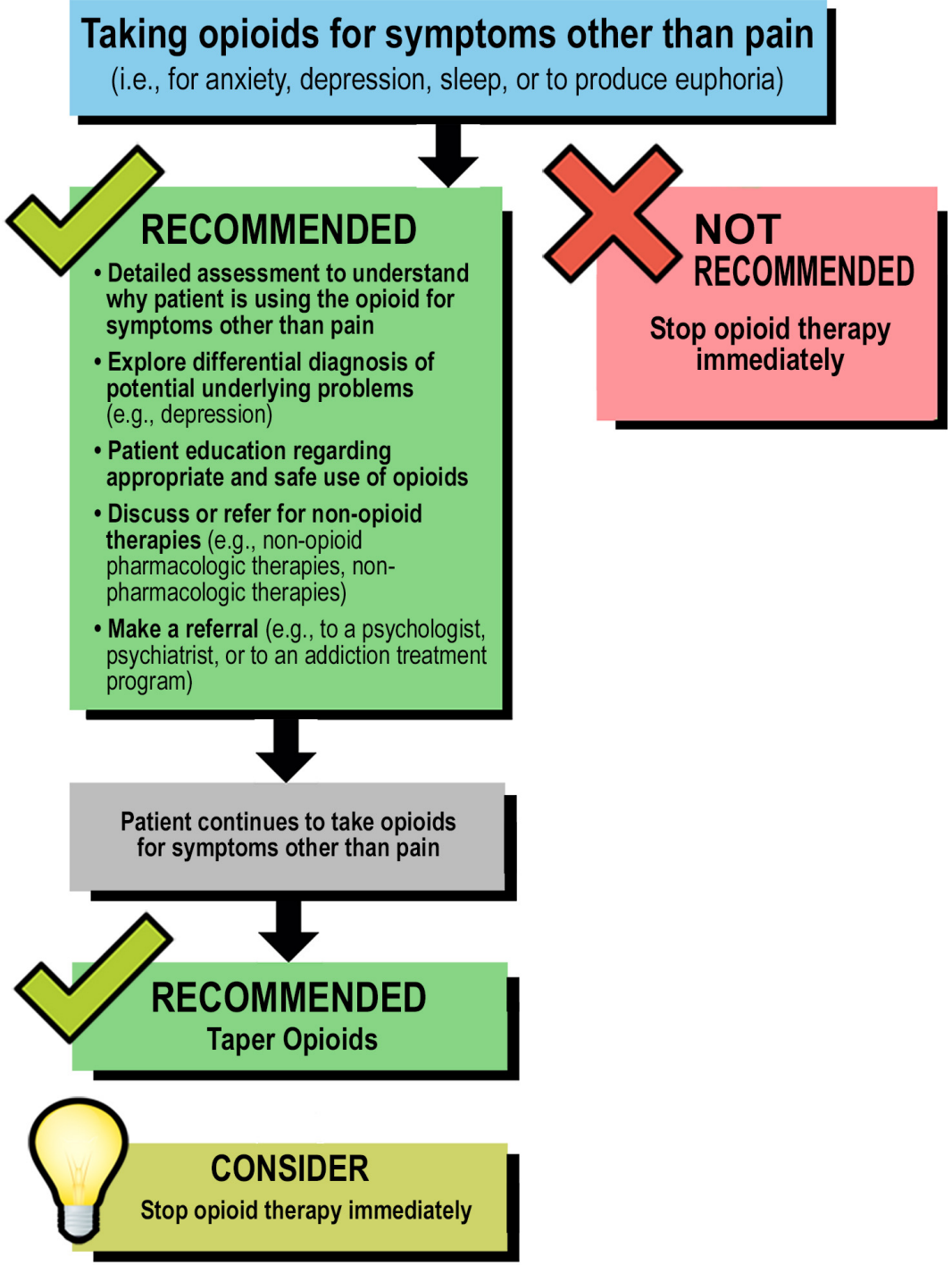
Study: opioid misuse in primary care

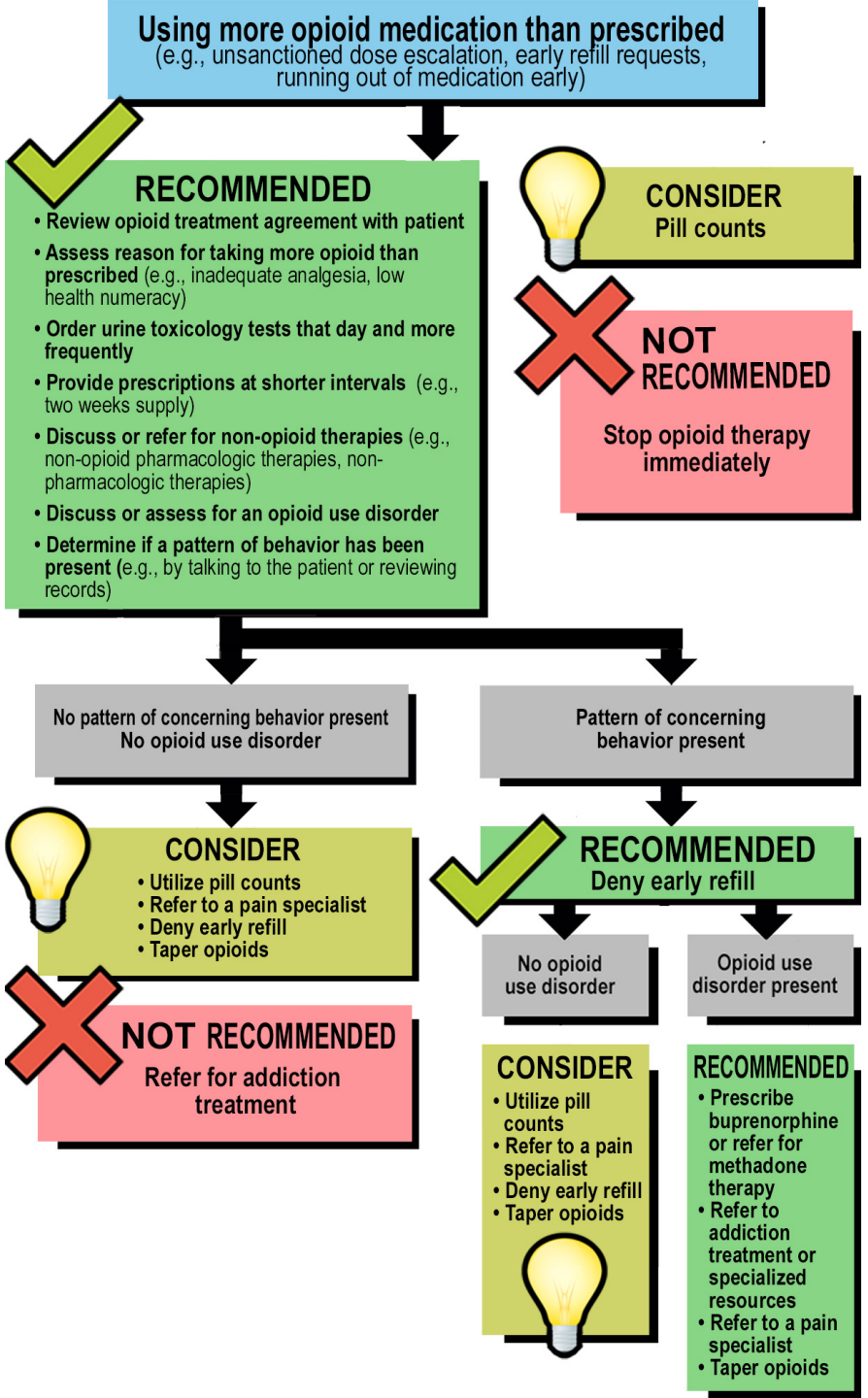
Common strategies across behaviors

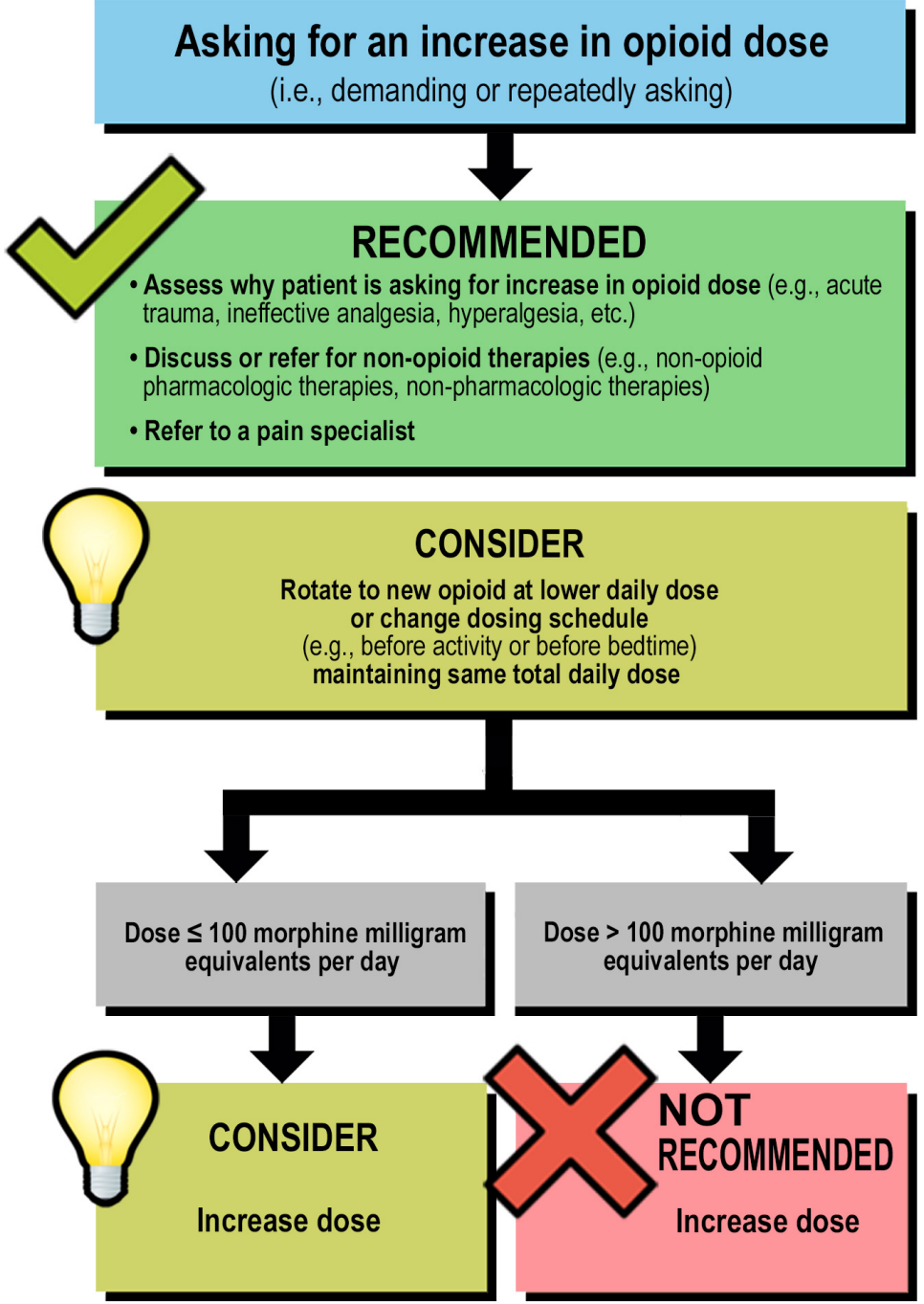
- Do not immediately stop abruptly
- Patient education
- Determine if there is a pattern present and if there is an opioid use disorder
- If there is an opioid use disorder, treat it
- If there is a pattern but no opioid use disorder, weigh benefits vs. risks
- Consider tapering/stopping

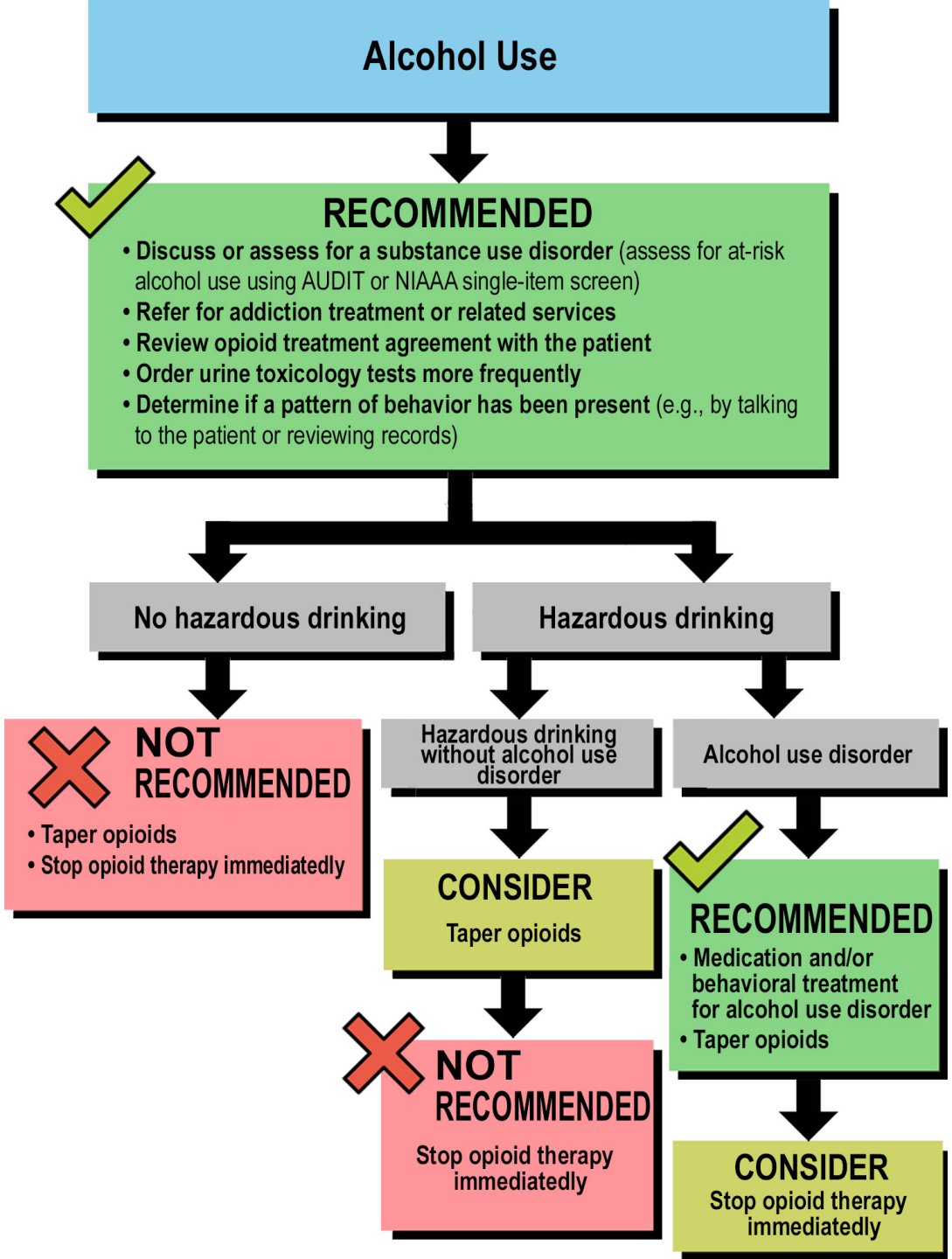
Merlin JS, *JGIM*, 2018.

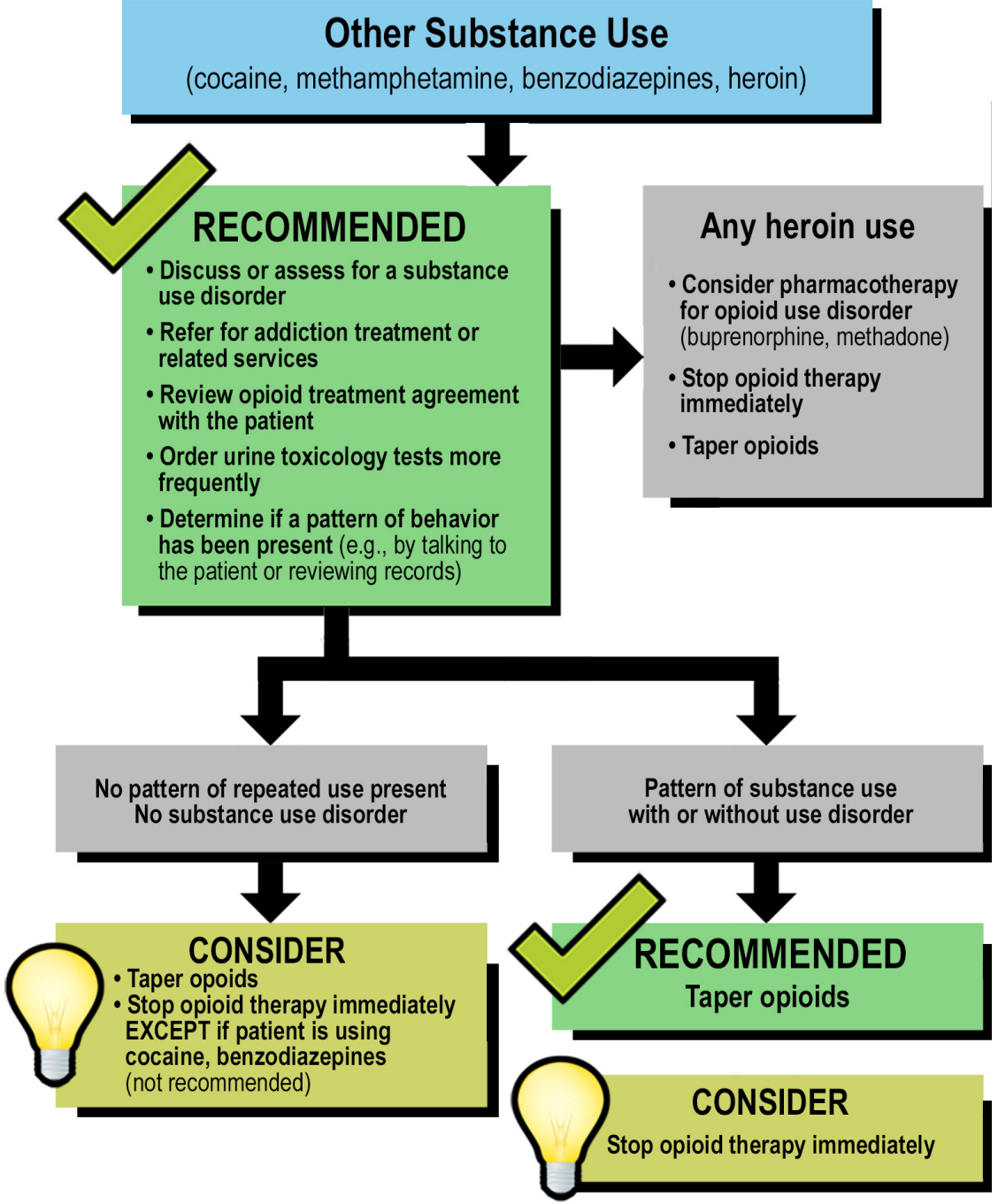

Missing Appointments with the Clinician who is Prescribing the Opioid
RECOMMENDED
• Consider structural factors (e.g., lack of transportation, people experiencing poverty)
• Determine if a pattern of behavior has been present (e.g., by talking to the patient or reviewing records)
• If first time: instruct patient to reschedule
• If second time: provide short prescription, only enough until next appointment
• Review opioid treatment agreement with the patient
• Require apppointment attendance if opioids are to be continued
• Give patient at least one chance to change behavior
NOT RECOMMENDED
Stop opioid therapy immediately
Patient continues to miss appointments
Hold prescription until patient sees their usual clinician
RECOMMENDED
Taper Opioids
CONSIDER
Stop opioid therapy immediately


Taking opioids for symptoms other than pain
(i.e., for anxiety, depression, sleep, or to produce euphoria)
RECOMMENDED
• Detailed assessment to understand why patient is using the opioid for symptoms other than pain
• Explore differential diagnosis of potential underlying problems (e.g., depression)
• Patient education regarding appropriate and safe use of opioids
• Discuss or refer for non-opioid therapies (e.g., non-opioid pharmacologic therapies, non-pharmacologic therapies)
• Make a referral (e.g., to a psychologist, psychiatrist, or to an addiction treatment program)
NOT RECOMMENDED
Stop opioid therapy immediately
Patient continues to take opioids for symptoms other than pain
RECOMMENDED
Taper Opioids
CONSIDER
Stop opioid therapy immediately


Using more opioid medication than prescribed
(e.g., unsanctioned dose escalation, early refill requests, running out of medication early)
RECOMMENDED
• Review opioid treatment agreement with patient
• Assess reason for taking more opioid than prescribed (e.g., inadequate analgesia, low health numeracy)
• Order urine toxicology tests that day and more frequently
• Provide prescriptions at shorter intervals (e.g., two weeks supply)
• Discuss or refer for non-opioid therapies (e.g., non-opioid pharmacologic therapies, non-pharmacologic therapies)
• Discuss or assess for an opioid use disorder
• Determine if a pattern of behavior has been present (e.g., by talking to the patient or reviewing records)
CONSIDER
Pill counts
NOT RECOMMENDED
Stop opioid therapy immediately
No pattern of concerning behavior present
No opioid use disorder
Pattern of concerning behavior present
CONSIDER
• Utilize pill counts
• Refer to a pain specialist
• Deny early refill
• Taper opioids
NOT RECOMMENDED
Refer for addiction treatment
RECOMMENDED
Deny early refill
No opioid use disorder
Opioid use disorder present
CONSIDER
• Utilize pill counts
• Refer to a pain specialist
• Deny early refill
• Taper opioids
RECOMMENDED
• Prescribe buprenorphine or refer for methadone therapy
• Refer to addiction treatment or specialized resources
• Refer to a pain specialist
• Taper opioids


Asking for an increase in opioid dose
(i.e., demanding or repeatedly asking)
RECOMMENDED
• Assess why patient is asking for increase in opioid dose (e.g., acute trauma, ineffective analgesia, hyperalgesia, etc.)
• Discuss or refer for non-opioid therapies (e.g., non-opioid pharmacologic therapies, non-pharmacologic therapies)
• Refer to a pain specialist
CONSIDER
Rotate to new opioid at lower daily dose
or change dosing schedule
(e.g., before activity or before bedtime)
maintaining same total daily dose
Dose ≤ 100 morphine milligram equivalents per day
Dose > 100 morphine milligram equivalents per day
CONSIDER
Increase dose
NOT RECOMMENDED
Increase dose


Alcohol Use
RECOMMENDED
• Discuss or assess for a substance use disorder (assess for at-risk alcohol use using AUDIT or NIAAA single-item screen)
• Refer for addiction treatment or related services
• Review opioid treatment agreement with the patient
• Order urine toxicology tests more frequently
• Determine if a pattern of behavior has been present (e.g., by talking to the patient or reviewing records)
No hazardous drinking
Hazardous drinking
NOT RECOMMENDED
• Taper opioids
• Stop opioid therapy immediatedly
Hazardous drinking without alcohol use disorder
Alcohol use disorder
CONSIDER
Taper opioids
RECOMMENDED
• Medication and/or behavioral treatment for alcohol use disorder
• Taper opioids
NOT RECOMMENDED
Stop opioid therapy immediatedly
CONSIDER
Stop opioid therapy immediatedly


Other Substance Use
(cocaine, methamphetamine, benzodiazepines, heroin)
RECOMMENDED
• Discuss or assess for a substance use disorder
• Refer for addiction treatment or related services
• Review opioid treatment agreement with the patient
• Order urine toxicology tests more frequently
• Determine if a pattern of behavior has been present (e.g., by talking to the patient or reviewing records)
Any heroin use
• Consider pharmacotherapy for opioid use disorder (buprenorphine, methadone)
• Stop opioid therapy immediately
• Taper opioids
No pattern of repeated use present
No substance use disorder
Pattern of substance use
with or without use disorder
CONSIDER
• Taper opoids
• Stop opioid therapy immediately EXCEPT if patient is using cocaine, benzodiazepines (not recommended)
RECOMMENDED
Taper opioids
CONSIDER
Stop opioid therapy immediately

Why consider Opioid Tapering?

- Pain, function & quality of life may improve with voluntary opioid tapering supported by multidisciplinary team

- Sometimes needed in patients with opioid misuse behaviors when buprenorphine is not feasible

Frank et al (2017)

Disclaimer

- High-quality evidence on tapering-related harms is limited
  - Can lead to withdrawal, psychological distress, unmasked OUD, increased pain
- Harm reduction
  - Frequent check ins
  - Short prescriptions
  - Naloxone
  - Interdisciplinary multimodal care.
- This is an area where new research is emerging.
- Policies make it challenging to provide individualized care

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

'How to' on opioid tapering

- Tapers work best when combined with psychosocial support[1]
- Give patient control over rate whenever possible
- One published example from a pain clinic:[2]
  - Education, go slow, 5% reduction 2x/1 mo, then 10%/week max
  - 75% of patients enrolled, 38% of those completed the study
  - Most completers reduced dose with minimal/no change in pain
- Switching to buprenorphine may also be a useful tapering tool[3,4]
  - Lower overdose risk: regardless of taper, the patient is safer

1. Frank (2017); 2. Darnell (2017); 3. Chou (2019)4. Powell (2021)

Buprenorphine Rotation

- Systematic Review: bup rotation a/w reduced pain
- Buprenorphine rotation may mitigate full agonist-related harms
  - E.g., inadequate analgesia, intolerable adverse effects, risky regimens (e.g., high dose), and opioid misuse
- Further studies needed to find ideal approach to bup rotation

Powell, V. D., Rosenberg, J. M., Yaganti, A., Garpestad, C., Lagisetty, P., Shannon, C., & Silveira, M. J. (2021). Evaluation of Buprenorphine Rotation in Patients Receiving Long-term Opioids for Chronic Pain: A Systematic Review. *JAMA Network Open, 4*(9), e2124152-e2124152. doi:10.1001/jamanetworkopen.2021.24152

Next steps (funded R34)

- Identify and operationalize implementation strategies for algorithms (short story: EHR integration, training, e-consults)
- Pilot trial

Key definitions

Serious illness: Carries a high risk of mortality AND either negatively impacts a person's daily function or quality of life, OR excessively strains their caregivers[1]

Palliative care: care for people with serious illness focused on improving quality of life for patient and family[2]

Note: Palliative care has moved "upstream"[3]

1. Kelley AS, *J Palliat Med,* 2018. 2. www.capc.org. 3. Kelley AS, *N Eng J Med,* 2010.

Key definitions cont'd

Opioid misuse:

- missing appointments
- taking opioids for symptoms other than pain
- using more opioid medication than prescribed
- asking for an increase in opioid dose
- angry/aggressive behavior related to opioid
- alcohol and other substance use

Opioid use disorder (OUD):

- Based on DSM-V criteria
- At the core: loss of control over opioid use, with important consequences

Merlin JS, *JGIM*, 2018.

Young S, Merlin JS, *Pain Med*, 2019.

What are some of the most important issues issues related to pain and opioid misuse/OUD in patients with serious illness?

Qualitative study of opioid mgmt challenges in serious illness

- National pall care clinician sample online
- Asked 7 open-ended questions re: challenges faced and decision-making
- Content analysis

Merlin JS, *Am J Hosp Pall Med*, 2019.

Results: opioid mgmt challenges in serious illness

- N=83
- 90% physicians
- 5% NP, 43% academic, 31% community

Merlin JS, *Am J Hosp Pall Med*, 2019.

Prescriber challenges faced

Care approach differences

"Cancer survivors who are free of disease whose oncologist has been prescribing high dose opioids for M years, only to decide this is not a g idea, then refer those patients to P clinic for 'weaning'… patients not on board."

"Sometimes…they just go next door to the Oncologist who then gives them as many [P]ercocets as they want."

Merlin JS, *Am J Hosp Pall Med*, 2019.

Decision-making

Factors related to disease or its treatment

When patient has curative intent of therapy, I am more conscious of the need to limit frequent escalations of medication due to future expectations to wean and/or stop opiate use in the future

Merlin JS, *Am J Hosp Pall Med*, 2019.

Decision-making

Prognosis: two alternative viewpoints

"If the patient is likely to die, we are more lenient. If the patient is dying, we are the most lenient."

"Risks/harms and benefits don't go away or lessen if patient has a poor prognosis."

Merlin JS, *Am J Hosp Pall Med*, 2019.

What is the best approach to the management of opioid misuse / use disorder in individuals with serious illness?

Modified Delphi Study to address this clinical question

- A Delphi study using expert panels can be conducted when no empirical evidence exists to answer a particular clinical question
  - Considered expert consensus-level evidence and may be used to generate clinical guidance
  - Determines whether consensus exists and if it exists, what it is

Shekelle PG, *West J Med,* 1999.

Methods

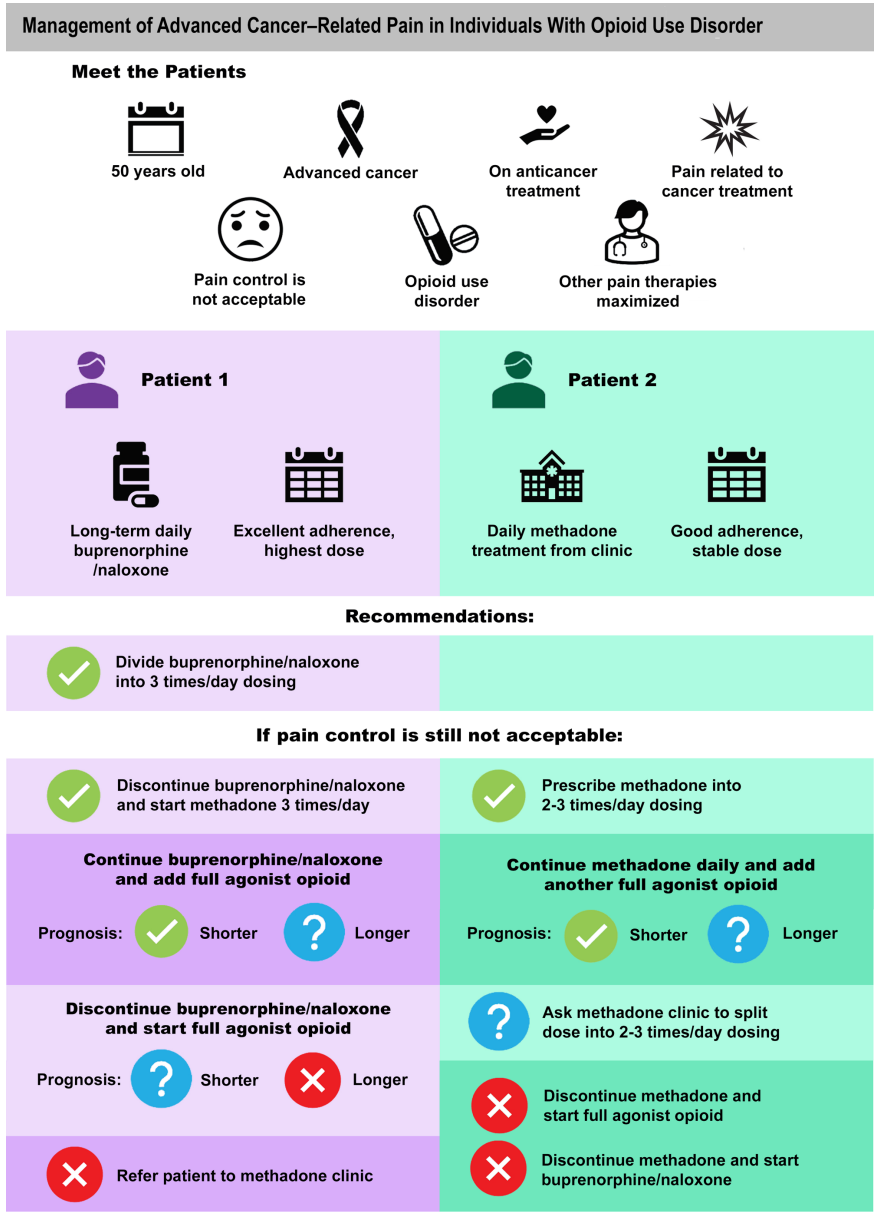
- 2 panels based on prognosis: weeks-months, months-years
- Developed common variations on scenario: 50 y/o, pain d/t cancer/treatment, unacceptable pain ctrl
- Participants: palliative care and addiction experts
- Rounds: 1) rate appropriateness of management strategies; 2) online review of R1 quantitative/qualitative results and discussion; 3) final rating

Merlin JS, *JAMA Netw Open,* 2021.

Results

- Of 129 invited experts: 120 (93%) participated in at least 1 round, 70 (84%) completed all 3 rounds
- Most of the experts held MD or DO degrees (115, 96%)

Merlin JS, *JAMA Netw Open,* 2021.



Merlin JS et al, *JAMA Netw Open,* 2021; Fitzgerald-Jones K, Merlin JS et al, JAMA Onc, 2022.

Merlin JS et al, *JAMA Netw Open,* 2021; Fitzgerald-Jones K, Merlin JS et al, JAMA Onc, 2022.

- Stimulant cases

Conclusions

- Experts favored NOT de-prescribing OUD treatment even at EOL
- De-prescribing opioids is an option but often avoided if possible
- Choice between bup/nx and methadone is complex
- Intriguing results regarding methadone prescribing and the role of methadone clinics

Merlin JS, *JAMA Netw Open,* 2021.

Next steps (pending K24)

- Identify and operationalize implementation strategies for management approaches
- Pilot trial

(Some) future directions

- Optimize opioid decision-making in individuals with serious illness
- Implement evidence-based practices for opioid misuse/OUD in patients with serious illness
- Improve care for individuals with comorbid OUD and pain in primary care and opioid treatment settings: IMPOWR
- Improve cannabis decision-making and communication
- Mentor the next generation of investigators in OUD/pain
- Continue to collaborate with amazing people

Thank you, amazing people!

Pitt

- Jane Liebschutz
- Hailey Bulls
- Deanna Wilson
- Our amazing staff

Montefiore

- Joanna Starrels
- Julia Arnsten
- Deepika Slawek

OHSU

- Ben Morasco
- Shannon Nugent
- Devan Kansagara

Yale

- Will Becker
- Jen Edelman
- Jen Kapo
- Bob Kerns

UAB

- Mike Saag
- Greer Burkholder

Others

- Diane Meier
- Christine Ritchie
- Mallory Johnson
- Judy Paice
- Katie Fitzgerald-Jones

…and many more!