Pain Management for Patients with Substance Abuse

Launette Rieb, MD, MSC, CCFP, FCFP, CCSAM, DABAM
Clinical Associate Professor, Department of Family Practice, University of British Columbia
Medical Consultant, Department of Family and Community Medicine, St. Paul’s Hospital, Vancouver
Canadian Addiction Medicine Research Fellow
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Faculty/Presenter Disclosure

• Faculty: Launette Rieb

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Learning objectives

1. Evaluate risk of Substance Use Disorders (SUD) in patients with chronic non-cancer pain (CNCP)

2. Minimize the likelihood of your patient developing a SUD with pain medications

3. Manage acute and chronic pain in patients with a current or past SUD
Remember

- All mood altering substances (prescribed or illicit) can reduce pain while intoxicated
- All substances (including pain medications) that cause dopamine release in the misolimbic system can be overvalued – even in the absence of true addiction – hence the emotional attachment around discussing opioids, cannabinoids, benzodiazepines and stimulants with patients

Common Tx Goals for Pain and SUD

- Correct sleep disturbance
- Stabilize mood
- Eliminate unnecessary medications
- Restore function

Screening and Assessment Tools

- SUD
  - AUDIT – alcohol
  - DAST - drugs
  - COMM – Current Opioid Misuse Measure
- Mood
  - PHQ9 or BDI – depression
- Pain
  - BPI - Brief Pain Inventory
- Function
  - PDI – Pain Disability Index
  - 5As (Universal Precautions)
Functional Assessment

Universal Precautions for Opioid Prescribing – The 5 As (Gourley, 2005)

1. Activities of daily living
   - Work, self care, mobility, leisure, sport, sleep
2. Analgesia
3. Adverse effects
4. Affect
5. Aberrant drug-related behaviors

Risk Assessment for SUD if Prescribed Opioid Medications

(Furlan 2010)

Canadian Opioid Use Guidelines-NOUGG

Best Practice for Opioid Therapy

- Complete history, physical, differential Dx
- Risk assessment SUD, psychiatric issues
- Medication review + urine drug screen
- Appropriate trial of non-opioid alternatives
- Pre/post-opioid pain and function questions
- Treatment agreement: 1 MD, visits, scripts
- Taper off benzodiazepines first – contraindicated
- Sufficient trial of opioid, establish efficacy
- Use Opioid Manager + PharmaNet each visit
Risk of SUD

- Those at highest risk:
  - Active SUD
  - Past Hx of SUD
  - Family Hx of SUD
  - Active psychiatric illness
  - Childhood trauma, esp. sexual abuse in women
  - Youth
  - Exposure:
    - Dose dependent rise in risk of SUD

Canadian Opioid Use Guidelines-NOUGG

Patients at High Risk for SUD

- Prescribe only for well-defined somatic or neuropathic pain conditions
- Relatively contraindicated in headache and fibromyalgia
- Start with lower doses and titrate in small dose increments
- Monitor closely for signs of aberrant drug related behaviors

NOUGG - tips

- How high can you go?
  - **Watchful dose = 200 mg** Morphine Equivalent Daily Dose (MEDD)
  - Patients who do not obtain significant (20 - 30%) drop in pain by 200 MEDD and should be re-evaluated, referred or taken off opioids
  - N.B. Worksafe BC watchful dose = 120 MEDD
  - N.B. Washington State = 120 MEDD since 80% of patients get relief below 80 mg MEDD
SUD in patients on LOT

- Systematic review and meta analysis
  - Based on history and physician suspicion alone rates of substance dependence with opioid therapy was under 5%, under 1% if no past hx SUD

- However 5 studies did UDS as well:
  - 21% of patients had either no prescribed opioid and/or a non-prescribed opioid in UDS
  - 15% had illicit drugs

  (Fishbain 2008)

Prescription Opioid Misuse and Addiction

- Estimates vary from 4% to 26%, or higher
  - Study (n=801) of pts with CNCP based on standardized interviews
    - 26% purposeful oversedation
    - 39% increased dose without prescription
    - 8% obtained extra opioids from other doctors
    - 18% used for purposes other than pain
    - 12% hoarded pain medications

  (Fleming et al. J Pain 2007)
Opioid Abuse, Addiction, Misuse: Dose-Dependent Effect

- Long-term prescribed opioid use (>90 days’ supply) associated with increased risk of an opioid abuse or dependence diagnosis vs. no opioid treatment
  - Low dose (1-36 mg MED/day): OR 15
  - Moderate dose (36-120 mg MED/day): OR 29
  - High dose (≥120 mg MEDD): OR 122

(Edlund 2014)

Non-Medical Prescription Opioid Use

MTF: Annual Use Prevalence 12th Graders

- Systematic review
  - Misuse was reduced between 7 and 23% (addiction, diversion, aberrant drug related behaviors)
  - Supports the effectiveness of treatment agreements and UDS to reduce substance misuse

(Starrels, 2010)
Contracts and Collateral Assessment

• Opioid contracts - e.g., CPSBC, WorksafeBC, Cnd opioid use guidelines, or write your own. (See appendix for examples)
• PharmaNet – prescription monitoring
• Urine drug screening – baseline before starting any addictive substance, then random q4-12 weeks, name synthetic opioids
• Pill counts – call back by MD or pharmacist
• With permission ask relatives/friends about sedation, sleep apnea, behavior

Cannabinoids – see my plenary

Case 1

Mr. A. – Impacted tooth extraction in a 53 year old male teacher with a hx of depression (MDD), and his parents have alcohol use disorders (AUDs)

• Use NSAID (e.g. ibuprofen 800 mg q8h)
• Returns day 1 postop, pain ++: Try a different NSAID – (e.g. ketorolac 10 mg q8h) plus acetaminophen 1g q6h
• Returns day 2 post op, pain unbearable: Examine – swollen and pus. Abx, to dentist. N.B. If opioid used – short scripts, discuss warning signs for SUD, collateral, firm stop (e.g. oxy 5 mg 1-2 q 6h prn x 2 d)
• Returns day 3 post op for more opioids: Examine, insist on return to dentist (instead of more opioids)
**Added Precaution**

- Additional care is needed in prescribing for those with a past history of substance use disorder
- **Relapse** can be triggered by
  - Pain
  - Stress
  - Re-exposure to drug of choice
  - Exposure to any drug that stimulates dopamine

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**Visual Cue & PET scan: Craving Alarm**

- Amygdala not lit up
- Amygdala activated

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**Non-opioid SUDs**

- All substances of abuse can produce pain relief during euphoria or sedation
- Patients confuse this momentary relief with pain control which it is not, but can drive pain
- Stabilization of the SUD is needed to treat the pain – e.g. alcohol, benzos, cocaine, etc.
- Even tobacco and caffeine can play a role in pain modulation, and should be addressed
Precautions if Any Active SUD

- Bubble pack medications
- Random call backs for pill counts
- RANDOM urine drug screens
  - Look for illicit substances, ensure taking prescription
  - Include ethyl glucuronide (ETG): 3-5d past alcohol use
- Put onto once daily formulations with daily witnessed ingestion at the pharmacy (no carries)
- Taper off opioids if drinking alcohol or on benzos

Opioid Detox Options

- Patients with physiologic dependence on opioids who need to come off can be assisted by a variety of approaches:
  - Symptom management (CINA, clonidine etc)
  - Replacement and tapering (if Rx for pain)
  - Agonist therapy (methadone or buprenorphine) for detox or maintenance
  - Antagonist therapy (naltrexone)
  - Screen for and address addiction processes
  - Engage in non-pharmacologic strategies
  - See my breakout session for details

Detox from Opioids or Benzos

- Negotiate rules (boundaries)
- Switch to a long half life medication
- Taper fixed percentage/time: 5-10% q1-2+ wks
  - Hospital/residential detox can be 5-10% per day
- Frequent visits, small quantities – daily if needed
- Increase supports and non-pharm coping skills
- Detox alone may help pain, but may leave a "chemical coper" with no means to soothe, so increase risk of relapse
Case 2

Mr. B: 48 yr old HIV+ HCV+ male with peripheral neuropathy, sleep disturbance, cocaine & alcohol use disorders now both in sustained abstinence (6 years), pain 8/10

Meds:
- Oxycodone/acetaminophen (5/325) 6 q6h – no evidence of current OUD, no pain relief
- Thus oxy 120 mg = 180 mg MEDD
- Temazepam 60mg hs 2-3x/wk (from his wife)
- Intolerable experience in the past with duloxetine, venlafaxine, and amitriptyline

Case 2, cont’d

Mr. C – Treatment:
1. Taper off oxycodone/acetaminophen 5/325:
   - Lower by 1 tablet q4 days until at 1 q6h
   - Then lower by ½ tab q4 days until off
2. Titrate onto gabapentin
   - Begin with HS dose - 100 mg, incr. q4d until at 300mg hs
   - Titrate up daytime doses by 100 mg until 300 tid - qid, then by 300mg weekly until 600 tid (2400 mg/d)
   - If no pain relief in 6 weeks at 2400 mg/d then taper off
   - If 2400 mg/d helpful can push the dose further to 3600
   - Neuromodulators can help ameliorate opioid withdrawal symptoms too which can help Mr. C.

Case 2, cont’d

Mr. C – Treatment, cont’d:
3. Taper temazepam
   - Stabilize nightly benzo to half current episodic dose
   - Slowly taper, or can use diazepam, remembering that neuromodulators can also help benzo withdrawal
   - Ashton protocol for benzo tapering may be needed
4. Nortriptyline may be better tolerated for sleep but he declined, can try quetiapine 25 mg hs and titrate up
5. Sleep hygiene techniques + relaxation/anger mgt
Case 2, cont’d
• **Result:** Pain better controlled, sleep still a challenge but improving with time
• **What if he was binging on alcohol and benzos?**
  • Offer residential detox. Not eligible for opioids – stop (or fast taper 10% per day).
• **What if he had requested more opioids instead of less?**
  • Explain that other medications are first line and need to be tried in sufficient doses. Explain that opioids have risks associated with use – outline them. Explain why this is considered a failed treatment attempt = opioids are no longer indicated

Case 2, cont’d
What if he had some pain relief and increased function with oxy/acetaminophen and was unresponsive to all other med categories?
• Once daily oral morphine formulation – which could go to a daily witnessed ingestion (DWI) if needed during initial monitoring, and be reverted back to DWI if there is cocaine or other drugs in the UDS
• **NOT eligible for carry doses of opioids if using cocaine or other illicit drugs**

Co-management of OUD and Pain
• When an Opioid Use Disorder is active, pain is much harder to treat due to dysregulation of all pathways involved with mood, pain, and behavioral reinforcement
• Withdrawal from opioids (which also happens with binging) lowers pain thresholds, producing more pain, driving use
• Must co-manage pain and addiction issues
Opioid Induced Hyperalgesia

- “OIH” Can occur with short term opioid use (e.g. intra-operative exposure)
- or long-term use (e.g. years of opioid use in patients with CNCP or those with opioid use disorders on methadone)
- Is dose dependent – higher the opioid dose, the higher the pain sensitivity to heat and cold
- Treatment:
  - Opioid lowering, rotation, elimination
  - NMDA antagonists, NSAIDs, gabapentinoids
  

Withdrawal Hyperalgesia

- When opioids are tapered or stopped the pain relieving properties cease but the pronociceptive pushback continues for a time with worsened hyperalgesia, known by a number of names
  - Opioid-abstinence hyperalgesia
  - Opioid withdrawal hyperalgesia
  - Withdrawal induced hyperalgesia (WIH)
- Is dose dependent
- May worsen with repeated exposure - w/d
- Treatment: Likely same as for OIH
- Beware old injury sites may hurt temporarily with opioid cessation (WISP)
  
  (Younger J 2008, Hooten WM 2010, Rieb 2016 under review)

Methadone for Pain – without addiction

Advantages of methadone for CNCP:
- Theoretically good for neuropathic pain: binds to NMDA receptor, blocks glutamate (one of the pathways of tolerance and opioid induced hyperalgesia, though can get)
- Long half life (24-36 hrs) so it can lower withdrawal induced pain if dosed daily, may need q6-8h dosing for analgesia

Disadvantages of methadone for CNCP:
- Methadone vs morphine 43% increased risk of death, even methadone 20mg or less HR = 1.5 (Ray, 2015)
- Review, 3 studies - limited info, efficacy (Haroutunian 2012)

Methadone should NOT be first line for CNCP (unless OUD)
NOUGG Guidelines
Managing Opioid Misuse and Addiction

For patients with chronic non-cancer pain who are addicted to opioids, three treatment options should be considered:

1. Methadone or buprenorphine treatment (Grade A)
2. Structured opioid therapy (Grade B), or
3. Abstinence-based treatment (Grade C)

NB. Only choice 1 and 3 are approved by CPSBC, and the American Pain Society (Chou 2008)

Consultation or shared care, where available, can assist in selecting and implementing the best treatment option (Grade C)

NOUGG Guidelines
Managing pain in those on methadone

Patients on Methadone or with a current SUD

• Mild to moderate acute/chronic pain treatment
  – High dose NSAIDs and acetaminophen
  – TCAs, SNRIs, neuromodulators (beware of street value of gabapentin)
  – Topicals, ice/heat, myofacial release techniques
  – stress reduction/mindfulness/breathing techniques
  – Counselling, AA, NA, social engagement
  – Exercise
  – Sleep hygiene

NOUGG Guidelines - methadone

Patients on Methadone for SUD

• Severe Acute/Chronic Pain Treatment
  – Consider all of the items on previous slide
  – Split methadone q6-8h and increase as needed
  – And/or …Additional opioid trial:
    • E.g. morphine, oxycodone, hydromorphone, witnessed inj.
    • Sunset clause if acute pain, consider consult if chronic
    • Lack of evidence to add a long term opioid to methadone
    • Rotation to buprenorphine/naloxone
  – In hospital get pain service or anesthesia to see
  – Procedures: nerve root blocks, epidurals, ketamine infusions, sympathetic blocks, regional blocks
**Specialized detoxes/conversions**

- Converting from other opioids to methadone or buprenorphine for detoxification or maintenance:
  - Requires specialized training and authorization
  - Once detoxed can block with naltrexone 50 mg/d x 6-12mo
  - See separate opioid lecture and detox lecture
- Note that buprenorphine is actually a full mu agonist for analgesia – as good as morphine, and it is a kappa antagonist which may help mood
- Novel protocols for CNCP pts on high dose opioids:
  - Out-patient protocol: Using buprenorphine patch as a bridge to bup/nx decreases precipitated w/d (Kornfeld, 2013)
  - In-patient protocol: Hydromorphone bridge (Berland 2014)

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**Methadone Maintenance Patients**

- “In order to determine if the patient’s pain is opioid responsive I ask them if they get pain relief 30 to 60 minutes after their [once daily] methadone dose and how long that relief lasts. If they get pain relief but it only lasts for 6 hours, then I believe their chronic pain is opioid responsive and the patient might benefit from additional opioids later in the day [e.g split methadone dosing]. If they get pain relief all day, I believe their pain is likely opioid withdrawal mediated pain that does not require additional opioids. If they get no relief from the methadone dose, I believe their pain is opioid resistant and would not benefit from opioid analgesics.”
- Dan Alford, MD, MPH, FACP – Medical director, Boston Medical Centre Office-Based Opioid Treatment Program

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**Treating pain in those with opioid use disorders on opioid maintenance**

- Patients on methadone maintenance with severe CNCP want to be heard, be given a diagnosis, be worked with, be given non-opioid and non-medication options for pain (Karasz, 2004)
Bup/nx and Pain

Retrospective chart review of CNCP patients on over 200 MEDD - converted from other opioids to bup/nx - pain scores averaged 8/10 pre-conversion, 4/10 post conversion

Case 3

Mr. Z.
- 61 year old IDU, HIV+, HCV+, polysubstance dependence, previous drug dealer currently on disability and working under the table doing home renovations, with insomnia and bilateral shoulder pain from multiple fracture-dislocations, and back pain from marked thoracic kyphosis and degenerative disc disease
- Asking for increases in morphine and diazepam, threatens to use heroin if denied
Case 3, cont’d

Mr. Z –

Current Medications beyond ARVs for HIV
- Methadone 100 mg/d twice weekly dispensed, first dose witnessed – “doesn’t help my pain”
- Morphine extended release (once daily formulation) 50 mg bid, twice weekly dispensed (no witnessed doses) – chewing, runs out early every dispensing cycle by 1-2 doses. “Only thing that gives me temporary relief”. Feels “nothing” if he swallows the pill whole. Wants 3 doses/d to chew
- Diazepam 10 mg hs now, wants 40mg/d like last yr
- Zopiclone 7.5 mg i-i hs
- When out of benzos, gets tryptophan from others, takes 1 pill (unknown strength) and can sleep
- Never tried and not interested in TCAs, SNRIs, gabapentinoids which he referred to as “bug pills”

Case 3, cont’d

Mr. Z –

Substance use hx – verbal report
- Caffeine: ½ jar of instant coffee/d, cigs: none
- Alcohol: “alcoholic” “trying to stop” - night before assessment “2 drinks”, “none for 3 weeks prior”
- Cannabis: 3.5 gm/d = 7 joints/d
- Heroin: “not now”. Started IV age 19 – most of his life off and on heroin dependence, or other opioid – reported drinking methadone up to 1000 mg at once on several occasions and still be able to walk around Vancouver. Has shot his methadone before
- Cocaine: not currently, 35 years of past IV use

Urine drug screen (point of care)
Positive (+) for methadone, opioid, benzos, THC
Negative (-) for cocaine, amphetamine, PCP

Case 3, cont’d

Mr. Z –

Assessment (beyond orthopedic condition)
- High risk for unintentional OD (mixing ETOH, benzos, and opioids – chewing extended release morphine into quick release)
- Not a good candidate for carry doses of any opioid (misuse of prescribed route of administration, active opioid use disorder, high diversion risk)
- MEDD over 700mg/d = failed opioid tx for pain
- May have opioid induced hyperalgesia
- Active alcohol and cannabinoid use disorders
- Not tried first line pain treatments
- Uses sarcasm and threats to try to get meds
### Case 3, cont’d

**Mr. Z – Recommendations**

- **Explain** the way he is taking morphine is unsafe, and is contraindicated for chronic pain on methadone especially with alcohol and benzodiazepines.
- **Explain** tolerance, withdrawal pain, and opioid induced hyperalgesia.
- **Change** all opioids to DWI.
- **Taper off morphine** (decrease by 10 mg every 4-7 days, he may be able to go faster since no effect).
- **Taper benzos:** Decrease diazepam 2.5 mg q 1-2 wks, then taper zopiclone by 3.5 mg in the same fashion, compounding lower at the end if needed.

### Case 3, cont’d

**Mr. Z – Recommendations, cont’d**

- **Offer** prescription for tryptophan 500 mg titrating up to 5 gms as needed before bed for sleep only because he reports good sleeps on this.
- **If** tryptophan ineffective for sleep – use nortriptyline 10 mg titrated to up every 4-7 nights as needed to max 100 mg (for sleep and pain).
- **If** more sedation needed use instead amitriptyline 25 mg hs titrated to 200 mg.
- **If** ineffective try quetiapine 25 mg hs titrated up to 200 mg hs, can also use 25 in the day for anxiety.

### Case 3, cont’d

**Mr. Z – Other considerations:**

- **Ensure** a thorough medical work-up has been done – e.g. physical, imaging, electrophysiologic studies.
- **Review** PharmaNet and Random UDS each visit.

**If** he had had had relief for the first 6 hours of methadone daily dose, **and** he didn’t have a history of methadone binging and shooting, **and** if UDSs were cleared once off morphine x3 months:

- could offer **a trial of split methadone** doses 22mg q8h (witness first dose, carry 2) and dose titration.
- return to DWI if no help or destabilizes.
Case 3, cont’d

Mr. Z – If neuropathic pain...

- A lower dose of cannabis is advised
- Venlafaxine can be offered starting at 37.5 mg/d titrating to 225mg/d to get pain relief from noradrenergic effect
  - Duloxetine (a sister SNRI) gets noradrenergic effect at low dose (30mg/d), not covered by Pharmacare
  - If ineffective or side effects taper over 2-4 weeks

Case 3, cont’d

Mr. Z – If neuropathic pain ...

Gabapentin

- Start low 100 mg hs, increasing by 100 mg hs every 3-4 days until 300 mg hs then add daytime doses until 300 mg tid, then can increase by 300 mg
- If no effect at 2400 mg after 6 weeks then taper: can back off 300-600 mg every 2-4 days
- If some benefit and no side effects at 2400mg/d can titrate to 3600mg/d only if added benefit.
- Nb Risk of diversion due to street value. May help him stop drinking. Increases the risk of unintentional OD
- Pregabalin is not covered by Pharmacare but is easier to dose, titrate and taper

Case 3, cont’d

Mr. Z – Recommendations, cont’d

- Non-medication treatment strategies can be employed if the patient is willing:
  - Physiotherapy, and a pool pass for self help
  - Sleep hygiene education
  - Cut caffeine to 3c or less/d
  - CBT 1:1 or group, peer support group
  - Nerve root blocks, epidurals, trigger point release massage, cortisone injections, etc.
Case 3, cont’d

Mr. Z –
Recommendations, cont’d

What if Mr. Z lands in hospital with a new painful issue?
• All non-opioid strategies should be considered 1st
• If an opioid is used, continue the methadone as usual and add a short acting opioid temporarily, witnessed by nursing staff and specify days and taper schedule (or PCA with lock out if anesthesia orders).
  • E.g. hydromorphone 2-4 mg q6h prn on days 1-4, then 1-2 mg pm q6h day 5, 1 mg pm day 6, then 1 mg hs pm day 7, faster taper if discharging

Case 3, cont’d

Mr. Z –
Recommendations, cont’d

What if Mr. Z could not stop drinking alcohol (on history or ETG positive UDS)?
• He is no longer a candidate for opioid therapy and can be offered detoxification (residential or outpatient) and long term treatment for all of his substance use disorders
• Offer hope: Recovery house, treatment for HCV
What if he was not on methadone and just binging on high dose street oxycodone?
• Convert to bup/nx
• Even if he is on methadone this conversion can be useful, though retention is somewhat lower

Medications are a fantastic tool, but if they are not working...

• Review the diagnosis – Repeat Hx/Px
• Consider opioid induced hyperalgesia, withdrawal hyperalgesia, addiction, diversion
• Screen for depression, anxiety, and PTSD
• Explore perception of disability & meaning
• Expand non-pharmacological treatments
• Ensure your prescribing is safe, effective, and cannot do more harm than good!!!
Summary

1. The treatment goals of both pain and SUD are similar – restore function, improve mood, ameliorate sleep cycle, reduce suffering, minimize medication burden and side effects.

2. If the patient is in recovery and has acute or chronic pain – discuss all options and risks before making a plan.

3. If the patient has a past history of a SUD or is at high risk for one then explore non-opioid options first when feasible, close monitoring.

4. If an active alcohol or benzodiazepine use disorder, then pt not eligible for conventional opioid therapy due to the elevated risk of unintentional overdose.

5. If an active opioid use disorder, then detox or buprenorphine/naloxone (bup/nx) or methadone maintenance therapy is recommended. If declined then other opioids are typically not recommended at this point by the CPSBC, though in the Cnd guideline other once daily opioids may be an option. An abstinence based treatment program may be in order.

6. Once on bup/nx or methadone for pain and addiction, non-opioid medications and non-pharmacologic strategies should be used for flares and mild to moderate new pain conditions.

7. If another opioid is added for severe pain then make it time limited.

8. If the pain condition is ongoing, consideration can be given to increasing the methadone or bup/nx. Caution should be applied and consultation obtained if possible before adding another opioid long term.
Summary

9. If the patient has an active cocaine or other stimulant use disorder then it is unwise to give take home doses of any opioid due to the risk of diversion and fueling the stimulant use.

10. Prescribing cannabinoids to people with cannabis use disorders or other active substance use disorders is contraindicated.

Thank you!

Bio & Disclosures

BIography
Dr. Rieb is a Clinical Associate Professor in the Department of Family Practice, University of British Columbia. She is certified by the American Board of Addiction Medicine and the Canadian Society of Addiction Medicine. Her graduate work was in the area of pain physiology. She is a medical consultant for Orion Health (Vancouver Pain Clinic), The Orchard Recovery Centre and the Immunodeficiency Clinic at St. Paul’s Hospital. She was the co-founder and first Medical Director of the St. Paul’s Hospital Goldcorp Addiction Medicine Fellowship. Dr. Rieb has been given a postgraduate teaching award from UBC.

DisclosureS
Dr. Rieb has no affiliation with commercial interests including the pharmaceutical industry.
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