Chronic Opioid Therapy Guideline Update
By Galen Goertzen, PharmD, BCACP; Edited by Tiffany Nguyen, PharmD

Key Points:

- To improve patient safety when prescribing opioids, minimize acute opioid prescribing, keep doses low, monitor appropriately, and avoid prescribing with other sedating drugs.
- Prescribe naloxone to your medium to high-risk patients on chronic opioid therapy to reduce the risk of overdose deaths.
- Encourage safe disposal of leftover opioids to avoid nonmedical use.

Background
Pain is one of the most common diagnoses that the average primary care physician deals with in a day, and opioids have been one of the primary options used for treatment. In the last couple of years, opioid overuse has received a great deal of attention as the safety and efficacy of these drugs have come into question. Since the year 2000, the rate of overdose death involving opioids has almost tripled. More than 28,000 people died from opioid overdose in 2014 alone.¹

In September, Group Health revised its Chronic Opioid Therapy (COT) guideline for the treatment of chronic non-cancer pain, with the intent to minimize practice variation, improve patient safety, ensure compliance with Washington State law, and ultimately increase patient and provider satisfaction. The specifics of the new COT guideline can be found on Group Health’s website. Following are some general principles that can be used to improve patient safety and efficacy when prescribing opioids for chronic pain.

- For acute pain, prescribe no greater quantity than needed for the expected duration of pain.
  ⇒ In most acute situations, a 3 day treatment with opioids is sufficient, with 7 days of therapy as a maximum.²
  ⇒ Sixty percent of patients who take opioids for 3 months are still on them 5 years later.³
- Use the lowest effective dose.
  ⇒ Keep patients to less than 40 morphine equivalents per day (MEDs), if possible.
⇒ Statistics show that a patient taking ≥120 MEDs is more than 122 times as likely to develop an opioid use disorder as a person who has not been prescribed opioids at all.\(^4\)
⇒ A person taking ≥100 MEDs is nine times as likely to overdose as a person taking less than 20 MEDs.\(^5\)

- Monitor your COT patient carefully.
  - A high risk COT patient needs to be seen at least once every 3 months.
  - Use an assessment tool, such as the PEG tool (page 27 of COT guideline) to monitor improvement in pain, function, and quality of life. If improvement is not seen, then discontinue COT.
  - Conduct urinary drug screens at appropriate intervals, based on risk category.
  - Consult Prescription Monitoring Program (PMP) at every COT visit.
  - Use provided tools to monitor for depression (PHQ-9 – see Appendix one of depression guideline) and opioid use disorder (ORT - appendix B of COT guideline)

- Avoid concurrent use of other sedating drugs which increases risk of overdose but do little to improve function.
  - Studies have shown that taking benzodiazepines concurrently with opioids increases the risk of overdose death by 4-10 times versus taking opioids by themselves.\(^6\)-\(^8\)
  - Other sedating medications such as the Z-drugs (sleepers such as zolpidem and zaleplon) and skeletal muscle relaxants also increase overdose risk in patients taking long-term opioids.
  - Poison control centers have reported increased use of hydrocodone, alprazolam and carisoprodol in combination, referred to as the “Holy Trinity,” “Houston Cocktail,” or “Triple Threat.” This combination is known to give an effect similar to heroin but also increases chances of overdose.\(^9\)

- Prescribe naloxone to all of your medium to high risk COT patients (See Clinical Pearl).
  - Several community-based programs have shown a reduction in overdose deaths associated with making naloxone available.\(^10\)
  - Overdose is most common in patients taking high doses of opiates, but it can occur at any risk level.
  - Consider prescribing naloxone for family members of high risk COT patients.
  - Narcan nasal spray is Group Health’s preferred naloxone product.

- Encourage patients to dispose of their leftover opioids in a safe manner in order to avoid future nonmedical use.
  - Much nonmedical use of opioids comes from use of unused opioids taken from the medicine cabinet of former users or from unused opioids from previous prescriptions.\(^11\)
  - According to the 2013 National Survey on Drug Use and Health (NSDUH) survey, over 50% of pain relievers obtained for nonmedical use came from friends or relatives.\(^12\)

Patients in King County may use medication disposal units at Group Health medical centers.

---

**New Opioid MED Safety Edit for Medicare Advantage Part D Members**

*By Janet Kim, PharmD*

**Key Points:**

- As of January 1, 2017, Medicare Advantage Part D (MAPD) patients who are taking a morphine equivalent dose (MED) of 100 mg/day or higher require stricter clinical review by the dispensing pharmacist to ensure patient safety.
• This new edit impacts all Part D health plans and all pharmacies servicing MAPD members, including Group Health (GH).

Background
• Centers for Medicare and Medicaid Services (CMS) mandates that all Part D sponsors implement a cumulative Morphine Equivalent Dose (MED) edit at the point of sale (POS), effective January 1, 2017.
• This new safety edit is intended to prospectively reduce risks from high-dose opioid use.

Description of new MED POS soft edit
• This MED POS soft edit or rejection will fire if GH MAPD members are taking a cumulative opioid dose of 100 mg MED/day or higher.
• Each opioid claim, as well as overlapping previous opioid claims filled, will roll up into the calculated cumulative MED/day (conversion factors will be used).
• Members in hospice care or with cancer will be excluded. Slight overlap of refills will be accounted for.
• CMS expects front-line pharmacists, not the Group Health Pharmacy Help Desk, to make the clinical and safety review and override the rejection when appropriate.
• Please note: GH pharmacies will request physician offices provide the following key safety elements in particular to guide the pharmacist safety review: chronic opioid therapy (COT) plan in place, opioid risk assessment (e.g. opioid risk tool or ORT) done at least once, depression screening (e.g. PHQ-9) completed within the past year, and Prescription Monitoring Program (PMP) checked within the past year. Documenting these elements and associated dates clearly within the chart notes or electronic health records will facilitate pharmacist review to override the alert so patients can obtain their opioid medications more quickly.

Evidence Review of Alternative Pain Management Approaches
By Bryan Davis, PharmD; Reviewed by Karen J. Sherman, PhD, MPH

Key Points:
• Complementary and alternative medicine (CAM) pain management approaches identified to have the strongest levels of evidence were: acupuncture and yoga for back pain; acupuncture and tai chi for osteoarthritis (OA) of the knee; massage therapy for neck pain; and relaxation techniques for severe headaches and migraine.
• Weaker levels of evidence suggest that relaxation approaches and tai chi may help with pain associated with fibromyalgia.
• Consider these alternative approaches as an adjunct therapy for a comprehensive pain management plan in addition to pharmacological therapies. Some details on coverage and processes can be found on the Group Health website.

Background
• The Department of Health and Human Services (HHS) has declared an opioid epidemic in the United States (US), with more than 650,000 opioid prescriptions dispensed a day.13
• Interest in alternative pain management strategies have grown substantially to treat the estimated 126 million adults experiencing some level of pain a year.14
• The Mayo Clinic Proceedings has developed a journal based CME activity and test based on an evidence evaluation of complementary health approaches.14
Efficacy and safety were evaluated for acupuncture, spinal manipulation (SM), massage therapy, relaxation techniques (including meditation), select natural supplements, tai chi, and yoga for five types of pain: back pain, knee osteoarthritis (OA), neck pain, severe headaches, and fibromyalgia.

Study Methodology

- A MEDLINE database search for articles published from 1/1/1966 through 3/31/2016 was performed to identify U.S. randomized control trials (RCTs).
- Interventions were evaluated by the preponderance of evidence, with “positive trials vs. negative trials.”

Results

Efficacy: Table 1 outlines the clinical trial data stratified by pain and treatment type. Select approaches are listed; further details can be reviewed in the full activity.

Table 1. Summary of Trials of Select Complementary Health Approaches by Type of Pain

<table>
<thead>
<tr>
<th>Approach</th>
<th># of RCTs included (N)</th>
<th>Population (s)</th>
<th>Primary Outcomes &amp; Study Measures</th>
<th>Results / Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Low Back Pain</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acupuncture</td>
<td>4 RCTs (1092)</td>
<td>Age range: 28-60 yrs</td>
<td>Self-report of pain intensity scales (numeric or visual)</td>
<td>2+ trials, 2 mixed 9-15% absolute reduction observed in pain intensity and function</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Primarily white</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yoga</td>
<td>6 RCTs (596)</td>
<td>Age range: 18+ yrs</td>
<td>Modified 24-point Roland Disability Scale</td>
<td>5+ trials, 1 – trial yoga vs. exercise: difference -1.8</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Primarily female</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Osteoarthritis of the Knee</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tai chi</td>
<td>4 RCTs (n/a)</td>
<td>Age range: 65-79 yrs</td>
<td>WOMAC total score or pain sub score</td>
<td>4 + trials WOMAC @ 12 week= –118.80 mm</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Primarily female</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Neck Pain</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Massage therapy</td>
<td>4 RCTs (n/a)</td>
<td>Age range: 20-60 yrs</td>
<td>Neck Disability Index (NDI) and visual pain scales</td>
<td>4 + trials NDI improvement: 39% vs 14%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Severe headaches / migraines</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Relaxation techniques</td>
<td>6 RCTs (n/a)</td>
<td>Age range: 12+ yrs</td>
<td>Headache Disability Index (HDI) and visual pain scales</td>
<td>6 + Trials ~10-20% reductions in HDI</td>
</tr>
</tbody>
</table>

(+) trials=approach with statistically significant improvements; (-) trials=no difference seen between groups; RCTs=randomized controlled trials; n/a=not available or reported; WOMAC=Western Ontario and McMaster Universities Osteoarthritis Index; yrs=years
Low back pain

- Acupuncture: 4 RCTs evaluated (N=1,092)
  - Cherkin et al. reported modest improvement in pain intensity and function compared with usual care (59-65% vs. 50%, P=0.02).\(^{15}\)
  - Wang et al. found a significant reduction in pain intensity in pregnant women and improved functional status compared with no treatment.
  - Two RCTs showed mixed results with comparison of active to sham acupuncture, which did not demonstrate significant differences.
- Yoga (hatha, vinyoga, iyengar): 6 RCTs evaluated (N=596)
  - Yoga was performed in 12-24 group sessions of 60-90 minutes duration.
  - Yoga improved pain and function, was superior to conventional therapeutic exercise, and similar to stretching.
  - Going to once-weekly classes provided similar improvements in pain intensity and function as with twice-weekly classes.
- Massage improved pain and function at 10 weeks, but was not sustained at 52 weeks.

Osteoarthritis of the Knee:
- Tai chi: 4 RCTs evaluated
  - Overall, tai chi (for 8-18 weeks) improved overall pain and Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) physical function more than controls. All improvements deteriorated after stopping sessions.

Neck Pain
- Massage therapy: 4 RCTs evaluated
  - Significant improvement on the Neck Disability Index (NDI) [39% vs. 14% (self-therapy control)] was seen at 10 weeks, but not evident by 26 weeks.\(^{18}\)
  - There was a dose-response relationship between the number and duration of massage sessions per week and improvement in the NDI score and neck pain intensity.\(^{19}\)

Severe headaches and migraine
- Relaxation techniques: 6 RCTs evaluated
  - Stress management, relaxation, biofeedback, written emotional disclosure, and neutral writing methods were evaluated for headache disorders.
  - All significantly decreased headache frequency and/or reduced headache disability scores.
  - Holroyd et al. compared relaxation techniques compared to tricyclic antidepressants. Both reduced chronic tension headaches similarly, but was best in combination (>50% reductions in headache index scores).\(^{20}\)

Safety: Generally minimal adverse effects were reported but included abdominal discomfort with supplements, muscle and joint soreness with tai chi and yoga, and pain or bruising with acupuncture.

Conclusion
- Consider the evidence and use clinical judgement to construct a tailored comprehensive pain management program for your patients.
- Clinicians do not need to make a referral for most CAM services, except for massage therapy.
- Many commercial patients have some level of coverage for CAM services or can receive discounts through programs such as Complementary Choices\(^{SM}\). Some information on Group Health coverage and benefits can be found on the Group Health provider website.
Clinical Question: How can the risk of venous thromboembolism be minimized in women taking oral contraceptives?

By Tiffany Nguyen, PharmD; Reviewed by Jeanne Lester, PharmD

Key Points:
- For patients at high risk of venous thromboembolism (VTE), progestin-only pills (POPs) are preferred over combined oral contraceptives (COCs).
- To minimize VTE risk in women on COCs, consider using COCs with low-dose estrogen (<35 mcg) and low-risk progestins such as levonorgestrel, norethisterone, or norgestimate.

Background
- Figure 1 compares the risk of VTE among different groups of women. Despite the increased risk of blood clots by 2-4 fold seen in COC users compared to nonusers, absolute risk is still much lower than during pregnancy and postpartum.21

Figure 1. Risk of Developing Blood Clots21

COCs vs. POPs
- Thrombotic risk is increased with higher ethinyl estradiol (EE) doses (>50 mcg) compared to COCs with <50 mcg of EE. Currently, most available COCs contain 20-35 mcg of EE.22, 23
- Patients on POPs carry similar VTE risks as those not on oral contraceptives. Thus, POPs are considered a reasonable choice for women at high risk of blood clots (Table 2).
- POPs are as effective as COCs when taken at the same time every day. If a pill is taken more than 3 hours late, a back-up method of birth control is recommended for the next 48 hours.24, 25

Table 2. The CDC Eligibility Criteria for Contraceptive Use: Patients at High VTE Risk26

<table>
<thead>
<tr>
<th>Patient Characteristics</th>
<th>Progestin-Only§</th>
<th>Progestin+Estrogen§</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smokes and is &lt;35 years old</td>
<td>No restriction</td>
<td>Benefits&gt;risks</td>
</tr>
<tr>
<td>Smokes &lt;15 cigarettes/day and is ≥35 years</td>
<td>No restriction</td>
<td>Risks&gt;benefits</td>
</tr>
<tr>
<td>Smokes ≥15 cigarettes/day and is ≥35 years</td>
<td>No restriction</td>
<td>Unacceptable risk</td>
</tr>
<tr>
<td>Obese (BMI ≥30 kg/m2)</td>
<td>No restriction</td>
<td>Benefits&gt;risks</td>
</tr>
<tr>
<td>Has history of VTE and at high risk for recurrent VTE*</td>
<td>Benefits&gt;risks</td>
<td>Unacceptable risk</td>
</tr>
<tr>
<td>Has history of VTE and at low risk for recurrent VTE#</td>
<td>Benefits&gt;risks</td>
<td>Risks&gt;benefits</td>
</tr>
<tr>
<td>Family history of VTE (1st-degree relative)</td>
<td>No restriction</td>
<td>Benefits&gt;risks</td>
</tr>
</tbody>
</table>

CDC= Center for Disease Control and Prevention § Includes implants, depot medroxyprogesterone acetate, and
progestin-only pills (POP); ¥ Combined contraceptives; Includes pill, patch, and ring; * High risk for recurrent VTE defined as having 1 or more risk factors: history of estrogen-associated VTE, pregnancy-associated VTE, idiopathic VTE, known thrombophilia, active cancer excluding nonmelanoma skin cancer, or recurrent VTE; #Patient has no risk factors for high risk of recurrent VTE.

**Choice of Progestin in COCs**
- The most commonly used progestins in COCs are levonorgestrel, norgestimate, norethisterone, drospirenone, and desogestrel. Levonorgestrel is associated with the lowest risk of blood clots.22, 23
- In 2012, based on observational studies, the FDA advised relabeling of all OCs containing drospirenone to state that they may be associated with a 3-fold higher risk of blood clots compared with OCs containing levonorgestrel.
- In 2014, a systematic review and meta-analysis (N=26 studies) found that the relative risk of VTE for COCs with desogestrel or drospirenone was 50-80% higher than for OCs with levonorgestrel.27
- In 2015, case-control studies using United Kingdom databases (N=10,562) found that drospirenone and desogestrel were associated with almost a 2-fold risk of VTE compared with levonorgestrel, whereas norethisterone and norgestimate had comparable risks as levonorgestrel.28
- Though desogestrel and drospirenone may increase VTE risk compared to levonorgestrel-containing COCs, the absolute excess risk remains small and is still considerably lower than the risk during pregnancy and postpartum.

**Conclusion**
- For women who are tolerating their drospirenone-containing OC therapy, use shared-decision making to decide whether it is appropriate to remain on therapy.29
- For new start patients, providers should consider overall VTE risk, patient preference, adherence to contraceptive method, and available alternatives.
- To minimize VTE risk, consider using a POP, or choose a COC containing low-dose ethinyl estradiol (<35 mcg) and progestins such as levonorgestrel, norethisterone, or norgestimate.

**FDA Medication Alerts and Announcements**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Safety Alert</th>
<th>Link</th>
</tr>
</thead>
</table>
| Testosterone and Other Anabolic Androgenic Steroids (AAS) | FDA Evaluating Risks Associated with Abuse and Dependence  
FDA approved class-wide labeling changes for all prescription testosterone products, adding serious safety risks (e.g., heart attack, heart failure, stroke) associated with abuse and dependence of testosterone and other AAS. | Link |
| Pioglitazone-containing Medicines         | FDA Updating Review for Pioglitazone and Risk of Bladder Cancer  
Updated FDA review concludes that use of type 2 diabetes medicine pioglitazone may be linked to an increased risk of bladder cancer. The labels of pioglitazone-containing medicines already contain warnings about this risk, and now the FDA has approved label updates to describe the additional studies that were reviewed. | Link |

[Return to top of section]
References


12) samhsa.gov. Results from the 2013 National Survey on Drug Use and Health Summary of National findings


23) Martin KA, Douglas PS. Risks and side effects associated with estrogens-progestin contraceptives. In: UpToDate. UpToDate, Waltham, MA. (Accessed on November 1, 2016.)


25) Kaunitz AM. Patient education: hormonal methods of birth control (Beyond the Basics). In: UpToDate. UpToDate, Waltham, MA. (Accessed on November 1, 2016.)


