Drug Utilization Review (DUR) Newsletter

COLORADO
Department of Health Care Policy & Financing

Select HCPF Medication Use Policy Updates

SUMMER 2022

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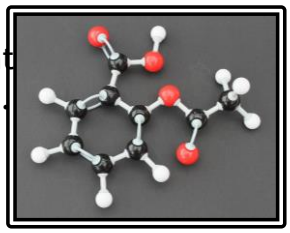
NEW Aspirin Guidelines for Primary Prevention More Factors to Consider



The US Preventive Services Task Force (USPSTF) has published a final recommendation statement on aspirin use to prevent cardiovascular disease. **The statement advises against starting aspirin for the primary prevention of cardiovascular disease in individuals aged 60 years or older.**

For those aged 40-59 years, the USPSTF suggests that aspirin could be considered in those at increased risk of cardiovascular disease (10-year risk of 10% or greater) but that the decision should be individualized through shared decision making. It notes that in the 40-59 age group, evidence indicates that the net benefit of aspirin use is small, and that persons who are not at increased risk for bleeding are more likely to benefit. More importantly, these recommendations only apply to people who do not have a history of cardiovascular disease and are not already taking daily aspirin.

The task force concluded that adequate evidence exists that low-dose aspirin has a small benefit to reduce risk for cardiovascular events (nonfatal myocardial infarction and stroke) in adults 40 years or older who have no history of cardiovascular disease but are at increased cardiovascular risk. Evidence shows that the absolute magnitude of benefit increases with increasing 10-year cardiovascular risk and that the magnitude of the lifetime benefits is greater when aspirin is initiated at a younger age.

However, aspirin use is not devoid of potential adverse events. The Task force added that adequate evidence exists that aspirin use in adults increases the risk for gastrointestinal bleeding, intracranial bleeding, and hemorrhagic stroke. The USPSTF determined that the magnitude of the harms is small overall but increases in older age groups, particularly in adults older than 60 years. For patients who are eligible and choose to start taking aspirin, the benefits become smaller with advancing age, and data suggest that clinicians and patients should consider stopping aspirin use around age 75 years. Controversy has always surrounded the protective effects of aspirin on colorectal cancer and the Task force clearly states that the current evidence still remains unclear regarding reduced risk of incidence or mortality.

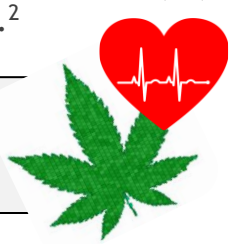
Finally, remember that aspirin is just one tool for reducing cardiovascular risk and patients can reduce their risk for a cardiovascular event in other ways such as regular exercise, eating a heathy diet, controlling blood pressure and diabetes, and by taking statins if they are at increased cardiovascular risk. When comparing these interventions to aspirin, aspirin only has a marginal value over and above all these other interventions.

WARNING: Cannabis May be Bad for Your Heart

In 2014, Colorado was the first state to allow cannabis to be sold from within a dispensary. Since this time, several states have either legalized, allowed for only medical use, decriminalized, or made cannabis fully legal. However, it is important to note that cannabis still remains a Schedule 1 substance according to Federal law. Within our state and nationwide, cannabis use has spiked, especially among young adults.[1] To this end, understanding the long-term safety risks has become critical.

When considering the cardiovascular (CV) complications associated with cannabis, much of the available published data are short term, observational, and retrospective in nature; lack exposure determination; exhibit recall bias; include minimal cannabis exposure with no dose or product standardization; and typically evaluate low-risk cohorts.[2] Additionally, the effect modification of mode of administration, dose, and chronicity of use of these CV complications is scant. Nonetheless, based on the effects of exogenous cannabinoids at the receptor level and the type of tissue involved, potential cardiovascular complications can be postulated. The major health concern is whether cannabis triggers or potentiates major adverse CV events such as myocardial infarction (MI), arrhythmias or stroke. Cannabis use may become a CV risk factor, similar to smoking.[2]

While the evidence is still inconclusive for cannabis use and adverse cardiovascular outcomes, recent data suggest a signal for an association, as well as the potential for cannabis use to be a potential risk ASCVD risk factor.



As with any psychotropic agent, cannabis has its adverse effects. Two recently published studies have provided insight into the cardiovascular risks. Using the American Behavioral Risk Factor Surveillance System survey of U.S. adults, Ladha et al evaluated the association between any recent cannabis use and MI history using a weighted logistic regression model that adjusted for demographic factors, socioeconomic factors, health-related behaviors, concomitant substance use and other comorbidities. Among 33,173 young adults (aged 18-44 years), 4610 respondents reported recent cannabis use. **Compared to non-users, cannabis users had a higher risk for MI (adjusted odds ratio (OR): 2.07, 95% confidence interval (CI): 1.12-3.82).** This association was similar in magnitude to associations seen for current tobacco smoking (adjusted OR 2.56, 95% CI 1.56–4.21) and smokeless tobacco use (adjusted OR 1.88, 95% CI 1.00–3.50). Chronic cannabis use (more than four times per month) and smoking cannabis as mode of administration was associated with higher odds of MI (adjusted OR: 2.31, 95% CI 1.18–4.50; adjusted OR: adjusted OR 2.01, 95% CI 1.02–3.98; respectively) compared to non-users. While higher risk of MI was associated with vaporization (adjusted OR 2.26, 95% CI 0.58–8.82) and edible consumption (adjusted OR 2.36, 95% CI 0.81–6.88), these findings were not statistically significant.[3]

In a cross-sectional analysis using the 2014–2015 nationwide Veterans Affairs Healthcare database and the Veterans with premature atherosclerosis (VITAL) registry, Mahtta et al categorized patients as having premature (n=135,703), extremely premature (n=7,716) or non-premature atherosclerotic cardiovascular disease (ASCVD) (n=1 112 455); stratified each cohort based on recreational substance use (e.g., tobacco, alcohol, cocaine, amphetamine, and cannabis); and evaluated the association. Compared with patients with non-premature ASCVD, patients with premature ASCVD had a higher use of cannabis (12.5% vs 2.7%, p<0.01) and, in adjusted models, cannabis use was independently associated with premature ASCVD (OR: 2.65, 95% CI 2.59 to 2.7), and the association was stronger in women than in men. Additionally, patients with polysubstance use had a graded response with the highest risk (~9-fold) of premature ASCVD among patients with use of four or more 4 recreational substances.[4]

DUR Board Member Spotlight

by Jenni Mun
PharmD Candidate
DUR Intern

Brian M. Jackson, MD, MA

Dr. Brian Jackson is an Intensive Care Physician at the Children's Hospital in Colorado and an Assistant Professor of Pediatrics at the University of Colorado School of Medicine. His role as an ICU physician involves providing care to pediatric patients from all over Colorado and eight other regions.

Dr. Jackson serves as Co-chair for the Ethics Committee at Children's Hospital, and he is also a part of the flight team at where he works to develop guidelines for the Medical Air Ambulance Program.

After attending Pomona College in California to pursue a degree in Religious Studies with a minor in Political Science, he moved to Washington, D.C., and attended the George Washington University School of Medicine. He continued his education by completing a master's degree program in Bioethics and Health Sciences.

Dr. Jackson enjoys providing care in different therapeutic areas and he became particularly interested in critical care. He loves getting to meet patients from diverse backgrounds, and it is rewarding to see his patients get better.

Aside from his professional duties, Dr. Jackson enjoys spending time with his wife and two kids . He also has a strong interest in theater. His current favorite Broadway show is *Come from Away*. He also enjoys cooking, discovering new recipes, and exploring new food places in Denver.

Dr. Jackson dedicates time to educate healthcare providers with limited pediatric critical care access by visiting rural towns and hospitals. He hopes to continue providing the best care for pediatric patients in need.

May 2022
DUR Board PDL Drug Classes Reviewed

- Tetracyclines
- Angiotensin Modifiers
- Pulmonary Arterial Hypertension Therapies
- Statins & Combinations
- Acne Agents, Topical
- Anti-Psoriatics
- Immunomodulators, Topical
- Topical Steroids
- Antiemetics
- *H.pylori* Treatments
- Pancreatic Enzymes
- Anticoagulants
- Erythropoiesis Stimulating Agents
- Benign Prostatic Hyperplasia (BPH) Agents
- Alpha Blockers
- Beta Blockers & Combinations
- Calcium Channel Blockers & Combinations
- Lipotropics
- Oral Isotretinoins
- Rosacea Agents
- Androgenic Agents
- Bile Salts
- GI Motility, Chronic
- Hemorrhoidal, Anorectal, and Related Topical Anesthetic Agents
- Proton Pump Inhibitors
- Non-Biologic Ulcerative Colitis Agents
- Anti-Platelet Agents
- Colony Stimulating Factors
- Phosphate Binders

Are you sure your patients who use opioids have **NALOXONE** available for an **overdose emergency**?

https://www.colorado.gov/hcpf/pharmacy-resources#PDL

The July 1, 2022 Colorado Preferred Drug List (PDL)

is available at

https://hcpf.colorado.gov/sites/hcpf/files/07-01-22%20PDL%20v2.pdf

Are you interested in observing a virtual Colorado DUR Board Meeting?

Board meetings are held once a quarter in

- February
- May
- August
- November

Meeting dates, times, agendas and minutes are posted on the DUR Board web page at https://hcpf.colorado.gov/drug-utilization-review-board

Zoom meeting information for public attendees is posted on the same web page a few days prior to each meeting

DUR Board Member Spotlight

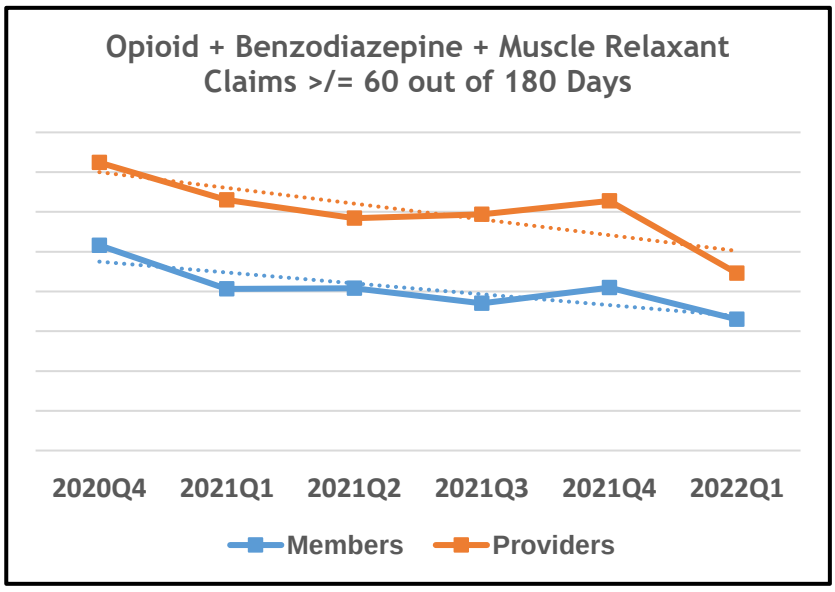
by Ryan Tran, PharmD Candidate DUR Intern

Shilpa Klocke, PharmD, BCPS

Dr. Shilpa Klocke is a Clinical Pharmacy Specialist in Neurology at Kaiser Permanente Colorado. Her role involves working with patients, prescribers, and nurses to assure the safe, effective, and affordable use of medications among patients living with various neurologic disorders. She engages in direct and indirect patient care, including clinical management of pregnant women with epilepsy and over 200 persons with multiple sclerosis. She also precepts students and residents, engages in clinical research, and participates in the drug utilization and formulary management process.

Dr. Klocke received her PharmD degree from the University of Wisconsin-Madison. Upon graduation, she obtained a PGY1 Pharmacy Practice Residency at the Parkland Health & Hospital System (PHHS) in Dallas, Texas. The second half of her PGY1 was so influential that she pursued a PGY2 in ambulatory care. However, Parkland was still developing its ambulatory care residency program so Dr. Klocke spent some time in the outpatient pharmacy as well as practicing at Costco pharmacy before becoming one of the first ambulatory care residents ever to train at PHHS. Dr. Klocke has a great passion for the ambulatory care setting because it fits her personality the best and, more importantly, she gets to know her patients and coworkers on a more personal level due to their constant interactions with one another. After finishing her PGY2 residency, Dr. Klocke worked at the ambulatory care clinic at Kaiser Permanente for a few years before her current position in Neurology (her true love) became available.

Outside of work, Dr. Klocke loves being active outdoors whether that is hiking, walking her dogs, or camping with conversion vans! She likes to read, cook, watch anything sci-fi related, spend time with family and friends, and travel (New Zealand and Iceland are noted as her favorite destinations thus far). In addition to providing her neurology specialty point of view, Dr. Klocke hopes to provide strategies to the DUR board so that Health First Colorado can continually provide access to safe, high quality medications for their patients in a smart and affordable way.



Use of opioid, benzodiazepine and skeletal muscle relaxant trio continues to steadily decline

The number of Health First Colorado members who receive an **opioid, benzodiazepine, and skeletal muscle relaxant concomitantly** for 60 or more days during a quarter continues to decline.

In many cases, the same prescriber does not authorize these medications.

Combined use of medications from these three drug classes may result in additive CNS depression, profound sedation and severe respiratory depression.

Our mission is to improve health care equity, access and outcomes for the people we serve while saving Coloradans money on health care and driving value for Colorado. https://hcpf.colorado.gov

The concerning and rising trend of gabapentin involvement in fatal drug overdoses

A recent *Morbidity and Mortality Weekly Report (MMWR)* suggests that gabapentin is increasingly involved in drug overdose deaths.[1] According to data from the State Unintentional Drug Overdose Reporting System (SUDORS) based on death certificate and medical examiner/coroner reports, the number of toxicology tests detecting gabapentin after fatal overdoses doubled between early 2019 and early 2020. About 90% of these cases also involved opioids, primarily illicitly manufactured fentanyl.[2]

- Gabapentin use is steadily increasing, and the drug may be used intentionally to potentiate the effects of opioids. It is generally considered safe and does not usually result in overdose on its own. However, when combined with other CNS depressants (such as opioids) the risk of respiratory depression, possibly fatal, is increased.
- Gabapentin exposures associated with intentional abuse, misuse, or unknown exposures reported to U.S. poison centers increased by 104% from 2013 to 2017.

In 2019, 69 million prescriptions for gabapentin were dispensed in the United States, making it the seventh most commonly prescribed medication in the nation. The number of toxicology tests detecting gabapentin after fatal overdoses doubled between early 2019 and early 2020.

- Most gabapentin-involved overdose deaths occurred among non-Hispanic White persons (83.2%) and persons aged 35–54 years (52.2%). Gabapentin-involved overdose deaths occurred with approximately equal frequency among men (49.7%) and women (50.3%).
- These findings highlight the dangers of polysubstance use. In the United States, although gabapentin is included on the list of substances recommended as part of a full postmortem toxicological panel,[3] it is not always analyzed or uniformly included on death certificates; therefore, overdose deaths involving gabapentin or with gabapentin detected are likely underestimated.

References

NEW Aspirin Guidelines for Primary Prevention: More Factors to Consider

1. Guirguis-Blake JM, Evans CV, Perdue LA, et al. Aspirin Use to Prevent Cardiovascular Disease and Colorectal Cancer: Updated Evidence Report and Systematic Review for the US Preventive Services Task Force. *JAMA*. 2022;327(16):1585-1597. doi:10.1001/jama.2022.3337. Available at: https://jamanetwork.com/journals/jama/fullarticle/2791401. Accessed May 2, 2022.

WARNING: Cannabis May be Bad for Your Heart

1. Department of Health and Human Services. Key Substance Use and Mental Health Indicators in the United States: Results from the 2020 National Survey on Drug Use and Health. October 2021. Available at: https://www.samhsa.gov/data/sites/default/files/reports/rpt35325/NSDUHFFRPDFWHTMLFiles2020/2020NSDUHFFR102121.htm. Accessed May 2, 2022.
2. Page RL II, Allen LA, Kloner RA, et al. Medical marijuana, recreational cannabis, and cardiovascular health: A scientific statement from the American Heart Association. Circulation 2020;142:e131–e152.
3. Ladha KS, Mistry N, Wijeysundera DN, et al. Recent cannabis use and myocardial infarction in young adults: a cross-sectional study. CMAJ 2021; 193: E1377-E1384.
4. Mahtta D, Ramsey D, Krittanawong C, et al. Recreational substance use among patients with premature atherosclerotic cardiovascular disease. Heart 2021;107:650–656.

The concerning and rising trend of gabapentin involvement in fatal drug overdoses

1. Mattson CL, Chowdhury F, Gilson TP. Notes from the Field: Trends in Gabapentin Detection and Involvement in Drug Overdose Deaths — 23 States and the District of Columbia, 2019–2020. MMWR Morb Mortal Wkly Rep 2022;71:664–666. DOI: http://dx.doi.org/10.15585/mmwr.mm7119a3. Accessed July 5, 2022.
2. Kuehn BM. Gabapentin Increasingly Implicated in Overdose Deaths. JAMA. 2022 Jun 28;327(24):2387. doi: 10.1001/jama.2022.10100. PMID: 35762989.
3. Davis, GG, Cadwallader, AB; Fligner, CL, et al. Position Paper: Recommendations for the Investigation, Diagnosis, and Certification of Deaths Related to Opioid and Other Drugs. Am J Forensic Med Pathol 2020;41(3):152-159. doi: 10.1097/PAF.0000000000000550. Available at: https://journals.lww.com/amjforensicmedicine/Fulltext/2020/09000/Position_Paper__Recommendations_for_the.2.aspx. Accessed July 5, 2022.

Images

1. Marijuana Leaf. Free*SVG. Public Domain Mark. SVG ID: 117669. https://freesvg.org/squares-mosaic-marijuana-leaf
2. Heart/ECG. Pixabay. Image by Gordon Johnson. https://pixabay.com/vectors/ekg-electrocardiogram-heart-art-2069872/
3. Aspirin molecular model. Wikimedia Commons. Creative Commons Attribution-Share Alike 3.0. Image by Bin im Garten. https://commons.wikimedia.org/wiki/File:Aspirin_8180.JPG#filelinks