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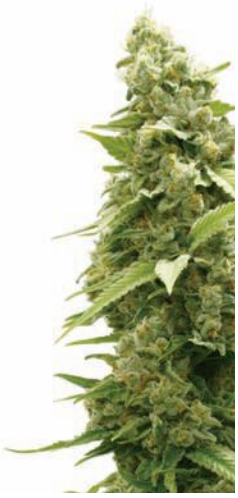
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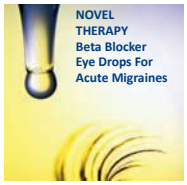
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BIG TOBACCO, BIG OPIOID, BIG WEED



The Successful Commercialization of Habituation & Addiction

by John C. Hagan, III, MD

Sham medical marijuana. How can it miss?
It's legal, it's addicting and, medical and moral judgments aside, it's a great investment.

In 1964, John, Paul, George and Ringo, a.k.a. The Beatles, lamented "Money can't buy me love." Money may not buy love but money can assuredly buy votes and elections. Money, lots and lots of it, bought victory in the November 2018 election for Show-Me State Amendment 2-medical marijuana (weed, pot, cannabis, MJ, Mary Jane, grass, ganja, 420). I shall refer to this as 'sham' medical marijuana because marijuana is not a drug and its popularity is more about THC than CBD. THC (tetrahydrocannabinoid) is the high/euphoria producing component of cannabis; CBD (cannabidiol) is the medicinal properties non-high producing component.



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Big Weed

"Big Weed" is the derisive name for the unseemly and avaricious conglomerate of cannabis growers, processors, distributors, dealers, Mexican drug cartels, users/abusers, investors, and other hanger-on's bent on making billions on medical, and inevitably recreational, marijuana.

Best estimates in 2018 are over $5 million was spent in Missouri promoting three sham medical marijuana referenda. The disorganized 'mom and pop' opposition spent less than $15,000. Big weed has been working to build support in Missouri for over 15 years.

Big Weed, and the high potency THC products it purveys, is the current darling of investors everywhere. The Wall Street Journal and investment advisors, such as The Motley Fool, predict cannabis stocks will experience the same exponential growth as Apple, eBay, and Amazon. By 2027 estimates are a $57 billion-dollar world marijuana market with $47 billion of that in North America.[1] How can it miss? It's legal, it's addicting and, medical and moral judgments aside, it's a great investment.

For $5 million Big Weed in Missouri got commercials, signs, billboards, out-of-state but on-the-payroll bogus medical experts extolling the purported (but largely unproven) benefits of weed for everything from menstrual cramps to cancer. State-wide rallies were skillfully orchestrated, social media was filled with promises of a medical panacea. Paid organizers worked first to obtain the necessary number of signatures to get on the ballot. These paid workers canvased city areas felt to be sympathetic to marijuana and/or with a sizeable percentage of recreation users. Once on the ballot workers turned out the vote.



Figure 1. Physicians, dentists, nurses, celebrities were paid to encourage people to smoke.
Source: Stanford Research into the Impact of Tobacco Advertising

Big Weed promised easier access, a higher 'high', and expanded marijuana choice with lower prices. Habituation, addiction, cannabis caused physical and mental disease, the present availability of three FDA approved CBD-based drugs for childhood seizures (Epidolex), chemotherapy nausea and vomiting (Marinol), and appetite stimulation (Cesamet), and the unified opposition of all Missouri's physician organizations were never mentioned.

When sham medical marijuana passed in Colorado, their healthcare organizations were uninvolved. When use of faux medical marijuana skyrocketed in the Centennial State it was only a matter of time till recreational pot was legalized. Problems related to easy access marijuana created catastrophic problems for Colorado physicians, hospitals, law enforcement, industry, and education. Driving under the influence of cannabis or mixed cannabis/alcohol increased with concomitant accidents, injuries, deaths, and disability. Colorado, due to sham medical and recreational marijuana has gone from one of the healthiest states in the USA to the fastest declining in public health parameters. What started as a referendum where oceans of money bought votes and won the election now directs how Missouri physicians practice medicine. Over the next decade widespread, high THC cannabis use will morph into a monstrous medical and social problem. (see related article page 482). Interested readers can find a summary of



Figure 2. Heroin was an over the counter product until 1914 and used for minor ailments.
Source: Prescription Drug Ads

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The Colorado physicians contacted Missouri physicians and urged us to oppose sham medical marijuana. To our credit, all the major state medical organizations came together and officially opposed all three sham medical marijuana referenda. This included the American Medical Association, Missouri State Medical Association, Missouri Association of Osteopathic Physicians & Surgeons, Kansas City Medical Society, St. Louis Metropolitan Medical Society, Greene County Medical Society, Missouri Pharmacy Association, and the organizations representing ophthalmology, emergency medicine, psychiatry, and family practice. Most medical groups also called on the FDA to change regulations to allow easier legitimate research on CBD cannabis; none of the sham medical marijuana referenda did so.

Noticeably, and inexcusably, sitting on the sidelines and remaining neutral was the Missouri Hospital Association. Other disappointments: Mothers Against Drunk Driving (MADD), school nurses' association, PTAs, religious denominations except the Baptists. Regrettably recommending "Yes" on Amendment 2: *The Kansas City Star* and *The St. Louis Post-Dispatch* newspapers.

Missouri law enforcement was vocal in opposition to easy marijuana. The Pueblo Colorado sheriff toured Missouri regaling our state police and sheriffs with the overwhelming amount of crime related to medical/recreational marijuana. Missouri law enforcement is bracing for a surge in marijuana-related crime and violence, including cartel illegal growing/selling.

As Nancy Pelosi infamously said in 2010, "We have to pass the bill so that you can find out what is in it." So too shall we in Missouri's health professions now try to understand what havoc Big Weed's voters have foisted on our profession. I predict in 6 to 12 years: that marijuana will be legalized for recreational use; widely diverted to younger and younger users and as socially accepted as alcohol; that medical and social problems from easy marijuana will parallel those that have predictably and inevitably occurred in other states like Colorado; that widespread marijuana use will be as detrimental to general health as tobacco abuse and the current opioid crisis.

Public health and social responsibility be damned, let's look how tobacco, opioids, and now marijuana have been marketed. Nothing sells like an addicting substance that many people can profit from marketing.

Big Tobacco

Doctors, nurses, dentists, pharmacists, as well as popular celebrities were put on the payroll to extoll how salubrious and healthy smoking tobacco was. (Figure 1) Physicians recommended cigarettes for rough throats, anxiety reduction, and other minor ailments. Physicians, especially with financial ties to the tobacco industry, denied any connection of tobacco use with heart/lung/blood vessel disease, cancer or other now-proven tobacco caused illnesses. Free cigarettes were distributed to the public including teenagers. Big Tobacco chemists learned how to ramp-up the habituating nicotine content of cigarettes. Taste enhancers such as menthol were added. Nefarious effects of smoking were falsely advertised to be ameliorated by filters on cigs. When evidence accumulated about the many serious health problems caused by tobacco use, studies paid for by Big Tobacco somehow failed to show any causation. When the evidence was overwhelming and undeniable, black box warnings were put on tobacco products and lawsuits

began. These eventuated in the 1998 Tobacco Master Agreement Settlement that stipulated Big Tobacco pay $206 billion over 25 years. See https://en.wikipedia.org/wiki/Tobacco_Master_Settlement_Agreement.

Tobacco continues to be a major health problem including soaring rates of e-cigarette use in the very young. Electronic 'vaping' of cannabis is common. The tort bar continues to reap profit suing Big Tobacco. And Big Tobacco just considers these judgment monies part of the cost of doing business. Big Tobacco also moved their addictive, health destroying product overseas, especially to under-developed countries with fewer health safe guards and far less litigation.



Figure 3. Figure 3. Russell Portenoy, MD, called by many 'The father of the opioid epidemic", while receiving industry monies encouraged physicians to prescribe 'low addicting potential' opioids. Also active was Kansas City's Center for Practical Bioethics.
Source: MedPage Today

Big Opioids

Opium, cocaine, and heroin were sold over the counter until the Harrison Narcotics Act of 1914. These products were said by their manufacturers to be non-addicting and ideal for treating many common and minor diseases. Oblivious and gullible physicians recommended heroin and opium for childhood coughs and a wide variety of everyday ailments. (Figure 2)

Many thousands of civil war veterans were given unrestricted access to morphine and syringes to deal with war wound pain and became addicted. Physicians unwittingly addicted hundreds of thousands of people, especially women with menstrual cramps and other common gynecological problems, by freely dispensing "Laudanum" which is opium in an alcohol base. After the addicting and health destroying properties of opium-based narcotics were belatedly recognized and regulated much of the highly addicting substances were manufactured and distributed by criminal networks. Until Purdue Pharma and the egregious multi-billionaire Sackler clan came along.[2,3] Contributing Editor Art Gale, MD, in *Missouri Medicine* has summarized how Purdue claimed their opioids were non-addicting and paid an astounding number of pain medicine specialists to shill their products. (Figure 3) Purdue was the first company to pay sales representatives bonuses based on the amounts of opioids their area physicians prescribed. In one year over $40 million was paid to Purdue sales reps. Dr. Gale's article can be found at: http://www.omagdigital.com/publication/?i=327880#{%22issue_id%22:327880,%22page%22:6}

The opioid crisis is one of the pre-eminent health problems of present-day America. The opioid industry used Big Tobacco's game plan: falsely claim unfettered health benefits for the product, deny addicting, habituating or unhealthful properties; pay pain-specialists to shill for them. The opioid industry was so successful that in the late 90s and early 2000s as much as $16-20 million in legal judgments were awarded against physicians, hospitals, clinics, nursing homes for withholding opioids from patients. Now the same lawyers are suing the same types of defendants for prescribing opioids. Tort lawyers will always find a way to flourish in the United States of Litigation. However, I am rooting for the numerous states' attorneys general in their collective efforts to win massive judgments against Purdue Pharma.

Big Weed

Big Weed, noting the success of Big Tobacco and Big Opioid, has successfully used the same *modus operandi*.

Extraordinary but unproven benefits are claimed for cannabis. Use of cannabis is purported to be non-habituating or addicting. Physicians, 'scientists', and alleged 'medical' users are paid to say nice things about medical marijuana. Money, money, and more money is poured into target states. Swarms of paid individuals collect signatures to place sham medical marijuana on the ballot. If marijuana is voted down, more money, more propaganda, more advertising is used and the issue appears in the next election. All it needs to pass is once.

Some of the contradictions on marijuana are staggering. People that think that the age for purchase of tobacco products should be raised to twenty-one support laws that make cannabis easily diverted to minors. People that think it should be illegal to sell sugary soft drinks have no problem with demonizing sugar but lionizing cannabis. They seem oblivious, perhaps intentionally so, to the voluminous and thoroughly researched literature on cannabis caused and aggravated diseases.[4,5]

Laura Kelly, newly elected governor of Kansas, is on record saying she supports medical marijuana but "done Kansas style." She believes, evidence to the contrary,[6] that pot will eliminate the opioid crisis. All states, including our own, show similar hubris. States believe they can release the evil cannabis genie from the bottle and make it behave. Evil cannabis genie will never behave.

At some future point the public, the tort bar, the medical profession, and the government will all understand that the claims of Big Weed were just as specious as those of Big Tobacco and Big Opioid. Then there will be a huge amount of litigation eventuating in class action lawsuits against Big Weed who will pay billions in reparations as did tobacco and opioids. There is so much money to be made off the habituated public that it will be just another ledger entry under the rubric "Costs of doing business."

Just how difficult is it dealing with addictive substances. Let's look at a group of intelligent, educated individuals knowledgeable in health matters and presumably wishing to stay healthy. Let's look at physicians and medical students. Fewer than 2% of US physicians smoke cigarettes down from over 50% in the early 1950s.[7] In the present general population about 16-17% smoke tobacco. Opioid addiction among physicians, nurses and other healthcare workers is said to be extremely high.[8] Physicians still prescribe too many opioids and are generally not comfortable recognizing and treating opioid addiction. What about marijuana? In a 2015 survey of physicians by Medscape,[9] 25% of physicians reported previous use of marijuana recreationally with 3% reporting current use. However, a 2018 study[10] shows that medical students world wide including the USA (note Table 1 in the reference) are very high (more ways than one) in their use of recreational marijuana. The overall prevalence of current marijuana use in medical students was 8.8%.[7] Hopefully, as with cigarette smoking, when physicians learn more about the detrimental effects of cannabis on general health fewer physicians and medical students will use cannabis for pleasure.

What started as a referendum where oceans of money bought votes and won the election now directs how Missouri physicians practice medicine. Over the next decade widespread, high THC cannabis use will morph into a monstrous medical and social problem.

Missouri, and soon the rest of our nation, has truly gone to pot!

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The Problem with the Current High Potency THC Marijuana from the Perspective of an Addiction Psychiatrist

by Elizabeth Stuyt, MD

Advocates for the legalization of medical and retail marijuana are quick to point out all the possible benefits that a community might see from such a venture. These include increased jobs, increased tax revenue, possible medical benefits and they advertise it as "safe" and "healthy" and "organic." They utilize the words "cannabis" and "marijuana" for everything without differentiating between the different forms of cannabis that can have very different effects on the mind and body.

Many people who have voted for legalization thought they were talking about the marijuana of the 1960s to 1980s when the THC content was less than 2%. However, without any clear guidelines or regulations from government officials, the cannabis industry has taken a page from the tobacco and alcohol industries' play book and developed strains of marijuana and concentrated marijuana products with much higher concentrations of THC, the psychoactive component that causes addiction. The more potent a drug is, the stronger the possibility of addiction and the more likely the person will continue to purchase and use the product.



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The active component in marijuana that people find so desirable was not really known until the 1960s when a research team in Israel found that after injecting THC into aggressive rhesus monkeys, they became calm and sedate.[1] This team discovered that there was a receptor in the brain that fit THC like a glove so they named these receptors cannabinoid receptors. It was not until the 1990s that this same team discovered why we have these receptors in our brain.[1] They discovered compounds produced by our bodies that fit into these receptors which they named anandamides, a Sanskrit word for "supreme joy." These receptors are found all over the brain and are still called endocannabinoid receptors but that is not because they are meant for people to take in THC.

The primary problem with the current available cannabis in dispensaries in Colorado is that the THC content is not like it used to be. Prior to the 1990s it was less than 2%. In the 1990s it grew to 4%, and between 1995 and 2015 there has been a 212% increase in THC content in the marijuana flower. In 2017 the most popular strains found in dispensaries in Colorado had a range of THC content from 17-28% such as found in the popular strain named "Girl Scout Cookie."[2] Sadly these plants producing high levels of THC are incapable of producing much CBD, the protective component of the plant so these strains have minimal CBD. For example the Girl Scout Cookie strain has only 0.09-0.2% CBD.

The flower or leaves that are generally smoked or vaped are only one formulation. We now have concentrated THC products such as oil, shatter, dab, and edibles that have been able to get the THC concentration upwards of 95%. There is absolutely no research that indicates this level of THC is beneficial for any medical condition. The purpose of these products is to produce a high, and the increased potency makes them potentially more dangerous and more likely to result in addiction.

Because there was initially no regulation on the edibles they have been made to look very similar to regular products that people consume such as chocolates, gummy bears, PopTarts etc. As a result there has been a significant increase in the accidental exposure/overdoses of children younger than nine in Colorado compared with the US at large.[3] New regulations beginning in 2019 require that all cannabis packaging in the state of Colorado must have a universal "THC" symbol on the label with the written warning "Contains Marijuana. Keep away from Children." All marijuana-infused products must have the universal symbol marked on at least one side of the "Standard Serving of Marijuana."

According to the 2014 Monitoring the Future Study, marijuana is by far the number one drug abused by eighth and twelfth graders.[4] Since legalization in Colorado, marijuana use in adolescents and those 18-25 has steadily climbed, well outpacing the national average. Colorado leads the nation in first time marijuana use by those aged 12-17, representing a 65% increase in adolescent use since legalization.[5] According to the Colorado Department of Public Health and Environment in 2015 the county of Pueblo, Colorado, has the highest prevalence of reported past month marijuana use by high school students at 30.1%.[6] It is well documented that when drugs are perceived as harmful, drug use decreases as we have seen with adolescent use of tobacco.[7] There is significantly less perception of harm by marijuana primarily because Colorado has normalized it as a society and allowed the perception that it is "organic" and "healthy" and that there is nothing wrong with it.

However, there are significant consequences of long-term or heavy marijuana use beginning in adolescence. Adolescence is a time of significant brain development. Normally during this period there is a significant increase in dopaminergic and glutamatergic stimulatory neurotransmitters and a decrease in serotonergic and GABAergic suppressive neurotransmitters located in the pre-frontal motor cortex – the last part of the brain to fully develop.[8] The prefrontal motor cortex or the "seat of judgement" is the last to fully develop and can take up to 25 – 30 years to fully develop. This equates to a great deal of learning, exploring and doing during this period, similar to stepping on the gas pedal and problems with impulse control and judgement, similar to problems stepping on the brake.

The reasons why adolescents are at such great risk for developing an addiction to drugs or alcohol is because this is a period with increased neurobiological based tendencies for risk taking with decreased suppressive and regulatory control, and this is a period of decreased parental monitoring and increase in peer affiliations, a "perfect storm."

The marijuana of old used to be classified as a hallucinogen and was thought to not cause addiction because there was no identified withdrawal syndrome. This has changed and with the increased potency of THC there is a definite recognized withdrawal syndrome which includes increased anger, irritability, depression, restlessness, headache, loss of appetite, insomnia and severe cravings for marijuana.[9] It has been reported that 9% of those who experiment with marijuana will become addicted; 17% of those who start using marijuana as teenagers will become addicted; and 25-50% of those who use daily will become addicted.[10] A 2015 study carried out in the UK found that high-potency cannabis use is associated with increased severity of dependence, especially in young people.[11]

Addiction is a problem with the learning and memory part of the brain and all drugs of abuse work in the same "reward pathway" where we learn to do anything such as eat and procreate. All drugs of abuse cause a release of dopamine from the nucleus acumbens that signifies salience and starts the process of long term potentiation which reinforces the learning. At the same time, the hippocampus which is vitally important for new memory and learning is negatively impacted by the chronic use of any addictive substance. These substances decrease neurogenesis in the hippocampus and actually cause shrinkage of the hippocampus and impair the ability to learn new things. This is true for alcohol, cocaine, methamphetamine, heroin, nicotine, and THC.[12] Animal studies have demonstrated impaired learning with all of these substances but the good news is that recovery is possible. When the use of addictive drugs is stopped and the animals are allowed to be in a recovery environment where they are free to exercise (voluntary exercise being one thing that improves neurogenesis) they can again learn new things.[13]

Human studies have shown that long-term (>10 years) and heavy (>5 joints per day) cannabis use compared with age matched non-using controls resulted in bilaterally reduced hippocampal and amygdala volumes ($p=.001$) and significantly worse performance on measures of verbal learning ($p<.001$).[14] There is evidence that recovery is possible in humans as well. A study of 40 male and 34 female long-term (@15 years) cannabis users versus 37 non-users, healthy controls divided the marijuana users into three groups; those that smoked predominantly THC in the previous three months, those who smoked a combination

of THC and CBD in the previous three months and former uses with a sustained abstinence of 29 months.[15] They found that cannabis users had smaller hippocampal volumes compared to controls but the users not exposed to CBD had an even greater (11%) reduced volumes (CBD appears to be somewhat protective). In the former users the hippocampal integrity was comparable to controls. The only problem with this study is they did not test for functional deficits to see if function improved along with hippocampal volume.

There are other important neurotransmitters that are very active during adolescence and include acetylcholine receptors (ACH) and endocannabinergic receptors (CB1). ACH helps us focus and concentrate and ACH innervation of the pre-frontal motor cortex reaches mature levels during adolescence.[16] These receptors in the brain are called nicotinic or nACHRs to differentiate them from the muscarinic receptors in the body. They are called nicotinic simply because nicotine binds to these receptors – not because we are supposed to use tobacco products. These receptors are involved in promoting or preventing neuronal cell death depending on the stage of brain development. Putting an exogenous form of nicotine in the developing brain, as in consuming tobacco, can dysregulate these fine tuning mechanisms during adolescence.

CB1 receptors regulate the balance between excitatory and inhibitory neuronal activity utilizing our own natural anandamides. Exposure to cannabis during adolescence disrupts glutamate which plays an important role in synaptic pruning in the pre-frontal motor cortex; disrupting normal brain development.[17] This is most likely why there are many studies demonstrating the negative effect on cognition and IQ in people who are exposed to marijuana beginning in utero through adolescence. In spite of this, nearly 70% of dispensaries in Denver, Colorado, recommend cannabis products to treat nausea in the first trimester of pregnancy.[18] This is basically bud-tenders practicing medicine without a license.

A study in New Zealand with a 20-year follow-up showed an average loss of 8 IQ points with early persistent teen use of marijuana.[19] If you already have a high IQ, a drop in 8 points may mean the difference between making As and making Bs, however for the person with an average IQ of 100 (50th percentile), a loss of 8 points can put that person in the 29th percentile with significant difficulty in functioning. A study out of Yale University tracked 1,142 students who achieved similar SAT scores and were enrolled in college.[20] They found that those who used minimal alcohol or cannabis had an average GPA of 3.1 at the end of the semester. Those who drank alcohol without using marijuana had an average GPA of 3.03 and those who used both alcohol and marijuana had an average GPA of 2.66.

Marijuana use is also correlated with creating or worsening many mental health problems including anxiety, depression, psychosis, and suicidal ideation. A prospective study in Australia followed 1,600 girls for seven years starting before they expressed symptoms of mental illness or substance abuse.[21] They found that girls who used marijuana at least once a week were twice as likely to develop depression than those who did not use, and those who used marijuana every day were five times more likely to suffer from depression and anxiety than non-users. A study of 307 adults with depression assessed symptoms, functioning and marijuana use at baseline, and three- and six-month intervals.[22] Researchers found that marijuana use was associated with poor recovery. Those aged 50+ increased their marijuana use compared to the youngest age group ($p<.001$) and the marijuana use worsened depression ($p<.001$) and anxiety ($p=.025$) symptoms. Marijuana use led to poorer mental health functioning compared to those who did not use marijuana ($p=.01$).

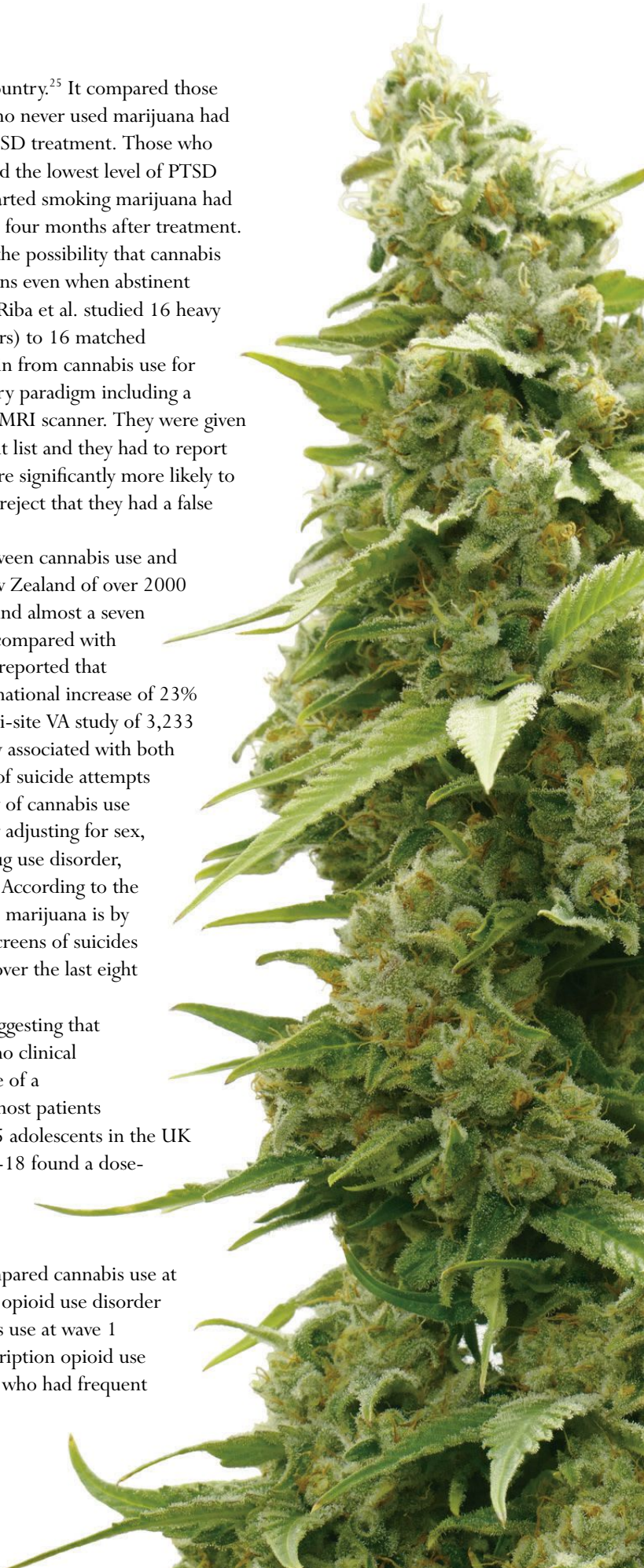
Numerous studies have demonstrated that using cannabis prior to the age of 15-18 significantly increases the risk of developing psychotic symptoms.[23] The risk is dose dependent and increases with greater frequency of use and with higher potency THC. A landmark study out of the UK analyzed 780 adults, ages 18-65, 410 with their first psychotic episode versus 370 matched healthy controls.[24] They found that use of high potency THC >15% resulted in a three times increased risk of psychosis, and if the use was daily there was a five times increased risk. Those using hash with <5% THC did not exhibit psychotic symptoms.

A growing number of states have identified PTSD as an approved condition for medical marijuana. However, this is not based on any research. There is no evidence that marijuana successfully treats PTSD and there is evidence that it can make it worse. Marijuana is not the answer for PTSD similar to the reason why benzodiazepines or alcohol are not the answer for PTSD. All these compounds do is provide temporary relief by numbing the individual and disconnecting them from the traumatic emotion. It does not resolve the trauma, and they have to continue to use multiple times a day in order to continue with the benefit. This can lead to increased addiction potential and withdrawal symptoms, cognitive impairment, a-motivational syndrome, and the potential for psychosis or worsening psychosis from the PTSD. An observational study done by the VA followed 2,276 Veterans who were treated for PTSD

in one of the VA PTSD treatment programs around the country.[25] It compared those using marijuana and those not using it and found those who never used marijuana had significantly lower symptom severity four months after PTSD treatment. Those who were using marijuana but stopped using it in treatment had the lowest level of PTSD symptoms four months after treatment, and those who started smoking marijuana had the highest levels of violent behavior and PTSD symptoms four months after treatment. Another conundrum that impacts treatment for PTSD is the possibility that cannabis users have an increased susceptibility to memory distortions even when abstinent and drug free which can compromise reality monitoring. Riba et al. studied 16 heavy cannabis users (daily for last two years – average of 21 years) to 16 matched cannabis naïve controls.[26] The cannabis users had to abstain from cannabis use for four weeks prior to the study. The study involved a memory paradigm including a study phase and a testing phase with the participant in an MRI scanner. They were given lists of four words to memorize and then shown a different list and they had to report if the words were on the previous list. Marijuana users were significantly more likely to have false recognition of the words and were less likely to reject that they had a false memory compared with the non-users.

Multiple studies have documented a relationship between cannabis use and suicidality. A large, longitudinal study in Australia and New Zealand of over 2000 adolescents and maximum frequency of marijuana use found almost a seven fold increase in suicide attempts in daily marijuana users compared with non-users.[27] A Congressional Hearing on April 27, 2017, reported that Veteran suicides were up 32% since 2001 compared to a national increase of 23% during the same time period. A 2017 cross-sectional multi-site VA study of 3,233 Veterans found that cannabis use disorder was significantly associated with both current suicidal ideation ($p<.0001$) and lifetime history of suicide attempts ($p<.0001$) compared to Veterans with no lifetime history of cannabis use disorder.[28] This significant difference continued even after adjusting for sex, PTSD, depression, alcohol use disorder, non-cannabis drug use disorder, history of childhood sexual abuse, and combat exposure. According to the Colorado Department of Public Health and Environment, marijuana is by far the most frequently encountered drug on toxicology screens of suicides among adolescents ages 10 – 19 and has been increasing over the last eight years.[29]

Misguided marijuana advocates have recently been suggesting that marijuana is a solution for the opioid epidemic. There is no clinical evidence of this and in fact, marijuana is found to be more of a "companion" drug rather than an "alternative" drug for most patients seeking addiction treatment in Colorado. A study of 5,315 adolescents in the UK with three or more measures of cannabis use from age 13-18 found a dose-response relationship between cannabis use trajectories in adolescence and nicotine dependence, harmful alcohol consumption, and other illicit drug use by age 21.[30] A large study of 34,653 individuals using NESARC data compared cannabis use at wave 1 (2001-2002 – 81% response rate) to prescription opioid use disorder at wave 2 (2004-2005 – 70.2% response rate).[31] Cannabis use at wave 1 was associated with a significant increase of having a prescription opioid use disorder at wave 2, with over four times the risk for those who had frequent use of marijuana.



There is evidence that prenatal exposure of cannabis can alter opioid gene function in humans. Fetal brains obtained from aborted fetuses from women who were using marijuana during their pregnancy were compared to those from women not using marijuana during pregnancy.[32] The researchers discovered impaired opioid-related genes in distinct brain circuits that they hypothesized may have long term effects on cognitive and emotional behavior. These findings are comparable to findings with animals. One study of prenatal cannabis exposure in rats found that the THC exposed rats exhibited shorter latency to first active lever press for heroin and had higher heroin-seeking during mild stress and drug extinction than animals not exposed to THC.[33] The THC exposed animals exhibited allostatic changes in the limbic encephalin systems in adulthood.

Another interesting study that supports the idea that cannabis use and opioid use are linked was in a randomized, double-blind, placebo controlled trial of naltrexone in non-treatment seeking cannabis smokers.[34] In a laboratory setting those receiving a placebo had 7.6 times the odds of self-administering active cannabis compared with those receiving daily naltrexone, an opioid receptor blocker.

If states continue to commercialize marijuana as has been done in Colorado we are destined to see many more people requiring treatment for addiction, depression, anxiety, suicidal ideation, and psychosis. We need to continually educate every one of the risks and increase prevention efforts to prevent children and adolescents from initiating marijuana use. This should include a strong ban on any advertising that appears to be directed toward youth – for all drugs including marijuana, tobacco, and alcohol. States will need to commit to increased funding for and availability of treatment options. The strongest recommendation would be to initiate regulations to limit the concentration of THC. Ideally this would be to less than 10% as there is no good research on concentrations greater than this for any medical condition and there is significant literature on the negative effects of high potency THC.

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Resident Access to the St. Louis County Prescription Drug Monitoring Program: Why PDMPs Matter and How to Gain Access

by Julia Lange, MD, Gary Gaddis, MD, Emily Varner, MPH, Spring Schmidt, PhD(c), Rachel Cohen, MPH & Evan Schwarz, MD

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The St. Louis County PDMP is likely to continue to be the de-facto Missouri state PDMP for the foreseeable future. It is user-friendly, rapidly accessible and presents information in a clear and useful format.



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Abstract

Prescription Drug Monitoring Programs (PDMPSs) permit physicians to determine whether patients obtained addictive substances from multiple physicians or pharmacies. In April 2017, the Saint Louis County Department of Public Health created its own PDMP. This manuscript evaluates evidence regarding the efficacy of PDMPs, in addition to discussing their impact on patient care and a provider's workflow. It also details how physicians can register to use the St. Louis County PDMP, Missouri's de-facto PDMP.

Foreword

This article grows from the 1st Annual Larry Lewis Symposium, held at Washington University School of Medicine in St. Louis in August 2017. The Symposium was a scientific forum addressing the current opioid epidemic.The purpose of this article includes:

* Educate *Missouri Medicine* readership regarding the "pro" and "con" evidence regarding efficacy of Prescription Drug Monitoring Programs (PDMPs).

* Emphasize that when a patient's PDMP data suggests they have an opioid use disorder (OUD), the next step is NOT to simply stop prescribing opioids.

* Facilitate increased access to and improved utilization of the St. Louis County PDMP, Missouri's de-facto PDMP.

* Instruct residents on how they can gain access to the St. Louis County PDMP.

Prologue/Clinical Vignette

Your first patient arrives with a "chief complaint" of "back pain flare-up." A brief chart review demonstrates frequent encounters for pain exacerbations. Upon entering the patient's room, you find a 35-year-old man with hips flexed and knees extended, while crying out in excruciating pain that "only oxycodone can help."

Upon examination, there are no physical abnormalities, his pain is distractible and inconsistent, and a negative straight leg raise sign is observed. At this point, the patient asks for benzodiazepines and opioids.



Figure 1: Cost of Opioid Epidemic in Missouri
Adapted with permission from The Missouri Hospital Association

Recalling a prior issue of *Missouri Medicine* that focused upon the current opioid epidemic you strongly suspect he has an OUD.[1]

You would like to know if he recently received opioids from another provider. In a prior issue of *Missouri Medicine*, you remember reading about PDMPs and are aware of the existence of the St. Louis County PDMP.[2] While not wanting to undertreat his pain, you are also unsure whether prescribing opioids is appropriate. You would like to have objective data to support your decision. You suddenly regret not having registered as an authorized user of the PDMP.

Let's learn how to resolve this dilemma after first reviewing why it is important to do so.

What is the Scope of the Problem?

Opioid[1] abuse is a growing epidemic in this country, particularly in the Midwest and Missouri. Between 2002 and 2011, 25 million Americans initiated nonmedical use of pain relievers, the majority of which were opioid analgesics; many developed substance use disorders (SUDs).[3] Unfortunately, physicians in training are not adequately taught how to diagnose, treat, or refer patients with SUDs to treatment, causing them to be poorly-prepared to do so.[4]

The rate of opioid overdose deaths due to prescription and illicit opioids in the United States has exploded, quintupling between 1999 and 2016.[5] In 2015 approximately 33,000 Americans died of an opioid-associated drug overdose.[6] That number rose to 42,249 in 2016.[5] Patients presenting to the emergency department (ED) following an opioid overdose rose 30% between July 2016 and September 2017.[7] Of overdose deaths from opioids, almost half are directly due to prescription opioids. The other half of decedents are likely to have utilized prescription opioids during initiation or maintenance of their OUD and subsequently switched to heroin.[6]

The Midwest was disproportionately affected, with a 70% increase during the same 14 months.[7] In Missouri there were 908 opioid-related deaths in 2016, a 35% increase over 2015.[8] To put that in perspective, 947 Missourians died in road accidents and 880 Missourians died from breast cancer that year.[9,10] The opioid epidemic was estimated to cost Missourians $12.6 billion in 2016, which represents 4.2% of Missouri's GDP (Figure 1) or nearly $1.4 million per hour.[11,12] While opioid-related deaths will never be zero, initiation of proper opioid stewardship programs including utilizing PDMPs and referral for OUD can decrease this number. Conceptually, using a PDMP to screen and intervene to prevent future morbidity draws similarities to physicians discussing mammograms, breast screening exams, or seatbelt and helmet usage with their patients.

Are PDMPs Effective?

The answer to this question may depend on how it is asked and how one judges the results. Sun et al. evaluated the effects of an automated PDMP query, embedded into an electronic health record (EHR), on opioid prescribing by emergency physicians in Washington State.[13] The algorithm was not associated with decreased opioid prescribing even in patients with evidence of previous "high-risk" opioid use. However, these results were derived from a database that extracted only selected components of the individual patient encounter records. Based on a single-center study, Hawk et al. concluded that although their state's PDMP was helpful toward identifying some patients' aberrant drug-related behavior, it was not able to detect most occurrences.[14] A recent systematic review including 17 manuscripts concluded there was insufficient evidence to determine whether PDMPs decreased fatal overdoses. However, low-strength evidence from ten studies did suggest a reduction in fatal overdoses and three studies demonstrated increased overdoses from heroin post-implementation.[15]

In this journal, Dr. John Lilly argued against enactment of PDMPs. He wrote that PDMPs do not decrease opioid-related unintentional deaths.[2] We believe this view derives from an incomplete consideration of the matter, as to decrease opioid-related deaths is not a PDMP's sole intended purpose. Mortality is a multi-factorial outcome,

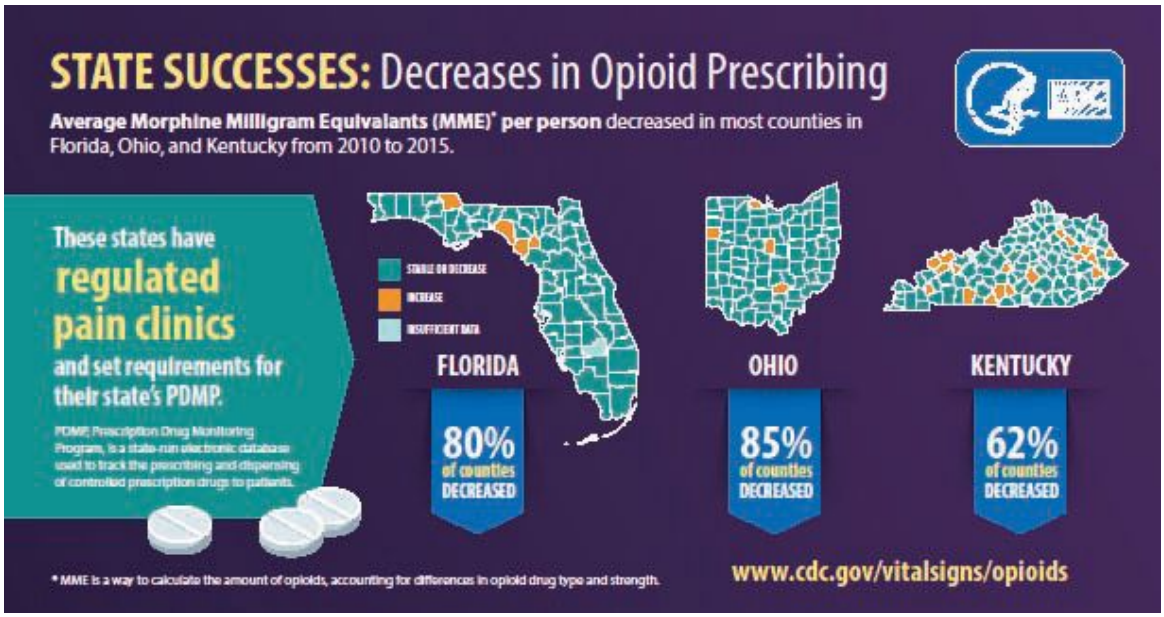


Figure 2: State Successes in Decreasing Opioid Prescribing: Florida, Ohio and Kentucky[23] Centers for Disease Control and Prevention. State Successes. https://www.cdc.gov/drugoverdose/images/vitalsigns/VS_State-Success-Graphic_508.pdf.

and in isolation, PDMPs are not expected to significantly impact mortality. However, data from Florida demonstrated decreased opioid-related deaths associated with their PDMP in 2017. According to the CDC, when multiple interventions including a PDMP were implemented, both opioid prescriptions and opioid-related deaths decreased. Further, in Florida, Ohio, and Kentucky, roll-out of state-wide PDMPs coincided with closer regulation of pain clinics and opioid prescribing decreased as a result (Figure 2).[16] Further, Dr. Lilly did not discuss the matter of the substantial direct and indirect costs to the state due to the opioid crisis.[11] Additionally, many states with effective PDMPs increased the number of patients enrolled in Medication Assisted Treatment (MAT), which will be discussed in a subsequent installment in this series.

Weiner et al. investigated emergency physicians' opioid prescribing in Ohio after a PDMP was introduced there in 2011 and after the state distributed opioid prescribing guidelines in 2012 advocating for prescribing no more than a three-day supply. After PDMP introduction, the number of opioid prescriptions decreased in 85% of the jurisdictions evaluated. Weiner's group found that the issuance of the guideline accelerated the already-declining rate of total opioid prescriptions and number of pills prescribed, which began after the PDMP was initiated.[17] Similar data were derived in Pennsylvania, where Suffoletto et al. found that at 15 Emergency Departments (EDs), opioid prescribing decreased in the first month after PDMP implementation (September, 2016) from 12.4 to 10.2% of patients. This decrease continued for each month between September 2016 and March 2017.[18] Bao et al. demonstrated a 30% reduction in ambulatory care center prescriptions of schedule II opioids associated with the implementation of PDMPs in 24 states.[19] Limiting the number of opioid prescriptions and pill counts could also limit the potential "black market" for prescription opioids, which was discussed at Senate hearings.[20]

Can PDMPs Assist Balancing Opioid Prescribing and Properly Managing Pain?

The goal of effective PDMPs is not to eliminate opioid prescribing, as opioids are necessary and appropriate to treat many painful medical conditions. The goal is instead to reduce inappropriate opioid prescribing, although reduction in total prescribing may be a natural consequence.

Physicians are public health advocates and take an oath to first do no harm (*primum non nocere*). It is challenging to balance the mission to alleviate suffering with the risk of contributing to a patient's likelihood of developing an OUD. Over the last 20 years, most OUDs began with oral opioids prescribed by physicians. While an increasing number of patients initiate OUDs with illicit opioids such as heroin and more are dying from illicit opioids, the fact remains that the majority of patients with an OUD still started with prescription opioids.[21–23] While most patients

Report	Study Subjects	Study Years	Principal Findings
Chen I, Kurz J, Pasanen M, et al. *Racial Differences in Opioid Use for Chronic Nonmalignant Pain*	397 patients over 18 years old with chronic pain presenting to 12 academic primary care settings throughout the U.S.	2002- 2003	Among patients treated in primary care clinics for chronic pain, 45.7% of Caucasians received an opioid prescription while only 32.2% of African Americans received an opioid prescription
Pletcher MJ, Kertesz SG, Kohn MA, Gonzales R. *Trends in Opioid Prescribing by Race/Ethnicity for Patients Seeking Care in US Emergency Departments*	156,729 patients of any age with any painful complaint presenting to noninstitutional general and short-stay hospital emergency departments throughout the U.S.	1993- 2005	Among patients who presented to an emergency department with pain-related complaints, 40% of Caucasians received an opioid prescription at discharge while only 32% of all other races received an opioid prescription at discharge
Tamayo-Sarver JH, Hinze SW, Cydulka RK, Baker DW. *Racial and Ethnic Disparities in Emergency Department Analgesic Prescription*	67,487 patients of any age with any complaint presenting to nonfederal, short-stay hospital emergency departments throughout the U.S.	1997- 1999	Among patients who presented to the ED with pain and received some type of analgesic during their stay, 34% of Caucasians, 23% of African Americans, and 23% of Latinos received an opioid analgesic
Heins JK, Heins A, Grammas M, et al. *Disparities in Analgesia and Opioid Prescribing Practices for Patients With Musculoskeletal Pain in the Emergency Department*	868 patients over 18 years old with musculoskeletal pain presenting to an academic emergency department in Alabama	2004	Among patients presenting with musculoskeletal pain to this emergency department, Caucasians were 86% more likely to receive an opioid during their stay, 81% more likely to receive a prescription analgesic at discharge, and 98% more likely to receive an opioid prescription analgesic at discharge than African Americans with similar complaints

Table 1: Racial disparities in opioid analgesic rates

exposed to opioids will not develop an OUD, our ability to predict who will is limited.

Physicians treating patients with pain must weigh the possibility of inappropriate prescribing against the possibility of under-treatment of pain. The 2016 CDC clinical guidelines for prescribing opioids for chronic pain stated that opioids were only indicated when their benefits outweigh their risks.[24] Additionally, multiple studies question the efficacy of opioids in the management of chronic pain, although they may still be indicated in patients with both acute and chronic pain.[25–27]

It is difficult to distinguish patients with pain who require opioids from those seeking opioids for inappropriate use or diversion. Many physicians believe that vital sign abnormalities such as hypertension and tachycardia are good indicators of pain. However, these are probably not useful surrogates.[28] Laboratory data also fail to provide accurate evidence of drug abuse. Standard urine drug screens (UDSs) only reliably detect morphine, codeine, and heroin (both metabolized to morphine). UDSs are less sensitive for semisynthetic opioids like oxycodone and hydrocodone and are ineffective tests for synthetic opioids such as fentanyl, meperidine, and methadone.[29] Further, collecting the specimen is challenging in busy environments such as EDs or hospital wards, and not useful at physician's offices, where test results may take multiple days to return.

Doctors thus often rely on clinical gestalt, but this is also imperfect and susceptible to racial/ethnic/gender biases, that can swing the pain management pendulum to oligoanalgesia. For example, numerous studies demonstrate a discrepancy in opioid analgesic use in Caucasian versus other racial and ethnic groups (Table 1).[30–33] Additionally, physician gestalt is not nearly as accurate as widely believed and has a poor ability to detect OUD.[34]

It is important to remember that decreased opioid prescribing via the use of a PDMP and proper analgesia are not mutually exclusive principles. However, oligoanalgesia is a potential side effect of stricter opioid prescribing policies. Nobody wants patients' pain to go untreated. The fear of opioids being under-prescribed, and the fear of patients suffering from widespread oligoanalgesia is a common argument against PDMPs. However, when PDMP data are used as intended, and when a patient experiencing pain presents for care while not receiving opioids from multiple prescribers, the PDMP may alleviate physician concerns about possible inappropriate prescribing. This may have been what occurred in the previously mentioned study from Washington where prescribing increased in some cases due to lack of concerning findings in the PDMP.[13]

Physicians may also worry that a tool reducing opioid prescribing may affect their patient satisfaction scores. One study evaluating the implementation of opioid prescribing guidelines demonstrated that physicians believed their patients' pain was just as well controlled with fewer opioids.[35] While not definitive proof of pain improvement, as patients were not surveyed, physicians did not have evidence that pain control was worse. Another study

also did not demonstrate an association between opioid administration and patient satisfaction scores.[36] While not a PDMP study, it shows that decreased opioid prescribing is not necessarily associated with decreased patient satisfaction. However, governmental agencies and hospital administration need to support physicians if satisfaction scores are negatively impacted by responsible opioid prescribing.

Despite this data, it is important to note that if not used properly as a tool or part of a larger plan, PDMPs do have the ability to drive patients to more dangerous illicit opioid use. Simply "cutting off" opioid prescriptions does not treat a patient's OUD and may increase the probability of them purchasing diverted prescription opioids or illicit opioids such as heroin.

Data derived from a PDMP should be used as a tool to initiate a discussion with the patient, and invites an opportunity to screen for SUDs. If the patient, once confronted, expresses interest in OUD treatment, then appropriate referral can follow. MAT improves mortality, and identification of an OUD via a PDMP assists physicians in discussing treatment prior to a patient overdosing. For patients with inadequate analgesia, the encounter represents an opportunity to place stricter limits on their prescribing plan, refer them to addiction or pain specialists, or introduce non-opioid analgesics and physical therapy where appropriate.

What is the St. Louis County Prescription Drug Monitoring Program?

The St. Louis County PDMP started as a grassroots project. Its belated launch in 2017, as well as its unusual "bottom-up" structure, can be attributed to opposition against establishing a PDMP by a powerful minority in the Missouri legislature. Opponents express privacy concerns, such as the Missouri government having access to medical information, cybersecurity threats, and the threat that someone might improperly obtain the information and use it inappropriately (e.g., commit a Health Insurance Portability and Accountability Act violation, which is a felony). However, many of these same concerns apply to any electronic health record or insurance-maintained database.

St. Louis County Council member Sam Page, MD, a former member of the Missouri General Assembly, supported a state-wide PDMP while a member of the legislature. Dr. Page later became a St. Louis County Councilman, and a locally-based PDMP was launched on April 25, 2017, in St. Louis County and City and 12 other participating jurisdictions. Subsequently, due to the hard work by many at the Saint Louis County Department of Public Health, the number of residents, fully-licensed doctors, and pharmacists in counties participating in the St. Louis County PDMP continues to grow. (https://www.stlouisco.com/Portals/8/docs/document%20library/PDMP/SubscribingCountyList.pdf)

The St. Louis County PDMP is fast and convenient to use. Any Missouri physician can register and utilize the PDMP as part of patient care, and can allow delegate access so that a medical assistant can use the PDMP for them, which saves physicians' time.[37] The PDMP also allows for bulk searching to further increase efficiency. Unfortunately, many Missouri providers are either not enrolled or not using the PDMP. Physicians may perceive time restraints, despite the fact that the query process takes less than 90 seconds. Even in the fast-paced environment of the ED, the authors often use it multiple times each shift. We hope that in the future the PDMP becomes embedded in the electronic medical record, similar to that which occurred in Washington. Lastly, use of the PDMP is voluntary. Depending on the situation, providers can choose not to check the PDMP prior to writing a prescription.

A St. Louis County PDMP query result shows the number of prescriptions filled by a patient, date written, date filled, filling location, and prescriber. It receives data from pharmacies in participating jurisdictions for schedule II-IV controlled substances, which is transmitted according to national standards established by the American Society for Automation in Pharmacy. Once uploaded, the PDMP vendor, Appriss®, validates, processes, and cleans the data prior to publication in the registry. Patients are identified by their name and date of birth. The provider can also view the patient's address and who wrote the prescription, if other safeguards are needed to verify the data's accuracy. This contrasts with the monitoring program established by an executive order of the former Governor.[38] That tool did not enable access to real-time, individual patient-level data as the St. Louis County PDMP does now.

So How Can I Use a PDMP To Improve the Quality of Care to My Patient?

So, what does the provider do if after reviewing the PDMP, they believe their patient has an OUD? PDMP data provide an opening for a conversation about drug abuse, the patient's readiness to quit, and drug abuse treatment options like MAT which includes methadone, buprenorphine, and naltrexone therapies. Fortunately, the St. Louis County PDMP can assist with this as well, as it

Figure 3:

How to Access and Utilize the St. Louis County PDMP

Physicians in Missouri can gain access to the St. Louis County PDMP by signing up with their email address at https://missouri.pmpaware.net.

Users are then prompted to select a user role:

- *Fully-licensed Physicians register as "Physician (MD/DO)"*
- *Residents must register as "Medical Resident."*
  - *Medical residents are delegate users in the PDMP until obtaining their own individual DEA # (not the institutional DEA+4).*
  - *Therefore, residents must obtain the approval of a fully-licensed Missouri physician willing to delegate access to the PDMP to the resident. This process is not complex.*
  - *At the end of the registration form, delegates will need to input their supervisory provider's email address.*
  - *Supervisory physicians must have an approved account in the PDMP before anyone who becomes their delegate can register.*
  - *Delegates will:*
    - *Enter the email address of their supervisory physician (typically the residency director) in the 'I am a delegate for:' section*
    - *Click 'Add,'*
    - *Then submit the registration.*
    - *This will trigger an email notification to the supervisory provider that a delegate has registered.*
- *All registrants must provide personal and professional information; required fields are marked with a red asterisk (*).*

All registrants are next prompted to provide validation documentation.

- *For physicians and residents, this is a copy of their medical license – either a copy of the blue medical license or online verification from Missouri Division of Professional Registration*
- *This can be obtained at:*
  - *https://pr.mo.gov/ > Licensee Search > Division Licensee Search Page.*
- *Documentation can be uploaded online, faxed to 314-615-0507, or emailed to PDMP.DPH@stlouisco.com.*

provides links to organizations such as the Substance Abuse and Mental Health Services Administration (SAMHSA). SAMHSA provides physicians with free tools and resources to assist patients with treatment once an OUD is diagnosed, runs a 24/7 referral helpline and MAT practitioner locator, and more.[39] While there are not enough resources for SUD treatment for those currently in need, it is hoped that increases in state and federal funding could improve what is currently available.

By failing to access information provided by the St. Louis County PDMP, the diagnosis of OUD may be missed or appropriate prescriptions could be withheld. While drug abuse treatment is the ideal outcome, there is value in identifying and documenting concerns to help future providers appropriately treat these patients or discuss other harm reduction practices. The St. Louis County PDMP was designed to be a non-intrusive tool used in conjunction with other care. However, if used in isolation, any PDMP is unlikely to improve care and may cause harm.

The Bottom Line

By obtaining access to and utilizing the St. Louis County PDMP, physicians have the ability to better identify and treat patients with OUD and can assist in changing the future of the opioid crisis in Missouri and the greater Midwest.

If the reader is interested in becoming a registered user of the St. Louis County PDMP, please follow the instructions in Figure 3.

Conclusion

The St. Louis County PDMP is likely to continue to be the de-facto Missouri state PDMP for the foreseeable future. It is user-friendly, rapidly accessible and presents information in a clear and useful format. Further, residents can become delegate-users once they secure a fully-licensed physician to serve as their supervising physician.

The Saint Louis County Department of Public Health continues to attract more counties to participate in its PDMP, and they have secured federal funding to ensure that new countries can join at no cost to the county until September 2019!

Author's Note

We use the term "opioids" to capture the more precise terms "opiate" (a naturally-occurring medication, such as morphine and codeine) and "opioid" (synthetic or semi-synthetic medications that have opiate-like effects and chemical structures). The word "narcotic" will not be utilized, because "narcotic" is a legal term, not a pharmacologic class of medications.

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Disclosure

None reported.

MM

Forecast for 2019 Legislative Session

by Heidi Geisbuhler

Prescription Drug Monitoring, Tort Reform, Scope of Practice... *the List Goes On*

Missouri's 100th General Assembly will convene on January 9, 2019, to begin their first session of legislative work. The legislature will work until adjournment on May 17, 2019. In between those dates, your MSMA lobbyists will be advancing a pro-physician agenda, while simultaneously heading off attempts to interfere with your profession. Following is a list of some of the issues we anticipate dealing with during the first five months of the new year.

Prescription Drug Monitoring Program (PDMP)

2018 was a quiet year for the effort to authorize a statewide PDMP. In the meantime, the St. Louis County program has only strengthened as counties and municipalities have become frustrated at the lack of a comprehensive state PDMP. This local PDMP now covers around 80% of the state's patients and 90% of its prescribers. In July 2017, the Governor issued an executive order that allowed the Department of Health and Senior Services to data mine prescription information from Express Scripts in a curious effort to identify over-prescribers. This new government surveillance program was launched early this year, causing confusion and frustration for physicians around the state. We anticipate the introduction of a comprehensive statewide PDMP bill this year. We will oppose efforts to mandate physician utilization of the PDMP. As things progress, we may come to realize the best way to implement a statewide PDMP is to allow the state to assume the St. Louis County program, thereby giving the state an operational head start.



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Prior Authorization Reform

We've heard from many MSMA members about their increasing exasperation with the prior authorization process in Missouri. More and more frequently, insurers are requiring physicians to obtain prior approval before providing medical services and pharmaceuticals to their patients. This burdensome process often creates unnecessary delays in patient care and requires physicians and their staff to spend valuable time on the phone defending their medical judgment instead of treating their patients. Legislation is currently in the works that would streamline the process, improving patient care and decreasing administrative headaches for our doctors.

Tort Reform

The state's tort reform coalition (of which, MSMA is a member) had a modest 2018. There were fewer tort issues this year that would have had a direct impact on physicians, but we continued to pursue some of the coalition's objectives. In the coming year, we expect to see the legislature debate tort reform issues relating to venue laws, punitive damages, and statute of limitations, among others.

APRNs

For a number of years we have battled the advance practice registered nurses over their scope of practice and their attempts to desecrate the collaborative practice act. We are anticipating that their advocates will once again introduce legislation to remove the collaborative practice requirement and the necessary patient protections that accompany it. In addition, we will likely seek to allow a standalone APRN license for those accomplished nurses under the authority of the Board of Registration for the Healing Arts. That board already oversees licensure for assistant physicians and PAs, two groups with nearly identical scopes of practice as APRNs. The nurses will likely oppose this effort, but we think it is a common sense change, and will perhaps open further avenues for compromise in the future.



Tanning Bed Prohibition

Forty-four states have some type of restriction on indoor tanning use by minors. In 2014, MSMA was instrumental in passing a law that required parental consent for minors who utilize tanning beds. Frequent exposure to ultraviolet rays by young people greatly increases their risk of developing melanoma. This year, we will again make an effort to completely ban the use of tanning beds by people under 17 years of age. If successful, Missouri will join 21 other states in this prohibition. MSMA has been part of a large coalition of organizations leading this effort, including the American Cancer Society, dermatology associations, and children's hospitals.

Fund Sweep

From time to time, the General Assembly finds itself in a financial pinch so seemingly dire that they try to sweep the professional licensure fees collected by the Board of Registration for the Healing Arts. That was case again last year, as several such "fund sweep" amendments were attempted during debate (none were successful). The Board of Healing Arts receives no public funding; its operating expenses are borne entirely from fees. Therefore, any skimming of those funds for other state purposes would, in effect, be a tax on physicians. We will watch for this financial sleight-of-hand as the session progresses.

Grab Bag

As is the case every legislative session, we are sure to contend with some issues we dealt with last year that failed to cross the finish line. Expect to see us contend with the annual effort to repeal the motorcycle helmet law. It is highly likely we will lock horns at some point with the chiropractors, athletic trainers, radiology technicians, physical therapists, and maybe the professional counselors as well. We will keep a watchful eye on the activities of the statewide MO HealthNet managed care companies, and fight for increased physician reimbursement and funding for public health initiatives. It's bound to be another busy year for organized medicine.

If you wish, there are a number of things you can do to assist us in these endeavors. First, please consider volunteering as the MSMA Physician of the Day in the Capitol. This rewarding program gives participants insight into MSMA's physician advocacy, and can initiate or further a relationship between MSMA members and their legislators. Plus… it's a lot of fun! You can find available dates on the MSMA Advocacy webpage. Second, there's no better way for you to support candidates that support organized medicine than through a PAC donation. Please consider giving. Finally, as a member, don't hesitate to reach out to the MSMA lobbyists when you have a question or concern. Advocacy on your and your patients' behalf is one of your many MSMA member benefits.

Follow our adventures during the 2019 legislative session in MSMA's weekly *Legislative Report*. The first edition will head out the door by email on January 11, 2019, and members will continue receiving it each Thursday throughout session.

White Coat Rally

MSMA is hosting a White Coat Rally on Tuesday, March 5, 2019. This event is an opportunity to visit the Missouri State Capitol to network and advocate on behalf of physicians and patients in the state. Legislators will deliver brief remarks on health care issues to the group from 9:00-10:00 AM in the first floor rotunda. Lunch will be provided to the group in the Capitol.

Throughout the rest of the day, we encourage attendees to meet with their local legislators, explore the building, and get to know fellow MSMA members. Some state specialty societies are planning to join the rally that day, so there may be additional meetings and presentations participants want to attend. All physicians and medical students are welcome to take part, even if you can only visit the Capitol for an hour or two!

For questions or to RSVP for lunch, visit www.msma.org/white-coat-rally or contact Heidi Geisbuhler at heidi@msma.org. **MM**

MSMA Membership Is Vital for All State Physicians

by Jeffery G. Copeland, MD

It sounds like the leaders and staff of the Missouri State Medical Association are never satisfied. We/ they are always beating the drum about physician involvement and increasing membership in the MSMA and other vital groups within organized medicine. That task is really no fun, mainly because it would seem the benefits of the actions we request would be self-evident to the highly educated group to which we address our appeal. Yet that does not appear to be true. In a perfect world, the main task of the physicians involved in the membership committee would be to provide a ready source of application documents. Sadly, that is not the case.

The other source of frustration is that we are usually talking to ourselves. It is not uncommon at meetings of local, state or national meetings of organized medical groups to see the same faces repeatedly for years, if not decades. And we are often talking about membership. This "preaching to the choir" experience could be worse (at least the people receiving the message are receptive), but if we are to achieve the goals of strengthening our intra-professional bonds and our collective strength to achieve beneficial changes in our medical world, we need the strength of numbers, i.e., we need more members, we especially need young members.

There appears to be a trend in our society to favor "lifestyle" over group membership. This takes the form of going to attend the soccer game, basketball game or some other family activities, which I certainly do not want to discourage, but it seems harder all the time to attract younger physicians into our fold and there is some natural attrition on the other end of the age spectrum.

The increased percentage of physicians who are employed by health systems is also thought to be partially responsible for this change, as there is often an allowance for memberships which is quickly consumed by specialty group dues.

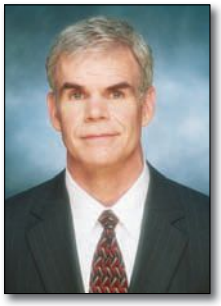
Then there are the various types of social media that seductively pull at our attention. Today, we can get lots of interaction sitting at home, rather than sitting with our peers in a doctors' lounge or at a meeting. It's just not the same interaction.

MSMA is an organization that benefits young physicians and hospital employed physicians as much as private practitioners. There exist numerous benefits to membership in organized medicine to make membership both logical and personally attractive. These include, in no specific order: the excellent advocacy MSMA provides the House of Medicine in the state legislature and to have a national voice on the larger stage of the AMA; the opportunity to get to know your Missouri peers better, both locally and across the state; access to numerous benefits that are attached to membership (it is worth going to msma.org and then to the dropdown: membership>membership perks for a complete list); the excellent Missouri Medicine journal which is among the best state journals in the country, as well as other publications from the Association which include a wryly written legislative report during session, Progress Notes to provide a brief periodic update on Association activities; support for scholarship program administration; and most recently, the opportunity to participate in the well-conceived Health Information Exchange called SHINE, which holds the promise to make patient's information securely available to anyone involved in their care, without the bounds of proprietary system EMRs.

This last benefit also holds the promise of empowering physicians with their own data source where consolidated data can be used for improvement of the care we provide as well as in our advocacy efforts. That is a very big deal.

Even though our MSMA dues are among the lowest in the country for a state medical association, it is important to know that our medical society knows how to work lean, with a very capable staff, each of whom actually performs several roles in the organization. We receive great value from these devoted people.

Lastly, a word about my personal favorite benefit – the



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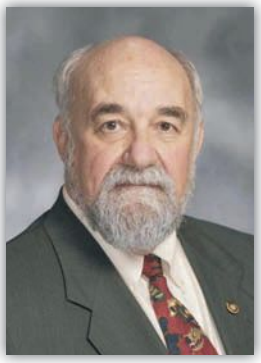
Greet Your Physician Legislators



Senator Bob Onder, MD (R)
State Senate District 2 (St. Charles)

- Hometown: Lake St. Louis
- Specialty: Allergy and Immunology
- MSMA Member since 1992
- Contact: bob.onder@senate.mo.gov

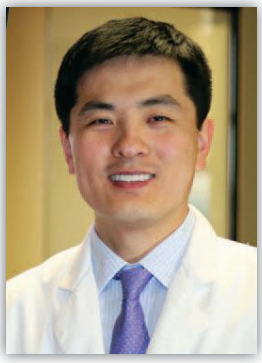
Beginning with his second term as Senator, Dr. Onder has been a tremendous friend to Missouri physicians throughout his tenure in the Senate. Last year, he offered heaps of support while we duked it out with Anthem. Dr. Onder just might end up as the Health Committee chair in 2019, and that would be a great place for an ally like him.



Representative Jim Neely, DO (R)
House District 8 (Cameron)

- Hometown: Cameron
- Specialty: Family Medicine
- MSMA Member since 2013
- Contact: jim.neely@house.mo.gov

Dr. Neely is starting his fourth term and has had a seat on the House Health and Professional Registration committees for several years now. He's consistently been a friend to MSMA and we're excited to have him back for another term.



Representative Elect Jon Patterson, MD (R)
House District 30 (Lee's Summit, Blue Springs, Independence, Unity Village)

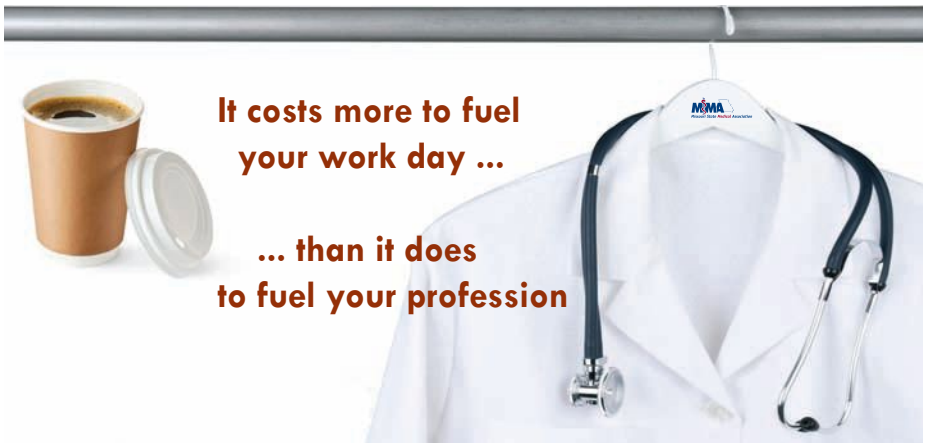
- Hometown: Lee's Summit
- Specialty: General Surgery
- MSMA Member since 2011
- Contact: jon.patterson.md@gmail.com

Dr. Patterson, beginning his first term, is a tireless physician advocate and MSMA is looking forward to working with him on the MSMA agenda in 2019.

opportunity to spend face time with my colleagues. It is my opinion that there are advantages to the physical meeting that are not available in any other way, not the least of which is the ability to receive information in the forms of body language, tonal inflection and a handshake. This contact builds the sense of community with people who share similar challenges and experiences better than other forms.

That same logic persists when it comes to our advocacy efforts in the legislature, so I would entreat each of you to consider a trip to Jefferson City in the role of Physician of the Day during session to make our physical presence familiar to our legislators. MSMA makes this a simple process and the legislators do take notice.

So, whether it is for professional responsibility, fiscal motivation or the desire for a sense of community, please stay or become a member of MSMA and do your best to recruit your peers, all of who would benefit similarly, to become members. Send in your 2019 soon or contact Haley Wansing hwansing@msma.org for a membership application. **MM**







"I think it's essential for early career physicians and residents who are training to be a physician to be involved in their state medical society because it helps connect them with the issues of the state, helps them network, helps them build relationships within their profession, and it helps them serve as a better citizen physician."

- Joanne Loethen, MD
Joined 2016



"One of the biggest benefits I get out of MSMA is feeling like I'm part of a larger group that's doing something to protect our patients and our profession, and we've had a lot of success."

Ramona Behshad, MD
Joined 2012

"MSMA provides a vehicle to capture your concerns, to combine them with other physicians with similar concerns and drive the policy position or policy question that can create change and create a different practice environment."



- Sam Page, MD
Joined 1989

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Despite Distractions, Legislators Look to Address Opioid Crisis

by Jonathan Patterson, MD

In what can only be described as a tumultuous session in the Missouri general assembly, a number of lawmakers have introduced legislation to address an increasingly devastating problem—opioid addiction and deaths due to overdoses. This no doubt reflects the epidemic nature of the problem: opioids resulted in 42,249 deaths in 2016, which represented a five-fold increase in opioid related deaths since 1999.[1] Public health advocates now warn that this is a far-reaching and urgent public health matter. As the abuse of opioids has increased, so too have the rates of heroin abuse, HIV and hepatitis C infection.[2]

Perhaps the simplest solution to help mitigate this crisis would be to reduce the prevalence of opioids in circulation. Analysis of the data clearly demonstrates that the increase in opioid related deaths has directly followed the dramatic increase in prescribing rates.[5] One way in which to achieve this goal would be to foster the growth of "takeback"programs, where individuals can dispose of narcotic pills in their possession.

In early July, the Governor signed Senate Bill 826, sponsored by Sen. David Sater. This law will allow "A Drug Enforcement Agency-authorized collector, in accordance with federal regulations, [to] accept unused controlled substances from ultimate consumers, even if the authorized collector did not originally dispense the drug."[8]. The Drug Enforcement Agency reports that in a similar nationwide program 456 tons of opioid pills were returned in one day.



Jonathan Patterson, MD, MSMA member since 2011, is a private practice general surgeon in Kansas City. He was just elected to the 30th District in the Missouri House of Representatives.
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If reducing opiate use is the goal, then patients must have a realistic understanding and expectation of pain. Interestingly, whether physicians like it or not, patients believe much of the blame lies with physicians. In a recent study, 33% of respondents placed most of the blame on physicians inappropriately prescribing pain killers.[6] Doctor grading websites, measurement of pain scores, and social media pressure physicians to prescribe opiates, lest they be judged harshly for not attending to a patient's pain. Rep. Jim Neely's amendment to SB 826 gives the department of mental health the task of developing a "treatment protocol containing best practice guidelines for the treatment of opioid-dependent patients." Such guidelines would help to establish prescribing norms that could be referenced by providers across the state.

Of course, no discussion about treating the opioid crisis would be complete without addressing a statewide prescription drug monitoring program (PDMP), which has been implemented in all states except for Missouri. Unfortunately, this legislation (House Bill 1619), sponsored by Rep. Holly Rehder, did not pass the general assembly in 2018.

A PDMP would give physicians a powerful tool to prevent addiction before it takes hold by a providing critical, real-time data about the patient's current opioid reserve. Multiple studies have demonstrated that a PDMP does in fact affect prescribing behaviors, especially in the emergency room, where patients are often treated by clinicians with whom they have no prior relationship and where the clinician has little or no information on the patient.[4]

It is for this reason that 33 health care associations (including MSMA) and 11 law enforcement agencies have advocated for a stated-wide PDMP. However, due to a small but entrenched faction of opposition in the general assembly, this legislation has not been able to be passed out of the senate and signed into law. Such delays in enacting this critical piece of legislation will continue to frustrate

practitioners of neighboring states, whose patients travel to Missouri and return home with opioid prescriptions.[4]

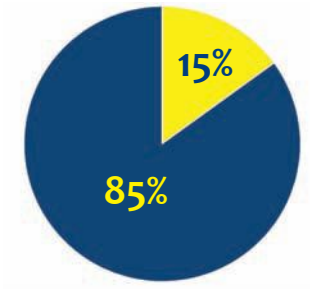
Given the size and scope of the problem, the opioid epidemic cannot be addressed with one or two pieces of legislation alone. It will take a combined effort from clinicians, patients, law enforcement, and lawmakers to make a demonstrable impact on opioid addiction and deaths. However, despite the distractions of this session, many legislators continued to propose reasonable changes that could be the catalyst for reducing the rates of opioid-related deaths. This combination of reducing opioids in circulation, establishing guidelines for the treatment of opioid abuse patients, and the development of a state-wide PDMP would be a very good start.

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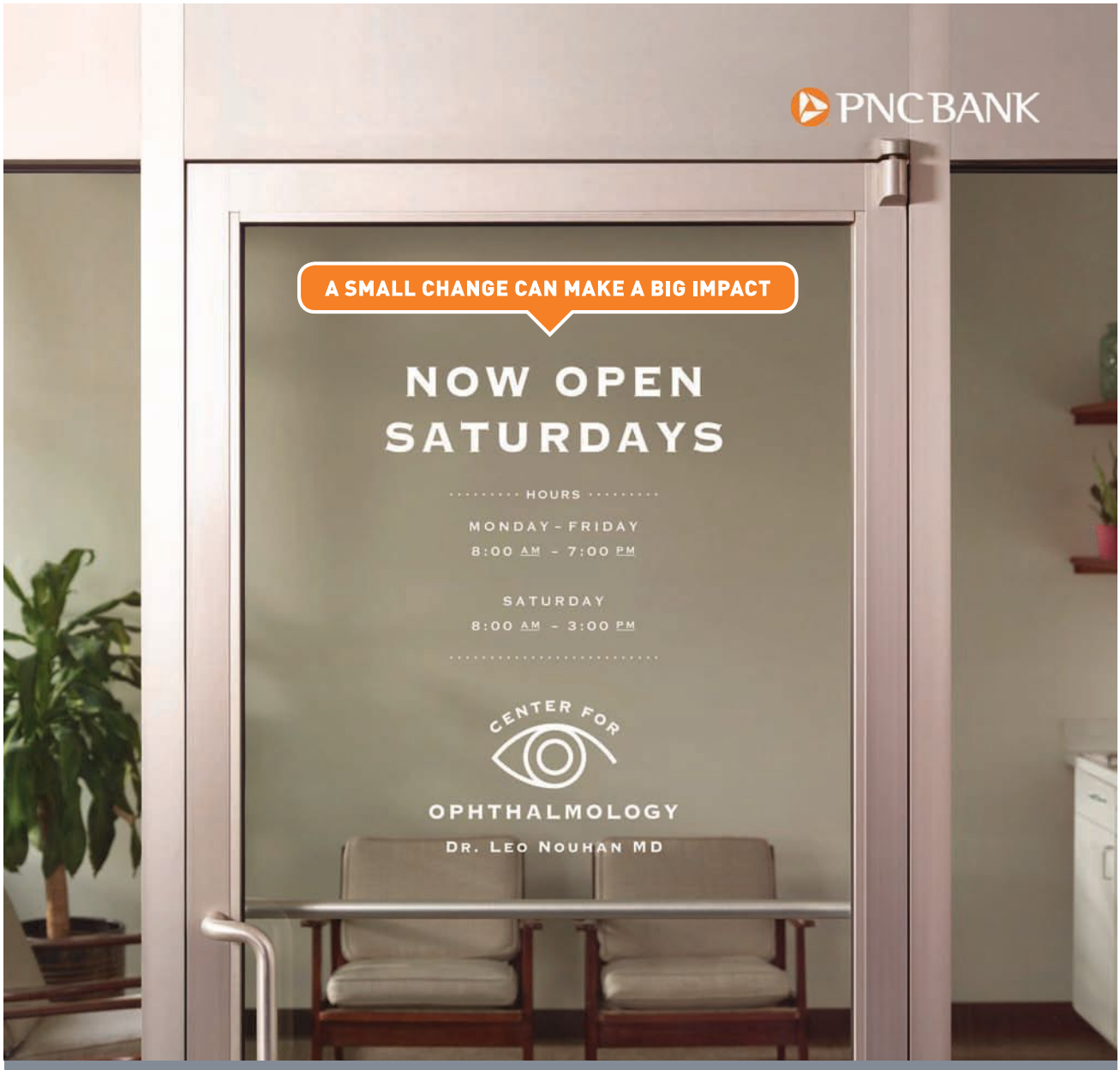
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Physician Advocacy: The AMA Interim Meeting 2018

by the Missouri Delegation to the AMA and compiled by Charles Van Way, III, MD

Each year, the House of Delegates (HOD) of the American Medical Association holds two meetings, an annual meeting in Chicago, in June, and a smaller meeting in November. In 2018, the interim meeting was held in National Harbor, Maryland, a suburb of Washington, DC, November 9-13. This meeting is intended to allow the organization to respond quickly to time-sensitive issues, and is focused on legislation and public advocacy.

The current AMA President, Barbara McAneny, MD, discussed barriers to health care in our dysfunctional system. She cited an example of a health plan denying pain medicine to a cancer patient, resulting in his suicide attempt. Restrictions on the use of opioids often result in their being withheld from patients who need pain relief. Further, reform of prior authorization procedures is currently a major priority for the AMA. Physician burnout has become too common. Electronic Health Records (EHR) are burdensome and the health system itself interferes with health care. Large health care systems are becoming too powerful. The AMA has fought large mergers, winning some and losing some. The increase in drug prices is also interfering with patient care. She summarized by saying that health care runs on our licenses. We have the power and the obligation to change the health care system.



Charles W. Van Way, III, MD, FACS, FCCP, FCCM, MSMA member since 1989, Missouri/AMA Delegate, and *Missouri Medicine* Contributing Editor, is Emeritus Professor of Surgery, University of Missouri - Kansas City.
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Jack Resnick, MD, chair of the Board of Trustees (BOT), discussed the proposed CMS rules to condense codes and cut reimbursement for evaluation and management services. The AMA has negotiated for improvements. Yet, the proposed new rules may still be disruptive.

James Madara, MD, the Chief Executive of the AMA, discussed the role of the AMA in reinventing medical education, improving the health of the nation, and reforming the dysfunctional health care system. The AMA has funded the Accelerating Clinical Education (ACE) in 32 schools. This year, the AMA put up $15 million for grants to reconfigure residency education. He also discussed the AMA's innovation in medical technology. First Mile Care, a spin-off from Health 2047, is focused on improving life style to reduce the development of type 2 diabetes. See www.health47.com. IHMI is a new data model which is designed to include social determinants of care and carry the promise of how clinical data is organized, recorded, and clinically shared. These new models are disruptive, he said, but physicians must be disruptive to repair the system and move forward.

OSMAP, the Organization of State Medical Association Presidents, meets the day before AMA meetings. Its meeting emphasizes current and controversial topics, especially new initiatives from the states. Dr. Gary Price discussed the results of the 2018 physicians survey by the Physicians Foundation, which showed, among other things, some 78% of physicians who responded had symptoms of burnout. Dr. McAneny discussed current AMA activities: sustainability of physician practices, enhancing medical education, and improving health outcomes. She also addressed the workforce shortage and the lack of residency slots and new residency programs. Congress has so far declined to provide funding through Medicare and Medicaid for increasing the number of residency slots. In fact, Congress wants to decrease such finding. We must find new funding sources. Dr. Resnick and Mr. Leonard Nelson, JD, discussed the activities of the Litigation Center, which supports medical-legal issues from local courts to the

Supreme Court. It currently is involved in over 100 cases.

Presentations from the state societies concerned adverse changes in Medicare, tort reform, and rising maternal death rates. Scott Ferguson, MD, reported on the efforts of the Arkansas state legislature, so far unsuccessful, to write tort reform into the state constitution. Mark Thompson and Vince Albanese presented on Delaware's use of blockchain technology to facilitate prior authorization. This technology is in the pilot phase. Nestor Ramirez, MD, from Illinois, reported on rising maternal death rates, both in his state, and nationally. The peak in mortality comes after delivery, with half occurring after 6 weeks. He advocated for "fourth trimester" care. Barbara Love, MD, speaking for the American College of Obstetrics and Gynecology, urged that state medical societies support the Activities for Alliance in Maternal Health. These guidelines emphasize simple measures, such as treatment of hypertension, diabetes, and acute heart failure. Florida reported on their "Healthy Floridians Initiative." This encourages healthy lifestyle with an emphasis on physical activity and good nutrition. The program will be rolled out in four areas in the state, with data collection to measure effectiveness.





MSMA members worked for their colleagues and patients at the national level at the American Medical Association (AMA) Interim Meeting in Washington, DC. Top, Missouri's AMA Delegates, from left, Elie Azrak, MD, St. Louis; Warren Lovinger, MD, Nevada, Mo.; Rebecca Hierholzer, MD, Kansas City; Edmond B Cabbabe MD, St. Louis; and James Conant, MD, St. Joseph. Bottom, Kansas City family physician, Michael O'Dell, MD, highlights resolutions from reference committee C at the Interim Meeting of the AMA House of Delegates.

Moving to the formal meeting of the House of Delegates, the AMA remains highly concerned about the increasing number of deaths secondary to opioid overdose, 60,000 in the last year. A major presentation on methods to deal with this epidemic was given, and several resolutions addressed it as well. But no one has easy answers. A lengthy resolution suggested a number of initiatives which have been found effective in locations around the country. The national push to "blame the doctor first" has slowed somewhat. Opioid use disorder is a chronic disease, and should be treated as such. There was general agreement on combined programs of community-based initiatives, modest legal reform, and pro-active medical treatment of the chronic opioid user will.

Resolutions and reports covered many topics. According to a BOT report, preventive care should not be subject to co-payments or other limitations. A resolution supported data collection on medical student and resident suicide, to try to find ways of preventing these tragedies. Prevention of gun violence was emphasized by several resolutions, which largely reiterated current AMA policy. A report from the Council on Medical Services (CMS) advocated access to certified Canadian pharmacies for personal drug purchases. The HOD added access to all certified foreign pharmacies, not just Canadian. An emergency resolution called for improvement in processes

dealing with sexual and non-sexual harassment within the AMA, and at meetings. This passed overwhelmingly.

There was increased concern over both smoking and "vaping" in children. E-cigarettes have become very popular in middle and high schools across the country. The fashionable e-cigarette marketed as Juul has even created a term, "juuling". The HOD passed a resolution that e-cigarettes should be prohibited for minors. There was discussion of the use of e-cigarettes as an aid to smoking cessation. Most delegates felt it was not very effective, and a resolution promoting it was rejected. A resolution supported banning flavoring agents in cigarettes and e-cigarettes. Since the meeting, the FDA has indeed recommended banning all flavored cigarettes, including menthol, and flavored e-cigarettes.

The HOD discussed migrant children. A resolution called for their proper medical care, opposed their detention, and promoted allowing unaccompanied minors to enter the US. This very political issue was referred to the BOT for further consideration. A resolution supported DALCA, Deferred Action for Legal Childhood Arrival. Many children who arrived legally when their physician parents immigrated with H-4 visas are now in legal limbo after they turn 21, largely because of case backlogs in the immigration system. Many of these individuals are now in medical school. This was also referred to the BOT.

Each meeting, the Board of Trustees (BOT) and several councils report on significant matters, usually in response to resolutions from previous meetings. This year, there were significant reports on physician free speech, violence prevention, methadone clinics, prescription drug monitoring programs, identification of animal-derived ingredients contained in prescription medications, treatment of children born with ambiguous gender identity, primary care workforce, and others. Several reports were sent back to the BOT or council for reconsideration, including competency of senior physicians, use of body-worn cameras by law enforcement, physician-assisted suicide, covering of mammography screening, and others. All of these reports are on the AMA web site, www.ama-assn.org.

There was much discussion over a report on physician-assisted suicide, from the Council on Ethical and Judicial Affairs (CEJA). Proponents introduced the term "aid in dying" as more acceptable than "physician-assisted suicide". This broader term covers some of what we regard as palliative care. Current AMA policy condemns physician-assisted suicide as unethical, regardless of whether or not it is legal in a given state. CEJA recommended against adopting "aid in dying" as a useful description of physician care at the end of life. The report was referred back to CEJA, AMA policy remains unchanged, and there will be an updated report at the 2019 annual meeting. .

In a side session by the Legislative Council, the election was analyzed. Health care was the top winning issue in the election for Democrats, specifically cost, access, and the Affordable Care Act. Medicare for all (and single payer) was an issue in some campaigns, but those who advocated it generally lost. Medicaid expansion was a big issue, including in Kansas and Missouri. Going forward, health policy issues will be ACA fixes, prescription drug prices, and possible MACRA reform. The fee schedule for E/M coding is still in play, although we have staved off the worst possible. Necessary budget cuts will loom over both the "lame duck" session and the next Congress.

Another side session discussed blockchain technology in health care. Blockchain use may enable true personal health records, with patients able to maintain their own health records, and control access to them. Other uses have been proposed, including maintenance of physician credentialing files and supply chain integrity. The technology is promising. But then, we have had a lot of promises from technology in the past. Does anyone else remember when EHR's seemed like a great idea?

Members of the Missouri delegation serve in leadership roles. David Barbe, MD, from Mountain Grove, MO, serves as Immediate Past President of the American Medical Association. Edmond Cabbabe, MD, of St. Louis, serves on the Council for Long Range Planning and Development. Charles Van Way, of Kansas City, MD, serves on the Steering Committee of OSMAP.

Missouri and Kansas are now the only members of the Heart of America (HOA) Caucus. The other two members, Arkansas and Oklahoma, both left to join the Southeast Caucus. For the future, our two states will remain together in the HOA. Rebecca Hierholzer, MD, of Kansas City, announced her retirement from the AMA delegation, after nine years of service.

Your AMA delegation continues to support your interests at the AMA. Keep those e-mails coming! And if you have particular concerns, submit a resolution by February 19 to the MSMA Annual Convention held at the Westin Crown Center in Kansas City on April 5-7. **MM**

Young Physician Leaders Represent MSMA at AMA

by Nita Kohli, MD & Albert Hsu, MD

The Young Physician Section (YPS) of the AMA includes any physicians who are less than 40 years of age or within the first eight years after their terminal residency or fellowship training. The AMA-YPS does not establish internal policy, focusing on resolutions and reports addressed by the full House of Delegates.

At the AMA national meeting at National Harbor, Maryland, AMA-YPS adopted two resolutions to be forwarded to the HOD in June, on peer support groups for second victims and on workplace bullying. The first resolution asked the AMA to encourage local physician wellness programs to develop peer support groups for "second victims" (healthcare providers involved in unanticipated adverse events, medical errors, and/or patient-related injuries). It also asked the AMA to work with others to survey all physicians in the US to quantitate the effects of stress and burnout, and its impact on our physician workforce. The second resolution asks the AMA to work with partners to develop a strategy to eliminate bullying in medical practice. AMA-YPS had an inspiring roundtable discussion on wellness and burnout among young physicians. Finally, a compelling seminar about "Blockchain in Health Care" discussed how blockchain may be useful in pharmacy supply chains and pharmacovigilence, healthcare monitoring and analytics, prior authorizations, billing, integrated AI for improved diagnostic capabilities, enrolling patients into research studies, and empowering patients to manage their own health and medical records.





Albert Hsu, MD, MSMA member since 2017 and Chair of the MSMA Young Physician Section, is a Reproductive Endocrinologist at the Missouri Center for Reproductive Medicine and Fertility in Columbia, Mo. Nita Kohli, MD, MPH, MSMA member since 2018, is the American College of Mohs Surgery representative to AMA-YPS and Dermatology Section Council. She is an Assistant Professor of Dermatology at Washington University, St. Louis, Mo.
Contact: scooberhsu@gmail.com

In the AMA-HOD, there was discussion about the CMS proposal to consolidate payment for E&M services, calling for congressional action before January 1 if CMS moves forward with a proposal to consolidate payment for services in the final physician fee schedule. Another issue was site of service differentials, given the ongoing disparities in Medicare payments for outpatient procedures across care settings. The AMA encouraged CMS to expand reimbursements for procedures performed in the office, to shift procedures from hospitals to more cost-effective office settings, and to have practice expense RVUs reflect the true cost of office procedures. A timely discussion on Veterans Day was had on "Ensuring Quality Health Care for Our Veterans," to ask the AMA to advocate for greater patient access to care for veterans outside the VA, improving the safety and quality of care in the VA, and ensuring recruitment and retention of VA physicians.

Other issues that were addressed by the AMA-HOD include:

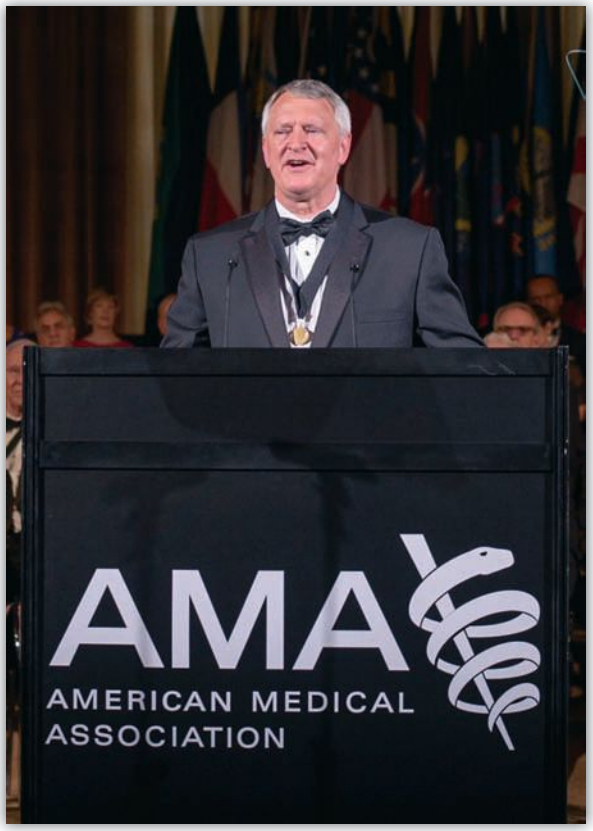
- Development of guidelines for responsible media coverage of mass shootings
- HIV post-exposure prophylaxis to survivors of sexual assault
- Reimbursement for services rendered during physician credentialing
- Prescription drug re-importation from other countries
- Advocacy for seamless interfaces between physicians' electronic health records, pharmacies, and prescription drug monitoring programs
- Opposition to Medicare Part B to Part D changes
- Protecting physician freedom of speech
- Opposition to step therapy in Medicare Advantage plans
- Opposition to mandatory licensing requirements for qualified clinical data registries
- Protection of physician-led medical education

If you or someone you know is a young physician who may be interested in getting involved in the MSMA-YPS and/or AMA-YPS, please contact Stephen Foutes at stephen@msma.org or 800-869-6762 and/or visit the AMA-YPS webpage at www.ama-assn.org/yps-annual-overview. **MM**

A Look Back on an AMA Presidency

by David Barbe, MD

No one, literally no one, not even my mother, could have imagined that when a local physician invited me to take his place as the MSMA 9th District Councilor back in 1987 it would ultimately lead to the presidency of the AMA. What a ride it has been and what a year an AMA presidency is. I was on the road almost 200 days during the year addressing issues that will impact our profession and our patients for years to come, speaking to students, residents, physicians, external audiences, the media and Congress, and representing US physicians to the world medical community. Grueling at times, but every minute of it was an amazing experience.



David O. Barbe, MD, MHA, MSMA member since 1985, is the American Medical Association Immediate Past President and a Family Physician from Mountain Grove, Missouri.
Contact: dbarbe_md@yahoo.com
Reprinted with permission from the Journal of the Greene County Medical Society.

The Issues

I was elected to the AMA Board in June 2009 during the height of the national debate on the Affordable Care Act that was eventually passed and signed into law in March 2010. Although the debate was heated (to say the least), both the AMA House and Board supported policies that would reduce the number of uninsured. The intensity of that issue during my first year was quite an initiation for a freshman member of the AMA Board.

Fast forward to June of 2016 when the AMA House of Delegates gave me the greatest honor of my professional career in selecting me to serve as AMA president. Then what happened? The national debate over healthcare reform was once again front and center in the November 2016 presidential and congressional campaigns. Those elections were immediately followed by efforts to undo the gains made under the Affordable Care Act, thrusting me once again into one of the most passionate and potentially divisive discussions facing our country and the profession of medicine.

As before, the AMA took a principled stand and, as the AMA spokesperson, I traveled the country advocating for maintaining coverage gains and patient protection provisions, protecting the safety net programs of Medicaid and CHIP, and stabilizing the insurance markets. I'm pleased to say that the gains remain mostly intact. However, there is much more to be done to improve affordability and further expand coverage.

During this time, our profession was also making the most significant change in Medicare physician payment in a generation with the AMA led repeal of the SGR and consolidation of the value payment programs into a single Medicare Quality Payment Program including the Medicare Incentive-Based Payment System or MIPS. I gave countless media interviews and live presentations that helped physicians understand how to either be successful in MIPS or how to avoid the penalties for the 2017 and 2018 performance years.

Ongoing efforts to address the opioid epidemic were part of almost every presentation. I am pleased to say that over the past few years, physicians have really stepped up and led the changes that resulted in a 22% decrease in opioid prescriptions, 50,000 physicians certified to prescribe buprenorphine and a leveling off in prescription opioid related deaths. However, with heroin and synthetic opioid related deaths continuing to rise – now

up to 135 deaths per day in the US – we must continue to advocate for broader availability and better coverage of non-opioid pain management and substance use disorder treatment.

Some of the most significant near-term wins are coming in regulatory relief, blocking unfavorable insurance payment proposals, blocking insurance mergers and reducing the prior authorization burden. In one physician audience after another, news of these wins brought encouragement and gave hope to physicians – many of whom had begun to lose sight of the joy in medicine.

In the same way, the AMA's efforts to bring the physicians and innovators together to shape and accelerate development of health care technology that works for physicians and patients and efforts like the AMA's Integrated Health Model Initiative that will bring more actionable information and decision support to physicians are generating excitement among physicians.

Physician burnout – or conversely, trying to restore the joy in medicine – is a high priority of the AMA and was a major point in my messaging to physicians and external audiences. The above initiatives are designed to address some of the underlying causes in the short and long term. However, as importantly, awareness of the extent of the problem and the urgent need to address it is now highly visible and a wide range of stakeholders are beginning to take steps to address the problem.

The above barely scratches the surface of what the AMA is doing for American medicine – and what I've been able to promote during my year as president. I haven't even touched on the AMA's major initiatives around accelerating changes in medical education (and soon to include GME), reducing the burden of chronic diseases such as diabetes and hypertension, addressing the opioid epidemic and gun violence, and the contribution to advancing medical knowledge through the JAMA family of publications. I could go on and on.

The Audiences and the Experiences

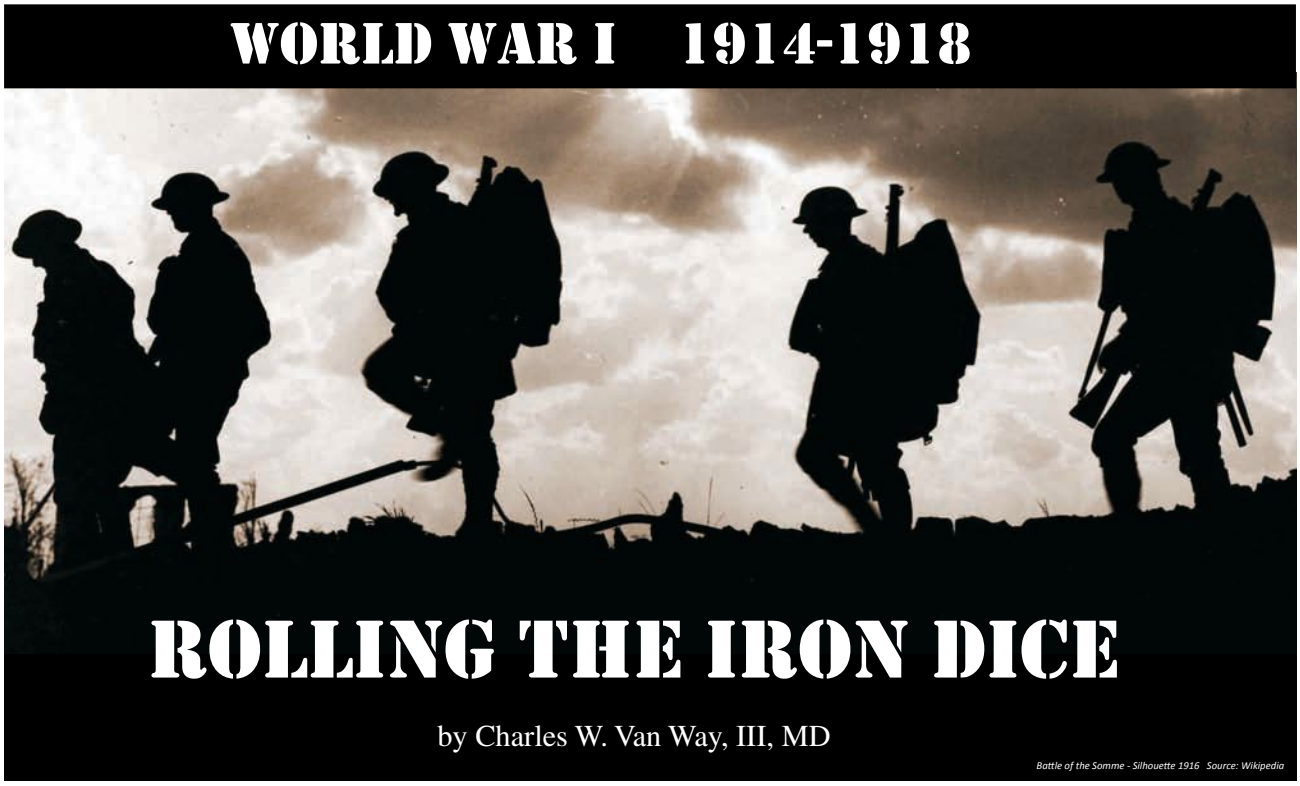
It was immensely gratifying to speak to physician audiences of all sizes and types across the country – from small county societies to small and large state societies and national specialty societies. At the end of every presentation, physicians would invariably come up to me and say, "I didn't have any idea the AMA was doing all that." That made me proud of the AMA and encouraged me to take the message to as many audiences as possible. My favorite audience was medical students. They are eager to learn not only clinical medicine but to learn about our profession, the challenges we face and how they can be involved in addressing those issues. They are also excited when they hear what the AMA is doing to make the practice of medicine better for physicians and patients.

Audiences outside of medicine were very interesting. I made many trips to Washington DC to meet with legislators on both sides of the aisle. The most substantive meetings were with leaders of the committees of jurisdiction and their staffs as they considered payment changes and regulatory relief. I did meet with CMS Administrator Seema Verma and her senior staff. No, I did not ever get summoned to the White House or meet with the President.

I was also impressed with the high regard with which I, as a representative of the AMA, was received by external audiences. I was often treated as a celebrity. One of the more notable experiences occurred at the end of a one-on-one meeting with the world-wide vice president of product development for Samsung. He said "I'd like to get a picture with you. My son is a medical student and he won't believe I met with the president of the AMA." I laughed and responded to him, "I need a picture too. My son is a medical student also, and he won't believe I met with the vice-president of Samsung!"

Epilogue

The breadth, depth and impact of the AMA's activities on behalf of physicians, patients and the health system in this country are nothing short of amazing. To have had the opportunity to lead the oldest, largest and most respected national physician organization was an experience that defies description. Almost any positive superlative that you can think of would apply to this past year. I was at the same time both humbled and extremely honored and found the entire experience exceptionally personally and professionally satisfying. I owe an immense debt of gratitude to you, my physician colleagues, that have mentored, encouraged, supported and worked along with me during my efforts to guide and lead our professional associations – the MSMA and AMA – to be what we need them to be "to promote the art and science of medicine and the betterment of public health." Thank you! **MM**



"If the iron dice must roll, may God help us." *-German Chancellor Theobald von Bethmann-Hollweg, 1914*

November 11, 2018, was the 100th anniversary of the armistice which ended World War I. Of course, until 1939, they called it the Great War, not the First World War. They didn't know that it was just the start of the bloody 20th Century. That November of 1918, there was great celebration across the world. Armistice Day became a national holiday, here and in many other countries. We celebrate it to this day, although we've changed the name to Veterans' Day.



Charles W. Van Way, III, MD, FACS, FCCP, FCCM, MSMA member since 1989, Missouri/AMA Delegate, *Missouri Medicine* Contributing Editor, Emeritus Professor of Surgery, University of Missouri - Kansas City, retired U.S. Medical Corps, Army Reserve Colonel.
Contact: cvanway@kc.rr.com
Co-published with Kansas City Medicine.

It was a brutal war. All across Europe, a third of a generation of young men died, killed by one another or dead from disease. In the now-hackneyed phrase, it changed everything. It ended the *Pax Britannica*, 100 years of world peace. Well, sort of peace, anyway. Except for the American Civil War. And the Crimean war. And others. It ended four empires – Russian, German, Austro Hungarian, and Ottoman. It was the beginning of the end for the French and British empires. Across Europe, it ended government by aristocracy. Lastly, the peace treaties completely re-drew the map of Europe, much as we know it today. They failed utterly to resolve the causes of war. As soon as a new generation of young men reached military age, 20 years later, Europe plunged back into a worse war. Or, as Churchill and others have called it, the 30 Years War of the 20th Century. It was even more destructive than the 30 Years War of 1618 to 1648, which devastated central Europe.

The Great War ushered in the Great Influenza Epidemic, which killed literally countless people around the world in 1918-19. Initial estimates were 20 to 30 million. Currently, historians think that 50 to 100 million

died. No one is sure, save that the number was very large. More people died of the epidemic than from the Great War itself. Ever since, epidemiologists have worried that it could happen again. True, medical treatment of pneumonia and of pulmonary failure has greatly improved. The conditions at the end of the Great War may be unlikely to recur. But the worry of another great flu epidemic is always with us.

And so is the fear of another Great War. World War III. Could it happen again? In the years before the war, a British author, Norman Angell, wrote *The Great Illusion* (1910). He argued that war among the great European powers was unlikely. His reasoning was that the economies of Europe were highly interdependent. War would be catastrophic. No national leaders would take their countries into war. He was, as we know now, half right. It was indeed catastrophic.

But at the outbreak of war, both national leaders and the people they led went into war enthusiastically. Even intellectuals wanted war. To paraphrase a sentiment attributed to the great German socialist writer Thomas Mann, "War would be a purifier, a great hope." In 1914, 93 of Germany's leading intellectuals, artists, and writers signed a manifesto supporting and justifying the war. And the militarists, who were strongly for the war, were typified by Colmar Freiherr von der Goltz, a German general and military writer, who wrote, "a long and bitter war was necessary for the sake of Germany's health." In August, 1914, large crowds gathered in Berlin, Austria, and other cities of the German and Austro-Hungarian empires to celebrate the beginning of the war.



The Meuse-Argonne Offensive, fought from September 26, 1918 until the Armistice of November 11, 1918, a total of 47 days.
Source: Wikipedia

Perhaps the French and British were less enthusiastic than the Germans? But there were demonstrations in support of war in London, Paris, and many other cities. This may have been simply patriotic fervor. Still, the British dived into war with enthusiasm. They had no compelling reason to go to war, only a vague conviction that Germany would be an uneasy neighbor across the English Channel and a desire to protect "Brave Little Belgium," based on a 75-year-old treaty obligation. Belgium, it should be noted, was internationally notorious for having made the Belgian Congo into a living hell over the previous 30 years. Yet, British popular support for the war was so great that until 1916, the British army of millions was made up entirely of volunteers, both from the British Isles and from the entire British Empire.

France had been spoiling for revenge ever since their humiliating loss in the Franco-Prussian war of 1870-71. Their war plans envisioned attacking the Germans south of Verdun, to regain the lost territories of Alsace and Lorraine. Defense was not a priority. Popular support for the war was universal. Even the Socialists, just as in Germany, abandoned their pre-war pacifism to support the war. Indeed, Clemenceau, Prime Minister in the latter part of the war, was a pre-war socialist.

So, could it happen again? After the Cold War, Frances Fukuyama wrote *The End of History and the Last Man* (1992). He contended that we now lived in a world dominated by liberal democracies, which would never make war on one another. At the time, this view was immensely popular. A quarter-century later it seems both naïve and irrelevant. The spread of democracy has become a retreat, and a third of the world is governed by autocracies.

We lived from 1945 to 1990 under the nuclear shadow of the Cold War. Through a combination of



Wounded Soldier Receiving Initial Care on the Battlefield (110th Infantry Regiment).
Source: www.worldwar1centennial.org

good judgement and luck, the world avoided World War III. Since the fall of the USSR, we've now had nearly 30 years of peace. OK, relative peace. Somewhere in the world, people have been killing one another pretty much constantly. But we've avoided a general conflagration. So far.

The unending wars of the Middle East look uncomfortably like the wars in the Balkans which preceded the First World War. Otto Bismarck said in 1888, "One day the great European War will come out of some damned foolish thing in the Balkans." Will the next world war come out of some equally foolish thing in the Middle East?

The most discouraging aspect of international affairs today is that no one really believes that a World War could happen again. Now, I came of age during the Vietnam War. Even at the height of that conflict, everyone knew that the greatest risk was escalation to a world conflict. And for all the misery of that war, it was successfully contained. But there was no doubt about that risk. One presidential campaign, in 1964, was heavily influenced by a video of a child followed by a mushroom cloud. No narration, no captions. Everyone knew, or thought they knew, that one candidate seemed more likely than the other to escalate the Cold War. Unfortunately, the winner went on to escalate the Vietnam War. But we didn't get Armageddon.

Do we have the same awareness today, of impending catastrophe? It's a generation after the end of the Cold War. No doubt that our political leaders, many of whom are over 60, remember the risk. But there is little evidence today that they are paying any attention. Other countries play with fire, with little apparent understanding that they might touch off a conflagration. We speak of the North Atlantic Treaty Organization (NATO) as if it were some kind of optional alliance. It is not. It was and is a guarantee that we would deter aggression, in order to prevent a general war. The United Nations seems to be fanning the embers rather than dousing the flames. Leaders of the European Union appear oblivious, squabbling over Brexit, bouncing among issues from immigration, to finance, to populism. And the US? Without descending to partisan politics, are there any adults left in Washington? Amidst the partisan squabbles, there seems little recognition that we live in a very dangerous world, and at a critical time.

Could the iron dice roll once again? Twice in the last 100 years, they have rolled across the world. No one wants a third world catastrophe. Yet, the danger is that someone will risk too much, not understanding the dangers. On the eve of the Great War, all sides were convinced that it would be a short war, decided by one or two big battles. "Over by Christmas," they said in August. Today, our military leaders, at least, know better. And so far, the 21st Century has been one of small, limited wars, involving the great powers only minimally. But the US has tens of thousands of troops in combat. More than that, some 450,000 are deployed overseas. The world is awash with conventional weapons, with poison gas and the atomic bomb available to too many countries. Some world leaders threaten others, in apocalyptic terms, and seem unaware of the risk. Nobody has pushed too far. Yet.

MM

A Meta Strada Li... "Halfway There"

by Joseph A. Corrado, MD

After my last posting, my wife, Donna, and I were cordially invited to attend the Kansas Medical Society Annual Meeting, joining their new president Dr. Robert Gibbs. Their reception and dinner was an opportunity to meet with the KMS Board of Trustees, and AMA president-elect, Dr. Patrice Harris, in a small group setting in the Topeka Country Club. A good time was had by all.

On Saturday, we went to the meeting which was held at their Kansas Medical Society Office in Topeka, which was quite an eye opener for me. They now have a new single day meeting format to accommodate the busy physicans' schedules, and have a wonderful space for their meetings. The key note speaker was Sam Quinones who spoke a few years ago at our own MSMA Annual Convention. He is a former *LA Times* reporter and author of *Dreamland*, the true tale of America's opiate epidemic, chronicling the opiate crisis in a small Ohio town, and how that town came together to address dependency and work toward economic and social revitalization. This was followed by Dr. Harris who currently chairs the AMA's opioid task force. They have released six key recommendations designed to better equip physicians as we seek to reduce opioid misuse within our own communities.

I met with the MSMA Alliance members at their Fall Conference after they had heard information and panel discussions on opioid rehabilitation at Westminster College. I joined them for dinner at the Buckshot Saloon in Kingdom City, and thanked them again for the important role they play in working with us.

Meeting again at the MSMA Council in Jefferson City I relayed the news that "SSM-mid Missouri" (consisting of Jefferson City and Mexico) were in a non-binding contract to be acquired by the University of Missouri Health System, which will certainly change the landscape of medicine in the middle of the state.



At the Kansas Medical Society Annual Meeting with, from left, Sam Quinones, Drs. Corrado, Robert Gibbs, Patrice Harris, and Jean Hausheer.

While attending the American College of Surgeon's Clinical Congress in Boston, I met with several AMA delegates. We all anticipated the upcoming Interim meeting.

Earlier this month I met with our colleagues in Pettis County at the 7:00 a.m. staff meeting of the Bothwell Regional Health Center in Sedalia. Greeted there by Drs. Stuart Braverman and David Kuhlmann and more solo practice dinosaurs, MSMA's Jeff Howell spoke convincingly of MSMA's patient and physician advocacy, and how much was accomplished this last year alone. Made ME want to join!

Mid-November was spent as part of the Missouri delegation to the AMA Interim meeting in Washington DC. Along with Kansas, which makes up the new, smaller Heart of America Caucus. We were challenged with many concerns affecting the House of Medicine. It gave me great pride to see physicians from all over the United States of America, no matter what specialty or political persuasion come together and tackle the multitude of problems we now face, from medical education reform to reimbursement issues almost always getting a consensus. Who said you can't herd cats? Again, reaffirming the necessity of organized medicine.

We have so much to appreciate during this season. I look forward in seeing you at your holiday county celebrations! Ciao for now! **MM**



Joseph A. Corrado, MD, FACS, a surgeon from Mexico, Mo., and MSMA member since 1982, is MSMA President for 2018-2019.
Contact: bigdocjoe@sbcglobal.net

MSMA Alliance Full Court Press Against Opioids

by Gillian Waltman

Your MSMA Alliance has been educating and encouraging physicians and communities about the sweeping opioid epidemic. At our October Fall Conference, we hosted several excellent speakers on the topic.

Held at Westminster College in Fulton, we received a warm welcome from Dr. David Roebuck, the Dean of Academic Affairs, who was excited to welcome the Alliance. He shared some personal background on his interest in opiate abuse About a dozen undergraduate students were invited to participate in the program as well.

Two different sessions comprised our afternoon presentations: *Identifying the Challenges Facing Missouri's Criminal Justice System* and *The Addiction Epidemic: A Community Problem with a Community Solution*. Invited speaker Isaac Amon, JD, LLM, is an adjunct professor at Washington University Law School. Until recently he worked as Director of Legislative and Constituent Services at the Missouri Department of Corrections (DOC) in Jefferson City, but was unable to attend. Two of his former colleagues from the Re-Entry program at the Director Ken Chapman and former parole officer Danielle Bellamy spoke on the difficulties facing individuals re-entering society after being both convicted and addicted. The speaker for the second session, Lauren Zehnle, MA, LPC, is a licensed professional counselor who runs a private practice for addiction counseling in St. Louis. MSMA Alliance Health VP Kelly O'Leary joined the three speakers for an animated panel discussion with great audience interaction, especially from the students. Donna Corrado did an excellent job as my appointed conference coordinator.

The guide for our private tour of the Marylebone Church and Churchill Museum following the program was well-versed in British history and it was an informative and worthwhile visit. MSMA President Joe Corrado, MD, joined us for dinner and gave us an update on what he has learned from his visits to medical societies within Missouri and all its contiguous states.

Alliance Presents Check to Physicians Health Program, which helps physicians with substance abuse.



From left, Alliance immediate past president Marsha Conant presents a check for $1,000 to Lisa Thomas, MD, Medical Director of Missouri Physicians Health Program at a recent MSMA Council Meeting. Gill Waltman announced that the check represented donations made at the end of Marsha's term as president, in honor of her service in 2017-2018.



Gillian Waltman is the 2018-2019 MSMA Alliance President and Professor, Ophthalmology, Saint Louis University, St. Louis, Missouri.
Contact: gillian.waltman@gmail.com

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The Alliance board meeting was held at the hotel the following morning. Pertinent board issues discussed were the disbanding of the Boone Medical Society Alliance and the concept of creating a new Alliance by reviving three now defunct mid-state Alliances.

Members and their spouses have been generous with their donations to the Alliance Holiday Sharing Card to support the Missouri State Medical Foundation and the AMA Foundation. Donors' names will be published in the upcoming issues of *Missouri Medicine*, *Show Me Alliance News*, and on the MSMA website.

The Alliance Day at the Legislature will be held February 19-20, 2019, in Jefferson City. Our Legislative Vice President Kirk Doan is the organizer. Our winter board meeting will be held the following day.

The Alliance Annual Meeting will be held in conjunction with the MSMA Annual Convention in Kansas City at the Westin Crown Center on April 5-7. Please mark your calendars for the Alliance Foundation Fundraiser Dinner to be held on Friday, April 5. In honor of my heritage, and also my (Monty Python) theme for this year "Look on the Bright Side," it is called "The British Invasion!" Kathy Weigand is chairing the event.

We are also holding a Cabi Fashion Show (another small fundraiser) after dinner on Thursday night. This was very popular last year at convention. Proceeds from both events will benefit the MSM Foundation. **MM**

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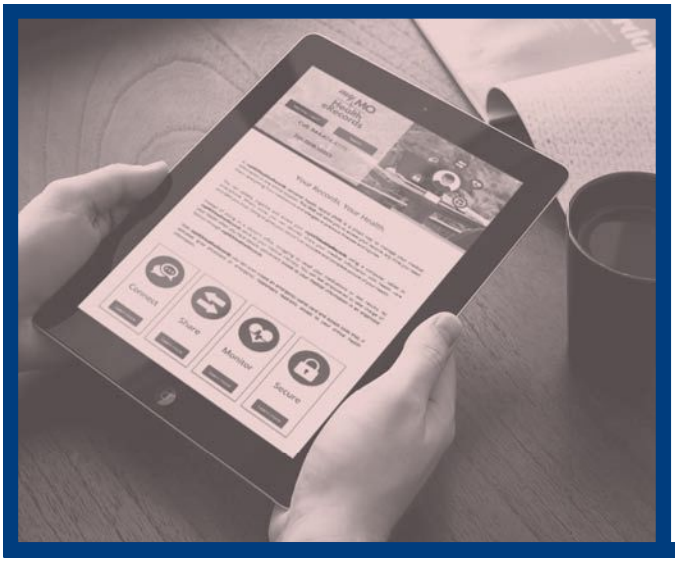
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Missouri Medicine in the News

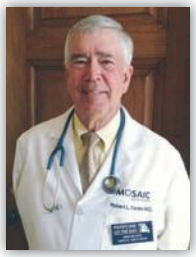
Did you make the news? Submit your success story and photo to hwansing@msma.org.

Missouri Medicine would like to publicly thank the following retiring Editorial Board members for their years of service: Mitch Botney, MD, Pulmonary Medicine-11 years; Juan Corvalan, MD, Psychiatry-20 years; Roger Jackson, MD, Orthopedics-13 years, and Charles Lederer, MD, Ophthalmology-17 years. Dr. Corvalan has been appointed the new Retired Physicians Representative on the Editorial Board.

Missouri Medicine would like to publicly thank the following non-Editorial Board experts who have done peer-review of submitted manuscripts in 2018: Charles Lederer, MD, Quinn L. Johnson, MD, Joseph Craft, MD, Alan R. Erickson, MD, William V. Stoecker, MD, Richard Griffey, MD, Scott Wingerter, MD, Alan R. Erickson, MD Scott Lucchese, MD, Robert D. Hall, PhD, JD, and Pradeep C. Bollu, MD.



John Collins, MD, and Sol Dubin, MD, have joined the team at Lafayette Regional Health Center. MSMA wishes both of you all the best. Your support as members of MSMA for a combined total of 82 years is immensely appreciated!



An MSMA member since 1977 and tireless advocate for organized medicine, Robert Corder, MD, is teaming up with The Center in downtown St. Joseph to provide treatment to pregnant women battling drug addiction. Though recently retired, Dr. Corder said his previous experience as an obstetrician, along with a desire to help his community, inspired his decision to practice once again.



Congratulations to David H. Perlmutter, MD, Dean of the Washington University School of Medicine and an MSMA member since 2016, for being named the Inaugural George and Carol Bauer Dean. He also is the Spencer T. and Ann W. Olin Distinguished Professor and Executive Vice Chancellor for Medical Affairs.



James Wirkkula, DO, an MSMA member since 2016, has re-joined the team at Bates County Memorial Hospital as a family medicine physician. Congratulations to you, Dr. Wirkkula.



William White, MD, (above, center), MSMA member since 1995 and MOSEPS member was awarded 2018 American Academy of Ophthalmology's Outstanding Humanitarian Service Award in a special ceremony in Chicago Illinois, October 2018. Dr. White organized and supervises numerous medical missions to Northern Haiti, the rudimentary hospital he helped build and equip is the only one of its kind in that large region of Haiti.



Congratulations to longtime MSMA member since 1996 Rick W. Wright, MD, the Jerome J. Gilden Distinguished Professor of Orthopaedic Surgery at Washington University School of Medicine in St. Louis on being named president-elect of the American Board of Orthopaedic Surgery.

Did you make the news? Submit your success story and photo to hwansing@msma.org.

MM

Correspondence

More Thoughts on Value of USPSTF Recommendations

Bravo to John C. Hagan, III, MD for his editorial in the July/August 2018 issue of *Missouri Medicine* regarding the USPSTF. They have also messed up the pap smear guidelines, all in an effort to save money, not to give excellent health care.

William Houck, MD, Obstetrics & Gynecology, Chesterfield, Missouri, MSMA Member since 1985

USPSTF: Skin Cancer Screening Recommendations

We read with great interest your editorial concerning the US Preventive Services Taskforce (USPSTF) skin cancer screening guidelines in the July/August 2018 issue of *Missouri Medicine*[1]. You emphasized the importance of visual skin cancer screening as a life-saving approach in the context of the controversial USPSTF recommendations.

We share your concerns regarding the USPSTF conclusion that current evidence on benefits of early detection and treatment of skin cancer is inadequate[2]. Melanoma five-year survival depends on the stage of the disease: over 98% for stage I, and only 18% for stage IV disease.[4, 5] This strongly suggests that in early stages, melanoma is a highly treatable condition. Most melanoma deaths might be prevented by total body skin cancer examination to identify early-stage melanomas, before they develop into an advanced life-threatening stage.[5] Skin is one of the only organs that can be safely inspected without any invasive procedures: visual skin cancer screenings are not only safe and easy, but among the most cost-effective medical tests.[5]

We agree that visual skin screening by a "clinician" for the "general population" may lead to misdiagnosis and overdiagnosis, among other possible harms.[2] We should therefore apply the data-driven screening guidelines that suggest benefit from targeting high-risk populations (based on age, personal and family history, physical features, and UV exposure), highly vulnerable to a delay in melanoma skin screening and diagnosis.[5] In addition, a "clinician" with less specialty dermatologic training may likely contribute to the mis- and overdiagnosing phenomenon; however, a specialty trained clinician is in a perfect position to detect and diagnose skin malignancies by routine visual examination.[5, 6]

There are well-documented reasons why randomized controlled trials of visual skin cancer screening in high-risk patients may not be possible. We respect and appreciate the invaluable work done by the USPSTF regarding disease prevention and preventive services. However, we strongly encourage the USPSTF to take into consideration input from experts in the field before making final recommendations.

Mirna Becevic, PhD, Show-Me ECHO Missouri Telehealth Network, University of Missouri, Columbia, Missouri. Jonathan Dyer, MD, Pediatric Dermatology, MSMA Member since 2006 and Karen Edison, MD, Dermatolgical Cancer/Disease, MSMA Member since 1991 at the University of Missouri Department of Dermatology Columbia, Missouri

1. J. Hagan III, "USPSTF: Quit Clowning Around with Our Health!," Missouri Medicine, July/August 2018 2018.
2. Force US Preventive Services Task, "Screening for Cancer: US Preventive Services Task Force Recommendation Statement," JAMA, vol. 316, no. 4, pp. 429-435, 2016.
3. American Academy of Dermatology, "Skin cancer," 2018. [Online]. Available: https://www.aad.org/media/stats/conditions/skin-cancer. [Accessed 12 September 2018].
4. M. Johnson, S. Leachman, L. Aspinwall, L. Cranmer, C. Curiel-Lewandrowski, V. Sondak, C. Stemwendel, S. Swetter, j. Vetto, T. Bowles, V. Dellavalle, L. Geskin, D. Grossman, K. Grossman, J. Hawkes, J. Jeter, C. Kim, J. Kirkwood, A. Mangold, F. Meysken, M. Ming, K. Nelson, M. Piepkorn, B. Pollack, J. Robinson, A. Sober, S. Trotter, S. Venna, S. Agarwala, R. Alani, B. Averbook, A. Bar, M. Becevic, N. Box, W. Carson, P. Cassidy, S. Chen, E. Chu, D. Ellis, L. Ferris, D. Fisher, K. Kendra, D. Lawson, P. Leming, K. Margolin, S. Markovic, M. Martini, D. Miller, D. Sahni, W. Sharfman, J. Stein, A. Stratigos, A. Tarhini, M. Taylor, O. Wisco and M. Wong, "Skin Cancer Screening: Recommendations for Data-Driven Screening Guidelines and a review of the US Preventive Services Task Force Controversy," Melanoma Management, vol. 4, no. 1, pp. 13-37, 2017.
5. N. Fleming, M. Grade and E. Bendavid, "Impact of Primary Care Provider Density on Detection and Diagnosis of Cutaneous Melanoma," PLOS One, vol. 13, no. 7, 2018.
6. American Cancer Society, "Survival Rates for Melanoma Skin Cancer, by Stage," 20 May 2016.

Clarification

The University of Missouri, The University of Missouri-Columbia School of Medicine and all of its departments did not take any position for or against the medical marijuana referenda in the Missouri November general elections. Any suggestion that the September/October 2018 *Missouri Medicine* cover implied an MU endorsement is erroneous.

Errata

Regarding May/June 115:3 2018, Pancreatic Adenocarcinoma by Ashley A. Vareedayah, MD, Samer Alkaade, MD & Jason R. Taylor, MD, page 230; should read, "The overall one- and five-year survival rates are 24% and 6% respectively." Page 235 first bullet, should read survival instead of mortality. **MM**

Missouri State Medical Association

161st Annual Convention

April 5-7, 2019 / Westin Kansas City at Crown Center
www.msma.org/annual-convention

PRELIMINARY PROGRAM

Pre-Convention Meetings

Thursday, April 4

2:30 pm	MSMA Insurance Agency Board Meeting
3:30 pm	MSMA Executive Committee
3:30-6:00 pm	Convention Registration
3:30-6:00 pm	Exhibitor Setup & Registration
5:00 pm	**MSMA Council Meeting**
6:30 pm	Alliance Dutch Treat Dinner
6:30 pm	**MSMA Council Reception & Dinner**

Convention Meetings

Friday, April 5

6:30 am-4:00 pm	Convention Registration
6:45 am	Moneta Group Investment Advisors Breakfast
7:00 am	**Exhibit Hall Opens/Continental Breakfast for all Conferees**
8:00 am	**Opening Session MSMA House of Delegates**
8:30 am	Alliance Board Meeting
10:00 am	Alliance General Assembly - Session I
10:00 am	**Reference Committee A**
10:30 am	**Reference Committee B**
11:00 am	Missouri Physicians Health Luncheon & Meeting
11:30 am	"Spirit of the Alliance" Awards Luncheon
Noon	SLMMS Caucus & Luncheon
Noon	KCMS Caucus & Luncheon
1:30 pm	**MSMA General Session**
3:30 pm	**MSMA General Session**
4:30 pm	Alliance Past President's Reception
5:00 pm	Organized Medical Staff Section Business Meeting
5:00 pm	Medical Student Section Business Meeting
5:30 pm	Medical School Alumni Receptions
7:00 pm	Alliance Foundation Fundraiser/Dinner
7:00 pm	Resident and Medical Student Mixer

Program subject to Change. Refer to Convention Official Program for times and meeting locations. For more information, contact MSMA's Benita Stennis, at 800-869-6762 or bstennis@msma.org.

Saturday, April 6

6:30 am-4:00 pm	Convention Registration
7:00 am	**Exhibit Hall Opens/Continental Breakfast for all Conferees**
All Day	CME Programs, Lectures & Meal Functions
7:00 am	International Medical Graduate Section Meeting
8:00 am	**MSMA General Session**
8:30 am	Alliance General Assembly - Session II
10:00 am	**MSMA General Session**
10:00 am	MMPAC Meeting
10:15 am	Resident and Fellow Section Business Meeting
10:30 am	Exhibit Hall Closes
10:45 am	Young Physician Section Business Meeting
11:15 am	Resident and Fellow Section/ Young Physicians Section/ Medical Student Section Program
Noon	SHINE of Missouri Product Theater
12:30 pm	Alliance Installation Luncheon
1:00 pm	AMA Issues
1:30 pm	**MSMA General Session**
2:30 pm	Missouri State Medical Foundation Meeting
2:30 pm	Alliance Board Meeting
3:00 pm	Component/Specialty Society Leaders Meeting
3:30 pm	OMSS Educational Session
5:15 pm	Reception: 50-Year Pin Recipients & MSMA Past Presidents
6:30 pm	**MSMA Presidential Inauguration**
7:30 pm	**MSMA Presidential Reception** *Entertainment, Hors d'oeuvres & Cash Bar*

Sunday, April 7

7:00 am	District Breakfasts & Caucuses
8:15 am	**Second MSMA House of Delegates**
Immediately Following Closure of the HOD	MSMA Council Meeting

www.msma.org/annual-convention

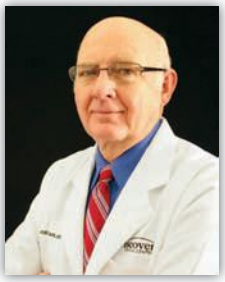
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Missouri State Medical Association

161st Annual Convention

April 5-7, 2019 / Westin Kansas City at Crown Center
www.msma.org/annual-convention

General Sessions



Friday, April 5 | 1:30 pm

The Science of Near-Death Experiences

John C. Hagan, III, MD
Editor, *Missouri Medicine*
Ophthalmologist
Kansas City, Missouri

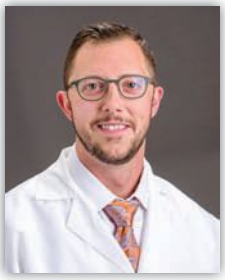


Friday, April 5 | 3:30 pm

Gen Nation: Making Sense of Generational Differences in the Workplace and Beyond*

Michael Wood, Co-Founder
747 Insights
Des Moines, Iowa

*No ABIM/MOC Points offered for this session



Saturday, April 6 | 8:00 am

Non-Opioid Pain Medicine (The Other Pills Used to Cure the Ills)

Nicholas Madaffer, MD
Assistant Professor
Physical Medicine & Rehabilitation
University of Missouri
Columbia, Missouri



Saturday, April 6 | 10:00 am

Alcoholics in the Hospital: Patients, Not Staff

Joan Shaffer, MD
Adult Intensivist
Mercy St. Louis
St. Louis, Missouri



Saturday, April 6 | 1:30 pm

Physician Suicide: The Silent Epidemic

Amanda Kingston, MD
Assistant Professor
Psychiatry
University of Missouri
Columbia, Missouri



Saturday, April 6 | 3:30 pm

OMSS PRESENTATION
Data & Leverage in Physician Employment Negotiations

Kyle Claussen, Vice President
Resolve Physician Agency
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Answering the Call: A Prospective Look at the Role of Timolol Eye Drops in the Treatment of Acute Migraine Attacks

by Sean Gratton, MD & Matthew Cossack, MD

We believe our work advances the notion that timolol eye drops are a safe, effective, and already widely available abortive treatment in select migraineurs.

The July/August 2014 issue *of Missouri Medicine* featured several articles about the use of beta blocker eye drops to treat migraine attacks.[1,2] These articles included a call for prospective studies to further investigate the effectiveness of these well-tolerated, affordable drugs in migraine. Answering the call put forth by John C. Hagan, III, MD and others, we performed a clinical trial, which was recently published in *JAMA Neurology* entitled "*Timolol eyedrops in the treatment of acute migraine attacks.*"[3] Our research helps to support the anecdotal experiences of Doctor Hagan, Carl V. Migliazzo, MD and others published in *Missouri Medicine*, and advances the argument that timolol eye drops are beneficial to some migraine sufferers.

We completed a randomized, placebo-controlled, single-blinded crossover study, which allowed for participants to serve as their own controls. Each subject was randomized to begin either with timolol maleate 0.5% or artificial tears drops. Subjects were seen monthly for four months, and each individual crossed over to the second drop at the two month halfway point after a three day washout period. The subjects were instructed to instill one drop into both eyes at the onset of migraine headache and thirty minutes later if needed. Subjects were asked to complete a headache evaluation sheet for each migraine attack suffered during the study period. The headache evaluation sheet tracked a number of different variables including migraine attack severity over time on a scale of zero to three. At the conclusion of the study prior to unmasking, subjects were asked to rate the effectiveness of each drop on a scale of one to four as well as which drop they preferred overall.

A total of 198 migraine attacks were studied among ten subjects. The subject-rated overall effectiveness of timolol was 2.4 compared to 1.4 with placebo. Four subjects found timolol highly effective compared to placebo while one subject found the opposite. 78% of migraines had a severity of none or mild at two hours on timolol compared to 57% with placebo. Several participants responded extremely well to the timolol, though we were unable to identify any factors that would predict responsiveness. Notably, one patient found such benefit from the artificial tear arm that she wished to replace her migraine medications with the artificial tear drops. There is a relatively high number of placebo responders in migraine patients.

Several factors were taken into consideration when determining how to best carry out this study. Patient





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safety was the number one priority, and for that reason we felt it was important not to deviate significantly from the established dosing of timolol maleate (one drop into the affected eye once a day in the morning).[4] To deviate substantially from the recommended dosing could, at least theoretically, put patients at higher risk of adverse events than would be expected after years of timolol maleate use for glaucoma. Additionally, doing so would have been a significant hurdle during our Institutional Review Board review, and may have required an Investigational New Drug Application (IND) to the Food and Drug Administration, which would have added substantially to the administrative and financial cost of the study.[5] It is possible that these decisions influenced the study results. For example, one might ask whether the effect of timolol would be more robust with a more aggressive dosing regimen (e.g. two drops into both eyes then repeated after ten minutes as a standard protocol). But for the reasons stated above we felt that a more aggressive dosing regimen was not appropriate.

When constructing the overall structure of the study, we used prior migraine abortive medication studies as a model. Specifically, we looked at triptan medications that do not utilize simple oral administration such as sumatriptan nasal spray and rizatriptan rapidly disintegrating tablet.[6,7] These studies were helpful in determining how best to instruct patients to use the timolol eye drops and in determining the best, well-validated, and widely recognized outcome measures for migraine attack assessment.

We note three significant limiting factors in our study: (1) lack of investigator blinding, (2) an imperfect placebo—as artificial tears tend to cause less of a burning sensation than timolol, and (3) a small sample size. The small sample size resulted from the unfunded nature of the study and difficulty recruiting without patient reimbursement. Despite these limitations, this pilot study allowed us to quantify the effect size to allow for power calculations. A future crossover study will require 86 patients to power a study with $\alpha \leq 0.05$ and $\beta \leq 0.2$.

Timolol eye drops provide an ideal and rapid route of delivery which avoids first pass metabolism and also achieves maximum plasma concentration within 15 minutes of administration.[2, 8] This pharmacokinetic advantage may not be ideal for chronic problems like glaucoma but is well-suited for the abortive treatment of migraines.[9] A reviewer from *JAMA Neurology* was initially concerned that the dose of timolol could alter systemic beta adrenergic receptor regulation. Timolol 0.5% is 5mg/ml and a maximum of 200 ul or 0.2 ml are absorbed with two bilateral sets of 50ul drops. That comes to a total of 1mg of timolol, in contrast to the dose for oral timolol, which is 10-30mg daily. We therefore do not believe the 0.4 to 1 mg of timolol given on a prior day influenced later migraines. Furthermore, the half-life of timolol ophthalmic is 4 hours. Thus 6 half-lives pass from day to day. We do not anticipate the small dose of 0.4 to 1 mg given inconsistently as an abortive treatment would have clinical significant effects on beta blocker receptor regulation.

Consistent with the relatively small systemic dose, there were no adverse systemic symptoms including hypotension or bradycardia reported in our study. One patient suffered a branch retinal artery occlusion while on placebo, which was thought to be unrelated to the study.

We are pleased to have published this work, and owe a debt of gratitude to Doctors Hagan and Migliazzo, and *Missouri Medicine*. We believe that, together, our work advances the notion that timolol eye drops are a safe, effective, and already widely available abortive treatment in select migraineurs.

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MM



Topical Beta Blockers for the Treatment of Acute Migraines in 2019

by Carl V. Migliazzo, MD & John C. Hagan III, MD

The use of beta blocker solutions for treatment of acute migraine has waited over 38 years for a large placebo-controlled study. We are making the same request of industry and academia today.

Migraine is the most prevalent neurological disease in the world. Migraine affects approximately 30 million Americans and is the leading medical cause of missed work and high among reasons listed for absent school days. The individual and national economic burden of migraine is enormous and patient suffering and disability incalculable. The advances in migraine therapy for this debilitating disease have been improving notably with triptans and the recently approved novel class of calcitonin gene related peptide (CGRP) inhibitors. The triptans may have serious side effects and must be used cautiously. CGRP inhibitors are expensive and may not be affordable to a large number of patients. Most migraineurs have some degree of dissatisfaction with their current therapy and would welcome new medications that are more effective, faster acting, safer, less expensive, and work synergistically with existing therapy. Beta blocker eye drops offer unique potential benefits when repurposed for migraines.



Carl V. Migliazzo, MD, (left) is a Kansas City ophthalmologist specializing in glaucoma treatment. John C. Hagan, III, MD, MSMA member since 1977, is a Kansas City ophthalmologist.
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We reported in *Missouri Medicine* in 2014,[1] a case report series of seven patients that had successfully used topical beta-blocker eye drops over multi-year intervals for relief of their acute migraines. These eye drops were often taken with their preferred oral analgesic. At the time, this was the largest case report series in the world's literature. We also referenced five smaller reports dating to 1980 of beta blocker eye drops used to successfully treat migraine.[2,3,4,5,6] Two additional studies effectively treating migraines with beta blocker eye drops have been identified.[7,8,] We, as well as all the authors of previously published papers, have recommended large, placebo-controlled studies. In the 38 years since this clarion call was made no such study has been performed.

Sean Gratton, MD, Mathew Cossack MD and others of the departments of ophthalmology and neurology at the University of Missouri-Kansas School of Medicine (UMKC) have recently reported[9] the world's first small, placebo-controlled, cross-over study of beta blocker eye drops for acute migraine. We commend them highly for their important work.

The UMKC study provided some useful data. (See page 506). Their study suffered from a lack of enrollment (only 10 patients out of a planned 26) which may have masked a true treatment effect. Seventy-eight percent of migraines had a severity of none or mild at two hours on timolol compared to 57% with placebo.



- **Migraine is a disabling, inherited neurological disease**
- **Migraine is the leading cause of disability among neurological disorders**
- **Migraine is ranked 7th highest cause of disability globally by the World Health Organization**

The subject-rated overall effectiveness of timolol was 2.4 out of a maximum of 4 compared to 1.4 with placebo. Notably 4 of 10 patients found beta blockers very effective while only 1 of placebo patients did. We consider these trends to be very encouraging.

What factors could have changed the significance of this study? Obviously, a larger enrollment would increase the power of the study. The authors have helpfully calculated that a future crossover study would require 86 patients to achieve significance at the .05% level. With only 10 patients, the UMKC study was not able to prove statistical significance. The difficulty of recruiting suitable patients indicates obtaining 86-100 appropriate subjects may require a cooperative multi-center testing protocol. The subjects would ideally have mild/moderate acute migraines without concurrent systemic or topical beta blocker therapy.

Another variable that we consider critical is the timing of the eye drop dosing. It is vital to instill the drops, one in each eye, at the first sign of an aura or migraine, and a second set within 10-15 minutes if patients do not experience major or complete relief. The UMKC protocol called for a second set no earlier than thirty minutes after the first set. After thirty minutes a migraine is usually well established and more difficult to control. The UMKC study decision to delay a second set of drops may have been necessary to secure approval from an Institutional Review Board. We have many anecdotal reports of success using beta blocker eye drops for acute migraine. We always suggest a second set of drops no later than 15 minutes after the first drops if still symptomatic. Patients report this as an important part of therapy.

Our clinical experience argues that obtaining rapid blood levels of the beta blocker is the primary factor in treatment success. It accounts for why oral beta blockers have been shown to be ineffective for acute migraines.[10,11] The oral route takes too long to obtain therapeutic blood levels and never catch up with the migraine pain/inflammatory cascade/cortical spreading depression. Often, patients will spontaneously comment that they didn't get their drops in soon enough after the onset of symptoms and their migraine progressed. Or, they missed their eyes with the drops and waited too long before instilling a second set. Instilling eye drops in pain, with or without a visual scotoma, can indeed be challenging, especially in patients who have not used eye drops routinely. The success of systemic beta blockers for migraine prophylaxis is explained by daily oral beta blockers achieving a constant therapeutic blood level. Instilling a second set of drops in 10-15 minutes would, we believe, have improved the UMKC final results.

Is there any increased risk from instilling more than one set of timolol eye drops within 10-15 minutes? We would argue there is not, assuming the usual and well-known contraindications of beta blocker usage are applied to patient selection. Timolol 0.5% solution contains 5.0 mg of timolol per ml. There are typically 20 eye drops in one ml of solution. One drop contains 0.25 mg of timolol (5 mg/20 drops). After a second set of drops into both eyes (4 drops total), even assuming all of the medication was absorbed systemically and none

spilled onto the lids, or absorbed into the eye, a total of one milligram was dosed into the systemic circulation. A typical intravenous injection of timolol for an acute cardiac event is in the range of one to four mg, well above the amount applied topically to the eye with two sets (4 drops total) of instillations. If an intravenous injection of these therapeutic doses of timolol is safe and approved for other indications, we believe that there little or no added risk from drops that contain a lower total dosage. Our clinical experience bears this out. We have not had any patient/physicians who have reported suffering an adverse event from a second set of drops instilled 10-15 minutes after the first set. We encourage rapid blinking after instillation to aspirate the beta blocker solution into the lacrimal duct for ultimate systemic absorption by the nasal-pharyngeal mucosa. With normal eyes, eyelids and patent nasal-lacrimal ducts, one drop of timolol 0.5% solution achieves 80% beta 1 and 2 receptor blockage in 10 minutes.[12] A second set should fully achieve almost complete beta receptor blockade. Note for migraine therapy the timolol solution must be used not the gel-forming version.

Eye drops are difficult for most people to instill and impossible for some. We feel eye drop instillation is not the most effective way to achieve rapid blood levels for migraine treatment. Sub-lingual or intra-nasal beta blocker administration is easier for virtually everyone and provides better, more predictable systemic absorption.[13] These dosing regimens are not FDA approved for timolol ophthalmic solution and would require new approval processes and possibly different chemical formulations. The FDA has issued guidelines to try and expedite new therapy for acute migraine[14] and the NIH has called for development of novel migraine therapy[15, 16] and is offering multiyear funding.

Given the cost of developing a new drug from the test-tube through FDA approval and marketing is estimated to be eight hundred million to one billion dollars, the cost of repurposing beta blockers by novel delivery for acute migraine would seem attractive to the pharmaceutical industry both because of the much lower costs of development and the greatly truncated testing and approval process. We hope the UMKC study will encourage industry to pursue this pathway. Alternatively, a consortium of research neurology departments might submit a NIH/Department of Defense grant request for a large placebo-controlled study.

The use of beta blocker solutions for treatment of acute migraine has waited over 38 years for a large placebo-controlled study. We are making the same request of industry and academia today.

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MM



Beta Blocker Eye Drops Have Dramatically Helped My Severe Migraines

by Carolyn Csongradi, MS

I've had migraine with auras since I was 20, which is now more than 50 years ago. I rarely have a headache without some form of aura – visual blurring, vertigo, facial numbness, language problems and confusion. The auras typically are the worst part of the migraine experience. I have a strong family history of migraine including hemiplegia – father, aunt, uncle, grandfather and includes both of my children – one of whom died in her teens during a seizure following a severe migraine episode.

Weather changes – usually cloudy, rainy days followed by bright sunshine are significant migraine triggers as are my failures to follow sensible sleep, exercise, and eating schedules. Over the past 30 years, I have tried a plethora of drugs, many of which have unacceptable side effects: atenolol, propranolol, nortriptyline, amitriptyline, indomethacin, valdecoxib, celecoxib, topiramate, prednisone, eletriptan HBF(sublingual). I have not used Botox or the newest injectables.

With advancing age and now mild persistent asthma, I no longer have access to Imitrex-type drugs or oral beta blockers, which do give me bronchospasm. This leaves me fewer options to deal not only with prophylactic migraine treatment but the frequent 'break through' headaches. Whoever said that one outgrows migraines forgot to ask me!

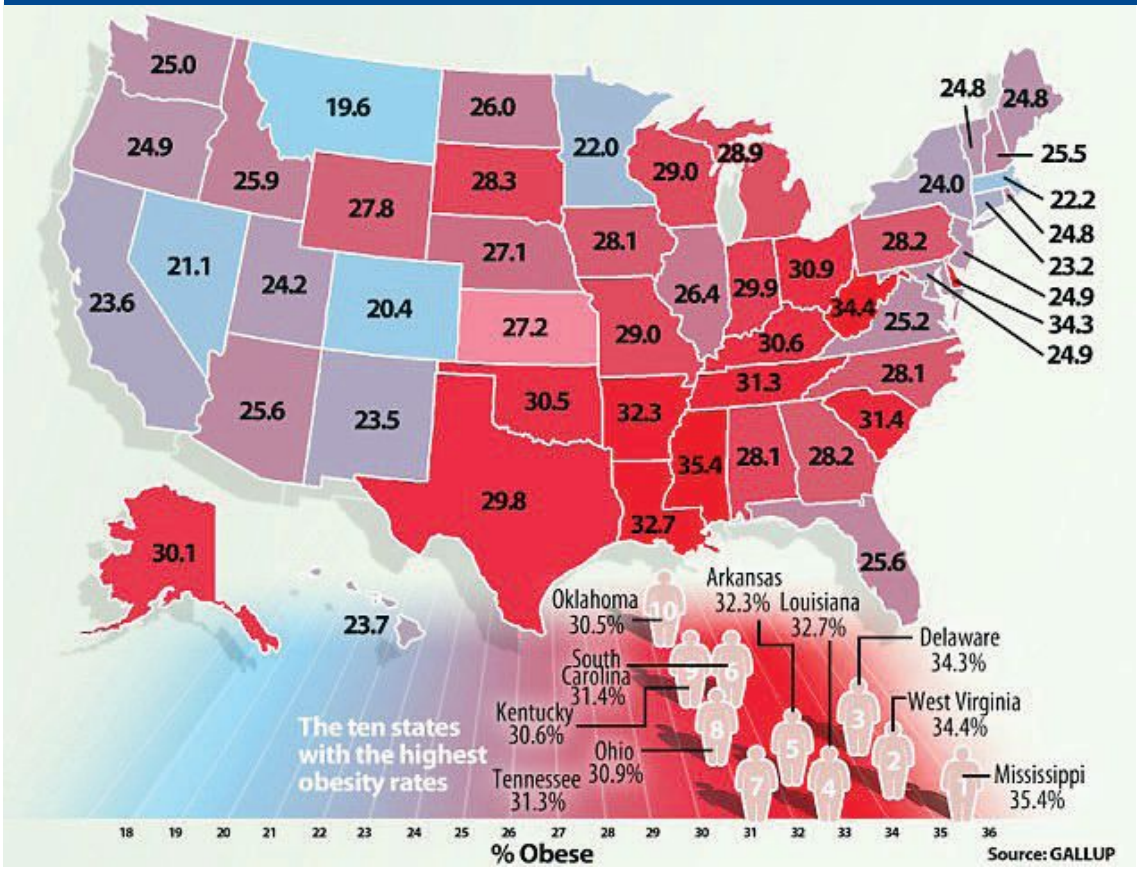
Currently, I take 75 mg of topiramate twice a day. As part of my allergic asthma treatment I also require daily Spiriva Respimat (2,5 mcg total) and inhaled corticosteroids. About 6 months ago while researching the internet, I discovered an article by doctors Migliazzo and Hagan suggesting the off-label use of timolol eye drops for the treatment of migraine. Voile!

Although not recommended for those who have bronchial asthma, my ophthalmologist agreed to let me try up to 2 drops in each eye of 0.25% Timolol eye drops for acute headaches. Since that time, I have successfully aborted many headaches using one or two drops of timolol 0.25% eye drops in only one eye at the first sign of discomfort without side effects. I put the drop(s) in the eye on the side where the aura or headache is occurring, keeping my eye open and blinking rapidly. The migraine symptoms resolve in less than 30 minutes. My life continues uninterrupted, including riding my horse Jules. (see photo) What a gift! **MM**



Carolyn Csongradi has a BS in chemistry from UC-Berkeley, Master degrees in neurosciences, and also education from Stanford University. She is a former adjunct faculty member of Santa Clara University.
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Sleep Medicine Single Series

Sleep Medicine: Stroke and Sleep

by Madihah Hepburn, MD, Pradeep C. Bollu, MD, Brandi French, MD & Pradeep Sahota, MD

We must increase awareness of the importance of diagnosing and treating obstructive sleep apnea in patients to reduce their risk of stroke and assist in their recovery following a cerebral ischemic event.



From top left, clockwise: Madihah Hepburn, MD, Pradeep C. Bollu, MD, Pradeep Sahota, MD, MSMA member since 2003, and Brandi French, MD, are in the Department of Neurology, University of Missouri - Columbia.
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Abstract

Cerebrovascular disease encompassing both ischemic and hemorrhagic strokes are among the leading causes of disability and mortality globally. The current evidence strongly suggests that identifying and addressing sleep disorders should be a part of both primary and secondary stroke prevention. Stroke and sleep are 'bedfellows' since sleep disorders, including sleep-disordered breathing, parasomnias, sleep-related movement disorders, insomnia, and hypersomnia are intimately intertwined with co-morbid cardiovascular conditions and increase stroke risk. Post-stroke sleep disorders also impact stroke rehabilitation, quality of life, and if left untreated can contribute to stroke recurrence.

Introduction

Vascular disease is a leading cause of mortality worldwide. In the United States, cerebrovascular disease (CVD) represents a large proportion of vascular events and approximately 795,000 persons/year have a new or recurrent stroke. The direct and indirect costs of cardiovascular disease and stroke are estimated to total more than 316 billion dollars including health care costs and lost productivity due to the morbidity of CVD.[1] The impact of CVD on quality of life and life expectancy underscores the importance of primary prevention with the identification and treatment of modifiable risk factors.

The traditional risk factors for CVD include atrial fibrillation, age > 65 years, hypertension, heart disease, carotid artery stenosis, tobacco use, diabetes mellitus, and dyslipidemias. However, there is increasing evidence that sleep disorders including sleep-disordered breathing (SDB), insomnia, hypersomnia, parasomnias, and sleep-related movement disorders are intimately intertwined with the cardiovascular conditions and increase the risk of cerebrovascular events.[2] Therefore, the identification and treatment of sleep disorders is an important step in risk factor modification and primary prevention of stroke.

Circadian Rhythmicity of Stroke

Observational studies have recognized that a temporal pattern of stroke events occurs in humans. Both ischemic and hemorrhagic strokes have a bimodal pattern with the major peak of events in the morning and a minor peak in the evening; with 20-40% of ischemic strokes occurring at night; especially at the onset of sleep.[3] This circadian pattern is independently linked to ischemic stroke even when other cardiovascular risk factors are adjusted.[4] This periodicity falls in the same lines of fatality of the strokes, with one study showing morning

strokes to be more likely to be fatal compared to afternoon strokes, even when variables of age, stroke severity, and gender were adjusted.[5] Although external factors such as seasonal variation; for example a higher frequency of stroke due to embolism and intracerebral hemorrhage (ICH) during the winter months, have been observed, more research suggests that endogenous factors are the main contributors to the temporal variation of stroke. These endogenous factors include diurnal variability of blood pressure, autonomic nervous system fluctuations, and hypercoagulability.

Blood pressure typically decreases in the evening by approximately 10% and has a surge in the morning at the time of awakening.[6] The autonomic nervous system also has a typical circadian pattern with a surge of sympathetic activity in the early morning, which correlates with the morning rise in blood pressure.[7] Additionally, our hemostatic balance is also affected by circadian rhythm with increased hematocrit and platelet aggregation and hypercoagulability occurring in the morning.[8] These endogenous factors may be the reason for the increased susceptibility to strokes in the morning..

A fair proportion of early morning or so-called, wake-up strokes have been observed to be embolic in nature. There seems to be a higher frequency of paroxysmal atrial fibrillation during the night and early morning hours.[9] The pathophysiology underscoring sleep and arrhythmia may be related to surges in autonomic activity which occur during sleep and trigger instability of cardiac electrical activity, such as REM induced surges of the autonomic nervous system. These changes in the vascular tone can lead to brief reduction of cardiac output and increase the risk of thrombus formation, which then may embolize during the periods of paroxysmal atrial fibrillation.[10]

Impact of Sleep Disorders on Stroke Risk

Elucidating the etiology of an acute stroke can affect outcomes and help to reduce recurrence of further events. The Trial of Acute Stroke Treatment (TOAST) categorized ischemic strokes based on etiology into five subtypes: Strokes due to large artery atherosclerosis, cardioembolic strokes, strokes due to small vessel occlusion, stroke of other determined etiology and cryptogenic strokes.[11]

The category of cryptogenic stroke is defined as ischemic cerebrovascular events in which the cause remains undetermined. The most frequent etiologies seen in this setting are paradoxical embolism via a patent foramen ovale or paroxysmal atrial fibrillation. Also, many of these cryptogenic strokes are found to be associated with sleep-disordered breathing (SDB). SDB is an umbrella term used to describe patterns of nocturnal breathing disturbances leading to ventilatory abnormalities such as hypoxemia and hypercapnia, and includes obstructive sleep apnea (OSA), central sleep apnea (CSA), sleep-related hypoventilation and Cheyne-Strokes Breathing (CSB). SDB is suspected in approximately 50-70% of acute stroke patients, and patients with recurrent cerebrovascular events are more likely to have SDB than those with a single cerebral ischemic event.[12] In this way, sleep and stroke become bedfellows because pre-existing sleep disorders increase the risk for stroke and acute strokes can lead to the development of SDB. After a stroke, the treatment of sleep disorders such as obstructive sleep apnea can augment functional recovery especially regarding ameliorating depression, increasing activities of daily living and improving attention and concentration.

The greatest prevalence of SDB is found among patients who are male and those with cryptogenic or recurrent strokes.[13] SDB has been associated with two to three times higher risk of incident stroke in several population studies. When investigating the link between obstructive sleep apnea and stroke, it has been difficult to determine if OSA and sleep are co-incident due to similar patient demographics namely gender, age, and presence of medical co-morbidities such as obesity, hypertension, hyperlipidemia, diabetes mellitus as opposed to a direct cause and effect of OSA leading to cerebral ischemia or infarction. A large population study, the Sleep Heart Health Study (SHHS) was a prospective cohort study of the cardiovascular effects of OSA. Approximately 5,000 patients were followed from the point of diagnosis of OSA until they either had an ischemic stroke or completed follow up at eight years. The study demonstrated that having OSA increases the risk of ischemic stroke, especially in men with moderate-severe OSA and suggested that having OSA as a co-morbidity increased the likelihood of stroke in this patient subset.[14]

The impact of disordered sleep breathing has many layers - its presence leads to and augments pre-existing co-morbidities which are typical risk factors for stroke. A cross-sectional analysis of a group of persons with SDB found after adjusting for confounding factors (age, gender, co-existing cardiovascular risk factors including obesity, hypertension, diabetes mellitus, hyperlipidemia) that a

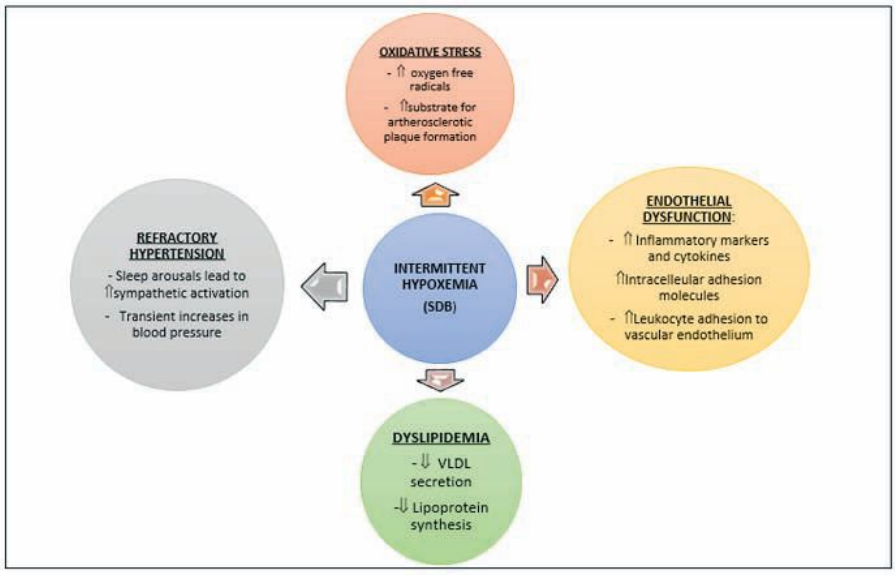


Figure 1: Overall contributors to plaque development are multifactorial

significant relationship exists between stroke and SDB. This study also showed that an Apnea Hypopnea Index (AHI) of ≥20 is associated with an increased risk of having a stroke within the next four years.[15] The presence of SDB portends an overall increased risk of cerebrovascular events.

The hypothesized mechanisms of SDB leading to stroke include fluctuations in the intrathoracic pressure due to apneas, intermittent hypoxemia, sympathetic activation and endothelial dysfunction. Due to sympathetic activation, there is vasoconstriction and hypertension along with direct endothelial damage and cardiac arrhythmias. The result is cerebral ischemia and damage due to the recurrent hypoxemia and variability in cerebral blood flow.[16] SDB preceding stroke affects multiple domains including the development of hypertension and early atherosclerosis by increasing platelet adhesion and vascular endothelial dysfunction.

In addition to the association between OSA and refractory hypertension and cardiac arrhythmia, there is also a key association between sleep apnea and systemic atherosclerosis. Overall contributors to plaque development are multifactorial as shown in Figure 1. The repeated hypoxemic events of OSA are implicated in atherosclerosis by increasing oxidative stress, endothelial dysfunction and causing dyslipidemia.

Impact of Stroke on Sleep

Changes in Sleep Architecture and EEG

Supratentorial strokes have been linked to the reduction in non-REM sleep and total sleep time, and this is more frequently seen with left-sided strokes. There may be an ipsilateral or bilateral reduction in sleep spindles also. A temporary reduction in REM sleep may also be observed in some cases of supratentorial stroke. This is more frequently seen with a right-sided stroke. Saw-tooth waves may be reduced after hemispheric stroke. Reduction in REM sleep can be seen after occipital strokes. Strokes in the ponto-mesencephalic junction and the raphe nucleus may cause a reduced amount of non-REM sleep while lesions in the lower pons can selectively reduce REM sleep.[1] Paramedian thalamus and lower pontine strokes can also result in lack of slow-wave sleep with preserved REM sleep.

Similarly, many changes in surface EEG recording can also be noted in the setting of strokes. Cortical and subcortical strokes can show evidence of neuronal dysfunction in the form of focal slowing. Sometimes, subcortical strokes may display diffuse neuronal dysfunction with intermittent bursts of ipsilateral or bilateral delta wave activity. Thalamic and brainstem infarcts may present with pathological EEG patterns like alpha coma, spindle coma and theta coma. While small infarcts may not produce any discernible EEG changes, massive infarcts may result in attenuation of EEG activity in the involved regions without any associated delta activity.

Insomnia after Stroke

Insomnia is defined as persistent difficulty with sleep initiation, duration, consolidation, or quality that occurs despite adequate opportunity and circumstances for sleep and results in some form of daytime impairment. Daytime symptoms typically include fatigue, mood issues, irritability, malaise, and cognitive impairment. Some patients with insomnia may also experience physical symptoms like muscle tension, palpitations, and headache. Under the international classification of sleep disorders, insomnia associated with stroke falls under the category of "Insomnia due to a Medical condition."

Insomnia is common in stroke patients and affects 20-56% of them. About 18% of the people reported

new-onset insomnia after their stroke. Insomnia typically occurs in the setting of the acute phase of the stroke. The development of insomnia may be related to the stroke location, with an increased prevalence in right hemispheric strokes as well as those within the thalamus or brainstem, including the pontine tegmentum and thalamo-mensencephalic region. Patients with strokes within the paramedian thalamus can also develop insomnia due to an inability to generate sleep spindles due to the involvement of the thalamoreticular system.. Along with stroke location, the development of insomnia in stroke patients may be due to multiple environmental factors such as being hospitalized, unfamiliar environments, loss of uninterrupted sleep and medication side-effects.[2] Overall post-stroke insomnia can increase anxiety, impair daytime energy levels, concentration and memory and therefore contribute to a suboptimal performance during rehabilitation.

Hypersomnia after Stroke

Increased sleepiness following stroke was mentioned by MacNish as early as 1830. Carl Wernicke in 1881 reported several patients in home autopsy showing punctate hemorrhages around the third ventricles and called it "Polioencephalitis Hemorrhagica Superioris," now called "Wernicke-Korsakoff syndrome." Mauthner in 1890 related to sleepiness and patients with sleeping sickness (encephalitis lethargica) to the presence of inflammatory lesions in the periventricular gray matter of the midbrain. The association between sleep-wake disorders and stroke became increasingly reported by the beginning of the 20th century. Von Economo in 1920 related that sleep might represent an active process of the brain and not just the absence of wakefulness and showed that hypersomnia was associated with lesions of the posterior hypothalamus. Manasseina and Kleitman also remarked on post-stroke hypersomnia in the classic monographs on sleep.[3,4] Post-stroke hypersomnia is defined as exacerbated sleep propensity with excessive daytime sleepiness, increased daytime napping or prolonged nighttime sleep following a cerebrovascular accident. The prevalence of hypersomnia in stroke patients ranges from 1.1% to 27%. Poststroke hypersomnia may be found after subcortical (caudate, putamen), upper pontine, medial ponto-medullary and cortical strokes affecting the reticular activating system (RAS). Paramedian or bilateral thalamic strokes present with sudden onset of coma, and when they awake, they can exhibit hypersomnia/sleep like behavior up to 20 hrs/day with deficits of attention, cognition, and memory.[5] Patients with stroke and hypersomnia are more likely to go to a nursing facility compared to those with stroke without hypersomnia, and the presence of hypersomnia may impair optimal stroke rehabilitation.

Stroke and Periodic Leg Movements

Restless leg syndrome (RLS) is an overwhelming urge to move the legs, that is worse with inactivity and at night and relieved by movement. RLS may be associated with sleep disturbance and involuntary movements of the legs during sleep, the periodic leg movements of sleep (PLMS). Overall, this occurs in 5-8% of the population and post-stroke PLMS has been associated with lesions of the pons and corona radiata.[6] Both RLS and PLMS have been linked to an increased risk of stroke, and this connection may be due to decreased sleep quality leading to an increased risk of cardiovascular disease. The duration of RLS may also be an independent predictor of asymptomatic cerebral small vessel disease, and this factor is associated with a higher rate of symptomatic stroke. Both disorders are associated with sympathetic hyperactivity which can affect the circadian rhythm of blood pressure, leading to more nocturnal hypertension and increased risk of atherosclerotic plaque rupture.[7] These factors cumulatively increase the risk of stroke.

Stroke and Parasomnia

Parasomnias are complex movements and behaviors during sleep which include REM sleep behavior disorder (RBD), nightmares, sleep paralysis, and other disorders of arousal including sleepwalking and sleep terrors. RBD consists of dream enactment behavior and vivid or unpleasant dreams and is frequently seen in neurodegenerative disorders such as Parkinson disease and multiple systems atrophy. Studies have established that individuals with RBD have a higher likelihood of also having concomitant stroke risk factors including diabetes mellitus and dyslipidemia. One study demonstrated that adults with RBD were 1.5 times more likely to develop stroke independent of other demographic variables including age, gender, hypertension, and tobacco use.[8] The mechanism linking RBD to stroke may be sleep fragmentation leading to increased sympathetic tone and

resulting in changes in heart rate variability and blood pressure surges which are cardiovascular events linked to stroke onset.

Sleep-Disordered Breathing After Stroke

Sleep-disordered breathing include a variety of diseases like Obstructive Sleep Apnea (OSA), Central Sleep Apnea (CSA), Sleep Related Hypoventilation, sleep-related hypoxemia and periodic breathing like Cheyne-Strokes Breathing (CSB).

A systematic literature search of PubMed databases published between January 1, 2001, and January 1, 2017, was performed to identify studies involving the treatment of obstructive sleep apnea in patients with acute ischemic stroke with continuous positive pressure ventilation and their functional outcomes including the impact on cognition, cardiovascular events, activities of daily living. Studies included randomized clinical trials and observational studies. Using MESH terms including 'stroke' and sleep apnea syndromes' as keywords, we found 429 articles, and of these, 27 were clinical trials, and 21 of the 27 trials were published within the last ten years. This demonstrates an increasing awareness of the importance of diagnosing and treating obstructive sleep apnea in patients to reduce their risk of stroke and assist in their recovery following a cerebral ischemic event.

The use of continuous positive pressure ventilation (CPAP) to treat patients following acute ischemic stroke has been beneficial in improving stroke severity. Initiating therapy early can have benefit in improving the overall NIHSS. Several trials have shown treatment with CPAP in the first few days after acute stroke trended toward greater NIHSS improvement.[9] The mechanism may be due to improved oxygenation and decreased the frequency of blood pressure surges associated with the apneas. Treatment with CPAP improved left ventricular function and allowed a more rapid normalization of cerebral vascular tone leading to the earlier return of normal cerebral autoregulation.[10]

Several studies have been performed in the rehabilitation setting with an aim to elucidate the benefits treating SDB would have on the overall functional status and cognitive recovery. A randomized trial in OSA patients admitted to a stroke rehabilitation unit with the premise that treating OSA in this group would enhance motor, neurocognitive and functional recovery found the CPAP group achieved improved functional outcomes, especially in stroke-related impairment as assessed by the Canadian Neurological Scale (CNS). They also achieved improved secondary outcomes including less depressive symptoms and less daytime sleepiness and fatigue.[11]

Another randomized controlled trial hypothesized that untreated OSA in patients was associated with a worse outcome regarding function and cognitive status during inpatient rehabilitation following an acute stroke. The study found that the group treated with continuous positive pressure ventilation (CPAP) had statistically significant improvement in domains of attention and executive function although overall did not demonstrate any more functional improvement compared to the placebo group after four weeks.[12] Albeit a small study, this provides some support that treating SDB can lead to improvement in certain cognitive domains.

The deficits related to a stroke are a function of focal injury to the cerebral cortex, and after an acute stroke, the brain reorganizes to improve and compensate for lost functions. Neurorehabilitation is multi-layered, involving physical, occupational and speech therapies as well as neuropsychological training to improve the overall daily living and cognitive functioning and sleep is a function which promotes recovery in all these domains.[13] In addition to SDB, disturbances of wakefulness are also associated with acute stroke, and this spectrum extends from hypersomnia, excessive daytime sleepiness, and fatigue. These conditions can also be intrinsically connected to disorders of breathing; for example, untreated sleep apnea can also be linked to fatigue and excessive daytime sleepiness.

Post-stroke CSA and CSB linked to lesions within the insula and thalamus affecting central autonomic networks which co-ordinate respirations.

Changes in Circadian Rhythm After Stroke

After an acute stroke, changes occur in the physiological circadian profile of blood pressure. As compared to normotensive persons, patients with both ischemic stroke and hemorrhagic strokes demonstrated a loss of the biphasic circadian variation. Normally nocturnal blood pressure drops approximately 10% or more, and after a stroke, this nocturnal dipping profile is eliminated.[14] Additionally, following a stroke, there are other alterations in the circadian rhythm, especially the sleep/wake cycle leading to sleep fragmentation and decreased sleep efficiency. This alteration in sleep/wake

cycle also correlates to the development of post-stroke apathy, which is defined as a syndrome of decreased goal-directed behavior including a lack of motivation, emotion or interest.[15] The disturbance of sleep architecture and the development of apathy following a stroke has consequences on rehabilitation performance and can negatively impact functional recovery.

Conclusion

There is a body of evidence which demonstrates that sleep disorders are intrinsically bound to both ischemic and hemorrhagic cerebrovascular events by increasing a patient's risk profile and as a sequela of an acute stroke. This underscores the importance of screening patients for sleep disorders especially SDB and appropriately manage them to help in the primary or secondary prevention of stroke which in the long run will decrease the morbidity and mortality of this potentially devastating disease.

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Disclosure

None reported. **MM**

Operationalizing Population Health Management in Practice

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Parents as Teachers.

Healthcare is looking to community-based organizations to establish meaningful partnerships to improve health outcomes.



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Abstract

We synthesized practitioner perspectives on how to integrate a community-based program into a healthcare system. Three focus groups and four in-depth interviews in Greene County, Missouri addressed: the population served, collaborations, service delivery design, training, data collection, and funding. Participants identified the following: integration as a way to increase population health outcomes through mutually beneficial partnerships; education and awareness of community-based resources; coordination of services to avoid duplication and maximize niche skills; smooth transitions across programs; and information sharing.

Introduction

Healthcare organizations are being propelled into the era of population health management[1] by changing reimbursement models that reward value rather than volume.[2] Improving population health outcomes will require a greater emphasis on modifiable factors, which account for up to 50% of population-level premature mortality;[3] medical care only accounts for 10-20% of health determinants.[4] Healthcare is looking to community-based organizations to establish meaningful partnerships to improve health outcomes.[5,6] Operationalizing this integration is still poorly understood.

Greene County, Missouri, has higher than average poverty, and a higher uninsured rate than Missouri and the U.S.[7,8] More than 94% of the 58,000 children live in a "healthcare shortage area" with only 44 pediatricians in the county.[9] Over 14,000 children in Greene County experienced poverty in the previous 12 months;[8] children living in poverty are less likely to be current on their vaccinations[10] and have higher rates of hospital admissions and death.[11-13]

In the city of Springfield, the largest town in Greene County, a population health integration model is being explored between Parents as Teachers (PAT) and healthcare organizations. PAT began in 1981 in Missouri. Today, it is federally recognized as a national, evidence-based home visiting model.[14] Families with children ages prenatal to six years can enroll in a local program through a variety of organizations, including schools. PAT services are delivered by trained parent educators (home visitors), and include early and routine child health and developmental screenings; personal visits; parent social support group connections; and referrals to community-based resources. The Springfield Public Schools PAT reaches approximately 6,000 children ages zero to six years annually.

This study is guided by the theoretical construct of population health management and health care integration with community-based programs to improve health outcomes.[1,6,15] We solicited stakeholder input on how to operationalize

integration of a community-based program (PAT) within the healthcare system in Springfield in order to establish meaningful partnerships to increase the likelihood of improving population health outcomes for Greene County residents.

Methods

The local maternal and child health coalition has a strong community presence and so recommended focus group participants who had been active in their communities and had worked together to increase the health and wellness of the children. It was important to include the perspectives of those who could act as partners in the potential implementation of an integration project. The coalition's focus on child health attracted participation from pediatric specialties; medical providers included nurses and pediatricians. Other medical provider specialties were not solicited if they had not been engaged with the community work.



PAT National Center (PATNC) staff members (including authors KJ and AY) recruited participants through email followed by phone calls to Springfield Public Schools PAT program, Federally Qualified Health Centers, major hospitals, foundation funders, and other healthcare providers/pediatricians.

Three focus groups were held in conference rooms at the Springfield School District building, each including 7-13 participants and lasting approximately 90 minutes. Lunch was provided as an incentive. One-on-one interviews were conducted with four participants that were not able to attend; each lasted approximately 30 minutes. All focus groups were audio-recorded. Facilitators began the focus group by thanking participants for their time and explaining the purpose of the focus group with a brief introduction of the Springfield PAT program.

Focus group questions were designed to gather participants' perspectives on the:

- Population Served: Populations served by the providers, and the strengths and challenges of families in their community. Sample question: What are some strengths of the families in your community?
- Partnerships/Collaborations: Ways participants partner, collaborate, and refer across organizations and systems. Sample question: How do you coordinate and communicate with partners?
- Service Delivery Design: Participants' vision for how PAT could integrate into the healthcare system and the practical implementation of that workflow. Sample question: What is your vision for Parents as Teachers in the medical system?
- Training/Technical Assistance: Training that would be necessary or helpful for successful integration. Sample question: What type of training/technical assistance needs to be in place to implement Parents as Teachers in the medical system?
- Data Collection: Data participants currently collect and track, and what would be helpful to collect and track for program service integration. Sample question: What additional outcomes would you be interested in tracking?
- Funding: How programs are funded or participants are reimbursed for services to determine if PAT integration into the healthcare system might fit a funding model. Sample question: How are you currently funded?

An external service transcribed the audio-recordings. PATNC staff validated the transcriptions, ensured data quality, and ensured participant anonymity. The four interviews were not recorded, but notes were taken. PATNC staff (led by KJ) used Microsoft Word to divide focus group and interview content into topic areas, summarize the content, and identify relevant themes through inductive analysis. Alignment to *a priori* categories was determined through deductive methods by multiple authors. PATNC staff compared results for validation, and to resolve disagreements. This study did not require Institutional Review Board approval.

Results

Participants

Participants included school nurses, pediatricians, hospital and clinic workers, school board members, county health department staff, behavioral health workers, a community hospital nurse care manager, representatives from funding agencies, a member of The Doula Foundation,



and a hospital communications staff member. Participants had varied experience with PAT programs, child health, and development.

Perspectives on the Population Served

Most participants served a general population; a few worked with high risk populations, including parents with high needs, children, or pregnant women. Participants reported that county residents faced a number of barriers, including high poverty rates, lack of mental health services, low educational attainment, instability with housing or insurance, substance abuse, and lack of transportation. In two of the focus groups, participants noted that the population they served was distrustful of home visitors as home visitors were seen as "with the state" and residents feared that home visitors would take their children away.

Partnerships/Collaborations

Participants noted that while community resources are available, residents often did not know how to access them. Despite residents' barriers to access services, most participants agreed that the residents care about their children's well-being.

Participants felt that their community worked well together. "If you're in the non-profit arena, that's an expectation that you work together and I think we do that as well as any community I've seen." Noted partnerships included the dental, mental health, and medical facilities collaborating to provide onsite care to Springfield Schools, and the Health Department's collaborative Healthy Living Alliance. Participants also noted the Early Childhood Coalition, the Pregnancy Coalition, and Head Start programs. One participant mentioned that the school district collaborates closely with a behavioral health provider; however, this is insufficient to overcome the provider shortage and long waiting lists. Participants noted the two hospital systems as strengths in the community, along with the collaborative spirit of the medical and social service organizations. However, not all participants perceived the hospitals as effective collaborators largely due to the fact that insurance restrictions do not allow patients the access they need. Insurance requires them to use one hospital and will not cover services at the other hospital. "One hospital system has a number of pediatric sub-specialists. Patients in the other system can't go across the street. They have to go up to St. Louis."

Service Delivery

Participants generated ideas on how to integrate PAT into the healthcare system around the following themes: 1) education and awareness of PAT; 2) information sharing and dissemination; 3) parent educators integrated inside health clinics to ensure services are not duplicated and parents can easily enroll; and 4) smooth transitions across programs.

Participants expressed surprise by the number of residents that did not know about PAT; awareness of community-based resources needs to improve, along with consistency of messaging to residents from various organizations. Medical providers also need to be educated on what community-based resources are available. Associating a program with a health system may strengthen program recognition for residents.

Generally, participants agreed that a parent educator housed in the medical facilities could reduce service duplication; improve the ability for services to strengthen their niche area of developmental screening, surveillance and parenting coaching; and improve program utilization. Participants noted PAT's strength in developmental screenings. A physician in Focus Group 1 emphasized pediatricians' skills in addressing health-related topics such as nutrition and safety. PAT parent educators are generally degreed professionals with training on administering, interpreting, and utilizing developmental screenings. Having parent educators complete developmental screenings, such as the Ages and Stages Questionnaire, sharing the results with a family's medical home, and educating parents on positive practices can save resources by preventing the clinic from duplication of effort and enriching a coordinated care model.

Providers, i.e., the nurses at the health department or doulas, have limited time to spend with new parents and children after birth. PAT can provide home visits until kindergarten.

One participant emphasized that programs housed in medical facilities not interrupt the flow of the clinic/hospital. Smooth program coordination was noted as an

important way healthcare and PAT programs would benefit from close collaboration.

Training/Technical Assistance

Consistent with educating medical providers on available community-based resources, several participants felt that it would be important that providers understand PAT services and expectations.

Educating providers on PAT services could be implemented through training. For some, this could count as professional development. Participants were enthusiastic about the possibility of continuing education opportunities. Conversely, parent educators would need to learn medical jargon and privacy regulations.

Data Collection

Hospitals and school districts collect family, individual, and caregiver information related to the health and development of children. One provider noted it is plausible to add a PAT box to a medical record.

While healthcare facilities and the other participating organizations already capture extensive data on families, the participants still noted some gaps, including documenting behavioral problems and measuring the effectiveness of the current community's maternal-child health programs.

Funding

Other than the first focus group, which included funders, discussions on how to fund programs was limited. Along with foundation funds, programs were funded by Medicaid or taxes. Currently, the mental health demand in the community exceeds funds identified for those services.

Discussion

Focus group participants identified key considerations for the integration of a community program into a healthcare system. The next steps include pilot testing the integration of PAT into primary care. Springfield's Federally Qualified Health Center Jordan Valley incorporates women's, children's, and dental services in one building. PAT would embed a parent educator to collaborate with providers. Future research will evaluate this effort.

Implications for Policy and Practice

- Integrated partnerships could build mutual benefit through: education and awareness of community-based resources; coordination of services to avoid duplication and maximize niche skills; smooth transitions across programs; and information sharing.
- These findings provide key considerations for healthcare organizations with population health initiatives when moving from "volume to value."
- Other communities might find our focus group results beneficial to use as talking points for their stakeholder discussions.
- Future work will report on lessons learned from integration, such as developing shared goals and outcomes, the ability to track patients across systems of care that do not technologically interact, and a feedback loop to support successes and identify opportunities for improvement.

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Disclosure

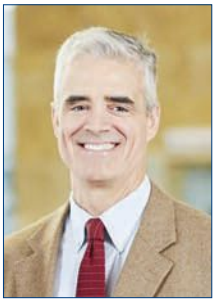
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Direct Anterior Total Hip Arthroplasty

by Gregory R. Galakatos, MD

As hospital-associated costs and consumer-driven healthcare become more important in the practice of total joint arthroplasty, more surgeons will continue examine surgical approaches/techniques along with other factors in order to drive improved patient outcomes.



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Abstract

The direct anterior approach to the hip for total joint arthroplasty has been suggested to have several advantages compared to other popular approaches through its use of a natural intramuscular and intra-nervous interval. Recent emphasis on tissue sparing and minimally invasive outpatient joint replacements has given rise to a significant increase in the utilization of direct anterior total hip arthroplasty (DAA). Proponents of this approach cite improved recovery times, lower pain levels, improved patient satisfaction as well as improved accuracy on both implant placement/alignment and leg length restoration. A number of variations of the procedure have been described and many authors have published their experiences and technical keys to successfully accomplishing this procedure. Described techniques have been performed using specifically designed instruments and specific fracture tables and intra-operative flouroscopy, however this approach may be performed using a regular table with standard arthroplasty tools with alternative patient positioning and without intraoperative imaging. This review summarizes several aspects of the direct anterior approach for total hip arthroplasty and its comparison to other popular approaches to modern hip replacement.

Introduction

There are several approaches to the hip joint that can be utilized for total hip replacement and these include with some variations the posterior approach (Moore or Southern), the lateral approach (Hardinge), the anterolateral approach (Watson Jones), and the direct anterior approach (Smith-Peterson). Although more recently popularized for hip arthroplasty, the direct anterior approach to the hip was originally described by Carl Heuter in 1881. Smith-Peterson is frequently credited with popularizing this technique through prolific use of this technique during his career after publishing his first description of the approach in 1917.[1] The anterior-based incision utilizes the interval to the hip joint between the tensor fascia lata and the sartorius muscles. Light and Keggi published their experience using this approach for hip arthroplasty in 1980, and Judet described the procedure with the use of a fracture table in 1985.[2] Recent desire to perform hip reconstruction through less invasive and tissue sparing as well as in an outpatient setting have been key factors in the newfound interest of this approach.

This has led to a surge in its use for hip replacement over the last 10-15 years. During this time, many authors have described variations of the technique and important pearls to safe and successful performance of anterior hip arthroplasty.[3] Although not as common, several have noted routine use of this technique for revision total arthroplasty as well as hemiarthroplasty for fractures.[4]

The direct anterior approach (DAA) can be used for patients of nearly all body habitus and hip conditions. Some anatomic features of the native hip and pelvis are recognized to make a direct anterior approach more difficult. Acetabular protrusio brings the femoral canal closer to the pelvis and can limit the access to the femur. Neck shaft angle with decreased offset positions the femoral canal deeper in the thigh, and factors associated with obese muscular males can limit the exposure. A potential disadvantage of the anterior approach is diminished access to the posterior column. If a patient has retained posterior acetabular hardware or posterior wall deficiency with augmentation contemplated, the anterior exposure might prove unsuitable.[5]

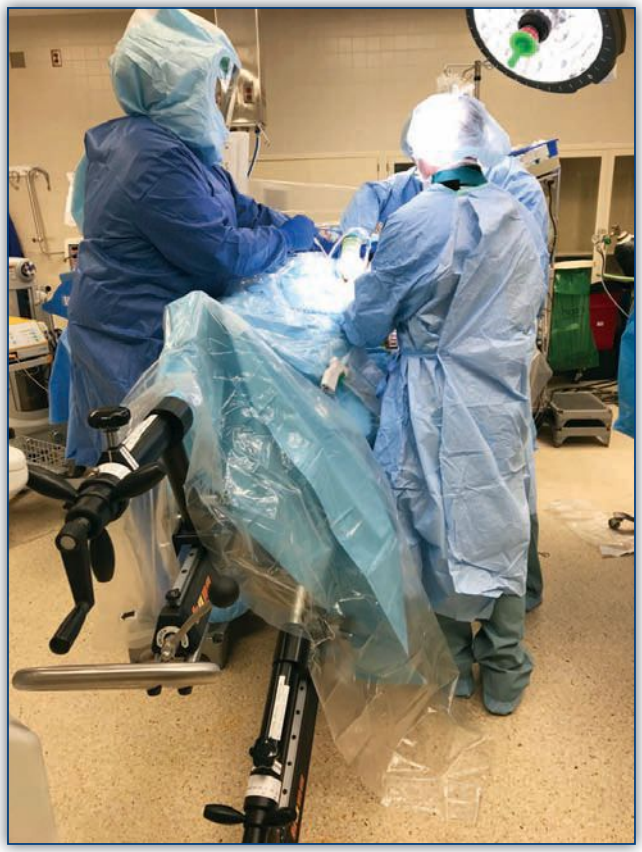


Figure 1. Surgical table set up with author's preferred draping technique on HANA table. Operative leg shown extended and adducted.

Surgical Technique

The vast majority of authors describing direct anterior approach position the patient supine on a fracture table or regular table. Michel et al. also reported performing anterior total hip arthroplasty in lateral decubitus position.[6] When using a regular operating room table, the patient is positioned with the hip located over the table break which can be reflexed to allow hyperextension of the hip joint. The contralateral leg is typically draped into the field and a mayo stand placed alongside to allow for figure-four adduction during the femoral exposure. The author's preferred method includes the use of a HANA or fracture table and a shower curtain laid across the patient or other draping system can be utilized. (Figure 1.)



Figure 2. Direct anterior approach specific retractors and instruments which are used to facilitate the approach.

Obese patients should have the pannus retracted with adhesive tape to avoid any possible interference with the exposure. Incisions vary by surgeon, however most authors rely on the ASIS and



Figure 3. Hip exposure with retractors and osteotome for femoral neck cut completion in minimally invasive direct anterior approach (DAA).

greater trochanter as anatomic landmarks for reference. An oblique incision is made originating 2-4 cm distal and lateral to the ASIS to a point a few fingerbreadths anterior to the greater trochanter. Dissection is taken deep to expose the overlying fascia of the tensor fascia lata (TFL) which is then incised along its fibers. Blunt finger dissection is utilized under the medial fascia and the interval is developed between the sartorius and the TFL. A wound protector can help minimize soft tissue, muscle, and skin damage caused by retraction.

The ascending branch of the lateral circumflex femoral artery and vein are identified over the intertrochanteric line and cauterized and the anterior hip capsule is exposed. Specific DAA retractors are useful for exposure. (Figure 2) A cobra type retractor is placed superior to the lateral capsule to retract the abductors and a second large Hohmann type retractor is placed inferior to the femoral neck. A curved third retractor maybe useful proximally to elevate the rectus tendon, especially in heavier patients. The anterior capsule can be partially excised, fully excised, or incised and tagged for retention and later repair. The femoral neck osteotomy can then be made either with a single cut or some prefer a napkin ring type parallel two cut technique to facilitate removal of the femoral head. An osteotome can be used to complete the cuts (Figure 3). Flouroscopy at this point can be useful to confirm the accuracy of the planned cuts. A corkscrew inserted through the cortical side of the femoral head or through the femoral neck cut will aid to spin the head and rupture the ligamentum flavum and assist with head removal.

Excellent exposure and visualization of the acetabulum can be achieved with the use of two or three retractors. A Mueller type retractor can be placed inferiorly on the posterior border of the acetabulum. Downward pressure on this retractor will bring the femur posterior. One or two retractors can be placed along the anterior acetabulum. Rim osteophytes and labrum are removed as well as the ligamentum flavum stump and soft tissue. An inferior capsular release may be useful for exposure. Reaming proceeds as in other approaches medially at first to reach the true floor then to anatomic position. Flouroscopy can be used to check the size and as well as inclination and version of the reaming and acetabular impaction seating. Screw fixation of the acetabular component may be added pending surgeon preference followed by liner impaction.

Femoral exposure on a HANA/fracture table is initiated then by external rotation of the femur typically over 90 degrees. A proximal femoral hook is placed for elevating the proximal femur to facilitate exposure. The leg is extended by lowering the leg to the floor followed by adduction of the extremity. For DAA arthroplasty on a standard table femoral exposure is accomplished by reflexing the table to extend the extremity and placing the leg figure-four under the opposite leg and knee. A cobra type retractor is placed on the femur medial to the neck cut and a double-pronged retractor is placed under the greater trochanter. Soft tissue releases are performed in the piriformis fossa and greater trochanter along while elevating the proximal femur with the hook device to visualize the osteotomy plane and allow for broaching and placement of a femoral trial component. A key advantage of DAA arthroplasty is the ability to evaluate leg length at this point in the procedure prior to final implant placement. The image of the trial



Figure 4. Radiographic image showing comparison of hips for leg length, fit and alignment.

components can compared to the preop plan, a preop image and/or the contralateral hip to confirm alignment, version, fit and leg length. (Figure 4)

Closure of the wound is initiated with repair of the capsule, if preserved, followed by closure of the TFL fascia with either running or interrupted suture. The use of a drain is optional. The subcutaneous tissue is closed with resorbable suture and skin is closed with technique of choice but glue technique with a long term adhesive dressing continued for two weeks may be useful in patients with a large pannus which can overly the incision.

Postoperative care is frequently initiated with the use of an abduction pillow along with anterior hip precaution instruction. Immediate weight bearing is allowed and the patient can be discharged when the patient is safely ambulating and can manage stairs. This is frequently within 23 hours and can occur on the same day of surgery as a true outpatient procedure.

Discussion

As with any surgical procedure there is a significant learning curve associated with the adoption of the anterior approach to the hip for arthroplasty. Outcomes related to anterior hip arthroplasty have been described in a number of studies, though the majority are retrospective with smaller samples sizes. A meta-analysis comparing the anterior and posterior approaches showed the anterior approach (DAA) may have potential advantages in patient reported pain and functional outcomes, post-operative length of stay, dislocations and postoperative narcotic requirements. It additionally noted that the DAA trended to higher rates of patients discharged to home versus a skilled facility and a larger percentage of acetabular cups placed within the "safe" zone of alignment due to the use of fluoroscopy.[6]

One retrospective study compared 41 DAA and 47 posterior approaches and found shorter hospital stay and fewer days to mobilization with the DAA. Incision length was shorter in the DAA, however lateral femoral cutaneous nerve injury and femoral fractures were more common and operative time was 20% longer.[7] Another report compared 419 patients receiving either a lateral approach or DAA and found similar operative times and blood loss, but less pain, shorter time to discharge and greater percentage of patients discharged directly home with the DAA.[8]

Another aspect of comparison in approaches to the hip involves functional capacity in the early and long term postoperative period. One prospective, randomized single surgeon study compared 43 DAA to 44 posterior approaches with endpoint analysis of normal ability to climb stairs and walk unlimited distances. The study revealed the DAA cohort performed better in the immediate post-op period with lower VAS pain scores on post-op day one, more patients climbing stairs and walking unlimited distances at six weeks and higher HOOS Symptom scores at three months. However, there were no significant differences at later time end points.[9] Other studies have found similar results that most advantages in functional outcome with DAA may be largely limited to the early postoperative recovery period of six to twelve weeks.[10-14]

A recent prospective, randomized Mayo clinic study compared 101 patients who were randomized to four surgeons. Two specialists were experts in DAA and the other two surgeons were experts on the "mini" posterior approach (MPA). The study documented quicker recovery by DAA subjects compared to the MPA patients. Specifically, advantages included discontinuing use of a walker (10 days post-op versus 14.5 days), discontinuing all walking aids (17.3 days versus 23.6 days), discontinuing narcotics (9.1 versus 14 days),

ascending stairs with gait aid (5.4 days versus 10.3 days), and walking six blocks (20 days versus 26 days). There was no difference in activity levels between the groups pre-op, and at two months and one year post op.[15]

Many studies have examined the relative complication rates associated with the DAA compared to other approaches to the hip. Some have noted as with all surgical procedures that complication rates correlate with surgeon experience and significantly drop after the first 40-100 cases.[16,17] Femoral fractures have been found to be of high incidence in initial experience with DAA likely due to excessive force for elevating the femur into the wound and poor exposure limiting access to the femur resulting in poor orientation for broaching and implant placement. Dislocation rates have been shown to be significantly lower with the DAA and several authors do not restrict patients with anterior hip precautions or abduction pillows postoperatively.[19-22] Lateral femoral cutaneous nerve injury and wound complications in some studies have been shown to be slightly higher with the DAA likely due to excessive traction on the soft tissues for exposure as well as the effect of a pannus resting on the incision in larger patients. Ring tissue protectors and extended sterile dressings have been suggested to improve this complication.[23-24]

Conclusion

Most standard approaches to hip arthroplasty have been shown to be safe and effective in the management of arthritis and with proper training and meticulous technique can be successful with exceptional patient satisfaction. There remains a significant learning curve associated with the DAA approach due to its recent popularization and lack of significant experience with this technique in residency training programs until the last decade. The growing emphasis for minimally invasive arthroplasty and improved and expedited functional results make this approach an attractive choice. As hospital associated costs and consumer driven healthcare become more important in the practice of total joint arthroplasty, more surgeons will continue examine surgical approaches/techniques along with other factors in order to drive improved patient outcomes.

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Disclosure

None reported. **MM**

Ovarian Cancer Survival in Missouri, 1996-2014

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To reduce disparities of ovarian cancer burden in Missouri, action is needed at multiple levels. Individuals at risk need to be informed and equipped with knowledge, skills and motivations to seek healthy lifestyles and timely medical check-up.



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Abstract

We evaluated relative survival (RS) for ovarian cancer (OC) overall, by demographic and by clinicopathological characteristics in Missouri. Survival data from the Missouri Cancer Registry were obtained for cases diagnosed 1996-2014. An improved OC survival, especially in late stage, was observed in the study period. Our findings showed demographic, especially race-associated, and geographical variations of OC survival. OC survival also differed by first course treatment received and histology. These differences indicate disparities in OC care.

Introduction

Among gynecologic malignancies, cancer of the ovary is less common than cancer of the breast and the uterus, but it has the highest fatality-to-case ratio, accounting for almost half of the deaths from cancers of the female genital tract.[1] In the U.S., 22,440 women were expected to be diagnosed with ovarian cancer (OC) and 14,070 women were expected to die from it in 2018.[2] According to a 2011 report, in Missouri (MO), ovarian cancer ranked tenth as a common invasive cancer among women; however, its death rate ranked in the top five.[3] Population-based cancer survival provides an indicator of the effectiveness of screening, early diagnosis and treatment. Survival differences between groups suggest disparities in access to early diagnosis and optimal treatment.

In addition to broad population-based implications, accurate survival statistics also offer patients an understanding of the disease nature and course and guide clinicians in counseling and management.[4] There is a lack of information on OC cancer survival among MO women. The aim of the study is to describe the relative survival (RS) for OC in MO overall, by demographic and by clinicopathological characteristics.

Methods

Data

Survival data from the Missouri Cancer Registry were obtained for cases diagnosed from 1996 through 2014. Using SEER*Stat, we analyzed five-year RS rates with follow-up through 2015. RS is the ratio of overall survival for cancer patients to the expected survival of a comparable group of individuals free of cancer.[5] RS provides a measure of excessive mortality experienced by cancer patients without needing cause of death information. For many cancer registries, cause of death information obtained from death certificate is either unavailable or unreliable due to misclassification errors or inherent ambiguities in determining the underlying cause of death (e.g., a metastatic site might be reported as the cause of death rather than the true underlying cause, the original cancer site).[5]

Demographic groups in the analysis included age (<40, 40-49, 50-64, 65+), race (white, black or other), marital status (single, married, separated, divorced, widowed

Figure 1. Five-year relative survival of ovarian cancer in Missouri by stage and year of diagnosis Note: The figure only shows trends from year 1996 through 2000 due to incomplete data for the estimation of five-year RS after year 2010.

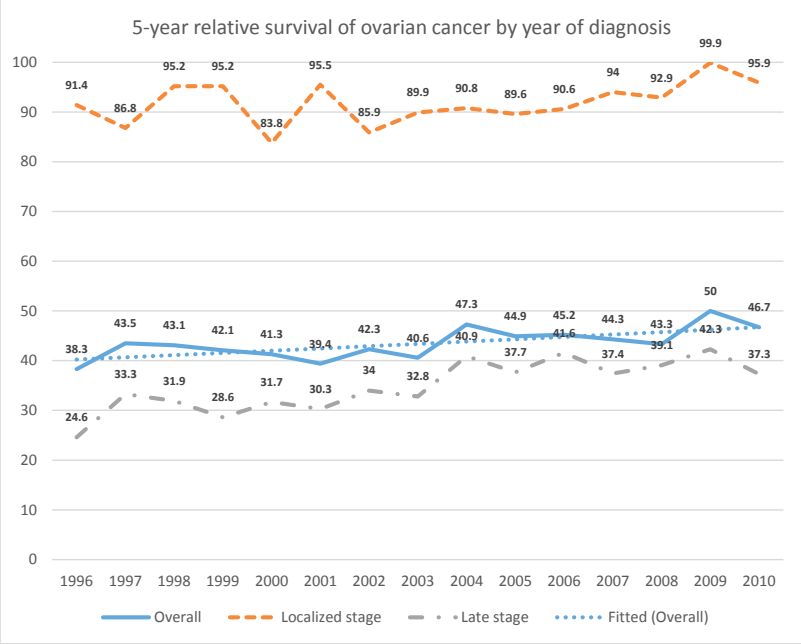


Table 1. Five-year relative survival of ovarian cancer by demographic characteristics in Missouri, 1996-2014.

	Relative survival	Number of cases
	% (95% CI)	
Age group		
<40	77.9 (73.8-81.5)	510
40-49	65.1 (61.6-68.5)	842
50-64	51.8 (49.5-54.1)	2296
65+	27.6 (25.8-29.4)	3398
Race		
White	44.2 (42.8-45.6)	6443
Black	38.9 (34.0-43.7)	501
Other	57.0 (41.2-70.0)	65
Marital status		
Single	52.9 (49.3-56.4)	968
Married	51.0 (49.1-52.9)	3454
Separated	47.0 (31.2-61.2)	48
Divorced	47.0 (41.1-49.2)	726
Widowed	23.1 (20.7-25.7)	1630
Unknown	39.7 (32.5-46.9)	210
Geographical regions		
Kansas City Metro	45.4 (42.3-48.5)	1307
Jackson County	43.6 (39.6-47.6)	786
St. Louis Metro	45.8 (43.5-48.0)	2492
St. Louis City	38.8 (33.1-44.5)	364
St. Louis County	46.6 (43.6-49.6)	1385
Central	41.4 (37.3-45.4)	757
Southwestern	44.1 (40.7-47.4)	1090
Southeastern	39.5 (35.6-43.4)	744
Northwestern	43.0 (36.8-49.1)	317
Northeastern	40.7 (34.5-46.8)	339
Metro vs. non-metro		
Metro	45.7 (44.1-47.3)	4962
Non-Metro	39.7 (37.3-42.1)	2084

or unknown), geographical region (Central, Southwestern, Southeastern, Northwestern, Northeastern, Kansas City metro and St. Louis metro), general metro vs. non-metro status based on 2003 Rural-Urban Continuum Codes, and MO's three most populous county or county equivalent over 1996-2014 (St. Louis City, St. Louis County, and Jackson County). RS was also analyzed by clinicopathologic characteristics including stage of diagnosis [localized, late (regional and distant) or unknown], first course treatment (surgery, no surgery or unknown), grade (well-differentiated, moderately differentiated, poorly differentiated, undifferentiated or unknown) and histological types (serous, epithelial not otherwise specified, endometrioid, mucinous, clear cell and other epithelial including mixed histology). Histology types were categorized using International Classification of Diseases for Oncology, 3rd Edition (ICD O-3) histologic codes. Ovarian cases were defined according to SEER's "Site Recode ICD-O-3/WHO 2008" variable. The first course treatment was based on codes for surgery at primary site.

Results

A total of 7046 OC cases were included in the analysis. From 1996-2014, OC RS in MO was 44%, slightly lower than the national rate of 46.5% (SEER-18 2007-2013). An increasing trend (annual percent change of 1.08% increase per year) of overall OC 5-year RS rates was observed in the study period (Figure 1), which is in line with the increasing national trend.

Table 1 displays OC RS by demographic characteristics at diagnosis from 1996 through

Table 2. Five-year relative survival of ovarian cancer by clinicopathologic characteristics in Missouri, 1996-2014.

	Relative survival	Number of cases
	% (95% CI)	
Stage of diagnosis		
Localized stage	92.7 (90.2-94.6)	1137
Late stage (R+D)	35.9 (34.4-37.3)	5332
Unknown	19.4 (15.9-23.1)	577
First course treatment		
Surgery	55.1 (53.5-56.6)	5411
Nosurgery	6.1 (4.7-7.7)	1330
Unknown	44.0 (42.6-45.3)	305
Grade		
Well-differentiated	88.1 (83.9-91.2)	548
Moderately differentiated	60.9 (57.3-64.2)	1004
Poorly differentiated	40.0 (37.8-42.1)	2702
Undifferentiated	37.0 (29.8-44.3)	322
Unknown	32.1 (30.0-34.2)	2470
Histology		
Serous	40.6 (38.6-42.6)	3052
Epithelial,not otherwise specified	26.1 (23.2-29.0)	1121
Endometrioid	78.5 (74.5-82.0)	675
Mucinous	68.4 (62.9-73.3)	419
Clear cell	68.5 (62.4-73.8)	338
Other epithelial including mixed histology	23.9 (19.3-28.8)	385

2014. Almost half of cases (n=3398 out of 7046) were diagnosed at age 65+; this group also had the lowest RS rate (28%) among all age groups. Most of the diagnosed cases in the analysis were white (n=6443). RS rates for white, black, and other were 44%, 39%, and 57%, respectively. Single and married women had relatively higher RS rates (53% and 51%, respectively) compared to those with other marital status. Among regions, Southeastern MO had the lowest (40%) and St. Louis Metro, the highest (46%) RS rate. Metro areas had higher RS rates than non-metro areas (46 vs. 40%). The City of St. Louis had a lower RS rate (39%) than St. Louis County (47%) or Jackson County (44%).

Table 2 presents OC RS by clinicopathologic characteristics. A majority of cases were diagnosed at late stage (n=5332) with five-year RS rate of 36%. RS rate for localized stage (n=1137) was 93%. Both stages experienced small but increased RS trends in the study period (Figure 1). Most patients underwent surgery as the first course treatment (n=5411); this group also had the highest RS rate (55%) compared to those who had no surgery (6%) or with treatment unknown (44%). With regard to grade classifications, those with well-differentiated OC (88%) and moderately differentiated OC (61%) had higher RS rates, compared to those with poorly differentiated (40%), undifferentiated (37%) or unknown (32%) grade for OC. More than half of the cases had poorly differentiated tumors or unknown grade status at the time of diagnosis (n=2702 and 2470, respectively). In terms of histological type, nearly half of the cases in the analysis were serous (n=3052). Among six categories of histological types, endometrioid OC had the highest RS rate (79%), followed by clear cell (69%), mucinous (68%) and serous (41%). Epithelial and other epithelial with mixed histology had the lowest RS rates (26 and 24%, respectively).

Discussion

Our findings suggested that, similar to the increasing national trend, OC survival has improved from 1996 to 2014 in MO.[1] This improved survival was observed especially in late stage tumors. During the past 30 years, the importance of tumor cytoreductive surgery has been recognized.[6] Likewise, adjuvant therapy for advanced-stage OC has also evolved with many new therapies introduced.[6] The improved survival for ovarian cancer seems promising. However, previous research noted that the survival gains have been predominately realized through prolonging the life expectancy of women with recurrent ovarian cancer, not through an increased cure rate.[7] This indicates the ongoing challenges in developing adequate screening and surveillance strategies to increase the cure rate of OC.[8,9]

Our findings showed a white-black OC survival gap in MO. Previous studies suggested that black patients are more likely to be diagnosed at later stage,[10] present with more aggressive tumors,[11] and have a poorer response to treatment.[12] In addition to biological and comorbidity differences,[13] the most concerning factor to racial disparities of cancer survival is the failure of black women to receive suitable cancer treatment, due to underuse of surgical resection and/or adjuvant therapy.[14] Indeed, our separate analysis showed that fewer black OC patients underwent surgery compared to their white counterparts

(67% vs. 77%). But for those black patients who received surgery, their RS was similar to white patients who received surgery: RS 54.1, 95% CI (47.7-60.10) and 55.0 (53.4-56.6) for blacks and whites, respectively (results not shown in Tables). Reasons underlying differential receipt of cancer treatment might include:

1) Unequal access to care, where black patients were more likely to be treated by physicians who were less well trained clinically and had more limited access to important clinical resources (e.g. specialists, high-quality imaging, high-quality ancillary services, and non-emergency hospital admissions) than physicians who treated white patients.[14]

2) Poor physician-patient relationship, where some physicians hold mistaken beliefs and implicit racial bias that black patients were more likely to be less educated, with poor social support and more likely to be at risk for non-compliance, therefore deter referring them for radical surgeries.[15,16] Perceived racism by patients can also undermine physician-patient relationship and result in mistrust and refusal to proceed with recommended treatment.[15,16]

3) Patients' misconception of cancer and its treatment may also adversely impact their willingness to undergo surgery.[17] Racial disparities in cancer care including OC care has been a long-term challenge in MO as well in the U.S.[18] This stresses the need to improve care access and utilization for black patients. Continued efforts to increase the number of the racial/ethnic minorities entering surgical specialties are warranted.[19] Expanding use of patient navigation programs where information and social support can be offered for black patients should also be strongly considered.[20]

Our findings also showed age-associated differences. Consistent with earlier findings, we saw a survival gap between the elderly (i.e., 65+) and younger groups. It has been reported that elderly cancer patients are less likely to receive potentially morbid treatments like surgery or chemotherapy regardless of the cancer stage,[21] Our separate analysis showed that the proportion of OC patients receiving surgery decreased as age increased (96%, 94%, 88% and 62% for age groups <40, 40-49, 50-64 and 65+ years, respectively) (results not shown in Tables). Older age is associated with higher rates of toxicity from chemotherapy and radiotherapy.[22-24] Less aggressive treatment plans are often given to older patients in consideration of their functional impairment, malnutrition, and comorbidity.[25-27] Additionally, there is insufficient evidence to determine how well they would respond to novel targeted therapy or combinations of chemotherapeutic agents due to their underrepresentation in clinical trials.[28,29] Caring for older cancer patients is complex, both medically because of comorbidities and polypharmacy, and psychosocially because of variable social support and financial constraints.[30] As the elderly continues to be the fastest growing subpopulation of cancer patients in MO as well as nationwide,[31] it is pressing to search for optimal treatment regimens and high-quality and patient-centered care plans for this frail patient population.[30]

In addition, we saw differences of OC survival across marital status in the study. Widowed OC patients had the poorest survival possibility due to the strong correlation between widowhood and old age.[32] Divorced and separated OC patients had slightly poorer survival compared to those who are married, which is possibly a result of lower social support from spouse.[33] Marriage directly imparts a benefit through social support, which promotes a married cancer patient receiving recommended or aggressive treatments.[34,35] Interventions centered on social support services might reduce survival disparities to those widowed, divorced, and separated OC patients.

Across geographical regions, we found rural areas, Southeastern MO and City of St. Louis had the lowest survival rates. Potential explanations for geographic variation in cancer survival include patients' characteristics, such as racial/ethnic background and health behaviors, and area-based characteristics, such as poverty and geographic access to healthcare.[36] Indeed, these two regions with poor survival identified in our study are areas where racial minorities and socioeconomically disadvantaged reside.[37] It is known that people with minority background and living in poverty are facing more barriers in cancer prevention and control.[18] They are less likely to engage in healthy lifestyles, less likely to access and use cancer care compared to their white and affluent counterparts.[18] Our study may suggest geographical disparities of OC in MO. Further studies are needed to better understand the factors predicting utilization of existing healthcare resources in these areas, and if these influence the OC survival outcome. Also, research on acceptability, accessibility and affordability of health care may inform efforts to increase utilization of healthcare resources among disadvantaged OC patients in these areas.

With respects to OC survival by clinicopathological characteristics, we found that OC patients who received sugary as the primary treatment had a much higher RS rate than those who did not have the surgical treatment. It appears that patients who underwent the debulking surgery or oophorectomyduring in the study period,[4] had

much improved survival compared to patients undergoing no surgery (RS for debulking, cytoreductive surgery, oophorectomy and no surgery were 35, 67% and 6.1%, respectively). However, we are cautious in making such a conclusion due to the uncontrollable confounding factors in the population-based cancer surveillance data. It is possible that patients from the registry database not undergoing the surgical treatments were experiencing medical comorbidities, with disease burden or other factors that place them in a high-risk group, which led to their poorer survival.[4] Because of unavailability of data, we also are not able to make a comparison between the effectiveness of treatments such as upfront debulking surgery or neoadjuvant chemotherapy. Neoadjuvant chemotherapy is the possible alternative treatment option to standard treatment in patients unable to undergo complete resection during primary debulking surgery.[38] Many randomized clinical trials attempted to determine the better primary therapy between upfront cytoreduction and neoadjuvant chemotherapy.[39-41] However, findings are mixed and further studies are warranted to clarify the precise role of each therapy in the management of advance OC.

Our study also showed that OC survival differed by histology. Similar observations were noted in other studies.[42,43] Serous carcinoma had lower survival compared to non-serous carcinoma, which may be related to the later diagnosis.[42] Serous carcinoma is found predominantly in later stage.[44] In contrast, mucinous, clear cell and endometrioid carcinomas tend to remain confined to the ovary.[44] Poorest survival was seen for unspecified tumors.[44] These unspecified carcinomas grow rapidly, usually exhibit extra ovarian spread, and have poor prognosis.[44] Our study added population-based evidence on OC survival in MO and suggests that OC is not a single disease, and that each subtype has its unique molecular profile and biological behavior, which requires relevant therapeutic strategy.[45]

Strengths and Limitations

To our knowledge, this study is the first to describe OC survival in MO with population-based registry data. We included multiple years of registry data and were able to stratify analysis based on available demographic and clinicopathological characteristics. We used RS as the outcome, which is advantageous compared with disease-specific survival or overall survival as it accounts for competing causes of death by adjusting the general survival rate for that same age, race, and date of diagnosis.[5]

Restrictions inherent with population-based cancer surveillance data limit our study. First, because cancer registries do not routinely collect the mode of diagnosis (i.e., symptomatic, screened, or incidental), it is impossible to rule out the effects of early diagnosis solely based on improved survival using population-based surveillance data. Lead-time bias, introduced by early detection, typically from screening or incidental detection with advanced imaging, potentially exists.[46] Also, the lack of pathologic validation for every case in cancer registry data could have led to misclassification of tumors.[4] Additionally, because of the nonrandomized nature of the registry data, we cannot test the hypothesis whether the improved survival was attributable by advanced treatment such as surgical and/or adjuvant therapy. It is possible that those who survived longer may represent a different subset of patients with respect to the natural history of the disease.[4]

Conclusion

This study showed an improved OC survival over time in MO and suggested demographical and clinicopathological disparities in OC. Race- and age-related variations in survival improvements may be explained, at least in part, by differences in care across these subpopulations. Findings on geographical difference of OC survival also indicate a need for improving detection and treatment in racially and socioeconomically disadvantaged regions. Our findings, from a population surveillance perspective, suggest OC survival differed by primary treatment plan received and by histological subtype. Future studies should include diverse populations and stratified analysis by different prognostic characteristics to set up specific strategies for OC patients. Our study is also a call for action. To reduce disparities of OC burden in MO, action is needed at multiple levels. Individuals at risk need to be informed and equipped with knowledge, skills and motivations to seek healthy lifestyles and timely medical check-up. Communities such as health care facilities, work places or faith-organizations are good venues to reach individuals, forming, and reinforcing health behaviors. Resources should be allocated to those socioeconomically disadvantaged, eliminating financial and access barriers to health care.

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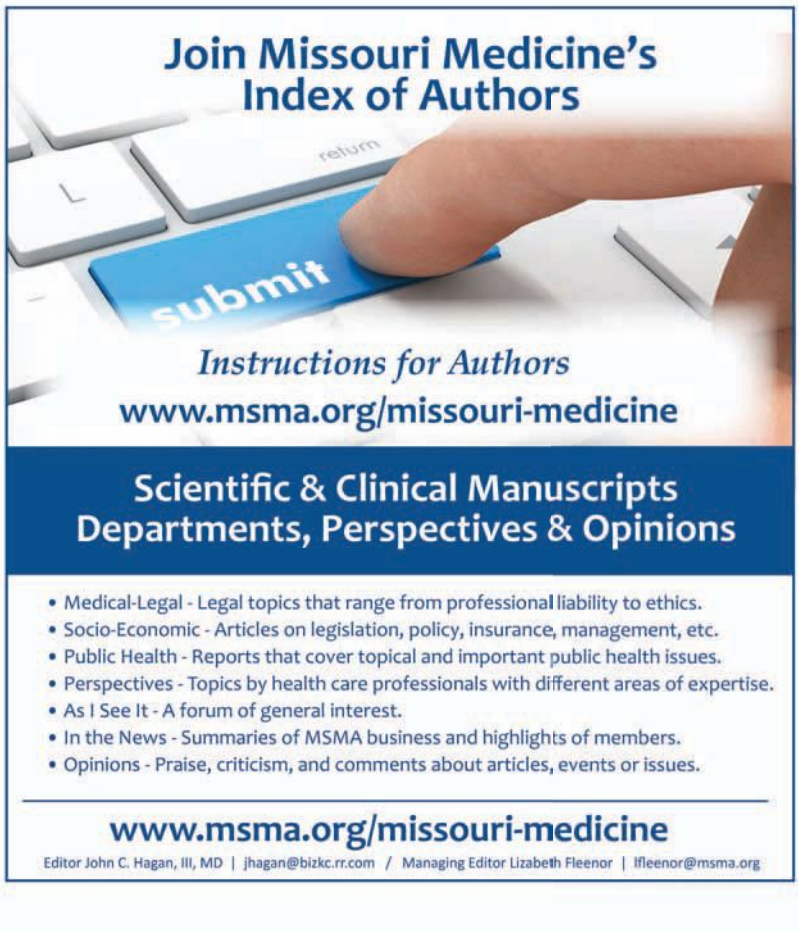
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