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The Journal of the Missouri State Medical Association – Since 1904

Volume 121 | Number 6 | November/December 2024 **www.msma.org/missouri–medicine**

GUEST EDITORIAL
As Hospitals Grow, So Does Your Bill
by David Wainer 414

FEATURE PERSPECTIVE
America's Broken Health Care System:
Can Doctors Lead the Fix?
by Alisa M. Berger, MD 416

PERSPECTIVE
Thwarting the Harm Caused by Private Equity in Surgical Practices … and Even in the NFL: Part 2
by Andrew Schlafly, JD 419



COVID-19 RETROSPECTIVE ANALYSIS
Optimizing Missouri's Preparation for the Next Pandemic: Lessons Learned from COVID-19: Part 1
by **David S. McKinsey, MD, Joel P. McKinsey, MD**, Julie R. McKinsey, BS & Maithe Enriquez, PhD 424

SCIENTIFIC PERSPECTIVE
Communication and Follow-Up of Noncritical Actionable Imaging Findings
by Govind Mattay, MD & **Andrew Bierhals, MD** 433

ADVOCACY
Countdown Begins for Missouri's General Assembly
by Jacob Scott, MA & Rachel Bauer, MPA 436

PRESIDENT'S FORUM
Time for Action!
by **David L. Pohl, MD** 441

AMA REPORT
Report of the American Medical Association Interim Meeting
by **Charles W. Van Way, III, MD**
& the Missouri AMA Delegation 442

MILITARY MEDICINE
Military Medicine and Medical Education in Missouri
by Ulysses Fernandez-Miro, Capt, DO, Pamala R. Huges, Lt Col, MD, Luke F. Jett, Lt, MD, Craig Krausz, MD, Richard K. Newman, Capt, DO, Brandon M. Parham, Capt, & Julie K. Gammack, MD 445

INSPIRING LIVES AND CAREERS
From Space Stations to the US Marines...From Engineering to Private Practice Surgery...A Physician is Right at Home
by **William Reynolds, DDS, MD** 452

MEDICAL | LEGAL
Beyond Malpractice: When Practice Becomes Criminal and Related Implications for Healthcare Providers
by Ashley Todd, JD & Tessa Carberry, JD 456

SCIENCE OF MEDICINE | FIRST WORLD LITERATURE REPORT
Timolol 0.5% Eye Drops for Essential Tremor: First Successful Case Report
by **John C. Hagan III, MD**
& **Steven C. Kosa, MD** 464

SCIENCE OF MEDICINE
Advancing Psychedelic-Assisted Therapy in Missouri (MO-PAT): Innovation at the Speed of Safety
by Danielle R. Adams, PhD, Torie Gettinger, PhD, Nathaniel Dell, PhD, Leopoldo J. Cabassa, PhD
& **Ginger E. Nicol, MD** 467

Revival of a Beast: The Challenges Facing the Management and Control of Syphilis in Missouri from 2000 to 2024
by Hilal Abdessamad, MD, Wassim Jamaleddine, MD, Christian Rojas-Moreno, MD
& Dima Dandachi, MD 474

Energy Drinks: A Clinical Primer and National Data Update
by Kevin Y. Xu, MD, Kevin T. Baumgartner, MD, Suraj Shankar, MD, **Alison Huckenpahler, MD, PhD** & Paul E Glaser, MD, PhD 481

Glucagon Like Peptide -1 Receptor Agonists for Weight Loss: A Primary Care Perspective
by **Kara Mohr, MD** & Clayton Butcher, MD 489

Pulmonary Embolism Education: Role of Generative Artificial Intelligence Models
by Rohma Zaidi, BA, Jonathan Asghedom, BS & Som Singh, MD 495

FROM YOUR ASSOCIATION
1 Picture = 1,000 Words 415
MMPAC Annual Membership 439
Correspondence 461
In the News 462
Errata 462
New Members 463
In Memoriam 463
2024 *Missouri Medicine* Index 499

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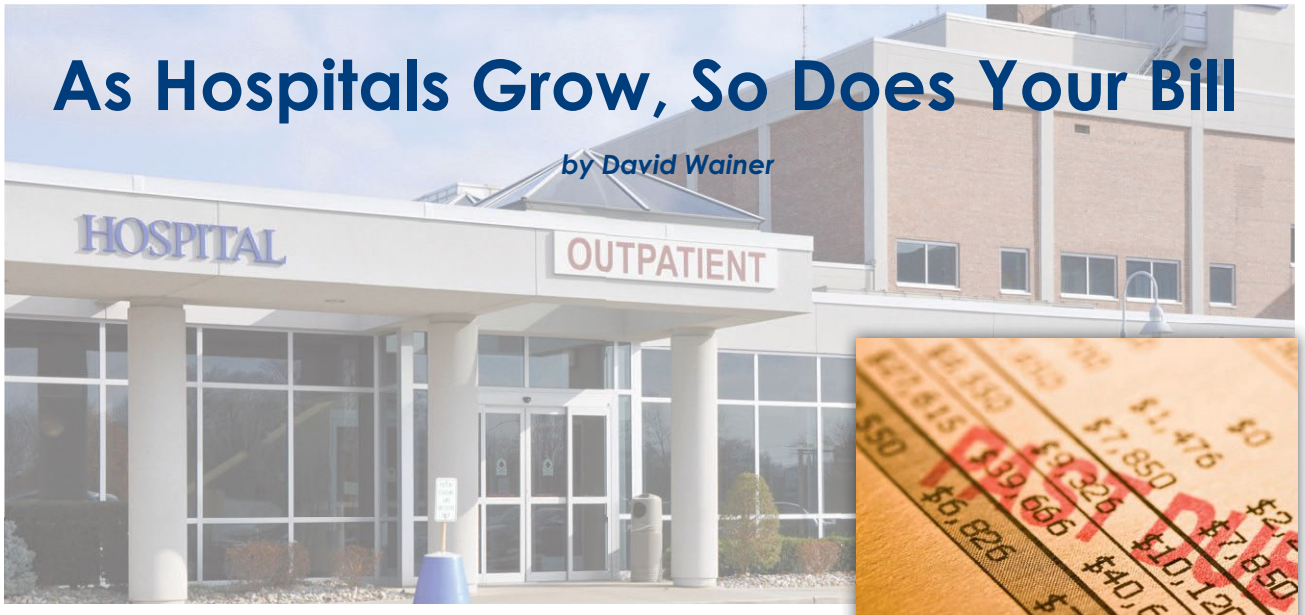
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As Hospitals Grow, So Does Your Bill

by David Wainer



If the fries at your local burger joint are soggy or if you're suddenly charged $25 for ketchup, you'll probably eat somewhere else next time. That's the beauty of competition.

Healthcare doesn't quite work that way. For starters, you don't always get to choose your medical provider—your insurer often does by contracting with them. And even the insurer can't easily walk away, either: Giant hospital systems are swallowing up big chunks of the country's healthcare system through vertical and horizontal integration. That leaves fewer parties with which to negotiate.

If McDonald's bought Burger King and then Wendy's, you could always cook at home instead, but nearly everyone needs to go to the doctor or the hospital at some point. Patients also aren't nearly as cost sensitive as they would be with other purchases because employers and insurers pick up much of the tab. They often don't even know the price ahead of time.

Hospital executives argue that mergers lead to improved efficiency and better outcomes for patients. But, after years of rampant consolidation between hospitals, most regions in the US are now dominated by a few large players. That has led to higher prices and no significant improvements in patient care.

Rising costs don't just lead to alarmingly high medical bills—they also make all of us worse off by increasing premiums, the bulk of which are paid by the nation's employers. That affects even people who rarely visit a doctor. As those premiums soar and employers look to offset the cost, they indirectly eat into people's paychecks.

Over the past two decades, there have been more than 1,000 mergers among the country's approximately 5,000 hospitals, according to a forthcoming paper in *American Economic Review: Insights.* During that period, the Federal Trade Commission took action against only 13 transactions, even though more than 200 of the deals would have met the FTC's bar for lessening competition. "The punchline is the FTC is underfunded, it's not enforcing enough and, as a result, lots of mergers that raise prices are happening," says Zack Cooper, a health economist at Yale University and one of the study's authors. "It's kind of a death by paper cuts."

More recently, the Biden administration has sought to beef up enforcement, especially when it comes to hospital mergers in the same geographic region, though this week it suffered a setback. Earlier this year, the FTC had challenged North Carolina-based Novant Health's acquisition of two other hospitals in the state from Community Health Systems, arguing that it would give Novant an "eye-popping 64% share of the market" in the Eastern Lake Norman area. On Wednesday, a federal court judge denied the FTC's bid for a preliminary injunction,



David Wainer is a healthcare columnist for the *Wall Street Journal*.
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arguing that the benefits of Novant acquiring struggling hospitals outweigh concerns about competition. Before the ruling, Novant said in a statement that the "FTC's one-size-fits-all opposition to all hospital transactions is, in this case, harmful to patients and dismisses compelling evidence that the transaction will enhance competition."

But tougher scrutiny on mergers between hospitals in the same geographic area has done nothing to slow down another approach to expansion: Hospitals buying up doctor's practices. Roughly one in every three healthcare dollars the US spends goes to hospitals. That is by far the largest cost category in American healthcare. To bring costs down, those paying for care with your money—insurers, the government and employers—have sought to move some of that spending into places like ambulatory surgery centers. Those are facilities where surgeries can be performed without hospital admission. Such efforts represent a major threat to large medical systems. In response, hospitals have snapped up or partnered with surgery centers and medical practices, too.

Hospitals aren't the only ones doing this. Insurers and private-equity firms all have been competing to acquire medical practices, with three out of every four doctors now working for either a hospital or a corporate owner. But sprawling health systems are by far the most dominant players, employing more than half of the country's doctors.

Some private-equity firms, as noted in the first article of this series, can raise prices without adding to overall quality of service by rolling up doctor's practices within a fragmented market. Hospital groups also increase their bargaining power with insurers when they acquire doctors. But it doesn't end there. After buying up physician groups, hospital groups collect billions of dollars in facility fees without really improving care, explains Cheryl Damberg, a senior health economist at nonprofit think tank RAND. They also use those practices to send more business their way. "Once a physician shifts from being at an independent practice to being employed or affiliated with a vertically integrated health system, they change their referral patterns and direct traffic to places like the hospital outpatient department," she says.

Another way to grow is by combining with hospitals in other regions through megamergers. In late 2022, Advocate Aurora Health and Atrium Health formed one of the country's largest nonprofit health systems, creating a medical powerhouse with more than $27 billion in annual revenue that linked up a major hospital system in the Midwest with one in the Southeast.

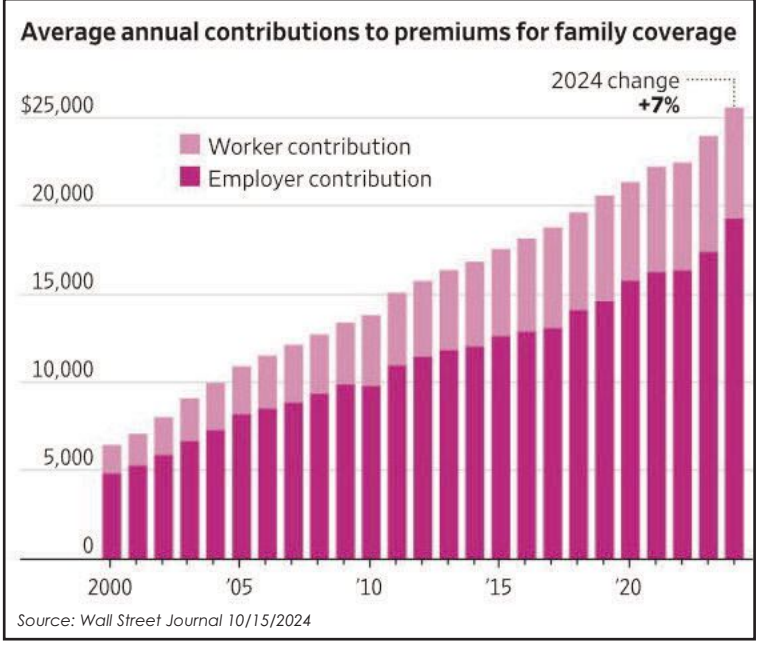
The deal faced pushback from various stakeholders who pointed out that employers in Wisconsin had sued Advocate Aurora, alleging the hospital system used its market power to gouge them. But because the two systems didn't have any geographic overlap—Advocate had a strong presence in Milwaukee and Chicago, while Atrium had headquarters in North Carolina—the FTC didn't challenge the deal.

Advocate Health, the merged entity, argued that the merger would make the combined system more accessible and affordable for all. Perhaps that will prove to be true, but at least three studies have now shown that mergers between hospitals in totally different geographies still contribute to higher prices. In a paper published in April, researchers found that six years after such deals, prices rose by about 13% on average compared with control hospitals. The reason is fairly straightforward: National employers prefer the ease of contracting with insurance plans that cover the whole country, so national hospital chains have more negotiating clout, explains one of the study's researchers, Daniel Arnold, a health economist at the University of California, Berkeley.

The bigger hospitals get, the more they can deploy bare-knuckle tactics to get what they want. For instance, they can demand guarantees that they will be included in all of an insurer's networks, even if a client doesn't want them, extensive *Wall Street Journal* reporting has shown.

Hospitals keep getting bigger while promising more access and affordability for patients. Instead, prices keep going higher. **MM**

1 PICTURE = 1,000 WORDS



Source: Wall Street Journal 10/15/2024

America's Broken Health Care System: Can Doctors Lead the Fix?

by Alisa M. Berger, MD



Physicians should not only be at the table of discussions regarding health care, but leading the inception and implementation of the solutions. Why aren't we? In part because we are too busy taking care of our patients.

America's health care system, much like Congress, is broken, and doctors have to be part of the solution. I don't know a single doctor who doesn't wish to improve our ability to increase access and the delivery of health services to our patients. Maintaining and/or improving the health of patients is our goal. That should be the goal of anyone associated with the health care system, but it's not. Currently, our system is infiltrated and plagued by profit. There's no quick fix or panacea. I have ideas on how to make improvements, but let me point out what I see as the biggest problems.

America's capitalist economy works well for many industries—but not all, and health care is not one of them. Health care is often not subject to the same standards of supply and demand and, therefore, cannot be considered a standard market. Insurance companies limit your choices when they force you to see someone "in-network," so your ability to choose the doctor you want is already curtailed, if not eliminated.

When your family member is sick, the typical response is to do everything to get them better. When that is an emergent situation, you don't stop and shop around for the best provider or cheapest deal. And despite what most people think, it's actually against the law to turn away a patient with an emergency due to lack of insurance. This is, in part, why community hospitals can no longer stay open. Such hospitals have to compete with for-profit facilities—



Alisa Berger, MD, is a practicing urologist in Texas.

This article first appeared at KevinMD.com and is reprinted with permission.

sometimes right next door–that usurp all the well-insured patients. Because they are bound to take care of emergent non-insured patients, who often make up a greater share of their population, they are bound to go broke. It's already happening as a community, and rural hospitals are forced to close their doors.

Hospitals do budget for indigent care, which is reimbursed by the government (you and me). Similarly, all those patients who can't afford to treat their chronic medical conditions who present in crisis to the ER with severe consequences of that neglect will get the services they need—which they cannot afford. So again, the government (you and I) are left to pay for that acute care—which is almost always much more than helping to subsidize the cost of maintaining their underlying diseases in the outpatient setting. So when you think about it, providing that basic level of health care to such patients is actually the economically smarter option. And clearly, it's the more humane and ethically appropriate thing to help prevent such morbidity when possible. There will always be non-compliance for sure, but most patients actually do want to take their meds—if they don't have to choose between that and paying for a roof over their head or putting food on the table. It's a win-win, so why are we not doing it? It's complicated, but I feel contributing factors are: corporate health care greed that gets its tailwind from capitalism, big players who pay the politicians, and polarized politics with taboo labels such as Obamacare and socialism.

The Big Players

I'd like to think that doctors are one of the big players. But as doctors, we know better. Physicians used to be considered the pillars of society. And sometimes, they still are. But more often, health care providers are often maligned and blamed for our current situation. Patients are shooting up doctors' offices and hospitals. Society has demonized doctors, and in a handful of cases, rightly so. There are some bad doctors out there who got into medicine for money. Or others who are now disenchanted with the practice and provide care based on reimbursement as opposed to the standard of care. Those bad apples are tainting the whole profession. But that's just it—they are bad apples among the bunch. Please know that most doctors really do want to help patients and keep them healthy.

Suffice it to say that physician salaries make up a minimal component of the overall health care expenditures at just 8.6% in 2011. And that was the second lowest among Western nations with a "modern" health care system. More than a decade later, physician salaries remain at 8.6% of health care spending. What most people don't recognize is that for the last 20 years, we've been getting paid a little less each year for the same services. What other industry is getting paid less each year for providing the same services? And it's just doctors—the other health care players have been getting incrementally more over this same time period. This explains why doctors now have to see more patients than they used to just to earn the same amount and cover the expenses—while the latter go up each year. And you can't pay your staff less each year—so that increase in overhead and staffing costs comes out of the doctor's salary. The medical assistant (MA) can now earn more at Buc-ee's or Costco than we can afford to pay them to work in our office. Therefore, the physician practice model pendulum has swung away from private practice and towards employment, being bought out by hospitals or, worse, private equity firms. The private practice solo physician is a dying breed; it's just not sustainable in our current system.

If doctor salaries are not the problem, what is? Let's start with the biggest player: insurance companies. It's in the interest of insurance companies to deny coverage and care as often as possible. It's expensive to keep you healthy. But it's even more expensive to try to treat you when you are sick. When we make being healthy (preventative care) a priority, in the long run, we all do better. But health care companies are in it for the bottom line—which is here and now. Denials of coverage for things practicing physicians have ordered are the norm. Prior authorizations have become such a nuisance that we are making state laws to help deal with this. Texas led the way with the gold card bill, which intended to exempt physicians with prior authorization approval rates of more than 90% from having to get prior authorizations at all. Unfortunately, it's rare for a

doctor to even know of their gold card status, and there is no punitive component when an insurance company doesn't comply.

Similarly, the Affordable Health Care Act (ACA), a.k.a. "Obamacare," enforced the 80/20 rule—which said that 80% of the premiums they collected had to be spent on medical claims. This was to both reduce insurance company profits and hopefully decrease premiums. My family and I got a check from my insurance company that next year for more than $500. But no surprise, we never got another check again because the insurance companies implemented workarounds—namely, increasing the costs of medical claims. So these laws end up having great intentions but with absolutely no practical impact.

While insurance companies placed the blame for rising rates on the ACA (which is technically accurate as it was their own reaction to the 80/20 rule), they still were able to increase the pay of their CEOs. The combined CEO salaries of the eight largest publicly traded insurance companies—including pharmacy CVS, which acquired insurer Aetna—was $143.5 million in 2017, up 14.4% from the year before. As of 2023, the top-paid insurance CEO made over $22 million. Meanwhile, premiums are rising at a much faster rate than overall wages—leaving the average American unable to even afford health insurance.

The next big player is drug companies. While the drug companies are paying their CEOs tens of millions, most Americans can't afford their prescriptions. In 2022, the top 10 pharmaceutical company CEOs made $28 million/year or more, with the highest paid getting more than $124.9 million/year. Thank God for Mark Cuban, Alexander Oshmyansky, and Cost Plus Drugs. Although they are a company seeking profits in order to stay in business, that's clearly not their motivation. The mission is clearly stated on their website: "We will provide low-cost, high-quality pharmaceuticals to the consumer… by any means possible." While Mark Cuban states, "I could make a fortune from this … But I won't. I've got enough money. I'd rather f— up the drug industry in every way possible." Why can't the government do something like this? Because the politicians are in the pockets of the big players.

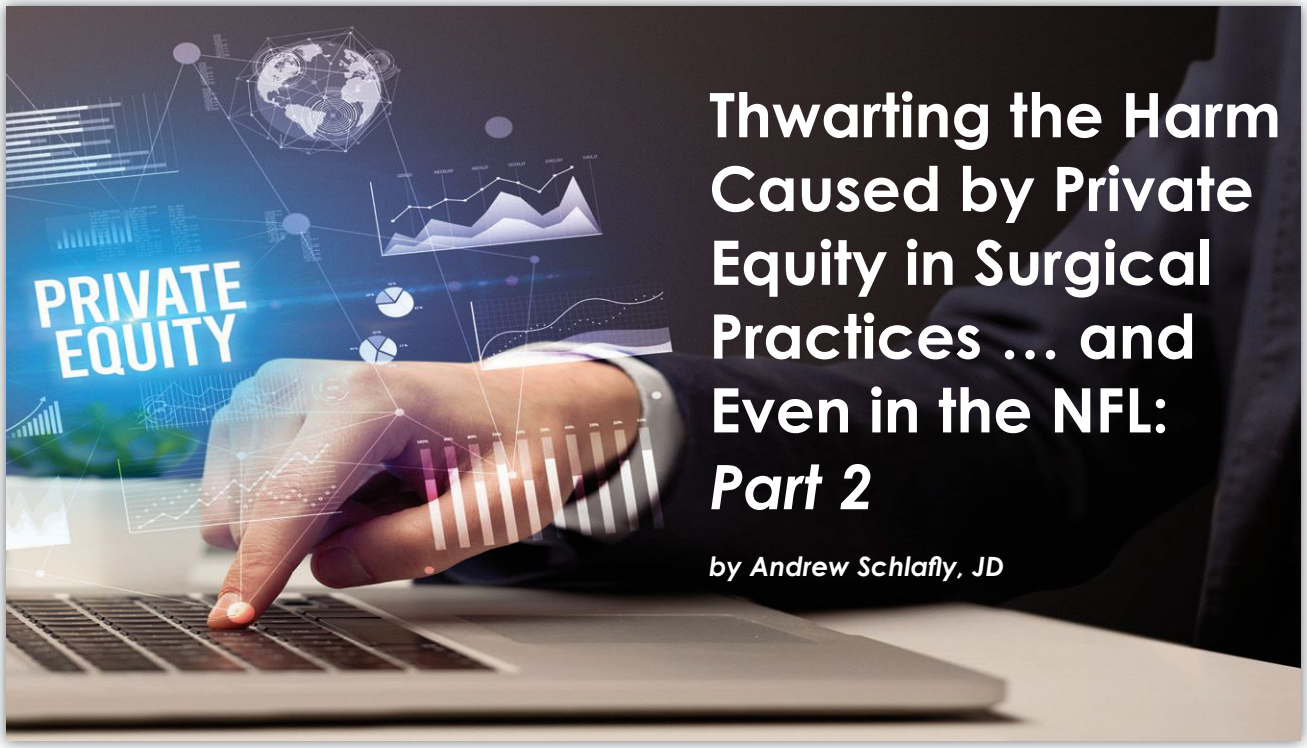
The final big player is the health care administration. From 1990 to 2012, the US health care workforce grew by 75 percent. All but five percent of that job growth was in administrative staff, not doctors. For every doctor, there were 16 health care workers, and only six of those were involved in actual patient care (nurses/aides). The other 10 represented purely administrative roles. And it's not from increased utilization as the number of days Americans spent in the hospital decreased by 12 percent, while hospital staff grew by 11 percent from 2002-2012. Why were all these people added? What are they doing? We do need someone to run a hospital and its staff, but what are all those extra people doing? Some even project this field will grow by 32% from 2019 to 2029! I cannot comprehend how the exorbitant 75% of the layers we now have are truly needed, nor that they result in improvement in patient care.

The economic structure that allows anyone and everyone to reap profits from the health care system, the insurance and drug company domination of the market and politicians, and the outsized ballooning of health administration are the biggest insults to the American health care system as this practicing physician sees it. The goal of our system needs to be the health and welfare of patients—which is almost uniformly the goal of all physicians practicing medicine. Physicians should not only be at the table of discussions regarding health care, but leading the inception and implementation of the solutions. Why aren't we? In part because we are too busy taking care of our patients to spend the time and money to educate and influence politicians. But politicians need to step aside and defer to those actually practicing medicine for solutions. As doctors, we also fight about the politics of medicine, but at the end of the day, patient care is what unites us—not getting re-elected. I'm ready to start addressing these problems and finding some practical solutions. Let's let doctors lead the way.

Sources

1. https://drive.google.com/file/d/1zXFZnfcH7ziZpFuf1lrXeGdGgyVqUQLn/view
2. 10 administrators for every 1 doctor. We deserve a better healthcare system - PNHP
3. Health Care Administration Job Outlook and Salary | USC EMHA Online

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Thwarting the Harm Caused by Private Equity in Surgical Practices … and Even in the NFL: *Part 2*

by Andrew Schlafly, JD

Isn't medical care as important as what happens on the gridiron?

In our first installment of this article (September/October 2024;121:328-332), we explained the harmful impact by private equity (PE) in taking over medical practices and hospitals. The predictable result has been more debt, more bankruptcies, higher prices, and less quality care, as we explained. This deprives patients of maximum access to affordable medical care. Good physicians are forced into retirement early, or are pressured into practicing solely for profit rather than doing what is best for their patients. "After private equity acquisition, hospital assets decreased by 24% relative to that of controls during two years," according to a recent article in *JAMA*. "Private equity acquisitions appear to have depleted, rather than augmented, hospital assets," it added.[1]

Tax loopholes are behind the skyrocketing assets available to PE managers, who are allowed to shift their compensation from the high income tax rates that everyone else pays to the far lower capital gains tax rates. With this unique benefit for PE, its assets have soared from only $1 trillion in 2006 to $8.2 trillion in 2023, which now exceeds one-seventh of the entire value of US stock markets combined. Flush with cash, in the past decade private equity has spent nearly $1 trillion on buying up medical practices.

Healthcare is especially attractive to PE both because there is an enormous, never-ending flow of money in this sector of the economy, and because healthcare is largely immune from recessions. Here in the US, healthcare is a record level of nearly 20% of our gross domestic product, totaling $4.5 trillion annually. This is far higher spending than anywhere else in the world, and much of the healthcare dollars goes to insurance companies and administrators, and now to PE managers.



Andrew Schlafly, JD, is General Counsel of the Association of American Physicians & Surgeons. This is part two.

In nearly every medical specialty, a substantial fraction of the groups are owned now by a private equity firm, particularly in metropolitan areas. For example, more than a quarter of emergency rooms in our country are owned by private equity firms now.

Even the NFL has begun allowing a private equity invasion into the ownership of the teams. In August of this year, PE firms obtained approval by NFL owners to buy up to 10% of individual teams, but with the restriction that this ownership interest must be held for at least six years before reselling it. NFL owners limited the list of eligible PE investors to merely a handful of approved firms.

Isn't medical care as important as what happens on the gridiron? If most PE firms are not considered ethical enough to buy into the NFL, then they should not be allowed to control medical decisions either. Yet there are almost no guardrails protecting patients and physicians against exploitive business practices of private equity as it continues to invade healthcare.

As explained a few months ago by Congress's Joint Economic Committee, in its report entitled "Predatory Private Equity Practices Threaten Americans' Health and the Economy":

Public companies bought by private equity management firms are approximately 10 times more likely to go bankrupt than a control group subject to the same market forces. That's largely because of how PE firms purchase companies. PE investors, typically wealthy individuals or institutional investors, often fund their acquisitions by taking out large loans. Frequently, about 70% of the money that PE investors use to buy a company will come from loans—allowing them to only pay 30% from their own funds. The acquired company then becomes responsible for paying off this debt. This is called a "leveraged buyout."[2]

The harm caused by private equity's invasion of surgical specialties is particularly acute. As every surgeon knows, sometimes the best advice to a patient is not to operate, but decisions not to operate result in fewer profits to the PE firm that purchased the practice for a short-term gain. Medical care is fundamentally different from selling a new computer or automobile, where every new transaction is to be promoted and encouraged in order to boost profits.

Private Equity Takeover of Surgical Specialties

The purchase by private equity of surgical specialties is considered to be the third of four phases of this invasion by PE into healthcare. The first phase was the acquisition by private equity of ambulatory surgery centers. The second phase was private equity investing in physician groups having exclusive contracts at hospitals, most notably emergency medicine and radiology. The fourth phase is private equity acquiring ownership of medication and patient management-related specialties, including primary care, cardiology, oncology, rheumatology, allergy, ophthalmology, and ear, nose and throat specialists.

Surgical practices are particularly susceptible to distortions caused by PE ownership, which can result in unnecessary or inappropriate surgeries in order to drive up short-term profits at the expense of the best decision-making for patients. The business model of PE acquisitions is to resell medical practices and other acquired targets within four to seven years of purchasing them, such that building long-term relationships with patients and others is not a goal of this approach. It is noteworthy that the NFL bans a quick exit in a few years, or "flipping," of an investment by PE of an NFL team, yet there is no such limitation on PE acquisitions in healthcare.

Debt is used heavily by PE acquisitions, and the recent run-up in interest rates caused valuations to decline because it becomes less affordable to pay off the interest charges while also paying a high price for a practice. As interest rates decline, it is predictable that the rate of private equity acquisitions will increase again.

The quick flipping of the investment has the effect of decreasing valuations further, similar to how a bankrupt owner of real estate is likely to sell off his property at fire-sale prices, and thereby tend to reduce the valuations in the neighborhood. Presumably this is why the NFL owners, who want to maximize the value of their own ownership interests in teams, have carefully prohibited PE firms from flipping their investments in a team within a short period of time.

More than 330 private equity takeovers of ophthalmology practices have occurred in the last six years. In 2019, the last year prior to Covid, takeovers of ophthalmology and optometry practices averaged 5.71 per month and, after the worst of the Covid pandemic, increased to 8.78 per month from January to September 2021.[3]

Lobbying by powerful private equity firms is changing the landscape of where mothers give birth. This year an influential private equity company that owns obstetrics practices successfully lobbied the

legislature in Florida to make it the first state to allow Caesarian sections to be performed outside of hospitals. Private equity overcame vocal opposition by the Florida Hospital Association to make this landmark change, which will likely shift most childbirth services to private-equity owned birthing centers rather than hospitals.[4]

As to dermatology, the aging American population makes dermatology practices an attractive target for private equity, and PE owns more than 10% of the dermatology market nationwide. But studies show that when PE takes over a dermatology practice, it subsequently generates a 5 to 17% increase in volume, while charging 3-5% more for routine appointments. PE also employs more physician assistants and nurse practitioners, rather than physicians.

"Get that money!!" screamed an August 2020 memo sent to employees in Michigan of Pinnacle Dermatology, a chain of 90 dermatology practices owned by private equity. "Don't forget the August bonus incentive for all patients scheduled in August! That's the easiest money you can make," the hard-charging PE management insisted of dermatologists in those clinics. A physician who questioned management was terminated, and she then shared her concerns with NBC News, which included "overlooked diagnoses, lost patient biopsies, questionable quality control in the company-owned lab and overbooking of patients without sufficient support staff."[5]

Policy Solutions

There are several policy approaches that can be taken to protect patients and physicians in Missouri, and nationwide, against the harm being inflicted by PE acquisitions of medical care.

Greater transparency and bans on non-compete provisions would help. So would strengthening laws against the corporate practice of medicine. Legislative committees could hold hearings to hear testimony from physicians who have witnessed first-hand the interference with patient care that PE acquisitions of medical practices and hospitals have caused.

The lack of transparency is what enables much of the wrongful disruption of medical care by PE managers to occur. Unlike publicly traded companies, private equity operates behind a shroud that lacks basic accountability as to leveraged financing of debt, the stripping of assets from acquired medical practices and hospitals, the upcoding and price increases to boost revenue, and the financial pressure to perform more operations or see more patients in a clinic.

Leveraged buyouts in healthcare, whereby assets are taken to enrich PE managers while new debt is imposed on the acquired entities, need not be permitted by any State. If the NFL can keep private equity on a short leash, so can the state of Missouri while protecting our most valuable assets: our medical practices and infrastructure that enable patients to obtain the medical care they need.

Non-compete agreements need not be allowed in healthcare either, on which PE acquisitions depend for their slash-and-burn strategy. Given that the Federal Trade Commission (FTC) has recently attempted to prohibit non-compete agreements nationwide across all occupations, which is being challenged in court due to the lack of congressional approval and sweeping scope of the FTC ban, Missouri should at least consider prohibiting non-competes in healthcare. Four other states have already broadly prohibited non-compete agreements: North Dakota (banned since 1865), Oklahoma (banned since 1890), California (its ban was strengthened in 2023), and Minnesota (banned in 2023).[6] It is contrary to the public interest for a physician to be limited by a non-compete agreement in his ability to set up a new practice in the same town to serve patients, whenever he feels that a PE manager is improperly controlling him or undermining care.

Strengthening state laws against the corporate practice of medicine would further deter PE firms from purchasing and managing medical practices purely for profit. Currently 33 states, not including Missouri, have laws against the corporate practice of medicine, although many of those states are not enforcing these laws in meaningful ways.

Missouri currently lacks any restriction on the corporate practice of medicine, and historically departed from the rule in many other states that have long prohibited this. Indeed, Missouri was one of the first states to interpret its laws to grant to corporations full rights to enter into contracts with physicians to provide medical services. In state ex rel. *Sager v. Lewin* (1907), a Missouri Court of Appeals somewhat naively held that:

" 'In all the larger cities, and connected with most of the medical colleges in the country, hospitals are maintained by private corporations, incorporated for the purpose of furnishing medical and surgical treatment to the sick and wounded. These corporations do not practice medicine but they receive patients and employ physicians and surgeons to give them treatment.' "[7]

The Supreme Court of Missouri has held that "unless prohibited by statute, a corporation has all the rights of contracting, under the common law, that an individual has. And corporations, when they are not restrained by their charters, may adopt all reasonable means in the execution of their business which a natural person may adopt in the exercise of similar powers."[8] This has been interpreted to permit the corporate practice of medicine in Missouri.

Subsequently, in 1962, the Attorney General of Missouri reinforced this permissiveness towards the corporate practice of medicine here by publishing his opinion that corporations have the full right to employ or contract with physicians in order to provide medical services, without the corporation being deemed to engage in the practice of medicine itself. As recently as 1967, Missouri and Nebraska were the only states that allowed the corporate practice of medicine.

This allowance of the corporate practice of medicine can be contrasted with the corporate practice of law, which is prohibited in every state. Law firms may not be acquired and distorted by private equity takeovers. Instead, only lawyers are allowed to own law firms. A state law could end the PE takeover of medical practices, and instead require that only physicians may own medical practices just as only attorneys may own law firms.

Finally, Missouri holds roughly $100 billion in state and local pension funds, some of which is presumably invested heavily in private equity funds. Laws could be clarified that the public has a right to full disclosure of how Missouri is using taxpayer dollars to invest in PE firms that, in turn, are making acquisitions in healthcare that ultimately harm the public. Missouri could divest its funds away from PE firms that fail to be fully transparent about their conduct with respect to healthcare acquisitions.

Individual Responses

The word has gotten out about how unpleasant it is to work for a medical practice owned by private equity. One survey found that approximately 65% of the medical residents were unwilling to work for a PE-owned medical practice.[9] If that percentage increases further, then PE managers may get the message and look elsewhere to do their leveraged buyout deals in search of squeezing out some profits somewhere.

Meanwhile, physicians should think twice before referring patients to medical groups that have been victimized by a PE takeover. Greater vigilance by physicians in recognizing which medical practices are controlled by private equity, and which ones remain independent, would be helpful when making referrals to patients. The more information that physicians can provide to patients about private equity, the better off both patients and physicians will be. PE managers can best be dealt with by understanding they are motivated solely by profits, not by medical decision-making that is best for patients.

When physicians become aware of "stealth roll-ups" by private equity in healthcare, then physicians should report this to the FTC, anonymously if desired. "Stealth roll-ups" are a clever but disingenuous tactic by PE firms to evade scrutiny of their anti-competitive conduct. A "roll-up" is the acquisition of many small entities, such as medical practices, in order to combine them into a large entity that will have sufficiently large market power to increase its prices without adequate competition. A "stealth" roll-up is the devious strategy by private equity to acquire and merge many small entities such that they are just below the radar of regulatory oversight, thereby evading reporting requirements that trigger FTC review. Fortunately, the FTC is onto this devious approach and will take action on complaints about it.

This is not to be confused with a "rollover", which is when an owner of a targeted practice is offered shares in the private equity-owned entity rather than receiving cash. A rollover enables a physician to remain a continuing owner after the acquisition rather than cashing out. The problem with rollovers in the acquisition of medical practices is that it can become very frustrating for the physician who is accustomed to directing his practice to then have to abide by the profit-maximizing tactics of the incoming PE managers who seek, for example, to increase surgeries and to upcode for higher reimbursements.

There is increased awareness at the FTC and among other public officials about the harm inflicted by private equity, and physicians should report such harm when they learn about it first-hand. The FTC has long been investigating violations of antitrust laws, but private equity firms with their sophisticated attorneys are clever in circumventing the Sherman Act that was enacted in 1890 to prohibit anti-competitive conduct. So the FTC has expanded its tools recently by invoking its own statute, the FTC Act, which allows this federal agency to block mergers based on a lower burden of proof and without having to define an antitrust market that is being harmed. The FTC depends on physicians and others to alert it to anti-competitive conduct by



Private Equity Intrusion into Medicine Is an Existential Threat to Medicine

by John C. Hagan III, MD

Almost all studies after private equity purchase show decreased quality and increased cost.

- https://lowninstitute.org/the-rising-danger-of-private-equity-in-healthcare/
- https://hms.harvard.edu/news/what-happens-when-private-equity-takes-over-hospital
- https://www.jec.senate.gov/public/index.cfm/democrats/2024/7/predatory-private-equity-practices-threaten-americans-health-and-the-economy
- https://www.amjmed.com/article/S0002-9343(23)00589-2/fulltext ttps://www.washingtonpost.com/opinions/2024/01/10/private-equity-health-care-costs-acquisitions/
- https://systemicjustice.org/article/the-private-equity-takeover-of-medicine/

The few studies showing Private Equity is good for medicine were financed by Private Equity.

- https://www.investmentcouncil.org/healthcare/

private equity firms. Typically the FTC enforcement actions are injunctive in blocking acquisitions and mergers, rather than punitive in nature.

Conclusion

"Using dollops of investors' cash and massive loans, private equity firms have taken over hundreds of hospitals, thousands of nursing homes, and tens of thousands of medical practices, leaving the hospitals, nursing homes, and practices—not the investors—on the hook to pay off the debt," wrote Steffie Woolhandler and others in August.[10] It is incumbent on physicians to speak out and object to this harmful intrusion on patient care by private equity.

The good news is that most medical residents have realized that they do not want to go work for a practice owned by private equity. When patients realize this too, then the exploitation of healthcare by private equity for short-term gain may end, and PE managers can then look for profits in the NFL rather than to the detriment of patients in healthcare.

References

1. https://jamanetwork.com/journals/jama/fullarticle/2821826?guestAccessKey=00d9206e-c4e5-468b-be37-9ba2a2b551fd&utm_source=For_The_Media&utm_medium=referral&utm_campaign=ftm_links&utm_content=tfl&utm_term=073024 (viewed Nov. 10, 2024).
2. https://www.jec.senate.gov/public/index.cfm/democrats/2024/7/predatory-private-equity-practices-threaten-americans-health-and-the-economy (viewed Nov. 10, 2024, emphasis added).
3. https://www.reviewofophthalmology.com/article/how-practices-are-making-private-equity-work (viewed Nov. 10, 2024).
4. https://www.wpbf.com/article/new-florida-law-allows-caesarean-sections-outside-hospitals-controversy-birth/60984028 (viewed Nov. 10, 2024).
5. Gretchen Morgenson, "'Get that money!' Dermatologist says patient care suffered after private equity-backed firm bought her practice," NBC News (Dec. 20, 2021) https://www.nbcnews.com/health/health-care/get-money-dermatologist-says-patient-care-suffered-private-equity-back-rcna9152 (viewed Nov. 10, 2024).
6. https://eig.org/state-noncompete-map/ (viewed Nov. 20, 2024).
7. State ex rel. Sager v. Lewin, 128 Mo. App. 149, 155, 106 S.W. 581, 583 (1907) (viewed Nov. 20, 2024).
8. State ex rel. McKittrick v. Gate City Optical Co., 339 Mo. 427, 436, 97 S.W.2d 89, 92 (1936) (viewed Nov. 10, 2024).
9. https://journals.sagepub.com/doi/10.1177/07488068221103638?icid=int.sj-full-text.similar-articles.1 (viewed Nov. 10, 2024).
10. Steffie Woolhandler, David U. Himmelstein, Elizabeth Schrier, and Hope Schwartz, "Private equity: health care's vampire," STAT (Aug. 19, 2024) https://www.statnews.com/2024/08/19/private-equity-health-cares-vampire/ (viewed Nov. 20, 2024).

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Optimizing Missouri's Preparation for the Next Pandemic: Lessons Learned from COVID-19: Part 1

by David S. McKinsey, MD, Joel P. McKinsey, MD, Julie R. McKinsey, BS & Maithe Enriquez, PhD

The United States (US), which spends far more on health care than any other country, suffered the worst COVID-19 associated mortality among 22 peer nations.[1] Missouri's performance was suboptimal in comparison to other states.[2] What happened? How can we do better with inevitable future pandemics?

This first article in a two-part series will review current knowledge about the source of COVID-19; assess the effectiveness and downsides of the control measures implemented in Missouri; describe the efficacy, toxicities, and benefits of COVID-19 vaccines; analyze the implications of temporal and regional variation in statewide mortality rates; and address the roles played by community-based interventions in reducing vaccine hesitancy. Lessons that should be applied to pandemic management in the future will be discussed.



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Figure 1.
Wuhan,
Hubei Province,
China
Source: Alamy

Did the Pandemic Originate From a Lab Leak or a Natural Source?

Controversy persists regarding the origin of SARS-CoV-2, the virus that causes COVID-19. Although the original source of the virus has not been confirmed, there is no question that the pandemic started in Wuhan, China (Figure 1). Two primary theories have been advanced: (1) that SARS-CoV-2 jumped from one or more animal species to humans in or near the Wuhan Huanan wet market, where many species of wild and domestic animals were caged and sold, or (2) that the pandemic started via a lab leak at the Wuhan Institute of Virology (WIV), either by spread from employees after a non-disclosed laboratory accident or by intentional nefarious activity.[3]

The COVID-19 Origin Act in 2023 directed US government agencies to determine which of the two competing theories held true. Differing opinions were expressed by the various intelligence agencies. However, after an extensive investigation, the conclusion of the Office of the Director of National Intelligence was that "all US agencies continue to assess that both a natural and a laboratory-associated origin remain plausible hypotheses."[4] The public does not have access to classified information reviewed by the federal agencies during their investigations. However, abundant published scientific literature provides insight into the most likely source of the pandemic.

Analysis of the first 155 cases of COVID-19 in Wuhan revealed spatial clustering in the wet market which almost certainly was the epicenter.[3,5] Cases were not identified near the WIV.[3] Some of the animal species kept at the market are highly susceptible to SARS-CoV-2.[6] Viral DNA was detected from environmental samples obtained near multiple cages[6] and is at the root of the SARS-CoV-2 phylogenetic tree.[3] However, at the onset of the pandemic when animals were euthanized, only a few were tested for virus, with negative results;[3] thus, scientists probably will not be able to confirm that cross-species transmission caused the initial outbreak.

Rhinolophus (horseshoe) bats are the hosts of all coronaviruses identified to date aside from SARS-CoV-2 which still has not been detected in bats.[3] Virologists maintain and publish catalogues of viruses studied at their laboratories. Of the 60 novel bat coronaviruses studied at WIV in 2018, the one most closely related to SARS-CoV-2, Banal-20-52, had more than 1,000 nucleotide differences and thus could not possibly have been manipulated to create SARS-CoV-2.[3] Virologists have not identified evidence of manmade genetic sequencing in the SARS-CoV-2 genome[3] and each of the US intelligence agencies concluded that SARS-CoV-2 was not genetically engineered and was not a weapon of bioterrorism.[4]

The preponderance of evidence continues to imply cross-species spillover to humans at the wet

market. Some who promote the lab leak theory cite the fact that multiple researchers at the WIV fell ill in the weeks prior to the pandemic's onset. A SARS-CoV-2 seroprevalence study was done on WIV researchers a few months after the pandemic started; all had negative serology tests.[3] Presuming that this information is accurate, the hypothesis that WIV researchers had undetected COVID-19 in November 2019, and thus triggered the pandemic a few weeks later, would be considered disproven.

What Did We Know About Pandemic Control Prior to 2020?

The public health community did not start from scratch in 2020 regarding its knowledge about the spread and control of pandemics. During the century prior to the onset of COVID-19, four influenza pandemics occurred: the 1918-19 Spanish flu, the 1957 Asian flu, the 1968 Hong Kong flu, and the 2009 Swine flu.

The 1918-19 influenza pandemic, which was by far the most lethal, has been extensively studied by epidemiologists.[7] Many of the control measures that were undertaken in Missouri in 1918, including closures of schools, theaters, and churches, and prohibition of public gatherings, in hindsight were demonstrably effective.[8,9] The duration of these closures and social distancing practices was significantly associated with reduction of mortality. A notable finding from analysis of the 1918 influenza pandemic was that the premature easing of school closures and other restrictions directly correlated with subsequent higher death rates nationwide.[8] In St. Louis, where public health measures were implemented with much less financially-motivated political opposition than in Kansas City, excess mortality was 34% lower.[8] St. Louis had the second lowest death rate among 17 US cities assessed,[8] a finding attributed to implementation of effective public health measures with strong and sustained support from local government.[9] Thus in 2020 it was well-known that closures and social distancing were likely to be effective tools for slowing the spread of the new pandemic.

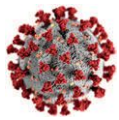
In 2004, the World Health Organization recommended that all countries develop plans for a potential pandemic, partly in response to the emergence of H5N1 Avian influenza in Asia.[10] In 2005 the US Department of Health and Human Services developed a strategy to coordinate and improve efforts to prevent, control, and respond to influenza viruses with pandemic potential.[11] This plan was updated three times. In 2019, the Global Health Security Index ranked the US among the top two countries worldwide in terms of preparedness.[12]

Did Control Measures Implemented During COVID-19 Work?

In hindsight many of the pandemic control measures undertaken nationally and locally were highly effective. Nonpharmaceutical pandemic mitigation strategies included shutdowns/closures, social distancing requirements, mask mandates, development and rollout of effective vaccines, and community partnerships to address vaccine hesitancy.

Mandate propensity, a summary measure of a state's requirements for physical distancing and mask use, and thus of the intensity of its public health response, was strongly associated with lower case rates and mortality.[36] Missouri ranked near the bottom of the 50 states on this measure.

It came as a surprise to most Americans at the onset of the pandemic that throughout our history the government has had the authority to order quarantines, shutdowns, and other limitations on the public. An early example in Missouri was General Order 11, issued in 1863 by US Brigadier General Thomas Ewing, which instituted martial law in Jackson, Cass, Bates, and northern Vernon Counties in retaliation for Quantrill's raid in nearby Lawrence, Kansas. Confederate sympathizers were ordered to vacate their properties, which were then set ablaze by Union soldiers. Less onerous, but



nonetheless challenging, limitations were placed on the population during World War I, when cigarettes, gasoline, and tires were rationed. Of note, coffee was not restricted and was provided in abundance to GIs in the trenches, the genesis of the phrase "Cup of Joe." In the early 20th century public health departments routinely isolated children with communicable infections in their homes. During World War II, the public was subjected to strict rations of silk, sugar, butter, gasoline, and canned milk.

Having faded from memory, closures and other restrictions were a highly unwelcome public health approach in 2020. Statewide pandemic mitigation measures in Missouri included closures of bars and restaurants from March 23 to May 4, 2020 and a stay-at-home order from April 6 to May 4, 2020.[2] Many other states had substantially longer shutdown periods. One analysis estimated that the combination of lockdowns and recommendations for mask use and hand hygiene saved hundreds of thousands of lives in the US during the first six months of the pandemic.[13] A second assessment concluded that social distancing in the US prevented millions of cases of COVID-19 in 2020.[14]

The impact of mask use during the COVID-19 pandemic has been studied extensively. Missouri cities and counties with mask mandates had reduced numbers of COVID-19 cases and significantly lower death rates during the Delta variant surge in 2021 than those that did not.[2] This finding was in concordance with other studies that demonstrated a salutary effect of mask use, including a systematic review that showed diminution of COVID-19 mortality by more than 50% in countries and US states with mask mandates.[15]

In a cohort of thousands of employees of a multi-hospital healthcare system in the St. Louis area early in the pandemic, community exposures were much more strongly associated with acquisition of COVID-19 than occupational exposures.[16] Disease incidence was more than twice as high among employees who had infected household contacts.[16] The results of this study suggest that mandated mask use in hospitals was effective in reducing SARS-CoV-2 transmission.

What Were the Downsides of Control Measures?

Control measures had downsides. A review of the extreme negative economic impact of shutdowns and closures is beyond the scope of this discussion. Standardized test scores among students plummeted to 50-year lows, representing the equivalent of a three-quarter year reduction in math and a half-year year diminution of reading scores.[17] Many schools mandated mask use after reopening. There was much controversy about whether masking in schools was necessary to prevent disease transmission, and regarding perceived negative effects of masking in children.

A multi-state, prospective study of secondary transmission rates of COVID-19 in K-12 schools in 61 US school districts from July to December 2021 found a 72% reduction in school-acquired cases in staff and students in schools that had universal masking policies.[18] An experimental study of children aged four to eight showed that face masks did not significantly impair basic language processing ability.[19] The investigators did find, however, that masks had a significant effect on the children's abilities to recognize emotions.[19] A randomized controlled trial of cognitive performance in fifth to seventh graders demonstrated that wearing face masks had no significant influence on children's attention and executive functions during school lessons.[20]

Anxiety, stress, and isolation skyrocketed in the population during COVID-19.[21-22] Some of the negative psychosocial impact likely was part and parcel of the exceedingly disruptive process of living through a once-in-a-century major pandemic during which more than a million Americans died. However, the various mitigation measures including societal shutdowns and distancing requirements that were imposed largely against the will of the public certainly had negative consequences.

Social isolation and disease containment strategies are known to exacerbate anxiety and depression.[23] A systematic review and meta-analysis of 42 studies in pediatric Emergency Departments published in the English language literature found that the relative risk for attempted suicide during the first two years of the pandemic was 1.22 (95%



confidence interval 1.08 – 1.37).[24] Reports to the US Poison Center for children increased in 2020 in comparison to the previous three pre-pandemic years.[25]

What Were the Risks and Benefits of Vaccinations?

Decades of research into structure-based vaccine design and the spike proteins of coronaviruses enabled the development of highly efficacious vaccines and the rollout of vaccination programs within a year after the genetic sequence of SARS-CoV-2 became available in January 2020.[26] One analysis estimated that during the first 10 months that vaccines were available, 1.6 million hospitalizations and 235,000 deaths were prevented in the US.[27] Another study estimated that if all American adults aged 18 years and older had been vaccinated between January 1, 2021 and April 30, 2022, almost 320,000 deaths would have been averted nationwide and 8,585 deaths would have been prevented in Missouri.[28]

Vaccine effectiveness of the 2023-2024 COVID-19 vaccine against symptomatic SARS-CoV-2 infection was 54% in the general population and 38% in adults with immunocompromising conditions.[29] By comparison, the 2023-2024 influenza vaccines were 41% - 44% effective in preventing flu-related hospitalization in adults.[30]

When COVID-19 vaccines were introduced, many concerns were raised regarding potential toxicities. Local and mild systemic side-effects of COVID-19 vaccination, including fatigue, are relatively common, but serious adverse events are extremely rare.[31] Although the mRNA COVID-19 vaccines rarely cause myocarditis, the risk is seven-fold lower than that associated with SARS-CoV-2 infection.[32] The currently recommended vaccines do not appear to cause infertility, Guillain-Barre Syndrome, Bell palsy, myocardial infarction, or thrombosis with thrombocytopenia syndrome.[33]

An annual updated COVID-19 vaccine is recommended by CDC for persons six months of age and older, with the exception of those aged ≥ 65 and the immunocompromised, who should be vaccinated every six months.[34] However, as of August 2024, only 22.8% of US adults ≥ 18 years had received the updated vaccine;[35] 91% of deaths in Kansas City,

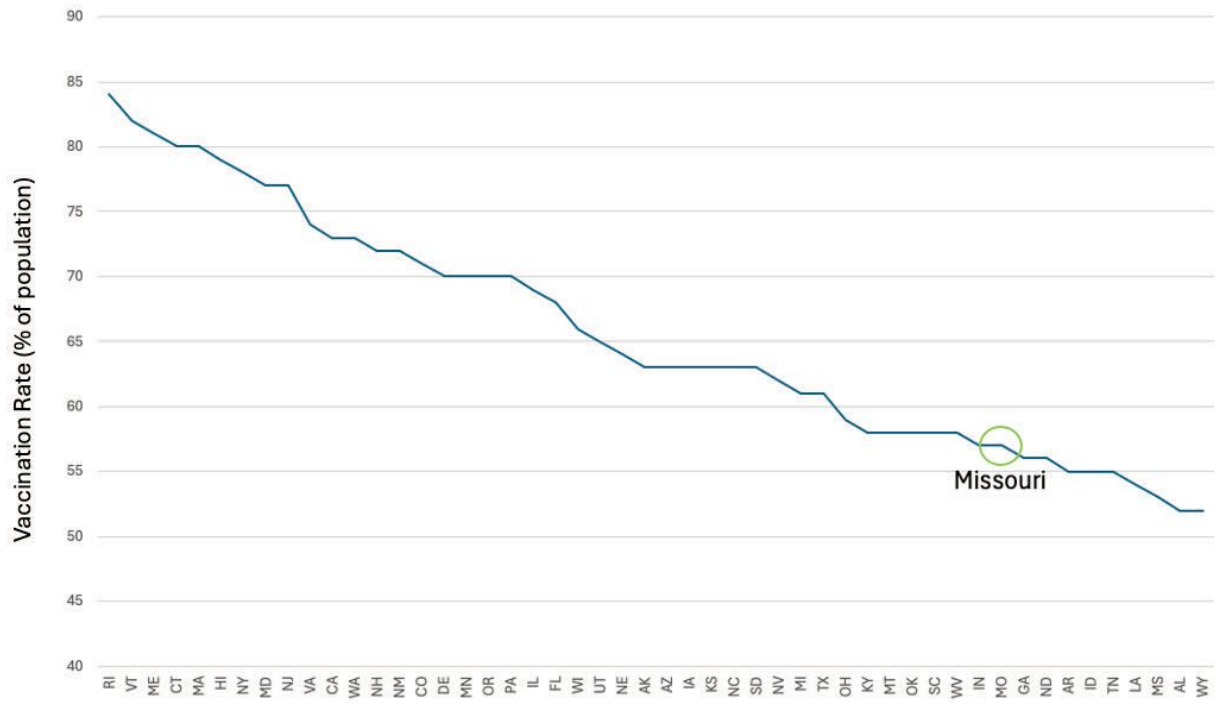


Figure 2. COVID-19 vaccination rate as of 8/3/22
Source: https://usafacts.org/visualizations/covid-vaccine-tracker-states/, accessed 8/18/24

Missouri, during the first eight months of 2024 occurred in individuals who were not up to date on their COVID-19 vaccinations. (Kansas City Health Department, personal communication)

What Were the Implications of Geographic Variability in Mortality?

COVID-19 morbidity and mortality rates among US states varied four-fold.[36] Missouri's mortality figure, 426 per 100,000 population per year, ranked 39th in the country as of mid-2022.[36] Assessment of factors associated with variation in death rates in subpopulations over time provides insight into potential strategies to reduce adverse outcomes.

Adverse social determinants of health correlated significantly with mortality, which was disproportionately higher in states with increased poverty rates, fewer mean years of education, limited access to quality health care, and lower levels of interpersonal trust.[36] During the first year of the pandemic, urban areas in Missouri experienced much higher death rates than rural regions, as had been the case during the 1918 influenza pandemic.[37] Native Americans, Hispanics, non-Hispanic Blacks, and persons with diabetes mellitus, obesity, or limited access to health care were at highest risk.[38] However, nationwide in 2021 the White population experienced the sharpest drop in life expectancy,[38] and in Missouri a shift occurred to much higher mortality in semirural counties, defined as those in which 1-49% of the population resided in urban areas. The Bootheel was the highest-risk area in the state, as it had been in 1918.[37]

Mandate propensity, a summary measure of a state's requirements for physical distancing and mask use, and thus of the intensity of its public health response, was strongly associated with lower case rates and mortality.[36] Missouri ranked near the bottom of the 50 states on this measure.[36]

After COVID-19 vaccines became available in December 2020, lack of vaccine uptake in the population was a strong predictor of mortality.[39.] During the Delta variant surge in the summer of 2021, unvaccinated persons were 14-fold more likely to die than those who were fully vaccinated.[39] In July 2022, long after access to vaccines was widespread,

Table 1. Missouri COVID-19 Scorecard, January 1, 2020 - July 31, 2022

Metric	Missouri	United States	Rank
Mortality per 100,000 population	426	372	39th
Mask mandate	No	39 other states had mandates	N/A
Stay-at-home orders (mean duration)	28 days	155 days	N/A
Closures of public places (mean duration)	42 days	215 days	N/A
Fully vaccinated (%)	57	67	41st
Living below poverty level (%)	13.2	11.5	36th
Years of education (mean)	12.7	13.3	23rd
Access to quality health care (%)	86	86.9	24th
Interpersonal trust (%)	37	40	38th

N/A: not applicable
Sources: Mo Med. 2022; 119: 98-105; Lancet; 401(10385): 1341l1360; https://usafacts.org/visualizations/covid-vaccine-tracker-states/state/missouri/ accessed 8/13/24

Missouri's vaccination rate ranked 41st in the country (Figure 2).

In 2021 the proportion of Missouri's population who were vaccinated was significantly reduced in counties with higher percentages of the community who had Hispanic/Latino or African ethnicity, were uninsured, were living below the poverty level, had high school education or less, or were working in the manufacturing sector.[40] In general vaccination rates were lowest in non-metropolitan communities in southern Missouri [40] and in counties with increased prevalence of tobacco use.[2]

We created Missouri's scorecard (Table 1) which shows its rankings in comparison with other states as of mid-2022 with regard to mortality, implementation of public health interventions, and population characteristics known to be associated with adverse COVID-19 outcomes. This table is updated from a prior version.[2] Based on the published literature summarized in the scorecard, and the personal observations of two of the authors (DM and JPM) who served as front-line workers throughout the pandemic at multiple hospitals with a mix of urban and rural patients, conclusions can be drawn. Missouri's extremely high mortality rate likely was secondary both to a combination of a large vulnerable urban population early in the pandemic when disease incidence was highest in St. Louis and Kansas City,[41] and, later, to low adoption of effective public health measures including masking and vaccination especially in less populated regions of the state.

What Was the Value of Community Partnerships?

An estimated 200,000 Americans are thought to have died due to anti-vaccine misinformation.[39] Although a segment of the population responded favorably to science-based messaging from national experts, vaccine hesitancy in hard-to-reach populations was a particularly vexing problem. Community partnered endeavors[42] provided a mechanism for community members, health care providers, and academic researchers to work together to develop and implement effective strategies to mitigate adverse COVID-19 health outcomes, enhance vaccine uptake, and provide accurate health information (Figure 3).[43]

The Missouri Center for Public Health Excellence partnered with 12 local public health agencies and provided valuable educational materials that likely contributed to substantially increased



Figure 3. A community partnership between a local chapter of the National Association of Hispanic Nurses, nurse researchers and a charter school serving under-resourced communities led to enhanced understanding of vaccine hesitancy and increased access to COVID-19 vaccines for children at the height of the COVID-19 pandemic.[43]

vaccination rates in each of the counties served.[44] Several barriers to vaccine acceptance in Southeast Missouri were identified, including a dearth of support from elected officials and local health departments' inadequate surge capacity for mass vaccination programs.[44]

The COVID-19 Response Network, a partnership between researchers at Saint Louis University and multiple health care providers and faith-based leaders in Southwest Missouri, provided community-based vaccine education in 16 predominantly rural counties.[45] Fear-based messaging was found to be counterproductive; appeals to the need to protect family members were much better-received. The authors concluded that "trust in the source of information was critical." Effective community-based approaches included use of peers and "meeting people where they are."[45] Two-way conversations were perceived much more favorably than one-way narrations.[45] Community-partnered endeavors have a proven track record of success for identifying and overcoming obstacles to implementation of best practices including vaccination.

Conclusion

We urge that the many lessons learned during the COVID-19 experience be used to optimize Missouri's preparations for the next pandemic. International wet markets, rife with potential for interspecies viral transmission, should be closed. Unpopular societal closures likely reduced the spread of illness. Masking decreased disease transmission and mortality. Although children and adolescents were at low personal risk for severe disease, masking in these age groups probably protected high-risk populations, without negative impact on educational advancement. Social isolation and anxiety were widely prevalent and can be anticipated to recur in future pandemics. An effective vaccine was developed and released within a year after identification of a novel virus, but widespread vaccine hesitancy cost many lives. Individual or small group tailored educational sessions with trusted members of the local community may be more effective in some settings for fostering vaccine acceptance than mass messaging from national authorities. The next article in this two-part series will address the challenges faced by our public health system during COVID-19 and the impact of opposition to pandemic mitigation strategies by elected officials.

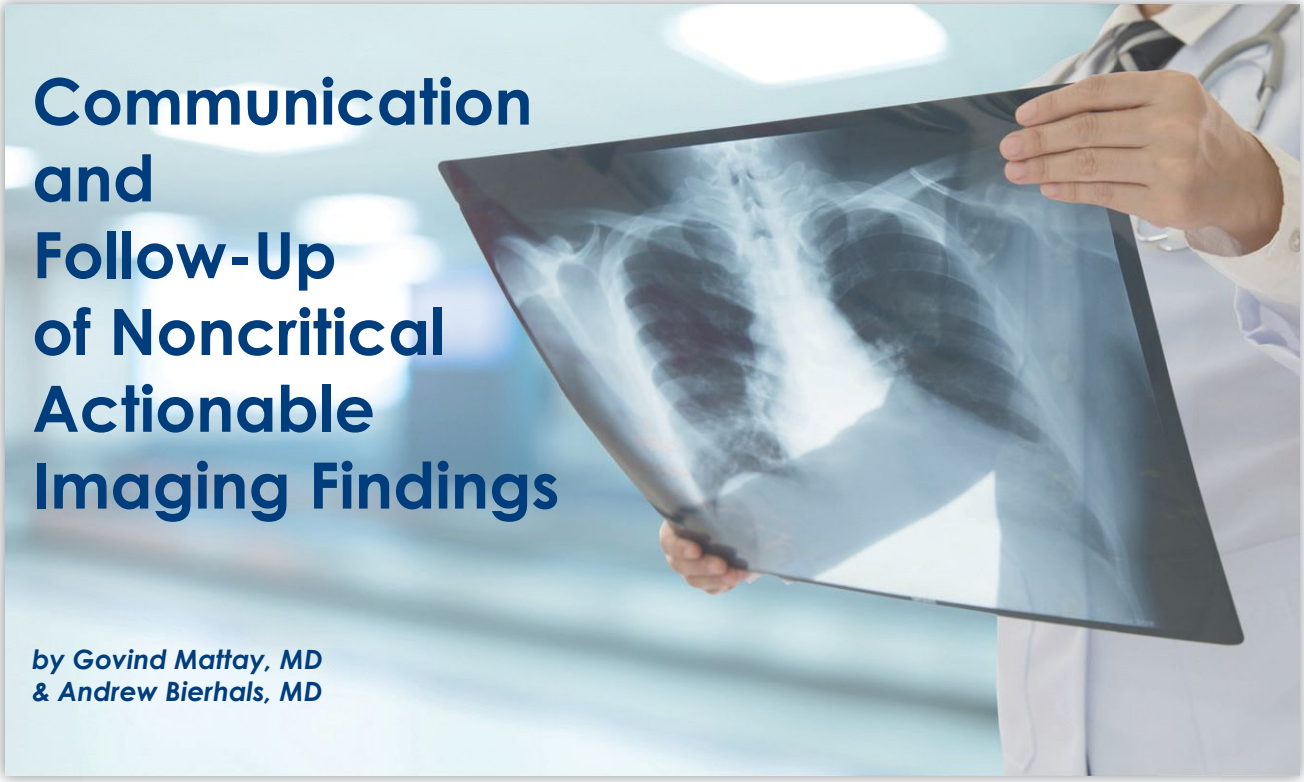
References

1. Woolf SH, Masters RK, Aron LY. Changes in Life Expectancy Between 2019 and 2020 in the US and 21 Peer Countries. JAMA Netw Open. 2022 5(4):e227067.
2. McKinsey DS, McKinsey JP, Hampson NB, Enriquez M. COVID-19 in Missouri 2020-2021: A Perspective on Origins, Spread & Controversies Part II. Mo Med. 2022; 119: 176-184.
3. Holmes EC. The Emergence and Evolution of SARS-CoV-2. Annu Rev Virol. 2024. doi: 10.1146/annurev-virology-093022-013037.
4. Office of the Director of National Intelligence. Potential links between the Wuhan Institute of Virology and the Origin of the COVID-19 pandemic. www.dni.gov/files/ODNI/documents/assessments/Report-on-Potential-Links-Between-the-Wuhan-Institute-of-Virology-and-the-Origins-of-COVID-19-20230623.pdf, accessed 8/13/24
5. Holmes EC, Goldstein SA, Rasmussen AL, et. al. The origins of SARS-CoV-2: A critical review. Cell. 202;184: 4848-4856.
6. Worobey M, Levy JI, Malpica Serrano L, et. al. The Huanan seafood wholesale market in Wuhan was the early epicenter of the COVID-19 pandemic. Science. 2022; 377:951-959.
7. Bootsma MC, Ferguson NM. The effect of public health measures on

the 1918 influenza pandemic in U.S. cities. Proc Natl Acad Sci U S A. 2007; 104:7588-93.
8. Hatchett RJ, Mecher CE, Lipsitch M. Public health interventions and epidemic intensity during the 1918 influenza pandemic. Proc Natl Acad Sci U S A. 2007;104: 7582-7
9. McKinsey DS, McKinsey JP, Enriquez M. Part I: The 1918 influenza in Missouri: centennial remembrance of the crisis. Mo Med. 2018; 115:183-188.
10. Bourrier MS, Deml MJ. The legacy of the pandemic preparedness regime: an integrative review. Int J Public Health. 2022; 67:1604961.
11. CDC. National pandemic strategy. CDC.gov/flu/pandemic-resources. Accessed 8/13/24
12. Cameron E, Nuzzo J, Bell J. Global Health Security Index. https://ghsindex.org/wp-content/uploads/2019/10/2019-Global-Health-Security-Index.pdf. Accessed 8/13/24
13. Yakusheva O, van den Broek-Altenburg E, Brekke G, Atherly A. Lives saved and lost in the first six month of the US COVID-19 pandemic: A retrospective cost-benefit analysis. PLoS One. 2022; 17:e0261759.
14. Hsiang S, Allen D, Annan-Phan S, et. al. The effect of large-scale anti-contagion policies on the COVID-19 pandemic. Nature. 2020; 584:262-267.
15. Talic S, Shah S, Wild H, et. al. Effectiveness of public health measures in reducing the incidence of COVID-19, SARS-CoV-2 transmission, and COVID-19 mortality: systematic review and meta-analysis. BMJ. 2021; 375:e068302.
16. Kwon JH, Budge PJ, O'Neil CA, et. al. Clinical and occupational risk factors for coronavirus disease 2019 (COVID-19) in healthcare personnel. Antimicrob Steward Healthc Epidemiol. 2022; 2:e123.
17. St. George D. American students' tests scores plunge to levels unseen for decades. www.washingtonpost.com/education/2022/09/01/student-test-scores-plunged-pandemic Accessed 8/14/24
18. Boutzoukas AE, Zimmerman KO, Inkelas M, et. al. School masking policies and secondary SARS-CoV-2 transmission. Pediatrics. 2022; 149: e2022056687
19. Bourke L, Lingwood J, Gallagher-Mitchell T, López-Pérez B. The effect of face mask wearing on language processing and emotion recognition in young children. J Exp Child Psychol. 2023; 226:105580.
20. Schlegtendal A, Eitner L, Falkenstein M, et. al. To mask or not to mask—evaluation of cognitive performance in children wearing face masks during school lessons (MasKids). Children. 2022; 9:95.
21. Loades ME, Chatburn E, Higson-Sweeney N, et. al. Rapid systematic review: the impact of social isolation and loneliness on the mental health of children and adolescents in the context of COVID-19. J Am Acad Child Adolesc Psychiatry. 2020;59:1218-1239.
22. King B, Adepoju OE, Woodard L, Oluyomi AO, Zhang X, Amos CI, Badr H. The effects of COVID-19 Lockdown on social connectedness and psychological distress in U.S. adults with chronic diseases. Int J Environ Res Public Health. 2023; 20:6218.
23. Shankar R. Loneliness, social isolation, and its effects on physical and mental health. Mo Med. 2023;120:106-108.
24. Madigan S, Korczak DJ, Vaillancourt T, et. al. Comparison of paediatric emergency department visits for attempted suicide, self-harm, and suicidal ideation before and during the COVID-19 pandemic: a systematic review and meta-analysis. Lancet Psychiatry. 2023;10:342-351.
25. Ciccotti HR, Spiller HA, Casavant MJ, Kistamgari S, Funk AR, Smith GA. Pediatric suspected suicides and nonfatal suicide attempts reported to United States Poison Control Centers before and during the COVID-19 pandemic. J Med Toxicol. 2023; 19:169-179
26. Fauci AS, Folkers GK. Pandemic preparedness and response: lessons from COVID-19. J Infect Dis. 2023; 228:422-425.
27. Steele MK, Couture A, Reed C, et. al. Estimated number of COVID-19 infections, hospitalizations, and deaths prevented among vaccinated persons in the US, December 2020 to September 2021. JAMA Netw Open. 2022; 5:e2220385.
28. Zhong M, Glazer T, Kshirsagar M, et. al. Estimating vaccine-preventable COVID-19 deaths among adults under counterfactual vaccination scenarios in the United States: a modeling study using observational data. J Pharm Pharmacol Res 2023; 7: 163-167
29. DeCuir J, Payne AB, Self WH, et. al. Interim effectiveness of updated 2023-2024 (monovalent XBB.1.5) COVID-19 vaccines against COVID-19-associated emergency department and urgent care encounters and hospitalization among immunocompetent adults aged ≥18 years - VISION and IVY Networks, September 2023-January 2024. Morb Mortal Wkly Rep. 2024; 73:180-188.
30. Frutos AM, Price AM, Harker E, et. al. CDC influenza vaccine effectiveness collaborators. Interim estimates of 2023-24 seasonal influenza vaccine effectiveness - United States. Morb Mortal Wkly Rep. 2024; 73:168-174.
31. CDC. COVID-19 vaccine safety. https://www.cdc.gov/vaccine-safety/vaccines/covid19.html?CDC_AAref_Val=https://www.cdc.gov/vaccinesafety/vaccines/Covid-19-vaccines.html Accessed 8/16/24
32. Voleti N, Reddy SP, Ssentongo P. Myocarditis in SARS-CoV-2 infection vs. COVID-19 vaccination: A systematic review and meta-analysis. Front Cardiovasc Med. 2022; 9:951314.
33. National Academies of Sciences, Engineering, and Medicine. 2024. Evidence review of the adverse effects of COVID-19 vaccination and intramuscular vaccine administration. Washington, DC: The National Academies Press. https://doi.org/10.17226/27746. Accessed 8/14/24
34. CDC. Interim clinical considerations for use of COVID-19 vaccines in the United States. https://www.cdc.gov/vaccines/covid-19/clinical-considerations/interim-considerations-us.html Accessed 8/17/24
35. CDC. COVID-19 vaccination coverage and vaccine confidence among adults.https://wwwl.cdc.gov/vaccines/imzmanagers/coverage/covidvaxview/interactive/adults.html. Accessed 8/17/24
36. Bollyky TJ, Castro E, Aravkin AY, et. al. Assessing COVID-19 pandemic policies and behaviours and their economic and educational trade-offs across US states from Jan 1, 2020, to July 31, 2022: an observational analysis. Lancet 2023; 401:1341-1360.
37. Sattenspiel L, Orbann C, Bogan A, et. al. Associations between rurality and regional differences in sociodemographic factors and the 1918-20 influenza and 2020-21 COVID-19 pandemics in Missouri counties: An ecological study. PLoS One. 2023; 18:e0290294.
38. Masters RK, Aron LY, Woolf SH. Life expectancy changes during the COVID-19 pandemic, 2019-2021: highly racialized deaths in young and middle adulthood in the United States as compared with other high-income countries. Am J Epidemiol. 2024; 193: 26-35.
39. Hotez P. Communicating science and protecting scientists in a time of political instability. Trends Mol Med. 2022; 28:173-175.
40. Lacy A, Khan MM, Deb Nath N, et. al. Geographic disparities and predictors of COVID-19 vaccination in Missouri: a retrospective ecological study. Front Public Health. 2024; 12:1329382.
41. McKinsey DS, McKinsey JP, Hampson NB, Enriquez M. COVID-19 in Missouri 2020-2021: A Perspective on Origins, Spread & Controversies, Part I. Mo Med. 2022; 119:98-105.
42. Schubotz, D. Participatory Research: Why and how to involve people in research. Sage, 2020
43. Molina R, Olmedo Y, El Corazon de la Tierra (Kansas City) Chapter of NAHN. Perceptions of COVID-19 Among Unvaccinated Hispanics. Hisp Health Care Int. 2024; 22:3-5.
44. Evans D, Norrbom C, Schmidt S, Powell R, McReynolds J, Sidibe T. Engaging community-based organizations to address barriers in public health programs: lessons learned from COVID-19 vaccine acceptance programs in diverse rural communities. Health Secur. 2023; 21(S1):S17-S24.
45. Ban A, Shrestha A, Van den Berk-Clark C, et. al. Through the eyes of community health workers: what was needed to increase COVID-19 vaccine uptake in the Missouri Southeast region. Front Public Health. 2024; 12:1286177.

MM

Communication and Follow-Up of Noncritical Actionable Imaging Findings



by Govind Mattay, MD & Andrew Bierhals, MD

As the number of imaging studies that are ordered continues to rise, and especially with the increased use of cross-sectional imaging, the number of NCAFs that are detected has increased.



Govind Mattay, MD, MBA, and **Andrew Bierhals, MD, MPH**, (pictured) are at the Mallinckrodt Institute of Radiology, Washington University School of Medicine, St. Louis, Missouri.

Importance of Noncritical Actionable Imaging Findings

Noncritical actionable findings (NCAFs), also known as incidental imaging findings (IIFs), are imaging findings that are unrelated to the primary purpose of a study but still warrant follow-up care.[1-5]

For example, a patient could present to the Emergency Department (ED) with chest pain and shortness of breath. The ED physician orders a computed tomography (CT) examination of the chest to look for a pulmonary embolism. The radiologist detects a pulmonary nodule as an NCAF when interpreting the examination. Depending on the appearance of this nodule and patient risk factors, this could warrant follow-up imaging or biopsy, to determine whether it represents malignancy.

NCAFs encompass a broad array of imaging findings that warrant timely follow-up care, including but not limited to lung nodules, solid organ (liver, pancreas, kidney, etc.) lesions, and vascular aneurysms.[1-5] Appropriate follow-up of NCAFs can lead to markedly improved patient outcomes. For example, if a suspicious pulmonary nodule detected

as an NCAF is biopsied and resected, this means a patient can be cured of early-stage lung cancer before it metastasizes.

As the number of imaging studies that are ordered continues to rise, and especially with the increased use of cross-sectional imaging, the number of NCAFs that are detected has increased.[6] The rate of follow-up of these NCAFs greatly varies across health systems and patient populations, and in many cases the rate of follow-up for NCAFs is very low.[7] If follow-up care for NCAFs is delayed or not performed, this can lead to poor patient outcomes and increased malpractice liability for all healthcare providers involved in the patient's care.[8-10]

Challenges in NCAF Follow-Up

There are many challenges in improving follow-up care for NCAFs, since the process for patients to receive care for NCAFs is long and complex.[11] There are several steps involved in directing patient to appropriate care for incidental findings and successfully closing the loop. Firstly, radiologists must accurately detect the finding within the imaging study. Secondly, the radiologist/imaging center must have a way of communicating the result with a clinician taking care of the patient or the patients themselves. Thirdly, the clinician must have a discussion with the patient about appropriate next steps. Fourthly, the clinician must order the appropriate follow-up care, whether it is another imaging study, a referral, or a biopsy. Then, this care must be scheduled and finally performed.

In our fragmented health care system, it is easily possible for failures to occur in any of these steps. Radiologists are inundated with high imaging volumes, and it is possible that they could not detect an NCAF in an imaging study. Even if the radiologist detects the finding and mentions it in the report, but does not provide a specific follow-up recommendation, it is possible that the clinician and patient will not know how to proceed.

Next, there are many possible failure points in appropriate communication of NCAFs to the correct clinician and the patient. Even if the NCAF and follow-up recommendation are mentioned in the radiology report, it is possible that the ordering provider does not see this information since they too are inundated with information on the many patients they are caring for. Additionally, often the clinician who orders the imaging study may not be responsible for coordinating appropriate follow-up care.

For example, many NCAFs are detected on imaging studies ordered by ED physicians, however ultimately the primary care physician is responsible for coordinating the follow-up. There are many additional such instances where NCAFs should be communicated between clinicians at handoffs of care so they do not get lost to follow-up: when patients are transferred between units within the hospital, when patients are discharged from the hospital, and when patients are referred to specialists. Lack of appropriate communication of NCAFs at handoffs is another important and addressable cause for delayed follow-up care.

Also, it is imperative that the patient is directly notified about the NCAF such that they are empowered to ensure that they get appropriate follow-up care. Lastly, there are additional barriers to patients receiving the follow-up care that include financial costs, access to health insurance, and poor health literacy.[11] The many potential failure points previously described are exacerbated in our fragmented health system. Often information is siloed in different electronic medical record databases, and records are not easily transferred. This makes it even harder to ensure that patients get appropriate follow-up care for NCAFs.

Solutions to Improve NCAF Follow-Up

Many health systems and corporations have developed solutions to address lack of follow-up of NCAFs. Several of these solutions share a common structure: radiology reports are queried for mention of an NCAF, NCAFs are stored in a tracking database, and finally there is some form of direct communication regarding the NCAF to the patient or provider.[11] Some institutions have chosen to institute templates that radiologists have the option of dictating into their report when describing an NCAF[12-13], while others utilize Natural Language Processing (NLP) algorithms to mine reports for mention of an NCAF.[14] The forms of communication regarding the NCAF also vary. Some organizations directly message patients, others send certified letters,[15] and others

use a combination of Electronic Health Record alerts and messages to ordering clinicians and patients.[11, 16] One method that has achieved a higher rate of success has been the use of care coordinators who directly contact patients or providers regarding incidental imaging findings to ensure follow-up has occurred. Overall, these programs have achieved varying success, with follow-up adherence rates ranging from 52%[17]-71%[16] after implementation.

The importance of NCAFs has also prompted several governing bodies to take action. The Centers for Medicaid and Medicare Services (CMS) has proposed several quality metrics that focus on health systems closing the loop on incidental imaging findings. The state of Pennsylvania passed the Patient Test Result Information Act (Act 112), which requires imaging centers to notify patients about NCAFs that require follow-up within three months. These actions represent steps in the right direction towards improving NCAF follow-up at a larger scale. However, early data has suggested that the effects of Act 112 are limited in improving rates of follow-up care completion.[15]

Health systems and healthcare providers should ensure that patients with NCAFs receive appropriate follow-up care to improve patient outcomes and limit malpractice liability. However, this is a difficult task, partially due to the multiple steps of communication that must occur for a patient to receive the appropriate follow-up care. Certain health systems have improved NCAF follow-up by implementing solutions that close the loop on these findings.

There remain multiple opportunities for improvement. Firstly, hospitals and healthcare systems which do not have programs to track NCAFs should look to implement these solutions. While these solutions may seem resource intensive, several recent studies have shown a positive financial impact of these solutions.[17,18] Secondly, health systems that have implemented these solutions should work to identify and address the specific factors that are leading to the 30-50% of patients that still do not receive appropriate follow-up. Solutions will likely vary based on the specific patient population, health system, and available resources. Finally, policymakers should find ways to align incentives such that health systems are rewarded for improving patient care through ensuring follow-up of NCAFs.

References

1. Domingo J, Galal G, Huang J, et al. Preventing delayed and missed care by applying artificial intelligence to trigger radiology imaging follow-up. NEJM Catal Innov Care Deliv. 2022;3(4):CAT-21.
2. Sistrom CL, Dreyer KJ, Dang PP, et al. Recommendations for additional imaging in radiology reports: multifactorial analysis of 5.9 million examinations. Radiology. 2009;253(2):453-461.
3. Mabotuwana T, Hall CS, Hombal V, et al. Automated tracking of follow-up imaging recommendations. AJR Am J Roentgenol. 2019;212(6):1287-1294.
4. Kadom N, Doherty G, Solomon A, et al. Safety-net academic hospital experience in following up noncritical yet potentially significant radiologist recommendations. AJR Am J Roentgenol. 2017;209(5):982-986.
5. Cochon LR, Kapoor N, Carrodeguas E, et al. Variation in follow-up imaging recommendations in radiology reports: patient, modality, and radiologist predictors. Radiology. 2019;291(3):700.
6. Aggarwal A, Lazarow F, Anzai Y, et al. Maximizing value while volumes are increasing. Curr Probl Diagn Radiol. 2021;50(4):451-453.
7. Blagev DP, Lloyd JF, Conner K, et al. Follow-up of incidental pulmonary nodules and the radiology report. J Am Coll Radiol. 2014;11(4):378-383.
8. Whang JS, Baker SR, Patel R, et al. The causes of medical malpractice suits against radiologists in the United States. Radiology. 2013;266(2):548-554.
9. Siegal D, Stratchko LM, DeRoo C. The role of radiology in diagnostic error: a medical malpractice claims review. Diagnosis. 2017;4(3):125-131.
10. Lorincz CY, Drazen E, Sokol PE, et al. Chicago, IL: American Medical Association; 2011.
11. Voreis S, Mattay G, Cook T, et al. Informatics Solutions to mitigate legal risk associated with communication failures. J Am Coll Radiol. 2022;19(7):823-828.
12. Santo EC, Dunbar PJ, Sloan CE, et al. Initial Effectiveness of a Monitoring System to Correctly Identify Inappropriate Lack of Follow-Up for Abdominal Imaging Findings of Possible Cancer. J Am Coll Radiol. 2016;13(12 Pt A):1505-1508.e2.
13. Cook TS, Lalevic D, Sloan C, et al. Implementation of an Automated Radiology Recommendation-Tracking Engine for Abdominal Imaging Findings of Possible Cancer. J Am Coll Radiol. 2017;14(5):629-636.
14. Domingo J, Galal G, Huang J, et al. Preventing delayed and missed care by applying artificial intelligence to trigger radiology imaging follow-up. NEJM Catal Innov Care Deliv. 2022;3(4):CAT-21.
15. Mattay GS, Mittl GS, Zafar HM, Cook TS. Early impact of Pennsylvania
Act 112 on follow-up of abnormal imaging findings. J Am Coll Radiol. 2020;17:1676-83.
16. Wandtke B, Gallagher S, et al. Reducing delay in diagnosis: multistage recommendation tracking. AJR Am J Roentgenol. 2017;209(5):970-975.
17. Mabotuwana T, Hall CS, Hombal V, et al. Automated tracking of follow-up imaging recommendations. AJR Am J Roentgenol. 2019;212(6):1287-1294.
18. Jhala, K., Lynch, E. A., Eappen, S., et al. Financial Impact of a Radiology Safety Net Program for Resolution of Clinically Necessary Follow-up Imaging Recommendations. J Am Coll Radiol. 2023; S1546-1440(23)01035-9.

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Countdown Begins for Missouri's General Assembly *Opens January 8*

by Jacob Scott, MA & Rachel Bauer, MPA

The 102nd General Assembly is winding down. Legislative action has ended, and we are past the election. We know who will be taking office and what new ballot initiatives they will be working with.

In these final days of 2024, all eyes are on the pending session and what may come out of this new group of lawmakers. One thing most Capitol denizens agree on is a renewed sense of hope. We have all been burning our sage to smudge out the bad juju that has plagued the legislative process for years and attempt to start fresh. Like a Phoenix rising from the ashes, the new year will usher in the beginning of the two-year-long 103rd General Assembly. So far, our hopes for good vibes are resonating. Many legislators are answering the call from their constituents to put differences aside and get to work. Per the constitution, prefiling for 2025 began December 1.

The legislature has been unable to accomplish much lawmaking—besides a budget—for the past several years. As such, many of the bills filed for next session will be repeats—three-peats, four-peats and so on—of legislation that has been filed for years.





Jacob Scott, MA, is Director of Legislative Affairs, and Rachel Bauer, MPA, is Director of Government Relations.

MSMA has worked on some great bills to protect physician-led, team-based care, and the state of public health. This coming session we will be back with our favorites and a couple new ideas as well. While our legislative agenda may be stuck on repeat, we believe these measures are important to protect the practice of medicine. Here is a list of just a few of the bills we will be bringing back for consideration by the legislature.

Covenants-Not-To-Compete

Every year a growing segment of the physician workforce becomes employed by hospitals and health systems instead of having independent practices. When we couple a large number of employed physicians with increased consolidation among those employers, it creates an unsettling effect on physicians and their patients.

Many times, physicians are forced to enter employment contracts that would prevent them from practicing medicine in the same geographical area as their employer should they leave their employment. Restrictive covenants stand in the way of a physician's ability to practice medicine and provide continuity of care for patients. These practices force physicians to up-end their families and move across the state or worse yet—leave our state to work.

No one wants to lose their doctor! We will be working to end covenants-not-to-compete in employment contracts between physicians and nonprofit healthcare facilities.

Emergency Department Physicians

Last session legislators were shocked to learn physicians are not always on staff in emergency departments (ED).

Emergency physicians are critical leaders of care teams in emergency situations, and we strongly believe emergency departments should be run by physicians when the ED is open. Having physicians on staff in all emergency departments not only helps with access to care but also ensures expectations and protects patients.

Graduate Medical Education Funding

Increasing opportunities for newly graduated doctors to stay in Missouri for residency is one way we are answering the call to address access in healthcare. We have worked hard to establish state funding for new residency slots. It is a big deal to have garnered the support and commitment of the state's general revenue funds to help us build a better pipeline of physicians to enter the workforce and serve patients. This coming session we will strive to maintain and hopefully increase the appropriations to the new GME program so we can keep talented Missouri medical students in our state for residency.



Prior Authorization Reform

Insurance companies have a chokehold on healthcare decisions. Prior authorization processes have become an arduous administrative burden wasting physician time and resources.

It is clear insurance companies covet cost control over patient care and best health outcomes. MSMA has been relentless in our continued and endless education and advocacy to rein in the way insurance companies use prior authorization to control physicians and direct care.

Patients shouldn't face delays in care or denial of care that they and their doctors believe are medically necessary. Studies show prior authorization can be so cumbersome and time-consuming patients wind up with worsening health conditions or even abandon care altogether. Physicians know what is best for their patients. We are working to get insurance out of the way.

Truth in Advertising and Title Protection

Patients have enough on their minds. We are working to stop the fraudulent misrepresentation of healthcare professionals to patients and potential patients. Titles matter—they are signals for patients as to what credentials are held by the people providing their care within a clinical setting.

The only healthcare professionals who should refer to themselves as physicians are physicians. The "ologist" designation means something. The suffix "ologist" refers to a specialist or expert in a particular scientific area of study. We will be working to help clear up confusion for patients and protect the highly specialized education and training that comes with the title "Doctor."



Offense and Defense



Though we believe we will have a robust offensive game plan this session, we are sure to spend plenty of time on defense as well. We are prepared for the return of a wide-ranging onslaught of bills aiming to expand scope-of-practice for non-physicians.

For years we have pushed back on bills that would attack physician-led care including adaptive questionnaires, independent practice for APRNs and CRNAs, naturopath licensure and optometrists performing surgery. This coming session will be no different. We will be there educating lawmakers and advocating on behalf of physicians, protecting the practice of medicine and patient safety in Missouri.

Last session you answered the call, volunteering as Doctor of the Day and showing up to testify before House and Senate committees. We need you to keep up the good work. Registration for Doctor of the Day volunteers is now open. Register at www.msma.org/DoctorDay. The revival of this advocacy opportunity was a hit last session. Physicians are highly regarded medical experts, and our legislators value your input.

We understand patient care is your top priority and physicians have little to no last-minute flexibility with scheduling. We promise to keep you informed as soon as we become aware of potential opportunities to testify on legislation during the committee process. If you are, or think you might be, interested in being a part of our rapid response team to deliver testimony please contact Rachel at rbauer@msma.org.

Physician Advocacy Day, or White Coat Day as it is widely known in the Capitol, will be here before we know it. If you haven't done so already, please save Tuesday, March 4, 2025, on your calendars. White Coat Day is our time to show our strength in numbers to not only lawmakers, but to other stakeholders in the healthcare industry.

Session will kick off on Wednesday, January 8; however, legislative action will likely stall until after the installation of all the newly elected statewide office holders on Monday, January 13, 2025. The inauguration filled with pomp and circumstance will begin at noon and will be followed by a festive evening of merriment at the Gubernatorial Ball at 6:30 pm. Speaker Jon Patterson, MD, will be greeting guests in the Speaker's office. Your MSMA staff will be there to congratulate and celebrate our many friends of medicine at the ball. If you would like to join us, please contact Rachel at rbauer@msma.org. The ball is open to the public and will be heavily attended.

Be on the lookout for the return of the *5 Things You Should Know* on Mondays and *Legislative Report* on Thursday once session begins.

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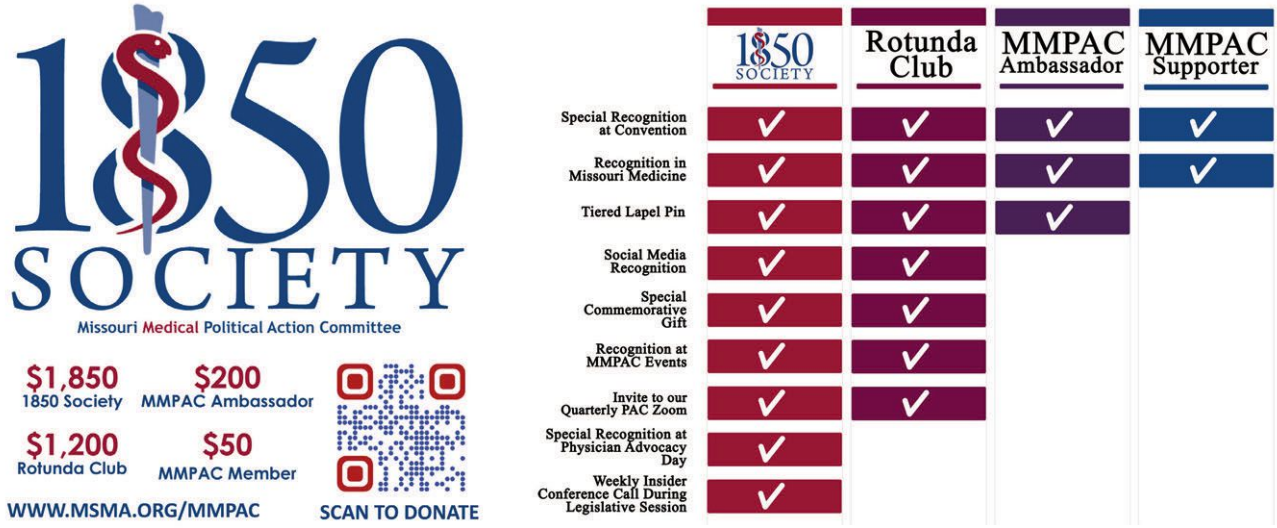
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MM

Time for *Action!*

by David L. Pohl, MD

At this writing, the elections are over, issues have been decided, and plans are being formulated for how we proceed forward. We are now faced with taking action to accomplish those goals on which we agree, how to mitigate the effects of those decisions on which we disagree, and how to do it in a manner that is respectful to our fellow citizens who see things differently than we do. Now begins the art of compromise. We need to remember that few things are forever, especially in the world of politics where "winners and losers" come and go. What should be a constant is our striving to make the world a better place than it was yesterday.

Many would say that, unfortunately, political activity is now a necessary part of the practice of medicine. However, we are fortunate to live in a society where we can become involved in determining the direction we wish our society to progress. Not every person elsewhere in the world has that privilege. It is a gift that should not be treated lightly. Not only do we have the opportunity to work for the improvement of our personal lives and those of our families, friends and associates, but we also have the responsibility to work for the betterment of the lives and situations of our patients and to alleviate the difficulties they may encounter while traversing the bureaucracy into which the modern medical system has evolved.

At the state level, which is where the MSMA predominantly works, the pre-filing of new bills for the upcoming legislative session began on December 1, 2024, in anticipation of the opening of the 103rd Legislative Session of the State of Missouri on January 8, 2025. We will face the usual and predictable challenges to Medicine that perennially seem to rise up from the dead, and will likely face a few new unanticipated developments that will seemingly come out of nowhere to occupy our time and energy—whether to support a good idea that we never thought would see the light of day, or to address the multitude of bad ideas which seemingly spring up and grow like weeds.

With the advent of the new year, I would like to ask you, as a physician, to make plans to assemble with your colleagues in Jefferson City on Tuesday, March 4, 2025, for our annual Physician Advocacy Day. Also, please consider signing up for the Doctor of the Day on Tuesdays and Wednesdays during the legislative session. These are the days during which most committees meet, and we would like to have you in attendance to help advance our positions. Lawmakers see our lobbyists frequently but tend to sit up a little straighter and become more attentive when a physician takes time from their practice to address the issues at hand. The great thing about the Doctor of the Day is that you no longer will need to triage medical issues for the assembly (something which may have impeded others in the past who were uncomfortable doling out medical advice in areas with which they were no longer familiar). Please go to the MSMA website at www.msma.org or email advocacy@msma.org for more information.

Finally, remember to reach out to your local legislators to offer your support and act as an information repository for them. Many legislators may be unfamiliar with the details and nuances of a particular bill and readily welcome the input of a physician on the issue. Getting involved does take some time and effort, but it pays off when we end up with reasonable and effective legislation to address our concerns.

Thank you to everyone in advance. And in the meantime, let's safely celebrate the upcoming holiday season with family and friends grateful for our freedoms, gifts and blessings. **MM**



David L. Pohl, MD, is a Radiologist from St. Louis, Missouri, and the 2024-2025 MSMA President.

Report of the American Medical Association Interim Meeting

by Charles W. Van Way, III, MD & the Missouri AMA Delegation

The 2024 Interim Meeting of the American Medical Association (AMA) House of Delegates (HOD) was at the Swan and Dolphin Hotels, Orlando, Florida, November 8-12. The Interim Meeting focuses on advocacy, particularly on current and pending legislation, other urgent issues, and ethics. The HOD considered 100 resolutions and 34 reports. The HOD was well attended, drawing 672 of 705 (95%) of delegates. Because the review and debate process has been improved and streamlined, the meeting went exceptionally well. And for anyone interested, the hotels are pricey, but very nice.

OSMAP, the Organization of State Medical Association Presidents, meets before the main meeting. Bruce Scott, MD, AMA President, discussed his priorities, as outlined below. Gary Price, MD, President of the Physician Foundation, discussed the results of the 2024 physician wellness survey. Burnout is still being reported at 60% rate, both practicing physicians and residents. Medical students have still a higher rate. A perceived stigma on seeking mental health care still inhibits such care.

Dr. Price noted that consolidation of health care systems has adverse effects on physician control and autonomy. Almost 80% of physicians are now employees of larger organizations, and 70% of those feel it hurts their ability to provide care. The advantages of consolidation of health care systems are not being realized.

A panel discussion by Texas, Florida, Maryland, and California presented several states' actions to stabilize state societies and to increase membership. This will be an ongoing initiative by OSMAP. The fragile health of many state societies is a matter of great concern.

In the opening session of the HOD, Dr. Scott discussed the current priorities of the AMA under his presidency. Physicians are trying to do more with too little support. Independent medical practice has become unsustainable. Physician Medicare payment has declined 29% since 2001. Another cut of 2.8% is projected for 2025, despite an estimated inflation burden of 3.5%. We need a rational payment system which will protect against inflation. "Budget neutrality" must be fixed. Congress must act now. A bill, HR 10073, has been introduced in the current "lame duck" session.

"Fix Medicare Now" was the major theme of the meeting. Inflation-adjusted physician payments have been reduced 29% in the last 20 years and will be cut another 3.5% in 2025. We must convince Congress that these cuts are totally unsustainable. Physician payments must be indexed to inflation, like all other participants in Medicare. MIPS has failed. Go to the website: www.fixmedicarenow.org.

James Madara, the outgoing Executive Vice President, reported on the continuing activities of the AMA. Membership has grown by 30% over the last 14 years, and finances are stable. The next EVP must consider governance, which should be streamlined and improved.

Medical education is a continuing concern of the AMA. The Council of Medical Education (CME) reported on a new initiative to rewrite and reform AMA policy on the spectrum of medical education. Existing policies date back to 1982, although with some more recent additions and changes. Reports on this will be coming out at least annually.

Sleep studies are difficult to obtain in many areas. Reimbursement for sleep studies is limited to physicians with certain certifications. To increase availability,



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MSMA thanks the members who represented Missouri at the American Medical Association Interim Meeting. From left: Drs. Ravi Johar, Charlie Van Way, Joe Corrado, Ed Cabbabe, Peggy Barjenbruch, Elie Azrak, and Joanne Loethen.



The AMA recognized delegates who served our country over Veteran's Day. Standing is Missouri's Charles Van Way, III, MD, is Colonel, US Army Reserve, Medical Corps.

resolution 605 called for expansion of reimbursement policy. This was referred to the Board of Trustees (BOT) which will issue a report and recommendation at the June meeting.

Increasing expense of attending AMA meetings has prompted shortening of the meeting. But resolution 609 asked for restoration of the original meeting length. Resolution 605 asked for direct reimbursement for delegates by the AMA. BOT Report 16 recommended continuing the existing grant program for short-term help, but not expanding it. A further report will be submitted to the AMA Annual Meeting in June. Further work will be done to mitigate costs and maintain participation.

There was brisk debate over Resolution 601, calling for reversing the policy (G630.140.4) which restricts where the AMA can meet. This is an emotional issue for many, because of restrictions on abortion and transgender care. States in the southern tier, which is favored for late fall meetings, are banned save for New Mexico and California. Florida is off limits after the 2024 and 2026 Interim Meetings, which were arranged some years ago. The AMA, which represents physicians in all states, has become strangely restrictive, being confined to only "blue" states. While this resolution was not adopted, the debate will continue at future meetings.

The increasing lethality of drug use continues to concern the AMA. Resolution 202 advocated a law enforcement approach, including support for Federal efforts to deal with the drug "crisis." Specifically, these include efforts to reduce importation, production, and selling of fentanyl and other dangerous drugs. There was significant opposition to this approach. The AMA supports the "public health" approach, which aims to make drug use less lethal.

Related to this, Council on Science and Public Health (CSPH) Report 1 discussed the problem of misleading advertising of cannabis products, and recommended policy supporting better regulation. Cannabis remains illegal at the Federal level, and state regulation varies widely. Many cannabis vendors advertise unproven health claims. The report recommended advocating stronger regulation and stronger enforcement of existing regulations.

Another perennial concern is Medicaid reform. Resolutions 803 and 807 advocated using health savings accounts (HSAs) in Medicaid. Many felt that the HSA

model is impractical for Medicaid. While these resolutions were not adopted, there was general support for giving more options under Medicaid.

Credentialling for new physician applicants is often delayed by insurance carriers. The AMA will urge the US Department of Labor to establish uniform credentialing standards and prompt action. The AMA also will urge requiring third party administrators to notify applicants within 45 days, after which an applicant is deemed to be eligible for payment of services.

BOT 15 reported proposed development of metrics for hospitals and health systems that would measure physician well-being. This would be nice, but such metrics will have to be developed. The use of unproven metrics in MIPS continues to be an issue. Many clinical performance and outcomes measures lack scientific validation and burden physicians without improving patient care. Resolutions 220 and 222 reaffirmed and expanded AMA advocacy for removal of unproven outcomes measures and associated mandates placed on physicians. There is support for eliminating MIPS entirely.

Resolution 817 called for expanding Federal subsidies to undocumented immigrants. This has been done in Washington state, with beneficial results for patients. There was support, but also concern for unintended consequences. It was recognized that this may not be consistent with political realities, and that it might have major budget implications at both state and Federal levels.

Augmented intelligence (AI) in medicine is an increasingly important issue. BOT 1 proposed policy, setting forth a number of guidelines. Health care AI must be designed, developed, and deployed in a manner which is ethical, equitable, responsible, accurate, and transparent. What is more, clinical decisions influenced by AI must be made with specified human intervention points during the decision-making process. This will be an ongoing concern.

There was continuing concern for the problems of rural health care, including inadequate payment, physician shortages, hospital closures, and excessive reliance on Medicaid. The AMA is already strongly in support of improving rural care. Resolution 811 called for improving the geographic allocation of practice cost by CMS and addressing the shortage of rural physicians. The lack of physician supervision in many emergency rooms, particularly in rural hospitals, was a highlight. Resolutions 201 and 203 affirmed that the preferred model of emergency care is the on-site presence of a physician in the emergency department whose primary duty is to provide care in that ED, but also supported state medical associations in developing appropriate rural exceptions.

There is an ongoing concern for physician and patient safety. Resolution 904 called for improved standards of radiation safety to protect physicians and all other health workers from the known hazards of radiation.

Resolution 228 advocated supporting legislation to re-instate the Chevron doctrine, which was reversed last year by the Supreme Court. This has implications on our interactions with a wide variety of Federal agencies. The question was referred to AMA staff for a study of the effect of this decision, especially on public health.

As usual, the HOD dealt with a mixture of physician-specific issues such as Medicare, and societal issues, care for transgender individuals, and the public health impact of climate change. The AMA sees itself as having an additional role beyond simple physician advocacy. There was less emphasis on societal issues than at previous meetings. The AMA is most effective when it works on issues affecting physicians and health care in general.

Several Missouri physicians continue to serve in leadership roles. **Edmond Cabbabe, MD**, serves on the Council for Long Range Planning and Development. **Elie Azrak, MD**, serves on the board of AMPAC, the AMA Political Action Committee. **Jerry Kennett, MD**, is on the AMA Foundation board. **Kelly Schmidt, MD**, is the past Chair of the Resident and Fellows Section. **Marc Mendelsohn, MD,** serves on the Council on Science and Public Health. **Charles Van Way III, MD**, is vice president of OSMAP, the Organization of State Medical Association Presidents.

Your AMA delegation would very much like to hear from physicians throughout Missouri about the issues discussed at the meeting, especially Fix Medicare Now. For further information, see the website https://fixmedicarenow.org. The business of the meeting is available on the AMA website. Highlights and details of this and previous AMA meetings are at: https://www.ama-assn.org/house-delegates/hod-organization/archive-house-delegates-meetings. The Annual Meeting of the HOD will be in Chicago, June 6-10, 2025. The AMA continues to advocate for physicians and their patients across the country. **MM**

Military Medicine and Medical Education in Missouri

by Ulysses Fernandez-Miro, Capt, DO, Pamala R. Huges, Lt Col, MD, Luke F. Jett, Lt, MD, Craig Krausz, MD, Richard K. Newman, Capt, DO, Brandon M. Parham, Capt, & Julie K. Gammack, MD

Introduction to Military Branches and Military Medicine

In the United States (US), military medicine plays a crucial role in ensuring the health and readiness of service members throughout the Department of Defense. Each military branch—Army, Navy, Air Force, Marine Corps, and Coast Guard—has its unique scope and duties within the broader context of national defense. Understanding each branch's distinctive responsibilities and educational initiatives is essential for understanding the comprehensive landscape of military medicine and medical education.

The intersection of military medicine and medical education is exemplified in Missouri and Southwest Illinois. Many longstanding and collaborative efforts exist between state institutions and the military to foster medical training and healthcare delivery excellence. By exploring these synergies, we can gain insights into the evolving landscape of military healthcare and its impact on medical education locally and nationally.



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National Scope and Duties

At the national level, military medicine encompasses many functions to support the health and well-being of active-duty personnel, veterans, and their families (Table 1). The branches collaborate closely through entities like the Defense Health Agency (DHA) to coordinate healthcare delivery, research, and medical training across the armed forces.

Military medical services focus on several key areas:

Combat Casualty Care: Providing advanced trauma care and medical support to wounded service members in combat zones.

Healthcare Delivery: Offering comprehensive medical services to active-duty personnel, retirees, and their families through military treatment facilities (MTFs) and civilian provider networks.

Medical Readiness and Training: Conducting specialized training programs to prepare healthcare providers for military-specific medical challenges.

Research and Development: Advancing medical research in infectious diseases, trauma care, and preventive medicine to improve health outcomes for military populations.

Scope of Missouri Military and Uniformed Services

In Missouri, military medical services are vital components of the state's healthcare landscape, facilitated by collaboration between military installations and civilian healthcare providers. Thousands of active, reserve-duty, and civilian employees of the military support the national and local health care needs of Missouri (Figure 1). [1] We are home to several military installations and medical

Table 1. Medical Corps and Services

Military Branch	Medical Branch	Key Operations
Army	Army Medical Corps	Medical care to Army personnel and families Combat casualty care Medical readiness training
Navy	Navy Medical Corps	Medical care for Navy and Marine Corps personnel and families Medical services on land and at sea Support of naval operations worldwide
Air Force	Air Force Medical Corps	Health and medical readiness of Air Force personnel and families Aeromedical evacuation Aerospace medicine and global health engagement
Marine Corps	Navy Medical Corps	Health and fitness of Marines Integration within Marine forces Expeditionary medicine and combat casualty care
Coast Guard	Coast Guard Health Services	Medical care to Coast Guard personnel and families Maritime readiness and rescue operations

centers that support training, deployment readiness, and healthcare delivery to service members and their families (Figure 2).

Healthcare Facilities

Military treatment facilities and Veterans Affairs (VA) medical centers in Missouri provide specialized care to active-duty personnel, veterans, and their dependents. These VA centers include the John Cochran and Jefferson Barracks branches of the VA Medical Center in St. Louis, the John J. Pershing VA Medical Center in Poplar Bluff, the Harry S. Truman Memorial Veterans' Hospital in Columbia, and the Kansas City, Missouri, VA Medical Center.

Military Bases, Branches, and Services

Fort Leonard Wood: Located in the Ozarks of Missouri, Fort Leonard Wood serves as a primary training center for the US Army, focusing on combat engineering, chemical defense, and military police operations.

Whiteman Air Force Base: Home to the 509th Bomb Wing, Whiteman AFB is a critical base for B-2 Spirit stealth bombers and supports a wide range of missions, including strategic deterrence and global strike capabilities.

Scott Air Force Base: Located in Illinois, near St. Louis, Scott AFB serves as a major hub for Air Mobility Command and supports global airlift and air refueling operations. Scott AFB is home to the sole Air Force Aeromedical Evacuation training squadron. Additionally, it also hosts the United States Transportation Command.

Missouri National Guard: The Missouri National Guard plays a crucial role in disaster response and relief efforts within the state, providing medical support, search and rescue operations, and logistical assistance during emergencies. During flooding events along the Missouri and Mississippi Rivers, Guard units provide essential support such as flood barrier construction, evacuation assistance, and medical aid to affected communities. Additionally, the Guard has played a pivotal role in responding to tornadoes and severe storms, conducting search and rescue operations, and delivering humanitarian assistance to impacted areas.

US Public Health Service Commissioned Corps (USPHS): Dedicated to protecting health and fighting disease, USPSH often partners with the National Guard for disaster preparedness and response to domestic emergencies. Seven Public Health Service sites operate in Kansas City, Missouri, St. Louis, Southwest Illinois, and Springfield, Missouri, locations, supporting 15 environmental and public health positions (Figure 2).[2] These offices support agencies such as the Food and Drug Administration, Department of Homeland Security, and Department of Defense.

Disaster relief, public health, and emergency response efforts highlight the critical role of military

Figure 1. Missouri Military Workforce by Branch



medical services in safeguarding public health and safety during emergencies and natural disasters within Missouri and its surrounding regions. By leveraging military resources and expertise, communities enhance their resilience and response capabilities in times of crisis.

Veterans Affairs Medical Centers

The US Department of Veterans Affairs (VA), via its Office of Academic Affiliations (OAA), coordinates education and training for medical, dental, nursing, associated health, and advanced fellowship programs nationwide. For nearly 80 years, the VA has supported the development of the healthcare workforce in more than 60 different professions. It is the largest enterprise for health care education and the second largest financier of health care training in the US. Each year, approximately 125,000 health profession trainees (HPTs) from 1,800 educational institutions serve our nine million veteran patients. Priority areas for VA training include primary care, mental health, and critical need services.[3]

Of the nation's 155 osteopathic and 37 allopathic medical schools, 99% have VA training affiliations for clinical education. Ninety percent of VA clinical sites engage in these academic affiliations. Each year, more than 50,000 medical residents and 30,000 medical students participate in VA training, an increase of 10% over the past five years.[4] This growth is largely due to the growing number of accredited US medical schools and the Veterans Access Choice and Accountability Act of 2014, establishing 1,500 new GME positions by 2020. Moving forward, more than 70% of practicing physicians in the US will have had a VA training experience.

Most of Missouri resides within the Heartland Veterans Integrated Service Network (VISN) 15 area, while southwest Missouri is included in VISN 16. Healthcare services are delivered at Missouri's four VA medical centers, 40 Community-Based Outpatient Centers (CBOCs), and other community healthcare facilities (Figure 2). Missouri and the Kansas City, Missouri, metropolitan areas support five accredited allopathic and two osteopathic medical schools, each having an educational affiliation with the VA. The state sponsors 18 graduate medical education institutions with 374 residency and fellowship programs.[4]

Military Medical Education

The US military medical education system has evolved significantly since the Army Medical Department was established in 1775 during the American Revolution. In the 19th century, the Civil War catalyzed the development of Army hospitals and medical colleges. The 20th century brought about rapid advancements in medical science, establishing specialized medical training programs within all military branches. Throughout its history, the US military medical education system has adapted to the evolving challenges of warfare while advancing medical knowledge through research and innovation.

Military medical education today is a complex network of institutions and programs dedicated to training medical professionals to serve the nation (Figure 3). Military medical training emphasizes clinical excellence, leadership, and readiness to provide care in austere environments. To foster a sustainable source of military physicians, the Uniformed Services Health Professions Revitalization Act of 1972 established two programs for physician training: 1)

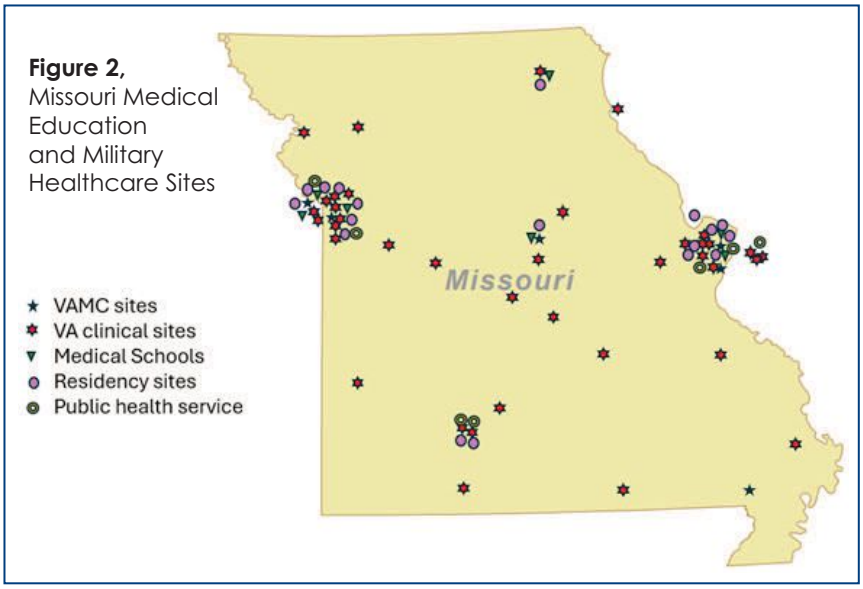


Figure 2, Missouri Medical Education and Military Healthcare Sites

the Health Professions Scholarship Program (HPSP) for students attending civilian medical schools, and 2) the Uniformed Services University of Health Sciences (USU) medical school.

Military Medicine Recruitment

The military's mission is to recruit the best, most highly qualified, and motivated prospective medical students, residents, and physicians to serve the nation's soldiers, airmen, seamen, and families. The Defense Health Agency (DHA) is a joint-service Military Health System whose mission is to support the National Defense Strategy and Service Military Departments by leading an integrated and highly reliable medical training, readiness, and health system. The main priority is to provide first-rate medical care and consistent in-strength, ensuring the health and wellness of service members to remain ready to accomplish any mission at any time.

The role of a military medical professional is a unique combination of active and reserve duty services, clinical care, and military officership. Reserve medical officers serve in their local community one weekend a month to supplement active-duty forces, train, and mentor service members, and ensure the medical readiness of the force. Physicians in the reserve also support humanitarian missions across the globe. Both active duty and reserve physician officers serve to support national defense and care for our nation's service members and their families.

Uniformed Services University of Health Sciences

The USU is the nation's only military health sciences university providing a spectrum of health professions education. Applicants must demonstrate rigorous academic standards and undergo a security clearance that meets the requirements for a military commission. USU is tuition-free and accepts 171 prior-duty and civilian students annually who become Army, Navy, Air Force, and Public Health Service officers. The curriculum includes basic sciences, innovative research, leadership training, and clinical practice tailored to the challenges of military medicine. Upon graduating, each officer completes an active-duty service commitment: seven years for the Army, Navy, and Air Force, and ten years for the Public Health Service (Figure 3). USU graduates serve in various clinical, research, and administrative roles within the military health system.

Health Professions Scholarship Program

HPSP supports undergraduate medical education for prospective civilian physicians who will enter the military workforce upon completion. It promotes the training and retention of medical professionals as active-duty military officers to support the mission of national defense. HPSP offers eligible candidates tuition-free medical education in exchange for a minimum two-year active-duty military service obligation.[5]

HPSP scholarships are available for accredited medical, dental, veterinary, nurse practitioner, clinical psychology, or optometry schools, located in the United States or Puerto Rico. The Army, Navy, and Air Force offer scholarships of varying lengths and the total number of slots available varies based on projected needs with each fiscal year. For example, in fiscal year 2025, the Army has a total of 340 scholarships to provide qualified students. Of note, the Navy and Air Force programs provide medical professionals to the Marine Corps and Space Force respectively.

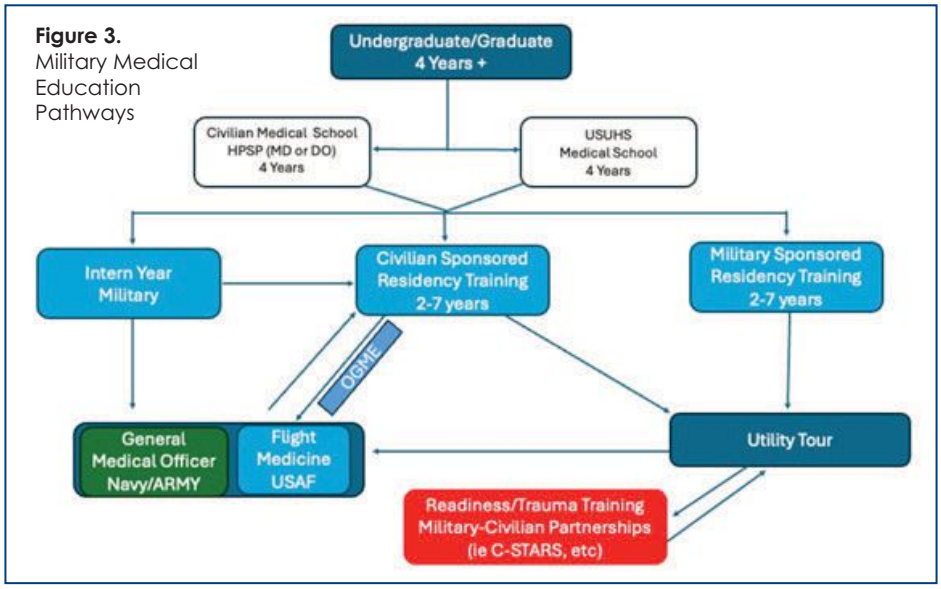


Figure 3. Military Medical Education Pathways

While students are in medical school, HPSP covers 100% tuition, required fees, textbooks, and many associated expenses of medical school. Additionally, it pays a monthly stipend to defray additional living expenses. Upon acceptance, the candidate is commissioned as an officer in their accepted service and placed into the Individual Ready Reserve. Scholarship recipients are expected to meet academic requirements for graduation and participate in 45 days annual training. These training opportunities can include medical rotations at military training facilities, medical school requirements, or officer professional development school. During medical school, candidates are eligible to apply for both military and civilian residencies of their choice with preference given to military residency positions. After graduating and earning a doctorate, HPSP recipients are commissioned as a Captain (O-3) in their respective military branches.

There are many other financial support options available to medical students, residents, and physicians for active duty, reserve military, and US public health service commitments.[5,6] Medical students interested in the reserve may be eligible for a stipend, health benefits, and years toward retirement. The Financial Assistance Program (FAP) for residents is an active-duty program that supplements their pay with a $40,000 annual grant, as well as a monthly stipend throughout residency. Residents who are interested in a reserve commission, can earn up to $250,000 in student loan repayment and a monthly stipend additive to their income. Practicing physicians can qualify for financial benefits such as loan repayment, accession bonuses, incentive pay, and board certification.

Missouri Military Medical Education

In addition to national responsibilities, each military branch engages with state-based institutions to promote medical education and training. There are nearly 90 unique military-civilian trauma center partnerships in the US, largely in collaboration with the Air Force.[7] Civilian trauma practice outside of deployment is considered a best equivalent for combat skill sustainment.[8] Military-civilian partnerships are prominent in Missouri, where military programs and educational institutions collaborate to advance healthcare. The military presence and partnerships within medical schools create unique medical education and research opportunities. Missouri and Southern Illinois training programs support many military deferred medical students and residents, active-duty teaching faculty, and reserve and retired officer physicians who are a part of the US Military. This partnership demonstrates the commitment of Missouri and Southwest Illinois to supporting the Armed Forces and promoting the health and well-being of the community.

SSM Health/Saint Louis University School of Medicine (SLUSOM) Family Medicine Residency

For over 25 years, SLUSOM and the 375th Medical Group at Scott Air Force Base have partnered in a uniquely integrated military-civilian family medicine residency. A total of 42 residents, 24 who are active-duty Air Force, are trained in the community-based program in O'Fallon, Illinois. Both civilian and military residents share educational and clinical spaces. They are taught by both military and civilian teaching physicians. HSHS St. Elizabeth's Hospital serves as the primary inpatient clinical site with adjacent military and civilian outpatient clinics providing continuity care for patients of all ages.

SSM Health/SLUSOM Emergency Medicine Residency

The SSM Health/SLUSOM emergency medicine residency is accredited for 24 positions. Six to eight of these positions are designated for military-matched active-duty Air Force residents through Operational Graduate Medical Education (OGME). This specialized training pathway is designed to produce medical officers capable of providing healthcare in dynamic, austere environments. The OEM track within OGME at SSM Health/SLUSOM has been active since 2017.

OEM integrates civilian residency training with military operational medical experience, culminating in developing highly skilled physicians prepared for deployment. In addition to SSM Health/SLUSOM, four other civilian partners offer emergency medicine training for the OEM program: The Ohio State University, Einstein Health Network, Mercy St. Vincent, and Virginia Commonwealth University. OEM focuses on developing emergency medicine physicians with the unique skill set required for flight surgeon roles. These physicians receive comprehensive training in emergency care and operational medicine. They also complete Aerospace Medicine Training at Wright-Patterson AFB and achieve their flight status in preparation for Flight Medicine upon graduation.

The Center for Sustainment of Trauma and Readiness Skills (C-STARS)

Based on his medical skills training lab at DePaul Hospital in Bridgeton, Missouri, the SLUSOM C-STARS program was established in 2002 by Colonel Michael Hayek, Air National Guard.[9] The program offers Air Force personnel simulation and hands-on training in an academic trauma center in partnership with civilian trauma teams.[10] This training experience in civilian trauma centers provides military surgeons with a greater trauma experience than they receive at their home station.[11] The St. Louis program conducts 19 advanced trauma skills courses annually for more than 300 military physicians and nurses. C-STARS has dedicated military faculty partners within the SLUSOM academic faculty and staff. The program utilizes classroom training, simulation, and clinical rotations at SSM Health Saint Louis University Hospital, an American College of Surgeons Level 1 Trauma Facility. C-STARS has since expanded to include programs in Ohio, Maryland, Nevada, and Nebraska. The Navy and Army have also established military-civilian trauma training partnerships like C-STARS.

Conclusion

Throughout Missouri, our physician workforce represents all military branches and includes active duty and reserve officers. Military physicians are vital assets for community health care, the US military service, and military-civilian educational partnerships. This partnership is achieved through the hard work, dedication, and support of service members, civilians, and their families. Missouri's motivated and supportive healthcare network fosters the environment required to remain focused on this critical mission. Physicians or prospective physicians who choose to serve will help maintain and advance a technologically savvy, modernized, and resilient healthcare system. Missouri is proud of its dedicated and inspired physicians who will drive military health's next evolution through adapting, innovating, and improving the care system through leadership, advanced training, research, and making extraordinary experiences ordinary.

References

1. "DoD Personnel, Workforce Reports & Publications" Military and Civilian Personnel by Service/Agency by State/Country. Defense Manpower Data Center, Accesses July 24. 2024. https://dwp.dmdc.osd.mil/dwp/app/dod-data-reports/workforce-reports.
2. "Commissioned corps of the us public health service. Where We Work. " U.S. Department of Health and Human Services, Accessed July 25, 2024, https://www.usphs.gov/about-us.
3. "Health Professions Education Statistics: Academic Year 2022-2023." U.S. Department of Veterans Affairs, May 9, 2024, www.va.gov/oaa/docs/OAA_Stats_Sheet_AY_2022-2023.pdf
4. "Accreditation Council for Graduate Medical Education (ACGME) – Public. Advanced Program Search". Accreditation Council for Graduate Medical Education. Accessed July 24.2024. https://apps.acgme.org/ads/Public/Programs/Search
5. "Health Professions Scholarship Program (Hpsp) Fact Sheet," United States Air Force, July 2024, https://www.airforcemedicine.af.mil/Media-Center/Fact-Sheets/Display/Article/425437/hpsp-fact-sheet/.
6. "Health Professions Scholarship Program (HPSP) and Financial Assistance Program (FAP)," U.S. Navy Bureau of Medicine and Surgery, Accessed October 14, 2024, https://www.med.navy.mil/Accessions/Health-Professions-Scholarship-Program-HPSP-and-Financial-Assistance-Program-FAP/.
7. Gurney J, et a. Data-driven readiness: A preliminary report on cataloging best practices in military civilian partnerships. J Trauma Acute Care Surg. 2022; 93(2S):S155-S159
8. Lee JJ, et al. Integrated military and civilian partnerships are necessary for effective trauma-related training and skills sustainment during the inter-war period. J Trauma Acute Care Surg. 2022; 92(4):e57-e76.
9. Thorson CM, et al . Military trauma training at civilian centers: a decade of advancements. J Trauma Acute Care Surg. 2012;73(6 Suppl 5):S483-9.
10. Grimm J.,et al, Saint Louis Center for Sustainment of Trauma and Readiness Skills: A Collaborative Air Force–Civilian Trauma Skills Training Program. J Emerg Nurs. 2016; (42(2): 104-107.
11. Schreiber MA, et al. Military trauma training performed in a civilian trauma center. J Surg Res. 2002; 104(1):8-14.

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Captain John C. Hagan III, USAF Medical Corp 1970-1972

During WWII my father had tuberculosis and was in a TB Sanatorium in Mt. Vernon, Missouri. Most of the eligible men and some of the women in my family, were on active duty in North Africa, Europe, and Pearl Harbor, Hawaii. After the war, I grew up hearing about their wartime military service which I greatly enjoyed. My father, who was killed in a plane crash when I was 10, lamented his inability to serve. He had no stories to tell. I grew up planning to join the military and tick that box for my family.



A young Doctor Hagan in 1970 in USAF "Boot Camp Light" for physicians, Sheppard Air Force Base Texas, temperature 118 degrees.

The opportunity arose during the Viet Nam War (1955-1975). In 1969, I finished medical school at Loyola University unsure of what direction in medicine or surgery to follow. I chose to join the United States Air Force (USAF). As an intern at Milwaukee County Hospital, I awaited orders on where I was to serve. I received a phone call at work from my wife. "Your orders came" my wife said in tears. I asked if I was going to Viet Nam. "No, it's worse, we are going to North Dakota."

Grand Forks AFB, North Dakota, turned out to be a rewarding experience. The friendships my wife and I made have lasted a lifetime. I was proud "to support the mission." I had official approval to do weekend *locum tenens* at a 12-bed hospital in Northwood, North Dakota. That was an awesome responsibility for a general medical officer. I was the only physician in a four-county area. I was sent to our sister base in Minot, North Dakota, to learn to triage ophthalmology. The first microscopic eye surgery case I assisted on made me certain ophthalmology was my calling in medicine. After completing service and beginning a residency at Emory University, the GI Bill was enormously helpful, allowing us to rent a home and accumulate no further educational debt.

Alas, things have not gone well for the armed forces in general and the Air Force in particular.[1] The planes are old, and there are not enough of the new ones. The Air Force plans to fly the venerable B-52 for almost 100 years! The force is seriously understaffed. A startling 77% of American youths do not meet the physical standards of military service. The ability of the US to prevail in a future military conflict is being continually eroded.

I treasure my time in the active and reserve military. I urge students and housestaff to consider the military as a way to dramatically reduce educational debt and serve with and care for those that guard our precious liberties.

References

1. Wicker R, Schmitt E. How the US Air Force Can Reclaim the Skies. Wall Street Journal October 13, 2024

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From Space Stations to the US Marines... From Engineering to Private Practice Surgery... A Physician is Right at Home

by William Reynolds, DDS, MD

It was the summer of 1951 in Washington DC that I entered the world. I was the second born child, but the family expanded to seven children by 1960. Dad worked for the US Navy surveying the North Slope of Alaska until the oldest child fell on a basement floor suffering a skull fracture and Dad was called back to Washington DC. My parents decided that he would take another job where he would be home in the evenings.



Dr. Reynolds at St. Patrick's Elementary School circa 1964.

Our family became corporate gypsies when our Dad entered the General Electric Company's space program division, moving our family to Philadelphia. St. Patrick's Elementary School in Malvern, Pennsylvania, was my first experience with the Sisters of St. Joseph and what was considered proper behavior. I was described as "All Boy" by the nuns.

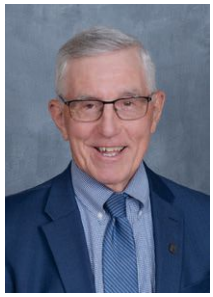
Growing up was exciting with the space program in full swing landing me in four high schools in four years on both coasts of the country, finally graduating high school in Scottsdale, Arizona. Engineering was all I thought of as I entered Arizona State University School of Engineering—calculus, differential equations, linear algebra, physics, chemistry, and engineering classes.

Dad transferred back east to work on another satellite, and I followed to enter the University of Maryland-College Park in the School of Engineering. I loved engineering, but I took a summer class in Zoology and fell in love with the life sciences, learning about parasites, protozoans, physiology, histology, comparative anatomy, and electron microscopy.

Upon graduating with honors from Maryland, I learned others had similar degrees; in fact, they had Masters and Doctorates and some post Doctorates. All were looking for jobs in our chosen fields. The first job I took was pumping gasoline at an APCO Station in Columbia, Missouri. I thought seriously of returning to engineering at Maryland but chose instead to enter graduate school at the University of Nebraska-Lincoln. Besides learning about Big 8 Football and the importance of the Nebraska-Oklahoma game, I spent time learning scanning and transmission electron microscopy, tissue culture techniques, cell differentiation, and genetics.

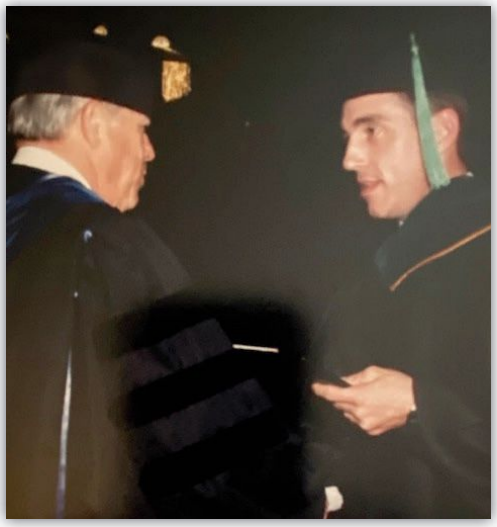
Nebraska's dental school was in Lincoln, and many of its students were living in the graduate student dorm. I spent time with these students and decided that I would apply to dental school. I entered the University of Missouri-Kansas City School of Dentistry. The dental school had an identical transmission electron microscope as Lincoln Nebraska did. I continued doing this type of work while in dental school as my skills were needed and working other jobs to keep the costs of dental school reasonable.

Boston University Hospital Department of Radiation Medicine and the Henry Goldman School of Graduate Dentistry had a joint Fellowship in Oral Oncology. Application and acceptance were successful



William Reynolds, DDS, MD, is a newly retired plastic surgeon in Springfield, Missouri, and a Contributing Editor to *Missouri Medicine*.

for the year after graduating dental school. I worked for Merrill Feldman DMD, MD, and Henry Goldman himself. All the math and physics in engineering was helpful in the radiation medicine department and being able to do electron microscopy and enjoying histology was helpful when working with Henry Goldman, who did everything—oral pathology, periodontics, research, and publications.





Left, Graduation from The University of Missouri -Kansas City Medical School 1988.

Right, LCDR William Reynolds DC, USNR Photo taken at Bethesda Maryland during a dental conference circa 1990.

During my time in Boston, Dr. Feldman took me to visit Padmakar P. Lele, MD, at MIT who was a neurosurgeon who became a physicist. His interest was ultrasound hyperthermia in the treatment of cancer. His lab was in a basement, and he had some graduate students in engineering. These graduate students had a difficult time with the surgery side, and I started working with the engineers who monitored the heating of the tumor as I prepared the experimental animals.

Dr. Lele had a great referral system from veterinarians throughout the local states. I remembered one case of a dog with a large ameloblastoma which was treated with ultrasound hyperthermia. Simply, the tumor disappeared. Drs. Feldman and Lele told me once that improving the treatment each year of any cancer survival rates by 2-3 % points would effectively be a cure after 40 years. Both have passed on, but they were right about survival rates.

I left Boston to begin private dental practice in Missouri. Boston was a wonderful experience but unaffordable to live in on a Fellows salary. Besides home was southwest Missouri and Mom and Dad were there. I met my future wife Julie who eventually went to law school at the University of Missouri-Kansas City graduating the same year as I graduated from medical school.

The dental practice did well, but I missed hospital work. So, after a few years an application to medical school was made and acceptance happened at the University of Missouri-Kansas City School of Medicine. It was a great four years. I intended to go into radiation medicine but soon found out I was a better surgeon than a radiation oncologist. It was on to general surgery.

I entered the US Naval Reserve as a Dental Corp Officer while in private dental practice. I felt everyone should serve at some time. This is a great country with a remarkable history of ordinary people serving to carry on traditions of service and sacrifice. Assigned initially to a Fleet Hospital, a transfer was made to a dental company in the 4th Marine Division-Fleet Service Support Group (FSSG- which no longer exists). I liked the way the Marines did things. It made sense, and I could keep up with the Marines. Continuing to drill as a Reservist during General Surgery Residency, I became the Battalion Surgeon 1st Battalion 24th Marines out of Detroit. I was in general surgery at Sinai Hospital of Detroit, and I had the support of the faculty. The Chairman of the Surgery Department was a WW II veteran as was one of the senior surgeons, who had served in Patton's Army in WW II.

When Saddam Hussein invaded Kuwait, the US military was on a war footing. The 1-24th Marines were activated, and I left General Surgery for a time. The 1-24th completed SOC training (Special Operations Capable) while in Okinawa, Japan. We were in reserve had the war not gone well. We never made it

to the dessert but instead were shipped to Subic Naval Base to Camp Tamez in the Republic of the Philippines. The 1-24th Marines were the Ground Combat Element (GCE) of MAGTF 4-90 (Marine Air Ground Task Force). Things were great there. I was allowed to operate at the Subic Naval Hospital with the general surgeons. I learned much about tropical parasitic diseases and the surgical implications, for example Oriental Cholangiohepatitis.



Staff Officers of 1/24th Marines in Okinawa Japan after SOC Training. Dr. Reynolds is the third from the right in the first row.

Two catastrophic events happened after Operation Desert Shield and Desert Storm finished. A very large volcanic eruption occurred in the Philippines. This was the Mount Pinatubo eruption and a massive tidal wave hit the coast of Bangladesh. The first was called Operation Fiery Vigil and the second was Operation Sea Angel.

Mount Pinatubo was the second largest eruption in the 20th century and required the evacuation of 58,000 people. The population of the Clark Air Force Base was evacuated over mountainous terrain to Subic Naval Base. The New People's Army (the armed branch of the Communist Party of the Philippines) was one of our major concerns. Eventually, the aftershocks ended, and the navy ships were allowed back into the harbor. The 1-24th Marines mission then included helping the relief at Subic. Fortunately, the 1-24th Marines was a Reserve Battalion with many of the officers were engineers in Detroit and many of the enlisted were card carrying union men who could work heavy machinery.

The natural disaster which unfolded in Bangladesh was noted worldwide. Nations around the globe responded to the needed relief. The American Relief was a US Navy relief effort. Medical supplies, food, clean water, and much more were provided. Another medical officer in the 1-24th Marines from Michigan helped this relief effort.

Upon returning to general surgery training in Detroit soon after Mount Pinatubo settled down, the Chairman of Surgery gave me a few days off before continuing as a resident. I kept a record of cases I had done while overseas and the chairman and faculty allowed me to advance to the next year in general surgery with approval of the American College of Surgeons. Also, I published the case of Oriental Cholangiohepatitis and other papers.

The opportunity to do a Burn Fellowship at the University of Kansas Medical Center was offered, and I accepted it because I had also been accepted into the Plastic Surgery Residency at KU the following year. I think of all the fields in surgery I have experienced, I have enjoyed burn surgery the most. It had the right amount of critical care, surgery, and reconstructive surgery. And those who worked in burn units would do nothing else. It is not uncommon that a nursing staff would say with pride "I am a Burn Nurse."

Burns injuries to the hands, face, perineum and feet are best handled by plastic surgeons in my opinion. Being a dentist also helped while at KU. John Heibert, MD, was a craniofacial surgeon and he understood how important occlusion was in jaw fractures and other facial injuries.

Time at KU was great. My family was growing, the work at KU was interesting and upon completion, Julie and I and the children all returned home to southwest Missouri. Interestingly, the Reynolds Family homesteaded in Spokane, Missouri, in 1892 along Chestnut Ridge. One of the sayings in this area is: "Everyone moves away but they all move back with time." I certainly did.

Continuing in the Reserves, I became the Regimental Surgeon 24th Marines in the Kansas City area. In training exercises at 29 Palms California,

Camp Pendleton and the Amphibious Warfare School in Coronado, California, I served as the MAGTF Surgeon.

I became an independent physician choosing not to sell my practice to one of the two major hospital systems in southwest Missouri. In retrospect, this was a good idea. I enjoyed being an employer rather than an employee.

The importance of organized medicine came home to me in private practice when I became a member of the local medical society, eventually becoming the president. As a member of the Missouri State Medical Society, I served as a delegate to the MSMA Annual Convention each year. There were many delegates and the collective efforts of the delegates, and the Council had a positive impact on issues facing our profession. And it still does.



Family Photo: First row Emma Reynolds (museum specialist) and Philip Weist (statistician) on their wedding day. Back row, L to R: Sarah Reynolds (engineer), Rachel Reynolds (landscape architect), wife Julie Reynolds (attorney), Bill Reynolds, Robert Reynolds (attorney), Laura Gowans (COO of KC Non-Profit).

I encourage any new graduate of a residency to join the local, state and national societies. These organizations represent you and your profession, and they have a positive impact on issues facing our professions.

Representative Jason Smith (Missouri's 8th Congressional District and Chairman of the House Ways and Means Committee) recently sent an e-mail which reported "unpredictable and shrinking reimbursement from the Medicare Physician Fee Schedule and burdensome quality reporting requirements." In plain talk, this means more paperwork and less patient care. He also noted when "a hospital system buys up a private practice, prices rise about 14% while preventable hospital admissions increase 13%." The AMA also recently reported that physicians pay has not increased since the early 2000s when adjusted for inflation.

It has been much better in private practice as an employer than in a hospital system as an employee. I am much happier retiring at the age of 72, with no burn out and no regrets. A new chapter in my family life has begun with retirement. Working in surgery— the staff, the patients, and my office staff will always hold a fond place in my heart. My continued work with the American Society of Plastic Surgeons on various committees is also rewarding. My favorite committees are the In-Service Examination Committee (writing the questions with a great group of plastic surgeons) and the Practice Management Committee. The Missouri State Medical Association has been an outstanding organization and I help as a Contributing Editor for *Missouri Medicine.*

Much of my time is spent re-reading books I have collected over the years especially on American history.

For new graduates from residency training, I say embrace the idea of independent private practice. You can open the possibilities of a great life and be much happier doing it. You are a member of the greatest profession there is, and you will do more service for the patients in your community, improving the health of the community, and improving the art and science of medicine and surgery. **MM**

Beyond Malpractice: When Practice Becomes Criminal and Related Implications for Healthcare Providers

by Ashley Todd, JD & Tessa Carberry, JD

In 2019, 23-year-old Elijah McClain died after Aurora, Colorado, Fire Rescue paramedics Jeremy Cooper and Peter Cichuniec administered a fatal dose of ketamine.[1] On a warm August night, Cooper and Cichuniec responded to a 911 call, and when they arrived on the scene Mr. McClain was already restrained and in handcuffs. Cooper was in charge of the call and responsible for the medical decisions related to Mr. McClain while Cichuniec was in charge of the crew and responsible for scene safety. Upon arrival, some members of Aurora Fire Rescue were informed that a carotid hold had been used on Mr. McClain, that he lost consciousness, and that he was "obviously on something."[2]





Ashley Todd, JD, (left) a Partner, and Tessa Carberry, JD, (right), an Associate of Husch Blackwell co-wrote this article. Husch Blackwell represents a full spectrum of healthcare providers and other businesses in developing compliance strategies, preliminary enforcement measures, employment concerns, and litigation matters. The information contained in this article should not be construed as legal advice or a legal opinion on any specific facts or circumstances. The contents are intended for general information purposes only, and readers are encouraged to consult their attorney concerning specific situations and specific legal questions.

Prior to administering ketamine to Mr. McClain, neither Cooper nor Cichuniec asked Mr. McClain if he consented to the administration of ketamine or how much he weighed. A correct dose of ketamine is 5 mg per kilogram of body weight. Cooper estimated Mr. McClain to be about 200 pounds indicating a 453 mg dose of ketamine. Mr. McClain, in fact, weighed 143 pounds. Notwithstanding, Cooper then administered 500 mg of ketamine in Mr. McClain's right deltoid—a dose for someone weighing 77 pounds more than Mr. McClain. The appropriate dose for Mr. McClain should have been closer to 325 mg. By the time Mr. McClain was placed on the gurney, he was unconscious, had no muscle tone, was limp, snoring, and had vomit coming from his nose and mouth. Shortly after being loaded into the ambulance, Mr. McClain had no pulse and was not breathing. While Mr. McClain would regain a pulse at the University of Colorado Medical Center, he would never regain consciousness.[3]

Initially, neither the police officers nor the paramedics were criminally charged following Mr. McClain's death, but, a few years later, Colorado Governor Jared Polis appointed Attorney General Phil Weiser as special prosecutor. He brought felony charges against the police officers and the paramedics.[4] On September 1, 2021, each paramedic was indicted on 11 criminal counts including manslaughter, criminally negligent homicide, assault in the second degree, and crimes of violence. Following a jury trial, the paramedics were both found guilty. In spring of this year, Cooper was sentenced to 14 months in jail and work release for criminally negligent homicide. Cichuniec was sentenced to five years in prison for criminally negligent homicide and assault for

unlawful administration of drugs.[5] In mid-September, Cichuniec was released from prison after a judge reduced his sentence to four years of probation.[6]

Prevalence of Healthcare Providers and Criminal Charges

The conviction and sentencing of Cooper and Cichuniec were major national news, but it is certainly not the first time a practitioner has been criminally charged as a result of treatment provided to patients. In other cases around the nation, healthcare workers have faced criminal charges as a result of alleged crimes committed in the scope of their work. Over 10 years ago, in 2011, Dr. Conrad Murray was found guilty of involuntary manslaughter following the death of Michael Jackson as a result of drugs administered by Dr. Murray.[7] Dr. Christopher Duntsch, a Texas surgeon who injured or killed more than 30 patients in the span of two years and was later deemed "Doctor Death."[8] Dr. Duntsch was charged with one count of injury to an elderly person and five counts of assault. In early September of this year, an Arizona doctor was sentenced to five years' probation after pleading guilty to manslaughter in connection with his role in providing "comfort and counseling to someone who couldn't live with the pain."[9] The district attorney's office concluded the woman had died "by means of assisted suicide." The Arizona physician was initially arrested and charged with second-degree manslaughter under a New York law that allows the charge for intentionally causing or aiding another person's suicide.

Although professional liability actions arising from civil suit or agency enforcement have presented a considerable risk for healthcare providers for decades, the pursuit of criminal culpability is a relatively new phenomenon gaining traction in many states.

Even beyond recent memory, healthcare practitioners have been charged criminally. In 2006, the *Journal of the Royal Society of Medicine* published a literature review of "Doctors charged with manslaughter in the course of medical practice, 1795–2005."[10] Notably, the study was conducted on medical practice in the UK, but the authors "identified 85 doctors charged with manslaughter" from 1795 to 2005. Interestingly, the numbers increased dramatically since 1990 and resulted from a mix of mistakes (37) or slips (17), and a minority because of alleged violations (16). Interestingly, not unlike the Elijah McClain case, "most cases in the 20th century involved errors in the administration or prescribing of medicines."[11] For example, in 1999 a "general practitioner administered 30 mg of diamorphine to a 55-year-old man suffering from lower back pain. The patient died from respiratory failure. The maximum recommended initial dose of diamorphine is 10 mg. The GP was charged with manslaughter and convicted." Similarly, in a 2001 case, "a surgeon guessed the patient's weight and inadvertently gave three times the recommended dose of lidocaine" resulting in the patient's death.[12] That doctor was charged with manslaughter, but later acquitted.

As demonstrated by the cases above, if practitioners are charged criminally, prosecutors seem to typically charge them with some version of manslaughter and/or assault. However, at times, practitioners are charged with more serious crimes. For example, last year, a nurse aide from Bridgeton, Missouri was charged with felony rape charges for assaulting a patient.[13] Around the same time, Missouri respiratory therapist Jennifer Hall, who was initially charged with two counts of first-degree murder, pleaded guilty to first-degree involuntary manslaughter in the deaths of two patients at a Missouri hospital and was sentenced to 18 years in the Missouri Department of Corrections.[14] Over the summer, a California plastic surgeon was charged with second-degree murder after leaving his patient

Table 1. Crimes and Definitions

Crime	Definition
First Degree Murder[27]	A person commits the offense of murder in the first degree if he or she knowingly causes the death of another person after deliberation upon the matter.
Second Degree Murder[28]	A person commits the offense of murder in the second degree if he or she: (1) Knowingly causes the death of another person or, with the purpose of causing serious physical injury to another person, causes the death of another person; or (2) Commits or attempts to commit any felony, and, in the perpetration or the attempted perpetration of such felony or in the flight from the perpetration or attempted perpetration of such felony, another person is killed as a result of the perpetration or attempted perpetration of such felony or immediate flight from the perpetration of such felony or attempted perpetration of such felony.
Voluntary Manslaughter[29]	A person commits the offense of voluntary manslaughter if he or she: (1) Causes the death of another person under circumstances that would constitute murder in the second degree under subdivision (1) of subsection 1 of section 565.021, except that he or she caused the death under the influence of sudden passion arising from adequate cause; or (2) Knowingly assists another in the commission of self-murder.
Involuntary Manslaughter – First Degree[30]	A person commits the offense of involuntary manslaughter in the first degree if he or she recklessly causes the death of another person.
Involuntary Manslaughter – Second Degree[31]	A person commits the offense of involuntary manslaughter in the second degree if he or she acts with criminal negligence to cause the death of any person

in the middle of a breast augmentation surgery to see other patients. The surgery patient went into cardiac arrest and died six weeks later. The surgeon pleaded guilty to manslaughter and aiding and abetting a person in practicing medicine without a license.[15] Even more recently, actor Matthew Perry suffered a fatal ketamine overdose in October 2023 and, just this summer, two of his doctors were federally charged in his death.[16] The first, Dr. Mark Chavez, agreed to plead guilty to one count of conspiracy to distribute ketamine. The second, Dr. Salvador Plasencia, was indicted on seven counts of distribution of ketamine and two counts of altering and falsifying documents or records related to the federal investigation. Dr. Plasencia entered a plea of not guilty and is set to go to trial in October.[17]

In early 2023, in an escalation from the charges in the Elijah McClain case, an Illinois paramedic and emergency medical technician ("EMT") were charged with first-degree murder after they strapped Earl Moore, Jr. facedown on a stretcher and transported him in that position.[18] Mr. Moore died from compressional and positional asphyxia. According to a press release by the City of Springfield Police Department, police responded to a call on December 12, 2022, and were "met with a resident who indicated the caller was suffering from hallucinations due to alcohol withdrawal."[19] Police then requested an ambulance and when the ambulance personnel arrived, they were escorted into the residence to Mr. Moore, who was not able to walk. The medical personnel "were not offering any assistance" to Mr. Moore in walking, but once the police got him outside, "the medical personnel place[d] the patient on the stretcher in a prone position and secured him to the stretcher prior to transport."[20] According to the civil complaint filed against, among other defendants, the paramedic and EMT, the providers did not assess Mr. Moore's medical condition and "[i]t is presently unknown what occurred during the ambulance ride."[21] This case has not yet gone to trial, and it remains to be seen what other evidence will be presented at trial.[22]

When Does Malpractice Become Manslaughter? And When Does Malpractice Become Murder?

Most practitioners are acutely aware of civil medical malpractice actions as a daily risk of medical practice. In Missouri, as with many other states, "[t]o make a submissible claim of [civil] medical malpractice, the plaintiff must establish that the defendant's acts or omissions: (1) failed to meet the requisite standard of care; (2) were performed negligently; and (3) caused [plaintiff's] alleged injuries."[23] "The basic philosophy in malpractice cases is that the [practitioner] is negligent by reason of the fact that he or she has failed to adhere to a standard of reasonable medical care and that consequently the service rendered was substandard and negligent."[24]

However, what many practitioners might have been less aware of or concerned about, and what the Elijah McClain case (or any of the other cases discussed above) has likely brought to the forefront of practitioners' minds, is the risk of criminal actions. Each state has its own criminal code with variations of the charges discussed in the cases above. In Missouri, these types of crimes are labeled as "offenses against the person" including murder, manslaughter, and assault.[25] "A crime generally consists of two elements: the physical, wrongful deed, or *actus reus,* and the guilty mind that produces the act, or *mens rea.*"[26]

Table 1 outlines the elements of murder and manslaughter in Missouri and the different *mens rea* required for each.

The determinative factor between the different levels of murder and manslaughter is the *mens rea*. In the Elijah McClain case, the paramedics were charged under the Colorado criminal code with manslaughter, criminally negligent homicide, assault in the second degree, and crimes of violence. Eventually, the jury found them guilty of criminally negligent homicide and assault for unlawful administration of drugs. Conversely, in the Earl Moore, Jr. case, the emergency medical providers are charged with first-degree murder and those charges are still pending a jury trial. While it is not yet clear if prosecutors will be able to prove the element of a first-degree murder charge, including the requisite *mens rea*, the juxtaposition of these two cases shows the variety of criminal charges available to prosecutors in these types of cases.

Licensure and Regulatory Implications of Criminal Convictions

A discussion of misconduct by healthcare providers such as those reviewed here would be incomplete without acknowledging the potential licensing and regulatory fallout associated with their criminal convictions. Licensing authorities in almost every state including Missouri[32] may impose discipline on licensees who have been convicted of offenses related directly to the delivery of emergency medical services, or those offenses reasonably related to the qualifications, functions, or duties of an activity regulated by the agency.[33] These agencies have considerable discretion as to the severity of discipline imposed, as well as what mitigating or aggravating factors are deemed relevant to discipline, such as the nature and seriousness of the crime, or the relationship of the crime to the licensee's fitness for continued practice.

In addition to state licensing agencies, the National Registry of Emergency Medical Technicians has published policy to establish eligibility requirements for national certification specific to criminal convictions. The policy requires affirmative disclosure of convictions and allows the Registry to suspend or revoke an individual's certification or to take other appropriate action with respect to certification, based on felony criminal convictions or *any* conviction that relates to crimes involving physical or sexual assault, abuse, or use of a dangerous weapon.[34] The Registry shares information it obtains related to convictions with other licensing authorities such as state departments of health.

Although professional liability actions arising from civil suit or agency enforcement have presented a considerable risk for healthcare providers for decades, the pursuit of criminal culpability is a relatively new phenomenon gaining traction in many states. In recent years, healthcare providers across the spectrum have been subject to expanding regulations—increasingly criminal in nature—that apply to the delivery of healthcare services. Most prominent among these are regulations related to

women's reproductive care following the repeal of *Roe v. Wade*, and to a wide variety of gender affirming care services. The cases discussed here offer a compelling narrative that criminal liability could attach to providers in some instances, but whether a broader trend toward criminalizing providers will prove beneficial for the industry as a whole remains to be seen. In any case, the debate acknowledges a fundamental understanding that healthcare providers, in particular emergency medical services personnel, are routinely placed in positions of public trust while providing care to an exceptionally vulnerable subset of patients, in settings that are largely unsupervised.

References

1. Sherry A. Reforms and heartbreak after final sentencing in Elijah Mcclain's death. NPR. May 1, 2024. Accessed September 16, 2024. https://www.npr.org/2024/05/01/1248194859/reforms-and-heartbreak-after-final-sentencing-in-elijah-mcclains-death#:~:text=Race-,Aurora%20Colorado%20paramedic%20sentence%20fatal%20botched%20arrest%20of%20Elijah%20McClain,Two%20cops%20were%20aquitted.
2. Grand Jury Indictment. *People v. Roedema, et al.*, Case No. 21CR782 (Adams Cnty. Colo. Sept. 1, 2021) https://ewscripps.brightspotcdn.com/32/1a/cc3b645a47a8b7b59f0fc0d7054e/2021-09-01-colorado-state-grand-jury-indictment.pdf.
3. *Id.*
4. *Id.*
5. Slevin C. Gruver M. Judge frees Colorado paramedic convicted in death of Elijah Mcclain from prison. AP News. September 14, 2024. Accessed September 16, 2024. https://apnews.com/article/elijah-mcclain-paramedic-sentence-probation-ketamine-9714cd7113c1bfead80714c0dbe461b9.
6. *Id.*
7. Medina J. Doctor is guilty in Michael Jackson's death. The New York Times. November 7, 2011. Accessed September 16, 2024. https://www.nytimes.com/2011/11/08/us/doctor-found-guilty-in-michael-jacksons-death.html.
8. Beil L. A surgeon so bad it was criminal. ProPublica. October 2, 2018. Accessed September 16, 2024. https://www.propublica.org/article/dr-death-christopher-duntsch-a-surgeon-so-bad-it-was-criminal.
9. Hill M. Ex-doctor pleads guilty to manslaughter in connection with suicide of Upstate New York Woman. AP News. September 3, 2024. Accessed September 16, 2024. https://apnews.com/article/assisted-suicide-homicide-new-york-9c385103705504b06c374f66c46119a8.
10. Ferner RE, McDowell SE. Doctors charged with manslaughter in the course of Medical Practice, 1795–2005: A literature review. *Journal of the Royal Society of Medicine*. 2006;99(6):309-314. doi:10.1177/014107680609900618.
11. *Id.*
12. *Id.*
13. FOX 2. Nurse's aide faces rape charges in alleged patient assault. FOX 2. September 15, 2023. Accessed September 16, 2024. https://fox2now.com/news/missouri/nurses-aide-faces-rape-charges-in-alleged-patient-assault/.
14. Missouri respiratory therapist Jennifer Hall sentenced in deaths of 2 patients. https://www.kctv5.com. August 19, 2023. Accessed September 16, 2024. https://www.kctv5.com/2023/08/19/missouri-respiratory-therapist-jennifer-hall-sentenced-deaths-2-patients/.
15. Mueller P. Bonita plastic surgeon guilty of manslaughter for botched surgery that led to mother's death. ABC 10 News San Diego KGTV. July 1, 2024. Accessed September 16, 2024. https://www.10news.com/news/local-news/south-bay-news/bonita-plastic-surgeon-guilty-of-manslaughter-for-botched-surgery-that-led-to-mothers-death.
16. Five defendants, including two doctors, charged in connection with actor Matthew Perry's fatal drug overdose last year. Central District of California | Five Defendants, Including Two Doctors, Charged in Connection with Actor Matthew Perry's Fatal Drug Overdose Last Year | United States Department of Justice. August 16, 2024. Accessed September 16, 2024. https://www.justice.gov/usao-cdca/pr/five-defendants-including-two-doctors-charged-connection-actor-matthew-perrys-fatal.
17. Leonard E. Doctor and alleged dealer charged in Matthew Perry's death agree to delay trial. NBC Los Angeles. September 4, 2024. Accessed September 16, 2024. https://www.nbclosangeles.com/investigations/doctor-alleged-ketamine-dealer-charged-matthew-perrys-death-agree-delay-trial.
18. Foody K. Prosecutor: Paramedics killed man by strapping him facedown. AP News. January 17, 2023. Accessed September 16, 2024. https://apnews.com/article/health-springfield-illinois-state-government-518d8beda0785e6e4c358d6c4bc50711.
19. Sangamon County State's Attorney Dan Wright announced First Degree Murder charges against two paramedics from an incident where the Springfield Police Department was the initial responding agency. https://www.springfield.il.us/Departments/Communications/PressReleasesHandler.ashx?imgid=1467.
20. *Id.*
21. Compliant, Washington v Lifestar Ambulance Service, Inc., No. 2023LA000014 (Sangamon Cnty., Ill. Jan 19, 2023) https://www.wcia.com/wp-content/uploads/sites/44/2023/01/FS-Moore-complaint-01.19.2023-1.pdf
22. Hassett C. Expert reports being gathered for EMS workers accused of first-degree murder. WICS. April 23, 2024. Accessed September 16, 2024. https://newschannel20.com/news/local/expert-reports-being-gathered-for-ems-workers-accused-of-first-degree-murder.
23. *Boehm v. Pernoud*, 24 S.W.3d 759, 761 (Mo. Ct. App. 2000).
24. *Aiken v. Clary*, 396 S.W.2d 668, 673 (Mo. 1965).
25. Mo. Ann. Stat. § 565.001, *et seq.*
26. *State v. Edgar*, 2 S.W.3d 896, 899 (Mo. Ct. App. 1999)
27. Mo. Ann. Stat. § 565.020
28. Mo. Ann. Stat. § 565.021
29. Mo. Ann. Stat. § 565.023
30. Mo. Ann. Stat. § 565.024
31. Mo. Ann. Stat. § 565.027
32. See Mo. Ann. Stat. §190.165(2); 19 CSR 30-40.342.
33. Mo. Ann. Stat. §190.165.
34. Certification policies +. National Registry of Emergency Medical Technicians. Accessed September 16, 2024. https://www.nremt.org/Policies/Certification-Policies.

Correspondence

PBMs and Rising Costs

I enjoyed reading your recent article on Pharmacy Benefit Managers (PBMs) and the skyrocketing cost of medicines in the September/October 2024 issue of *Missouri Medicine*. I have some comments about PBMs and their impact on pharmacies like mine.

"It's not the way I wanted it to go," he says sadly. "You do what you're supposed to do. You go to college, get a doctorate, start a small business in a small town, support the community and it's not even close to being a viable option. This isn't because the community didn't support us. It's because we lose money on every prescription we fill." Those are the words of Tom Wullstein, owner of Brandon Pharmacy.[1] He is talking about his own pharmacy which closed in September, but the same words could have been said by over a thousand pharmacy owner/operators this year alone.

I conducted a study recently to determine how many pharmacies are closing in the US. From January 1 to September 1, 2024, exactly 2,275 pharmacies—4% of all community pharmacies in the country—have closed.[2] Those pharmacists that speak out call out the unfair pricing tactics of PBMs as a culprit.

The Federal Government has recently taken a significant interest in PBMs and their role contributing to an unfair prescription drug market, the creation of pharmacy deserts, and inducing higher drug prices. In July, the House Oversight Committee created a report on PBMs and held an illuminating hearing[3] in which they questioned the CEOs of the three dominant PBMs. The Federal Trade Commission (FTC) released a scathing interim staff report on their ongoing Section 6b study of the PBM industry[4]—so scathing that Cigna Group chose to sue the FTC for defamation. The report is fascinating reading for anyone trying to understand PBMs. Additionally, the FTC filed a complaint[5] against the big three PBMs for their role in the dramatic increase in the price of insulin over the past 20 years. The complaint contains damning evidence—an OptumRx executive quipped that Viatris should set their insulin price high in order to "cover the PBMs rebate guarantees #milliondollarideas."

Some states have successfully regulated the worst abuses of PBMs by common reforms:

1) Require PBMs to become licensed to create a mechanism for oversight, and entrust oversight to a competent and adequately-funded enforcement agency – some states have chosen their insurance department, some the Attorney General's office.

2) Pass meaningful legislation regulating the practices that PBMs engage in: formulary placement, prior authorizations, appeals, affiliated-pharmacy steering, pricing manipulation, audit abuse, etc. Would-be reformers can look to Oklahoma's Patient's Right to Pharmacy Choice Act[6] as a model.

In addition to state level efforts, federal legislation is also needed. House Resolution 90967, the Pharmacists Fight Back Act, contains a number of provisions that would dramatically reform the PBMs' role in federal programs, by setting the price of medications at a legible and fair price in those programs. In the current pharmacy system, drug prices, including patient copayments, pharmacy reimbursements, and plan pay amounts are determined by a multitude of factors at the whim of PBM pricing managers[8]. Pharmacy operators are left feeling that they are operating a slot machine in Las Vegas instead of a professional business—most drugs will reimburse at two cherries ($0.47), and very rarely a few will reimburse at triple 7s ($3,000), seemingly at random. HR 9096 would enforce a single pricing mechanism across all federal programs—the average cost to a pharmacy to buy a drug plus the average cost to operate a pharmacy. This would make drug pricing fair and legible to a layman, and allow pharmacies to continue to serve their communities.

Meaningful PBM reform is in sight for the first time in a generation. Pharmacists and patients are desperate for help.

Benjamin Jolley, PharmD
Senior Fellow, Healthcare,
American Economic Liberties Project

References

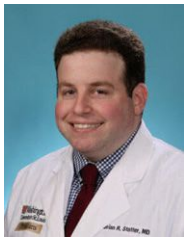
1. https://www.brandonvalleyjournal.com/content/dwindling-insurance-reimbursements-ends-brandon-pharmacy%E2%80%99s-14-year-run
2. https://benjaminjolley.substack.com/p/2275-pharmacies-have-closed-so-far
3. https://oversight.house.gov/hearing/the-role-of-pharmacy-benefit-managers-in-prescription-drug-markets-part-iii-transparency-and-accountability/
4. https://www.ftc.gov/news-events/news/press-releases/2024/07/ftc-releases-interim-staff-report-prescription-drug-middlemen
5. https://www.ftc.gov/system/files/ftc_gov/pdf/d9437_caremark_rx_zinc_health_services_et_al_part_3_complaint_public_redacted.pdf
6. https://oklahoma.gov/content/dam/ok/en/oag/documents/divisions/pbm/patients-and-consumers/Patients%20Right%20to%20Pharmacy%20Choice%20Act%2006.27.2024.pdf
7. https://www.congress.gov/bill/118th-congress/house-bill/9096
8. https://x.com/redlgb1969/status/1845926919486808255

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In the News

Missouri Medicine Announces New Board Member

Missouri Medicine announces new Editorial Board members. Board members are selected on the basis of exceptional professional accomplishment and expertise in their specialty.



Brian R. Stotter, St. Louis, the new Editorial Board member for Nephrology. He is Assistant Professor Pediatrics, at Washington University School of Medicine in St. Louis, Missouri. He was a Fellow in Nephrology at Children's Hopstial in Boston, Massachusetts.

He replaces **Gary Singer, MD**, who is with Midwest Nephrology Associates in Saint Peters, Missouri, whom we thank for his service.

Thank You Invited Peer-Reviewers 2024

Missouri Medicine would like to publicly thank the following invited non–Editorial Board experts who have done peer–review of submitted manuscripts in 2024:

Stephen B Carr, MD, Charles Lederer, MD, Bhanu Telugu, PhD, Elizabeth Bryda, PhD, David G. Ingram MD, Joseph Brunworth, MD, Amit Mathur, MD, Kevin Black MD, Abid M. Bhat, MD, Rajeev Aurora, PhD, Manjamalai Sivaraman, MD, Matthew Lindquist, DO, Romayne L. Kurukulasuriya MD, Shannon McGuire, MD, Sarah Eddington, MD, Kaushik Ravipati MD, Eric J. Lenze, MD, Vrinda Trivedi MD, David McKinsey, MD, John Vukich, MD, and Vance Thompson, MD.

Errata

The title of the editorial in the September/October 2024 *Missouri Medicine* by John C. Hagan, III, MD, was inadvertently omitted. The title should have been printed and read: "Hear Today & Gone Tomorrow." The Journal regrets this error.

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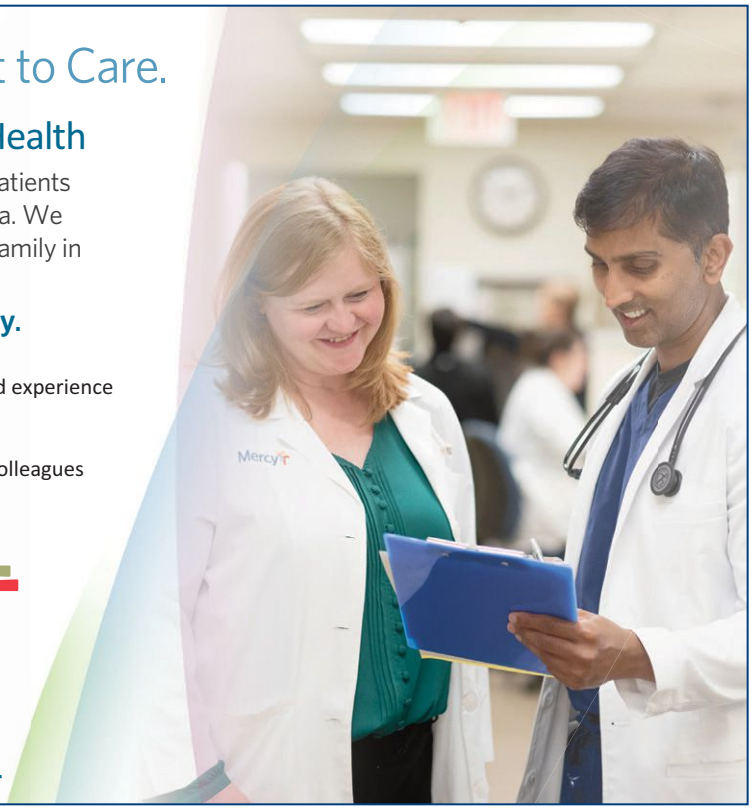
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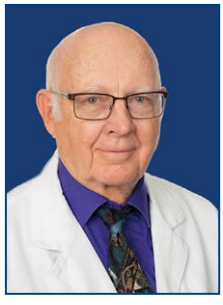


New Use for an Old Medicine

Timolol 0.5% Eye Drops for Essential Tremor: First Successful Case Report

by John C. Hagan III, MD & Steven C. Kosa, MD

All physicians treating essential tremor should be aware of the successful use of prn timolol 0.5% eye drops or nasal spray for tremor suppression.



John C. Hagan, III, MD, (pictured) is an ophthalmologist and editor of *Missouri Medicine*. **Steven C. Kosa, MD**, is a neurologist specializing in headache treatment. Both are in Kansas City, Missouri.

Abstract

This paper presents a new treatment modality, timolol 0.5% eye drops either topical to normal eyes or preferably by a compounded nasal spray for episodic use in patients with mild to moderate essential tremor. This would primarily be patients wishing to damp their tremors on certain occasions or who were not able to tolerate daily oral beta blockers. We believe this to be a first literature report.

Introduction

All neurologists and many primary care physicians will treat patients with essential tremor (ET). The tremor is in the range of 4-12 Hz and typically increases with purposeful movements. ET increases in incidence and severity with age and oftentimes has a hereditary component; the exact causation is unknown and could be multifactorial. While many cases are mild causing no or minor functional problems some ET patients progress to severe disability. An in-depth review of ET is beyond the scope of this manuscript; excellent reviews are available.[1]

There are a variety of treatments for essential tremor with more in development. The most common first line medication is oral β-adrenergic blockers (beta blockers). Oral daily propranolol is the most commonly used beta blocker and provides satisfactory abatement of tremors in 50-70% of cases.[2]

The purpose of this paper is to present a new treatment modality, timolol 0.5% either topical to normal eyes or by a compounded nasal spray, for episodic use in patients with mild to moderate ET. This would primarily be patients wishing to dampen their tremors on certain occasions or who were not able to tolerate daily oral beta blockers.

We believe this to be a first literature report of a patient with essential tremor, intolerant of daily oral beta blocker, treated successfully with timolol topical to her eyes.

Case Report

A 78-year-old female had moderate essential tremor which was well controlled with an oral beta blocker. She began to have common beta blocker side effects including chronic cough and orthostatic hypotension. The oral beta blockers were discontinued and the side effects abated. Her tremors returned and were noticeable to friends, family, and were troubling to her. She mentioned this to author JCH3 who is her ophthalmologist. She said she didn't mind the tremor most of the time but when she went to church, played bridge, or her grandchildren came over her tremors caused a great deal of embarrassment. JCH3 has published extensively on the novel use of timolol 0.5% beta blocker for acute migraines.[3-11] Her family physician was contacted and he agreed to try the novel treatment

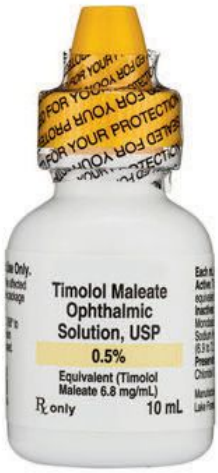


Figure 1. Timolol eye drops are rapidly systemically absorbed and reach therapeutic blood levels faster than oral beta blockers. Because of this, they may be useful for other conditions such as migraine, essential tremor and cardio-vascular disease. They are much less expensive than other medications used in these conditions. A 10 ml. generic bottle is priced $6-$15 USD. (2024)

for her essential tremor. Test drops were instilled while she was in her physician's office without side effects and there was damping of her tremor. Thereafter, she used one drop of timolol 0.5% in each eye prior to social events. The tremor abated to an inconspicuous level and remained so for up to 12 hours.

Discussion

In the 1960s, beta blockers were developed by Scottish pharmacologist James W. Black for cardio-vascular indications. Dr. Black was awarded the 1988 Nobel Prize in Medicine for his pioneering work. Beta blockers remain among the most widely prescribed and effective medications to the present day. They are relatively inexpensive and safe when standard beta blocker contra-indications are observed and the patient monitored for side effects.

Two serendipitous observations were subsequently made in patients put on oral beta blockers for cardio-vascular indications:

1. Patients with migraine often had improvement in their headaches.

2. Patients with chronic open angle glaucoma often had significant lowering of their intraocular pressure. These two physiological effects are useful in treating patients with migraine or glaucoma.

Neurologists subsequently used daily oral beta blockers as a successful preventive for migraine.[12] Intermittent oral beta blockers, taken at migraine first onset, did not prove successful.[13] For over 50 years, it was not investigated why there were diametrically different responses to oral beta blockers in acute and preventive migraine therapy.

Ophthalmologists pursued the use of timolol in eye drop form for treating chronic open angle glaucoma and found it highly effective.[14] Timolol was FDA approved in 1978 and quickly became the most widely used glaucoma medication (Figure 1). Side effects were soon observed and attributed to systemic absorption. Standard beta blocker contra-indications and careful monitoring were instituted.

Carl V. Migliazzo, MD, a glaucoma specialist, noted his patients with migraines frequently reported improvement of headaches when they used their timolol eye drops. Beginning about 1999-2000, he treated informally, empirically, and successfully acute migraine patients peripheral to his ophthalmology practice. In 2014, Migliazzo and Hagan reported[3] the first successful case series (N=7) of acute migraines treated by timolol 0.5% eye drops instilled at first onset of acute migraine drawn from Migliazzo's patient base. They determined oral beta blockers fail to treat acute migraines because systemic absorption from the gut and first-pass metabolism are so slow that therapeutic blood levels never eventuate. In beta blockers for migraine prevention the quotidian oral dosing maintains therapeutic levels.

In a normal eye, timolol drops instilled topically flow quickly through the lacrimal duct to the nasopharynx onto nasal mucosa where systemic absorption is extremely rapid and not subject to first-pass metabolism. Therapeutic levels of beta blocker are usually present 10-15 minutes post installation.[15] Because the eye drops work by systemic absorption on nasal mucosa, and eye drops are difficult to instill for some and certain ocular conditions contra-indicate application to the eye, nasal spray delivery was recommended when used for acute migraine treatment.[6] Initially, a 0.25% timolol nasal spray was formulated by the national O'Brien Compounding Pharmacy. In a small unreported series of patients, successfully using timolol 0.5% topical to the eye for acute migraine, users found the lower strength timolol was not effective. It is important to use only 0.5% timolol therapeutically. An addendum noting this change of concentration is in press (International Journal of Pharmaceutical Compounding). Nasal spray 0.5% timolol was recently first reported for effective treatment of a series of refractory migraine patients (62.5% successful repeated use; N=16) referred to a headache clinic (Figure 2).[10] The usual dosage is one drop each eye or one spray each nostril as quickly as possible at onset of headache. The dosage may be repeated, if necessary, in 15 minutes but no more than four drops or four sprays in any 24-hour period. Patients frequently take other acute migraine medications and often find them synergistic.

In an editorial accompanying the 2014 case series,[4] it was suggested that any condition that would benefit from rapid achievement of beta blocker therapeutic blood levels might be suitable to treat by topical to the eyes or nasal delivery; listed among these conditions was essential tremor.

Figure 2. Timolol 0.5% in a compounded nasal spray formulation from O'Brien Pharmacy (Kansas City) is more convenient and easier to use than eye drops and has faster onset. There are numerous potential therapeutic uses including acute migraine and essential tremor. Cost for a 15 ml nasal spray is $77.45 USD (July 2024) Other local compounding pharmacies should be able to produce the spray using the updated formula in reference [6].



When the opportunity arose to test this hypothesis for essential tremor, with the consent of the patient and her physician, topical timolol 0.5% proved successful. The well-known side effects of beta blockers are more common when taken daily than episodically. Thus, this patient was able to tolerate intermittent treatment with beta blocker drops but not able to tolerate daily oral beta blocker.

Two patients in the nasal timolol for acute migraine study[10] with essential tremor and migraines noted an improvement in their tremor when taking the timolol nasal spray. They subsequently intermittently used nasal spray for both their acute migraines and essential tremor. (Kosa personal communication 2024)

While this is a first literature report of beta blocker eye drops specifically prescribed for treatment of known essential tremor, there is a case report of a glaucoma patient using timolol drops who was switched to the non-beta blocker drop latanoprost.[16] Tremors developed after discontinuance of the timolol eye drop. Neurological evaluation confirmed a diagnosis of essential tremor. The patient was cautiously restarted on timolol eye drops; the tremors stopped and the patient tolerated the medication. Another study reported the successful use of daily timolol eye drops as a preventive medication for chronic migraines.[17] There does not seem to be any benefit to using timolol eye drops daily versus oral beta blocker pills for migraine prevention unless there is a large cost differential. However, as in the case presented, using timolol eye drops on select occasions may be tolerated in some essential tremor patients that are unable to tolerate daily oral beta blockers.

In patients unable to instill eye drops or who have conditions such as lacrimal duct stenosis or ectropion that negate the effectiveness of beta blocker eye drops, compounding pharmacies should be able to prepare a nasal spray of timolol 0.5% at a reasonable price.[6] Additional large, placebo-controlled studies are warranted for novel indications of timolol in solution delivered topical to normal eyes or nasally.

Conclusion

All physicians treating essential tremor, especially those patients that wish only to suppress their tremor on special occasions, should be aware of the successful use of prn timolol 0.5% eye drops or nasal spray.[3,1]

References

1. Younger DS. Editor. Handbook of Clinical Neurology, Vol. 196 (3rd series) Motor System Disorders, Part II: Spinal Cord, Neurodegenerative, and Cerebral Disorders and Treatment. https://doi.org/10.1016/B978-0-323-98817-9.00012-0 2023 Elsevier B.V.
2. Shukla W. Diagnosis and Treatment of Essential Tremor. CONTINUUM (MINNEAP MINN). 2022. 28(5, MOVEMENT DISORDERS):1333–1349.
3. Migliazzo CV, Hagan III JC. Beta Blocker Eye Drops for the Treatment of Acute Migraines. Missouri Medicine. 2014;111(4):284-289
4. Hagan III JC. A Eureka Moment? Beta Blocker Eye Drops for Acute Glaucoma. Missouri Medicine 2014;112(4):280-282
5. Hagan III JC. Letter to the Editor: A Randomized, Double-Blinded, Placebo-Controlled, Cross Over Study Evaluating the Efficacy and Safety of Timolol Ophthalmic Solution as an Acute Treatment of Migraine." Kansas Journal of Medicine. Volume 13 (2020): KJM Supplement 2: Frontiers Edition. https://journals.ku.edu/kjm/article/view/15733
6. Hagan III JC, Everett E, Chamberlain T. Compounded Beta-blocker Nasal Spray for Treatment of Acute Migraine: A New Therapeutic Modality. International Journal of Pharmaceutical Compounding 2020; 24:194-197 Note addendum in press use 0.5% timolol not 0.25%
7. Hagan III JC. It Should Not Be This Difficult to Engage Pharma in an Effective, Safe, Inexpensive Product for Acute Migraine, the Third Most Prevalent Disease in the World. Missouri Medicine. 2022;119(1):4-6
8. Hagan III JC. Systemic Review and Meta-analysis of Acute Treatments for Episodic Migraine in Adults" JAMA. 2021;326(16):1636. https://doi:10.1001/jama.2021.14060
9. Migliazzo CV, Hagan JC III. Topical Beta Blockers for the Treatment of Acute Migraines in 2018. Missouri Medicine. 2018;115(6):508-509
10. Kosa SC, Hagan III JC. Nasally Delivered 0.5% Timolol Beta Blocker Successfully Treats Acute Migraines in a Referral Headache Clinic: A Case Series. Missouri Medicine 2024; 121(1):33-36
11. Hagan III JC. Attention Pharma & Headache Researchers! Nasal Spray Timolol May Be the Next Great Thing for Acute Migraine. Missouri Medicine 2024;121(1);4-5
12. Shamliyan TA, Kane RL, Taylor FR. Migraine in adults: Preventive pharmacologic treatments. Agency for Healthcare Research and Quality (US); 2013 Apr. Report No.: 13-EHC068- EF. http://www.ncbi.nlm.nih.gov/pubmed/23700633
13. Fuller GN, Guiloff RJ. Propranolol in Acute Migraine: A Controlled Study. Cephalalgia. 10(5):229-233, 1990 Oct
14. Zimmerman FJ, Kaufman HE. Timolol: A ☒-Adrenergic Blocking Agent for the Treatment of Glaucoma. Arch Ophthalmol. Arch Ophthalmol. 1977;95(4):601-604. https://doi.org:10.1001/archopht.1977.04450040067008
15. Duchateau GS, Zuidema J, Merkus FW. Bioavailability of Propranolol After oral, Sublingual, and Intranasal Administration. Pharm Res. 1986;3:108-111 https://doi.org/10.1023/A:1016345504153
16. deCalesta P. A Case of Essential Tremor Masked by the Topical Beta Blocker Timolol Maleate. 1998; College of Optometry https://commons.pacificu.edu/opt/1230
17. Etemadifar M, Abedi MR. The Preventive Role of Topical Timolol in Treatment of Migraine Headaches. 2005;10(5):288-291

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Advancing Psychedelic-Assisted Therapy in Missouri (MO-PAT): Innovation at the Speed of Safety

by Danielle R. Adams, PhD, Torie Gettinger, PhD, Nathaniel Dell, PhD, Leopoldo J. Cabassa, PhD & Ginger E. Nicol, MD

To proactively facilitate the safe and effective implementation of PAT for Missourians, it is paramount to develop the infrastructure and stakeholder partnerships necessary to support the accessibility and quality of this promising new treatment.



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Abstract

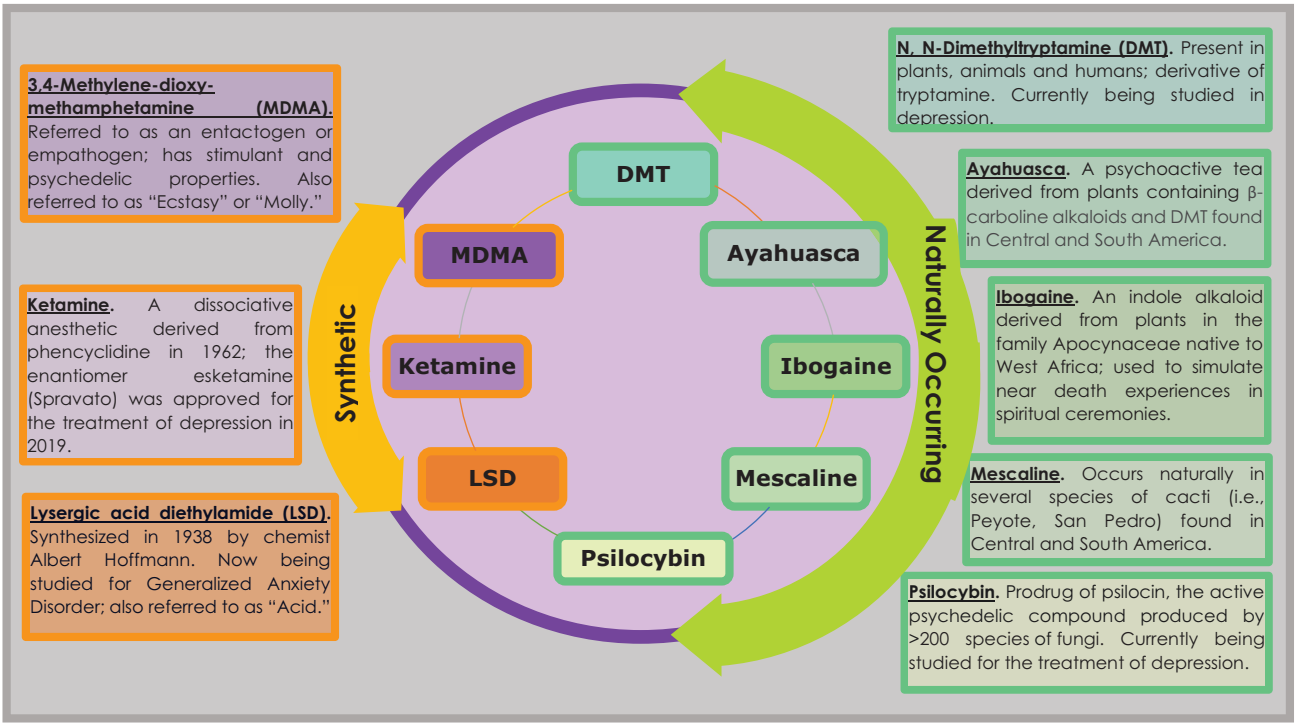
The United States is facing a growing behavioral health crisis. Now more than ever, novel, safe and effective treatments are needed. Over the past decade, clinical trials of psychedelic-assisted psychotherapies (PAT) have shown promising results for treating a number of common behavioral health conditions with minimal adverse effects. This article provides a brief historical and sociopolitical context surrounding PAT, discusses unanswered questions related to the safety and quality of PAT, and charts a pathway forward through the complex policy, legal, and social barriers to uptake for the state of Missouri in its consideration of PAT as a behavioral health treatment. With careful consideration and proper infrastructure, PAT could represent a paradigm shift in how the field approaches the prevention, treatment, and potential recovery of behavioral health conditions. We outline how Missouri can be at the forefront of advancing the science and practice of PAT – cautiously.

Introduction

After decades of nearly dormant research due to federal restrictions, psychedelics (e.g., psilocybin) are returning to mainstream culture as medicines that hold promise to provide fast-acting and sustained relief from common but debilitating behavioral health conditions like depression, substance use disorders, eating disorders, anxiety and psychological distress associated with life-threatening illnesses (e.g., cancer), and post-traumatic stress disorder (PTSD) when paired with psychotherapy.[1–5] In a field where modest medication efficacy is the rule, greater efficacy is often at the cost of tolerability, and where few people achieve remission or lasting treatment effects, safe and effective treatment innovations such as psychedelic-assisted psychotherapy (PAT) are necessary.[6]

The resurgence of psychedelic research comes at a time when the United States is faced with a growing behavioral health crisis. Demand for behavioral health services has soared in recent years and has been further exacerbated by the COVID-19 pandemic, which has been associated with increased depression and anxiety symptoms.[7] Overdose deaths and deaths by suicide in the United States are at record highs.[8,9] Despite the urgent

Figure 1: Synthetic and Naturally Derived Psychoactive Substances with Psychedelic Properties.



need for fast-acting, long-lasting, effective behavioral health treatments, limited access to the available treatment options remains a persistent problem.[10] The longstanding workforce shortage has been exacerbated by poor reimbursement rates, chronic underfunding of the behavioral health system, low compensation, and poor working conditions for clinicians,[11] and is projected to worsen given the current unmet need and continued increase in demand.[12]

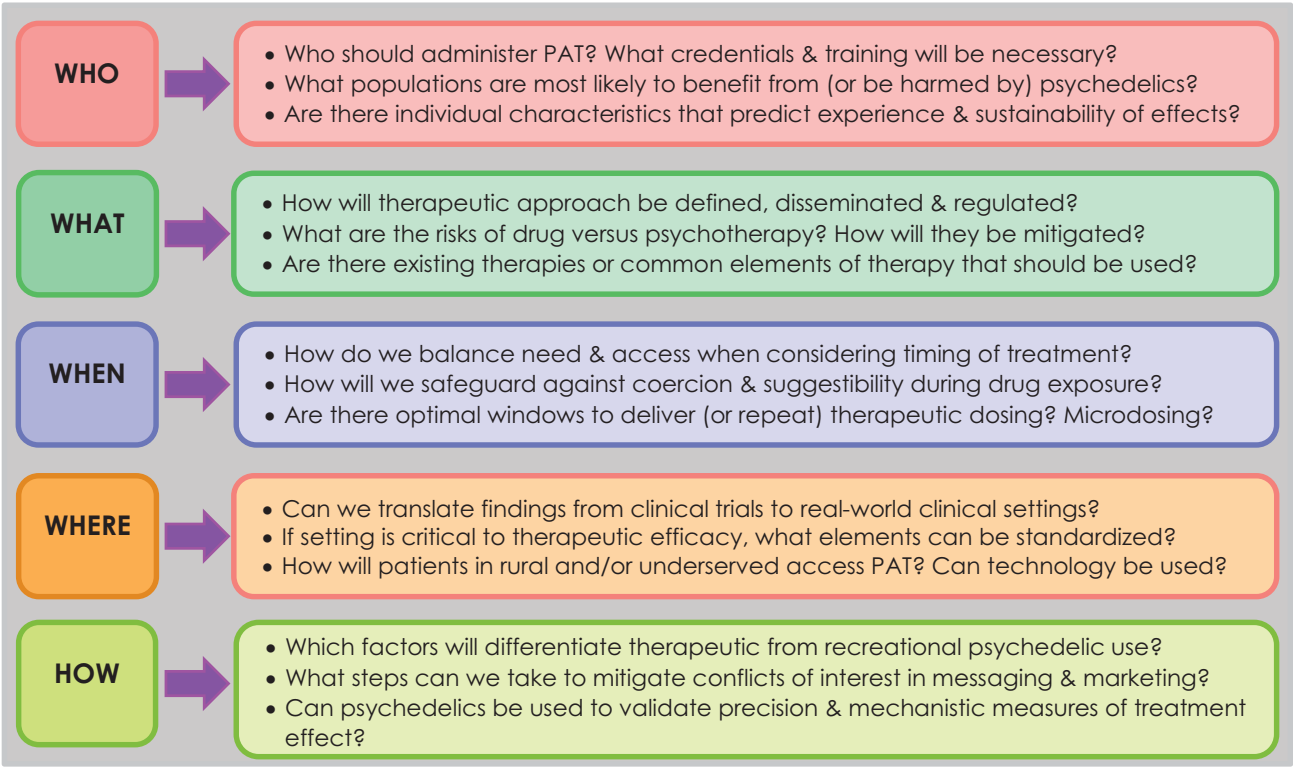
The purpose of this article is to provide a brief historical and sociopolitical context surrounding PAT, discuss unanswered questions related to the safety and quality of PAT, and chart a pathway forward through the complex policy, legal, and social barriers to uptake for the state of Missouri in its consideration of PAT as a behavioral health treatment. As the behavioral health crisis worsens and PAT continues to show promise in clinical trials and real-world experiments such as those in Oregon, increasing access to PAT should be at the top of key stakeholders' minds.[13] Missouri is at an advantage: we have major research universities at the forefront of studying psychedelics, state lawmakers sponsoring legislation to increase access to PAT for veterans, and we can learn lessons from state legalization and decriminalization of psychedelics for medicinal purposes prior to federal rescheduling and approval by the U.S. Food and Drug Administration (FDA) approval.

History and Sociopolitical Context

While definitions of what constitutes a 'psychedelic' molecule may vary, they generally include 'synthetic drugs (e.g., Lysergic acid diethylamide [LSD]),' and naturally occurring 'botanical' compounds (e.g., psilocybin, Figure 1). When ingested, these psychoactive compounds can lead to altered states of perception and consciousness, changes in cognition, heightened emotion, and increased self-awareness.[14] PAT is often described as a mystical and transformative experience in which the individual may undergo changes in consciousness, confront challenging and suppressed emotions, process and reframe difficult feelings, and find a renewed meaning.[14] Classic psychedelics (N, N-Dimethyltryptamine (DMT), lysergic acid diethylamide LSD, and psilocybin) are hypothesized to exert these effects as 5-hydroxytryptamine $(5\text{-HT})_{2A}$ receptor agonists.[15]

Naturally occurring psychedelic compounds such as psilocybin have been used for spiritual ceremonies (as a means of healing, gaining spiritual insights, facilitating life transitions) and in other traditional rites in some indigenous groups for millennia.[16] Beginning in the early 1900s, synthetic psychedelics such as 3,4-Methylenedioxymethamphetamine (MDMA), LSD, and ketamine were synthesized, and eventually,

Figure 2: Outstanding Research Questions in Psychedelic-Assisted Therapy (PAT).



their medicinal properties were tested. In the 1950s and 60s, hundreds of research studies of varying quality were conducted on naturally occurring and synthetic psychedelics, especially LSD, documenting the unique ability of these compounds to aid in treating a variety of behavioral health disorders.[17]

However, the recreational use of psychedelics in the 1960s helped to shepherd in the counterculture, where influential social figures like Dr. Timothy Leary encouraged young people to "turn on, tune in, and drop out" of society, seen by many as an existential threat to prevailing social norms at the time.[18] Under the Controlled Substance Act of 1970, psychedelics were categorized as Schedule I drugs, the most restrictive class of drugs considered to have 'no accepted medical use,' and research on psychedelics was halted for decades.[19]

Although federal research stalled, the 'psychedelic renaissance' is now upon us. The use of psychedelics is shifting from counterculture to mainstream with a heightened focus on their healing benefits. The FDA has acknowledged the therapeutic potential of psychedelic drugs. For example, in 2017 MDMA-assisted therapy received breakthrough therapy designation for the treatment of PTSD, and in 2018 and 2019, psilocybin-assisted therapy received breakthrough designation for treatment-resistant depression (TRD) and major depressive disorder (MDD), respectively.[20] In March of 2024, LSD received breakthrough designation for the treatment of generalized anxiety disorder.[8] Although FDA does not regulate or comment on efficacy of behavioral therapies, psychedelic treatments uniquely work to rapidly promote nerve cell growth, differentiation, and connectivity, a process broadly referred to as 'neuroplasticity.' The rapid onset necessitates careful attention to both the mental and physical contexts ('set and setting') immediately surrounding exposure to psychedelic drugs to optimize the effects of the drugs for healing, as well as to promote safety. In August of 2024, the FDA rejected MDMA as a treatment for PTSD, requiring that the industry sponsor, Lykos, conduct more research, in turn setting back the approval timeline for this medicine.[21] Psilocybin-assisted therapy is anticipated to be reviewed in 2026. Increasing access to PAT for individuals with behavioral health conditions, especially veterans, has garnered bipartisan support. However, even with legislative reform at the state level, until rescheduling occurs, PAT remains illegal at the federal level.

Over the past decade, clinical trials of PAT have shown promising results for treating behavioral health conditions and symptoms beyond PTSD, MDD, and TRD; these include anxiety associated with life-threatening illnesses (e.g., cancer), chronic pain syndromes, eating disorders, and substance use disorders.[2,22–25] A meta-analysis on the safety of psychedelics in a supervised medical context found nine serious adverse events were reported (i.e., acute transient anxiety and delusions) for more than 1,000 administrations of psychedelic substances, and the majority of side effects (e.g., nausea, headaches, increased heart rate and blood pressure) were moderate and occurred only in the hours following intake.[26]

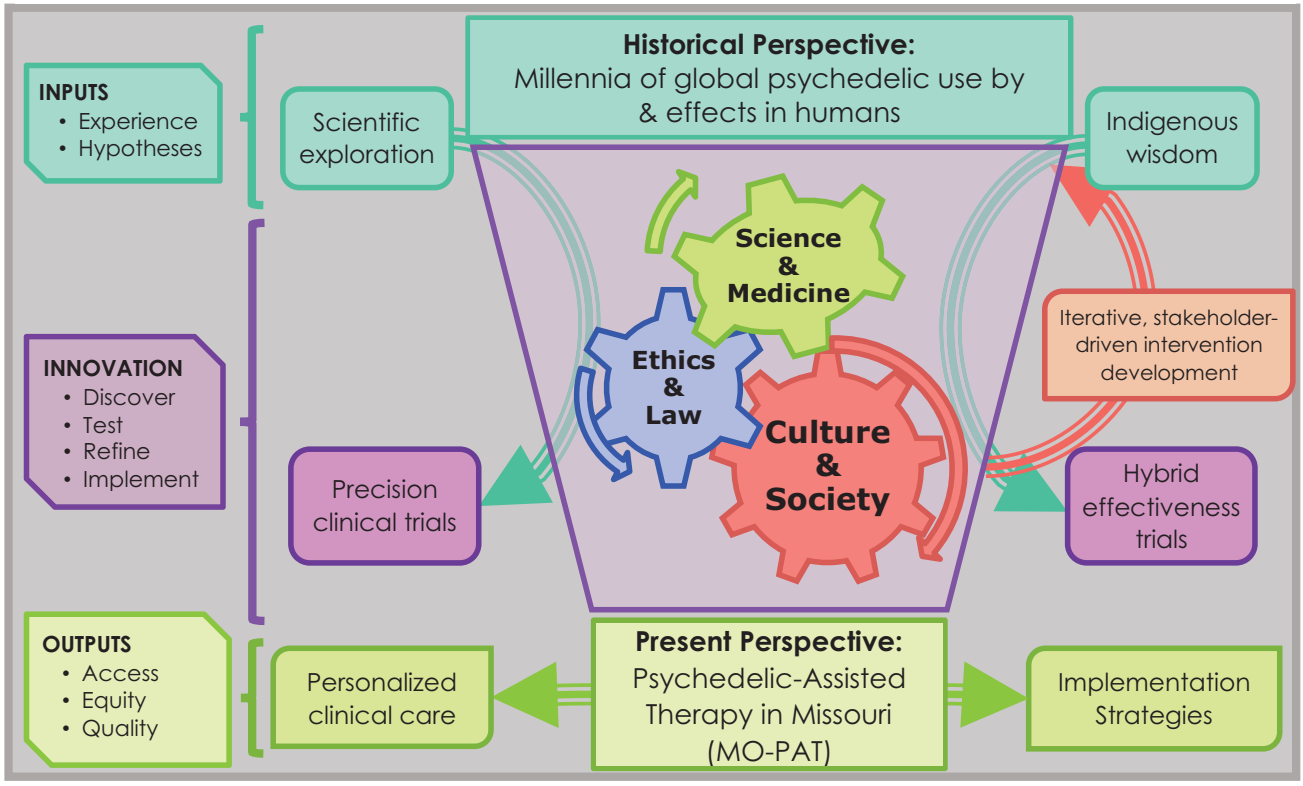
Despite the potential benefits and relatively safe risk profile of psychedelics for the treatment of behavioral health conditions, there remain several challenges and unanswered questions related to biological and psychological mechanisms of action, risks, safety, tolerability, short and long-term effectiveness, dose-response relationship, identification of populations that would benefit most, legality, implementation (administration, cost/reimbursement, equitable access), and policy (Figure 2). Addressing these questions now is especially important as the FDA contemplates approval of the use of PAT before federal legalization and several states (Oregon and Colorado) have approved the use of PAT for medicinal purposes.

Missouri Call to Action

We are at a critical crossroads to harness the potential of PAT to alleviate suffering in often hard-to-treat, disabling behavioral health conditions. The increasing commercial availability and direct-to-consumer marketing of psychedelic products (e.g., ketamine) juxtaposed with the long and costly process of conducting large clinical trials for FDA approval creates a complex and rapidly evolving legal and regulatory landscape that will be difficult for clinicians and patients to safely navigate, especially when we are experiencing a protracted behavioral health crisis. Stories of the profound and rapid transformational effects of psychedelics, for those who are suffering and cannot access appropriate care, offer a seductive beacon of hope. However, stories of significant harm when psychedelics are ingested without the proper medical supervision and therapeutic support can literally be life-threatening. These stories highlight the potential for significant dangers and underscore the urgency of identifying solutions for overcoming implementation challenges and addressing unanswered questions related to the use of psychedelics for the treatment of behavioral health conditions. With PAT, we face an incredible opportunity to re-imagine behavioral health service delivery—with careful consideration and proper infrastructure, it could represent a paradigm shift in how the field approaches the prevention, treatment, and potential recovery of behavioral health conditions.[27] Missouri has the opportunity to be at the forefront of advancing the science and practice of PAT —cautiously.

What is needed is a coordinated effort to adopt and scale PAT for marginalized populations in Missouri. In Figure 3, we provide a roadmap that gives an iterative framework for the development and implementation of PAT in Missouri. A variety of inputs exist to ground this work. First, we must begin by acknowledging and respecting the historical knowledge, indigenous wisdom, and practical experience with medicinal use of naturally-occurring psychedelics since antiquity.[28,29] Scientific exploration of PAT evolved slowly following the introduction of the Controlled Substances Act in the 1970s and 80s, but has exploded in the past three decades, building a robust literature that should be expanded to now generate and test hypotheses regarding safety, quality, and equity (Figure 2). We can learn from implementation experiences in Oregon, California and Colorado, where psychedelics have been decriminalized or legalized for medical use. Next, we must look to innovation to generate tools and solutions that can be used to address remaining gaps in knowledge, using rigorous methodologies such as precision clinical trials and hybrid effectiveness/implementation studies to discover, test, refine, and implement PAT.[30,31] Finally, the outputs of this work should address three key components: access (ensuring that those who need and want treatment can get it in a timely and affordable manner), equity (ensuring that those who need it the most get it first), and quality (ensuring that PAT achieves its intended outcomes of improving participants quality of life and reduced symptomology). To achieve these goals, we recommend the use of 1) personalized clinical care and 2) implementation strategies to support the uptake, implementation, and sustainability of PAT in routine clinical practice [Adams DR, Allen H, Nicol GE, Cabassa LJ. Moving psychedelic-assisted therapies from promising research into routine clinical practice: Lessons from the field of implementation science. Translational Behavioral Medicine. 2024 Oct 17:ibae053]. Throughout each of these stages, the processes will be impacted by culture and society at large (e.g., the de-

Figure 3: Knowledge, Experience & Iterative Innovation for PAT Implementation in Missouri.



stigmatization of psychedelics), ethics and law (e.g., state and federal level regulations related to PAT), as well as advancements in science and medicine (e.g., advances in science catalyze new treatment paradigms or research methodologies).

Missouri has long been at the forefront of psychedelics research. For example, the Department of Psychiatry at Washington University (WashU) School of Medicine in St. Louis conducted one of the first clinical trials of LSD in the early 1950s.[32] In that study, LSD was given to a total of 29 patients, mostly those hospitalized with psychosis or mania. The investigators observed that following their LSD exposure:

"…some of the patients were then able to re-evaluate the emotional meaning of some of their symptoms and improved. Most were better able to organize their ideas in relation to real rather than fancied problems and were seen to experience and express relevant emotion. Two of the patients [both psychoneurotic] … were improved sufficiently to discontinue treatment."[33]

In 2023 WashU Medicine completed the first modern clinical trial of psilocybin in humans in the state of Missouri since the 1950s, using precision functional brain mapping, a neuroimaging approach pioneered by WashU researchers.[34] In the study, a single 25 mg dose of psilocybin caused global desynchronization of the connections between brain networks in healthy volunteers. Though network synchronization reestablished itself over a period of a few hours or days, small differences in the brain's connections between the default mode network and other brain networks persisted for weeks, indicating there may be a window of optimal neuroplasticity that can be harnessed for targeted transformational psychotherapeutic healing.[34]

Now, WashU is home to the Center for Holistic, Interdisciplinary Research in Psychedelics (CHIRP), a Transcend Initiative supported by WashU's Here & Next Strategic Plan.[35] In addition to supporting university-wide, translational pilot research projects, the Center, jointly led by the Department of Psychiatry and the Brown School of Social Work, also incorporates private-public collaboration through the conduct of clinical trials for FDA approval of psilocybin for MDD and TRD, and community-based participatory research methods in planning the next phase of effectiveness and implementation research with psychedelics.

The medicinal use of psychedelics is gaining popularity among the Missouri veteran community, and bipartisan bills legalizing compounds like psilocybin are being proposed in the state. The veteran suicide rate in

Missouri is significantly higher than the national rate,[36] and Missouri politicians of all political affiliations are taking note. In 2022, Missouri lawmakers began an effort to pass legislation related to making psilocybin available to veterans in research settings, though bills were struck down in 2022 and 2023. A 2024 Missouri House Bill 1830 and Senate Bill 768 led by Republicans would have allowed military veterans who are at least 21 years old and are diagnosed with a qualifying condition such as PTSD or substance use disorders to access laboratory-tested psilocybin in a research setting legally, but the House Bill ultimately died in the chamber.[37,38] Meanwhile, a separate budget proposal that would spend $10 million from state opioid settlement funds to study the use of psilocybin to treat opioid use disorder passed the full House but was ultimately cut in the Senate committee.[39] While there has been no formal legislation passed in Missouri related to the use of psychedelics for behavioral health treatment, it is encouraging to see Missouri lawmakers spearheading the effort to increase the availability of these treatments for veterans.

Missouri is in an advantageous position to learn about implementation processes from states that have already begun the process of decriminalizing the therapeutic use of and legalizing psilocybin. In 2020, Oregon became the first state to legalize and decriminalize the use of psilocybin through regulated service centers.[13] Oregon Psilocybin Services, housed within the Oregon Health Authority Public Health Division's Center for Health Protection directs the Oregon Health Authority to license and regulate the manufacturing, transportation, delivery, sale, and purchase of psilocybin products and the delivery of psilocybin services.[40] An Advisory Board comprised of experts across disciplines was appointed in 2021 to make recommendations on the requirements, specifications, and guidelines for licensing, regulating and providing psilocybin services in Oregon.[41] Colorado, which passed a law decriminalizing and legalizing psilocybin, ibogaine, mescaline, and DMT for medicinal uses, is also on the verge of creating state-licensed "healing centers" where individuals can pay for a supervised PAT experience.[42] Other states, such as Maryland, Utah, Alaska, and Minnesota have passed legislation to create a task force to study and advise on legalizing certain psychedelic substances in the use of behavioral health treatments.[38]

Missouri would also benefit from the creation of a task force as a first step to engage necessary stakeholders. This task force, composed of key stakeholders including experts in behavioral health intervention development and testing, behavioral health services delivery, health equity research, large-scale multisite clinical effectiveness trials, implementation science, and policy, as well as representatives from indigenous communities, community providers (e.g., social workers, primary care physicians, psychiatrists, etc.), regulatory leaders, policymakers, representatives from advocacy organizations, and patients and caregivers with lived experiences of behavioral health conditions and psychedelic use, would be responsible for advising on policies for access, use, and conduct of research. Academic leaders are well positioned to effectively lead this type of task force as they are responsible for upholding the scientific integrity of PAT. Community-based participatory research principles and ethical principles that honor and are informed by indigenous medicine traditions should be infused throughout to integrate stakeholders' perspectives and wisdom, ensure equity and access, and inform implementation strategies.[43,44]

Missouri will also need to establish monitoring programs to track outcomes relevant to public safety, such as drug diversion and crimes related to illicit distribution, and public health concerns, such as exposures during pregnancy and ingestion by minors. Any FDA approval for the clinical use of psychedelics will almost certainly require risk evaluation mitigation strategy (REMS), a program that monitors medications with a high potential for serious adverse effects.[45]

To proactively facilitate the safe and effective implementation of PAT for Missourians, it is paramount to develop the infrastructure and stakeholder partnerships necessary to support the accessibility and quality of this promising new treatment. Further, throughout the regulatory and legislative process, PAT stakeholders must prioritize equity, centering the voices of Black, Brown, and Indigenous communities that have been impacted by the devastating "War on Drugs" era. A cohesive, community-engaged, and comprehensive approach will help to shape policy and regulations and ensure safe and equitable implementation of PAT in real-world settings throughout Missouri.

References

1. Calder A, Mock S, Friedli N, Pasi P, Hasler G. Psychedelics in the treatment of eating disorders: Rationale and potential mechanisms. Eur Neuropsychopharmacol. 2023;75:1-14. doi:10.1016/j.euroneuro.2023.05.008

2. Ko K, Kopra EI, Cleare AJ, Rucker JJ. Psychedelic therapy for depressive symptoms: A systematic review and meta-analysis. J Affect Disord. 2023;322:194-204. doi:10.1016/j.jad.2022.09.168

3. Luoma JB, Chwyl C, Bathje GJ, Davis AK, Lancelotta R. A meta-analysis of placebo-controlled trials of psychedelic-assisted therapy. J Psychoactive Drugs. 2020;52(4):289-299. doi:10.1080/02791072.2020.1769878

4. van der Meer PB, Fuentes JJ, Kaptein AA, et al. Therapeutic effect of psilocybin in addiction: A systematic review. Front Psychiatry. 2023;14:1134454. doi:10.3389/fpsyt.2023.1134454

5. Peck SK, Shao S, Gruen T, et al. Psilocybin therapy for females with anorexia nervosa: A phase 1, open-label feasibility study. Nat Med. 2023;29(8):1947-1953. doi:10.1038/s41591-023-02455-9
6. Kelly K, Posternak M, Jonathan EA. Toward achieving optimal response: Understanding and managing antidepressant side effects. Dialogues Clin Neurosci. 2008;10(4):409-418.
7. Vahratian A. Symptoms of anxiety or depressive disorder and use of mental health care among adults during the COVID-19 pandemic — United States, August 2020–February 2021. MMWR Morb Mortal Wkly Rep. 2021;70. doi:10.15585/mmwr.mm7013e2
8. Spencer MR, Miniño AM, Warner M. Drug overdose deaths in the United States, 2001–2021. Accessed August 22, 2024. https://stacks.cdc.gov/view/cdc/122556
9. Curtin SC. Provisional estimates of suicide by demographic characteristics: United States, 2022. Published online 2021.
10. Adams DR, Pérez-Flores NJ, Mabrouk F, Minor C. Assessing access to trauma-informed outpatient mental health services for adolescents: A mystery shopper study. Psychiatr Serv. 2024;75(5):402-409. doi:10.1176/appi.ps.20230198
11. Last BS, Crable EL. Policy recommendations for coordinated and sustainable growth of the behavioral health workforce. Milbank Q. Published online July 25, 2024. doi:10.1111/1468-0009.12711
12. Bureau of Health Workforce. Health Workforce Projections. Accessed August 22, 2024. https://bhw.hrsa.gov/data-research/projecting-health-workforce-supply-demand
13. Oregon Health Authority :Oregon Psilocybin Services: State of Oregon. Accessed September 4, 2024. https://www.oregon.gov/oha/ph/preventionwellness/pages/oregon-psilocybin-services.aspx
14. Pollan M. How to Change Your Mind: What the New Science of Psychedelics Teaches Us About Consciousness, Dying, Addiction, Depression, and Transcendence. Penguin; 2018.
15. López-Giménez JF, González-Maeso J. Hallucinogens and serotonin 5-HT2A receptor-mediated signaling pathways. In: Halberstadt AL, Vollenweider FX, Nichols DE, eds. Behavioral Neurobiology of Psychedelic Drugs. Springer; 2018:45-73. doi:10.1007/7854_2017_478
16. Schultes RE, Hofmann A. Plants of the Gods: Their Sacred, Healing, and Hallucinogenic Powers. Healing Arts Press; 1992.
17. Belouin SJ, Henningfield JE. Psychedelics: Where we are now, why we got here, what we must do. Neuropharmacology. 2018;142:7-19. doi:10.1016/j.neuropharm.2018.02.018
18. Leary T. Turn On, Tune In, Drop Out. Ronin Publishing; 2009.
19. Siegel JS, Daily JE, Perry DA, Nicol GE. Psychedelic drug legislative reform and legalization in the US. JAMA Psychiatry. 2023;80(1):77-83. doi:10.1001/jamapsychiatry.2022.4101
20. MindMed. MindMed Receives FDA Breakthrough Therapy Designation and Announces Positive 12-Week Durability Data From Phase 2B Study of MM120 for Generalized Anxiety Disorder. March 7, 2024. Accessed June 24, 2024. https://ir.mindmed.co/news-events/press-releases/detail/137/mindmed-receives-fda-breakthrough-therapy-designation-and-announces-positive-12-week-durability-data-from-phase-2b-study-of-mm120-for-generalized-anxiety-disorder
21. Reardon S. MDMA therapy for PTSD rejected by FDA panel. Nature. Published online June 5, 2024. doi:10.1038/d41586-024-01622-3
22. Luoma JB, Chwyl C, Bathje GJ, Davis AK, Lancelotta R. A meta-analysis of placebo-controlled trials of psychedelic-assisted therapy. J Psychoactive Drugs. 2020;52(4):289-299. doi:10.1080/02791072.2020.1769878
23. Calder A, Mock S, Friedli N, Pasi P, Hasler G. Psychedelics in the treatment of eating disorders: Rationale and potential mechanisms. Eur Neuropsychopharmacol J Eur Coll Neuropsychopharmacol. 2023;75:1-14. doi:10.1016/j.euroneuro.2023.05.008
24. van der Meer PB, Fuentes JJ, Kaptein AA, et al. Therapeutic effect of psilocybin in addiction: A systematic review. Front Psychiatry. 2023;14:1134454. doi:10.3389/fpsyt.2023.1134454
25. Robinson CL, Fonseca AC, Diejomaoh EM, et al. Scoping review: The role of psychedelics in the management of chronic pain. J Pain Res. 2024;17:965-973. doi:10.2147/JPR.S439348
26. Romeo B, Kervadec E, Fauvel B, et al. Safety and risk assessment of psychedelic psychotherapy: A meta-analysis and systematic review. Psychiatry Res. 2024;335:115880. doi:10.1016/j.psychres.2024.115880
27. Yehuda R, Lehrner A. Psychedelic therapy—A new paradigm of care for mental health. JAMA. 2023;330(9):813-814. doi:10.1001/jama.2023.12900
28. Jay M. Mescaline: A Global History of the First Psychedelic. Yale University Press; 2019. doi:10.2307/j.ctvgc61q9
29. Fotiou E. The role of Indigenous knowledges in psychedelic science. Published online March 1, 2020. doi:10.1556/2054.2019.031
30. Curran GM, Landes SJ, McBain SA, et al. Reflections on 10 years of effectiveness-implementation hybrid studies. Front Health Serv. 2022;2. doi:10.3389/frhs.2022.1053496
31. Lenze EJ, Nicol GE, Barbour DL, et al. Precision clinical trials: A framework for getting to precision medicine for neurobehavioural disorders. J Psychiatry Neurosci JPN. 2021;46(1):E97-E110. doi:10.1503/jpn.200042
32. Busch AK, Johnson WC. L.S.D. 25 as an aid in psychotherapy; preliminary report of a new drug. Dis Nerv Syst. 1950;11(8):241-243.
33. Rucker JJH, Iliff J, Nutt DJ. Psychiatry & the psychedelic drugs. Past, present & future. Neuropharmacology. 2018;142:200-218. doi:10.1016/j.neuropharm.2017.12.040
34. Siegel JS, Subramanian S, Perry D, et al. Psilocybin desynchronizes brain networks. medRxiv. Published online August 24, 2023:2023.08.22.23294131. doi:10.1101/2023.08.22.23294131
35. Ebsworth-Goold E. A strategic vision for Washington University's next 10 years. The Source. October 3, 2022. Accessed September 10, 2024. https://source.washu.edu/2022/10/a-strategic-vision-for-washington-universitys-next-10-years/
36. U.S. Department of Veteran Affairs. Missouri Veteran Suicide Data Sheet, 2021. Accessed August 20, 2024. https://www.mentalhealth.va.gov/docs/data-sheets/2021/2021-State-Data-Sheet-Missouri-508.pdf
37. Adlin B. Second Missouri House panel approves bill To legalize psilocybin therapy for Veterans. Marijuana Moment. April 18, 2024. Accessed August 26, 2024. https://www.marijuanamoment.net/second-missouri-house-panel-approves-bill-to-legalize-psilocybin-therapy-for-veterans/
38. Psychedelics Legalization & Decriminalization Tracker. Psychedelic Alpha. Accessed August 26, 2024. https://psychedelicalpha.com/data/psychedelic-laws
39. Adlin B. Missouri lawmakers strip $10 Million In psilocybin research funding from budget bill. Marijuana Moment. April 25, 2024. Accessed August 26, 2024. https://www.marijuanamoment.net/missouri-lawmakers-strip-10-million-in-psilocybin-research-funding-from-budget-bill/
40. Oregon Health Authority: Oregon Psilocybin Services: State of Oregon. Accessed August 26, 2024. https://www.oregon.gov/oha/ph/preventionwellness/pages/oregon-psilocybin-services.aspx?utm_source=OHA&utm_medium=egov_redirect&utm_campaign=https%3A%2F%2Fwww.oregon.gov%2Fpsilocybin
41. Legislature OR. ORS 475A.225 – Members of Or. Psilocybin Advisory Bd. Accessed August 26, 2024. https://oregon.public.law/statutes/ors_475a.225
42. Colorado Proposition 122, Decriminalization and regulated access program for certain psychedelic plants and fungi initiative (2022). Ballotpedia. Accessed September 4, 2024. https://ballotpedia.org/Colorado_Proposition_122,_Decriminalization_and_Regulated_Access_Program_for_Certain_Psychedelic_Plants_and_Fungi_Initiative_(2022)
43. Wallerstein N, Duran B. Community-based participatory research contributions to intervention research: The intersection of science and practice to improve health equity. Am J Public Health. 2010;100(Suppl 1):S40-S46. doi:10.2105/AJPH.2009.184036
44. Celidwen Y, Redvers N, Githaiga C, et al. Ethical principles of traditional Indigenous medicine to guide western psychedelic research and practice. Lancet Reg Health – Am. 2023;18. doi:10.1016/j.lana.2022.100410
45. Penn A, Yehuda R. Preventing the gaps in psychedelic research from becoming practice pitfalls: A translational research agenda. Psychedelic Med. 2023;1(4):198-209. doi:10.1089/psymed.2023.0017

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MM

Revival of a Beast: The Challenges Facing the Management and Control of Syphilis in Missouri from 2000 to 2024

by Hilal Abdessamad, MD, Wassim Jamaleddine, MD, Christian Rojas-Moreno, MD & Dima Dandachi, MD

As syphilis makes a comeback, we notice that similar risk factors are shared across Missouri that are exacerbating the epidemic.



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Abstract

Syphilis is an old disease that remains to be a major threat in the modern world. In the last decade, we have seen an exponential rise in the number of new cases. While this surge is universal, some places appear to be more affected than others, such as the southern and midwestern states in the United States. In Missouri, the syphilis epidemic strikes almost everywhere, from rural to metropolitan areas, affecting various age groups and sub-populations. We conducted this narrative review focusing on published data regarding syphilis in Missouri, and discussing contemporary risk factors for such an unprecedented spread, and treatment and prevention options. While rurality, social stigma, and medication shortage play a role in this disease spread, new plans are being adopted in the state for mitigation of its burden.

Introduction

Among sexually transmitted infections (STIs), syphilis is one of the most ancient, evidenced by the art produced in that time (Figure 1).[1] The initial painless ulcer, often goes unnoticed, and sometimes not diagnosed until the latent phase. Additionally, there is a lack of an effective vaccine. For these reasons, it has become humanity's "old foe," surging at unpredictable times, including this current time.[2] In addition, being an intra-cellular pathogen with few effective antimicrobials makes syphilis a "hard to treat" organism.[3]

Syphilis causes significant morbidity and mortality when not treated early. Besides, congenital syphilis (CS) can have severe and irreversible complications, which can be all prevented by awareness, screening, and treatment.[4]

To this day, syphilis continues to be a worldwide problem, where the World Health Organization (WHO) estimates more than 7.1 million people have been infected in 2020.[5] The Centers for Disease Prevention and Control (CDC), reported a sharp increase in the prevalence of syphilis in the United States (US) from 101,590 in 2017 to 176,713 in 2021,[6] and a 24% increase in CS from 2019 to 2020.[7]

The CDC reported that between 2017 and 2021, there was a 72% increase in primary and secondary syphilis (PSS) cases across the US, and 219% increase for CS. Missouri (MO) had an even higher increase at 157% for PSS, and 593% for CS.[8] 2021 marked

the highest number of CS cases in Missouri since 1994, with 63 new diagnoses.[9]

Understanding the barriers to sexual health prevention measures in the Midwest is essential to curtail the surge. We provide a narrative review of literature on syphilis in MO, to better understand the challenges in its screening, diagnosis, treatment and prevention.

Methods

Literature search: In this narrative review, we searched Pubmed, Google Scholar, and Scopus.

Gray literature: In addition, we searched Ovid's Health Management Information Consortium (HMIC) and MedNar for a deep web search.

We searched for all articles about syphilis in MO, except for treatment since it is not state-specific. We used the keywords syphilis AND Missouri, with at least one of the phrases "sexually transmitted," "outbreak," "infection control," "prevention," "treatment," and "epidemiology." Synonyms included were "treponema," "STI," and, "Midwest" and "infection."

Our inclusion and exclusion criteria were as follows:

All publications discussing any of the following were included:

1. Syphilis in the state of Missouri between 2000 and 2024.
2. Difficulties in syphilis management that apply to the Midwest.
3. Syphilis diagnostic approaches.
4. Treatment options for syphilis.
5. Prevention interventions for syphilis in MO.

Publications were excluded if they met any of those criteria:

1. Not in English.
2. Non-human studies.
3. Syphilis epidemiology outside MO.
4. Publications explaining syphilis to the general population for awareness.



Figure 1. "The Syphilitic", Albrecht Dürer (1496)[63]

5. Experimental new treatments for syphilis.
6. Studies from outside the US that are not discussing treatment options.
7. Case reports.

The search yielded 1,316 results. Rayyan.ai[10] was used to sort the publications and remove duplicates before the first screening. After removing 248 duplicate articles, 1,068 remained.

Data management: After the search, a two-step review of all results was conducted by HA and WJ. The first step included the title and abstract search that excluded 947 publications, leaving 121 articles for the second screening. The second step included a full-text review of the 101 articles. A total of 49 publications met all inclusion and exclusion criteria and were included in this review (Figure 2).

Data Extraction and Synthesis: Data was extracted manually and synthesized thematically, for the burden, challenges in screening, diagnosis, treatment, sexual health, and prevention.

Quality Assessment: Data was evaluated by the two authors (HA and WJ) independently to minimize bias. Any article that was included by at least one reviewer was included in the full-text screening.

Results

Epidemiological Changes in Missouri

In the 1990s, syphilis cases were declining every year, to almost double between 2001 and 2002 from 16.7% to 33.3%.[11] In 2008, a CDC-led survey among men who have sex with men (MSM) in different US cities, including St. Louis, showed that 76 had multiple sexual partners in the past year, and among them 54% had condomless sex. In this sample, only 35% had been tested for syphilis. As a result, the CDC recommended annual screening for syphilis.[12]

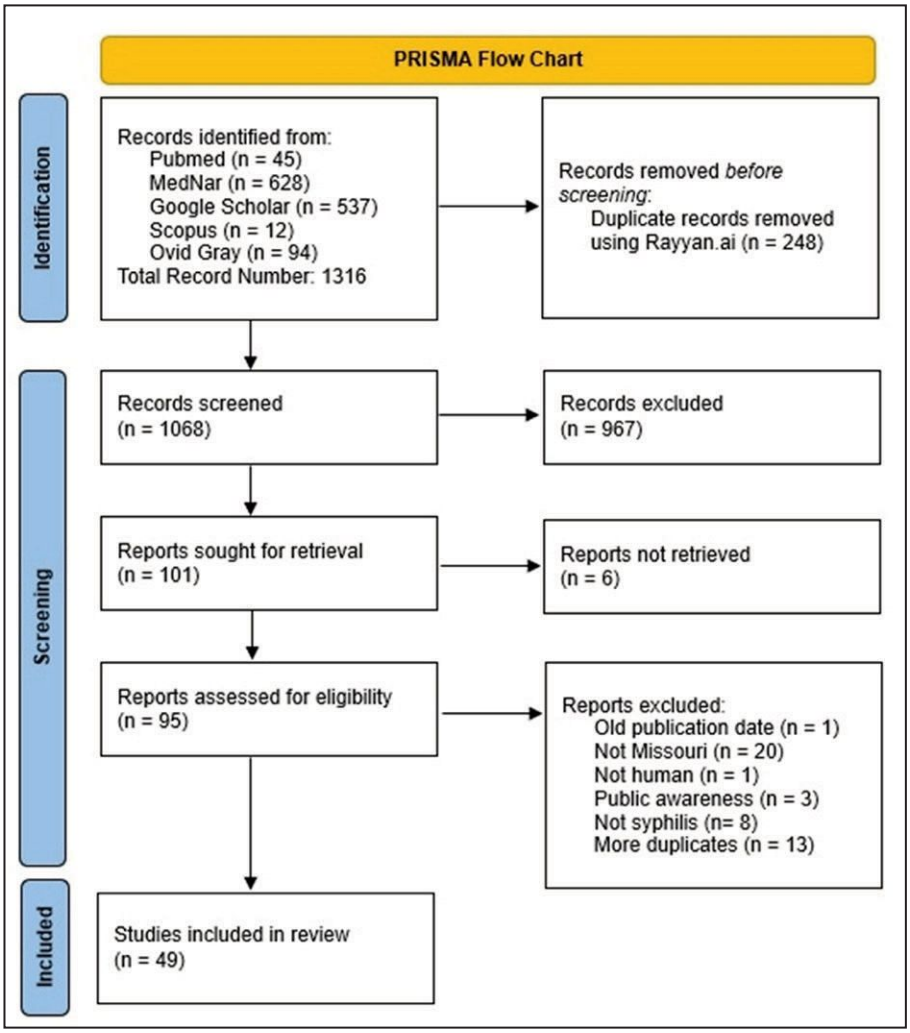


Figure 2. PRISMA Flowchart for Present Study

Another report from the CDC in 2010, stated that the rates of CS started increasing in 2007 after a historical low in 2004-2005. [13] The trends in the Midwest followed the national ones. Of those cases, 29% were detected at delivery and the overall case-fatality rate reached up to 7% among infants.[13] In 2017, case numbers hit a record high for the first time since 1993.[14]

In 2015, the first state-specific statistics for syphilis among MSM were published. MSM had 53.9% and 93% higher risk of syphilis than men who have sex with women only (MSW) and to women, respectively.[15] Up to 60% of cases in the US were black.[16] Compared to other states, MO had the 13th highest rate of syphilis among MSM and the 24th highest overall. MO had 37% (777/2,096) syphilis cases and 60% (3/5) CS in the West North (WN) Central states.[16] Furthermore, MO State Health Profile showed an increase in PSS from 2.3/100,000 in 2011 to 5.1/100,000 in 2015.[17]

In 2019, Bernstein et al. classified Missouri as an intermediate-risk state for primary, secondary, and CS.[18] They demonstrated an association between CS and urbanization and an association between PSS and violent crime, People Who Inject Drugs (PWID), poor socioeconomic status, and rejection of same-sex marriage.[18] The CDC described the association between PSS and drug use, linking the two epidemics together in a national trend that is also applicable to the Midwest states, where the percentage of PWID among those who have PSS increased from 4.5 in 2013 to 12.5 in 2017.[14]

In a retrospective observational study published in 2020, Reno et al. demonstrated that sexual health and drug use should be tackled to address the rising numbers of syphilis in Missouri.[19] Despite having the highest numbers of new cases of early syphilis in PWID in Kansas city and St. Louis, the largest increase in such cases between 2012 and 2018 occurred in rural areas.[19] This was linked to poorer access to healthcare, lower levels of sex education, and decreased access to syringes and drug rehabilitation programs in such counties, suggesting a possible solution would be in addressing such issues on a public health level.[19]

New cases of syphilis continued to increase in Missouri from 1,914 cases (31.2/100,000) in 2018 to 4,176 cases (67.6/100,000) in 2022.[20] Currently, Missouri has one of the highest prevalences of CS (CDC, 2021),[21] St. Louis is the 5th leading US city in terms of STI rates in 2024 [22] and Kansas City is struggling with a massive surge of new cases, approaching 39.8/100,000 people in some of its counties as per January 2024.[23]

However, despite mandated reporting of syphilis cases, complications in 2023 remain underreported.[24] In 2023, the incidence of STIs, including syphilis, continues to increase in MO. Vallery et al. recommended yearly reporting of cases, sex education, and addressing unemployment and poverty.[25] In addition, racism, homophobia, and xenophobia are barriers to screening and treatment for STIs and in addition to poor healthcare access and IV drug use in Missouri.[25]

Challenges in Screening

As with other STIs, early recognition and treatment is the best strategy in preventing spread and complications.[7] In 2003, a 22-laboratory network reporting system in Kansas City found that syphilis was under-screened and underreported.[26] In the same year, the CDC put a plan to eliminate syphilis by 90% by 2005 and set clear screening and reporting guidelines.[27] In 2005, Feinstein reported a high false-positive screening rate, making interpretation difficult and resulting in unnecessary stigma and restrictions.[28]

In 2013, McNicholas et al. screened 8,347 female participants seeking primary health services for STIs and found that 8% had at least one infection. Black women had the highest prevalence.[29] This high prevalence among blacks might be explained by the lack of trust in the healthcare system, especially after the historical Tuskegee study.[30]

Missouri had adopted the CDC recommendation for syphilis screening in the first trimester of pregnancy, and a repeat test in the third trimester in high-risk individuals.[31] In 2016, the US Preventive Services Task Force (USPSTF) recommended that all pregnant women should be screened at least once for syphilis, in addition to high-risk individuals, including people who have unprotected sex, multiple sexual partners, syphilis exposure, People Living With HIV (PLHIV), and PWID.[32]

Diagnostic Challenges

The diagnosis of syphilis can be challenging, due to non-automated testing, subjective interpretations, and low specificity.[33] It includes a two-step approach. The traditional algorithm starts with non-treponemal tests, the venereal disease research laboratory (VDRL) or rapid plasma reagent (RPR), that, if positive, are to be followed by confirmatory treponemal tests such as T. pallidum enzyme immunoassay (TP-EIA), particle agglutination (TPPA) or fluorescent treponemal antibody absorption (FTA).[33] Non-treponemal tests remain positive after treatment which makes it hard to interpret re-infection and decreases sensitivity for latent infection.[33] The reverse algorithm starts with a treponemal test if positive, reflexes to a non-treponemal test, but it has higher false-positive results in populations with low prevalence.

In the late 2010s, the Food and Drug Administration (FDA) cleared a new diagnostic approach, the "BioPlex 2200 Syphilis Total & RPR," which is automated and offers both tests simultaneously.[33] This was important as it decreased sample processing time, especially in high-burden areas, and overcame the problem of operator dependence.[33]

Challenges in Treatment

The treatment of choice for syphilis is intramuscular benzathine penicillin G and intravenous procaine penicillin for neurosyphilis.[34] In case of penicillin allergy in neurosyphilis, CS, or syphilis in pregnancy, the CDC recommends desensitization or ceftriaxone as a last resort; while in adults with PSS, doxycycline or tetracycline is recommended.[34]

However, penicillin has been in shortage in the US since the 1990s due to costs and failure of supply to meet the demands.[35]

In 2007, Stoner illustrated that azithromycin use in syphilis had a high failure rate due to prevalent molecular resistance in Treponema pallidum, while ceftriaxone in daily doses for 8-10 days was an acceptable alternative with close monitoring.[36]

After the coronavirus pandemic, the FDA listed benzathine penicillin G on their shortage webpage and the CDC recommended using doxycycline for adults when possible.[37,38] In July 2023, it became a debate whether to declare this shortage as a "public health emergency" due to high numbers of children with CS in many US states including Missouri.[39] As a result, in January 2024, the FDA temporarily allowed benzathine benzylpenicillin import from France, especially after national drug suppliers declared it would take until mid-2024 to end this shortage.[46] However, the shortage of penicillin G is global.

As patients allergic to penicillin often tolerate cephalosporins, Cao et al. demonstrated in a multicentered study in Jiangsu, China, that ceftriaxone 1g intravenous daily administration for PSS in healthy adults was non-inferior to penicillin G. Tsai et al.

concluded in 2014 that doxycycline twice daily for two weeks is a good alternative when penicillin G is not available.[41]

In the UK, an acceptable alternative treatment (except for neurosyphilis) is ampicillin plus probenecid to increase ampicillin's bioavailability.[42] In Japan, because penicillin G was not available before 2022, a 1,500 mg ampicillin daily dose was used successfully for 14 days in early and 28 days in late syphilis.[42] A study from Spain failed to show the non-inferiority of linezolid against penicillin in early syphilis and recommended against it.[43]

Several ongoing trials are assessing alternative treatments. For example, the National Taiwan University Hospital is conducting a phase 4 trial comparing penicillin, doxycycline, and ceftriaxone.[44]

For now, the CDC urges the use of doxycycline when feasible and not contraindicated at times of shortage, to prioritize penicillin for CS, pregnant females and children.[45]

Prevention

In 2015, 4% of high-school students had sex before age 13, 36% had at least one sexual encounter, and 26% were sexually active. However, only 56% reported using condoms.[46] These findings made it imperative to promote sexual health, acceptance, parent-child communication, sex education, screening, and prevention. As of January 2024, schools in Missouri are not obliged to incorporate sex education into their curricula, but as per Statute § 170.015, they are required to give health education that would include HIV prevention.[47]

According to the CDC, sex education makes people more likely to delay sexual encounter to a later age, limit the number of sex partners, and practice safe sex.[48] It has to be well structured, though, taught by trained people, respect the needs of all people including LGBTQ+, engage with families, and be non-judgmental.[48] Sex education makes people more inclined to report any symptoms they have and screen themselves more for STIs.[49]

In 2015, Bolan et al. discussed daily doxycycline 100mg daily as Pre-Exposure Prophylaxis (PrEP) in MSM and found that it was effective in decreasing the incidence of syphilis, gonorrhea, and chlamydia, but the results were not statistically significant.[50]

Since screening is key in prevention, the COVID-19 pandemic resulted in less testing in 2020 and 2021, translating to underreporting of new cases and more transmission, according to CDC.[7] Many public health workers were reassigned for the pandemic in those years, and there was a decrease in state funding for syphilis, which likely lead to a surge in new cases in 2022. [51]

Doxycycline 200mg taken once within 24 hours of a sexual encounter as post-exposure prophylaxis (PEP) is preventative in 70%. However, there are concerns this can lead to doxycycline resistance in syphilis.[52] The 2021 CDC update on STIs stated that "more research is needed" to determine doxycycline PrEP or PEP effectiveness for proper prevention. As per the New York Department of Health, PEP should be prescribed to all cisgender men and transgender women who are at risk and have had an STI or who have condomless sex with multiple MSM partners.[53] No information of doxycycline PEP is mentioned on Missouri's Department of Health website.

Discussion

Containing the alarming rise in syphilis cases will require a robust public health approach. Valleroy et al. demonstrated the need to address socioeconomic factors such as unemployment, sex education, and stigma, especially around HIV, which has a strong association with syphilis.[25] Furthermore, the CDC stated that certain communities are "hit especially hard" by this STI epidemic, including MSM and certain races such as black, American Indian, and Alaska Native, which are the groups that face more social barriers to healthcare.[54]

Missouri is ranked 12th among all 50 states regarding syphilis prevalence. The syphilis rates in the Midwest are quickly going up.[55] However, it should be noted that when specific cities are compared, it ranks among the top five, with St. Louis having the highest numbers.[56]

Syphilis, despite being an ancient disease, continues to be one of the rapidly increasing problems in Missouri. Social stigma, lack of sex education, and focus on sexual health, socioeconomic challenges, and low health literacy fosters high-risk sexual behavior and reluctance to disclose their status to sexual partners. Residents of rural areas face additional problems related to transportation barriers.[57]

Prevention is always key, and public health approaches are almost always the most important and cost-effective interventions.[58] However, preventive measures are slow to be implemented; including the lack of PEP recommendations.

In addition to global and local treatment shortages. More studies are needed in the US generally, and in Missouri specifically, to see the feasibility and effectiveness of alternative non-penicillin pharmacotherapy.

Hopeful initiatives include, the CDC providing more

than five million dollars in funding for STI prevention efforts and to invest in disease intervention specialists.[59] Prenatal screening is now legally required for every pregnant woman's first clinic visit. In high-risk areas, it is also required at 28 weeks and delivery.[59] In its major cities, Missouri is becoming more inclusive towards the LGBTQ+ community, especially in Columbia, Kansas, and St. Louis.[60] On February 20, 2024, Columbia City became a "sanctuary for LGBTQ residents," and implemented measures of protection of marginalized groups.[61] Being 97% rural by area, many projects such as the Hotspot Project aim to improve phone and internet connectivity to promote telehealth and access to care. Several new projects are being funded by the US Department of Agriculture to improve healthcare access to rural regions.[62]

Conclusion

As syphilis makes a comeback, we notice that similar risk factors are shared across Missouri that are exacerbating the epidemic. Adopting a more inclusive judgement-free approach with adequate education and awareness is crucial to mitigate risky behavior, which is only gets worse with more stigma. Rurality is a problem that is still to be solved for better healthcare access, and investing in alternatives to penicillin in PSS would offer good alternatives in times of shortage. Efforts are currently being made by the state, but consistency in objective plan deployment remains much needed.

Limitations

This is a narrative review, the publications included are heterogeneous and cannot be compared heads on, therefore no biostatistical methods could be used.

References

1. Tampa M, Sarbu I, Matei C, Benea V, Georgescu S. Brief History of Syphilis. J Med Life. 2014;7(1):4-10.
2. Stamm LV. Syphilis: Re-emergence of an old foe. Microb Cell. 2016;3(9):363-370. doi:10.15698/mic2016.09.523
3. STAMM LV. Syphilis: antibiotic treatment and resistance. Epidemiol Infect. 2015;143(8):1567-1574. doi:10.1017/S0950268814002830
4. Schmidt R, Carson PJ, Jansen RJ. Resurgence of Syphilis in the United States: An Assessment of Contributing Factors. Infect Dis (Auckl). 2019;12:1178633719883282. doi:10.1177/1178633719883282
5. Syphilis. Accessed January 24, 2024. https://www.who.int/news-room/fact-sheets/detail/syphilis
6. Sexually Transmitted Disease Surveillance, 2021. Published April 11, 2023. Accessed January 24, 2024. https://www.cdc.gov/std/statistics/2021/default.htm
7. Impact of COVID-19 on STDs. Published April 11, 2023. Accessed January 24, 2024. https://www.cdc.gov/std/statistics/2021/impact.htm
8. missouri.pdf. Accessed January 24, 2024. https://www.cdc.gov/std/dstdp/sti-funding-at-work/jurisdictional-spotlights/missouri.pdf
9. Health Advisory: Increased Incidence of HIV and Syphilis Co-Infection Among Missourians of Child-Bearing Potential. stlouis-mo.gov. Published November 2, 2023. Accessed January 24, 2024. https://www.stlouis-mo.gov/government/departments/health/news/increased-incidence-hiv-syphilis-co-infection-child-bearing-potential-health-advisory.cfm
10. Rayyan – Intelligent Systematic Review - Rayyan. Published November 8, 2021. Accessed May 16, 2024. https://www.rayyan.ai/
11. Primary and Secondary Syphilis --- United States, 2002. CDC. https://mednar.com/mednar/desktop/en/service/link/track?redirectUrl
12. HIV Risk, Prevention, and Testing Behaviors Among Men Who Have Sex With Men --- National HIV Behavioral Surveillance System, 21 U.S. Cities, United States, 2008. CDC. https://mednar.com/mednar/desktop/en/service/link/track?redirectUrl
13. Congenital Syphilis --- United States, 2003--2008. CDC. https://mednar.com/mednar/desktop/en/service/link/track?redirectUrl
14. Grey JA/ T. Increased Methamphetamine, Injection Drug, and Heroin Use Among Women and Heterosexual Men with Primary and Secondary Syphilis — United States, 2013–2017. PubMed Central. Published online February 15, 2019. doi:10.15585/mmwr.mm6806a4
15. State-Specific Rates of Primary and Secondary Syphilis Among Men Who Have Sex with Men — United States, 2015 | MMWR. CDC. https://mednar.com/mednar/desktop/en/service/link/track?redirectUrl
16. Summary of Notifiable Infectious Diseases and Conditions — United States, 2015 | MMWR. CDC. https://mednar.com/mednar/desktop/en/service/link/track?redirectUrl
17. Missouri - 2015 State Health Profile. CDC. https://mednar.com/mednar/desktop/en/service/link/track?redirectUrl
18. Bernstein KT/ G. Developing a Topology of Syphilis in the United States. PubMed Central. Published online September 2018:S1-S6. doi:10.1097/OLQ.0000000000000817
19. Reno H/ F. The Emerging Intersection Between Injection Drug Use and Early Syphilis in Nonurban Areas of Missouri, 2012-2018. Pubmed. Published online September 2, 2020. doi:10.1093/infdis/jiaa056
20. Table 20. Total Syphilis* — Reported Cases and Rates of Reported Cases by State/Territory and Region in Alphabetical Order, United States, 2018–2022. Published November 30, 2023. Accessed February 14, 2024. https://www.cdc.gov/std/statistics/2022/tables/20.htm
21. AtlasPlus - Maps. Accessed February 20, 2024. https://gis.cdc.gov/grasp/nchhstpatlas/maps.html
22. These U.S. Cities Have the Highest STD Rates [2024]. Innerbody. Accessed February 20, 2024. https://www.innerbody.com/std-testing/std-statistics
23. Kansas City has seen a massive increase in syphilis cases in the past decade. Here's what to know. KCUR - Kansas City news and NPR. Published January 3, 2024. Accessed February 20, 2024. https://www.kcur.org/health/2024-01-03/kansas-city-has-seen-a-massive-increase-in-syphilis-cases-in-the-past-decade-heres-what-to-know
24. Jackson DA/ M. Reported neurologic, ocular, and otic manifestations among syphilis cases — 16 states, 2019. PubMed Central. Published online July 13, 2022. doi:10.1097/OLQ.0000000000001673
25. Valleroy E, Reed A, Lightner JS. Population-level predictors of sexually transmitted infection rate changes in Missouri: an ecological study. Arch Public Health. 2023;81:12. doi:10.1186/s13690-022-01019-6
26. Hoffman MA, Wilkinson TH, Bush A, et al. Multijurisdictional approach to biosurveillance, Kansas City. Emerg Infect Dis. 2003;9(10):1281-1286. doi:10.3201/eid0910.030060
27. Kahn RH. Recommendations for Public Health Surveillance of Syphilis in the United States.
28. Feinstein AR. Does "Health Promotion" Really Promote Health? The American Journal of Economics and Sociology. 2005;64(1):427-434.
29. McNicholas C, Peipert JF, Maddipati R, Madden T, Allsworth JE, Secura GM. Sexually transmitted infection prevalence in a population seeking no-cost contraception. Sex Transm Dis. 2013;40(7):546-551. doi:10.1097/OLQ.0b013e31829529eb
30. Lynn JJ. The Lived Experience of Urban Plus-Sized Black Women in a Midwestern City.
31. Warren HP/ C. State Requirements for Prenatal Syphilis Screening in

the United States, 2016. PubMed Central. Published online September 2018:1227-1232. doi:10.1007/s10995-018-2592-0
32. Lee KC/ NM. Sexually Transmitted Infections: Recommendations from the U.S. Preventive Services Task Force. Pubmed. Published online December 1, 2016. https://mednar.com/mednar/desktop/en/service/link/track?redirectUrl
33. Tesfazghi MT/ A. Clinical Performance of the BioPlex 2200 Syphilis Total & RPR Assay at a Tertiary Medical Center with a High Rate of Syphilis. PubMed Central. Published online January 2, 2019. doi:10.1128/JCM.01487-18
34. Kennedy AK, Kaushik G, Dubinsky EL, Huseynli A, Jonson-Reid M, Plax K. Direct and Indirect Cost Savings From Sexually Transmitted Infection Testing, Treatment, and Counseling Among Foster Youth. Sexually Transmitted Diseases. 2022;49(1):86. doi:10.1097/OLQ.0000000000001511
35. McDonald R. Vital Signs: Missed Opportunities for Preventing Congenital Syphilis — United States, 2022. MMWR Morb Mortal Wkly Rep. 2023;72. doi:10.15585/mmwr.mm7246e1
36. Stoner BP. Current Controversies in the Management of Adult Syphilis. Clinical Infectious Diseases. 2007;44(Supplement_3):S130-S146. doi:10.1086/511426
37. Shortage of Penicillin G Benzathine (Bicillin L-A). Clinicians. Accessed February 20, 2024. https://www.vdh.virginia.gov/clinicians/shortage-of-penicillin-g-benzathine-bicillin-l-a/
38. Clinical Reminders during Bicillin L-A® Shortage. Published July 26, 2023. Accessed February 20, 2024. https://www.cdc.gov/std/dstdp/dcl/2023-july-20-Mena-BicillinLA.htm
39. Syphilis Emergency Looms in the US as Drugs Run Low. Bloomberg.com. https://www.bloomberg.com/news/articles/2023-07-26/us-officials-weigh-deeming-a-syphilis-emergency-as-drugs-run-low. Published July 26, 2023. Accessed February 20, 2024.
40. FDA allows imports of syphilis drug from France amid nationwide shortage. FOX 2. Published January 11, 2024. Accessed February 20, 2024. https://fox2now.com/news/national/fda-allows-imports-of-syphilis-drug-from-france-amid-nationwide-shortage/
41. Tsai JC, Lin YH, Lu PL, et al. Comparison of Serological Response to Doxycycline versus Benzathine Penicillin G in the Treatment of Early Syphilis in HIV-Infected Patients: A Multi-Center Observational Study. PLOS ONE. 2014;9(10):e109813. doi:10.1371/journal.pone.0109813
42. Ando N, Mizushima D, Omata K, et al. Combination of Amoxicillin 3000 mg and Probenecid Versus 1500 mg Amoxicillin Monotherapy for Treating Syphilis in Patients With Human Immunodeficiency Virus: An Open-Label, Randomized, Controlled, Non-Inferiority Trial. Clinical Infectious Diseases. 2023;77(5):779-787. doi:10.1093/cid/ciad278
43. Ubals M, Nadal-Baron P, Arando M, et al. Oral linezolid compared with benzathine penicillin G for treatment of early syphilis in adults (Trep-AB Study) in Spain: a prospective, open-label, non-inferiority, randomised controlled trial. The Lancet Infectious Diseases. 2024;0(0). doi:10.1016/S1473-3099(23)00683-7
44. National Taiwan University Hospital. Treatment Responses of Early Syphilis to Single-Dose Ceftriaxone Plus Doxycycline Versus Single-Dose Benzathine Penicillin G Plus Doxycycline in PLWH. clinicaltrials.gov; 2023. Accessed December 31, 2023. https://clinicaltrials.gov/study/NCT05980871
45. Syphilis - STI Treatment Guidelines. Published January 16, 2024. Accessed February 23, 2024. https://www.cdc.gov/std/treatment-guidelines/syphilis.htm
46. Missouri Summary Report. Analysis of State Health Education Laws.
47. Missouri State Profile. SIECUS. Accessed February 21, 2024. https://siecus.org/state_profile/missouri-state-profile-23/
48. What Works In Schools: Sexual Health Education | DASH | CDC. Published April 11, 2023. Accessed February 23, 2024. https://www.cdc.gov/healthyyouth/whatworks/what-works-sexual-health-education.htm
49. Craig-Kuhn MC, Schmidt N, Lederer A, et al. Sex education and STI fatalism, testing and infection among young African American men who have sex with women. Sex Educ. 2021;21(4):404-416. doi:10.1080/14681811.2020.1809369
50. Bolan RK, Beymer MR, Weiss RE, Flynn RP, Leibowitz AA, Klausner JD. Doxycycline Prophylaxis to Reduce Incident Syphilis among HIV-Infected Men who have Sex with Men who Continue to Engage in High Risk Sex: A Randomized, Controlled Pilot Study. Sex Transm Dis. 2015;42(2):98-103. doi:10.1097/OLQ.0000000000000216
51. MSc JC MD. Syphilis surge: The great imitator strikes again. Published April 2, 2024. Accessed May 16, 2024. https://www.idsociety.org/science-speaks-blog/2024/syphilis-surge-the-great-imitator-strikes-again/
52. Park JJ, Stafylis C, Pearce DD, et al. Interest, Concerns, and Attitudes Among Men Who Have Sex With Men and Health Care Providers Toward Prophylactic Use of Doxycycline Against Chlamydia trachomatis Infections and Syphilis. Sexually Transmitted Diseases. 2021;48(9):615. doi:10.1097/OLQ.0000000000001395
53. DiMarco DE, Urban MA, Fine SM, et al. Doxycycline Post-Exposure Prophylaxis to Prevent Bacterial Sexually Transmitted Infections. Johns Hopkins University; 2023. Accessed February 23, 2024. http://www.ncbi.nlm.nih.gov/books/NBK597440/
54. CDC Newsroom. CDC. Published January 1, 2023. Accessed January 24, 2024. https://www.cdc.gov/media/releases/2023/s0411-sti.html
55. Weber L. As Syphilis Invades Rural America, A Fraying Health Safety Net Is Failing To Stop It. KFF Health News. Published April 18, 2019. Accessed February 23, 2024. https://kffhealthnews.org/news/syphilis-invades-rural-america-missouri-health-care-infrastructure-crumbling/
56. Syphilis cases in Missouri have jumped 259% in the last few years. Here's what to know. STLPR. Published January 9, 2023. Accessed February 23, 2024. https://www.stlpr.org/health-science-environment/2023-01-09/syphilis-cases-in-missouri-have-jumped-259-in-the-last-few-years-heres-what-to-know
57. Hadjimohammadi A. HIV prevention, education improve in Missouri. But stigma still stands • Missouri Independent. Missouri Independent. Published December 1, 2023. Accessed February 23, 2024. https://missouriindependent.com/2023/12/01/hiv-prevention-education-improve-in-missouri-but-stigma-still-stands/
58. Velmovitsky PE, Bevilacqua T, Alencar P, Cowan D, Morita PP. Convergence of Precision Medicine and Public Health Into Precision Public Health: Toward a Big Data Perspective. Front Public Health. 2021;9:561873. doi:10.3389/fpubh.2021.561873
59. CDC STI State Profile Missouri.pdf. Accessed February 23, 2024. https://www.cdc.gov/std/dstdp/sti-funding-at-work/jurisdictional-spotlights/missouri.pdf
60. Missouri All-Stars: Three Cities Lead the Way in LGBTQ Equality. Human Rights Campaign. Published October 19, 2017. Accessed February 23, 2024. https://www.hrc.org/news/missouri-all-stars-columbia-kansas-city-and-st-louis-lead-the-way-in-lgbtq
61. Columbia passes LGBTQ sanctuary city ordinance. Here's how the council voted. Columbia Daily Tribune. Accessed February 23, 2024. https://www.columbiatribune.com/story/news/local/2024/02/20/columbia-missouri-now-lgbtq-sanctuary-city-what-that-means/72657910007/
62. USDA Helps Expand Access to Rural Health Care in Missouri. Rural Development. Published July 27, 2023. Accessed February 23, 2024. https://www.rd.usda.gov/newsroom/news-release/usda-helps-expand-access-rural-health-care-missouri
63. Piro A, Tagarelli A, Quattrone A. 'The Syphilitic' by Albrecht Dürer (1471–1528). Sex Transm Infect. 2014;90(7):544-544. doi:10.1136/sextrans-2014-051597

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Energy Drinks: A Clinical Primer and National Data Update

by Kevin Y. Xu, MD, Kevin T. Baumgartner, MD, Suraj Shankar, MD, Alison Huckenpahler, MD, PhD & Paul E Glaser, MD, PhD

Caffeine consumption is a multi-faceted phenomenon that has a continuum of behaviors, ranging from excessive daily use to daily use without functional impairment to complete abstinence.



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Abstract

This article describes estimates of energy drink uptake using national-level data in the US and provides clinical strategies for evaluating patients with unhealthy energy drink consumption. Our approach is grounded in the paradigm of harm reduction, which supports incremental change while recognizing people's dignity, autonomy, individualism, and accountability.[1] Rather than urge complete abstinence, we emphasize the importance of helping people understand energy drinks' potential harmful effects independently of whether individuals are ready to abstain from energy drinks.

Caffeine Content Unknown in Energy Drinks

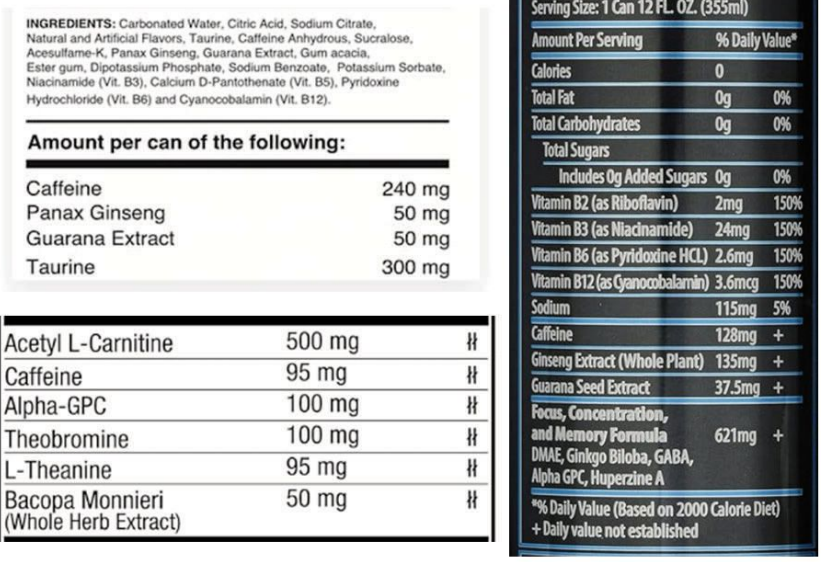
Energy drinks represent nearly 10% of all sugar-sweetened beverages worldwide.[2] The target consumer market for energy drinks consists heavily of young adults,[3] a population less tolerant of caffeine's effects and at heightened risk of adverse effects.[3] Surveys suggest that half of college students consume at least one energy drink per month, with common reasons including the desire to increase energy, reverse the effects of alcohol (a misconception described in detail in article), and/or compensate for poor sleep.[4]

Protected by the 1994 Dietary Supplement Health and Education Act, energy drinks are grouped together with natural dietary supplements described as Generally Regarded as Safe (GRAS) by government regulators, owing to the inclusion of specialty ingredients not commonly found in juices and soft drinks such as amino acids (taurine), yerba mate, guaraná, ginseng, B-complex vitamins, and other ingredients.[5] The stimulating effects of energy drinks are not only due to caffeine and specialty ingredients but also the rush caused by a high dosage of carbohydrates and sugars.[6]

Due to their GRAS status, energy drinks often do not report their caffeine content, nor provide warning labels advising proper use.[7] In cases where drinks do disclose their content, labeling inaccuracies are common.[5] Some energy drinks may contain up to 70% more caffeine on average than the 0.02% caffeine threshold for GRAS products.[8-10] Yet, the FDA has not re-evaluated energy drinks' GRAS status in recent

decades.[10] While most soft drinks fall within the FDA's limit of no more than 65 mg of caffeine per 12 ounces,[11] energy drinks are suspected to contain far greater amounts of caffeine, ranging from 50 to 550 mg per bottle.[12] As shown in Figure 1, energy drinks may sometimes report the quantity of caffeine, yerba mate, and guaraná separately, without disclosing the precise quantity of caffeine contained in the mate and guarana contents.

Figure 1: Examples of nutrition and supplement facts for selected energy drinks (available for sale on www.amazon.com)

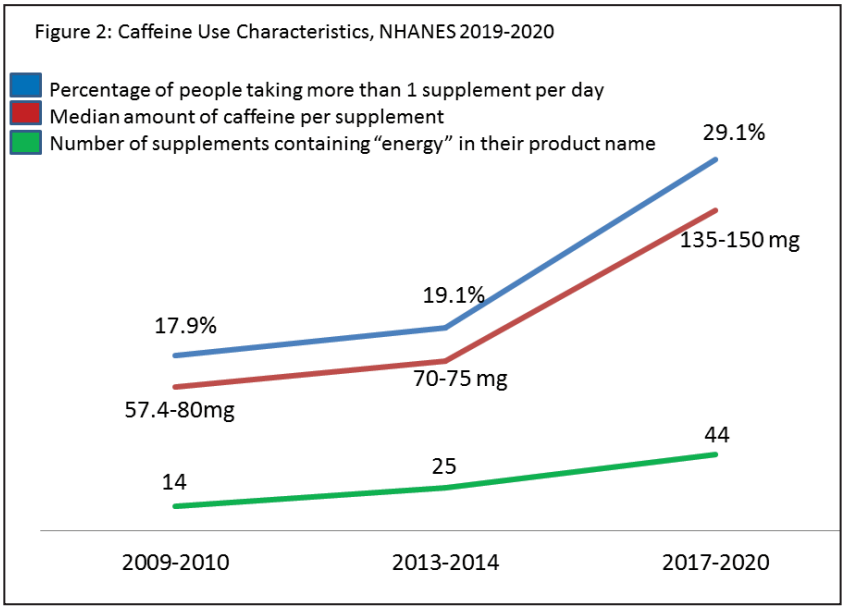


Energy drinks are altering the debate about the risk/benefit ratio for caffeinated beverages, which has historically been grounded in controversy surrounding whether caffeine use disorder is a valid diagnosis. After all, caffeine consumption is considered "more a dedicated habit" than a risk factor for "compulsive addiction" due to its mood and alertness-enhancing effects at low doses.[13,14] Most people can consume caffeine throughout the life-span without sustaining functional impairment. Many individuals report improvements in subjective alertness and decreased fatigue immediately after consuming energy drinks,[15,16] supporting the popularity of energy drinks among athletes who report improved short-term strength and endurance.[17-21] While caffeine use disorder remains without formal Diagnostic and Statistical Manual of Mental Disorders (DSM) diagnostic criteria, the DSM-5 recently added criteria for caffeine withdrawal and intoxication, as studies show that caffeine withdrawal and intoxication can cause functional impairment among chronic consumers of caffeine.[22-24] Per DSM-5 guidelines, caffeine withdrawal is defined as prolonged daily use of caffeine with 3+ symptoms, occurring within 24 hours of reduction in use, including headache (the most common symptom[3]), fatigue, dysphoria, depressed mood, irritability, concentration deficits, and flu-like symptoms.[25] Caffeine intoxication is also included in the DSM, with symptoms including insomnia, rambling speech and flow of thought, increased psychomotor activity and restlessness, nervousness and excitement, diuresis, gastrointestinal upset.[25]

Caffeinated Dietary Supplement Consumption Increase

Because there is limited data on trends in energy drink consumption in the US, we conducted preliminary analyses using the publicly-available National Health and Nutrition Examination Surveys (NHANES), which encompass face-to-face interviews and physical examinations in a nationally representative sample of approximately 5,000 individuals per two-year cycle. The NHANES survey's dietary supplement questionnaires contain data (i.e., brand, amount, caffeine content) on prescribed and over-the-counter dietary supplements reported by NHANES participants based on past 24-hour recall.

Using SAS 9.4, we computed the number of dietary supplements containing the term "energy" in their product name as a proxy for energy drink consumption. We also calculated the median amount of caffeine content (mg) per supplement, as well as the percentage of supplements (containing "energy" in the product name) consumed more than once daily. As shown in Figure 2, the number of supplements containing "energy" in the product name increased steadily from 2009 to 2020, rising from 14 in 2009-2010 to 44 in 2017-2020. The median caffeine content, across all supplements, increased from 57.4-80mg in 2009-2010 to 135-150 mg in 2017-2020. Whereas 17.9% of dietary supplements containing



the term "energy" in the product name were reportedly taken >1 per day in 2009-2010, this figure increased to 29.1% in 2017-2020.

There are limitations associated with our preliminary analyses. After all, caffeinated dietary supplements in the NHANES data do not capture all available energy drinks, and not all dietary supplements containing the term "energy" are necessarily energy drinks. Yet, such trends have important implications; multiple professional organizations (including the American Academy of Pediatrics[26]) recommend children and adolescents not consume energy drinks owing to current gaps in our knowledge of caffeine content and risk level. There is also no legal age limit to buying energy drinks, and the overtones of caffeine being a GRAS dietary supplement may lead consumers to believe that "more is better."[3] While studies suggest that energy drink consumption increased nearly 10-fold across children and adolescents in the 2010s,[27] up-to-date data remains sparse on the risks and benefits of energy drinks in children and young adults. While death from caffeine intoxication is thought to be rare,[28] energy drink-related toxicity reports are also underestimated, as data relies on self-reported signs and symptoms when many consumers may not be able to link their symptoms to energy drink consumption.[7]

Harm Reduction for Safer Caffeine Consumption

Harm reduction (the framework of mitigating risk without the goal or expectation of completely eliminating risk) can be useful for helping patients with unhealthy energy drink consumption, particularly since many patients may not be ready to completely cut energy drinks out of their routine. Rather than help people move from active energy drink consumption to a state of abstinence, harm reduction strategies aim to optimize the safety of energy drink consumption regardless of whether they are ready to cut down. We provide a clinical checklist (Table 1, created via expert clinician consensus) to guide physicians through the evaluation of young adults engaged in unhealthy energy drink consumption.

Evaluate for Caffeine Toxicity

1. Outpatient generalists must consider whether the patient needs to go to the emergency room. Caffeine intoxication is characterized by tachycardia, neuropsychiatric excitation (ranging from anxiety and tremor to status epilepticus), nausea and vomiting, and metabolic abnormalities including hypokalemia and hyperglycemia.[29] As with most poisonings and intoxications, caffeine toxicity exists on a spectrum; patients with mild tremor, mild sinus tachycardia, or mild gastrointestinal upset do not typically require medical intervention, while patients with significant tachycardia, seizure, or intractable vomiting should be referred to the emergency department for evaluation and treatment.

2. Cardiovascular changes, seizures, and gastrointestinal problems are expected in cases of caffeine poisoning. Tachycardia is essentially universal in caffeine intoxication; the rhythm is typically sinus tachycardia, but patients with severe poisoning or comorbid cardiac conditions may experience dysrhythmias, myocardial infarction, or cardiac arrest.[30] Although premature atrial contractions were initially thought to be associated with high caffeine intake, studies have shown that this is not

Table 1

Clinical Case Challenge: A 21-year-old college student presents to her primary care doctor for recurrent panic attacks and reports that she had not slept for 36 hours. Her history of present illness is significant for one year of sustained low mood, "poor quality" sleep, day time fatigue, headaches, stomach aches, passive suicidal ideation, and irritability. Four months ago, she initiated a selective serotonin-reuptake inhibitor, which was up-titrated to a therapeutic dose with limited benefit. She had been diagnosed with attention-deficit hyperactivity disorder (ADHD) at age 16; she had a prescription for amphetamine salts (Adderall XR) in high school but discontinued it in 12th grade. Notably, she reports consuming approximately six energy drinks in the afternoons for the last 2 years. After trying Red Bull for the first time at a college orientation week party (where it was mixed with alcohol), she escalated her energy drink consumption in order to "power" herself through a heavy freshman year course load. Lately, she feels as if she cannot function without energy drinks. ***What might your work-up look like for this patient?***
Framework for an Office-Based Energy Drink Workup **Evaluate for Caffeine Toxicity** [ ] Physical exam and vitals; electrocardiogram (if clinically indicated) [ ] Readily apparent signs and symptoms of caffeine poisoning should prompt emergency department referral [ ] Complete blood count, pregnancy test, comprehensive metabolic panel, total creatinine kinase, thyroid studies [ ] Dipstick urinalysis; urine drug screen with confirmatory testing and blood alcohol level (if clinically indicated) **Evaluate for Treatable Mental Health Conditions** [ ] Depression; anxiety disorders; bipolar and psychotic disorders [ ] Attention-deficit hyperactivity disorder; substance use-related problems (i.e., alcohol, vaping/nicotine, marijuana) [ ] Consider referral to psychiatry or counseling/psychotherapy **Focus on Preventive Health Care** [ ] Primary care follow-up [ ] Dentist referral [ ] Motivational interviewing; discuss why patients were drawn to energy drinks in the first place and whether safer alternatives may exist

the case in the general population, although caffeine intake is associated with an elevated risk of premature ventricular contractions.[31] Blood pressure is usually elevated, and widened pulse pressures the difference between systolic blood pressure and diastolic blood pressure) may be observed. Hypotension may develop in very severe intoxication due to profound tachycardia resulting in inadequate diastolic filling time or due to peripheral vasodilation mediated by beta-2 agonism. Visits to the emergency department specifically related to energy drink consumption–often for rapid heart rate, palpitations, or chest pain–increased nearly 20-fold in the 2000s.[32 33] While the moderate consumption of energy drinks (<200 mg caffeine/day) is not known to correlate with clinically relevant cardiovascular changes in most individuals,[34 35] a recent study more than 50% of a sample of healthy subjects developed a long QTc interval with light activity following energy drink consumption.[36] Seizures should be expected in severe caffeine poisoning, and may be recurrent and difficult to control.[29] Gastrointestinal upset can be profound and lead to hypovolemia. Hyperglycemia and hypokalemia—both due to the effects of catecholamine release provoked by caffeine—can be useful diagnostic markers.

3. Laboratory evaluation may be needed in some cases. People without readily apparent signs and symptoms of caffeine poisoning do not necessarily need a laboratory evaluation outpatient. In patients with moderate-severe symptoms requiring referral to the emergency department or another acute care environment, clinicians should obtain diagnostic testing including complete blood count, electrolytes, total creatinine kinase, thyroid studies (as thyrotoxicosis can mimic caffeine intoxication), and an electrocardiogram. Testing for serum acetaminophen should be pursued in any patient with a known or suspected intentional overdose. Direct testing for caffeine in blood has limited availability and does not typically play a role in acute management. Clinicians should also consider ordering a pregnancy test in reproductive-age women, as high caffeine consumption has been found to correlate with increased risk for adverse birth outcomes, such as miscarriage and small-for-gestational-age infants.[37] The treatment of caffeine intoxication severe enough to require emergency medical care involves targeted sedation with benzodiazepines or other GABAergic sedatives, anti-emetics, intravenous hydration, management

of metabolic disturbances, and in very severe cases intravenous beta-blockers, vasopressors, inotropes, and/or emergent hemodialysis.[38]

Evaluate for Treatable Mental Health Problems

1. Energy drink consumption may suggest unmet mental health needs. Unhealthy energy drink consumption is often comorbid with treatable mood and anxiety disorders.[39] Yet, the relationship between caffeine consumption and mental illness is complex. Symptoms of anxiety and depression can be produced by both caffeine withdrawal and caffeine consumption,[40] and clinicians are recommended to evaluate caffeine intake as part of routine psychiatric assessment.[41] While a cross-sectional study suggested that coffee and caffeine consumption were associated with a lower risk of depressive symptoms.[42] the authors urged caution on interpretation of their results due to confounding. Other studies found that after adjustment for confounders, people who used energy drinks frequently were more likely to experience depressed mood and heightened sleep difficulty[43, 44] compared to moderate and infrequent energy drink consumers.[45] A recent meta-analysis shows that caffeine intake is associated with an increased risk of anxiety disorders in healthy individuals without psychiatric disorders,[46] while caffeine intake can also exacerbate symptoms in individuals with preexisting anxiety-spectrum disorders.[47] Studies also found that adolescents with higher levels of caffeine consumption are more likely to experience insomnia compared to peers with lower levels of caffeine consumption.[48, 49] Caffeine's effects can be particularly problematic for patients with serious mental illnesses (i.e., bipolar and psychotic disorders) who are sensitive to sleep disruption.[50, 51]

2. Energy drinks are not a substitute for SSRIs or psychotherapy. Past literature[52, 53] on the effects of caffeine on mood were conducted on lower risk thresholds than the amounts contained in energy drinks. Improvements to mood from caffeine may be short-lived, as energy drink consumption was associated with a transient decrease in anxiety and depressive symptoms that returned to baseline after the effects of caffeine wore off.[53] Overall, it is difficult to differentiate between improvements to mood as a consequence of reversing caffeine withdrawal (among habitual consumers who developed tolerance and dependence) and caffeine's direct effects on mood and cognition.[3]

3. Energy drinks are not a substitute for ADHD medication. Teens with ADHD often report using caffeine to "self-medicate" ADHD symptoms. However, the observational nature of existing analyses on the caffeine-ADHD relationship hinders our ability to infer causation.[54, 55] Consumers of energy drinks were nearly 70% more likely to exhibit symptoms of ADHD (i.e., hyperactivity and inattention) compared to peers who did not consume energy drinks.[56] On one hand, adolescents with ADHD were twice as likely as peers without ADHD to consume caffeinated beverages in the afternoon and evening;[57] yet, caffeine consumption was not consistently associated with ADHD symptom severity.[55] Importantly, psychostimulants such as methylphenidate and amphetamines consistently are significantly more effective than caffeine for the treatment of ADHD.[58]

3. Inquire about whether energy drinks are being mixed with alcohol. The co-consumption of alcohol and caffeine increased in popularity since the 2000s,[59] with nearly 50% of young adult samples reporting that they used energy drinks in tandem with alcohol.[4] Consumers often incorrectly believe that caffeine may counteract the CNS depressant effects of alcohol. Yet, in reality, caffeine reduces sleepiness without alleviating alcohol-related impairment (i.e., "wide-awake drunkenness").[60] Thus, people may underestimate their degree of impairment while consuming energy drinks with alcohol,[61] and are more likely to experience dehydration and alcohol poisoning than peers who do not mix caffeine and alcohol.[60] Studies raised concern for increased risk of alcohol dependence,[62, 63] and driving while intoxicated[64] among people who consume caffeine and alcohol together. Of concern, chronic alcohol consumption may increase the half-life of caffeine by over 70%.[65]

4. Non-judgmentally, ask your patients about substance use. Studies showed a correlation between energy drinks use and a myriad of non-alcohol substance use-related problems; for instance, US national survey data of middle and high school students illustrated associations between energy drink consumption and 30-day cigarette and marijuana use.[66] Associations between regular energy drink consumption and smoking among adolescents were also observed in European samples,[67] paralleled by Canadian studies showing an increase in sensation-seeking, depressive symptoms, and substance use among energy drinks users relative to peers who do not consume energy drinks.[68]

Focus on Preventive Health Care

1. Do not neglect primary care labs and work-up. Sugar is the second most prominent ingredient in energy drinks after water, and thus clinicians should evaluate for diabetes[69-71] and dental caries[7 72] associated with chronic energy drink consumption. Patients may also develop hypertension, cardiovascular problems,[73-75]and renal dysfunction[7, 76] Because studies suggest that some patients with sleep apnea may turn to caffeine to promote wakefulness,[77] history should be gathered regarding sleep-disordered breathing, and sleep studies should be considered if clinically appropriate. Studies also suggest that people with narcolepsy may also turn to caffeine for management of drowsiness.[78]

2. Engage your patients in conversation about safer caffeine consumption. Consistent with the spirit of motivational interviewing, clinicians should explore the benefits patients are deriving from energy drinks (i.e., managing an overwhelming workload; relief from depression; influence of social norms). Perceived benefits such as improvements in athletic performance, wakefulness, and reaction time should be explicitly acknowledged and weighed against potential risks. Recognizing that abstinence is not necessarily the goal, clinicians should assess their patients' readiness for change and discuss caffeinated alternatives to energy drinks that may be safer (i.e., flavored coffee, tea/chai), if patients are open to such discussions. While patients may not be ready to discontinue energy drinks, they may, however, be open to discussion about ways to engage in safer alcohol and drug use.

Conclusion

Caffeine consumption is a multi-faceted phenomenon that has a continuum of behaviors, ranging from excessive daily use to daily use without functional impairment to complete abstinence. Defining risk-reduction levels for energy drinks—a crucial step in any harm reduction initiative—is hindered by a dearth of research investigating the safety and mental health risks/benefits of specialty ingredients in energy drinks and their interactions with caffeine. For instance, while some articles suggest that 100+ mg caffeine/day for adolescents and 2.5 +mg caffeine/kg of body weight for children correlates with increased risk of caffeine toxicity and adverse cardiovascular events,[79] research has not established clear safety thresholds.[80] Because there is no consensus on the threshold for safe caffeine consumption, data is urgently needed to inform definitions for energy drink consumption risk levels and illustrate how changes in consumption risk may correspond to functional impairment.

References

1. Hawk M, Coulter RWS, Egan JE, et al. Harm reduction principles for healthcare settings. Harm Reduct J 2017;14(1):70. doi: 10.1186/s12954-017-0196-4 [published Online First: 2017/10/27]
2. Park S, Blanck HM, Sherry B, et al. Factors associated with sugar-sweetened beverage intake among United States high school students. J Nutr 2012;142(2):306-12. doi: 10.3945/jn.111.148536 [published Online First: 2012/01/10]
3. James JE, Rogers PJ. Effects of caffeine on performance and mood: withdrawal reversal is the most plausible explanation. Psychopharmacology (Berl) 2005;182(1):1-8. doi: 10.1007/s00213-005-0084-6 [published Online First: 2005/07/08]
4. Malinauskas BM, Aeby VG, Overton RF, et al. A survey of energy drink consumption patterns among college students. Nutr J 2007;6:35. doi: 10.1186/1475-2891-6-35 [published Online First: 2007/11/02]
5. Narine C, Weller J, Mathieson K. Energy Drink Use in Adolescents With and Without ADHD: Trends and Influences. Innov Clin Neurosci 2021;18(4-6):28-32. [published Online First: 2022/01/05]
6. Kaminer Y. Problematic use of energy drinks by adolescents. Child Adolesc Psychiatr Clin N Am 2010;19(3):643-50. doi: 10.1016/j.chc.2010.03.015 [published Online First: 2010/08/05]
7. Reissig CJ, Strain EC, Griffiths RR. Caffeinated energy drinks--a growing problem. Drug Alcohol Depend 2009;99(1-3):1-10. doi: 10.1016/j.drugalcdep.2008.08.001 [published Online First: 2008/09/24]
8. Harris JL, Schwartz M, Brownell K, et al. Sugary Drink FACTS: Evaluating Sugary Drink Nutrition and Marketing to Youth; 2011. .
9. Markey EJ, Durbin RJ, Blumenthal R. What's all the BUZZ about? A Survey of Popular Energy Drinks Finds Inconsistent Labeling, Questionable Ingredients and Targeted Marketing to Adolescents; 2013.
10. Pomeranz JL, Munsell CR, Harris JL. Energy drinks: an emerging public health hazard for youth. J Public Health Policy 2013;34(2):254-71. doi: 10.1057/jphp.2013.6 [published Online First: 2013/03/15]
11. Pennington N, Johnson M, Delaney E, et al. Energy drinks: a new health hazard for adolescents. J Sch Nurs 2010;26(5):352-9. doi: 10.1177/1059840510374188 [published Online First: 2010/06/12]
12. Ishak WW, Ugochukwu C, Bagot K, et al. Energy drinks: psychological effects and impact on well-being and quality of life-a literature review. Innov Clin Neurosci 2012;9(1):25-34. [published Online First: 2012/02/22]
13. Nehlig A. Are we dependent upon coffee and caffeine? A review on human and animal data. Neurosci Biobehav Rev 1999;23(4):563-76. doi: 10.1016/s0149-7634(98)00050-5 [published Online First: 1999/03/12]
14. Satel S. Is caffeine addictive?--a review of the literature. Am J Drug Alcohol Abuse 2006;32(4):493-502. doi: 10.1080/00952990600918965 [published Online First: 2006/11/28]
15. Howard MA, Marczinski CA. Acute effects of a glucose energy drink on behavioral control. Exp Clin Psychopharmacol 2010;18(6):553-61. doi: 10.1037/a0021740 [published Online First: 2010/12/29]
16. Alford C, Cox H, Wescott R. The effects of red bull energy drink on human performance and mood. Amino Acids 2001;21(2):139-50. doi: 10.1007/s007260170021 [published Online First: 2001/10/23]
17. Souza DB, Del Coso J, Casonatto J, et al. Acute effects of caffeine-containing energy drinks on physical performance: a systematic review and meta-analysis. Eur J Nutr 2017;56(1):13-27. doi: 10.1007/s00394-016-1331-9 [published Online First: 2016/10/21]
18. Perez-Lopez A, Salinero JJ, Abian-Vicen J, et al. Caffeinated energy drinks improve volleyball performance in elite female players. Med Sci Sports Exerc 2015;47(4):850-6. doi: 10.1249/MSS.0000000000000455 [published Online First: 2014/07/23]
19. Gallo-Salazar C, Areces F, Abian-Vicen J, et al. Enhancing physical performance in elite junior tennis players with a caffeinated energy

drink. Int J Sports Physiol Perform 2015;10(3):305-10. doi: 10.1123/ijspp.2014-0103 [published Online First: 2014/08/27]
20. Forbes SC, Candow DG, Little JP, et al. Effect of Red Bull energy drink on repeated Wingate cycle performance and bench-press muscle endurance. Int J Sport Nutr Exerc Metab 2007;17(5):433-44. doi: 10.1123/ijsnem.17.5.433 [published Online First: 2007/11/30]
21. Abian-Vicen J, Puente C, Salinero JJ, et al. A caffeinated energy drink improves jump performance in adolescent basketball players. Amino Acids 2014;46(5):1333-41. doi: 10.1007/s00726-014-1702-6 [published Online First: 2014/03/07]
22. Strain EC, Mumford GK, Silverman K, et al. Caffeine dependence syndrome. Evidence from case histories and experimental evaluations. JAMA 1994;272(13):1043-8. [published Online First: 1994/10/05]
23. Juliano LM, Evatt DP, Richards BD, et al. Characterization of individuals seeking treatment for caffeine dependence. Psychol Addict Behav 2012;26(4):948-54. doi: 10.1037/a0027246 [published Online First: 2012/03/01]
24. Hughes JR, Oliveto AH, Liguori A, et al. Endorsement of DSM-IV dependence criteria among caffeine users. Drug Alcohol Depend 1998;52(2):99-107. doi: 10.1016/s0376-8716(98)00083-0 [published Online First: 1998/11/04]
25. Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, Text Revision (DSM-5-TR). 2022
26. Committee on N, the Council on Sports M, Fitness. Sports drinks and energy drinks for children and adolescents: are they appropriate? Pediatrics 2011;127(6):1182-9. doi: 10.1542/peds.2011-0965 [published Online First: 2011/06/01]
27. Vercammen KA, Koma JW, Bleich SN. Trends in Energy Drink Consumption Among U.S. Adolescents and Adults, 2003-2016. Am J Prev Med 2019;56(6):827-33. doi: 10.1016/j.amepre.2018.12.007 [published Online First: 2019/04/22]
28. Cappelletti S, Piacentino D, Sani G, et al. Caffeine: cognitive and physical performance enhancer or psychoactive drug? Curr Neuropharmacol 2015;13(1):71-88. doi: 10.2174/1570159X13666141210215655 [published Online First: 2015/06/16]
29. Willson C. The clinical toxicology of caffeine: A review and case study. Toxicol Rep 2018;5:1140-52. doi: 10.1016/j.toxrep.2018.11.002 [published Online First: 2018/12/07]
30. Laskowski LK, Henesch JA, Nelson LS, et al. Start me up! Recurrent ventricular tachydysrhythmias following intentional concentrated caffeine ingestion. Clin Toxicol (Phila) 2015;53(8):830-3. [published Online First: 2015/08/19]
31. Dixit S, Stein PK, Dewland TA, et al. Consumption of Caffeinated Products and Cardiac Ectopy. J Am Heart Assoc 2016;5(1) doi: 10.1161/JAHA.115.002503 [published Online First: 2016/01/28]
32. Thorlton J, Colby DA, Devine P. Proposed actions for the US Food and Drug Administration to implement to minimize adverse effects associated with energy drink consumption. Am J Public Health 2014;104(7):1175-80. doi: 10.2105/AJPH.2014.301967 [published Online First: 2014/05/17]
33. Hoyte C. The toxicity of energy drinks: myth or reality? Clin Toxicol (Phila) 2013;51(8):729-30. doi: 10.3109/15563650.2013.825268 [published Online First: 2013/08/24]
34. Parmenter K, Wardle J. Development of a general nutrition knowledge questionnaire for adults. Eur J Clin Nutr 1999;53(4):298-308. doi: 10.1038/sj.ejcn.1600726 [published Online First: 1999/05/20]
35. Ehlers A, Marakis G, Lampen A, et al. Risk assessment of energy drinks with focus on cardiovascular parameters and energy drink consumption in Europe. Food Chem Toxicol 2019;130:109-21. doi: 10.1016/j.fct.2019.05.028 [published Online First: 2019/05/22]
36. Kozik TM, Shah S, Bhattacharyya M, et al. Cardiovascular responses to energy drinks in a healthy population: The C-energy study. Am J Emerg Med 2016;34(7):1205-9. doi: 10.1016/j.ajem.2016.02.068 [published Online First: 2016/05/11]
37. Greenwood DC, Alwan N, Boylan S, et al. Caffeine intake during pregnancy, late miscarriage and stillbirth. Eur J Epidemiol 2010;25(4):275-80. doi: 10.1007/s10654-010-9443-7 [published Online First: 2010/03/23]
38. Hoffman RS, Nelson LS, Goldfrank LR, et al. Goldfrank's Toxicologic Emergencies, Eleventh Edition: McGraw-Hill Education 2019.
39. Kaur S, Christian H, Cooper MN, et al. Consumption of energy drinks is associated with depression, anxiety, and stress in young adult males: Evidence from a longitudinal cohort study. Depress Anxiety 2020;37(11):1089-98. doi: 10.1002/da.23090 [published Online First: 2020/08/28]
40. Bodur M, Kaya S, Ilhan-Esgin M, et al. The caffeine dilemma: unraveling the intricate relationship between caffeine use disorder, caffeine withdrawal symptoms and mental well-being in adults. Public Health Nutr 2024;27(1):e57. doi: 10.1017/S1368980024000399 [published Online First: 2024/02/02]
41. Winston AP, Hardwick E, Jaberi N. Neuropsychiatric effects of caffeine. Advances in Psychiatric Treatment. 2005;11(6):432-439. doi:10.1192/apt.11.6.432.
42. Wang L, Shen X, Wu Y, et al. Coffee and caffeine consumption and depression: A meta-analysis of observational studies. Aust N Z J Psychiatry 2016;50(3):228-42. doi: 10.1177/0004867415603131 [published Online First: 2015/09/05]
43. Clark I, Landolt HP. Coffee, caffeine, and sleep: A systematic review of epidemiological studies and randomized controlled trials. Sleep Med Rev 2017;31:70-78. doi: 10.1016/j.smrv.2016.01.006 [published Online First: 2016/02/24]
44. Weibel J, Lin YS, Landolt HP, et al. Regular Caffeine Intake Delays REM Sleep Promotion and Attenuates Sleep Quality in Healthy Men. J Biol Rhythms 2021;36(4):384-94. doi: 10.1177/07487304211013995 [published Online First: 2021/05/25]
45. Park S, Lee Y, Lee JH. Association between energy drink intake, sleep, stress, and suicidality in Korean adolescents: energy drink use in isolation or in combination with junk food consumption. Nutr J 2016;15(1):87. doi: 10.1186/s12937-016-0204-7 [published Online First: 2016/10/16]
46. Liu C, Wang L, Zhang C, et al. Caffeine intake and anxiety: a meta-analysis. Front Psychol 2024;15:1270246. doi: 10.3389/fpsyg.2024.1270246 [published Online First: 2024/02/16]
47. Klevebrant L, Frick A. Effects of caffeine on anxiety and panic attacks in patients with panic disorder: A systematic review and meta-analysis. Gen Hosp Psychiatry 2022;74:22-31. doi: 10.1016/j.genhosppsych.2021.11.005 [published Online First: 2021/12/07]
48. Pollak CP, Bright D. Caffeine consumption and weekly sleep patterns in US seventh-, eighth-, and ninth-graders. Pediatrics 2003;111(1):42-6. doi: 10.1542/peds.111.1.42 [published Online First: 2003/01/02]
49. Orbeta RL, Overpeck MD, Ramcharran D, et al. High caffeine intake in adolescents: associations with difficulty sleeping and feeling tired in the morning. J Adolesc Health 2006;38(4):451-3. doi: 10.1016/j.jadohealth.2005.05.014 [published Online First: 2006/03/22]
50. Kim E, Robinson NM, Newman BM. A Brewed Awakening Neuropsychiatric Effects of Caffeine in Older Adults. Clin Geriatr Med 2022;38(1):133-44. doi: 10.1016/j.cger.2021.07.009
51. Frigerio S, Strawbridge R, Young AH. The impact of caffeine consumption on clinical symptoms in patients with bipolar disorder: A systematic review. Bipolar Disord 2021;23(3):241-51. doi: 10.1111/bdi.12990
52. Grosso G, Micek A, Castellano S, et al. Coffee, tea, caffeine and risk of depression: A systematic review and dose-response meta-analysis of observational studies. Mol Nutr Food Res 2016;60(1):223-34. doi: 10.1002/mnfr.201500620 [published Online First: 2015/11/01]
53. Petrelli F, Grappasonni I, Evangelista D, et al. Mental and physical effects of energy drinks consumption in an Italian young people group: a pilot study. J Prev Med Hyg 2018;59(1):E80-E87. doi: 10.15167/2421-4248/jpmh2018.59.1.900 [published Online First: 2018/06/26]
54. Lara DR. Caffeine, mental health, and psychiatric disorders. J Alzheimers Dis 2010;20 Suppl 1:S239-48. doi: 10.3233/JAD-2010-1378 [published Online First: 2010/02/19]
55. Agoston C, Urban R, Horvath Z, et al. Self-Medication of ADHD Symptoms: Does Caffeine Have a Role? Front Psychiatry 2022;13:813545. doi: 10.3389/fpsyt.2022.813545 [published Online First: 2022/02/22]
56. Schwartz DL, Gilstad-Hayden K, Carroll-Scott A, et al. Energy drinks and youth self-reported hyperactivity/inattention symptoms. Acad Pediatr

2015;15(3):297-304. doi: 10.1016/j.acap.2014.11.006 [published Online First: 2015/02/14]
57. Cusick CN, Langberg JM, Breaux R, et al. Caffeine Use and Associations With Sleep in Adolescents With and Without ADHD. J Pediatr Psychol 2020;45(6):643-53. doi: 10.1093/jpepsy/jsaa033 [published Online First: 2020/05/10]
58. Ioannidis K, Chamberlain SR, Muller U. Ostracising caffeine from the pharmacological arsenal for attention-deficit hyperactivity disorder--was this a correct decision? A literature review. J Psychopharmacol 2014;28(9):830-6. doi: 10.1177/0269881114541014 [published Online First: 2014/07/06]
59. O'Brien MC, McCoy TP, Rhodes SD, et al. Caffeinated cocktails: energy drink consumption, high-risk drinking, and alcohol-related consequences among college students. Acad Emerg Med 2008;15(5):453-60. doi: 10.1111/j.1553-2712.2008.00085.x [published Online First: 2008/04/29]
60. Al-Shaar L, Vercammen K, Lu C, et al. Health Effects and Public Health Concerns of Energy Drink Consumption in the United States: A Mini-Review. Front Public Health 2017;5:225. doi: 10.3389/fpubh.2017.00225 [published Online First: 2017/09/16]
61. Ferreira SE, de Mello MT, Pompeia S, et al. Effects of energy drink ingestion on alcohol intoxication. Alcohol Clin Exp Res 2006;30(4):598-605. doi: 10.1111/j.1530-0277.2006.00070.x [published Online First: 2006/04/01]
62. Marczinski CA, Fillmore MT, Maloney SF, et al. Faster self-paced rate of drinking for alcohol mixed with energy drinks versus alcohol alone. Psychol Addict Behav 2017;31(2):154-61. doi: 10.1037/adb0000229 [published Online First: 2016/11/08]
63. Marczinski CA. Can energy drinks increase the desire for more alcohol? Adv Nutr 2015;6(1):96-101. doi: 10.3945/an.114.007393 [published Online First: 2015/01/17]
64. Arria AM, Caldeira KM, Bugbee BA, et al. Energy Drink Use Patterns Among Young Adults: Associations with Drunk Driving. Alcohol Clin Exp Res 2016;40(11):2456-66. doi: 10.1111/acer.13229 [published Online First: 2016/10/21]
65. George J, Murphy T, Roberts R, et al. Influence of alcohol and caffeine consumption on caffeine elimination. Clin Exp Pharmacol Physiol 1986;13(10):731-6. doi: 10.1111/j.1440-1681.1986.tb02414.x [published Online First: 1986/10/01]
66. Terry-McElrath YM, O'Malley PM, Johnston LD. Energy drinks, soft drinks, and substance use among United States secondary school students. J Addict Med 2014;8(1):6-13. doi: 10.1097/01.ADM.0000435322.07020.53 [published Online First: 2014/02/01]
67. Holubcikova J, Kolarcik P, Madarasova Geckova A, et al. Regular energy drink consumption is associated with the risk of health and behavioural problems in adolescents. Eur J Pediatr 2017;176(5):599-605. doi: 10.1007/s00431-017-2881-4 [published Online First: 2017/02/24]
68. Azagba S, Langille D, Asbridge M. An emerging adolescent health risk: caffeinated energy drink consumption patterns among high school students. Prev Med 2014;62:54-9. doi: 10.1016/j.ypmed.2014.01.019 [published Online First: 2014/02/08]
69. Malik VS, Schulze MB, Hu FB. Intake of sugar-sweetened beverages and weight gain: a systematic review. Am J Clin Nutr 2006;84(2):274-88. doi: 10.1093/ajcn/84.1.274 [published Online First: 2006/08/10]
70. Malik VS, Popkin BM, Bray GA, et al. Sugar-sweetened beverages and risk of metabolic syndrome and type 2 diabetes: a meta-analysis. Diabetes Care 2010;33(11):2477-83. doi: 10.2337/dc10-1079 [published Online First: 2010/08/10]
71. Hu FB, Malik VS. Sugar-sweetened beverages and risk of obesity and type 2 diabetes: epidemiologic evidence. Physiol Behav 2010;100(1):47-54. doi: 10.1016/j.physbeh.2010.01.036 [published Online First: 2010/02/09]
72. Higgins JP, Tuttle TD, Higgins CL. Energy beverages: content and safety. Mayo Clin Proc 2010;85(11):1033-41. doi: 10.4065/mcp.2010.0381 [published Online First: 2010/11/03]
73. Grasser EK, Yepuri G, Dulloo AG, et al. Cardio- and cerebrovascular responses to the energy drink Red Bull in young adults: a randomized cross-over study. Eur J Nutr 2014;53(7):1561-71. doi: 10.1007/s00394-014-0661-8 [published Online First: 2014/01/30]
74. Grasser EK, Miles-Chan JL, Charriere N, et al. Energy Drinks and Their Impact on the Cardiovascular System: Potential Mechanisms. Adv Nutr 2016;7(5):950-60. doi: 10.3945/an.116.012526 [published Online First: 2016/09/17]
75. Garcia A, Romero C, Arroyave C, et al. Acute effects of energy drinks in medical students. Eur J Nutr 2017;56(6):2081-91. doi: 10.1007/s00394-016-1246-5 [published Online First: 2016/06/18]
76. Clauson KA, Shields KM, McQueen CE, et al. Safety issues associated with commercially available energy drinks. J Am Pharm Assoc (2003) 2008;48(3):e55-63; quiz e64-7. doi: 10.1331/JAPhA.2008.07055 [published Online First: 2008/07/04]
77. Aurora RN, Crainiceanu C, Caffo B, et al. Sleep-Disordered Breathing and Caffeine Consumption Results of a Community-Based Study. Chest 2012;142(3):631-38. doi: 10.1378/chest.11-2894
78. Aldosari MS, Olaish AH, Nashwan SZ, et al. The effects of caffeine on drowsiness in patients with narcolepsy: a double-blind randomized controlled pilot study. Sleep Breath 2020;24(4):1675-84. doi: 10.1007/s11325-020-02065-6 [published Online First: 2020/03/28]
79. Seifert SM, Seifert SA, Schaechter JL, et al. An analysis of energy-drink toxicity in the National Poison Data System. Clin Toxicol (Phila) 2013;51(7):566-74. doi: 10.3109/15563650.2013.820310 [published Online First: 2013/07/25]
80. Temple JL. Caffeine use in children: what we know, what we have left to learn, and why we should worry. Neurosci Biobehav Rev 2009;33(6):793-806. doi: 10.1016/j.neubiorev.2009.01.001 [published Online First: 2009/05/12]

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Glucagon Like Peptide -1 Receptor Agonists for Weight Loss: A Primary Care Perspective

by Kara Mohr, MD & Clayton Butcher, MD

The recent advances in obesity medicine have led to many changes in the approach to patients with obesity and there is hope that this can be a manageable disease thus mitigating the consequences of it.



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Abstract

In this article we review the glucagon like peptide -1 receptor agonist (GLP-1) medications and discuss how to approach using them for weight loss and management in non-diabetic patients.

Introduction

"Hey Doctor, I know this person who has been using a shot for weight loss, do you think that's something I could try?"

This has become a daily conversation in primary care and for good reason. According to the World Health Organization (WHO), as of 2022 one out of eight people in the world were living with obesity; a rate that has more than doubled since 1990.[1] To say this another way, 43% of adults were overweight and 16% were obese. Obesity is now the most prevalent chronic disease worldwide.[2] Obesity is defined using a combination of a body mass index (BMI) of 30kg/m^2 or greater and overweight is defined as BMI 25kg/m^2 to 29.9kg/m^2, or increasing waist circumference in men: waist circumference > 40 inches (102 cm), in women: waist circumference > 35 inches (89 cm). According to the 2021 Behavioral Risk Factor Surveillance Survey, the rates in Missouri adults are even higher with prevalence of 37.2% being obese and 32% being overweight.[3]

Obesity results from an imbalance of energy intake and energy expenditure, but is also multifactorial due to environment, psychosocial factors, and genetics. Not only that, adipose tissue accumulates when a person is overweight or obese and functions as an organ. Adipose tissue uses energy, has vascular supply, and grows. It also secretes hormones, adipokines, and inflammatory cytokines.

Obesity is chronic, progressive, and relapsing with increased morbidity and mortality and reduced quality of life. Adults in their 20s with obesity are estimated to have a reduced lifespan from 5.6 to 10.3 years.[4] The Global Burden of Disease study reported over 4.7 million deaths yearly due to obesity.[5] The leading causes of death associated with obesity are cardiovascular disease, chronic kidney disease, type 2 diabetes, and cancer of various types.[4] In addition, obesity is associated with

hypertension, hyperlipidemia, obstructive sleep apnea, metabolic dysfunction associated with steatotic liver disease, and osteoarthritis. Patients with obesity are at higher risk of mental health disorders, physical and sexual dysfunction.[4]

Many of the effects of obesity can be halted, reversed, and prevented by losing weight. Traditionally, weight loss centered around discussions of reduced caloric intake and increased physical activity. This is difficult because weight loss activates central and peripheral compensatory mechanisms that counter weight loss and favor weight gain.[4] When lifestyle intervention is the sole treatment, weight is typically regained even with continued compliance.[6] Treatment requires a comprehensive approach that includes lifestyle interventions, pharmacotherapy and in some instances, bariatric surgery. If it were simple to overcome obesity, we would have already done it. Fortunately, through research we have a better understanding and way to approach treating obesity. Despite this there is still some hesitancy in using medication for weight loss which comes from a variety of reasons including, but not limited to, lack of recognition of obesity as a disease, lack of provider experience, biases, concerns about safety and efficacy, cost, and lack of reimbursement.

Medications

Up until recently, the medications used to treat obesity were not very effective and had many limiting side effects and contraindications. These included phentermine, orlistat, phentermine/topiramate (Qsymia) and bupropion/naltrexone (Contrave). To date, there are two GLP-1s approved for weight loss; liraglutide (Saxenda) and semaglutide (Wegovy), and one GLP-1 and gastric inhibitory polypeptide also know as glucose-dependent insulinotropic polypeptide receptor agonist (GIP), tirzepatide (Zepbound).

These medications work by mimicking the natural GLP-1 which is an incretin peptide released from cells in the bowel.[5] It enhances insulin secretion in the hyperglycemic state, inhibits glucagon secretion, delays gastric emptying, regulates food preference, and reduces food intake by increasing satiety thru central appetite suppression. Some studies suggest the delayed gastric emptying is only in the first hour and overall gastric emptying did not seem to be affected.[7,8] GLP-1 is also expressed in the brainstem, endocrine pancreas, and immune system. Part of the GLP-1 action is to activate metabolism of brown fat and adipose redistribution with decreased visceral fat and relative increase in lower-body subcutaneous fat deposition.[8] GIP is also an incretin hormone involved in energy and nutrient metabolism through cell surface receptor signaling in the brain and adipose tissue.[2]

Liraglutide was the first GLP-1 approved for weight loss and was studied in the Satiety and Clinical Adiposity-Liraglutide Evidence (SCALE) trials.[9] The initial SCALE study evaluated the efficacy of liraglutide 3mg once daily in individuals with BMI greater than 27kg/m^2 with one or more comorbid conditions or BMI greater than 30kg/m^2. After 56 weeks, mean weight loss was 8.4kg in the liraglutide group and 2.8kg in the placebo group (p value <0.001).[10] In addition, 33.1% of trial participants lost greater than 10% of their body weight in the liraglutide group and 10.6% in the placebo group (p value <0.001).[10] The SCALE obesity and prediabetes trial evaluated the effect of liraglutide 3mg daily versus placebo plus lifestyle intervention in individuals with BMI greater than 30kg/m^2 and prediabetes and showed fewer people were diagnosed with diabetes in the liraglutide arm (2% vs 6% liraglutide vs placebo, respectively).[11] The SCALE Intensive Behavioral Therapy (IBT) study compared participants receiving IBT to liraglutide 3mg versus placebo. Over 56% of participants achieved mean weight loss of 7.5% with liraglutide versus 4% with placebo. In addition, 30.5% vs 19.8% (p value = 0.0469) reported greater than 10% weight loss with liraglutide versus placebo, respectively.[12] More than 15% weight loss was seen in 18.1% in the liraglutide group and 8.9% in the placebo group (p value=0.0311). [12]

Table 1. Medication Dosage and Frequency[15,16,17]

Medication	Liraglutide (Saxenda)	Semaglutide (Wegovy)	Tirzepatide (Zepbound)
Frequency	Daily injection with dose increased weekly	Weekly injection with dose increased every 4 weeks	Weekly injection with dose increased every 4 weeks
Starting dose	0.6mg	0.25mg	2.5mg
Dose increases	1.2mg	0.5mg	5mg*
	1.8mg	1mg	7.5mg
	2.4mg	1.7mg*	10mg*
	3.0mg*	2.4mg*	12.5mg
			15mg *
***Denotes maintenance dose**			

The Semaglutide Treatment Effect in People with Obesity (STEP) trials evaluated the safety and efficacy of semaglutide for weight loss. The STEP 1 trial compared semaglutide to placebo over 68 weeks in individuals with BMI greater than or equal to 30 kg/m^2 or greater than or equal to 27 kg/m^2 with one or more weight-related comorbidity and showed that semaglutide was associated with a 14.9% weight loss whereas placebo was 2.4% (p value <0.001).[7] The STEP 3 trial, which looked at the effect of semaglutide versus placebo as an adjunct to IBT, showed that continued semaglutide at 2.4mg was associated with slightly more weight loss, up to 17.4%, whereas when switched to placebo there was weight gain and overall weight loss was only 5.9% with both groups continuing lifestyle interventions.[7]

Tirzepatide was studied in the SURMOUNT-1 trial and was shown to have average weight loss of 15% with the 5mg dose, 19.5% with 10mg and 20.9% with the 15mg dose, whereas the placebo group had 3.1% weight loss.[2] Similar to the STEP 1 trial, SURMOUNT-1 included individuals with BMI greater than or equal to 30 kg/m^2 or greater than or equal 27 kg/m^2 with one or more weight-related comorbidity, except diabetes, and patients were treated over 72 weeks. Participants also had improvement in waist circumference, systolic and diastolic blood pressure, fasting insulin level, lipid levels, and A1c with most of the participants who had prediabetes achieving normoglycemia.[2] This demonstrates a significantly decreased 10-year predicted atherosclerotic cardiovascular disease risk.[13] Recently, semaglutide was approved for reducing risk of cardiovascular events in patients with cardiovascular disease who are obese or overweight. This approval was based on the SELECT trial which showed a 20% reduction in cardiovascular events in patients with BMI 27kg/m^2 or higher and preexisting cardiovascular disease without diabetes.[14]

Approach to Therapy

Medications are indicated when adult patients have failed non-pharmacologic methods such as diet modification, increased activity, and have a BMI of 30kg/m^2 or higher or BMI 27kg/m^2 or higher with an obesity related comorbidity such as hypertension, hyperlipidemia, heart disease, or obstructive sleep apnea. Semaglutide is indicated for weight loss in pediatric patients over the age of 12 with obesity.

The use of medications for weight loss needs to be an adjunct to diet and lifestyle changes to ensure the weight loss is sustainable. Ideally, this would be with a multidisciplinary team. Working with a dietician may help patients alter their food choices, but discussion of decreasing caloric intake is also helpful. Most international guidelines recommend at least a 500kcal daily energy deficit for weight loss.[4] According to the American Heart Association and the Academy of Nutrition and Dietetics, as long as the diet is balanced and healthy the macronutrient composition is not significant.[4] The recommended amount of exercise is 150 minutes per week of moderate intensity.[4] This includes both endurance exercise and strength training. For long-term weight loss maintenance

Table 2. Drug Interactions[15,16,17]

Medication	Effect	Next Steps
Medications with hypoglycemia as a side effect (ex. Antidiabetic agents, beta-blockers, etc)	Can increase risk of hypoglycemia	Educate patients on signs and symptoms of hypoglycemia and what to do in a hypoglycemic emergency
Furosemide	May increase serum concentration of furosemide	• Educated patients on side effects • Closer lab monitoring of electrolytes and renal function • Dose adjustment of furosemide as indicated
Levothyroxine	May increase serum concentration of levothyroxine	• Educated patients on signs and symptoms to monitor for • Closer lab monitoring of thyroid function • Dose adjustment of levothyroxine as needed
Oral hormonal contraceptives	May decrease serum concentration of contraceptive	Switch to an alternative contraceptive method or add a barrier method for four weeks after initiated and four weeks after dose escalation
Warfarin	Tirzepatide may increase serum concentration of warfarin	• Educate patients on risk and effect of potentially elevated INR • Closer lab monitoring of INR

there would need to be an increase in weekly exercise to three hundred minutes, which is typically not sustainable.[4] Additionally, individual or group sessions in a weight management program should be considered. Having patients track intake and physical activity has been shown to be helpful.

These medications are subcutaneous injections that patients do on their own. Liraglutide is daily, while semaglutide and tirzepatide are weekly. Liraglutide is a multiple use pen that requires a new needle with each injection and patients dial the pen to their dose, semaglutide and tirzepatide are single use pens.[15,16,17]

Once patients decide to start medication, they should be counseled on side effects and how to take the medication. They can be injected into the abdomen (most common), fatty part of the thigh, or upper arm. The cost can be prohibitive, most insurances require prior authorization and making patients aware of this up front helps reduce frustration and phone calls/messages. At this time, Medicaid and Medicare will not cover them for weight loss. Each of the three medications has coupons on the manufacturer website patients can apply for, however, if they have government insurance, they are exempt from qualifying. It should be noted that the cost of future healthcare needed from consequences of obesity is likely to be more than that of the medication. There have also been ongoing shortages of some of the doses of the medications. Once started, the dose should be increased every four weeks (or weekly if using liraglutide) until maintenance dose is achieved (Table 1). If there are significant side effects a slower titration may be helpful but is usually limited by insurance.

Side-effects and Interactions

Most side effects are gastrointestinal and include nausea, vomiting, diarrhea, and constipation. These effects tend to be mild to moderate and are transient, mostly following dose increases.[5,7] Patients should be counseled on adequate water intake. Nausea can sometimes be alleviated by eating smaller amounts but more frequently, diarrhea and constipation can be mitigated with increased fiber intake.[6] Other helpful changes include eating slowly, stopping eating when satiated, and avoiding high fat foods.[7] Antiemetics may be considered if the smaller portions and diet changes are made

Table 3. Missed Doses[15,16,17]

Medication	Administer dose as soon as possible)	Skip dose and give at next scheduled time	Other
Liraglutide (Saxenda)		Resume once-daily regimen with next scheduled dose if 1 or 2 days are missed	If ≥ 3 days missed, reinitiate at 0.6mg dose
Semaglutide (Wegovy)	If ≤ 5 days since last dose	If > 5 days since last dose	
Tirzepatide (Zepbound)	If ≤4 days since last dose	If > 4 days since last dose	

but there are still significant side effects. Studies report that the discontinuation rate due to adverse effects were lower with semaglutide than liraglutide (3.2% vs 12.6% respectively).[6] Despite these side effects, trials showed that nausea and vomiting did not really contribute to patients' weight loss, it was the lower energy intake that has been thought to be responsible for the weight loss. Given that the gastrointestinal side effects are transient, and patients continue to lose weight it is likely not the side effects causing the weight loss.[8]

They are contraindicated in pregnancy, in patients with a personal or family history of medullary thyroid cancer or multiple endocrine neoplasia syndrome type 2.[7] Some suggest that it not be used with patients with a history of pancreatitis as there have been rare cases reported. In the STEP trials there was no notable increase in the incidence of acute pancreatitis with the 2.4mg dose of semaglutide.[6] Although rare, hypoglycemia, acute kidney injury, angioedema, and anaphylaxis have been reported. There has been an association with increased heart rate, usually one to four beats per minute, and so this should be monitored.[7] Rapid weight loss is associated with increased risk of gallbladder disease and so patients need to be made aware of signs and symptoms to monitor for. Patients with renal and/or hepatic dysfunction may need closer monitoring as this may affect the pharmacokinetics and bioavailability.[5] In January 2024 there was an alert from the Food and Drug Administration about concerns for suicidal thoughts and actions, this investigation is ongoing. Preliminary evaluation has not found evidence that use of these medications causes suicidal thoughts or actions.

There are some notable drug interactions. With the potential for delayed gastric emptying absorption of other medications should be considered.[6] Most of the drug interactions are increased risk of hypoglycemia therefore education about symptoms is important. Other drug interactions are noted in Table 2.

Monitoring

Close follow-up is essential to success as well. Once started, follow-up within a few weeks allows discussion with patient on side effects and ongoing diet/lifestyle changes. It also allows continued documentation of weight to demonstrate success with the weight loss efforts. Notably, vital signs should be reviewed as there may need to be adjustments of other medications as the benefits of weight loss come through, especially blood pressure medications. It is important for patients to be aware of symptoms of low blood pressure.

Once a patient is on maintenance dose, follow-ups can be spread out, however, it may be beneficial to see patients more frequently if they continue to have weight loss or are not having the expected maintenance of weight. Since obesity is a chronic and relapsing disease, patients should be made aware that use of these medications is expected to be ongoing. Patients should know there is expected weight loss in the up titration but usually a plateau and then maximum weight loss after taking the maintenance dose for a year, then continued use of the medicine is meant for weight maintenance.[7,8] Providers and patients should be aware that metabolic adaption is likely the reason for the plateau and not a poor response or resistance to the medication.[7,8] That being said,

if there is not at least 4-5% weight loss after 12 weeks on maintenance dose, the medication should be discontinued. If a dose is missed it can be made up as in Table 3. Of note as well, if a patient is undergoing a non-emergent surgery, newer anesthesia consensus-based guidance recommends holding GLP-1s up to a week in advance given possible gastroparesis leading to aspiration risk.[18] If a patient is undergoing a surgery, it may be best to have anesthesia give guidance on their preference of preoperative GLP-1 management.

Conclusion

The recent advances in obesity medicine have led to many changes in the approach to patients with obesity and there is hope that this can be a manageable disease thus mitigating the consequences of it. With just 5% weight loss, there is noticeable improvement in health and reduced risk of complications. Weight loss would also be expected to reduce risk of cardiovascular disease, chronic kidney disease, metabolic dysfunction associated with steatotic liver disease, type 2 diabetes, and other diseases.[3] With these medications most patients can achieve this 5% goal and as high as 20%. Some studies also suggest that GLP-1s may have a role to play in many other disease processes including Alzheimer's, Parkinson's, strokes, chronic pain, polycystic ovarian syndrome, and cancer.[19]

References

1. World Health Organization. Obesity and overweight. www.who.int. Published March 1, 2024. https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight. Accessed April 14, 2024.
2. Jastreboff AM, Aronne LJ, Ahmad NN, et al. Tirzepatide Once Weekly for the Treatment of Obesity. N Engl J Med. 2022;387(3):205-216. doi:10.1056/NEJMoa2206038
3. Nickelson PF. Missouri's Public Health at a Glance. Mo Med. 2023 Jan-Feb;120(1):4-7. PMID: 36860611; PMCID: PMC9970341. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9970341/pdf/ms120_p0004.pdf Accessed April 30, 2024
4. Blüher M, Aras M, Aronne LJ, et al. New insights into the treatment of obesity. Diabetes Obes Metab. 2023;25(8):2058-2072. doi:10.1111/dom.15077
5. Moore PW, Malone K, VanValkenburg D, et al. GLP-1 Agonists for Weight Loss: Pharmacology and Clinical Implications. Adv Ther. 2023;40(3):723-742. doi:10.1007/s12325-022-02394-w
6. Bergmann NC, Davies MJ, Lingvay I, Knop FK. Semaglutide for the treatment of overweight and obesity: A review. Diabetes Obes Metab. 2023;25(1):18-35. doi:10.1111/dom.14863
7. Chao AM, Tronieri JS, Amaro A, Wadden TA. Semaglutide for the treatment of obesity. Trends Cardiovasc Med. 2023;33(3):159-166. doi:10.1016/j.tcm.2021.12.008
8. Ard J, Fitch A, Fruh S, Herman L. Weight Loss and Maintenance Related to the Mechanism of Action of Glucagon-Like Peptide 1 Receptor Agonists. Adv Ther. 2021;38(6):2821-2839. doi:10.1007/s12325-021-01710-0
9. Drucker DJ. GLP-1 physiology informs the pharmacotherapy of obesity. Mol Metab. 2022;57:101351. doi:10.1016/j.molmet.2021.101351
10. Pi-Sunyer X, Astrup A, Fujioka K, Greenway F, Halpern A, Krempf M, Lau DC, le Roux CW, Violante Ortiz R, Jensen CB, Wilding JP; SCALE Obesity and Prediabetes NN8022-1839 Study Group. A Randomized, Controlled Trial of 3.0 mg of Liraglutide in Weight Management. N Engl J Med. 2015 Jul 2;373(1):11-22. doi: 10.1056/NEJMoa1411892. PMID: 26132939.
11. le Roux CW, Astrup A, Fujioka K, et al. 3 years of liraglutide versus placebo for type 2 diabetes risk reduction and weight management in individuals with prediabetes: a randomised, double-blind trial [published correction appears in Lancet. 2017 Apr 8;389(10077):1398]. Lancet. 2017;389(10077):1399-1409. doi:10.1016/S0140-6736(17)30069-7
12. Wadden TA, Tronieri JS, Sugimoto D, et al. Liraglutide 3.0 mg and Intensive Behavioral Therapy (IBT) for Obesity in Primary Care: The SCALE IBT Randomized Controlled Trial. Obesity (Silver Spring). 2020;28(3):529-536. doi:10.1002/oby.22726
13. Hankosky ER, Wang H, Neff LM, et al. Tirzepatide reduces the predicted risk of atherosclerotic cardiovascular disease and improves cardiometabolic risk factors in adults with obesity or overweight: SURMOUNT-1 post hoc analysis. Diabetes Obes Metab. 2024;26(1):319-328. doi:10.1111/dom.15318
14. Lincoff AM, Brown-Frandsen K, Colhoun HM, et al. Semaglutide and Cardiovascular Outcomes in Obesity without Diabetes. N Engl J Med. 2023;389(24):2221-2232. doi:10.1056/NEJMoa2307563
15. Saxenda (liraglutide) [package insert]. Novo Nordisk. U.S. Food and Drug Administration website. https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/206321s007lbl.pdf. Revised October 2018. Accessed April 30, 2024.
16. Wegovy (semaglutide) [package insert]. Novo Nordisk. U.S. Food and Drug Administration website. https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/215256s000lbl.pdf. Revised June 2021. Accessed April 30, 2024.
17. Zepbound (tirzepatide) [package insert]. Lily. U.S. Food and Drug Administration website. https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/217806s000lbl.pdf. Reviewed November 2023. Accessed April 30, 2024.
18. Joshi, G et al. American Society of Anesthesiologists Consensus-Based Guidance on Preoperative Management of Patients (Adults and Children) on Glucagon-Like Peptide-1 (GLP-1) Receptor Agonists. www.asahq.org. https://www.asahq.org/about-asa/newsroom/news-releases/2023/06/american-society-of-anesthesiologists-consensus-based-guidance-on-preoperative Accessed May 1, 2024
19. Zhao X, Wang M, Wen Z, et al. GLP-1 Receptor Agonists: Beyond Their Pancreatic Effects. Front Endocrinol (Lausanne). 2021;12:721135. Published 2021 Aug 23. doi:10.3389/fendo.2021.721135

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Pulmonary Embolism Education: Role of Generative Artificial Intelligence Models

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This study demonstrates that there is a need for generative artificial intelligence models to become more accessible by including simplified responses with comprehendible diction.



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Abstract

The growing use of generative artificial intelligence (AI) in the public sphere allows for a greater degree of disseminating information worldwide. For patients, there is a growing body of literature exploring how the generative artificial intelligence models can be used in improving the health literacy of patients, especially in cases of acute pulmonary embolism, where patients require deep, concise understanding of there disease and management. This study measured the readability of the generative responses created by publicly available AI models, and found that ChatGPT, Google Gemini, and Microsoft CoPilot do not currently meet the United States readability recommendations. Given the growing use of these models, future investigation on the longitudinal readability measures may help profile how these generative AI models adapt in their deep learning processes.

Introduction

Pulmonary embolism is a common cause of cardiovascular death, coming in third following strokes and heart attacks.[1,2] There have been developments in treating pulmonary embolism, with treatments typically consisting of anticoagulation and with thrombolysis being used on other occasions.[3,4] This wide array of treatment options has led physicians to establish guidelines for the management and diagnosis of both deep vein thrombosis (DVT) and pulmonary embolism.[3,5]

While there have been great developments made in the treatment and diagnosis of pulmonary embolism, there is still a greater need for improvements in the accuracy and comprehensibility of information available regarding the general information, risk factors, and treatments for pulmonary embolism. In the literature, it has been well established that the internet and social media are common sources of healthcare information for patients.[6,7] While the internet has become an educational source for patients, a substantial component of its medical information is often misleading and commonly leads patients to forming more questions rather than having answers.[8] Unfortunately, patients may also often face difficulties distinguishing biased information, and thus gain inaccurate information from product or service endorsements.[8] While online websites and google searches have been examined in regards to patient education in pulmonary embolism, general artificial intelligence models remain yet to be explored.[9,10]

Generative artificial intelligence models have grown to be popular for users, as it uses data to predict outcomes and curate responses

for users.[11–14] The accuracy and comprehensibility of responses from generative artificial intelligence models have been explored previously for various pathologies, such as arrhythmias.[12] For pulmonary embolism, generative AI models can play an important role in education for patients by informing them of symptoms, risks, and treatments.[13] This is vital, as pulmonary embolism can progress rapidly and cause sudden death if not treated quickly.[15] If generative artificial intelligence models can serve as an educational resource, patients can rely on the information they find and clinicians can feel confident regarding the source of the patient's medical knowledge. While generative artificial intelligence models can provide answers to medical questions, the accuracy and understandability of its responses for questions pertaining to pulmonary embolism remains yet to be explored. The aim of this study is to explore the readability of generative artificial intelligence models by assessing responses to patients' frequently asked questions concerning pulmonary embolism.

Methodology

This study utilized responses from publicly available generative artificial intelligence models to evaluate the quality and readability of the most commonly asked questions by patients. Similar to previous literature, this study acquired 20 of the most frequently asked questions regarding pulmonary embolism utilizing the Google RankBrain algorithm.[16–20] These questions were selected if they were both unique and pertaining to pulmonary embolism. After the questions were selected, they were categorized using Rothwell's classification by two individuals. Any disagreements between a classification were brought to a third, senior author who would make the final decision on the classification.

Once these questions were extracted, they were applied to three different generative artificial intelligence models- Google Gemini, ChatGPT, and Microsoft CoPilot.[21–23] These models were chosen due to their popularity in growing literature.[24,25] Responses for these questions were pasted onto a document, and then analyzed for readability. To assess readability, formulas like Gunning Fog, Flesch Kincaid, and Flesch Reading Ease were used to score the responses. These formulas were specifically utilized due to their prevalence in previous literature, making them well established for analyzing readability.[26–28] After the scores for each response were obtained, they were analyzed for statistical significance. A one-way analysis of variance (ANOVA) was utilized, with the p-value being less than 0.5.

Results

A total of 20 questions were extracted regarding pulmonary embolism from the Google RankBrain algorithm. These questions were subsequently classified according to Rothwell's classification—they were classified as fact-, value-, or policy-based. Of the 20 questions, 30% were fact-based, 30% were value-based, and 40% were policy-based (Figure 1). Following Rothwell's classification, each question was then applied to three different generative artificial intelligence models—Gunning Fog, Flesch Kincaid, and Flesch Reading Eases—thus generating a total of 60 responses. Each response was scored, and a total of 180 scores were generated.

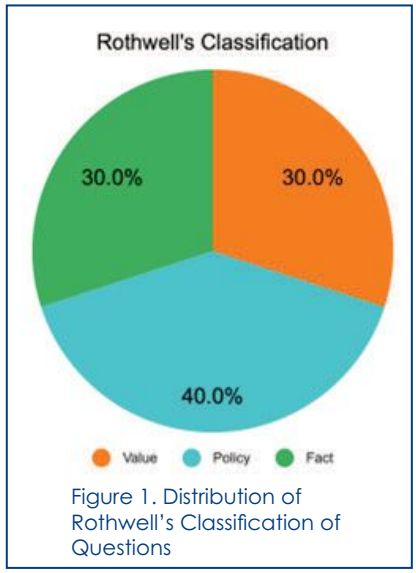


Figure 1. Distribution of Rothwell's Classification of Questions

The mean Gunning Fog score was lowest for responses from Google Gemini, with a score of 11.68 ± 1.30, correlating to the reading level of a high school junior. The mean Gunning Fog score was highest for responses from ChatGPT, with a mean of 13.705 ± 1.43. This score is correlated to the reading levels of a college sophomore. Microsoft CoPilot had a mean Gunning Fog score of 12.555 ± 1.96, which is equivalent to that of a high school senior.

For Flesch Kincaid, the responses for Google Gemini had the lowest mean score. The score was 9.95 ± 1.50, which is correlated to an average reading level, equivalent to a high school freshman. In comparison, the Flesch Kincaid mean score was highest for ChatGPT, with a score of 12.055 ± 1.48. This reading level is comparable to that of a college student. The mean Flesch Kincaid score for Microsoft CoPilot was 10.355 ± 1.54, which is equivalent to a high school sophomore.

Regarding Flesch Reading Ease, the highest mean score was seen for Google Gemini, with a score of 47.895 ± 9.42. This score is comparable to the reading level of a college graduate, making it more advanced. Furthermore, the lowest mean score for Flesch Reading Ease was seen in ChatGPT, with a score of 33.175 ± 9.99. This score is

Table 1. Mean Readability Scores and Standard Deviation

	Gunning Fog	Flesch Kincaid	Flesch Reading Ease
ChatGPT	13.705 ± 1.43	12.055 ± 1.48	33.175 ± 9.99
CoPilot	12.555 ± 1.96	10.355 ± 1.54	44.535 ± 10.81
Google Gemini	11.68 ± 1.30	9.95 ± 1.50	47.895 ± 9.42

comparable to the reading level of a university graduate and has a higher readability level than Google Gemini. Once again, Microsoft CoPilot was in the middle, with a mean Flesch Reading Ease score of 44.535 ± 10.81.

Utilizing ANOVA, there was a significant statistical difference in the mean readability scores between the generative artificial intelligance models. Specifically, Gunning Fog (p=0.000778), Flesch Kincaid (p=0.00009), and Flesch Reading Ease (0.000056) all demonstrated statistically significant differences in readability for Google Gemini, ChatGPT, and Microsoft CoPilot.

Discussion

Currently, health literacy has been a topic of interest, especially since it can address disparities in healthcare. Pulmonary embolism has been disproportionately affecting specific socioeconomic and racial populations, and health literacy may be an effective intervention to address the barriers they face.[29,30] Previous studies have demonstrated efforts to address disparities within health literacy for pulmonary embolism, and these studies have shown that health literacy improves patient outcomes for pulmonary embolism.[31,32] To address the disparities in the effects of pulmonary embolism, it could be beneficial to utilize generative artificial intelligence models for patient education. Generative artificial intelligence models can be useful to clinicians by assisting physicians, nurses, and other healthcare workers with handling critical situations more effectively.[32] Patients can also benefit from general artificial intelligence models, with patients often making more educated decisions and having a greater understanding of treatments.[33] This study focuses on the understandability and accuracy of generative artificial intelligence models in the context of pulmonary embolism. Understanding the readability of various public general artificial intelligence models can give an overview of its accessibility regarding pulmonary embolism.

This study compares the readability of three publicly accessible generative artificial intelligence models. To improve health literacy, readability of the text must be addressed. Generally, it is recommended that all health materials and online health information should meet a sixth-grade reading level to be accessible for the public.[33, 34] By improving readability, there can be an increase in health literacy for all, thus potentially playing a role in addressing socioeconomic and racial disparities.

The scores obtained from this study indicate that the mean Flesch Kincaid score and Gunning Fog score are highest for ChatGPT, and the mean Flesch Reading Ease score is lowest for ChatGPT. The scores for these readability formulas (Table 1) indicate that the text is fairly difficult to read, comparable to the reading level of a college student. This means that ChatGPT does not meet the reading level to be accessible to the public and may formulate responses that are difficult for patients to comprehend. Comparatively, Google Gemini had the lowest Gunning Fog and Flesch Kincaid scores, and the highest Flesch Reading Ease score (Table 1). These scores are generally correlated with a reading level of a high school student, thus making the text more "readable" than ChatGPT for the public. However, although Google Gemini demonstrates greater readability than ChatGPT, it also does not meet the recommended reading level. Microsoft CoPilot had Flesch Reading Ease, Flesch Kincaid, and Gunning Fog scores in between that of Google Gemini and ChatGPT.

These findings suggest that patients may find Google Gemini more accessible and understandable when compared to Microsoft CoPilot or ChatGPT. It should be noted that the responses found in generative artificial intelligence models should only be considered as supplemental information or general education, rather than medical advice or replacement of evaluation by clinicians. Though generative artificial intelligence models have become publicly accessible and are able to formulate responses, they have yet to tailor their responses to be more accessible to the public. Likewise, generative artificial intelligence models serve as a tool for clinicians to educate their patients if the content and quality of the material is appropriate, but are not to be used as a primary tool to educate patients at this point in time. It

is imperative for clinicians to provide keen oversight as the use of these tools continues to proliferate.

While this study included commonly searched questions via the RankBrain algorithm, these questions may not be inclusive of all the questions that patients may ask. A potential way to add to this study would be to increase the sample size by looking into other search engines. Additionally, many patients may not have access to the internet or other digital resources. Future studies can include asking patients directly about their questions regarding pulmonary embolism and analyzing the differences from the questions generated by the RankBrain algorithm.

Conclusion

While the mean readability scores generated for ChatGPT, Google Gemini, and Microsoft CoPilot do not meet the readability recommendations, Google Gemini generated responses for pulmonary embolism have the highest readability. This study demonstrates that there is a need for generative artificial intelligence models to become more accessible by including simplified responses with comprehendible diction. Addressing readability of generative intelligence models can make these tools more accessible to the public. This in turn can increase health literacy and reduce socioeconomic and racial disparities in patient education for pulmonary embolism.

References

1. Doherty S. Pulmonary embolism An update. Aust Fam Physician. 2017;46(11):816-820.
2. Essien EO, Rali P, Mathai SC. Pulmonary Embolism. Med Clin North Am. 2019;103(3):549-564. doi:10.1016/j.mcna.2018.12.013
3. Di Nisio M, van Es N, Büller HR. Deep vein thrombosis and pulmonary embolism. Lancet Lond Engl. 2016;388(10063):3060-3073. doi:10.1016/S0140-6736(16)30514-1
4. Trott T, Bowman J. Diagnosis and Management of Pulmonary Embolism. Emerg Med Clin North Am. 2022;40(3):565-581. doi:10.1016/j.emc.2022.05.008
5. Konstantinides SV, Meyer G, Becattini C, et al. 2019 ESC Guidelines for the diagnosis and management of acute pulmonary embolism developed in collaboration with the European Respiratory Society (ERS). Eur Heart J. 2020;41(4):543-603. doi:10.1093/eurheartj/ehz405
6. Zhao Y, Zhang J. Consumer health information seeking in social media: a literature review. Health Inf Libr J. 2017;34(4):268-283. doi:10.1111/hir.12192
7. Lee K, Hoti K, Hughes JD, Emmerton L. Dr Google and the consumer: a qualitative study exploring the navigational needs and online health information-seeking behaviors of consumers with chronic health conditions. J Med Internet Res. 2014;16(12):e262. doi:10.2196/jmir.3706
8. Ullrich PF, Vaccaro AR. Patient education on the internet: opportunities and pitfalls. Spine. 2002;27(7):E185-188. doi:10.1097/00007632-200204010-00019
9. Hansberry DR, D'Angelo M, White MD, et al. Quantitative analysis of the level of readability of online emergency radiology-based patient education resources. Emerg Radiol. 2018;25(2):147-152. doi:10.1007/s10140-017-1566-7
10. Frontiers | Health literacy in patients with pulmonary embolism: development and validation of the HeLP (Health Literacy in Pulmonary Embolism)-Questionnaire. Accessed July 21, 2024. https://www.frontiersin.org/journals/public-health/articles/10.3389/fpubh.2023.1167499/full
11. Chakraborty C, Bhattacharya M, Pal S, Lee SS. From machine learning to deep learning: Advances of the recent data-driven paradigm shift in medicine and healthcare. Curr Res Biotechnol. 2024;7:100164. doi:10.1016/j.crbiot.2023.100164
12. Feeny AK, Chung MK, Madabhushi A, et al. Artificial Intelligence and Machine Learning in Arrhythmias and Cardiac Electrophysiology. Circ Arrhythm Electrophysiol. 2020;13(8):e007952. doi:10.1161/CIRCEP.119.007952
13. Sallam M. ChatGPT Utility in Healthcare Education, Research, and Practice: Systematic Review on the Promising Perspectives and Valid Concerns. Healthc Basel Switz. 2023;11(6):887. doi:10.3390/healthcare11060887
14. Boscardin CK, Gin B, Golde PB, Hauer KE. ChatGPT and Generative Artificial Intelligence for Medical Education: Potential Impact and Opportunity. Acad Med J Assoc Am Med Coll. 2024;99(1):22-27. doi:10.1097/ACM.0000000000005439
15. Roy PM, Douillet D, Penaloza A. Contemporary management of acute pulmonary embolism. Trends Cardiovasc Med. 2022;32(5):259-268. doi:10.1016/j.tcm.2021.06.002
16. Singh SP, Ramprasad A, Luu A, Zaidi R, Siddiqui Z, Pham T. Health Literacy Analytics of Accessible Patient Resources in Cardiovascular Medicine: What are Patients Wanting to Know? Kans J Med. 2023;16:309-315. doi:10.17161/kjm.vol16.20554
17. Shen TS, Driscoll DA, Islam W, Bovonratwet P, Haas SB, Su EP. Modern Internet Search Analytics and Total Joint Arthroplasty: What Are Patients Asking and Reading Online? J Arthroplasty. 2021;36(4):1224-1231. doi:10.1016/j.arth.2020.10.024
18. Sajjadi NB, Shepard S, Ottwell R, et al. Examining the Public's Most Frequently Asked Questions Regarding COVID-19 Vaccines Using Search Engine Analytics in the United States: Observational Study. JMIR Infodemiology. 2021;1(1):e28740. doi:10.2196/28740
19. Fassas SN, Peterson AM, Farrokhian N, et al. Sinus Surgery and Balloon Sinuplasty: What Do Patients Want to Know? Otolaryngol Neck Surg. Published online February 8, 2022:01945998221076803. doi:10.1177/01945998221076803
20. Digital Patient Education on Xanthelasma Palpebrarum: A Content Analysis - PMC. Accessed December 12, 2023. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10605081/
21. ChatGPT. Accessed April 6, 2024. https://openai.com/chatgpt
22. Gemini - chat to supercharge your ideas. Accessed April 16, 2024. https://gemini.google.com/
23. Copilot. Accessed April 6, 2024. https://copilot.microsoft.com/
24. Giannakopoulos K, Kavadella A, Aaqel Salim A, Stamatopoulos V, Kaklamanos EG. Evaluation of the Performance of Generative AI Large Language Models ChatGPT, Google Bard, and Microsoft Bing Chat in Supporting Evidence-Based Dentistry: Comparative Mixed Methods Study. J Med Internet Res. 2023;25:e51580. doi:10.2196/51580
25. Kaftan AN, Hussain MK, Naser FH. Response accuracy of ChatGPT 3.5 Copilot and Gemini in interpreting biochemical laboratory data a pilot study. Sci Rep. 2024;14:8233. doi:10.1038/s41598-024-58964-1
26. Wong K, Levi JR. Partial Tonsillectomy. Ann Otol Rhinol Laryngol. 2017;126(3):192-198. doi:10.1177/0003489416681583
27. Soliman L, Soliman P, Gallo Marin B, Sobti N, Woo AS. Craniosynostosis: Are Online Resources Readable? Cleft Palate-Craniofacial J Off Publ Am Cleft Palate-Craniofacial Assoc. 2024;61(7):1228-1232. doi:10.1177/10556656231154843
28. Hillyer GC, Beauchemin M, Garcia P, et al. Readability of Cancer Clinical Trials Websites. Cancer Control J Moffitt Cancer Cent. 2020;27(1):1073274819901125. doi:10.1177/1073274819901125
29. Dronamraju VH, Lio KU, Badlani R, Cheng K, Rali P. PERT era, race-based healthcare disparities in a large urban safety net hospital. Pulm Circ. 2023;13(4):e12318. doi:10.1002/pul2.12318
30. Ojukwu CP, Nwagha TU, Agbo LC, Ezeigwe AU, Okorie P. Knowledge Levels and Predictors of Venous Thromboembolism among Pregnant Women in Nigeria: A Cross-Sectional Survey for the "Move for Flow" Programme. West Afr J Med. 2023;40(8):799-807.
31. Mefford MT, Zhou H, Fan D, et al. Health Literacy and Treatment Satisfaction Among Patients with Venous Thromboembolism. J Gen Intern Med. 2023;38(7):1585-1592. doi:10.1007/s11606-022-07852-3
32. Fischer S, Kalch A, Küchler C, et al. Health literacy in patients with pulmonary embolism: development and validation of the HeLP (Health Literacy in Pulmonary Embolism)-Questionnaire. Front Public Health. 2023;11:1167499. doi:10.3389/fpubh.2023.1167499
33. Jayakumar P, Moore MG, Furlough KA, et al. Comparison of an Artificial Intelligence-Enabled Patient Decision Aid vs Educational Material on Decision Quality, Shared Decision-Making, Patient Experience, and Functional Outcomes in Adults With Knee Osteoarthritis: A Randomized Clinical Trial. JAMA Netw Open. 2021;4(2):e2037107. doi:10.1001/jamanetworkopen.2020.37107

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Advertisers

Acrisure, LLS 242
Frost Law ..... CV3 May/June
Mercy 31,101, 203, 249, 363, 462
MO Physicians Health Program 26, 32, 95, 125, 241, 325, 413
Moneta ..... 126, 274, CV3 July/Aug, CV3 Sept/Oct
MSM Foundation ..... CV2 Jan/Feb, Mar/Apr, May/June, July/Aug, Sept/Oct, Nov/Dec
ProAssurance ..... CV3 Jan/Feb, Mar/Apr, May/June,July/Aug, Sept/Oct, Nov/Dec
VOC ..... CV3 Mar/Apr

Advocacy

Not All Heroes Wear Capes! Sometimes They Just Donate
by Jacob Scott, MA 255
Countdown Begins for Missouri's General Assembly
by Jacob Scott, MA & Rachel Bauer, MPA 436

American Medical Association

Report of the American Medical Association Annual Meeting
by Charles W. Van Way, III, MD/MO Delegation 250
Report of the American Medical Association Interim Meeting
by Charles W. Van Way, III, MD/MO Delegation 442

Annual Convention

MSMA President 244
MSMA Alliance President 245
State of the Association Address 246
Resolution and Policy Actions 249
Presidential Address 254
50-Year Physician Pin Recipients 255
Credentials & Appointments 256
Elections 258
Council Minutes Summary 259
Convention Sponsors 266
Reports of the Delegate Handbook 267
Attendance 275

As I See It

Learning to be Vulnerable
by Joanne Loethen, MD 11
The Harm from Private Equity's Takeover of Medical Practices and Hospitals
by Andrew Schlafly, JD 328

Author Listing

Hilal Abdessamad, MD 474
Rayyan Abid 385
Danielle R. Adams, PhD 467
Abdulbaki Agbas, PhD 87
Arpit Aggarwal, MD 195
Arpana Agrawal, PhD 333
Aseel Alkhader, MD 60
Riya Aradhyula 206
Jonathan Asghedom, BS 495
Komal Ashraf, MD 149
Rajeev Aurora, PhD 310
Navpreet Bains, DO 127
Deepa Baswaraj, MBBS 52
Rachel Bauer, MPA 436
Abid Bhat, MD 60, 379
Kimberley Beier, BS 68
Sydney Bell, BA 220
Ecenur Tuc Bengur, MD 277
Alisa M. Berger, MD 416
Andrew Bierhals, MD 433
Kevin J. Black, MD 37
Lynn Bock, MS 225
Suzanne G. Bollmeier, PharmD 403
Meelie Bordoloi, MD 195
Barbara Braddock, PhD 225
J. Patrick Brooks, MD 395
Kevin T. Baumgartner, MD 481
Clayton Butcher, MD 489
Leopoldo J. Cabassa, PhD 467
Tessa Carberry, JD 456
Steven B. Carr, MD 136
Wesley Chen, MD 149
Michael Chicoine, MD 128, 136
Amy L. Clark, DO 206
Ellen E. Fitzsimmons-Craft, PhD 345
Mary-Ann P. Czak, JD 198
Victoria Damba, DO 99
Dima Dandachi, MD 474
Daniel J. Davis, PhD 170
Louis P. Dehner, MD 262
Nathaniel Dell, PhD 467
Patricia I. Dickson, MD 276
Lauren Draper, MD 204, 220
Sarah Dubin MD 364
Samuel DuMontier, DO 373
Ila Durkin, MD 195
Paige Ekert, MS 297
Maithe Enriquez, PhD 424
Greg Flaker, MD 52
Arthur Gale, MD 201
Gary Gaddis, MD, PhD 105, 189
Julie K. Gammack, MD 445

Lancer G. Gates, DO 6, 99
Sabrina Genovese, BS 142
Torie Gettinger, PhD 467
Nikki Gill, MD 391
Paul E. Glaser, MD, PhD 481
Ashraf Gohar, MD 60, 379
Jessica A. Gold, MD 14
Catherine Gooch, MD 297
Sean Goretzke, MD 225
Gary S. Gottesman, MD 297
Sai Goutham 170
Scott Griggs, PhD, PharmD 403
Benjamin Grin, MD 81
George Grossberg, MD 271
Sumit K. Gupta, MD, MPH 164
Sharon Gustowski, DO 76
John C. Hagan, III, MD 4, 33, 180, 242, 326, 464
Marc B. Hahn, DO 66
Karen Harbert, MPH 317
Jennifer Heeley, MD 277
Jennifer Heithaus, MD 225
Fletcher Hoague, MS 220
Carlton Homan, BS 395
Albert L. Hsu, MD 184
George Hubbell, MD 317
Alison Huckenpahler, MD, PhD 481
Pamala R. Huges, Lt Col, MD 445
Amanda E. Hull, MD 184
Omar Hussein, MD 60
Jordyn Huston, MD 206
Nicholas C. Jacobson, PhD 345
Wassim Jamaleddine, MD 474
Rachel Jensen, PhD 304
Luke F. Jett, Lt, MD 445
Emma C. Johnson, PhD 333
Quinn Johnson, MD 156
Fareed Jummah, MD 127, 136
Diana Jung, MD 364
Timothy Kable, MD 373
Inamullah Khan, MD 142
Kris Kappel, JD 257
Parashar Koirala, MD 102
Edina Kosa, MSc 87
Steven C. Kosa, MD 33, 464
Craig Krausz, MD 445
Krithika Kumarason, MD 225
Bornali Kundu, MD, PhD 149
Mark J. Lambrechts, MD 164
Emily V. Leary, PhD 164
Su Han Lee, BSc 87
Joanne Loethen, MD 11
Will Lubaroff 246
Lisa M. Luetkemeyer, JD 257
Poornaashri Malarvannan, MD 206
Maggie Mannebach, JD 257
Thornton Mardis, MA 68
Govind Mattay, MD 433
David S. McKinsey, MD 424
Joel P. McKinsey, MD 424
Julie R. McKinsey, BS 424
Janette McVey, MD 156
Mark M. Miller, MA 21
Eric A. Millican, MD 184
Ulysses Fernandez-Miro, Capt, DO 445
Kara Mohr, MD 489
Trecia Moore, JD 198
Christian Rojas-Moreno, MD 474
Bryan Munoz, MS 68
Vithya Murugan, PhD 220
April Tyus-Myles, MD 27
Sowjanya Naha, MD 44
Brook V. Nelson, MD 113
Richard K. Newman, Capt, DO 445
D'Angeleau Newsome 76
Paula F. Nickelson, MEd 10
Ginger E. Nicol, MD 467
Thorklid Norregaard, MD 149
Ravi Nunna, MD 127, 142
Michelle Oliva, MSN 284
Ashlie Otto, RN 317
Michael Ortiz, MD 142
Melinda Owens, RN 220
Brandon M. Parham, Capt 445
Pooja Patak, MD 364
Vimita Patel, MD 271
Kami Pearson, MS 68
Duyen Pham, BSc 87
David L. Pohl, MD 248, 355, 441
Shulamit Portnoy, MD 225
Sara S. Procknow, MD, PhD 289
John Puetz, MD 231
Daniel Quay, MA 317
Adnan I. Qureshi, MD 127
Garrett Rampon, MD 368
Lacey E. Raper, MA 184
Kaushik Ravipati, MD 136
Margaret Reynolds, MD 304
William Reynolds, DDS, MD 452
David Roelofsz, MD 368
Stephanie A. Rolin, MD 14
Pradeep Sahota, MD 44
TThomas Sanford, MD 310
Paul Santiago, MD 142
Joshua M. Sappington, MD 350
Andrew Schlafly, JD 328, 419
Crystal Schollmeyer, RN 317
Jacob Scott, MA 255, 436
Susie Sharpe, MD 357

James Shelton, MD 156
Morgan C. Shields, PhD 14
Suraj Shankar, MD 481
Zhengye Si, MA. 164
Ajay Singh, MD 391
Som Singh, MD 495
Kathleen Sisco, MSN 284
Marwan Shinawi, MD 304
Farhan Siddiq, MD 127, 149
Turner Slicho, DO 76
Manjamalai Sivaraman, MD 44
Bradley S. Spence, MD 164
Christopher Streiler, MD 373
Kaitlyn Stumpe, BS 225
Deepti Sudhakar, BS 206
Hannah S. Szlyk, PhD 14
Lindsey Smith Taillie, PhD 96
Farzana Tariq, MD 127, 136, 142, 149
Sarah Von Thaer, MD 156
Ashley Todd, JD 456
Rebecca L. Tominack, MD 340
Michael Ortiz-Torres, MD 136
Katharyn Turner, DO 225
Alecia C. Vogel, MD, PhD 37
Charles W. Van Way, III, MD 116, 250, 442
David Wainer 414
Maxwell Wallace, MD 225
Terri Weaver, PhD 220
Julie A. Weber, RPh 340
Judith Weisenberg, MD 304
Jason Werner, MD 220
Laura White, NP 289
Barbara Y. Whitman, PhD 235
Kevin Y. Xu, MD 14, 481
Andrew Youkilis, MD 149
Reddy Yeddula, DVM 170
Asma Zaidi, PhD 68
Rohma Zaidi, BA 495
Lawrence Zhang, MD 38
Jason Zweig, MD 379

Editorials

Attention Pharma & Headache Researchers! NasalSpray Timolol May Be the Next Great Thing for Acute Migraine
by John C. Hagan, III, MD 4
Big, Bold Warning Labels Can Steer People Away from Junk Food
by Lindsey Smith Taillie, PhD 96
Too Much Exercise? Here's the Rundown
by John C. Hagan III, MD 180
Like a Fine Wine, *Missouri Medicine* Continues to Improve with Age
by John C. Hagan III, MD 242
Hear Today & Gone Tomorrow
by John C. Hagan III, MD 326
As Hospitals Grow, So Does Your Bill
by David Wainer 414

Medical-Legal

Physician Organizing: Trends and Takeaways
by Trecia Moore, JD & Mary-Ann P. Czak, JD..... 198
The "Rights" Prescription: Navigating Copyright Law in Practice of Medicine
by Kris Kappel, JD, Lisa M. Luetkemeyer, JD & Maggie Mannebach, JD 257
Beyond Malpractice: When Practice Becomes Criminal and Related Implications for Healthcare Providers
by Ashley Todd, JD & Tessa Carberry, JD..... 456

***Missouri Medicine* Departments**

1 Picture = 1,000 Words 9, 163, 197, 415
2024 Missouri Medicine Index 499
2024 Annual Convention Schedule 3
Book Review 425, 428
Correspondence..... 121, 268, 360, 431
Errata 184, 268, 350
In Memoriam 463
In the News 31, 270, 360, 462
MMPAC Annual Membership 439
New Members 32, 124, 203, 269, 361, 463
Statement of Ownership, Management & Circulation ... 363

Perspectives by Subheading

Feature Perspective

Medical Illustration State of the Art & Future Considerations - Part II
by Mark M. Miller, MA 21
Creating State-Funded Residency Programs: How They Did It in Rural Indiana
by Albert L. Hsu, MD, Lacey E. Raper, MA, Amanda E. Hull, MD & Eric A. Millican, MD..... 184
A Long-Standing Partnership: Walsworth Celebrates 100 Years with Missouri State Medical Association
by Will Lubaroff 246
America's Broken Health Care System: Can Doctors Lead the Fix?
by Alisa M. Berger, MD 416

Inspiring Lives & Careers

From Aspiration to Impact: Paving the Path in Healthcare and Inspiring Future Generations
by April Tyus-Myles, MD 27
My Story
by Charles Van Way, III, MD 116
My Life in the Golden Age of Medicine
by Arthur Gale, MD 201
A Path Chosen Long Ago and Where It Went
by Louis P. Dehner, MD 262
The Extraordinary Journey of a Physician-Artist
by Susie Sharpe, MD 357
From Space Stations to the US Marines...From Engineering to Private Practice Surgery...A Physician is Right at Home
by William Reynolds, DDS, MD 452

Military Medicine

Military Medicine and Medical Education in Missouri
by Ulysses Fernandez-Miro, Capt, DO, Pamala R. Huges, Lt Col, MD, Luke F. Jett, Lt, MD, Craig Krausz, MD, Richard K. Newman, Capt, DO, Brandon M. Parham, Capt, & Julie K. Gammack, MD 445

Perspective

The State of Missouri's Public Health
by Paula F. Nickelson, MEd 10
Mental Illness and Violence Among People Experiencing Homelessness:
An Evidence-Based Review
by Kevin Y. Xu, MD, Jessica A. Gold, MD, Hannah S. Szlyk, PhD, Stephanie A. Rolin, MD & Morgan C. Shields, PhD 14
Beta Blocker Nasal Spray for Actue Migraine
by Parashar Koirala, MD 102
The Generous Reimbursement of Non-Physician Clinical Services - Part I: A Deep Dive into the Resource-Based Relative Value Scale
by Gary Gaddis, MD 105
Mental Health and the Graduate Medical Education Trainee: Emergent Concerns
by Brook V. Nelson, MD 113
The Generous Reimbursement of Non-Physician Clinical Services - Part 2: An Indication for Non-Physician Education Reforms
by Gary Gaddis, MD, PhD 189
Effects of Pornography on Youth: A Review
by Meelie Bordoloi, MD, Ila Durkin, MD & Arpit Aggarwal, MD 195
Easy Availability of Marijuana and Other Cannabis Derived Products: What is the Missouri Poison Center Seeing?
by Rebecca L. Tominack, MD & Julie A. Weber, RPh 340
Thwarting the Harm Caused by Private Equity in Surgical Practices … and Even in the NFL: Part 2
by Andrew Schlafly, JD 419

Retrospective Analysis

Optimizing Missouri's Preparation for the Next Pandemic: Lessons Learned from COVID-19: Part 1
by David S. McKinsey, MD, Joel P. McKinsey, MD, Julie R. McKinsey, BS & Maithe Enriquez, PhD 424

Scientific Perspective

Pediatric Palliative Care: A Place for Hope
by Lauren Draper, MD 204
Current Screening Tests/Biomarkers for Alzheimer's Disease: Implications for Clinicians
by Vimita Patel, MD & George Grossberg, MD 271
Eating Disorders Care and the Promises and Pitfalls of Artificial Intelligence
by Ellen E. Fitzsimmons-Craft, PhD & Nicholas C. Jacobson, PhD 345
Hearing Loss: The Silent Pandemic That is Finally Being Heard
by Joshua M. Sappington, MD 350
Cannabis and Psychosis: Weeding Out Fact from Fiction
by Emma C. Johnson, PhD & Arpana Agrawal, PhD 333
Communication and Follow-Up of Noncritical Actionable Imaging Findings
by Govind Mattay, MD & Andrew Bierhals, MD 433

President's Forum

Cyber Attacks on Interoperable Electronic Health Records: A Clear and Present Danger
by Lancer G. Gates, DO 6
MSMA & MAOPS: Pitching Our Advocacy Tent
by Lancer Gates, DO & Victoria Damba, DO 99
Back to the Basics
by David L. Pohl, MD 248
Getting Involved: Let's Hear Your Voice!
by David L. Pohl, MD 355
Time for Action!
by David L. Pohl, MD 441

Science of Medicine | Feature Series
Listed by Issue Release Date & Theme

January/February 2024:
Innovations in Treatment: Pain,Depression, Opioid Use & Neurodegeneration
Presented by Kansas City University, Kansas City, Missouri

KCU Sharpens Focus on Population Health and Equity Through New Center of Excellence
by Marc B. Hahn, DO 66
The Neurochemistry of Depression: The Good, The Bad and The Ugly
by Kami Pearson, MS, Kimberley Beier, BS, Thornton Mardis, MA, Bryan Munoz, MS & Asma Zaidi, PhD 68
Integration of Osteopathic Manipulative Treatment for Patients with Chronic Pain
by Sharon Gustowski, DO, Turner Slicho, DO & D'Angeleau Newsome 76
Opioid Use Disorder in Missouri: An Evidence-Based, Public Health-Oriented Approach
by Benjamin Grin, MD 81
Human Platelet Derived Mitochondrial OPA-1 Isoforms and Interaction With TDP-43 in Neurodegenerative Diseases
by Su Han Lee, BSc, Duyen Pham, BSc, Edina Kosa, MSc & Abdulbaki Agbas, PhD 87

March/April 2024:
The New Age of Neurosurgery
Presented by University of Missouri - Columbia, Columbia, Missouri

Advances in the Endovascular Management of Cerebrovascular Disease
by Ravi Nunna, MD, Farzana Tariq, MD, Fareed Jummah, MD, Navpreet Bains, DO, Adnan I. Qureshi, MD & Farhan Siddiq, MD 127
Seven Decades of Neurosurgery at MU Columbia
by Michael Chicoine, MD 128
Advances in Cranial Surgery
by Farzana Tariq, MD, Fareed Jumah, MD, Kaushik Ravipati, MD, Michael Ortiz-Torres, MD, Steven B. Carr, MD & Michael R. Chicoine, MD 136
Cutting Edge Developments in Spine Surgery at the University of Missouri
by Ravi Nunna, MD, Farzana Tariq, MD, Michael Ortiz, MD, Inamullah Khan, MD, Sabrina Genovese, BS & Paul Santiago, MD 142
Role of Functional neurosurgery in Improving Patient Outcomes in Epilepsy, Movement Disorders, and Chronic Pain by Wesley Chen, MD, Farzana Tariq, MD, Komal Ashraf, MD, Thorklid Norregaard, MD, Andrew Youkilis, MD, Bornali Kundu, MD, PhD & Farhan Siddiq, MD 149

May/June 2024:
Happy Kids & Happy Families: Modern Pediatrics
Presented by Saint Louis University School of Medicineand SSM Health Cardinal Glennon Children's MedicalCenter, St. Louis, Missouri

Diabetes and Dyslipidemia Screening in Pediatric Practice
by Jordyn Huston, MD, Deepti Sudhakar, BS, Poornaashri Malarvannan, MD, Riya Aradhyula & Amy L. Clark, DO 206
Managing the Mother-Baby Dyad Affected by Substance Disorder: A Statewide Quality Collaborative Initiative
by Kimberly Spence, MD & Alison Williams, DNP 212
Institutional Experience with Investigation and Service for Acute and Post-Traumatic Stress in the Pediatric Intensive Care Unit
by Jason Werner, MD, Sydney Bell, BA, Lauren Draper, MD, Fletcher Hoague, MS, Melinda Owens, RN, Vithya Murugan, PhD & Terri Weaver, PhD 220
Improving Access to Autism Evaluation: A Coordinated Developmental-Behavioral Pediatrics and Pediatric Neurology Diagnostic Pathway
by Barbara Braddock, PhD, Katharyn Turner, DO, Krithika Kumarason, MD, Lynn Bock, MS, Kaitlyn Stumpe, BS, Maxwell Wallace, MD, Jennifer Heithaus, MD, Sean Goretzke, MD & Shulamit Portnoy, MD 225
Hemophilia Gene Therapy: Another Blessing or Another Curse?
by John Puetz, MD 231
Prader-Willi Syndrome: The More We Know, the Less We Know
by Barbara Y. Whitman, PhD 235

July/August 2024:
Washington University & the Future of Psychiatry
Navigating the Genomics Revolution
Presented by Washington University School of Medicine, St. Louis, Missouri

Genetics is Scary
by Patricia I. Dickson, MD 276
Genetics and Primary Care: Raising Awareness and Enhancing Cooperation
by Ecenur Tuc Bengur, MD & Jennifer Heeley, MD .. 277
Medical Genetics for the Undiagnosed and Rare Patient: "Chasing Zebras"
by Kathleen Sisco, MSN & Michelle Oliva, MSN 284
Hypermobile Ehlers Danlos for the Primary Care Provider
by Laura White, NP & Sara S. Procknow, MD, PhD 289

Metabolic Bone Disease: An Overview
by Catherine Gooch, MD, Paige Ekert, MS & Gary S. Gottesman, MD 297
The DESSH Clinic: A New Multidisciplinary Clinic to Address the Complex Needs of Individuals with a Rare Genetic Disorder
by Margaret Reynolds, MD, Judith Weisenberg, MD, Rachel Jensen, PhD & Marwan Shinawi, MD 304

September/October 2024:
Breathe Easy - Pulmonary Medicine Advances Presented by University of Missouri-Kansas City School ofMedicine/University Health, Kansas City, Missouri

Update on Asthma Management Guidelines
by Sarah Dubin MD, Pooja Patak, MD & Diana Jung, MD 364
Lung Cancer in Missouri
by David Roelofsz, MD & Garrett Rampon, MD 368
Sarcoidosis: A Review of the Guidelines and What's To Come
by Timothy Kable, MD, Samuel DuMontier, DO & Christopher Streiler, MD 373
Insomnia in Adults in the Primary Care Clinic Setting
by Jason Zweig, MD, Ashraf Gohar, MD & Abid Bhat, MD 379
Non-CPAP Therapies for Obstructive Sleep Apnea in Adults
by Rayyan Abid, Lawrence Zhang, MD & Abid Bhat, MD 385

Science of Medicine | First World Literature Report

Nasally Delivered 0.5% Timolol Beta Blocker Successfully Treats Acute Migraines in a Referral Headache Clinic: A Case Series
by Steven C. Kosa, MD & John C. Hagan III, MD 33
Timolol 0.5% Eye Drops for Essential Tremor: First Successful Case Report
by John C. Hagan III, MD & Steven C. Kosa, MD 464

Science of Medicine | Feature Review

Brain Imaging in Routine Psychiatric Practice
by Alecia C. Vogel, MD, PhD & Kevin J. Black, MD ... 37
The Microbiome: From the Beginning to the End
by Rajeev Aurora, PhD & Thomas Sanford, MD 310

Science of Medicine

Insomnia: A Current Review
by Sowjanya Naha, MD, Manjamalai Sivaraman, MD & Pradeep Sahota, MD 44
Syncope in Athletes: A Prelude to Sudden Cardiac Death?
by Deepa Baswaraj, MBBS & Greg Flaker, MD 52
Home Sleep Apnea Testing for Obstructive Sleep Apnea
by Omar Hussein, MD, Aseel Alkhader, MD, Ashraf Gohar, MD & Abid Bhat, MD 60
Obesity and Anesthesia: Challenges in the Perioperative Period
by Sarah Von Thaer, MD, Janette McVey, MD, James Shelton, MD & Quinn Johnson, MD 156
Telehealth Visits have Lower Non-attendance than Traditional Orthopaedic Clinic Visits
by Bradley S. Spence, MD, Mark J. Lambrechts, MD, Zhengye Si, MA, Emily V. Leary, PhD & Sumit K. Gupta, MD, MPH 164
CRISPR Advancements for Human Health
by Daniel J. Davis, PhD & Sai Goutham Reddy Yeddula, DVM 170
Improved Assessment: The Path to Better Maternal Outcomes in Missouri
by Daniel Quay, MA, Ashlie Otto, RN, George Hubbell, MD, Karen Harbert, MPH & Crystal Schollmeyer, RN 317
Management of Visually Significant Vitreous Opacities
by Nikki Gill, MD & Ajay Singh, MD 391
The Status of Cadaver-Based Anatomy Instruction in Missouri Medical Schools
by J. Patrick Brooks, MD & Carlton Homan, BS 395
The Role of Pharmacy Benefit Managers and Skyrocketing Cost of Medications
by Suzanne G. Bollmeier, PharmD & Scott Griggs, PhD, PharmD 403
Advancing Psychedelic-Assisted Therapy in Missouri (MO-PAT): Innovation at the Speed of Safety
by Danielle R. Adams, PhD, Torie Gettinger, PhD, Nathaniel Dell, PhD, Leopoldo J. Cabassa, PhD & Ginger E. Nicol, MD 467
Revival of a Beast: The Challenges Facing the Management and Control of Syphilis in Missouri from 2000 to 2024
by Hilal Abdessamad, MD, Wassim Jamaleddine, MD, Christian Rojas-Moreno, MD & Dima Dandachi, MD 474
Energy Drinks: A Clinical Primer and National Data Update
by Kevin Y. Xu, MD, Kevin T. Baumgartner, MD, Suraj Shankar, MD, Alison Huckenpahler, MD, PhD & Paul E Glaser, MD, PhD 481
Glucagon Like Peptide -1 Receptor Agonists for Weight Loss: A Primary Care Perspective
by Kara Mohr, MD & Clayton Butcher, MD 489
Pulmonary Embolism Education: Role of Generative Artificial Intelligence Models
by Rohma Zaidi, BA, Jonathan Asghedom, BS & Som Singh, MD 495

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