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**MEDICAL JOURNAL**

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Josiah "Jody" Rich, MD, co-authored study which reports  
opioid addiction treatment in prisons reduces overdose deaths



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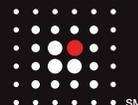
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## Expert opinions

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I RECENTLY REVIEWED an article submitted for publication in a neurology journal providing an “expert opinion” on how to use a new drug. The first surprise was that the first author was not a recognized expert in the field, and was primarily an administrator, who possibly had no experi-



ence using the new drug. Of the seven other authors, only one probably had any “hands-on” experience, and most probably had absolutely no experience treating people with the disease, let alone with the new drug. However, the authors represented only half the expert consensus panel. The other eight authors also, surprisingly, were not recognized experts. All were, however, paid consultants to the drug company that owned the drug.

I pointed this out to the editors, of course. And, while I know some of these experts, and am quite certain that none of them would be overtly biased by their financial relationship to the company, it could not look anything but suspicious to a reader who did not know these people personally. In my review, I pointed out that I, too, was a paid consultant to this company, and that the editors should take into account that I had not been invited to be part of this consensus panel. Hence, I might be biased because I was overlooked, that

I missed a payday, and authorship on another publication. Why I was not invited, I can only guess at. It is even possible that I was invited and couldn’t attend, as I am poor at keeping track of these sorts of things and my memory is not the most reliable. On the other hand, not only do I

have actual experience with the drug, which, I believe, are at least informed by experience, but I’ve also published my experience, unlike all of the “experts.”

I have sometimes discussed in these columns the problems associated with medical decision making, deciding between “evidence-based medicine,” which is data driven, but based on data from trials which used stringent entry criteria. This is required to be sure that their population represented a relatively “pure” example of the problem to be treated, and also to maximize the chance that the experimental drug would be successful. However, the patients in most studies were most likely not exactly like the one in front of you in the office, and therefore not really in the database. Yes, they were diabetic, but no, they were not morbidly obese or intellectually impaired, or had asthma. “Experience-based medicine (EBM),” which often reflects the last two or three patients you saw with similar problems to the one in front of you,

often suggests different approaches than evidence-based medicine. This type of EBM, of course, has its own problems, and my experience may be very different than yours.

There are always two sets of studies that spring to mind when I think about the two “EBMs.” One was on the use of quetiapine to treat psychosis in PD patients. While three double-blind, placebo-controlled trials were negative, most experts, myself included, think it does actually work and I continue to use it. The other was the CATIE study, an observational study to demonstrate that the second generation of antipsychotics caused less tardive dyskinesia than the first generation. The huge, multi-centered trial was developed by leaders in the field and turned out showing that there was no difference. That set the stage for various groups to publish papers explaining the “wrong” outcome of the study. Even we “experts” have feet of clay.

I did not think well of the article. My review recommended that the editors reject it. As of this writing I don’t yet know their decision. I doubt it will be accepted as my review was too harsh, and, my suggestion that an average reader, seeing that all the “experts” were paid consultants, and that the premise of the article was how, rather than why, this drug should be used, might surmise that this was a piece planted by the drug company. That thought, alone, is likely to kill the piece.

I don't like rejecting articles, but each journal has its own standard, and articles pretending to be expert advice should come from experts in the field they are talking about, not "meta experts," that is, people who are experts about issues related to the topic of interest but not really the topic itself. The set of experts who consulted on the bad manuscript, were international experts in pharmacology, but had absolutely no experience with the drug they were talking about in the niche of Parkinson's disease. Having interacted with many experts in schizophrenia, I can assure you that being expert in schizophrenia does not readily translate into expertise in Parkinson's disease.

I think that if I had reviewed the same article by authors who truly had expertise, I would have written the same critique I submitted to the journal editors, except for the criticisms based on their

lack of actual experience. While I would have challenged their suggestions, citing my own experience, I would have recommended publication, believing that biological variation and human variation in the observers would account for the differing opinions. I would have asked the editors to invite a companion opinion piece, preferably by me. If that did not occur I would have written a letter to the editor when the article was published.

Since I wrote the above I have co-authored an expert set of guidelines for a different movement disorders problem, and, am happy to say, am not a consultant for any company involved in this field, and, I have actual, hands-on experience. I am, I think, an expert. This doesn't mean I'm right and that my recommendations should be followed, but does mean they should be taken seriously. ❖

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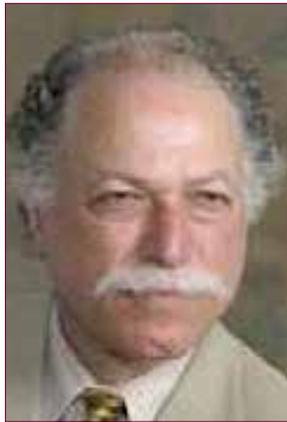
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## Coronary Stent Placement in Patients with Stable Angina – an Ongoing Debate

KENNETH S. KORR, MD, FACC

**T**HE RESULTS OF THE RECENT ORBITA trial (1) in Britain have re-ignited the discussion over the role of Percutaneous Coronary Intervention (PCI) in stable angina patients, prompting this recent headline in the *New York Times*: “Heart Stents Are Useless for Most Stable Patients...” (2) The unique feature of this trial included a “sham” intervention, unprecedented in stenting trials, marking this as the first double-blind placebo-controlled interventional trial, similar in design to more typical, randomized, placebo-controlled pharmacological studies. The intent of this design was to mitigate any perceived beneficial placebo effect among the stent patients. The trial included 200 patients with stable coronary artery disease (>70% single vessel stenosis) who received 6 weeks of optimal medical therapy (OMT) followed by randomization to either stent placement or a “sham” procedure without a stent. At 6-week follow-up, while still on OMT, there was no difference in exercise time on a treadmill stress test in the stented vs. the “sham” patients.

The fact that the investigators could successfully perform a placebo-controlled interventional trial was noteworthy in and of itself. Placebo-controlled device trials are uncommon and many physicians have ethical concerns



withholding an established therapy. The investigators demonstrated that such a trial is possible and safe, and this will likely serve as a stimulus for similar studies in the future. Beyond that, the results of the study were less than overwhelming. Increases in exercise time, as a surrogate for coronary ischemia, may not be the best measure of symptom relief, especially in patients on medical therapy with beta blockers. The sample size was small, only 200 patients compared to larger trials like the COURAGE study (3) discussed below. While there were improvements in incremental exercise time in the stent group, these did not reach statistical significance and might have achieved significance with a larger sample size. Furthermore, increases in exercise time are imprecise and subjective and change from week to week. A single stress test at 6-week follow-up may be a relatively short period upon which to base treatment conclusions. These methodological issues have caused many interventional cardiologists to question whether the results would have been more revealing if the study population had been 400–500 patients and with a longer period of follow-up of 6 months. Nonetheless, this study has stirred considerable discussion in the interventional and

general cardiology communities and it is anticipated that the investigators will continue to present longer-term follow-up data in these patient groups going forward.

Looking at this from a broader treatment perspective, the role of PCI in the management of coronary artery disease has evolved considerably in the 41 years since Andreas Gruntzig performed the first percutaneous transluminal coronary angioplasty (PTCA) in Zurich in 1977.(4) The introduction of coronary stents in the late 1990s substantially improved the success and safety of PCI and reduced the incidence of emergency coronary bypass surgery (CABG) for failed PCI from 1.0% to 0.1%. The improved efficacy of coronary stenting made it particularly attractive as a treatment modality for patients with acute myocardial infarction (MI) and other unstable coronary syndromes, where it quickly became the preferred treatment approach.

Currently, PCI with coronary stent placement has been well established by numerous randomized control trials (5) as the standard of care for the majority of patients with ST elevation MI, non-ST elevation MI and other acute coronary syndromes. Interventional quality measures include door-to-balloon times of less than 90 minutes (the time from the patient's arrival at the door to the ER until a balloon is passed into the occluded coronary artery) and many of these procedures are being performed

in hospitals without onsite coronary bypass surgical back-up. The majority of PCI procedures are now performed for patients with acute unstable coronary syndromes.

### But what about the role of PCI in patients with stable angina?

Stable angina pectoris is defined as reproducible exertional symptoms, usually chest discomfort, of at least 6 months duration while anything short of this is usually considered new onset and thus less stable or unstable angina. This may be an important distinction when applying trial results to individual patients. One of the earliest studies to address the role of PCI in stable angina patients was the ACME trial, (6) which compared balloon angioplasty to medical therapy in 212 patients with significant single-vessel coronary artery disease and found more freedom from angina and improved exercise duration among the angioplasty group at 6 months follow-up. It is hard to extrapolate and compare these results to present-day treatment options as the study was performed in the pre-stent era where the results of PTCA were less favorable and less durable than they are with current stent technologies. And medical therapy has also evolved considerably in the past 25 years.

In a more recent study of 2,300 patients with stable angina and predominantly single vessel disease randomized to OMT alone vs. OMT plus PCI with stent placement, the COURAGE trial investigators (3) demonstrated no significant difference in rates of death, myocardial infarction or stroke up to 4.5 years of follow-up. The degree of angina relief, however, was significantly higher in the PCI group, although there

was also substantial improvement in the medical-therapy alone group. Critics of this study have pointed to the difficulty in recruiting patients with very high grade stenoses (ie >90% proximal LAD stenosis) suggesting that the trial selected out a lower risk subset of patients who would do as well on medical therapy. However, similar results have been observed in other trials, none of which have demonstrated an advantage of revascularization over medical therapy in regard to death or MI. However, in many trials, up to 50% of patients “crossed over” to revascularization with PCI or CABG due to persistent symptoms that were refractory to antianginal drug therapy (7).

### So what is the current role of PCI in patients with stable angina?

Clearly, many stable angina patients can be well controlled for long periods of time with optimized medical therapy (including aspirin, beta blockers, nitrates, statins and ACE inhibitors). For patients whose symptoms cannot be easily controlled, those who have lifestyle issues, cannot tolerate optimal medical therapy or in whom symptoms progress over time, PCI with stent placement clearly has a role. A 2008 reassessment of the role of PCI concluded that for patients with stable angina and well-preserved left ventricular function, already on an excellent medical regimen, the long-term outcome is usually excellent. In this setting, PCI may not decrease cardiac mortality, which should be already quite low. However, PCI remains very effective in decreasing symptoms and ischemia as well as markedly decreasing the need for subsequent procedures. (7)

It will be interesting to see if future randomized placebo-controlled inter-

ventional device trials will add further to our understanding of the role of PCI in these patients. Until then, PCI along with medical therapy will continue to have a role in the management of patients with varying degrees of stable angina.

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# Clinical Challenges in the Growing Medical Marijuana Field

JONATHAN BARKER, MD

## ABSTRACT

Unique clinical challenges arise with the growing number of patients who possess medical marijuana cards. Medical marijuana patients with mental disorders can have worsening symptoms with marijuana use. Often there is sparse continuity of care between the patient and the medical marijuana practitioner. Lack of communication between the patient's treating practitioners and the practitioner who has authorized the medical marijuana can be problematic. This article is a discussion of the new clinical challenges practitioners are likely to encounter with the growing number of medical marijuana patients.

**KEYWORDS:** cannabis, cannabinoid, cannabidiol, medical marijuana

## BACKGROUND

According to an article published in the Providence Journal in 2015, the number of Rhode Island medical marijuana patients increased from 4,849 in 2013 to 11,620 in 2015.<sup>1</sup> The Rhode Island Department of Health issued a statement entitled, "Minimum Standards for Authorizing Medical Marijuana," on September 30, 2011.<sup>2</sup> This statement expressed that "The Rhode Island Department of Health (HEALTH)'s Board of Medical Licensure and Discipline has concerns over its ability to safely regulate the management of patients seeking authorization for medical marijuana." Physicians who choose to authorize medical marijuana cards should be aware that the Massachusetts Board of Medicine recently suspended the license of two physicians due to their practice of authorizing medical marijuana.<sup>3</sup>

The endocannabinoid system is extremely complex, and we know relatively little about it. THC is one of more than 60 cannabinoids present in the cannabis plant.<sup>4</sup> While there certainly may be medicinal properties of cannabinoid receptors, the current practice of dispensing a highly variable drug to the population at large and observing what happens is not only unscientific, it is dangerous. The Institute of Medicine gave the following statement upon review of the clinical uses of cannabis:

"If there is any future for marijuana as a medicine, it lies in its isolated components, the cannabinoids and their

synthetic derivatives. Isolated cannabinoids will provide more reliable effects than crude plant mixtures. Therefore, the purpose of clinical trials of smoked marijuana would not be to develop marijuana as a licensed drug but rather to serve as a first step toward the development of nonsmoked rapid-onset cannabinoid delivery systems."

Presently, potential clinical conditions with symptoms that may be relieved by cannabis include nausea, wasting syndromes (such as AIDS and cancer), chronic pain, inflammation, multiple sclerosis, some forms of muscle spasticity, and glaucoma.<sup>5</sup> There is research suggesting that cannabidiol (CBD) has anti-epileptic and antipsychotic properties.<sup>6,7,8,9,10</sup>

There are special cases of severe conditions, such as treatment-resistant intractable epilepsy or end-stage diseases, for which cannabis extracts may be more beneficial than traditional FDA-approved anti-epileptic medications. However, working with patients who are using medical marijuana, even for appropriate indications, presents special challenges.

For example, I saw two patients in an outpatient, partial hospitalization day program who each reported to me during the initial intake session that they had an outpatient physician prescribing them medical marijuana. Both were daily smokers. One had become paranoid and delusional. The other was manic and had physically assaulted hospital staff. I advised both patients about the dangers of cannabis, and the potential for cannabis to worsen mania and psychosis. I was put in a difficult position when one of the patients responded by saying his outpatient psychiatrist gives him a medical marijuana card. Having two different doctors with seemingly opposing messages about cannabis confused the patient; one doctor saying it was good for the patient, and one doctor saying it was bad.

The following are issues commonly encountered in treating patients who use medical marijuana, and some suggestions for dealing with these challenges:

1. Gaining trust of the patient and forming a therapeutic alliance.

The patient may not know whom to trust. Another doctor with whom the patient has already formed a therapeutic alliance gives the patient the authority to purchase medical marijuana. This means the patient's other doctor thinks marijuana is good for them. The patient likes using

marijuana, and may even be addicted to its use. Now a new doctor tells the patient that marijuana is not good for his/her mental health.

For the patient who is manic with no insight into the mania and enjoys being manic, it is easier to continue with the marijuana-prescribing doctor and fire the doctor opposing the use of marijuana. For the patient who has paranoid delusions that are real in the patient's mind, and now hears that the delusions are being exacerbated or caused by the marijuana, it is easier to trust the marijuana-prescribing doctor.

2. Treating the patient's mental illness knowing that the patient will continue to use marijuana.

If the patient wants to continue to use marijuana but is also accepting treatment, should the doctor agree to start treatment knowing that the patient will continue to use marijuana? A similar question could be asked of a patient who has a stimulant-induced mania and is unwilling to stop the stimulants. Should the doctor treat with antipsychotic or mood-stabilizing medicine to counteract the stimulant-induced mania knowing that the patient has no intention of stopping the offending agent?

3. Contacting the outpatient provider who is providing the patient with the medical marijuana card when the patient does not want providers communicating with the medical marijuana-authorizing provider.

Patients may not give you permission to contact the marijuana-authorizing doctor because they are afraid if you talk to the marijuana-authorizing doctor, they will no longer be able to renew the medical marijuana card from that doctor.

I suggest the following for outpatient providers who are faced with the above challenges:

1. As the new provider, you should be well educated about the research accounting for the dangers and benefits of cannabis in different areas of medicine. I suggest starting the conversation with the patient by acknowledging the confusion he or she might be experiencing. By explaining the science, the patient is more likely to view you as an expert on the subject, which will make it easier for the patient to trust you.

2. I suggest continuing treatment if the patient trusts you enough to start engaging in treatment, but does not want to stop the cannabis use. With treatment, either medication or psychotherapy, the patient may gain a better understanding of the ways in which cannabis is affecting his/her mental health and agree to discontinue its use. The alternative is that the patient may continue the cannabis use without the treatment you could provide.

3. If the patient does give permission to contact the marijuana-authorizing doctor, I would suggest doing so to provide the doctor with information about the patient's mental state while using cannabis. If the patient does not give you

permission, I would suggest not breaching confidentiality unless there is an emergency, because you are likely to drive the patient out of treatment if you do so. Furthermore, marijuana is easy enough to obtain. The patient is likely to continue its use even if you breach confidentiality and the marijuana-authorizing doctor agrees not to continue providing the patient with a medical marijuana card.

### Acknowledgment

I wish to thank Edward Silberman, MD, and Devra Barter, MS, for helping with the review process of this manuscript.

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## Child sexual exploitation: cautionary lessons from England

ANISH RAJ, MD

**KEYWORDS:** commercial sexual exploitation of children, domestic minor sex trafficking, abuse

The sexual exploitation of children is an issue that continues to be under-recognized and inadequately confronted by those with the moral and professional responsibility to protect vulnerable youth. Recent studies have demonstrated that both healthcare providers and law enforcement personnel are often unaware of the presenting characteristics and legal status of victims.<sup>1,2</sup> This unfamiliarity is further exacerbated by prevailing misconceptions. Child sexual exploitation and abuse, including forms such as the trafficking of minors, have historically been incorrectly regarded as exclusively international practices; ones perpetrated by violent men against foreign girls with the notion of human smuggling falsely being equated with the trafficking of persons. Largely due to the lack of empirical data and absence of standardized guidelines, first-line providers in many institutions lack the knowledge base or appropriate means to intervene. However, it is imperative that we recognize that inaction, regardless of etiology, is unacceptable.

The child protection scandal that yielded substantial international media coverage during the summer of 2014 and led to the development of widespread awareness campaigns throughout

England was the revelation of decades of organized child sexual abuse in the town of Rotherham. Of note, these findings and subsequent movements garnered remarkably minimal attention in the United States. While the absence of any such scandals stateside involving organized child abuse on the magnitude of Rotherham's is certainly comforting, it does beg the question: Have the seeds already been sown, and we simply have not uncovered them yet? It stands to reason that our children would best be served by reviewing and learning from the procedural lapses that transformed lives in Rotherham, so that we can strive for a proactive approach to get ahead of the issue instead of relying on a reactionary one.

An independent inquiry published in 2014 and commonly referred to as the Jay report shed light on the alarming prevalence of child sexual exploitation in England and the widespread systematic failures that facilitated its perpetuation. The comprehensive investigation conservatively estimated that between 1997 and 2013 over 1,400 British children were sexually exploited in Rotherham – a moderately sized town with a population of 258,400.<sup>3</sup> All the affected youth were under 16 at the time of initial exploitation.<sup>3</sup> Nearly half of these children came from a home with domestic violence; a fifth had a parent struggling with addiction; over a third had a parent with mental

health issues.<sup>3</sup> More than a third of the victims had previously interfaced with child welfare services, and almost two-thirds had documented truancy.<sup>3</sup> The appalling forms of coercion and abuse included, but were not limited to, girls as young as 11 being “raped by multiple perpetrators, trafficked to other towns and cities in the north of England, abducted, beaten, and intimidated.”<sup>3</sup> One victim even disclosed that she considered gang rape “a usual part of growing up in the area of Rotherham in which she lived.”<sup>3</sup> Fear-invoking tactics also involved violent threats or actual assaults on victims' families. One of the most concerning aspects was the lack of coordinated action by law enforcement and social services despite years of mounting evidence of the organized abuse. The 2014 Jay report and subsequent inquiries noted that multiple testimonies submitted by residential staff and youth workers were suppressed or altogether ignored for years.<sup>4</sup> The reasons for this negligence reek of bureaucracy, but were also complicated by survivors often being labelled as unreliable witnesses or consenting to their situations. Furthermore, while social services had identified child sexual exploitation as a referral category in 2001, the local police department did not have a similar designation until 2013.<sup>4</sup> Consequently, cross-communication of information between disciplines was markedly hindered, and many lives

were impacted. As Gladman and Heal declare, “It should not have occurred. It did not need to happen. It was all so unnecessary.”<sup>4</sup>

Strikingly, few accounts even mention the role of pediatricians (or general practitioners). At best, this reflects an oversight. However, at worst, these constitute numerous missed opportunities to intervene. Outside of acute hospital visits for suicide attempts or the completion of sexual assault kits, much of the provisioned health care in Rotherham seems to have been facilitated by outreach programs and sexual health service organizations. The irony is that one of the cornerstones of pediatric medicine is continuity of care and recognizing the subtle warning signs of physical, mental, or social decline. A United Kingdom general practitioner observed in the aftermath of Rotherham that “sometimes there is a pattern” – a pattern that should be within our scope to identify and gives us the opportunity to intervene.<sup>5</sup>

The children and families of Rotherham were systematically let down at every step. Preventative measures were unsuccessful, early identification and intervention were absent, inadequate support was provided by child welfare services, and the legal system did not strengthen victims’ resolve to disclose. Recognizing these failures brings us back to our central question: If there is not already an undiscovered Rotherham brewing in the United States, what can be done to prevent one? Given the lack of standardized practice and nationwide variability in responses, our young persons are certainly not immune from a situation like that in Rotherham. When even one child is at risk, no child is safe.

Similar to England in the 1990s and early 2000s, there is presently no consensus on the scale of child sexual exploitation in the United States. We must prepare by educating ourselves and those around us, especially as the literature base grows on identifiable risk factors and recommended trauma-informed approaches.<sup>6</sup> We also need to account for children that are frequently absent from care. Missing scheduled appointments and chronic truancy are red flags that should be noted and followed up on. Pediatric patients, by virtue of their age, have an adult responsible for them. Providers should liaise with child welfare services and law enforcement to ensure that no child falls through the cracks (e.g. patients for whom a wayward petition has been filed). When encountered, exploited youth should be identified as victims and survivors. As a healthcare worker states in a British mini-series, “There’s no such thing as a child prostitute. What there is, is a child who is being abused.”<sup>7</sup> Words matter. Extensive linguistic research, especially in the realm of addiction medicine, has demonstrated that terminology with traditionally negative connotations can influence attitudes during care provision and contribute to stigma. Clinical experience suggests most youth do not disclose their involvement initially and possibly ever. We must believe them when they do. While federal legislation (e.g. Trafficking Victims Protection Act) mandates broad protection for minor victims, states contrast in their interpretation of regulations. As of late 2015, 34 states had passed variations of Safe Harbor legislation designed to decriminalize youth involvement and divert away from juvenile justice

systems.<sup>8</sup> Whereas Rhode Island has not yet formally secured Safe Harbor legislation, a multi-agency collaboration recognized as the Rhode Island Human Trafficking Task Force (RI HTTF) produced a state-wide protocol to ensure that pediatric survivors of commercial sexual exploitation are not criminalized and instead plugged in with recovery services as soon as possible.<sup>9</sup> States also tend to differ on whether sexual exploitation that does not involve household members or caregivers falls under the purview of child welfare services (i.e. mandated reporting). In light of the RI HTTF protocol, any individual in the state of Rhode Island that suspects commercial sexual exploitation of a child, regardless of perpetrator, is to notify the Division of Children, Youth & Families (DCYF) immediately.<sup>9</sup> While Rhode Island has made progress in recent years, considerable work remains to be done, and it will be important to review corresponding outcomes and determine which interventions prove the most effective. As soon as possible, all states will need to come together and determine a consistent, evidence-based, and multi-disciplinary approach to protecting vulnerable youth.

As healthcare providers, we must be aware of our local regulations and resources. If a child is seeking help, it is our responsibility to know where referrals ought to be made and what services can be offered. It is said that those who fail to learn from history will inevitably repeat it. Thus, let us learn from the experiences of our British counterparts so that we can best serve all children going forward. ❖

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## The elephant – or donkey – in the exam room

VISHAL KHETPAL, MSC; MADELINE PESEC, AB

**KEYWORDS:** physician-patient communication, medical school, culture of medicine, political polarization

With the commission of the Flexner Report in 1910, leaders in medicine sought to characterize the profession as pure and objective, encouraging their colleagues to recede from traditional pursuits in the public arena. And today, most strive to rise above the mud slinging of politics, at least publically.

Today's medical students find themselves studying medicine in a time of profound political change as global populist movements take rise and as our country is embroiled in hyper-partisanship. Fellow students, here and elsewhere, are creating new groups and organizing around issues like abortion and racial injustice. Lectures on subjects normally inert to shifting political trends, like neuroanatomy and brain tumors, feature digressions into concerns over the potential elimination of biomedical research funding from the National Institutes of Health (NIH). One of our psychology exams even featured a vignette about a boy suffering from adjustment disorder after his father was deported, a question which took on a political undertone given the persistent rhetoric regarding deportation espoused by the current administration.

In all fairness, most medical students

– of any era – have probably attended a lecture in which a professor detours into an unwarranted, but well-intentioned, commentary on topical political debates, like the legalization of medical marijuana or the bioethics of abortion. But what used to be an occasional (and memorable) event has morphed into a regular presence in our lecture hall, perhaps unbeknownst to our professors. During our first year in medical school, it wasn't uncommon to hear two, or even three, of these diatribes daily in the immediacy of the new administration.

At our clinical mentoring sites, idle conversations about the weather and basketball have been replaced by the latest scoop in Washington. The political tumult over the past year has even forced itself past the waiting room, as the psychosomatic symptoms of post-election stress disorder, described by a number of mental health professionals in recent months, still invariably creep into our case write-ups and oral presentations to our preceptors.<sup>1</sup> On one occasion, we witnessed a patient's adjustment disorder from the outcome of the election, likely contributing to recent episodes of nausea and anxiety, go undiscussed during his follow-up visit for diabetes. Would the resident have dived into this recent development if the patient's case of adjustment disorder was due to something less socially uncomfortable, like losing his job, or a death in the family? Perhaps so.

It seems that we're not alone in making these observations. An editorial written by Dr. Reshma Jagsi, in *JAMA Oncology* (January 2017), chronicled how concerns over continued insurance coverage, fear of religious discrimination, and other contentions of politics have invaded her exam rooms since the recent election.<sup>2</sup> And although Jagsi and other prominent physicians often note that their training discouraged them from discussing politics in the clinic, evidence from a study of primary care physicians conducted in 2006 suggests that this advice is often discarded in medical practice. Most providers (83%) had indeed discussed politics with patients in the past decade and nearly 50% had initiated such discussions themselves.<sup>3</sup>

More recently, we've also come to understand that politics is not an inert factor in the clinic; it impacts medical decision-making by physicians. One notable study, published in the *Proceedings of the National Academy of Science* in 2016 by Hersh and Goldenberg, found that physicians registered as Democrats or Republicans dramatically differ in their medical counsel when presented with politically charged issues, like gun stewardship, marijuana, sex work, and abortion.<sup>4</sup>

Taken together, these statistics paint a reality that substantially differs from common wisdom: that politics are trivial for objective medical practice, and

certainly not an appropriate topic for the exam room. Given its prevalence and influence, it is strange that appropriate ways to navigate politics in the exam room have not been taught to us in our medical school, nor at others, to the best of our knowledge.

On a national level too, it seems that politics has been regarded *persona non grata* in the exam room. The American Medical Association's Code of Medical Ethics offers relatively little guidance on the subject, noting that "physicians have the right, and even occasionally the moral obligation to undertake political action themselves," but in ways which are "not disruptive to patient care."<sup>5</sup> The section focuses on maintaining good relationships with co-workers and avoiding litigation, rather than offering recommendations for clinical comportment, an important component of professionalism.

Because of these factors, medical students are left with little advice on how to grapple with politics in the exam room, when it inevitably presents itself. This lack of protocol is certainly not because politics is controversial; medical schools regularly teach students how to talk about other uncomfortable topics. Indeed, of the three topics traditionally excluded from dinner table conversation as social taboos – sex, religion and politics – we have received extensive training on two. We learn how to discuss the complexities of religion, both as sources of conflict or solace for our patients, through opportunities to practice conversations and engage in thorough discussions about this topic with our mentors. Early in our experiences in medical school, we are also taught non-judgmental methods to

broach the topic of sexual practices, the diseases that may be transmitted, and specifics on protection. Like actors in a theater company, we practice asking standardized patients about the most personal elements of their social and sexual history until our faces no longer flush red with embarrassment. Yet among our preparations for the more uncomfortable topics that may arise in the exam room, politics is rarely, if ever, mentioned.

When it does surface in the clinic, medical students are handed down a folk wisdom of sorts, built on hunches and previous missteps. Searching for answers, we directly asked three physicians, who serve as mentors for medical students at our university, about how they approach the subject of politics in the exam room. And perhaps unsurprisingly, we received three thoughtful, but different, answers.

Dr. A shared that her approach is patient dependent, and relies upon her experienced ability to "read a room." As an internist, she stressed the importance of subtle, but noticeable, self-disclosure in long-term relationships with patients. Her approach, after the election, has involved using pins on her white coat, presenting her support for the LGBT community and the Black Lives Matter movement, to communicate her views non-verbally. In conversations, Dr. A avoids discussing politics unless relevant to health, such as in the case with our patient's adjustment disorder discussed earlier in this essay. She is concerned with how the doctor-patient relationship will evolve alongside increasing political vitriol, as well as with the partisan divides emerging between health professionals.

Dr. B recommended, first and foremost, to be a mirror to the patient, should politics appear in the exam room. He emphasized that any communication in the exam room, given how short the average patient visit is today, should be purposeful. "Politics," Dr. B shared, "should be discussed like any other subset of non-medical, but complicated topics which might surface in the doctor-patient relationship." For the patient presenting with political stress disorder, his advice emphasized employing the clinical gaze, and using objectivity to understand how the patient's processing of events impacts their health.

Finally, Dr. C looked to his past training in the Israeli healthcare system to shape his attitude toward political conversation in the exam room. In Israel, politics are pervasive, even violent at times. In response to this tense political climate, Dr. C shared that physicians have become extremely apolitical figures within their communities. He notes that while different groups may face discrimination outside of the clinic, in his decade in the country, he never fielded a complaint about differential treatment inside the walls of the clinic. While it is general wisdom in the United States not to talk about politics with patients, Dr. C observed this taboo to be much stronger in Israel, where physicians and patients alike make a strong effort to steer clear of political topics. But in the United States, Dr. C has observed politics gradually creeping into the exam room in recent years, and reports seeing many patients, especially after the last presidential election, whose anxiety about politics complicates their comorbidities. His advice to young doctors is to work with the patient to design

an intervention – which could include political engagement or advocacy – that will be helpful to them in alleviating their anxiety. However, he adds, “when in doubt, stay neutral.”

It is abundantly clear, from our conversations with three physicians, that previous generations of physicians have learned how to navigate politics by observing their own mentors and accumulating good clinical sense over time. But in this time of political turmoil, perhaps more formalized guidance is warranted, for both medical students and weathered physicians.

What this guidance should look like isn't for us, as untested medical students, to say. Perhaps one option could be to take the path of Dr. A, and offer self-disclosure of political stances non-verbally, through office signs and pins, while limiting any verbal discussion of politics to relevant issues of health for our patients. Another could be to take Dr. B's advice, and effectively serve as an impartial sounding board for our patients, as they process political issues alongside other elements of daily life, whether positive or negative. We could learn from physicians like Dr. C and look to our counterparts who practice abroad in countries like Israel, marked by severe political division. And finally, we could seek advice from other professions, like teaching, which also have had to contend with a new

reality of political polarization while maintaining inclusive and objective environments.

These approaches and others, tempered by trial and error, surely exist in our country's clinics and wards. Before taking any path, however, a frank discussion within the medical school community, as well as outside of it, is needed for the sake of tomorrow's doctors, and ultimately our patients.

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### Disclaimer

The views expressed by the authors in this manuscript do not necessarily reflect the views of the Warren Alpert Medical School of Brown University.

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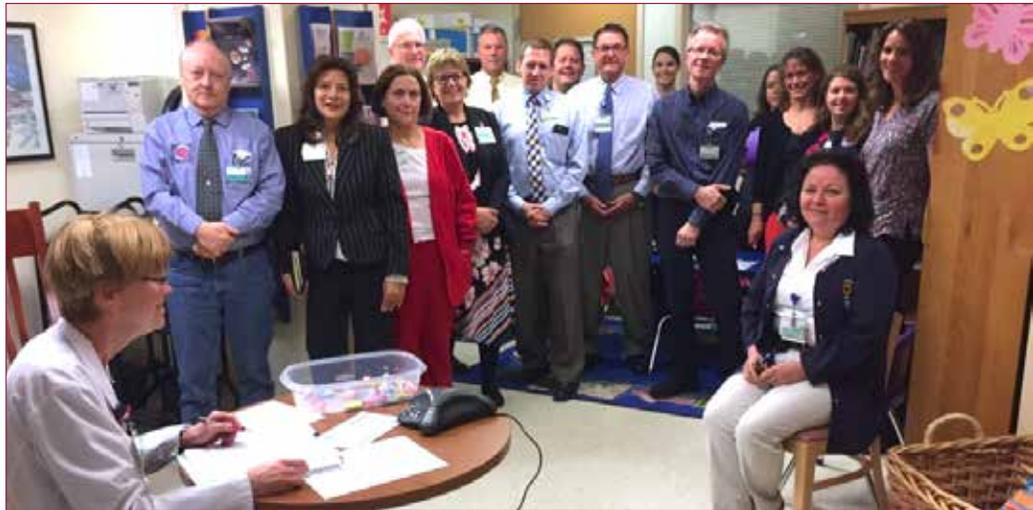
**"Collecting the Uncollectible"**

## Daily Safety Briefs (DSB) focus on improving safety at Hasbro Children's Hospital

IVONA SEDIVA, MD; LINDA SNELLING, MD

Daily Safety Briefings (DSB) are reports from front-line units and ancillary departments to enhance awareness of immediate or potential problems affecting patient safety and care. They also enhance communication across all disciplines. Patient safety briefs improve outcomes by increasing the timeliness and quality of information teams share with each other, and by producing greater accountability. Staff members are encouraged to bring forth concerns and propose solutions.<sup>1</sup>

Hasbro Children's Hospital started DSB in November 2013 after reviewing DSB methods at Cincinnati Children's Hospital and providing education on DSB for all participants. Briefings start every weekday at 11:45 a.m. sharp and last 10–15 minutes. We begin with reporting the number of days since our last serious harm event. Representatives from 31 units and departments report on any safety issues that have occurred in the past 24 hours, and they look ahead to identify any predictable issues in the next 24 hours. One hundred percent attendance is rewarded monthly by Real Inspiring Hero Certificates and notification is sent to departments with low-attendance rates. Each department follows a customized reporting template. For example, inpatient nursing reports on census, discharges, scheduled admissions, acuity, number of rapid response calls and children who are monitored for risks of deterioration, as well as staffing issues, and any safety issues in the last 24 hours. Good catches and near misses also are reported. Safety measures are



Myra Edens, MSN, RN, NE-BC, FACHE leading DSB

enacted to prevent near misses from reaching patients in the future.

Between November 2013 and November 2017, we identified 961 safety concerns. The average time to resolution was 7.5 days, but many issues were resolved the same day. Complex system issues may take a few weeks to months to complete. For example, we identified an unintended system issue where changes targeting adult units at Lifespan resulted in consequences adversely affecting monitoring on pediatric units. We track reports in a database to allow timely review by designated hospital leaders across departments. The date the issue is resolved is reported back at the subsequent briefings.

DSB has become an important part of daily operations at Hasbro Children's Hospital. Department leaders encourage concerns to be brought up by all staff in a timely manner, and report back

on resolution. Full participation and feedback improves transparency and creates situational awareness, improves collaboration between departments, and demonstrates that every single person in the hospital, no matter his/her position or direct patient contact, is essential to our mission: "Delivering Health with Care."

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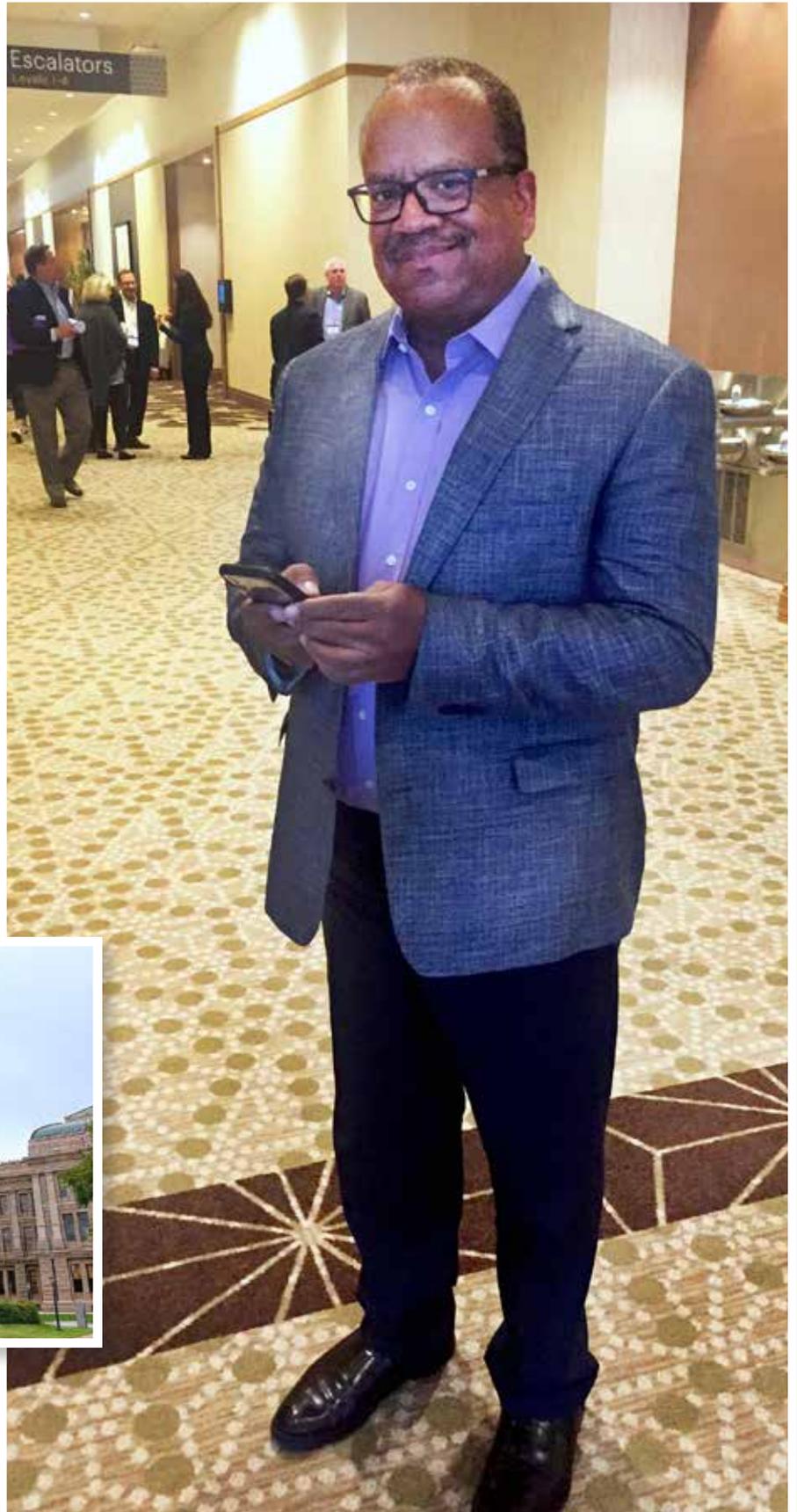
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### AUSTIN, TEXAS

**Keith D. Carter, MD**, President, American Academy of Ophthalmology (AAO); President, Board of Trustees, Association of University Professors of Ophthalmology (AUPO); and Lillian C. O'Brien and Dr. C.S. O'Brien Chair in Ophthalmology and Chairman and Head, Department of Ophthalmology, University of Iowa Carver College of Medicine; takes a moment from his busy schedule to view the *RI Medical Journal* while attending the AUPO Annual meeting in Austin, Texas.



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## Neurotherapeutics: Recent Developments

SYED RIZVI, MD, EMHL  
GUEST EDITOR

Diseases of the nervous system often have devastating outcomes. Unfortunately, treatments for neurological disorders, which primarily tend to be progressive, are very limited. The last two decades have seen game-changing clinical developments in neuroimmunology and neuro-intervention. In this section, we will review some recent progress in four different subspecialties of neurology.

### Multiple Sclerosis (MS)

Treatment of MS, that is, slowing of disease progression, has evolved from no evidence-based treatments prior to 1994 to 14 different FDA-approved disease-modifying agents in 2017. As the treatments become more effective, the threshold for tolerating disease activity has decreased. Most MS specialists now aim for NEDA (No evidence of disease activity based on MRI, relapse and disability progression). The treatment choices have expanded and offer a more aggressive approach but with increasing risk of serious adverse events. Progressive Multifocal Leukoencephalopathy (PML) has now been associated with several of the disease-modifying agents. Wong et al. review the current options in the treatment of MS.

### Stroke

The acute management of cerebrovascular disease has undergone a dramatic change in the last few years. Several studies have validated the use of aggressive and early intra-arterial intervention and in selected cases expanded the window of intervention for up to 24 hours. There is also increasing evidence supporting a more aggressive approach towards detecting atrial fibrillation and secondary prevention. Mac Grory et al. review the latest advances in stroke management

### Parkinson's Disease (PD)

PD continues to be a frustrating and difficult to manage neuro-degenerative disorder. Several new agents including different formulations of Levodopa and dopamine now offer additional options for optimizing care in these patients. Device-based treatments including Deep Brain Stimulation (DBS) and Levodopa Carbidopa Intestinal Gel (LGIC) are increasingly used in a select group of patients. D'Abreu reviews the latest in the management of PD. Unfortunately, no intervention has been shown to slow progression.

### Epilepsy

Uncontrolled epilepsy carries significant risk of morbidity and mortality. Up to 30% of patients continue to have seizures despite appropriate treatment with multiple agents. These patients benefit from a comprehensive evaluation at an epilepsy center with experience in epilepsy surgery. Bayer et al. review the surgical options for management of intractable epilepsy.

### Guest Editor

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# Moving Towards a Cure for MS: Increased Immunosuppression and Striving for No Evidence of Disease Activity (NEDA)

BRIAN WONG, MD; JONATHAN CAHILL, MD; SYED RIZVI, MD, EMHL

## ABSTRACT

Multiple sclerosis (MS) is a chronic central nervous system demyelinating disease. The cause is unknown, but likely results from a combination of genetic predisposition and environmental exposures leading to autoimmune destruction of the brain and spinal cord. The most common phenotype of MS is relapsing-remitting (RRMS), characterized by episodes of neurological symptoms, typically lasting days to weeks, followed by symptom remission. After years of disease, the majority of RRMS cases transform into secondary progressive MS (SPMS), characterized by slowly worsening symptoms and progressive neurological disability, which may or may not be also accompanied by superimposed relapses. A third distinct phenotype, primary progressive MS (PPMS) is characterized by slowly worsening neurological symptoms and disability from disease onset, without clinical relapses.<sup>1</sup>

The first disease-modifying agent was approved by the FDA in 1993. There are now 14 FDA-approved disease-modifying therapies (DMTs) with almost all agents indicated for relapsing forms of MS. The medical management of multiple sclerosis has changed dramatically over the past decade as the number of available DMTs has increased (See Table 1).

Most of the newer agents have been shown to decrease clinical relapse rates to a greater degree than the older agents. These DMTs frequently also decrease the rate of disability progression in MS. With the increased immunosuppression of the newer therapies comes the potential for more serious side effects. Balancing efficacy with potential adverse events is a primary consideration of patients and clinicians treating MS today. The potential for near complete control of the disease is becoming a reality in select cases, and a new goal of “no evidence of disease activity” (NEDA) may be supplanting the previous aim of relapse rate reduction.

**KEYWORDS:** multiple sclerosis, NEDA, disease-modifying therapy, PML

## ESCALATION VS. INDUCTION THERAPY

Early in the disease course, multiple sclerosis is characterized by periods of inflammation associated with demyelination and axonal injury. However, as the disease reaches a later progressive phase, inflammation and relapses become less prominent and neurodegeneration becomes the more defining feature of the illness. It has been proposed that aggressive treatment early in the disease course may have a greater effect on morbidity in multiple sclerosis because it is during this period that DMTs have the greatest opportunity to reduce inflammation. Two strategies used in selecting the best DMT to treat an individual MS patient are “escalation” and “induction” therapy.<sup>2</sup> An escalation approach has been widely utilized in the treatment of multiple sclerosis since the 1990s. This entails starting a patient on a first-line agent (typically glatiramer acetate or interferon-beta) and transitioning to a second-line agent only in the event of disease progression while on therapy. This is a reasonable strategy, as a patient may be well controlled on an agent with a long safety profile history. However, this approach does not take into consideration how early or late a patient is in their disease course or the degree of initial clinical or radiographic activity. Ultimately, the majority of patients starting treatment with glatiramer acetate or interferon-beta will continue to show evidence of disease activity. If there truly is a critical period early in the disease course where DMTs can provide the greatest impact, an aggressive approach may instead be warranted. This practice is analogous to induction chemotherapy for some cancers. Induction therapy is the alternative strategy where drugs with the highest efficacy are used for a defined period of time as an initial treatment despite their increased risk of serious side effects. Using an induction strategy to control inflammatory disease activity early in the course of MS, may ultimately decrease long-term disability.<sup>2</sup>

## FIRST-LINE AGENTS

Glatiramer acetate and several interferon-beta preparations (See Table 1) are frequently considered first-line agents. Each of these self-injectable agents reduces relapse rates in relapsing MS by modest amounts (approximately 30–35% relapse rate reduction), but their effectiveness in preventing long-term disability progression is limited.<sup>3</sup>

The three oral agents approved for relapsing MS represent an advance in the treatment of the disease by reducing relapse

**Table 1.** Disease-modifying agents for multiple sclerosis

Drug	Brand name	First FDA-approved	Dosing and administration	Indication
Interferon-beta 1b	Betaseron, Extavia	1993	0.25mg SC every other day	Relapsing MS
Interferon-beta 1a IM	Avonex	1996	30mcg IM weekly	Relapsing MS
Glatiramer acetate	Copaxone	1996	20mg SC daily or 40mg SC three times a week	Relapsing MS
Mitoxantrone	Novantrone	2000	12mg/m <sup>2</sup> IV every 3 months to lifetime max 140mg/m <sup>2</sup>	Relapsing MS and SPMS
Interferon-beta 1a SC	Rebif	2001	22-44mcg SC three times a week	Relapsing MS
Natalizumab	Tysabri	2004	300mg IV every 28days	Relapsing MS
Fingolimod	Gilenya	2010	0.5mg PO daily	Relapsing MS
Teriflunomide	Aubagio	2012	7-14mg PO daily	Relapsing MS
Dimethyl fumarate	Tecfidera	2013	240mg PO twice a day (after initial titration)	Relapsing MS
Peginterferon-beta 1a	Plegridy	2014	125mcg SC every other week	Relapsing MS
Alemtuzumab	Lemtrada	2014	12mg IV daily x5 days, then x3 days one year later	Relapsing MS
Daclizumab	Zinbryta	2016	150mg SC monthly	Relapsing MS
Ocrelizumab	Ocrevus	2017	600mg IV every 6months (with first dose split)	Relapsing MS and PPMS

rates to a greater degree when compared to the self-injectable agents, and in some cases showing decreased rates of disability progression.<sup>3</sup> Fingolimod and dimethyl fumarate both reduce relapse rates vs. placebo by approximately 50%.<sup>4,5</sup> Fingolimod also reduces relapse rates compared to an active comparator, intramuscular interferon beta-1a.<sup>6</sup> Teriflunomide reduces relapse rates by approximately 30% in relapsing MS and decreases the risk of sustained disability progression compared to placebo by ~26% over a two year period.<sup>7</sup>

Despite the improvements in efficacy with the oral agents, there are still many patients who experience clinical relapses, new MRI disease activity, and disability progression on these medications. Unfortunately, clinicians' ability to predict from disease onset which patients will fail to respond to the first-line injectable or oral agents is limited.

### MONOCLONAL ANTIBODIES: MORE EFFICACIOUS, BUT GREATER RISK

To justify the use of agents with increased serious side effects, the disease severity may be considered. Some patients with multiple sclerosis have a rapidly progressive course and respond poorly to first-line agents. In this population, the risk of serious side effects from a second-line agent may be acceptable. Using a Canadian database containing 5891 patients with adult-onset MS, an attempt was made to define aggressive multiple sclerosis (AMS). The three definitions proposed were: (1) Expanded Disability Status Scale (EDSS) 6 or greater within 5 years of MS

symptom onset, (2) EDSS 6 or greater by age 40, or (3) secondary progressive course within 3 years of a relapsing-onset course. Depending on the definition, between 4–14% of patients were characterized as having aggressive multiple sclerosis. There was a higher likelihood of aggressive MS in patients who were male, older at symptom onset, or presented with PPMS.<sup>8</sup>

An aggressive treatment approach could also be considered to achieve a disease activity free status in multiple sclerosis. The term “no evidence of disease activity” (NEDA) has emerged to describe this disease activity-free state.<sup>9</sup> More specifically, NEDA-3 has been defined as: (1) absence of relapses, (2) absence of focal MRI activity, and (3) absence of confirmed disability progression. While NEDA-3 captures inflammatory disease activity well, it may not fully account

for the neurodegenerative component of MS. Thus another more stringent definition was developed. NEDA-4 includes the criteria included in NEDA-3, but also requires an annualized rate of brain volume loss of less than 0.4%.<sup>10</sup> Since brain volume loss has been shown to correlate with disability progression and cognitive decline, this definition may more accurately reflect a complete absence of disease activity. However, other researchers have noted that NEDA criteria do not fully capture disability related to MS, neglecting some cognitive measures, visual function, fatigue, and pain.<sup>11,12</sup>

Natalizumab was first approved by the FDA for the treatment of relapsing forms of MS in 2004. The medication is a humanized monoclonal antibody which binds to the  $\alpha_4$  subunit of  $\alpha_4\beta_1$  and  $\alpha_4\beta_7$  integrins on the surface of lymphocytes. Binding to these integrins blocks lymphocytes' ability to interact with endothelial cell receptors (VCAM-1 and mucosal addressin-cell adhesion molecule 1) and prevents lymphocyte migration into the central nervous system. In clinical trials, natalizumab reduced clinical relapses (67% relapse-free at two years), new MRI disease activity (97% free of gadolinium enhancing lesions at two years), and disability progression (no EDSS disability progression in 29% compared to 17% of placebo).<sup>13</sup> The number of patients who met all the criteria satisfying NEDA-3 was not included in the final analysis of the study; however, a smaller Italian study of 152 patients with RRMS treated with natalizumab demonstrated that 34% of patients were able to maintain NEDA-3 status after 7 years of follow-up.<sup>14</sup>

Alemtuzumab, another intravenous infusion agent, was approved for use in the treatment of relapsing forms of MS in November 2014. Alemtuzumab is a humanized anti-CD52 monoclonal antibody which binds to the CD52 receptor on B and T lymphocytes causing a long-lasting depletion of lymphocytes. Alemtuzumab is given as an infusion over 5 days initially, repeated once for a cycle of three more days after one year. Most patients do not require further treatment for a period of five or more years. Alemtuzumab is perhaps the only true induction agent for the treatment of relapsing forms of MS. Following depletion, there is a subsequent slow repopulation of these cells. In clinical trials compared to subcutaneous interferon-beta 1a, alemtuzumab was superior in achieving an endpoint equivalent to NEDA-3 (referred to as “freedom from disease activity” in the study). 39% (139/360) of patients in the alemtuzumab arm maintained freedom from clinical or radiographic disease at 24 months compared to 27% of patients in the interferon beta 1a group. Furthermore, patients treated with alemtuzumab had less brain atrophy on MRI.<sup>15</sup>

The newest disease modifying agent, Ocrelizumab, was approved by the FDA in March, 2017 for both relapsing and primary progressive forms of MS. Ocrelizumab is a humanized monoclonal antibody that targets the CD20+ receptor found on pre-B cells, mature B cells, and memory B cells. This receptor is not present on stem cells or plasma cells. Thus the medication should preserve existing humoral immunity and potential for B cell reconstitution. The mechanism is identical to rituximab and only differs in that ocrelizumab is a humanized antibody rather than a chimeric antibody. In clinical trials of relapsing MS, ocrelizumab patients achieved NEDA-3 approximately 47% of the time, compared to approximately 27% in subcutaneous interferon-beta 1a.<sup>16</sup> The rate of brain volume loss in the ocrelizumab group compared with the subcutaneous interferon-beta 1a group was also decreased to a statistically significant degree in one study.

Ocrelizumab has also been shown to be effective in primary progressive MS. Although NEDA does not apply to PPMS and was not a secondary end point in this trial, the ocrelizumab patients had statistically significant better outcomes in disability progression (~25% relative risk reduction), volume of T2 lesions, and mean percentage change in brain volume when compared to placebo.<sup>17</sup> Based on this clinical trial, ocrelizumab became the first FDA-approved agent for the treatment of PPMS.

The mainstay of relapse treatment continues to be intravenous high-dose methylprednisolone. Acthar Gel (repository corticotropin injection) is used in rare cases where IVSM is not tolerated.

### AUTOLOGOUS HEMATOPOIETIC STEM CELL TRANSPLANTATION

While modern disease modifying agents have demonstrated improved efficacy in minimizing disease progression in RRMS, autologous hematopoietic stem cell transplantation

(AHSCT) for the treatment of MS, which can be considered the ultimate in induction therapies for MS, has also shown encouraging results. AHSCT for MS patients began in 1995 and by 2008 approximately 400 cases had been performed worldwide.<sup>18</sup> Although protocols from early transplantations varied greatly, even initial data showed a slowing of disease progression in a majority of patients following treatment. However, the procedure carries significant risk and transplant-related mortality was initially as high as 7.3%.

The protocol for AHSCT varies at each institution, but in general involves four main steps. First, hematopoietic stem cells are mobilized, typically using granulocyte colony stimulating factor. Then hematopoietic stem cells are collected in the patient’s circulating blood. The patient’s remaining immune cells are then eradicated via a “conditioning” regimen using one or several chemotherapeutic agents, and lastly the previously harvested stem cells are reintroduced to the patient.<sup>18</sup>

AHSCT has demonstrated NEDA status rates of 78–83% at 2 years and 60–68% after 5 years.<sup>19</sup>

### ADVERSE EFFECTS AND MINIMIZING RISK

Because NEDA is a new concept in the MS treatment field, specific NEDA rates of the older agents are not readily available. In longitudinal follow-up studies for the older agents, and in the clinical trials for the newer agents, NEDA status rates between 13–46% have been reported after two years of treatment. Direct comparison of NEDA status rates is impossible due to variations in the study populations.

Decisions about disease-modifying therapy must be made with consideration given to risks and side effects as well as efficacy. There are few serious side effects from the older self-injectable agents, but with newer oral and infusible agents, treating neurologists must monitor for specific side effects (See **Table 2**) including hepatic dysfunction, cardiac arrhythmia, and ocular disorders.

With the increased immunosuppression of the newer highly effective agents, there is increased risk of possible serious infections, secondary autoimmunity, and malignancy. One such serious infection is progressive multifocal leukoencephalopathy (PML), which is a rare brain infection that can be fatal. PML is associated with several of the DMTs used for MS, and in the highest risk patients may occur at a rate of 13/1000 individuals. Therefore, carefully selecting the appropriate DMT for each patient is critical.

Despite the increasing number of medications, the cost of each of these drugs remains prohibitively high for many patients. On average, treatment with one of these agents costs \$55,000/year and decision-making often requires consideration of insurance coverage limitations.

### CONCLUSIONS

As newer therapies are used more frequently as the initial treatment in MS, and therapies are modified and refined to minimize side effects, there will likely be improved long-term outcomes and increasing rates of NEDA. The goals for

an individual patient starting treatment for MS today are shifting from reducing relapses to completely controlling the disease clinically and radiographically. Reducing disability in the long-term and decreasing morbidity of the disease over many years is becoming a reality. Although none of the treatments discussed here is a cure for MS, the field is increasingly moving toward that goal as patients and providers become less accepting of new symptoms, signs, or MRI changes.

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**Table 2.** Common and serious potential side effects of the disease-modifying agents

Drug	Common side effects	Serious potential side effects
Interferon-beta	Post-injection flu-like symptoms Liver function abnormalities Depression	Rare
Glatiramer acetate	Injection site reaction (skin irritation)	None
Mitoxantrone	Few	Heart failure (0.4%) Hematological malignancy (0.8%)
Natalizumab	Few	PML JCV + patients (1/1000 patients) JCV – patients (extremely rare)
Fingolimod	Few	Macular edema (0.1%) Heart block (0.1%) PML (extremely rare)
Teriflunomide	Mild alopecia	Hepatic dysfunction (uncommon)
Dimethyl fumarate	Gastrointestinal upset, Abdominal cramping Flushing	PML (extremely rare)
Peginterferon-beta 1a	Post-injection flu-like symptoms Injection site reaction Depression Liver function abnormalities	Rare
Alemtuzumab	Infusion reaction	Immune thrombocytopenic purpura (ITP) (1%) Autoimmune thyroid disease (30%) Serious infections (uncommon) Glomerular disease (0.3%)
Daclizumab	skin rash	hepatic dysfunction (rare)
Ocrelizumab	Infusion reaction	Breast cancer? (unclear evidence)

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# Updates in Stroke Treatment

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## ABSTRACT

In this article, we discuss major advances in the treatment and prevention of ischemic stroke that have taken place in the past 3 years. The most important advance in acute stroke treatment is the validation and widespread adoption of intra-arterial therapies for the treatment of acute ischemic stroke. Five clinical trials spanning multiple continents were published in early 2015 that proved that intra-arterial treatment – both with and without tPA – is beneficial in improving functional recovery after stroke. Emerging literature (including the DAWN trial) also suggests that patients can be treated up to 24 hours after the onset of symptoms based on the size of the infarct core obtained using MRI Perfusion or CT Perfusion imaging. With respect to stroke secondary prevention, widespread adoption of long-term cardiac monitoring has increased the detection rate of atrial fibrillation (as demonstrated in the EMBRACE and CRYSTAL-AF trials). Pioglitazone (an oral hypoglycemic agent of the thiazolidinedione drug class) was shown in the IRIS trial to reduce the risk of recurrent stroke in patients with impaired glucose tolerance who had not developed type 2 diabetes mellitus.

**KEYWORDS:** Ischemic stroke, transient ischemic attack, mechanical thrombectomy, atrial fibrillation, embolism, pioglitazone

## INTRODUCTION

The last 3 years have represented a paradigm shift in the treatment and prevention of ischemic stroke. Overwhelmingly, the most important change has been a comprehensive demonstration of the efficacy of interventional treatment for acute ischemic stroke. In addition to this, there have been advances in medical therapy for the prevention of recurrent stroke, new strategies for the detection of atrial fibrillation and a plethora of new oral anticoagulants for use in the prevention of stroke of embolic origin.

## INTERVENTIONAL THERAPY FOR ACUTE ISCHEMIC STROKE

The most important advance in the field of stroke neurology since the discovery of tissue plasminogen activator (tPA)

occurred in 2015. Thrombus retrieval using intra-arterial therapies was demonstrated as being both safe and highly effective in the treatment of acute ischemic stroke. This has led to a rapid uptake in its use in the United States and across the world and has galvanized the neurologic community to improve systems of care and rapid access to stroke treatment centers.

The use of mechanical devices to treat acute ischemic stroke was the subject of controversy in the field of stroke neurology for over a decade. Multiple trials<sup>1,2</sup> had demonstrated that mechanical clot retrieval devices improved the rate at which arteries were re-canalized after an acute occlusion, but no trials had demonstrated that this necessarily improved functional outcomes. For example, the Merci device<sup>3</sup> (Mechanical Embolus Removal in Cerebral Ischemia) used a corkscrew mechanism to penetrate a clot and then retrieve it. (**Figure 1**) It was effective at achieving the goal of removing clots but was associated with a high rate of complications, specifically arterial dissection.

The Penumbra device<sup>5</sup> used a gentle suction mechanism at the proximal end of a clot to attempt to gradually retract it. (**Figure 2**) It was associated with a lower rate of complications but also never shown to improve functional outcome.

In early 2015, five clinical trials were published in quick succession demonstrating the efficacy of a new generation of devices to treat acute ischemic stroke: MR CLEAN<sup>6</sup>, ESCAPE<sup>7</sup>, EXTEND-IA<sup>8</sup>, SWIFT PRIME<sup>9</sup> and REVASCAT<sup>10</sup>. These trials mostly used a stent retriever device. (**Figure 3**) This device introduces an undeployed stent directly in to the core of a clot, then expands the stent, leaving it in situ for approximately 5 minutes. This causes a clot to become enmeshed in and adherent to the stent before being extracted.

The results of the trials are depicted in **Table 1**:

A meta-analysis<sup>11</sup> of these trials confirmed that mechanical thrombectomy led to reduced disability at 90 days with an odds ratio of 2.49. The number needed to treat (NNT) was only 2.6 to achieve one favorable outcome. In addition, the risk of death at 90 days and the risk of cerebral hemorrhage were no higher than that of tPA alone. In the last few months, the investigators for the MR CLEAN trial showed that the benefits seen at 90 days persisted after 2 years of follow-up of their original trial subjects.<sup>12</sup>

Intravenous tPA and intra-arterial clot retrieval can only be delivered if a person presents within the “therapeutic

Figure 1. The Merci device<sup>4</sup>

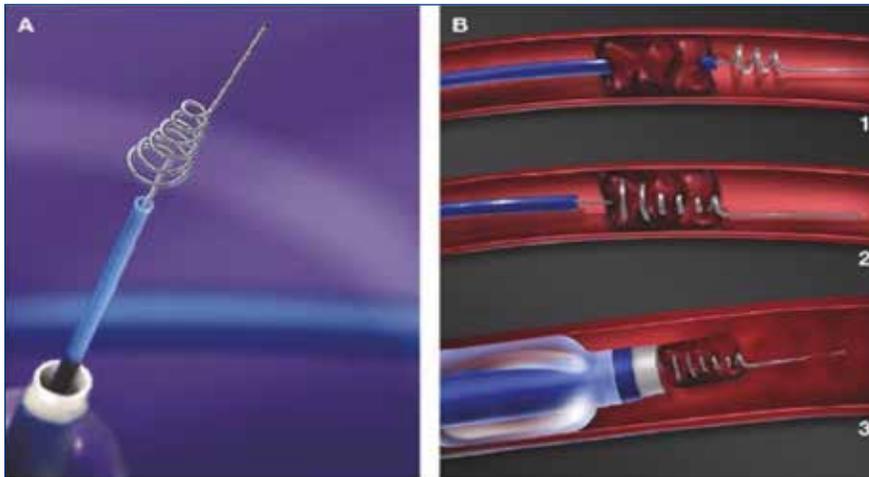


Figure 2. The Penumbra device<sup>5</sup>.

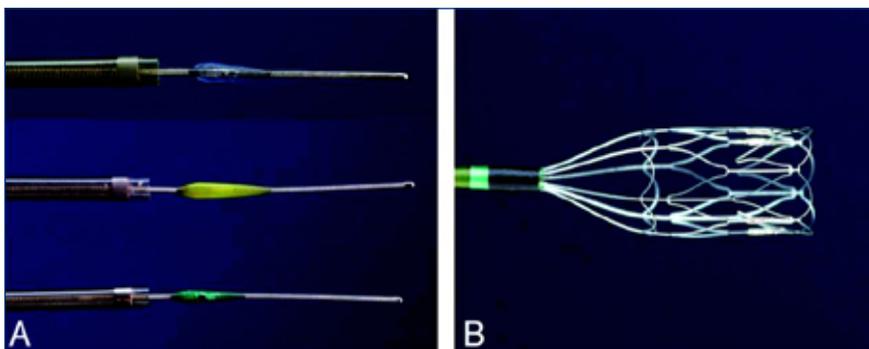
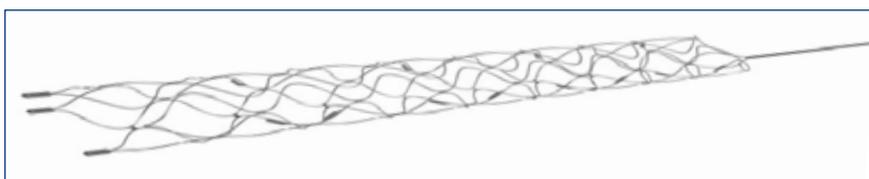


Figure 3. The Stent Retriever Device.



[www.medtronic.com/us-en/healthcare-professionals/products/neurological/revascularization-stroke/solitaire.html](http://www.medtronic.com/us-en/healthcare-professionals/products/neurological/revascularization-stroke/solitaire.html)

“window” – 4.5 hours for tPA and 6–12 hours for intra-arterial therapy. Therefore, an enormous challenge in the field of stroke neurology is the treatment of strokes that present late (after 12 hours) or from sleep (so-called “wake-up strokes”). The DAWN trial<sup>13</sup> (Clinical Mismatch in the Triage of Wake Up and Late Presenting Stroke Undergoing Neurointervention with Trevo) was recently completed. This was a randomized, controlled trial of thrombectomy vs. best medical therapy in patients who had a stroke beginning between 6 and 24 hours prior to presentation and who would not have not strictly been eligible for treatment with intra-arterial therapy. However, in this trial the investigators performed an assessment of the size of the “core infarct” (the area of dead tissue that is felt not to be salvageable) using magnetic resonance imaging (MRI) or computed tomography perfusion (CTP) imaging. They enrolled patients with a core infarct volume of <50 cc and a large stroke syndrome (NIHSS >20) meaning that the person’s stroke syndrome was worse than their imaging demonstrated, suggesting that there was a large volume of brain tissue that was salvageable. Using this protocol, they enrolled people presenting late in their “stroke window” and perform intra-arterial clot retrieval safely. Of 206 subjects, those treated with intra-arterial clot retrieval, achieved a favorable functional outcome in 48.6%, in comparison to 13.1% of patients in the control arm.

Table 1. The results of the trials.

Trial	Number of patients	Intervention	Outcome measure	Enrollment criteria	Result
MR-CLEAN(6)	500 (233 in intra-arterial treatment group vs. 267 in control group)	Stentriever	mRS at 90 days	Within 6 hours of symptom onset	OR of 1.67 for functional independence
ESCAPE(7)	316 (165 in intra-arterial group vs. 150 in control group)	Any thrombectomy device	mRS at 90 days	Within 12 hours of symptom onset	OR of 2.6 for functional independence
EXTEND-IA(8)	70 (35 patients in each group)	Stentriever	mRS at 90 days	Ischemic core of <70ml on CT Perfusion	71% functional independence in treatment group vs. 40% in control group
SWIFT PRIME(9)	196 (98 patients in each group)	Stentriever	mRS at 90 days	Within 6 hours of symptom onset	60% functional independence in treatment group vs. 35% in control group
REVASCAT(10)	206 (103 patients in each group)	Stentriever	mRS at 90 days	Within 8 hours of symptom onset	OR of 2.1 for functional independence

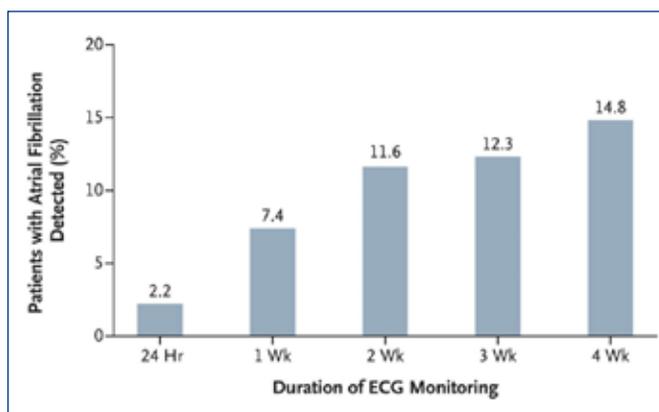
## DETECTION OF ATRIAL FIBRILLATION AFTER ISCHEMIC STROKE

Approximately one-third of all strokes are labelled as cryptogenic i.e., there is no cause identified despite a comprehensive workup. There is, however, growing recognition that paroxysmal atrial fibrillation is challenging to diagnose and can easily be missed with only short-term cardiac telemetry. So, a large proportion of patients with “cryptogenic stroke” may have atrial fibrillation that has simply not been diagnosed. Since strokes due to atrial fibrillation are eminently preventable – anticoagulation with inexpensive, widely available medications such as coumadin reduce the risk of stroke due to atrial fibrillation by approximately two-thirds<sup>14</sup> it is important to evaluate. Even brief bouts of atrial fibrillation substantially increase the risk of stroke.<sup>15</sup> The fact that strokes due to atrial fibrillation are so severe – and so treatable – lends an urgency to its detection.

Two recent trials are informative in this regard:

1) EMBRACE<sup>16</sup>: The EMBRACE trial was a study of patients aged 55 years and above who had suffered a cryptogenic stroke or cryptogenic TIA in the 6 months preceding screening and who had no evidence of atrial fibrillation after 24 hours of cardiac telemetry. The investigators randomized them to either a further 24 hours of telemetry or 30-days of continuous ambulatory cardiac rhythm monitoring. The primary outcome measure was the detection of 30 seconds of continuous atrial fibrillation. In the intervention group, 16.1% of patients were found to have new paroxysmal atrial fibrillation in contrast to a 3.2% of patients in the control group. They also demonstrated a very clear, incremental yield with an increased length of monitoring time. (Figure 4)

**Figure 4.** Incremental yield of prolonged ECG monitoring for the detection of atrial fibrillation in patients with cryptogenic stroke or TIA.<sup>16</sup>



This increased rate of diagnosis of atrial fibrillation resulted in an increased rate of anticoagulant therapy: 18.6% of the intervention group vs. 11.1% of the control group. This trial highlights the fact there is a significant

proportion of people who have been historically diagnosed with “cryptogenic” stroke who have probably had occult atrial fibrillation.

2) CRYSTAL-AF<sup>17</sup>: The CRYSTAL-AF trial examined the use of an insertable cardiac monitor (ICM) for the purpose of detecting paroxysmal atrial fibrillation. An ICM is a small device that is placed under the skin of the chest through a very minor outpatient procedure with no need for sutures or anesthesia. It has the ability to continuously monitor heart rate and remotely transmit data. The device is left in place for up to 3 years at a time and is well tolerated. The CRYSTAL-AF investigators enrolled patients aged 40 or older who had a stroke or TIA within the preceding 90 days and labelled as cryptogenic after a work-up which included 24 hours of EKG monitoring. 441 were successfully randomized to either the intervention group (ICM insertion) or the control group (with no specific protocol for heart rhythm monitoring specified). They also used the primary outcome of 30 seconds of continuous atrial fibrillation. In the patients assigned to the control group, the rate of atrial fibrillation diagnosis was only 1.4% at 6 months of follow-up whereas in the intervention group it was 8.9%. Only 2.4% of ICMs had to be removed in this study – the most common reason being local infection, pain or irritation.

The lower detection rate of atrial fibrillation in the CRYSTAL-AF study compared with the EMBRACE study may reflect the younger population that was studied in that trial. Alternatively, it could represent technical differences between the ability of an ICM and an ambulatory Holter monitor to detect atrial fibrillation. Both of these trials used 30 seconds of atrial fibrillation as a cutoff and so they may still underestimate the true prevalence of atrial fibrillation.

The growing recognition of embolism as a major cause of stroke – especially in those people diagnosed with a cryptogenic stroke – has led to the creation of a new clinical construct: embolic stroke of undetermined source (ESUS).<sup>18</sup> This refers to a stroke that appears embolic (i.e. it is multifocal, based in the watershed zone or cortically-based) and is too large to simply represent a lacunar infarct (i.e., is greater than 1.5cm in maximal diameter) but for which no cause can be found. The potential causes include atrial fibrillation, sub-stenotic or aortic arch atherosclerosis, and cardiac shunt. Recently, atrial dysfunction or cardiopathy in the absence of atrial fibrillation has been proposed as a mechanism in patients with ESUS. This is based on the fact that serum, ECG, and echocardiographic biomarkers of atrial cardiopathy have been shown to be associated with embolic risk in the absence of atrial fibrillation.<sup>19</sup> In addition, recent studies showed no temporal relationship between sub-clinical atrial fibrillation and embolic events, arguing that atrial fibrillation is a biomarker of atrial cardiopathy which in turn is the direct cause of stroke in most patients with this arrhythmia.<sup>19</sup>

## INSULIN RESISTANCE AND THE SECONDARY PREVENTION OF STROKE

Insulin resistance is a phenomenon observed in those with type 2 diabetes but also in approximately half of all people without diabetes who have had a stroke or TIA. There is a rich basic science literature on the interaction between insulin resistance and atherosclerosis, inflammation and thrombosis. This generated interest in whether or not treating insulin resistance itself would aid in the secondary prevention of ischemic stroke. The IRIS trial (Insulin Resistance Intervention after Stroke)<sup>20</sup> was designed to test whether administration of pioglitazone (a member of the thiazolidinedione drug class of oral hypoglycemic agents) would reduce the risk of recurrent stroke. In this trial, Kernan et al<sup>20</sup> (2016) studied patients 40 and older who had suffered an ischemic stroke or TIA in the 6 months prior to enrollment. Specifically, within that population they studied patients with evidence of insulin resistance but not frank type 2 diabetes. Patients were randomized to either pioglitazone (at a dose of 15mg which was ramped up to 45mg if well-tolerated) or placebo. Follow-up took place over 5 years and the primary outcome was the occurrence of stroke or myocardial infarction. 3876 patients were randomized to either pioglitazone or placebo – 1939 in the pioglitazone group and 1937 in the placebo group. This trial had a positive outcome: 11.8% of patients administered placebo reached the primary outcome over the 5 year follow-up period whereas only 9.0% of the patients administered pioglitazone did. The p-value for this result was significant at 0.007. Among secondary analyses, it was also noteworthy that the rate of progression to type 2 diabetes was lower in the pioglitazone group.

The results of this trial are impressive but there are a number of important caveats:

The risk of bone fractures was high in the group treated with pioglitazone: 5.1% of patient suffered a bone fracture in the treatment group compared with only 3.2% in the control group ( $p < 0.003$ ).

All patients with stroke or TIA were included in the trial irrespective of the cause of their stroke/TIA. Stroke is the endpoint of multiple, diverse disease states and not a disease itself per se. For instance, approximately 7% of patients in this trial had atrial fibrillation. A stroke due to atrial fibrillation would not be expected to be prevented by a medication that addressed insulin resistance. This point serves to caution against prescribing pioglitazone to a patient who has suffered a stroke, prior to first carefully evaluating the mechanism of the stroke.

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# Parkinson's disease: A Quick Update

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## ABSTRACT

Parkinson's disease is a neurodegenerative disorder characterized by motor and non-motor symptoms. Although the diagnosis still relies on the presence of motor signs, new diagnostic criteria have been proposed to incorporate recent observations in order to improve accuracy. The cornerstone of therapy remains dopamine replacement with L-Dopa. However, new therapies, with different modes of action, or administration have become available to improve management.

**KEYWORDS:** Parkinson's disease, movement disorder, extrapyramidal, tremor, deep brain stimulation

## BACKGROUND

Parkinson's disease (PD) is a neurodegenerative disease, characterized by motor and non-motor symptoms. The prevalence of the disease ranges from 100 to 200 per 100,000 people and its annual incidence is approximately 15 per 100,000. Men are more frequently affected than women and age of onset is variable, usually after age 50. Onset earlier than 40 years is observed in less than 5% of the cases. Aging increases the risk of developing the disease. Monogenetic forms are responsible for less than 10% of the cases, and the majority of cases are considered idiopathic. (1) In this paper, we will discuss the most recent published diagnostic criteria for PD as well as the most recent clinically available treatments.

## CLINICAL DESCRIPTION

The diagnosis of PD relies mostly on clinical expertise. Recently the International Movement Disorders Society published a proposed new set of criteria (2). In summary, the first step is to diagnose the presence of Parkinsonism defined by bradykinesia (slowness of movement, and decrement in amplitude or speed on continuous movement), in combination with either rest tremor, rigidity (velocity-independent resistance to passive movement), or both.

The second step in diagnosing "clinically established PD" requires the absence of absolute exclusion criteria; the presence of at least two supportive criteria; and no "red flags."

The diagnosis of clinically probable PD can be made in the absence of absolute exclusion criteria and the presence of red flags counter balanced by supportive criteria. Exclusion criteria include findings on the neurological examination suggestive of signs not seen in PD such as cerebellar, pyramidal or eye movement abnormalities. The most important red flags are rapid progression of gait and balance impairment, lack of progression of disease not attributable to treatment, and absence of any of the common non-motor features of the disease.

## IMAGING STUDIES

Imaging is not helpful in diagnosing PD and is used only for atypical cases. 123I-ioflupane SPECT (DatSCAN) is approved for distinguishing essential tremor from PD and is probably also helpful, although not approved, for distinguishing drug-induced parkinsonism from PD. DaT is normal in ET and DIP. However, DaTSCAN is also abnormal in patients with other forms of primary Parkinsonism which attack the dopaminergic cells in the basal ganglia (3) Therefore DaT, if normal, excludes the diagnosis of PD but a positive scan does not make the diagnosis.

## TREATMENT

PD treatment involves a combination of life style measures, medication and, in some cases, surgery. In the following section, we will discuss newer therapeutic interventions.

### Exercise

Exercise improves motor and non-motor symptoms, such as pain, sleep and mood. Most experts agree that exercise should be encouraged as part of the treatment (4). There are no data to suggest an optimal exercise strategy, so that common sense dictates that the regimen chosen should: (a) take into consideration safety, motor and cognitive constraints and other medical comorbidities; (b) be an activity the patient is comfortable with; (c) be one the patient will likely adhere to.

### Medication

The choice of the initial therapy of patients with PD takes into account age, employment status, presence of comorbidities, cognitive status, active psychiatric issues, and patient

preference. There are no therapies known to slow disease progression. Even though there is no consensus on the best time for therapy to be initiated, there is also no reason to withhold therapy in those with clear symptoms in order to prevent future treatment-related complications.

#### *Motor symptoms*

**1) Levodopa:** A precursor in dopamine synthesis remains the superior drug in symptom control. A new formulation of carbidopa/levodopa is available. Rytary ( Impax Laboratories, Hayward, CA, USA) is an oral, extended-release capsule that contains beads of levodopa and carbidopa with differing rates of absorption, allowing for a decreased dosing frequency. Rytary is FDA approved for both drug naive patients and those with motor complications by increasing "on" times, without worsening troublesome dyskinesias. Its side effect profile and tolerability are similar to other levodopa preparations. (5, 6) There are no long-term data on starting patients directly on Rytary compared to immediate release (IR) levodopa. The major indication to switch a patient from the IR formulation to Rytary is the presence of wearing off, especially if the patient is already receiving IR at a frequency of over 4 doses a day. The ratio for conversion is approximately 2:1 (Rytary: IR levodopa), and it can be done overnight. Since part of the formulation contains IR granules, patients should be advised to avoid taking medication with food (at least 30- minute interval). Rytary can take up to 8 weeks for the full benefit to be observed after the switch, and dose adjustments are usually required (7).

**2) Dopaminergic agonists (DA):** DA bind to post-synaptic dopamine receptors. They can be used as monotherapy in patients with early disease or as adjunctive therapy in later disease stages. The main adverse effects are nausea, vomiting, edema, hypotension, excessive daytime sleepiness and sleep attacks, impulse control disorders and hallucinations, especially in elderly patients. The most commonly used are pramipexol, ropinirole and rotigotine. Apomorphine has a different profile from other agonists with potent D1 and D2 agonist action. Apomorphine is available as an intermittent injection and in other countries as a continuous infusion. It has poor bioavailability after oral ingestion. The ideal subjects are on an optimized oral schedule, are able to both recognize their "off" state and to inject themselves (or have a caregiver to do it). Indications are the need for rescue medication (early morning "off", delayed "on", unpredictable "offs") or gastroparesis. Subcutaneous apomorphine is rapidly absorbed and peak plasma concentration is achieved in 10 to 20 minutes, with a clinical effect lasting from 45 to 60 minutes. First apomorphine injection should be monitored particularly for hypotension and nausea. Side effects include nausea, injection site reactions, postural hypotension, confusion, psychosis, impulse control disorders, and rarely hemolytic anemia and eosinophilic syndrome. (8) Nausea is so common that an antiemetic is always started before

the first dose, and is required for ongoing treatment in about half the cases.

**3) MAO-B inhibitors** increase dopamine availability by inhibition of monoamine oxidase B, which metabolizes dopamine. They can be used as monotherapy in mildly symptomatic young subjects or as adjunctive therapy. Side effects include nausea, vomiting and insomnia (selegiline). Safinamide (XADAGO), the newest agent, has dopaminergic action, by selective and reversible inhibition of MAO-B, and nondopaminergic properties due to voltage-gated sodium and N-type calcium channels inhibition, modulating glutamate release. It is indicated as adjunctive treatment in patients with PD experiencing "off" episodes, as it increases "on-time" with no increase in bothersome dyskinesias. Efficacy as monotherapy has not been established. Common adverse events (AEs) include dyskinesia, insomnia, somnolence, dizziness, headache, cataract, orthostatic hypotension, nausea and falls. (9, 10) Relative efficacy of MAO-b inhibitors is unknown. Safinamide is a reversible MAO-b inhibitor, unlike selegiline and rasagiline. Thus the effects of safinamide begin much sooner than the older drugs, and resolve much sooner if discontinued.

**4) Amantadine:** amantadine extended release capsules (GOCOVRI) is the first and only FDA-approved medicine for treatment of dyskinesia in patients with Parkinson's disease receiving levodopa therapy, with or without concomitant dopaminergic agents. It reduces both off times and well as levodopa-induced dyskinesias in PD patients with dyskinesias (11). There are no data to determine if this formulation is more effective than the generic form of the drug, which is usually given 2 or 3 times daily.

#### *Non-motor symptoms*

**1) Pimavanserin:** is a selective 5-HT<sub>2A</sub> inverse agonist with a lower affinity for 5-HT<sub>2C</sub> and sigma-1 receptors. It lacks dopaminergic, muscarinic, adrenergic, and histaminergic activity. (12) Data suggests a high benefit/risk profile with number need to treat (NNT) <10 (using a very conservative definition of improvement), number needed to harm (NNH) was ≥ 10 (although not statistically different from placebo) and the likelihood to be helped by taking the medication was consistently over 1 (13). Pimavanserin is the only drug with FDA approval for the treatment of hallucinations and delusions associated with PD psychosis. (12)

**2) Droxidopa:** is an oral norepinephrine precursor approved for the treatment of neurogenic orthostatic hypotension caused by primary autonomic failure. Studies show a good safety profile with NNT <10, NNH from 23-302. Droxidopa is 7.8 times more likely than placebo to provide clinical benefit than drug discontinuation due to an adverse event. (14) Droxidopa has been studied in patients with PD showing similar results, leading to decreased number of falls and increased standing systolic blood pressure. (15, 16)

### Device-aided treatments

Response to levodopa is a prerequisite for all therapies below as neither is helpful in patients not responsive to the drug. Patients with drug-resistant tremor may respond well to DBS, though, when L-Dopa is not helpful.

**1) Levodopa-carbidopa intestinal gel (LCIG)** is an aqueous gel containing a combination of levodopa and carbidopa (20 mg and 5 mg respectively per milliliter) delivered directly to the proximal jejunum *via* a percutaneous endoscopic gastrostomy tube with a jejunal extension connected to a portable, programmable infusion pump. By bypassing gastric emptying, levodopa is steadily absorbed producing stable plasma concentrations, thus decreasing motor complications (dyskinesia and motor fluctuations). Dose is individually titrated, and after a morning bolus a continuous infusion is administered over 16 hours, with further bolus if necessary. LCIG may be administered as monotherapy, or with adjunctive therapies. The treatment may be continued for as long as it is beneficial. Procedure/device related adverse events are reported in 76% of subjects; 17% of those are considered serious. Most frequent non-procedure/device adverse events are dyskinesias, chronic polyneuropathy (due to vitamin B deficiencies), stoma infection and weight loss. (17, 18)

**2) DBS:** The two main sites of DBS placement are the subthalamic nucleus (STN) and the globus pallidus (GPi). STN-DBS improves off-drug score compared with preoperative off-drug condition; decreases off-time during the day; improves quality of life; and allows the decrease in levodopa equivalent daily dose resulting in the reduction in levodopa-induced dyskinesia. (19) A recent analysis in the German health care system suggested that STN-DBS at earlier stages of the disease is cost effective in patients younger than 61 years when compared with the best medical treatment (20). GPi-DBS also provides improvement in motor scores associated with reductions in dyskinesias with modest or no decrease in dopaminergic therapy. Complications of DBS are either related to surgery, implanted material or by stimulation itself. Severe adverse events such as death or permanent disability are rare, and occur in less than 2% of the cases, while hardware-related adverse events are observed in 9% of the cases. Much more common are reversible adverse effects of stimulation, which may happen in up to 20% of patients. Long-term follow-up demonstrates sustained benefits of STN-DBS and GPi-DBS despite disease progression. Practitioners should be aware that DBS does not slow disease progression and should be considered another symptomatic therapy. It is considered a stand-of-care treatment, covered by all insurers.

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# Fighting Fire with Fire: Surgical Options for Patients with Drug-Resistant Epilepsy

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## ABSTRACT

While antiepileptic drugs (AEDs) provide adequate seizure control for most patients with epilepsy, ~30% continue to have seizures despite treatment with two or more AEDs.<sup>1</sup> In addition to direct harm from seizures, poor epilepsy control correlates with higher mortality, morbidity,<sup>2,3</sup> and cost to the healthcare system.<sup>4</sup> In the subset of patients with persistent seizures despite medical management, surgical intervention and neuromodulation may be more effective. Primary care physicians and general neurologists should be aware of non-AED treatment options that are standard of care for drug-resistant epilepsy (DRE).

**KEYWORDS:** Drug-resistant epilepsy, surgical treatment of epilepsy, vagal nerve stimulation, responsive neuro-stimulation

## DRUG-RESISTANT EPILEPSY: ITS CONSEQUENCES

Epilepsy affects ~1% of the United States population.<sup>1</sup> Despite an expanding selection of AEDs, many patients continue to have seizures, even with AED polypharmacy.<sup>1</sup> The International League Against Epilepsy (ILAE) defined drug-resistant epilepsy (DRE) as failure of adequate trials of two appropriate, well-tolerated antiepileptic medications (whether as monotherapies or in combination) to achieve sustained seizure freedom.<sup>5</sup>

DRE is associated with higher long-term morbidity and mortality<sup>3</sup> including sudden unexplained death in epilepsy (SUDEP), accidental injury and death, cognitive decline, as well as psychiatric and psychosocial comorbidities.<sup>2</sup> SUDEP is defined as non-traumatic, non-drowning-related sudden death in a person with epilepsy which may or may not be related to recent seizure but is not due to status epilepticus, with autopsy that is unrevealing of an obvious anatomic or toxic cause of death,<sup>6</sup> and is thought to be related to seizure-induced cardiac arrhythmias. SUDEP is the most common epilepsy-related cause of death, with an incidence of up to 9.3 deaths per 1000 person-years among some with DRE.<sup>6</sup> The strongest risk factor for SUDEP is recurrent seizures.<sup>6</sup>

Seizures impede patients' freedom to pursue education and careers,<sup>7</sup> drive,<sup>6</sup> and live independently. AED side effects

can also adversely affect quality of life (QOL),<sup>8</sup> and have implications for patients' overall health. Patients with DRE require more ER visits and hospitalizations, longer hospital stays, more office visits, and accumulate up to double the healthcare costs of those with stable epilepsy.<sup>4</sup>

## EPILEPSY CENTERS

Neurologists differentiate seizures that are "generalized" in onset (e.g. seizures arising from the entire brain at onset) from those that are "focal" or "partial" (e.g. seizures starting from one part of the brain). Classification systems for epilepsy are complex, relying on factors including clinical history, physical examination, EEG and MRI findings. Therefore, all patients with epilepsy should have a neurologist, preferably one with additional training in epilepsy. The National Association of Epilepsy Centers (NAEC) recognizes four levels of epilepsy care. Level 1 care consists of evaluation at an emergency department or primary care office, while level 2 care involves assessment by a general neurologist. Levels 3 and 4 are offered at specialized epilepsy centers, which provide a comprehensive approach to DRE.<sup>9</sup> The NAEC recommends referral to an epilepsy center if seizure freedom is not achieved within one year of treatment.<sup>9</sup> Earlier referral is recommended if the epilepsy diagnosis is in question, or in the following additional situations: to distinguish epileptic from psychogenic non-epileptic events; to optimize seizure control in non-refractory patients; to integrate neurologic and psychiatric care; and to optimize AED management for family planning. Other epilepsy center services include surgical evaluation, counseling on epilepsy-related dietary modifications, and care for developmental disabilities. The Brown-Rhode Island Hospital Comprehensive Epilepsy Program is a level 4 epilepsy center.

## PREOPERATIVE EVALUATION

DRE rates are higher in focal epilepsy (35%) than in generalized epilepsy (25%).<sup>6</sup> Some focal epilepsies are associated with an underlying lesion, such as a stroke, tumor or vascular malformation, whereas others lack an overt structural abnormality apparent on MRI. Feasibility of surgical intervention should be explored as soon as focal DRE is diagnosed, since intervention can result in seizure reduction or seizure-freedom, with associated potential benefits including improved morbidity and mortality, better QOL, improved

psychiatric outcomes, and decreased AED requirement.<sup>1,3</sup>

Preoperative workup includes long-term video EEG monitoring and high-resolution brain MRI. Further investigations can include positron emission tomography, single photon emission computed tomography (SPECT), magnetic resonance spectroscopy, subtraction ictal SPECT co-registered to MRI, functional MRI, and magnetoencephalography.<sup>10</sup> In many cases, patients initially diagnosed with 'non-lesional' epilepsy are found to harbor a subtle lesion using these techniques.

Neuropsychological testing is used to assess for potential preoperative cognitive impairments and to predict postoperative neuropsychological outcomes.<sup>10</sup> For patients with temporal lobe epilepsy (TLE), Wada testing defines language localization and risk-stratifies the patient regarding possible postoperative memory impairment.<sup>10</sup> This test involves anesthetizing one hemisphere while a neuropsychologist performs rapid testing to characterize language and memory function in the contralateral hemisphere.

Our epilepsy center conducts multidisciplinary conferences to review potential surgical candidates. This forum draws upon the expertise of specialists from epilepsy, neurosurgery, neuroradiology and neuropsychology departments to formulate an individualized approach for each patient. Depending on the patient's needs, the team may include other specialists such as a psychiatrist, nutritionist, and social worker.

After the first phase of preoperative testing, some patients are found to be good surgical candidates and are referred to neurosurgery. Other patients may be deemed poor candidates for resective or ablative surgery for various reasons, such as the determination that the seizure focus stems from an important structure needed for language or mobility, or the finding of seizures from multiple foci. However, recent advances in the treatment of epilepsy offer hope for patients facing these difficult situations. Alternatives include an ever-growing list of AEDs, hormonal treatments, low glycemic index dietary approaches, and neuro-stimulation devices.

### **SURGICAL OPTIONS AND OUTCOMES IN EPILEPSY**

Temporal lobe epilepsy (TLE) is among the most common focal epilepsies,<sup>11</sup> and is sometimes associated with scarring of the mesial structures including the hippocampus, called mesial temporal sclerosis (MTS). TLE is the focal epilepsy syndrome most amenable to surgery, and anterior temporal lobectomy (ATL) is the most common epilepsy surgery.<sup>12</sup> Therefore, many studies of surgical outcomes in focal epilepsy have emphasized the study of TLE patients who undergo ATL. Classically, ATL consists of the removal of some anterior-lateral temporal cortex plus resection of the amygdala, para-hippocampal cortex, and hippocampus.<sup>9,12</sup> Many such patients have MTS demonstrated on MRI and this subgroup has historically done extremely well with surgical intervention. More recently, selective ablation of the mesial temporal lobe structures (hippocampus and amygdala) using

laser-thermal technology has demonstrated nearly equivalent outcomes for seizure control and improved neuropsychological outcomes due to sparing of lateral neocortical structures and adjacent white matter tracts.<sup>13,14</sup> Other surgeries for focal epilepsy include topectomy, in which cortex is removed while sparing underlying white matter, as well as lesionectomy, extratemporal lobar or multilobar resections, multiple subpial transection, and hemispherectomy.

In a landmark randomized controlled trial (RCT) of surgical versus medical management in patients with drug-resistant TLE, resection resulted in seizure-freedom in 58% when evaluated one year after surgery, compared with 8% with medical management;<sup>7</sup> a second RCT demonstrated 73% seizure-freedom after two years of follow-up among patients who had surgery within two years of developing DRE, compared with 0% seizure-freedom in medically-managed patients.<sup>1</sup> Approximately 45% of patients were seizure-free after resection for extra-temporal lobe epilepsy.<sup>1</sup>

Data suggest that the earlier the surgery, the better the outcome.<sup>1</sup> Sex and age do not affect surgical outcomes.<sup>1</sup> While older age was previously thought to be a relative contraindication to epilepsy surgery, a retrospective analysis of ATL for MTS showed that age at surgery did not independently affect seizure recurrence.<sup>8</sup> Although patients with an identifiable lesion are more likely to experience postoperative seizure reduction or seizure freedom,<sup>1</sup> patients with non-lesional DRE can also benefit from surgery if seizures are well-localized on EEG.

Even when patients do not achieve total seizure-freedom postoperatively, reduction in seizures can be quite significant. A meta-analysis of studies of medically refractory TLE cases treated with surgical resection at 13 centers, 67.2% of patients achieved seizure-freedom and an additional 20% experienced improvement.<sup>7</sup> Thus, 87% of the patients achieved significant seizure reduction with surgery. Many patients with DRE experience numerous seizures each day, so reduction in seizure burden can be life-changing for patients and caretakers. Additionally, a systematic review of QOL for adults after epilepsy surgery has shown that QOL is significantly improved after surgery, with the most significant gains seen in those attaining seizure-freedom.<sup>1</sup>

NAEC-published data indicates that of the ~750,000 patients in the USA with DRE, a mere 2,459 patients, on average, underwent resection surgery each year from 2012 through 2015.<sup>15</sup> Several factors limit the identification and treatment of potential surgical candidates. First, many with DRE are not referred to an epilepsy center. DRE patients also vary in the degree to which seizures are disabling, and may forgo evaluation if the patient and treatment team feel that the seizures are not disruptive or limiting to quality of life.

### **SURGICAL RISKS AND ALTERNATIVES**

Risks associated with epilepsy surgery are defined by the location of the epileptic focus. For example, TLE surgery is

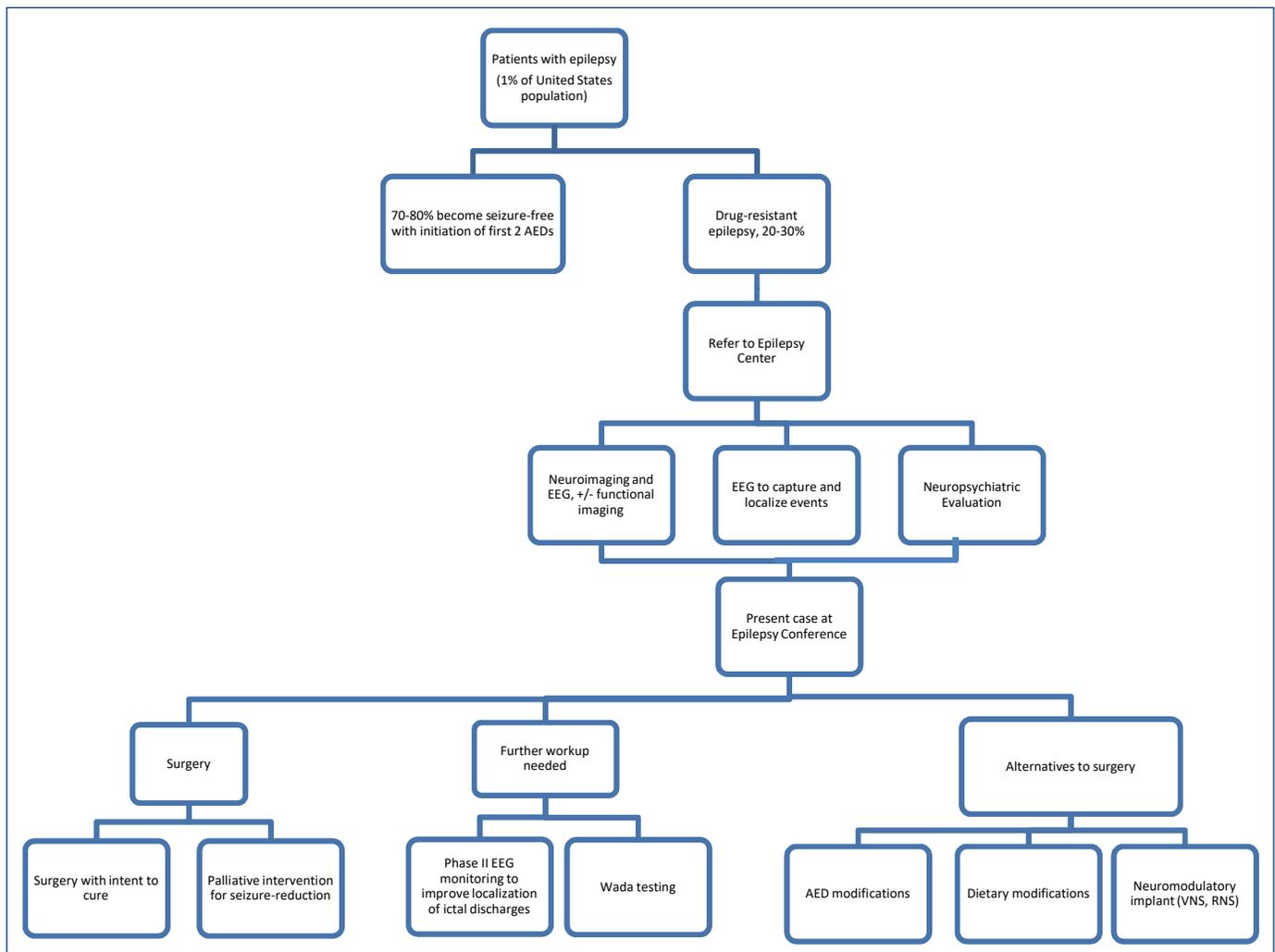
associated with risks of language deficit, memory impairment, motor impairment, visual field cut, cranial nerve injury, and behavioral/personality changes depending on the location of the focus.<sup>10</sup> With newer, less invasive and more tissue-sparing techniques for epilepsy surgery, the incidence of these has decreased. Reviews of epilepsy surgery have shown that operative mortality ranges from 0.1% to 0.5%.<sup>1</sup>

Apart from resective surgery, alternative options include vagus nerve stimulation (VNS) or responsive neuro-stimulation (RNS). VNS is an option to treat DRE which is not amenable to conventional resection, and for patients with persistent DRE after surgical resection.<sup>12</sup> VNS implantation involves surgical placement of a generator below the clavicle, with a stimulating wire connected to the left vagus nerve, to deliver intermittent stimulation.<sup>12</sup> The mechanism of action of VNS is speculated to relate to desynchronization of cortical activity.<sup>16</sup> A meta-review of 14 VNS outcomes studies demonstrated that ~50.9% of patients achieved a >50% reduction in seizure frequency.<sup>16</sup> The efficacy of VNS increases over approximately two years

following implantation.<sup>17</sup> Bilateral or multifocal epilepsy may be associated with even better VNS outcomes.<sup>18</sup> Common but generally tolerated side effects include hoarseness and neck-tingling.<sup>16</sup>

RNS was FDA-approved in 2013 for patients 18 years or older with focal DRE and no more than two epileptic foci. RNS implantation involves neurosurgical placement of subdural or depth electrodes near the focus. Seizure pattern-detectors in the device are programmed to trigger direct cortical stimulation upon detection of an ictal buildup.<sup>19</sup> Electrical stimulation at the onset of ictal discharge is intended to interrupt propagation of the discharge before the seizure generalizes and the patient becomes symptomatic. The RNS System Pivotal trial, a multicenter RCT to evaluate short-term efficacy of RNS versus sham treatment, demonstrated a 37.9% decrease in mean seizure frequency in the treatment group, compared to 17.3% seizure reduction in the control group.<sup>17</sup> Patients receiving RNS treatment demonstrated statistically significant improvements in verbal functioning, visuospatial ability, memory, social function, health concerns, and

Figure 1. General approach to evaluation in DRE



cognition at one and two years post-implantation.<sup>19</sup> There were also significant improvements in QOL scores.<sup>19</sup> Some common complications and side effects of RNS noted during the Pivotal trial included implant site pain, local swelling or infection, headache, and dysesthesia.<sup>19</sup> Another disadvantage is the necessity of repeated surgery for battery changes, with an average battery life of 3.8 years.

## CONCLUSIONS

The care of patients with DRE necessitates a multidisciplinary approach with integrated access to specialized diagnostic tools that guide the care team toward individualized treatment plans for each patient. Surgery is helpful for a subset of DRE patients. Many patients can achieve seizure-freedom after surgery. In those not achieving complete seizure-freedom, surgery can lead to a meaningful reduction in seizures, reduce risk of seizure-associated injury, and allow for reduction in medication burden. Even when the patient is disinterested in or hesitant to pursue surgery, referral to an epilepsy center can help to optimize the AED regimen, manage comorbidities and AED complications, manage key life transitions that affect epilepsy care, and explore neuromodulation among other options.

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# Suboptimal Opioid Prescribing: A Practice Change Project

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## ABSTRACT

In the U.S. in 2015, the proportion of people dependent on opioids approached one percent, and opioid overdose rivaled auto accidents as the leading cause of accidental death. The literature suggests a credible link between increased opioid prescribing and increased opioid addiction. Accordingly, some have suggested that limiting the number of opioid prescriptions (and the number of doses per prescription) might be effective in reducing the number of opioid-related deaths. Toward this end, we designed and piloted an evidence-based quality-improvement project in four urgent care clinics. Results of the intervention were monitored with data from a state-sponsored prescription drug-monitoring program (PDMP) by comparing opioid prescribing before and after adoption of the guideline, and in this manner, a statistically significant ( $P < 0.05$ ) decline in the rate of opioid prescribing was revealed. On average, 2.43 fewer opioid prescriptions were written, per provider, per week, in weeks five through eight after promulgation (5.21, SD =4.37) than in the eight weeks before promulgation (7.64, SD =7.73). Our results suggest that implementing a simple opioid-prescribing guideline, with monitoring, can reduce sub-optimal opioid prescribing, and therefore the volume of opioids available in the community for diversion, abuse, and addiction.

**KEYWORDS:** opioid prescription, opioid epidemic, urgent care, prescribing guidelines, practice change

## INTRODUCTION

In the U.S. in 2015, the proportion of people dependent on opioids approached one percent (809 per 100,000),<sup>1</sup> and the mortality rate from opioid overdose exceeded 10 per 100,000. In the same year, the number of opioid deaths (33,091) in the U.S. approached the number of traffic fatalities (35,092), rivaling the latter for the most important cause of accidental death in the nation.<sup>2</sup>

Opioid prescribing, which began increasing in the U.S. in the early 1990s, has been linked to increasing numbers of people addicted to opioids, and, in turn, increasing numbers of opioid overdose incidents and deaths.<sup>3</sup> In Rhode Island, the opioid “epidemic” (of overdose incidents and deaths) has

been especially problematic. For example, in 2015, Rhode Island’s age-adjusted death rate from “drug-induced causes” was 28.9 per 100,000, 68 percent higher than the overall U.S. rate (17.2 per 100,000), and 5th highest among the 50 states and the District of Columbia. Furthermore, Rhode Island’s current standing represents a significant deterioration over the past decade and a half. In fact, since 1999, the state’s age-adjusted drug-induced death rate has doubled twice. At that time, Rhode Island’s rate was 5.8 per 100,000, 15 percent lower than the overall U.S. rate (6.8), and 24th highest among the 50 states and the District of Columbia. Rhode Island’s death rate from drug-induced causes has been especially high in the past several years.

On the basis of the *prima facie* correlation between trends in opioid prescribing and trends in opioid addiction, opioid overdose incidents, and opioid-induced deaths, some have suggested that by reversing the trend in opioid prescribing, one might reverse the trends in untoward outcomes, as well. Recent literature indicates that prescribing guidelines, combined with prescription monitoring, may be used to help health prescribers make more informed choices in the use of analgesics.<sup>4,5</sup> Accordingly, we designed and piloted a practical, evidence-based quality-improvement project to limit opioid prescribing in urgent care settings, focusing on the treatment of acute pain.

## SETTING

The pilot was implemented in four privately owned urgent care centers (“the centers”) under common management in the State of Rhode Island, staffed by 14 physicians and mid-level practitioners. The centers care for the usual mix of urgent care complaints, which include acute pain associated with minor injuries, infections, and inflammations, for which opioids may be prescribed. The combined average number of patients seen in the clinics is 2.75 patients per provider per hour. The patients seen through the clinics are pediatric through geriatric, with 95% being adult and the majority of the children being in the adolescent age group. All forms of medical insurance including all major insurances, state health coverage and self-pay are accepted at OSUC clinics. Prior to the pilot, the centers had adopted an electronic medical record system in which the default maximum for opioid prescribing is 15 doses, which amounts to

3–5 days’ use at one dose every four to six hours. Prescribers may exceed the default, but it serves as a reminder of current guidelines from the Centers for Disease Control and Prevention (“CDC”):

“Patients who are prescribed opioids for acute pain are more likely to use opioids long-term, and a greater amount of early opioid exposure (taking opioids for a longer time or at higher doses) is associated with greater risk for long-term use. Physical dependence on opioids is a physiologic response in patients exposed to opioids for more than a few days. Several previous guidelines on opioid prescribing for acute pain from emergency departments and other settings have recommended prescribing <3 days of opioids in most cases, whereas others have recommended <7 days or <14 days. The Guideline recommends that if opioids are needed in cases of acute pain (not related to major surgery or trauma, such as acute back pain, sprained ankle), ≤3 days will often be sufficient – unless circumstances clearly warrant additional opioid therapy – and that more than 7 days will rarely be needed. If pain continues longer than expected, providers should re-evaluate the patient to make sure nothing was missed.”<sup>6</sup>

An examination of the prescribing behavior of the centers’ 14 providers in the eight weeks prior to implementation of the pilot (based on prescriber-specific reports generated by Rhode Island’s Prescription Drug Monitoring Program – PDMP<sup>7</sup>), demonstrated restraint in the use of opioids. On average, most prescriptions were written for 2–5 doses, equivalent to 1–2 days’ treatment. Only one prescriber differed substantially from this profile, with an average of 30 doses per prescription, equivalent to 5–7 days’ treatment. Given this laudable starting point, the pilot focused primarily on *whether or not* to prescribe opioids – as opposed to non-opioid analgesics – for treatment of acute pain.

**INTERVENTION**

The intervention was composed of three elements: provider education, guidelines for opioid prescribing, and monitoring of prescribing behavior.

**Provider Education**

A PowerPoint presentation with supplemental hand-outs was developed from the “CDC Guideline for Prescribing Opioids for Chronic Pain – United States”<sup>7</sup> (and key references therein), and presented to all prescribers in each of the four centers. The CDC’s “Guideline” contains a wealth of information on opioid use and misuse, including an assessment of the relation between short-term use of opioids for acute pain and long-term use of opioids for chronic pain.

**Guidelines**

The following guidelines were adopted:

- 1) Before prescribing opioids, assess the patient’s prescrip-

tion history, by generating a patient-specific report from Rhode Island’s Prescription Drug Monitoring Program database (“PDMP”). Assess patterns of opioid use, and look for other prescriptions which may cause adverse reactions in combination with opioids, such as benzodiazepine.

- 2) Limit all opioid prescribing to a 7 days’ supply.

**Monitoring of Prescribing Behavior**

Opioid prescribing was monitored before and after adoption of the guidelines, to assess the effect of the pilot. Provider-specific prescribing profiles generated by Rhode Island’s PDMP were used for this purpose.

**ASSESSMENT OF THE INTERVENTION**

Using PDMP profiles, we compared opioid prescribing in the eight weeks before adoption of the guideline, t(0), in weeks 1–4 post-adoption, t(1), and in weeks 5–8 post-adoption, t(2). The data from pre- and post-intervention PDMP reports were compared in EXCEL spreadsheets. We summarized opioid prescribing using means, standard deviations, standard errors, and upper and lower 95% confidence intervals. (See Tables 1 and 2.) Paired t-tests were conducted to assess the statistical significance of changes in opioid prescribing, using P < 0.05 as a cut-off for tests of statistical significance.

**RESULTS**

The summary statistics in Table 1 demonstrate a decline in the average number of opioid prescriptions written per provider per week over the course of the pilot. The decline was immediate. On average, 1.89 fewer opioid prescriptions were written per provider per week in the four weeks post-intervention, t(1), as compared with the eight weeks pre-intervention, t(0). Over 14 providers, this amounts to 106 fewer opioid prescriptions written, or about 577 doses dispensed. The decline was sustained in weeks 5–8 post-intervention,

**Table 1.** Mean number of opioid prescriptions per provider per week across four urgent care settings, as measured in three time periods:  
 t(0): weeks minus 8 through minus 1 before adoption of new prescribing guidelines  
 t(1): weeks plus 1 through plus 4 after adoption of new prescribing guidelines  
 t(2): weeks plus 5 through plus 8 after adoption of new prescribing guidelines

Period	Mean	Std. Deviation	Std. Error Mean
t(0) Average of 8 weeks before Intervention t(0) N=14	7.64	7.53	2.01
Average of weeks 1-4 after Intervention t(1) N=14	5.75	7.38	1.97
Average of weeks 5-8 after Intervention t(2) N=14	5.21	4.47	1.16

but with less variation in the number of opioid prescriptions written per provider, i.e., with *more uniformity of prescribing across providers*, as revealed by the standard deviations calculated for t(0), t(1), and t(2): 7.53, 7.38, and 4.77, respectively.

Turning to **Table 2**, the decline in opioid prescribing between t(0) and t(2) was found to be statistically significant ( $P < 0.05$ ), on the basis of the paired t-test. Other declines, i.e., between t(0) and t(1) and between t(1) and t(2), did not achieve statistical significance, primarily because of the rather large standard deviations computed for paired comparisons in t(0) and t(1).

**Table 2.** Differences in the mean number of opioid prescriptions per provider per week across four urgent care settings, as measured in three time periods:

t(0): weeks minus 8 through minus 1 before adoption of new prescribing guidelines

t(1): weeks plus 1 through plus 4 after adoption of new prescribing guidelines

t(2): weeks plus 5 through plus 8 after adoption of new prescribing guidelines

	Paired Differences					t	df	Sig. (1-tail)
	Mean	Standard Deviation	Standard Error	95% Confidence interval of the difference				
				Lower	Upper			
t(0) vs. t(1) (N=14)	1.07	1.76	3.08	-3.02	3.14	0.61	13	p=0.27
t(1) vs. t(2) (N=14)	-3.50	2.12	4.51	-6.15	3.87	-1.64	13	P=.060
t(0) vs. t(2) (N=14)	-2.43	1.23	1.51	-4.39	-0.47	1.97	13	p=0.035

## DISCUSSION

Although reducing the number of people addicted to opioids is the goal of our intervention and others like it, the effects of such interventions will, unfortunately, not be seen immediately, so obstinate is the problem. Nevertheless, what *can* happen immediately is a reduction in the number of opioid doses available for diversion in the community. Our results suggest that a simple opioid prescribing intervention, combining provider education, a simple prescribing guideline, and prescription monitoring, can decrease the number of opioid prescriptions written by urgent care providers. Ostensibly, the patients who *might* have been treated with opioids were treated with alternative medications or therapies, thereby reducing the number of *unnecessary* opioid doses available for diversion.

Can similar results be obtained in other settings? Quite possibly. Certainly, the simplicity of our intervention lends itself to a wide variety of settings, as “*initial*” opioid prescribing for *acute* pain occurs in virtually all settings in

which opioids are prescribed. In continuity-of-care settings, of course, it is also desirable to institute parallel guidelines for the use of opioids in the treatment of *chronic* pain.

In any setting, however, we believe that *monitoring*—with the use of PDMP reports— is key. Fortunately, PDMP systems have become more common—and accessible—across the United States, which should facilitate the use of PDMP reports in interventions such as the one we piloted.

Finally, we offer a related—and of late, crucial—caveat: In today’s opioid-saturated world, providers—in all health-care settings—*must* be equipped to assess and to refer those

patients whom they suspect to be developing or to have developed a dependency on these medications. Simply limiting the number of doses prescribed, without additional support, such as may be effected by means of an appropriate referral to a center specializing in the treatment of chronic pain or of opioid addiction, *may* encourage some patients to seek an illicit source of prescription opioids or of heroin—or so it would seem, despite a scarcity of studies on this very issue.<sup>8</sup> Certainly, there is a connection between the use of prescribed opioids and heroin use among “recent users of heroin,”<sup>9</sup> and this, in and of itself, calls for prudence, not only in prescribing, but in the evaluation of patients

and the potential need for referral to pain or addiction specialists. Again, provider awareness and *education* is key, not to mention some form of goal-setting and monitoring (of assessment and referral practices). In this vein, the Rhode Island Department of Health, among many other public health agencies, recommends adoption of a protocol called “Screening Brief Intervention and Referral to Treatment” or simply “SBIRT.”

### Screening Brief Intervention and Referral to Treatment (SBIRT):

Consider screening all patients annually or upon entry to your practice to assess potential risk for substance abuse. Tools such as the Opioid Risk Tool (ORT) as well as DAST 10 (Drug and Alcohol Screening Tools 10) and several more tools available from Substance Abuse and Mental Health Services Administration (SAMHSA).<sup>10</sup> [For additional information on SBIRT from SAMHSA, see: <https://www.samhsa.gov/sbirt> ]

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## A 57-year-old man with a spontaneous carotid artery dissection

PAUL COHEN, MD; NICHOLAS MUSISCA, MD; WILLIAM BINDER, MD

*From the Case Records of the Alpert Medical School of Brown University Residency in Emergency Medicine*

**DR. PAUL COHEN:** Our patient is a 57-year-old male who presented to the emergency department complaining of acute onset left-arm heaviness, paresthesias, and weakness while typing on his computer. The initial symptoms lasted for approximately 20 minutes, and the patient activated emergency medical services (EMS), who administered aspirin while en route. By the time the patient arrived to the emergency department his symptoms had mostly abated. Review of systems was positive for two days of mild shortness of breath and intermittent tinnitus in his right ear. The patient's past medical history includes hypertension and hyperlipidemia for which he takes felodipine and simvastatin. He uses tobacco and has a family history of heart disease and stroke.

The patient's physical exam was unremarkable. His temperature was 36.8°C, HR 71, BP 154/96 mmHg and oxygen saturation 97% on room air. His lung, cardiac and abdominal exam were normal, and pulses were 2+ in the bilateral radial and posterior tibial arteries. The patient had a normal neurologic examination. He was alert and oriented, there was no apraxia or neglect appreciated, and his speech was fluent and without aphasia. His cranial nerves II-XII were intact, his tone was normal and no fasciculations were noted. Sensation was intact to light touch, temperature, and proprioception bilaterally. There was no dysmetria with finger to nose. The patient had no ataxia.

**DR. LAURA MCPEAKE:** What was your primary consideration for this patient and what was done?

**DR. COHEN:** Our main concern included a primary neurologic event such as an ischemic or hemorrhagic stroke, TIA, cervical artery dissection, hemiplegic migraine, and radiculopathy. ACS was briefly considered given the patient's shortness of breath and left arm heaviness. Other neurologic mimics such as hypoglycemia and post-ictal paralysis were viewed as unlikely given the patient's history, exam, and normal blood sugar.

The patient's ECG, laboratory work-up, and non-contrast CT of the brain were unremarkable. Given the suspicion



**Figure 1.** Patient's CT scan showing a dissection of the right internal carotid artery.

for dissection, a CTA of the head and neck was performed, which demonstrated a high-right cervical internal carotid artery dissection. (Figure 1). CTA and MRA have replaced angiography for the diagnosis of cervical artery dissections.<sup>1</sup> While there is no clear benefit of one imaging modality over the other, CTA is often easier to obtain, demonstrates intraluminal abnormalities, and has been reported to have a greater accuracy in diagnosing vertebral artery dissections.<sup>2</sup> On the other hand, MRI/MRA does not involve ionizing radiation and provides better visualization of the brain in acute ischemic stroke.

**DR. CATHERINE CUMMINGS:** Did the patient have a history of recent trauma or have other risk factors? How common is a spontaneous dissection?

**DR. COHEN:** In the United States, the annual incidence of spontaneous carotid artery dissection is believed to be

2.5–3/100,000, although this number is probably underestimated as some patients are asymptomatic.<sup>3,4</sup> It is slightly more common in men than women. The Cervical Artery Dissection and Ischemic Stroke Patients (CADISP) consortium, established in 2009, has attempted to elucidate risk factors for spontaneous dissections. Reasons for arterial injury are believed to be multifactorial. Some recent small studies suggest that predisposing hereditary connective tissue disorders may be highly prevalent in patient with spontaneous cervical artery dissections, but recognizable phenotypes such as fibromuscular dysplasia (most commonly implicated), Ehlers-Danlos syndrome type IV, and Marfan syndrome are noted in only approximately 5% of cases.<sup>5,6</sup>

Cervical carotid artery dissections can be due to major or minor trauma. Whereas penetrating and significant blunt trauma are obvious causes of a dissection, seemingly innocuous events may be responsible for an injury to the internal carotid artery. Almost 1/3 of patients do not describe an inciting mechanical event.<sup>7</sup> Carotid artery dissections have been reported after engaging in such activities as amusement park rides, playing basketball, coughing and sneezing, scuba diving, sexual intercourse, volleyball, as well as other activities. Chiropractic manipulation has also been implicated as a cause for a carotid artery dissection.<sup>4,7</sup>

While our patient did not have any known trauma, he did report a recent bout of bronchitis several days prior to presentation, and stated he had paroxysms of coughing and sneezing over the past week. Although it is certainly not typical for patients with minor trauma to develop a dissection, it is possible that our patient may have had an underlying inflammatory process or structural abnormality leading to arterial injury.<sup>8,9</sup>

**DR. WILLIAM BINDER:** Your patient reported left-arm heaviness. Are carotid artery dissections a common cause of stroke and/or a transient cerebral ischemia?

**DR. NICHOLAS MUSISCA:** Although cervical artery dissections are estimated to account for approximately 2% of all ischemic strokes in all ages, they account for nearly 20% of strokes in young and middle-aged patients.<sup>10</sup> The average age of those presenting with stroke secondary to dissection are about 46 years old, and they often do not have the usual risk factors for atherosclerotic strokes.<sup>11,12</sup> In fact, cerebral ischemia – TIA or infarct – is one of the most common presenting symptoms of dissection, occurring in up to 67% of all patients.<sup>13</sup> It is also notable that subarachnoid hemorrhage may develop from intracranial artery dissection.<sup>14</sup>

The symptoms seen in carotid artery dissections are often related to the arterial injury sustained. Dissections of the carotid artery can be a result of an intimal tear or disruption of the vasovasorum. A tear in the intima can lead to the formation of a fibrin thrombus and result in an artery-to-artery embolism or occlusion, causing hypoperfusion and ischemic

symptoms. Subadventitial lesions (between the media and adventitia) usually result in aneurysm (and pseudoaneurysm) formation and compression neuropathies.<sup>15, 16</sup>

**DR. JAMES MONTI:** What clinical features should we be on the lookout for? Does carotid dissection present differently than vertebral artery dissection?

**DR. MUSISCA:** In addition to cerebral ischemia, which occurs more frequently with vertebral artery dissection (77% vs 60%),<sup>11</sup> the most common initial symptoms of dissection is head and neck pain (80%).<sup>13</sup> Neck pain is typically more common in vertebral artery dissections, while pain in the eye, ear, or face is more commonly found in carotid artery dissection.<sup>11,17,18</sup> Headache is noted to be approximately equal in both types of dissection and tend to present ipsilateral to the dissection. Concomitant presence of a carotid bruit in carotid artery dissections has a poor sensitivity of 33%.<sup>4,13</sup>

Ischemia from carotid dissections generally affects MCA and ACA territories, thereby causing contralateral hemiparesis, hemisensory loss, aphasia, hemineglect, pulsatile tinnitus and/or monocular vision loss. Horner's syndrome (and partial Horner's) is seen in carotid artery dissection less frequently and typically presents without anhidrosis as the ischemia is secondary to localized compression of the sympathetic fibers travelling in the internal carotid artery plexus.<sup>4</sup> Ischemia due to a vertebral artery dissection may affect the brainstem and cerebellum, leading to symptoms such as ataxia, dysmetria, dysphagia, and vertigo and may cause anhidrosis.

**DR. WHIT FISHER:** Should the treatment of acute cerebral ischemia change based on whether it is secondary to dissection?

**DR. COHEN:** Acute ischemic stroke in the Emergency Department should be treated according to standard stroke practice. This includes treating eligible patients with thrombolytic therapy in the acute period instead of withholding it due to hypothetical concern for possible cervical artery dissection and worsening expansion of the dissection. Numerous studies note that the efficacy and complications of thrombolysis for patients with ischemic stroke associated with cervical artery dissection are comparable to patients with ischemic stroke from other causes.<sup>19-23</sup>

**DR. ANDREW NATHANSON:** What is the standard of care for treatment of carotid artery dissection?

**DR. COHEN:** Stroke prevention with antithrombotic therapy remains the basis for the treatment of patients with dissection. The AHA/ASA recommends that patients with ischemic stroke or TIA with concomitant cervical artery dissection be treated with either antiplatelet or anticoagulant

therapy for at least 3 to 6 months. However, no clear benefit has been established when comparing these therapies.<sup>24-26</sup> Antithrombotic treatment should begin immediately except for those who received thrombolysis or sustained significant trauma. Patients who received thrombolysis can generally be started on therapy after 24 hours. The timing of initiating antithrombotic therapy in trauma patients varies and depends on the specific injuries present; however, it is generally believed that these patients should be started early given the significant stroke rates without treatment.<sup>27</sup> One important caveat is that in patients who do not present with a neurologic event, or if the carotid lesion is found incidentally, the risk of stroke is low, suggesting that patients who present later in the course of the disease are at lower risk for an ischemic event.<sup>16</sup>

**DR. AMY BASS:** When is endovascular therapy used?

**DR. COHEN:** Endovascular interventions such as thrombectomy, intra-arterial thrombolysis, angioplasty, and stent placement may be employed in specific circumstances. The Society for Vascular Surgery guidelines recommend that medical therapy be employed as first-line treatment, and that those remaining symptomatic or with significant progression of the dissection on medical therapy be considered for intervention.<sup>28-30</sup> Interestingly, several studies have found endovascular therapy as an acute therapeutic intervention for ischemic stroke due to carotid dissection to be safe and efficacious.<sup>31</sup>

While some reports suggest that patients who develop a pseudoaneurysm have a mostly uneventful course, other studies suggest that there is a risk of thromboembolic disease. A single institution study in a series of 120 patients with pseudoaneurysms found that 13.8% enlarged with interval studies, and that > 3% had recurrent TIAs and 14% had non-ischemic symptoms. The authors citing this study intervene on enlarging pseudoaneurysm because they likely represent non-healing dissections leading to false lumen filling, and can cause discomfort and neuropathy due to mass effect.<sup>32</sup>

**DR. MELANIE LIPPMAN:** How was this patient treated and what was his outcome?

**DR. COHEN:** Our patient was initiated on 325mg aspirin daily and on his three-month follow-up was noted to only have intermittent tinnitus that had decreased in severity. The patient's good outcome is consistent with the favorable prognosis typically seen with cervical artery dissections.

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# Human Papillomavirus (HPV) Vaccination Coverage among Rhode Island Adolescents, 2008–2016

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 SUE DUGGAN-BALL, MPA; PATRICIA RAYMOND, RN, MPH

Human papillomavirus (HPV) is the most common sexually transmitted infection in the United States, with the highest rates of infection among people in their late teens and early 20s.<sup>1,2</sup> Although most HPV infections are asymptomatic and transient, certain types can cause cancers of the cervix, vagina, and vulva in women; cancers of the penis in men; and cancers of the anus and oropharynx as well as genital warts in men and women.<sup>1,3</sup> Every year in the United States, an estimated 19,200 women and 11,600 men are diagnosed with a cancer caused by HPV, and most of these cancers could be prevented with vaccination.<sup>1,2</sup>

The Centers for Disease Control and Prevention (CDC) recommends routine HPV vaccination for boys and girls at 11–12 years of age before exposure to HPV to protect against cancers and genital warts caused by HPV infections.<sup>1,3</sup> HPV vaccine is administered as a 2- or 3-dose series depending on age of vaccine initiation.<sup>1,3</sup> In Rhode Island, HPV vaccine has been available to providers through the state supplied vaccine program since November 2006 for girls and since July 2011 for boys.

This report describes 1) trends of HPV vaccination coverage among adolescents 13–17 years of age, and 2) missed opportunities to administer the HPV vaccine in Rhode Island.

## METHODS

We analyzed data from the 2008–2016 National Immunization Survey-Teen (NIS-Teen). NIS-Teen has collected HPV vaccination information among adolescents aged 13–17 years since 2008 for girls and since 2011 for boys in each of the 50 states and selected areas. NIS-Teen uses a random-digit-dialed telephone interview with parents/guardians of eligible adolescents to collect socio-demographic information and vaccination provider contact information. Providers are then contacted by mail, containing a standard questionnaire, to report the immunization history from the adolescent’s medical records.<sup>4</sup> HPV vaccination coverage estimates presented in this report are based on provider-reported immunization information.<sup>4</sup>

In this report, up-to-date (UTD) doses of HPV vaccination were defined as completion of a 3-dose series for 2008–2015, and completion of a 2- or 3-dose series for 2016, as specified in the CDC’s updated schedule.<sup>1,3</sup> A missed opportunity to administer the HPV vaccine was defined as a healthcare

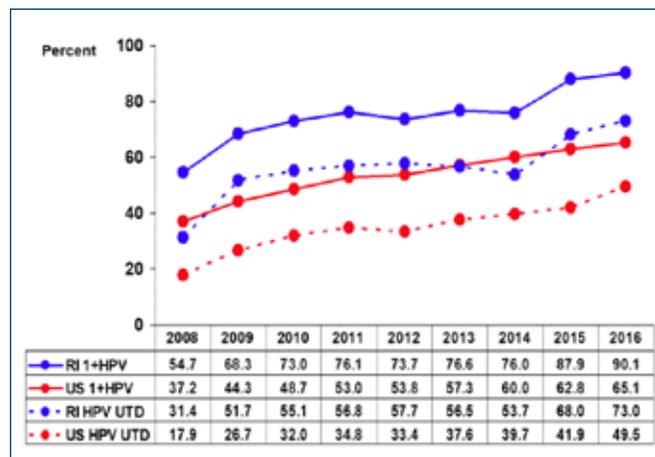
encounter where the adolescent received at least one adolescent vaccine (Tdap or MCV4) but did not receive the first dose of HPV vaccine. Trends of HPV vaccination coverage were presented from 2008 to 2016 for girls (n=1,534) and from 2012 to 2016 for boys (n=957) separately. Logistic regression was used to test the statistical significance of linear trend. Differences in vaccination coverage were considered statistically significant if  $p < 0.05$ .

## RESULTS

### Trends in HPV Vaccination Coverage for Girls

Figure 1 shows the trends in HPV vaccination coverage with  $\geq 1$  dose and UTD doses among girls 13–17 years of age. For Rhode Island girls, the overall trends in HPV vaccination coverage increased significantly during 2008–2016 for both  $\geq 1$  dose and UTD doses ( $p < 0.001$  for both trends). More specifically, between 2008 and 2010, the early stage of vaccination, coverage with  $\geq 1$  HPV vaccine dose increased from 54.7% to 73.0% ( $p < 0.01$ ) and coverage with UTD doses increased from 31.4% to 55.1% ( $p < 0.001$ ). However, coverage rates leveled off during 2010–2014 for both  $\geq 1$  dose and UTD doses. Between 2014–2016, the most recent data available, coverage with  $\geq 1$  dose and UTD doses increased significantly, from 76.0% to 90.1% ( $p < 0.01$ ) and from 53.7% to 73.0% ( $p < 0.01$ ), respectively.

Figure 1. Trends in HPV vaccination coverage among girls 13–17 years of age, Rhode Island vs. United States, 2008–2016



Overall, HPV vaccination coverage rates among Rhode Island girls were significantly higher than the U.S. throughout the years, for both  $\geq 1$  dose and UTD doses. During 2008–2016, the differences in coverage rates between Rhode Island and the U.S. girls ranged from 16.0 percentage points in 2014 to 25.1 percentage points in 2015 for  $\geq 1$  dose, and ranged from 13.5 percentage points in 2008 to 26.1 percentage points in 2015 for UTD doses.

### Trends in HPV Vaccination Coverage for Boys

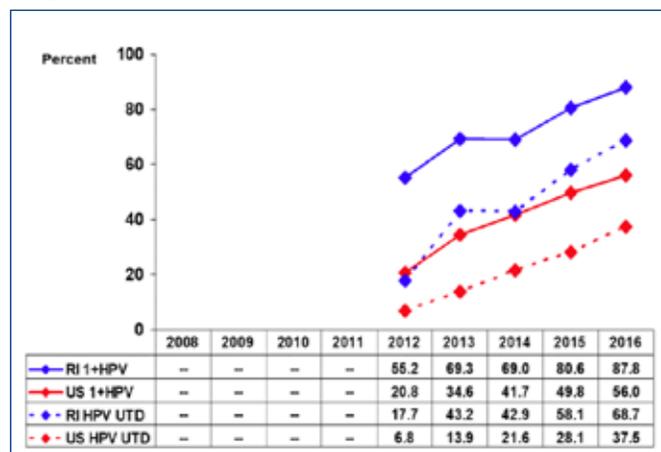
The overall trends in HPV vaccination coverage among Rhode Island boys increased significantly during 2012–2016, for both  $\geq 1$  dose and UTD doses ( $p < 0.001$  for both trends) (Figure 2). More specifically, between 2012 and 2013, the early stage of vaccination, coverage rates increased significantly from 55.2% to 69.3% for  $\geq 1$  dose ( $p < 0.05$ ) and from 17.7% to 43.2% for UTD doses ( $p < 0.001$ ). However, between 2013 and 2014, coverage rates for both  $\geq 1$  dose and UTD doses did not change at all. During 2014–2016, coverage rates for  $\geq 1$  dose and UTD doses increased significantly again, from 69.0% to 87.8% ( $p < 0.001$ ) and 42.9% to 68.7% ( $p < 0.001$ ), respectively.

Overall, HPV vaccination coverage rates among Rhode Island boys were also significantly higher than the U.S. throughout the years. During 2012–2016, the differences in coverage rates between Rhode Island and the U.S. boys ranged from 27.3 percentage points in 2014 to 34.7 percentage points in 2013 for  $\geq 1$  dose, and ranged from 10.9 percentage points in 2012 to 31.2 percentage points in 2016 for UTD doses.

### Differences in HPV Vaccination Coverage by Gender

Since HPV vaccine was introduced in 2006 for girls and in 2011 for boys, coverage rates for girls were higher than boys throughout the periods. However, the differences in HPV vaccination coverage between boys and girls in Rhode Island narrowed significantly during 2012–2016 due to faster increase in vaccination rates among boys than girls. Gender differences in HPV vaccination coverage decreased from 18.5 percentage points in 2012 to 2.3 percentage points in 2016 for  $\geq 1$  dose, and from 40.0 percentage points in 2012 to 4.3 percentage points in 2016 for UTD doses. In fact, gender

**Figure 2.** Trends in HPV vaccination coverage among boys 13–17 years of age, Rhode Island vs. United States, 2012–2016

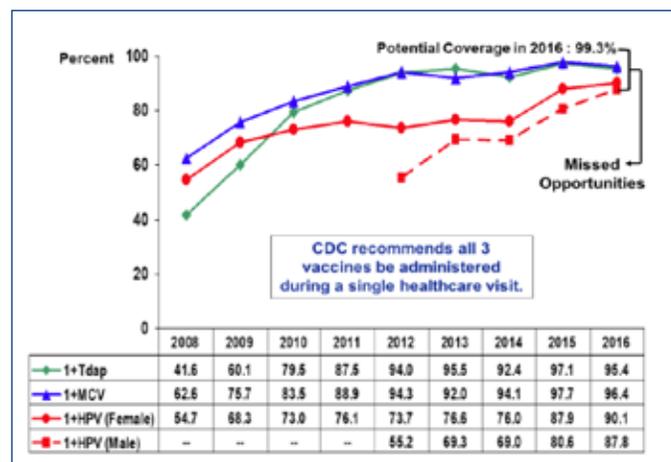


differences in coverage with  $\geq 1$  dose and UTD doses were no longer statistically significant in Rhode Island in 2016.

### Missed Opportunities in HPV Vaccination

Figure 3 presents the coverage trends of three adolescent vaccines in Rhode Island – Tdap, MCV4, and HPV vaccines. CDC recommends that providers administer these adolescent vaccines at a single visit at ages 11–12 years to reduce the likelihood of missing opportunities for vaccination.<sup>1</sup> If these vaccines are administered at a single visit as recommended, coverage rates for  $\geq 1$  Tdap,  $\geq 1$  MCV4, and  $\geq 1$  HPV vaccine doses should be the same.

**Figure 3.** Missed opportunities in HPV vaccination among adolescents 13–17 years of age, Rhode Island, 2008–2016



During 2012–2014, coverage with  $\geq 1$  dose of HPV vaccine among girls and boys was significantly lower compared to the other two adolescent vaccines, indicating that there were substantial missed opportunities for administering HPV vaccine at visits when Tdap or MCV4 vaccine was given. Since 2014, coverage with  $\geq 1$  dose of HPV vaccine has increased significantly among both boys and girls, whereas the coverage of the other two vaccines remained stable. As a result, the difference in coverage between  $\geq 1$  dose of HPV vaccine and the other two vaccines narrowed significantly. If missed opportunities had been eliminated, the potential coverage rate for all three adolescent vaccines would have reached 99.3% in 2016 in Rhode Island. In 2016, the differences between potential and actual coverage rates for  $\geq 1$  HPV vaccine dose was 9.2 percentage points among girls and 11.5 percentage points among boys. (In 2014, the estimated potential coverage was 98.3%, and the differences between potential and actual coverage rates for  $\geq 1$  HPV vaccine dose was 22.3 percentage points among girls and 29.3 percentage points among boys.)

### DISCUSSION

HPV vaccination coverage rates among Rhode Island adolescents 13–17 years of age were significantly higher than the U.S. In fact, Rhode Island has maintained the highest coverage rates in the nation during all study years.

However, in 2016, UTD doses for girls (73.0%) and boys (68.7%) were still well below the Healthy People 2020 goal of 80% coverage. Although HPV vaccination coverage in Rhode Island stagnated during 2010–2014 for girls, and during 2013–2014 for boys, we have achieved new and rapid increases since 2014. Recommended actions for healthcare providers and public health actions to improve HPV vaccination coverage are summarized below.

### Recommended Actions for Rhode Island Healthcare Providers

Healthcare providers (HCPs) play a critical role in improving HPV vaccination rates. HCPs should educate parents that HPV vaccine is safe and effective in preventing cervical cancer and genital warts, and that the vaccine series is most effective when administered before exposure to HPV.<sup>1-3</sup> To eliminate missed opportunities for vaccination, HCPs should provide a strong recommendation for HPV vaccine, since provider recommendation is the best predictor of vaccination, and routinely administer HPV vaccine the same day as other adolescent vaccines. Reminder/recall systems, use of KIDSNET (Rhode Island's Integrated Child Health and Immunization Information Systems) to monitor coverage rates, and using every encounter (well and sick visits) to assess vaccination status could improve HPV series completion rates.

### Public Health Actions to Improve HPV Coverage Rates

Rhode Island has historically had higher HPV and other adolescent and childhood vaccination rates when compared nationally due to many factors. Rhode Island is a universal vaccine purchase state, one of only eight universal vaccine purchase states. All vaccine (for insured and uninsured) that is routinely recommended for children and adolescents is purchased by the state and provided to healthcare providers at no cost. Healthcare providers do not have to order vaccine privately or separate vaccine, therefore cost is not a barrier to the provider or the patient. In August 2015, the Rhode Island Department of Health (RIDOH) added HPV vaccine to the school immunization requirements to improve HPV vaccination coverage rates for students entering 7th grade.<sup>5,6</sup> In the fall of 2016, Rhode Island's Vaccinate Before You Graduate (VBYG) program ([http://www.health.ri.gov/programs/detail.php?pgm\\_id=1010](http://www.health.ri.gov/programs/detail.php?pgm_id=1010)), a school-located immunization catch-up program for high school students, expanded to include public middle school students.<sup>6</sup> This expansion was initially funded by CDC's Prevention and Public Health Funding (PPHF). PPHF funding also provided an opportunity to build upon "AFIX" (Assessment, Feedback, Incentive, Exchange), a quality improvement practice to increase immunization coverage rates. The Office of Immunization hired a physician consultant to visit healthcare providers' offices identified with low HPV vaccination coverage rates. The visits include a review of all childhood and adolescent immunization coverage rates; however, a primary focus is on HPV vaccination. The consultant assesses current practices, addresses missed opportunities, and provides strategies for increasing HPV vaccination coverage rates.<sup>6</sup>

During 2/2015–10/16, the physician consultant completed

67 visits. All visits included participation of  $\geq 1$  practice clinician. Of the 67 practices receiving AFIX visits, 51 had increases in  $\geq 1$  HPV dose vaccination coverage of at least 5%. Rhode Island applied for and received another PPHF award in 2016 to increase HPV vaccination coverage rates through AFIX activities, which includes the successful physician-to-physician visits.

There are at least three limitations in this report. First, UTD doses were defined differently between 2008–2015 and 2016. If the updated HPV dosing schedule was applied retrospectively, vaccination rates with UTD doses for 2008–2015 might have been slightly higher. Second, HPV vaccination coverage might have been underestimated due to the possible incompleteness of provider-verified vaccination histories. Third, estimates of HPV vaccination coverage by gender in Rhode Island might be unreliable because of small sample sizes.

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### Disclosure

The authors have no financial interests to disclose.

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# Rhode Island Monthly Vital Statistics Report

## Provisional Occurrence Data from the Division of Vital Records

VITAL EVENTS	REPORTING PERIOD		
	AUGUST 2017	12 MONTHS ENDING WITH AUGUST 2017	
	Number	Number	Rates
Live Births	1,085	11,445	10.8*
Deaths	781	10,332	9.8*
Infant Deaths	3	69	6.0#
Neonatal Deaths	3	54	4.7#
Marriages	791	7,214	6.8*
Divorces	325	3,089	2.9*
Induced Terminations	84	1,951	170.5#
Spontaneous Fetal Deaths	75	728	63.6#
Under 20 weeks gestation	73	666	58.2#
20+ weeks gestation	2	62	5.4#

\* Rates per 1,000 estimated population

# Rates per 1,000 live births

Underlying Cause of Death Category	REPORTING PERIOD			
	FEBRUARY 2017	12 MONTHS ENDING WITH FEBRUARY 2017		
	Number (a)	Number (a)	Rates (b)	YPLL (c)
Diseases of the Heart	204	2,315	219.2	3,109.5
Malignant Neoplasms	186	2,235	211.6	5,534.5
Cerebrovascular Disease	36	432	40.9	430.0
Injuries (Accident/Suicide/Homicide)	75	887	84.0	14,156.0
COPD	53	485	45.9	462.5

(a) Cause of death statistics were derived from the underlying cause of death reported by physicians on death certificates.

(b) Rates per 100,000 estimated population of 1,056,298 ([www.census.gov](http://www.census.gov))

(c) Years of Potential Life Lost (YPLL).

NOTE: Totals represent vital events, which occurred in Rhode Island for the reporting periods listed above.

Monthly provisional totals should be analyzed with caution because the numbers may be small and subject to seasonal variation.

**When you hear hoof beats,  
*it could be zebras.***



**Be prepared for the unexpected.**

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## RIMS NOTES: News You Can Use

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**RIMS NOTES: NEWS YOU CAN USE**

This issue sponsored by

Welcome to the current issue of *RIMS Notes*, your concise, bi-weekly bulletin to keep RIMS members up to date on RIMS, the legislature, and highlights of our advocacy efforts.

**Volume 1 - Number 21**

For more information about our Sponsors, please visit [here](#).

**What's New**

**On October 14 CMS published its Final Rule for implementing MACRA.** All physicians must take careful note of the momentous changes in how Medicare will pay starting in little more than 2 months. On October 20, AMA released two new documents to help physicians understand the Final Rule and what it means for their practices. AMA's new [chart](#) provides an outline, while AMA's new [summary document](#) provides detail of MACRA. The Final Rule incorporates a number of improvements that AMA fought for to ease the transition for doctors.

**Membership Activities**

**The Medical Society's new website** debuted September 22, 2016. The URL is unchanged: [www.rimed.org](#), but everything else has been rebuilt from the ground up in fulfillment of strategic planning and consulting done last winter. You will like what you see.

**December 1** Back by popular demand! [Paint and Wine](#) at the Muse Paint Bar, 117 North Main Street, Providence. Register through the [Member Portal](#) on RIMS' website. Unleash your inner artist.

**Keeping You Posted: Opioids**

**New Prescription Limits are in Effect!** By state law effective June 28, 2016, initial opioid prescriptions for outpatient adults shall entail no more than 30 morphine milligram equivalents (MMEs) or 20 total dosages. Review the impact of these important new laws [here](#).

**Co-prescribing** FDA now requires strong warnings for combined use of opioid analgesics, prescription opioid cough products, and benzodiazepines. The action is part of a national effort led by Rhode Island Director of Health, Nicole Alexander-Scott, MD, MPH, to highlight the dangers of co-prescribing.

**Surgeon General to physicians: Take the pledge!** Vivek H. Murthy, MD, MBA, calls on America's doctors to [Turn the Tide](#) on the opioid crisis. Read his [letter](#). Take the pledge.

**This Date In History - 23 Years Ago**

October 21 is National Mammography Day, and October is Breast Cancer Awareness Month. President Bill Clinton designated the third Friday of October as Mammography Day in 1993.

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Contact Sarah if you've missed an issue, [sstevens@rimed.org](mailto:sstevens@rimed.org).



## Working for You: RIMS advocacy activities

### February 1, Thursday

Meeting with Board of Medical Licensure and Discipline regarding physician profiles  
Webinar on Safe Consumption Spaces  
Meeting with House leadership regarding legislation  
Meeting with Department of Health regarding physician mental health issues: Bradley J. Collins, MD, President  
Legislative hearings  
House Majority Leader Shekarchi fundraiser: Herbert Chen, MD; CJ Malgieri, MD

### February 2, Friday

Medically Supervised Injection Facility/ Harm Reduction Center work group, RIMS offices  
Public hearing on regulations, Department of Health  
Meeting with Thundermist Healthcare

### February 5, Monday

Conference call with Anchor Medical and Department of Health regarding Diabetes Prevention Program (DPP)  
House Special Legislative Commission on School Start Times: Susan Duffy, MD  
RIMS Council Meeting: Bradley J. Collins, MD, President

### February 6, Tuesday

RIMS Physician Health Committee: Herbert Rakatansky, MD, Chair  
AMA Advocacy Resource Center conference call regarding social media  
Legislative hearings

### February 7, Wednesday

Legislative hearings: Martin Weinstock, MD; Helena Kuhn, MD; and Mary Teeple, MD, testified on bill to ban minors from tanning booths.

### February 8, Thursday

Meeting with RI Quality Institute regarding Health Information Exchange updates  
SIM Steering Committee: Peter Hollmann, MD, President-elect  
Legislative hearings  
Sen. Majority Leader McCaffrey fundraiser

### February 9, Friday

Meeting with Massage Therapy Association regarding alternative pain treatment legislation



## Best Practices Regarding Opioid Prescribing

### Register Now!

#### **Best Practices for Pain Management and Opioid Prescribing: Fulfilling the New Opioid CME Mandate**

Crowne Plaza, Warwick

#### **Saturday, March 3**

Appropriate Prescribing, Potential for Dependence, Pharmacology, and Addiction.

#### **Saturday, March 24**

Alternatives for Opioid Pain Management: Chiropractic Care, Medical Marijuana, Physical Therapy, and Acupuncture.

CME applied for. These courses fulfill the requirements set forth in Department of Health Regulations, *Prescriber Training Requirement for Best Practices Regarding Opioid Prescribing*.

Physician prescribers holding a Controlled Substance Registration (CSR) must fulfill this specific training requirement only once and must do so before the next renewal of their CSR (June 2018).

Conference call with Blue Cross Blue Shield of RI regarding joint Diabetes Prevention CME event

### February 12, Monday

Meeting with Physicians for Fair Coverage regarding legislation

### February 13, Tuesday

AMA National Advocacy Conference, Washington, DC: meeting with Congressional delegation, Peter A. Hollmann, MD, President-elect and staff

### February 14, Wednesday

Board of Medical Licensure and Discipline Governor's Task Force on Overdose Prevention and Intervention

Meeting with Department of Health regarding physician mental health issues: Bradley J. Collins, MD, President

### February 15, Thursday

MA/RI Medical Group Managers Association presentation regarding legislation  
Mental Health and Substance Use Disorder Coalition meeting at RIMS

Meeting with Office of the Health Insurance Commissioner regarding legislation: L. Anthony Cirillo, MD  
Legislative Hearings

### February 16, Friday

Annual meeting of health care lobbyists at RIMS

### February 20, Tuesday

Improving End of Life Care Coalition  
AMA Advocacy Resources conference call regarding prior authorization

### February 21, Wednesday

Primary Care Physicians Advisory Committee, RI Department of Health

### February 23, Friday

Medically Supervised Injection Facility/ Harm Reduction Center work group meeting, RIMS offices

### February 27, Tuesday

AMA Advocacy Resources conference call regarding APRN Compact  
Interested parties meeting on laser safety legislation, Michael E. Migliori, MD, Chair, RIMS Public Laws Committee, Representative Kathleen Fogarty, bill sponsor  
Legislative hearings

### February 28, Wednesday

Workers Compensation Advisory Committee meeting  
Legislative hearings

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## RIMS CORPORATE AFFILIATES

The Rhode Island Medical Society continues to drive forward into the future with the implementation of various new programs. As such, RIMS is expanding its Affinity Program to allow for more of our colleagues in health-care and related business to work with our membership. RIMS thanks these participants for their support of our membership.

Contact Marc Bialek for more information: 401-331-3207 or [mbialek@rimed.org](mailto:mbialek@rimed.org)



[www.nhpri.org](http://www.nhpri.org)

Neighborhood Health Plan of Rhode Island is a non-profit HMO founded in 1993 in partnership with Rhode Island's Community Health Centers. Serving over 185,000 members, Neighborhood has doubled in membership, revenue and staff since November 2013. In January 2014, Neighborhood extended its service, benefits and value through the HealthSource RI health insurance exchange, serving 49% the RI exchange market. Neighborhood has been rated by National Committee for Quality Assurance (NCQA) as one of the Top 10 Medicaid health plans in America, every year since ratings began twelve years ago.

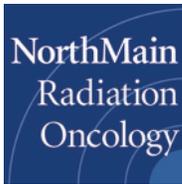


[www.ripccpc.com](http://www.ripccpc.com)

RIPCPC is an independent practice association (IPA) of primary care physicians located throughout the state of Rhode Island. The IPA, originally formed in 1994, represent 150 physicians from Family Practice, Internal Medicine and Pediatrics. RIPCPC also has an affiliation with over 200 specialty-care member physicians. Our PCP's act as primary care providers for over 340,000 patients throughout the state of Rhode Island. The IPA was formed to provide a venue for the smaller independent practices to work together with the ultimate goal of improving quality of care for our patients.



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# Brookdale Overview

## Independent Living *An ideal retirement living experience*

- Spacious apartments with minimal maintenance
- Restaurant-style dining
- Plenty of planned activities every day

## Assisted Living *The right choice for people who need extra help with daily activities*

- Qualified staff assists with taking medication, dressing, bathing, etc.
- Floor plans, from studio to two-bedroom apartments
- Activities and events for various levels of acuity

## Alzheimer's & Dementia Care *Person-centered care for people at various stages*

- Programs that leverage the latest dementia care research
- A care philosophy defined by more than the symptoms of Alzheimer's & dementia
- An experienced staff who help residents thrive

## Rehabilitation & Skilled Nursing *For short-term surgical recovery or long-term rehabilitation*

- Around-the-clock, licensed nursing care
- Providing clinical resources in a comfortable setting that feels like home
- A mission and focus to helping residents get well and then get home as quickly as possible

## Personalized Living *For people who just need a little help with things*

- One-on-one non-medical services for home care needs
- Additional personal needs for those in assisted living or home such as escorts to doctor appointments and more

## Home Health *For qualified people in need of therapy or rehabilitation — all in the comfort of home*

- Get Medicare-certified assistance from experienced professionals
- Many healthcare services such as wound care and stroke therapy

## Therapy *Specialized programming personalized to encourage recovery*

- An emphasis on education, fitness and rehabilitation that helps seniors retain or enhance their independence
- Most insurances accepted

## Hospice *Promoting comfort by addressing the full range of needs of patients and families*

- Primary focus of quality of life
- Specially trained staff help families and patients cope with overwhelming feelings accompanying end-of-life care

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# The Rhode Island Network

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## JAMA study reports opioid addiction treatment in prisons reduces later overdose deaths



Dr. Josiah "Jody" Rich directs the Center for Prisoner Health and Human Rights at The Miriam Hospital in Providence and is an advisor to Rhode Island's Overdose Prevention Task Force. [Photo: Mike Cohea/Brown University]

and director of the Center for Prisoner Health and Human Rights at The Miriam Hospital in Providence. "With this study, we wanted to see if that intervention could impact statewide overdose mortality, and the answer is a resounding yes."

**DR. TRACI GREEN**, an adjunct associate professor of emergency medicine and epidemiology at Brown, a senior researcher at Rhode Island Hospital and a researcher at Boston Medical Center's Grayken Center for Addiction, is the study's lead author. She said Rhode Island's program could be a national model for how to begin turning the tide in the opioid epidemic.

"People have been searching for some way to stop overdose deaths," said Green, who is also an associated professor in Boston University's schools of medicine and public health. "Here we have a program that's shown to work, and it's absolutely replicable in other places. Not only do we see that a statewide program treating people using medications for addiction treatment is possible and reduces deaths, but also this approach intervenes on the opioid epidemic at its most lethal and socially disrupting point – incarceration – to give hope and heal communities."

### A unique program

The program grew out of work done by Rhode Island Governor Gina M. Raimondo's Overdose Prevention and Intervention Task Force. Both Green and Rich are expert advisors to the Task Force and study's co-authors included the two Task Force co-chairs, **NICOLE ALEXANDER-SCOTT, MD, MPH**, the director of the Rhode Island Department

PROVIDENCE, BROWN UNIVERSITY – A treatment program for opioid addiction launched by the Rhode Island Department of Corrections was associated with a significant drop in post-incarceration drug overdose deaths and contributed to an overall drop in overdose deaths statewide, a new study finds.

The program, launched in 2016 and the only one of its kind in the nation, screens all Rhode Island inmates for opioid use disorder and provides medications for addiction treatment (MAT) for those who need it. Comparing the six-month period before the program was implemented to the same period a year later, the study showed a 61 percent decrease in post-incarceration deaths. That decrease contributed to an

overall 12 percent reduction in overdose deaths in the state's general population in the post-implementation period.

While the study, published in *JAMA Psychiatry*, was designed as a preliminary evaluation of the program, the results suggest that comprehensive MAT treatment in jails and prisons, with linkage to treatment in the community after release, is a promising strategy for rapidly addressing the opioid epidemic nationwide, the researchers say.

"This program reaches an extremely vulnerable population at an extremely vulnerable time with the best treatment available for opioid use disorder," said study co-author **DR. JOSIAH "JODY" RICH**, professor of medicine and epidemiology at Brown University

of Health, and **REBECCA BOSS, MA**, the director of the Rhode Island Department of Behavioral Healthcare, Developmental Disabilities, and Hospitals.

The nature of opioid use disorder, Rich says, makes incarcerated populations especially vulnerable to overdose. People who use opioids build a tolerance, meaning they require an ever-increasing dose to get the same effect. That tolerance quickly evaporates during incarceration, when people are forced off the drugs.

“They may have stopped using while incarcerated, but nothing has been done to change the pathways in the brain responsible for addiction,” Rich said. “So when they get out, people are likely to relapse, and with their tolerance gone, they’re at high risk for overdose.”

Decades of research from around the globe have shown that MAT is the best path to recovery for people with opioid use disorder, Rich says, whereas simple detox or “cold turkey” fails 90 percent of the time.

The MAT program implemented by the Rhode Island Department of Corrections (RIDOC) consists of three different drug therapies. Two drugs, methadone and buprenorphine, are opioid medications that help to reduce withdrawal symptoms like drug craving. The third drug, naltrexone, blocks people from experiencing the high normally associated with opioid use. Clinical criteria are used to tailor the best treatment for each individual patient.

“While comprehensive treatment for opiate use disorders has not been the traditional role of correctional facilities, we have shown that it is feasible,” said **DR. JENNIFER CLARKE**, medical programs director at RIDOC, an associate professor of medicine at Brown and director of the RIDOC MAT program. “Providing treatment saves lives and helps people become productive members of society, positively engages them with their communities and families which makes for healthier and safer communities.”

The treatment is administered to inmates by CODAC Behavioral Health, a nonprofit provider of medications for addiction treatment contracted by RIDOC to provide MAT inside correctional facilities. Upon release, former inmates can continue their treatment without interruption at CODAC, primary care providers, or other Centers of Excellence in MAT locations around the state. Patients are also assisted with enrolling or re-enrolling in health insurance to make sure they are covered when they return to the community.

While a handful of programs elsewhere in the nation provide one MAT drug or another to certain segments of incarcerated populations, Rhode Island’s is the only one that makes the full suite of MAT available to every individual coming in or leaving the correctional system. Medications are continued if they are on them when they arrive and started if they need them upon arrival or prior to release.

### Fewer overdose deaths

The study was designed as a preliminary assessment of the program’s effectiveness in reducing overdose deaths among recently incarcerated people, meaning those who had been incarcerated within a year of their deaths.

The research showed that the number of recently incarcerated people who died from overdose dropped from 26 in the first half of 2016 – before the program started – to just nine in the first half of 2017, after the program’s implementation. The decrease in post-incarceration overdose deaths, which occurred within six to 12 months of initiating the program, was a major contributor to the overall decline in overdose deaths among Rhode Island’s general population in the two study periods. The number of deaths fell from 179 in the 2016 period to 157 in the 2017 period.

“What’s remarkable is that between 2016 and 2017 there was a huge jump in the amount of fentanyl and related

compounds available on the illicit market,” Rich said. “So in the face of a worsening overdose risk, we actually saw a decline in overdose deaths. We’re quite confident that that happened because we’ve given people these medicines and they’ve stayed on them long enough to avoid an overdose.”

The researchers say the study’s positive results likely underestimate the effect of the program. Though launched in the summer of 2016, the program wasn’t fully up and running at all locations in the correctional system until early 2017. So the 2017 study period doesn’t capture the fully operational program.

The research team plans to perform further evaluation of the program, looking at longer-term outcomes among those treated with MAT, as well as how the program might affect re-incarceration and other population-level outcomes. But these early data make a strong case that this type of intervention could help stem the tide of opioid overdoses, the researchers say.

“People may say, well, Rhode Island is a small state and that’s why they were able to implement this,” Green said. “But there are state and county correctional systems all over the country that are the same size as Rhode Island’s. They could all be doing this, and this study tells us that they should be.”

Rich agreed that Rhode Island’s program should serve as a model for similar programs across the country.

“If people are concerned about overdose deaths in their community, they should demand that a similar program of comprehensive MAT be promptly implemented in the correctional facilities that service their community,” Rich said.

The research was funded by the Centers for Disease Control (NU17CE 002740) and the National Institutes of Health (K24 DA022112, R21 DA044 443, T32 DA013911, P30 AI042853). ❖

### CNE, Partners to begin formal discussions with Lifespan

Care New England and Partners HealthCare have approached Lifespan and will begin formal discussions to explore how all three health care providers might work together to strengthen patient care delivery in Rhode Island, according to a joint statement on behalf of Care New England, Partners HealthCare, Brigham and Women’s Hospital and Lifespan released on Tuesday, February 27.

It stated: “By combining the talent, experience and resources of our like-minded, provider-based organizations, we envision creating a national model that fully leverages the integration and coordination of care. In doing so, we are better equipped to meet market challenges and mandates to improve outcomes while reducing health care costs.” ❖

### Yale New Haven Health and South County Health end merger talks

NEW HAVEN, CT AND WAKEFIELD, RI – Yale New Haven Health and South County Health have mutually decided to end talks regarding a possible merger of Westerly Hospital (a member of Yale New Haven Health) and South County Hospital. As a result of this decision, the organizations released the following joint statement this week:

“Over the past several months, we have collectively reviewed a potential partnership between Westerly Hospital and South County Hospital, exploring opportunities to develop a single delivery network for patients in the region. Unfortunately we were not able to identify a mutually acceptable plan that would meet the needs of our respective communities. We believe this is the right course at this point in time and we each remain committed to delivering excellent care for the communities we serve.” ❖



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## Study finds young children with suicidality, PTSD at higher risk for hospital readmission

*First research to connect factors with long-term prognosis*

PROVIDENCE – A Bradley Hospital study found that young children with oppositional defiant disorder (ODD), behavior marked by disobedience to authority, and co-occurring suicidal thoughts and behavior or posttraumatic stress disorder (PTSD) are at increased risk for readmission following hospital-based psychiatric treatment and may require a higher level of long-term care. While treatment through Bradley Hospital's Pediatric Partial Hospital Program has been found effective in changing patients' behavior, the study suggests that additional treatment at the early onset of suicidal or PTSD symptoms may be needed. The paper was published online in *Child Psychiatry and Human Development*.

"We've seen the important connection between suicidal ideation and poor long-term mental health outcomes among adolescents, but by studying these links in young children, we can better understand, predict, and more effectively address the long term mental health needs of our youngest kids," said **JOHN BOEKAMP, PhD**, clinical director of the Pediatric Partial Hospital Program at Bradley Hospital and the study's principal investigator.

Study participants were 261 children age three to seven who entered the study at the time of their initial partial hospital admission. They were evaluated for suicidal thinking and behavior, as well as other psychiatric conditions such as depression and aggressive

behavior. Researchers then analyzed children who returned to the partial hospital program to better understand readmission factors. The study was conducted from 2010 to 2015.

Of the 261 children in the study, 23 percent (or 61 children) were subsequently readmitted – with most readmissions occurring within one year. Findings showed that younger children with suicidal thoughts and behavior and PTSD needed readmission sooner.

"We want to be able to get started on implementing higher quality treatment and after-care planning for these children as soon as we've identified risk factors that are a cause for concern. Early intervention here is key," added Boekamp. ❖



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## Alpert Medical School receives \$50M gift

PROVIDENCE, BROWN UNIVERSITY – A new \$50 million gift for Brown University's Warren Alpert Medical School will propel efforts to transform biomedical research and discovery into treatments and cures for disease.

The gift from Brown Chancellor **SAMUEL M. MENCOFF**, a Class of 1978 alumnus, and his wife, **ANN S. MENCOFF**, will help the medical school secure its position as a world-class center of innovation

in biology and medicine, said Brown President **CHRISTINA PAXSON**.

Half of the Mencoff family gift will be dedicated to establishing endowed chairs and providing funding to support outstanding researchers – from laboratory scientists to physician-scholars – whose discoveries alleviate illness and disease. The remaining \$25 million will support medical education and research.

The gift will support the Brown Institute of Translational Science (BITS), which is part of the Warren Alpert Medical School. BITS is establishing teams of scientists and clinicians who convert scientific discoveries into medical breakthroughs that are tested in the clinic and brought to patients in the marketplace. ❖

## Butler Hospital's Memory and Aging Program one of the first sites to start Tauriel AD clinical trial

PROVIDENCE – The Memory and Aging Program (MAP) at Butler Hospital has launched another research trial for Alzheimer's disease (AD). As one of the first to register a participant, the purpose of the study is to assess the safety, tolerability, and efficacy of RO7105705, an experimental drug in people with early to mild signs of AD.

The new study, called Tauriel, is a clinical trial sponsored by Genentech, Inc., a member of the Roche Group. The trial is designed for people with mild cognitive impairment or mild AD dementia, determined through cognitive testing and brain images showing levels of amyloid protein and tau protein tangles associated with AD.

"Alzheimer's disease is an imminent public health crisis, currently without a cure," said **DR. DANIELLE GOLDFARB**, neuropsychiatrist at Butler Hospital and an investigator on the study. "Adding this clinical trial to the many underway here, allows us to learn more about the disease and possible treatments."

Butler Hospital is one of the first of 125 research centers worldwide to place someone in this trial. Participants, age 50 to 80 years old with mild cognitive impairment or mild AD dementia, will be followed for two or more years, with regular appointments to administer the infusion and conduct tests and procedures. As a double-blind, placebo-controlled study, neither the research team nor the participants know whether the active RO7105705 or matching placebo is being administered.

**DR. STEPHEN SALLOWAY**, director of the Memory and Aging Program, calls this study "a big step in the war against Alzheimer's."

He said, "This study brings new clinical trial options for patients with early Alzheimer's disease, and because the study uses a new PET scan technique to visualize and measure the effects of this intervention on tau pathology, it could also prove to be a major advance in brain imaging." ❖



Phillips Academy  
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### CONSULTING PSYCHIATRIST

Phillips Academy seeks to establish a contractual relationship with a consulting psychiatrist to provide on campus psychiatric care during the academic year which runs from late August to mid-June. Students will be referred to the consulting psychiatrist by the academy's medical director and psychological counselors or the student's personal home psychiatrist. For complete listing, go to:

[www.andover.edu/about/employment/administrator-and-staff](http://www.andover.edu/about/employment/administrator-and-staff).



### OFFICE SPACE AVAILABLE

The Rhode Island Medical Society has 442 square feet of newly renovated office space (3 contiguous offices of 200 sq ft, 121 sq ft and 121 sq ft), complete with convenient sheltered parking and the opportunity for tenants to share three well-equipped meeting spaces, break room, office machinery, etc. on the western edge of downtown Providence. Suitable for a small non-profit organization, boutique law firm, CPA firm or other office-based small business.

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## Recognition



**Welch Award 2017:** Pictured from left to right are Robert Insoft, MD, senior vice president of quality and chief medical officer; **Edie McConaughy, CNM**, winner of the Richard P. Welch Award, Clinical; Mary Welch, wife of Dick Welch; **Lori Bailey**, winner of the Richard P. Welch Award, Non-Clinical; and Matt Quin, RN, MSN, senior vice president of patient care services and chief nursing officer.



**Mattis Award 2017:** Pictured from left to right are Robert Insoft, MD, senior vice president of quality and chief medical officer; Noreen Mattis; **Jennifer Silva**, 2017 winner of the Noreen Mattis Award for Excellence in Patient and Family Centered Care; Therese Stafford, 2016 Noreen Mattis Award winner; and Matt Quin, RN, MSN, senior vice president of patient care services and chief nursing officer.

## Women & Infants staff members receive awards of excellence

Women & Infants Hospital recently presented its annual customer excellence awards at the sixth annual Patient, Family, and Community Centered Care Summit, "Celebrating the Patient and Family Experience," held on Wednesday, January 24, 2018.

Receiving the awards were Edie McConaughy, CNM, of Warwick, clinical winner of the Richard P. Welch Award; Lori Bailey of North Providence, non-clinical winner of the Richard P. Welch Award; and Jennifer Silva of Rehoboth, MA, winner of the Noreen Mattis Award for Excellence in Patient and Family Centered Care.

**EDIE MCCONAUGHEY**, a certified nurse midwife in the Midwifery Department who has worked at Women & Infants for more than 25 years, was nominated by department director Elisabeth D. Howard, CNM, PhD, FACNM, on behalf of the entire department. In nominating her, Howard said, "On a daily basis, Edie has shown herself to be exemplary in patient care, teaching, and collaborating with nurse and physician colleagues. Edie always places the woman and family she is caring for at the center of the obstetric team."

**LORI BAILEY**, who works in Food and Nutrition, was nominated by a colleague in Women & Infants' Carter Family Neonatal Intensive Care Unit (NICU) who wrote about Lori's involvement with a lunch delivery program for families who are caring for their baby in the NICU. The program was established through a partnership with the Philanthropy Department and the NICU Family Advisory Council.

**JENNIFER SILVA**, a member of the NICU Family Advisory Council (NFAC), was nominated separately by two council members. One wrote, "Jenn is more than just a council member, she is an advocate for families who is always willing to do what it takes to make sure NICU families have what they need...Her passion and dedication shows as you walk through the NICU family room which she has taken as her personal project to keep comfortable and welcoming...The NICU is a better place because of Jenn, and our NFAC is beyond blessed to have her." ❖

## Rhode Island Hospital cardiothoracic intensive care nurses earn Silver Beacon Award

PROVIDENCE – Rhode Island Hospital's cardiothoracic intensive care nursing staff was recently recognized by the American Association of Critical-Care Nursing (AACN) with a Silver Beacon designation, the third such designation for the unit.

The Rhode Island Hospital CTIC unit is one of only 42 across the country to achieve

this level, indicating the unit meets or exceeds evidence-based criteria in leadership structures and systems, staffing and staff engagement, communication, knowledge management, learning and development, evidence-based practice and processes, and outcome measurement.

Rhode Island Hospital Senior Vice President and Chief Nursing Officer

**BARBARA RILEY, DNP**, says the CTIC nurses are highly skilled and dedicated to excellence, which is reflected in the Beacon designation. "The citizens of Rhode Island are fortunate to have professionals of this caliber ready to care for them when they need it most," she says. "This is great news for both our nurses and our patients." ❖

## Recognition

### Southern New England Rehabilitation Center reaccredited

The Southern New England Rehabilitation Center (SNERC) has been re-accredited for three years by the Commission on Accreditation of Rehabilitation Facilities (CARF), an international accrediting body focused on helping organizations measure and improve the quality of their inpatient rehabilitation programs and services. This accreditation recognizes SNERC's success in delivering high-caliber patient-centered care and validates the organization's drive to meet and exceed nationally and internationally accepted standards of care. SNERC is one of only three CARF-accredited rehabilitation programs in Rhode Island.

SNERC was re-accredited through January 31, 2021 for its Stroke Specialty Rehabilitation, as well as Inpatient Rehabilitation for adults, children and adolescents. The CARF surveyors noted that SNERC "employs strong and dedicated staff members who are tenured. The staff members are innovative and remain current in evidence-based practice." The surveyors also recognized strong supportive leadership and a commitment to outreach in the community.

"This achievement is an indication of SNERC's dedication and commitment to improving the quality of life for our patients," said **DAVID KOBIS**, President of Our Lady of Fatima Hospital, which is home to SNERC's inpatient rehabilitation program. "We are proud to be recognized for quality by CARE, which is considered the premiere accrediting body for rehabilitation programs."

Founded in 1966, CARF is an independent, non-profit accreditor of health and human services in a number of areas including medical rehabilitation. CARF-accredited service providers are recognized for their commitment to excellence.

This year, SNERC is celebrating its 30th year of delivering comprehensive rehabilitation services. The Center's skilled staff of professionals led by medical director **KHIN SEIN YIN, MD**, provide a full range of coordinated rehabilitation care. SNERC's 24-bed inpatient center offers rehabilitation programs for people who have experienced serious injury or illness that limits their abilities to function in everyday settings. The Center's clinical staff maintains academic affiliations to help train future rehabilitation professionals. ❖

### Roger Williams' Weight Loss Surgery program reaccredited for three years

The Weight Loss Surgery program at Roger Williams Medical Center has been reaccredited for three years as a Comprehensive Center by the Metabolic and Bariatric Surgery Accreditation and Quality Improvement Program (MBSAQIP). The center has held this accreditation since 2005. More than 3,000 people have had their weight loss surgery at Roger Williams Medical Center. The Weight Loss Surgery team at Roger Williams, under the leadership of surgeon **DR. DIETER POHL**, has been performing bariatric surgery for more than 16 years.

MBSAQIP works to advance safe, high-quality care for bariatric surgical patients through the accreditation of weight loss surgery centers. A bariatric surgical center achieves accreditation following a rigorous review process during which it proves that it can maintain certain physical resources, human resources, and standards of practice. All accredited centers report their outcomes to the MBSAQIP database.

"We are pleased to work with MBSAQIP to ensure we are meeting high standards for bariatric surgery," said Dr. Pohl. "Our continuing accreditation lets patients know we are meeting national goals related to safe and high-quality bariatric surgery." ❖

### Women & Infants Fertility Center named Nursing Center Of Excellence

The Fertility Center at Women & Infants Hospital of Rhode Island been named a Nursing Center of Excellence by the Nurses' Professional Group of the American Society for Reproductive Medicine (ASRM).

The Fertility Center is the only such program in Rhode Island to achieve this recognition for nursing care.

"Nurses play a key role in providing compassionate, comprehensive care to patients, not to mention their importance in patient and family education and satisfaction," said **MATT QUIN, RN**, senior vice president of patient care services and chief nursing officer at Women & Infants. "We are so proud of the nurses in our Fertility Center on this achievement, and are appreciative of the collaborative work that was done with SEIU 1199 New England, which helped support the funding for this application process."

A center may achieve center of excellence designation if at least 50 percent of the practice's registered nurses and/or nurse practitioners are experienced in reproductive endocrinology nursing and have completed additional training through ASRM. At Women & Infants' Fertility Center, 61 percent of their nursing staff – 10 registered nurses and one certified nurse midwife – completed the certificate examination. Six additional nurses have already begun the coursework and preparation for the exam. ❖



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## Appointments

### Syeda Maria Sayeed, MD, joins Southcoast Physicians Group



FALL RIVER – **SYEDA MARIA SAYEED, MD**, has joined the Rheumatology department as a member of the Southcoast Physicians Group.

Dr. Sayeed earned her medical degree at Dow Medical University in Karachi, Pakistan. She completed her residency at Memorial Hospital of Rhode Island. Dr. Sayeed also completed her fellowship in Rheumatology at the University of Vermont.

She is a member of the American Medical Association, the Rhode Island Medical Society, and the American College of Physicians. ❖

### John J. Holiver elected chair of HARI Board of Trustees; Michael Souza named vice chair

The Hospital Association of Rhode Island (HARI) has recently welcomed CharterCARE Health Partners Chief Executive Officer **JOHN J. HOLIVER**, as the newly-elected chair of the HARI Board of Trustees.

Holiver was named Chief Executive Officer of CharterCARE Health Partners in July 2016, having served previously as interim President of Roger Williams Medical Center. Prior to joining Prospect Medical Holdings in 2015 as Chief Integration Officer, Holiver held several executive leadership positions in the Steward Health Care System.

In addition, Chief Executive Officer of Landmark Medical Center and the Rehabilitation Hospital of Rhode Island Michael Souza was recently elected the vice chair of the HARI Board of Trustees. Souza joined the Prime Healthcare system in 2017.

Prior to becoming CEO of Landmark Medical Center and the Rehabilitation Hospital of Rhode Island, Souza served in several roles at Hospital Association of Rhode Island, including president of the association. Souza joined HARI in 2009 from Signature Healthcare in Brockton, MA, where he served as corporate controller and was responsible for the accounting, reporting and control functions of the corporation's various entities. He also served as director of financial planning at Landmark Medical Center. ❖

### Clinical audiologists, Drs. Stephany Briggs, Brianna Schiff, join Women & Infants

Clinical audiologists Stephany Briggs, AuD, CCC-A, F-AAA, of Providence, and Brianna Schiff, AuD, CCC-A, F-AAA, of Warwick, have joined the Department of Audiology at Women & Infants Hospital, providing hearing services for children and adults of all ages. Both audiologists are Care New England Medical Group providers.



**DR. STEPHANY BRIGGS** received her doctoral degree in audiology from the University of Connecticut and completed her externship at Rhode Island/Hasbro Children's Hospital. She is a fellow of the American Academy of Audiology and holds a Certificate of Clinical Competence in Audiology (CCC-A) from the American Speech-Language-Hearing Association. She works with children, adults, and families in the diagnosis and management of hearing loss. Dr. Briggs' main areas of interest are electrophysiology and pediatric diagnostic audiology.

**DR. BRIANNA SCHIFF**, who was inspired to become an audiologist by her brother who has hearing loss, attended Muhlenberg College and graduated summa cum laude and Phi Beta Kappa with a degree in neuroscience. She then earned a doctoral degree in audiology from Montclair State University and was elected to the Alpha Epsilon Lambda Graduate Honor Society. She completed her fourth year clinical externship at JFK Medical Center Johnson Rehabilitation Institute. Dr. Schiff is a fellow of the American Academy of Audiology, holds a Certificate of Clinical Competence in Audiology (CCC-A) from the American Speech-Language-Hearing Association, and is a member of the Educational Audiology Association. Her areas of interest include auditory brainstem response testing, diagnostic testing, educational audiology, and genetics of hearing loss. ❖



## Appointments

### Peter J. Snyder, PhD, joins URI as VP for Research and Economic Development

KINGSTON – The University of Rhode Island has named **PETER J. SNYDER, PhD**, to the position of vice president for Research and Economic Development and professor of Biomedical and Pharmaceutical Science. He succeeds Gerald Sonnenfeld, the former vice president of the division, who retired in December 2017.

Snyder has served as senior vice president and chief research officer at Lifespan Health System since 2008.

Prior to joining Lifespan in 2008, he served as an early clinical leader at Pfizer Inc., as a professor of psychology at the University of Connecticut, and as chief of the Division of Behavioral Neurology at Allegheny General Hospital in Pittsburgh. Snyder is an internationally renowned expert in Alzheimer's disease, and he is editor-in-chief for one of the journals of the Alzheimer's Association. He will



move his laboratory and active research program to the Ryan Institute for Neuroscience, and he plans to continue to mentor promising graduate students and junior faculty.

Snyder earned his bachelor's degree with high honors in neuroscience and psychology from the University of Michigan, his master's degree in psychology from Michigan State University and his doctorate in clinical psychology from Michigan State. He was a clinical neuropsychology resident in the Departments of Neurology and

Psychiatry, Long Island Jewish Medical Center, Albert Einstein College of Medicine, and he completed the Wilder Penfield Post-Doctoral Fellowship (awarded by the American Epilepsy Society) at the Comprehensive Epilepsy Center at Albert Einstein College of Medicine. ❖

## Obituary



**DR. GEORGE PHILLIP LEWIS, JR**, 84, died January 31, 2018 surrounded by his family.

He met his wife, Elaine Nunes, in high school, while working as an orderly at Newport Hospital. Elaine was a nurse's aide.

They married at Jesus Savior Church in Newport and then moved to Queens, NY while he finished medical school and Elaine worked as a nurse at Children's City Hospital. They were married for 59 years.

He graduated from Providence College and New York Medical School. He completed his internship at Rhode Island Hospital. He served in the U.S. Army as a Captain in the medical corps in several locations including Tokyo. After completing his surgical residency at St. Vincent's Hospital in Bridgeport, CT, he moved his growing family back to the Newport area. Upon returning to Newport, he opened his medical practice on Touro Street and was a surgeon at Newport Hospital. He served as Chief of Surgery at Newport Hospital and was a member of the American College of Abdominal Surgeons, American College of Physicians Executives, American Medical Association and the Rhode Island



Medical Society. He also served on the Board of Trustees at Newport Hospital and the Bank of Newport. He was a founding partner of Blenheim Newport and served as President and Medical Director until 1999.

Dr. Lewis retired from his medical practice in 1998. He then trained and received his pilot's license. He enjoyed flying for many years and was an avid reader, gardener and painter. He enjoyed sailing with his family on Narragansett Bay and camping with his children and grandchildren.

He was known in the Newport area for his work in medicine as a general surgeon. His treatment of patients, co-workers and staff was compassionate and kind. His colleagues and his family enjoyed his sense of humor and his shenanigans.

Besides his wife, he is survived by his children, George of Colorado, Dianne (Jim) of Virginia, Maureen (Michael) of Rhode Island, Peter of Massachusetts, Suzanne (Todd) of Pennsylvania, Karen of Rhode Island and 16 grandchildren and 1 great grandchild. His greatest love was spending time with his wife, children, grandchildren and his great-granddaughter.

Donations may be made in Dr. Lewis' memory to St. Augustin's Church PO Box 357, Newport, RI 02840 or to St. Jude Children's Research Hospital, 501 St. Jude Place, Memphis, TN 38105, [www.stjude.org](http://www.stjude.org). ❖