One Size Fits None? Treatment Algorithms and Guidelines in Psychiatry and Neurology

Andrew A. Nierenberg, MD

A hypothetical algorithm of treatment algorithms or a guideline to treatment guidelines would be of little use to practitioners of psychiatry or neurology because they would become obsolete as soon as their creators disseminated them. New knowledge simply comes too fast to be integrated into these fanciful compendiums of compendiums. And such knowledge is invariably incomplete. Nevertheless, treatment guidelines proliferate at an impressive rate. If only we had more data; if only the guidelines were more detailed, then we would be more certain about what to do for our patients. A marvelous short story, "On Exactitude in Science" by Jorges Luis Borges may be instructive....

".....the Cartographers Guilds struck a Map of the Empire whose size was that of the Empire, and which coincided point for point with it......The following Generations, who were not so fond of the Study of Cartography as their Forebears had been, saw that that vast Map was Useless, and not without some Pitilessness was it, that they delivered it up to the Inclemencies of Sun and Winters. In the Deserts of the West, still today, there are Tattered Ruins of that Map, inhabited by Animals and Beggars;...."

—Suarez Miranda, Viajes de varones prudentes, Libro IV, Cap. XLV, Lerida, 1658

Perhaps I am being too harsh, cynical, or pessimistic. After all, algorithms and guidelines can serve a useful purpose, ie, they can serve as an introduction to the sequence of evidence-based steps that can inform clinicians about potential options for the most straightforward and uncomplicated of clinical scenarios for the average patient. If these are to be useful, how

can clinicians use them? Do clinicians routinely or regularly consult these to inform their clinical decisions? Should health care organizations require that their clinicians use these and justify deviations from them? And couldn't these be implemented by less experienced and less trained technicians? After all, how difficult could it be to follow a treatment algorithm or guideline?

Forgive me for falling back into being critical, but policy makers are suggesting such things. Look at "The Innovator's Prescription" by Christiansen and colleagues.1 They make a cogent argument that the medical field would benefit from moving from intuitive medicine to precision medicine, using infectious diseases and cancer as examples. Precision medicine has a well-defined method of diagnosis with a treatment to match. A penicillin responsive bacterial infection should be treated by penicillin. Makes sense, a "no brainer". In fact, one does not need advanced training to implement a prescription of penicillin. One does, however, need advanced training to manage the complications that could result, eg, if the patient takes less penicillin than prescribed and ends up with a penicillin resistant infection or if serious adverse effects occur. For psychiatry and neurology (and their interface), perhaps we will eventually get closer to precision medicine with the current push for personalized medicine and appropriate biomarkers.

Should we be moving towards technicians implementing precision medicine? Would you want you or your loved ones to be treated in such a way? As a clinician, would you want to be constrained by such a system? Would it serve your patients well? As Klein wrote, "Algorithms

are brittle and often don't work well in the shadows, whereas skilled decision makers are more resilient and sensitive to context and nuance.... In addition, algorithms can get in the way when we need people to develop and sustain skill and expertise".2 Perhaps algorithms would be appropriate for the simplest of problems. In one of our conversations, my colleague Gary Sachs told me that the problem is physicians do not like these because one size does not fit all. What we really need are decision support systems, not decision replacement systems. We need systems that augment and enhance our judgment and provide us with information that helps us make better decisions. What we need are well-trained doctors, nurses, and physician assistants who are capable of "adaptive decision making". What will happen when these algorithms and guidelines become automated and embedded within electronic medical record systems? Will outcomes improve? Will physicians accept them? Many will develop such systems and companies will spring up to disseminate them. We will need to assess if these systems yield better outcomes than what Christensen and colleagues refer to as "intuitive medicine". I can only imagine that their utility (or lack thereof) will become clearer in time. Perhaps in 10 or 20 years, practices will be dominated by these. Or perhaps we will find their remnants when we go walking in the "Deserts of the West....". CNS

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US FDA APPROVES DOXEPIN FOR THE TREATMENT OF INSOMNIA

The United States Food and Drug Administration approved doxepin (Silenor, Somaxon Pharmaceuticals) for the treatment of insomnia characterized by difficulty with sleep maintenance. Dosing should be individualized with a minimum dosage of 3 mg/day and a maximum dosage of 6 mg/day for adults and in the elderly. Doxepin should be taken 30 minutes before a patient goes to bed.

Approval was based on six clinical studies of 1,423 patients between 18–93 years of age suffering from chronic or transient insomnia. In multiple studies of adults, elderly patients, and patients suffering from transient insomnia, doxepin was more effective than placebo.

The most common side effects found in clinical trials of doxepin were drowsiness, upper respiratory tract infections, and nausea.

For more more information, please consult doxepin's full prescribing information (www.silenor.com) — Christopher Naccari

AAN PUBLISHES NEW PARKINSON'S DISEASE TREATMENT GUIDELINES

The American Academy of Neurology (AAN) recently published new guidelines for the pharmacologic treatment of the non-motor symptoms (sleep disorders, sensory symptoms, autonomic dysfunction, mood disorders, and cognitive abnormalities) in Parkinson's disease patients. The guidelines, written by Theresa A. Zesiewicz, MD, FFAN, and colleagues are intended to provide physicians with recommendations on treating these common yet unrecognized symptoms of Parkinson's disease.

In order to develop these guidelines, the committee searched medical databases from 1966 to 2006 to find 3,369 citations and found 46 articles were relevant to the treatment of non-motor symptoms in Parkinson's disease patients.

For the treatment of erectile dysfunction, the AAN recommends prescribing patients sildenafil citrate 50 mg because it has been found it to improve this condition.

For the treatment of constipation, they recommend isosmotic macrogal (polyethylene glyocl) because it improves bowel movement frequency as well as stool consistency. They also found that increasing a patient's daily intake of water and fiber also relieved constipation.

For the treatment of insomnia, they recom-

mend levodopa-carbidopa because it has been found to improve sleep-associated motor functions as well as decrease spontaneous nighttime leg movements. For excessive daytime sleepiness, the researchers recommend modafinil, however, not every study found objective improvement with the medication. For the treatment of fatigue, they found that methylphenidate might be useful, however, concerns about its addictive qualities might hinder its usefulness. (Neurology. 2010;74(3):924-931.) —Christopher Naccari

SCHIZOPHRENIA PATIENTS HAVE IMPROVED HIPPOCAMPAL PLASTICITY POST-EXERCISE

The positive benefits on physical health via aerobic exercise has been greatly documented. However, research into the positive benefits of aerobic exercise on patients suffering from mental disorders continues to shed new light on the benefits of exercise.

Frank-Gerald Pajonk, MD, and colleagues from The Saarland University Hospital in Germany, investigated16 males 18–40 years of age suffering from chronic and relapsed schizophrenia (as per *International Classification of Disease, Tenth Edition* criteria) and compared them to 8 healthy males. The duration of illness was 10.4 years with few positive and moderate negative symptoms.

Pajonk and colleagues chose to assess the efficacy of aerobic exercise in these patients because schizophrenics have been found to have lower hippocampal volume and exercise has been found to increase hippocampal plasticity. Thirteen patients exercised 30 minutes, 3 times a week for 12 weeks, the remaining 11 patients played table football for 40 minutes, 3 times a week for 3 months. In order to assess the efficacy of exercise on the hippocampus, the researchers took magnetic resonance images (MRIs) of each patient's hippocampus.

The researchers found that hippocampal volume is plastic in response to aerobic exercise in both healthy patients and in patients suffering from schizophrenia. After exercising, schizophrenia patients where found to have a 12% increase in relative hippocampal volume while healthy patients had a 16% increase. There was no change in the patients that did not exercise. The schizophrenia patients were also found to have a 35% increase in N-acetylaspartate to creatine ratio in the hippocampus.

A confirmatory study which will focus on neurobiological markers which mediate hippocampal growth and analyzing methods which might improve cognitive functioning and functional outcome is forthcoming. (*Arch Gen Psychiatry*. 2010;67:133-143.) —*Christopher Naccari*

FMRI REVEALS FUNCTIONING BEHIND STUNTED EMOTIONAL PROCESSING IN GENERALIZED ANXIETY DISORDER

In a recent imaging study, patients with generalized anxiety disorder (GAD) demonstrated inhibited emotional processing. This, according to researchers, was explained by the inability of GAD patients' brains to regulate the amygdala by engaging the pregenual anterior cingulate.

The investigation, headed by Amit Etkin, MD, PhD, at Stanford University, and colleagues, focused on implicit emotional regulation in GAD. Etkin and colleagues scanned 17 GAD patients

(mean 31.5 years of age, 65% female) and 24 healthy comparison subjects (mean 36.5 years of age, 75% female) with functional magnetic resonance imaging (fMRI) while displaying happy or fearful facial expressions. Each image was overlaid with a "happy" or "fear" caption. Some facial expressions had mismatching captions.

The comparison subjects non-intentionally regulated the emotional conflicts presented by mismatched captions. The GAD group, however, had impaired emotional adaptability and delayed reaction times. fMRI and performanceresults were so significantly correlated with symptoms that patients could be divided accurately by that sole criterion.

This study was funded by grants from the National Institute of Health and the residencey program of the Veterans Affairs—Palo Alto Health Care System. (Am J Psychiatry. Epub February 1, 2010). —Lonnie Stoltzfoos

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