

INTERNATIONAL HEALTH NEWS

William R. Ware, PhD - Editor

NUMBER 255

MARCH 2015

24th YEAR



The measles outbreak in the US has been heavily featured in the news lately. Central to the media coverage is finger pointing at parents who for various reasons decide not to have their children vaccinated. Some of the more radical critics propose separating children from these parents and pressing criminal charges. The parents are being characterized as irresponsible and choosing an action that puts not only their children but the public at risk. Vaccination requirements for attending school will no doubt be strengthened. It is being proposed in some states that personal reasons would no longer be accepted for refusing permission; only religious conviction could qualify for a waiver. One state is even considering eliminating that. It is not the intention of this editorial to get into the vaccine debate, but the view projected on the evening news ignores what may be an important aspect of the decision not to vaccinate, loss in faith. Faith has been lost in the companies that manufacture vaccines. The integrity of studies that back up the official position regarding efficacy and risk, and now called into question is the potential bias and conflicts of interest of those pushing the hardest for universal and forced acceptance of the merits and safety of vaccination. Challenged by disbelief is this giant pillar in mainstream preventive medicine and the position that the science is clear and cannot be questioned.

It is easy to understand the origin of this loss of faith. One source has been a few magazine, newspaper and internet news service articles concerning the manner in which the pharmaceutical industry conducts business. Examples include huge amounts of money (billions) in criminal fines paid over the past few years in the US by many major pharmaceutical companies without admission of wrongdoing for which they were convicted. In addition, there have been stories concerning whistleblowers that were engaged in industrial or governmental vaccine research and claimed to have participated in or were aware of fraud in the conduct of studies intended to demonstrate efficacy or safety. For those who wanted in-depth investigative reporting and documentation, there are now several recent books available written by scientists, frequently medical doctors, which provide detailed and depressing accounts of the manner in which the industry conducts both research and marketing. These might well totally destroy anyone's faith. Some who have lost faith would simply point out that it is not possible to reliably ascertain the risk and the benefit, since what is involved is frequently not really straightforward science, but politics, fraud, and conflicts of interest mixed in with managed and orchestrated clinical research.

The internet and social media of course have been a major source of faith destruction with a number of anti-vaccination websites and highly efficient spreading of information both true and false. One important contribution these efforts have made is to acquaint the public regarding the US Government unprecedented blanket indemnification of drug companies from liability associated with harm from vaccines. Perhaps to placate critics who considered this a violation of basic rights, the US government set up a vaccine injury court to hear claims of harm. There have been thousands of claims and for some vaccines, a high proportion allowed with compensation paid. Both the existence of this court, its public records and the successes in winning reinforces the belief among those who have lost faith in what they are being told by the media, public health authorities and their physicians, i.e. that vaccines are safe. In fact, it is not hard to believe that the court documents represent the tip of an iceberg

and this reinforces the belief that there is an intentional lack of transparency and adequate, honest adverse event tracking. The thousands of case histories on the anti-vaccination websites also reinforce this view. The internet also widely carried the whistleblower story of cherry picking of data in a CDC sponsored clinical study on vaccination and autism which shifted the results to indicate no risk. Horror and related stories are picked up by the social media and spread to millions. The allegations and insinuations rampant in the internet and social media coverage of vaccine issues are of course just that, and many of the issues raised unfortunately may never be resolved. However, for those who have lost faith, denials from the accused now carry no weight. The same can be said for recommendations from sincere public health authorities and physicians who by and large must follow the guidelines and official wisdom. Unfortunately even skilled and knowledgeable researchers may never be able to discover the truth concerning benefit vs. risk.

Wishing you and your family good health,

William R. Ware, PhD, Editor

Highlights

Statins for almost all diabetics	p. 5
Most cardiovascular risk calculators appear inaccurate	p. 7
Tight glycemic control and over-treatment of older adults with diabetes	p. 8

AMAZING THINGS IN BRAIN NEUROPLASTICITY HAPPENING IN WISCONSIN

The rehabilitation of individuals with pathological or trauma-related brain dysfunction is generally a slow process involving mental and physical exercises augmented by such activities as meditation. Implementation requires trained therapists and the success is highly variable. For example, the dysfunction can be associated with multiple sclerosis, Parkinson's disease, stroke, brain trauma, etc. There is a widespread need for better and faster rehabilitation, a need that is growing with the increased prevalence of the underlying diseases and as well the growing incidence of traumatic brain injury in military conflicts and sports. In what follows, a remarkable and revolutionary approach to this problem and this crisis will be described.

Some readers may have read the bestselling book *The Brain That Changes Itself* by Norman Doidge, M.D., a psychiatrist on the research faculty at Columbia University Department of Psychiatry and on the faculty of the University of Toronto's Department of Psychiatry. A new book by this author titled *The Brain's Way of Healing* has just been published. The subtitle is *Remarkable discoveries and recoveries from the frontiers of Neuroplasticity*. Chapter 7 of this book is devoted to a description of research at the University of Wisconsin that in the near future may revolutionize the treatment of a set of neurological problems which accompany a remarkably diverse set of disorders. The laboratory has the name *Tactile Communication and Neurorehabilitation Laboratory* (TCNL) and is run by Yuri Damilov, a Russian neuroscientist, Mitch Tyler, a biomedical engineer and Kurt Kaczmarek, an electrical engineer. The mission of the center is to study the theory and application of what they term *applied neuroplasticity* which is related to the brain's ability to reorganize in response to new information, needs and stimulation, and to develop solutions for sensory and motor disorders. Dr. Doidge is uniquely qualified provide the up-to-date report on the activities and achievements of this laboratory.

The beneficial effects of stimulating the brain with electrical pulses, light or magnetic fields has received considerable attention over the past decade. However, the benefits and durability have been variable although sometimes very good, although one invasive approach of implanting electrodes in the brain is complex and carries risks. The Wisconsin group has developed a unique device called the Portable Neuromodulation Stimulator (PoNS) for non-invasive stimulation of the brain with electrical pulses that appears to offer a very successful approach to neurorehabilitation and appears to have a remarkable diversity of applications. The approach makes use of the fact that the tongue can be used as an effective interface for transmitting electrical signals to the brain. They have developed a device with 300 electrodes that is placed on the tongue and transmits pulses in a certain pattern. Brain scans were used to identify the areas of the brain stimulated and refine the protocols and now a number of patients have now been successfully treated at the TCNL. The protocol involves both brain stimulation and exercises directed at the disability in question, a combination which appears to facilitate the activation of the plasticity of the brain to revert to normal function in damaged areas and for specific dysfunctions. One of the inventors calls it “*neuroplasticity on demand*.” The device is small, held in the mouth, and can be used while on a treadmill, walking, doing balancing or other exercises, or engaging in mental exercises. Some beneficial results appear within minutes, others develop over hours, days, weeks or longer. In the clinical work of the center, patients are trained to use the device and given a protocol of activities and exercises to follow. The treatments continue at home with regular follow-up and for some last months or even longer.

How does this device work? The researchers believe that the neuromodulation due to the electrical pulses, which travel from the tongue through cranial and facial nerves to the brain stem and then throughout the brain, activate or reactivate neurons and related structures involved in human functions. Put another way, neuromodulation is thought to enhance the neuroplasticity of the brain, its ability to restructure or relearn in response to new experiences, sensory input and functional demands. The plasticity of the brain allows abnormal brain function and activity to move toward normal, called a state of homeostasis, when properly stimulated. Thus the simultaneous use of targeted physical, occupational and cognitive exercises simultaneous with the electrical stimulation.^{1;2}

The results they have achieved are sensational and unbelievable, go directly against the modern conventional thinking that one locates a brain target and treats it. Thus there is skepticism. In particular, the nonspecificity of the approach suggested by the diverse disorders impacted goes against the view that each illness is best treated by a unique chemical or magic bullet that targets a specific microscopic or biochemical defect. This skepticism ignores the fact that the device is the result of research, including functional MRI, leading to knowledge of the specifications and patterns of the electrical stimulation to which the receptors, neurons and synapses of the tongue respond and transmit to the brain. Let's look briefly at the case histories from TCNL recounted in Dr. Doidge's book which involve four different disorders and then look at what is in the peer-reviewed literature.

- **Multiple Sclerosis (MS).** The patient was a well-known opera singer who had lost his singing voice, most of the rest of his voice, and was disabled to the point of needing two full arm canes to walk. He was at the peak of his career when this disaster struck. It actually took nine years to get from his symptoms to the diagnosis of MS. He was referred to the Wisconsin TCNL. After two twenty minute sessions, he was able to hum a tune. After four, he was able to sing again. At the end of a week he was near his original vocal powers. By the end of his two-week stay in Madison, his other MS symptoms started to improve and this man who needed two canes when he arrived, performed a tap-dance for the team. He continued to use the device at home to reinforce his gains.
- **Parkinson's Disease (PD).** An eighty year-old patient had suffered from PD for twenty-three years. She could not walk, maintain balance, and her tremor made difficult most normal daily activities. So bad was her speech that she could not maintain a conversation. She was described as “frozen into the immobility of advanced Parkinson's disease.” After two weeks of treatment with the device, she had regained her speech, the ability to walk and the tremor was diminished. The walker was no longer needed. Aside from the residual tremor, she appeared completely normal. The PD is not totally gone, but she leads a normal life. Her son once found her standing on a table painting a ceiling.
- **Stroke.** The patient was a fifty-four year old woman whose stroke had left her unable to speak, write, read, cough, or make any noise at all. Thinking ability had deteriorated and sensory problems

prevented her from understanding conversation if there was any background noise. In addition, there was a profound deterioration in visual processing. Four and a half years after the stroke most of her deficits remained. Her sister lived in Madison, and had heard about the TCNL lab. The patient was accepted for therapy. Changes were remarkably rapid. Even by day three, most of the deficits described above were vastly diminished. She continued the treatments at home and regarded the results as “life changing.” She stopped using the device after six months and has had no relapse.

- **Multiple Sclerosis (MS).** This account comes from another institution which was studying the device to provide better evidence for the TCNL team. The research concerned patients with relapsing, remitting or progressive MS. Eight patients were involved. Most needed canes, one a walker. After treatment, all seven who had needed canes were able to walk faster, longer, and go up and down stairs without having to hold the railing. Not only was walking and balance improved, other MS symptoms improved. One patient returned to playing tennis, one was able not only to walk well, but run. Nevertheless, MS was not cured, but simply ceased to be a serious quality of life factor, i.e. a huge change. The patients all continued at home to use the device, but the account does not give details.
- **Traumatic brain injury (TBI).** The success with the above disorders caused the Wisconsin team to start recruiting victims of traumatic brain injury. Two case histories provided in Dr. Doidge’s book make it clear that the PoNS protocol achieved remarkable improvements in the deficits due to this type of injury. What is really interesting is that both individuals were reinjured in a car accident and it was found that the protocol also was effective for this scenario. The results from TCNL on TBI have attracted the attention of the US military which is going to test this approach on injured soldiers. There are obviously also athletes waiting in the wings.

In 2014 the Wisconsin group published in the *Journal of Neuroengineering and Rehabilitation* the results of a randomized double blind controlled study, a so-called pilot trial.³ The trial involved 10 treated and 10 control subjects who exhibited gait difficulties associated with MS, a serious problem with this disease. The intervention consisted of the simultaneous use of the device and rehabilitation therapy, the latter involving gait, balance and relaxation training with the device in place. Both the treated and control groups used the device, but the control group were exposed to much lower intensity even though they thought they had the same intensity adjustment option as those treated who adjusted the intensity to near the discomfort threshold whereas the controls were told they could not feel anything because of individual variation. After two weeks of in-laboratory training on a one-to-one basis with a trainer, during the remaining 12 weeks the program was carried out at home.

The results indicated a very significant improvement in a standard gait score in the treated group, and for the control group, once the training period was over, a small increase and then decrease in the score, with the average remaining well below the treated group. It was concluded that tongue-based neurostimulation may significantly amplify the benefits of exercise for improving gait problems in individuals with MS.

Other recent published clinical and experimental studies from the group include the use of functional MRI to show neuromodulation of individual brainstem nuclei by the device in balance-impaired individuals,⁴ and two brain network studies also on balance impaired individuals.^{5,6}

Currently, there are four clinical trials organized by Helius Medical Technologies, the company involved in the commercial development of the device. The company target for submission to the US FDA for regulatory approval is early to mid-2016.

The following trials are underway or scheduled to start soon.

- Pilot study: Chronic balance deficit in mild to moderate traumatic brain injury. Underway at TCNL
- Pilot study: Chronic balance and gait deficit due to MS. Montreal Neurological Institute starting February 2015.

- Pivotal phase 3 trial: Chronic balance deficit in mild to moderate traumatic brain injury. Oregon Health Sciences University, Orlando Regional Medical Center and Montreal Neuro-feedback Institute, starting February 2015.
- Pivotal phase 3 trial: Chronic balance and gait deficit due to MS. Montreal Neurological Institute and Hospital. Starting Q3 2015.
- The company has also entered into an agreement with the US military to test the device for treating traumatic brain injury. Veterans need to be aware of this because these studies will be recruiting patients.

The PoNS device currently has the status of an investigational device and is not available in the US or Canada pending further testing and regulatory approval. After approval, it may only be available on prescription or through a physician or clinic administering therapy. Other countries have different regulations and the device may soon be widely available.

The above discussion concentrates on neuromodulation by electrical stimulation targeted at facilitating changes attributed to neuroplasticity of the brain. It is very important to realize that this is just one of many techniques that have been utilized in an attempt to achieve this goal. Each chapter of Dr. Doidge's new book explores a different approach and he emphasizes that some approaches work better than others due to individual variability and the disorder or disorders being treated. The focus here has been on one technique that is simple and seems to have a number of applications and appears remarkably effective. Someone having problems that might respond to neuromodulation may need to consult several experts in this field. Reading Dr. Doidge's book cover to cover is highly recommended.

BOTTOM LINE

The research described above has opened new vistas in brain rehabilitation and offers great hope to those who suffer from the large assortment of problems directly related to mental dysfunction. Some might say it is one of the biggest advances in the treatment of brain disorders in the history of neurology. There does not appear to be another rehabilitation protocol that offers relief as fast or as extensively or for so many disorders as that based on the PoNS device combined with targeted physical and mental therapy. Even though the device and protocols are yet to be approved in North America, awareness of these advances is important. There will no doubt be studies in which one can enroll and some studies may still be enrolling. The device and protocol may soon become available in countries with lower regulatory barriers for this type of therapy before this happens in North America, and it appears that suitable versions of the device are nearly ready to be manufactured. Because the training period for the patient is short and the device is then used at home along with other prescribed interventions, for North Americans even travel to a foreign country might be worthwhile. Also, the Wisconsin group has found no adverse side effects, and in fact, one of the inventors in the group reports having used the device daily for several years just to see if any turned up. None were observed. IHN will keep readers informed on progress in what appears to be a very exciting area of neurodegenerative therapy. Also, consult the website of Helius Medical Technologies for updates and announcements of additional trials that may be of interest to some readers (www.heliusmedical.com).

STATINS FOR ALMOST ALL DIABETICS

In November 2013 new guidelines were proposed by two American professional medical groups concerning the indications for prescribing statin drugs. Estimates quickly followed suggesting that if followed, these new guidelines would increase the number of Americans taking statins by 13 million and for all over the age of 40, about half would now be on statins, a dream come true for the pharmaceutical industry. These new guidelines included the recommendation that all diabetics between the ages of 40 and 75 should be placed on statin therapy regardless of their cholesterol levels or other risk factors. Diabetes has historically been a factor viewed as conferring high risk of cardiovascular disease on a par with a history of this disease. The American Diabetes Association (ADA) has just made news by going along with these new guidelines, so we now have the imprimatur of this influential organization along with the American Heart Association and the American College of Cardiology.

Perspective can be gained by considering that in the CDC 2014 report based on 2012 data; about 30 million individuals in the US had diabetes, of which 21 million were actually diagnosed. In the age group ≥ 45 there were about 25 million of which about 18 million were diagnosed. This is roughly the age group in question although if half those diagnosed are already on statins, this represents 9 million new candidates for a prescription renewable for life since the disease is progressive and incurable except by such dietary interventions recently discussed in IHN, which are of course off the radar of mainstream medicine and will no doubt remain there for a number of years. This provides incentive for revisiting the benefits of statins in the case of diabetics.

Individuals with diabetes have enhanced risk of coronary heart disease and vascular disease in general. In the context of true primary prevention in non-diabetics, statins provide only a small (approximately 1%) absolute benefit in terms of acute coronary events and no impact on mortality. Thus it is of interest to examine this therapy in diabetics. The original studies that influenced a number of versions of the ADA standard of care,⁷ were three primary prevention lipid-lowering studies where it was possible to stratify by diabetes and the identify the presence or absence of baseline CHD, thus obtaining information on the role of statins in risk reduction in the context of primary prevention of acute CHD events in type 2 diabetics. It is thus of interest to look at the individual primary prevention trials. The results were as follows for absolute percent risk reduction (ARR), the numbers needed to treat to prevent one event (NNT), the relative risk reduction (RRR) and number with no benefit for the endpoint of fatal and non-fatal heart attack over 4-5 years (calculated from reported events over the study period).

Table 1. Primary prevention trials of statins among patients with diabetes

TRIAL	ARR	NNT	RRR	NO BENEFIT
ASCOT ⁸	0.6%	166	16%	99.4%
ASPEN ⁹	0.7%	142	27%	99.3%
CARDS ¹⁰	1.9%	53	36%	98.1%

The very small average absolute risk reduction (1.1%) with large NNT (91) seen in the above table was also found in studies of cohorts where diabetes is present in only in a small fraction or absent altogether. In this essentially non-diabetic population, when meta-analyses were rigorously restricted to primary prevention statin trial,¹¹ absolute risk reduction for major CHD events was 1.0% and the NNT 100. Thus it is interesting that in the context of primary prevention with statins, there is little difference between diabetics and non-diabetics.

The largest meta-analysis of statin trials where both diabetes and primary vs. secondary prevention were stratified was the Cholesterol Treatment Trialists' Collaborators (CCT) study. This is the key citation in most justifications of statins for diabetics. The results are summarized below for the composite endpoint of heart attack (MI), coronary-related deaths, stroke, or coronary revascularization over 4-5 years, calculated from reported event numbers.¹² Most participants in these trials were at elevated risk of adverse CVD events. Note that the composite endpoint includes the soft outcome of revascularization which because it is dependent on a number of factors including physician views and non-medical incentives, inflates the number of events.

Table 2. Summary of outcomes from Cholesterol Treatment Trialists' Collaborators study

CATEGORY	ARR	NNT	RRR	NO BENEFIT
Diabetes and no vascular disease	2.6%	39	27%	97.4%
Diabetes along with vascular disease	5.3%	19	20%	94.7%
No diabetes and no vascular disease	1.6%	63	22%	98.4%
No diabetes with vascular disease	5.0%	20	21%	95%

These results illustrate the greater impact of statins in secondary prevention. The result for diabetics with no vascular disease is somewhat higher than in CARDS, ASPEN and ASCOT discussed above, presumably because of the expanded endpoint which increases event rates. The results for no diabetes

and no vascular disease are slightly higher than those reported above, 1.6% vs. 1.1%.¹¹ Note that the RRRs in both tables are highly misleading and deceptive.

There is growing suspicion that a significant and perhaps major part of the action of statin drugs involves non-lipid lowering (pleiotropic) effects, of which there is a long and impressive list containing actions that can influence acute events, but have nothing to do with lower circulating cholesterol.¹³⁻¹⁵ This may partly explain the higher absolute risk reduction in secondary prevention trials seen in Table 2.

When absolute benefits are small and most do not benefit, as the data presented above suggests, focus shifts to side effects. A partial list includes increased risk of diabetes and its progression, hearing loss, transient global amnesia, gout, peripheral neuropathy, cataracts, bradycardia, muscle wasting, severe myopathy, cognitive impairment and liver dysfunction. For liver dysfunction, cataracts and myopathy, the number needed to treat to harm one patient with statin therapy cited by advocates of this therapy has been estimated for men at 142, 52 and 81 and for women 136, 33 and 259, respectively.¹⁶ However, and this is very important, most critics believe that adverse events are significantly under-reported, downplayed or prevalence data suppressed. Thus these NNTs should probably be much smaller and shift the risk/benefit toward unacceptable risk of side effects. The terrible aspect of statin side effects is that they can be confused with symptoms of other common diseases including those of aging, can take several years or even more to exhibit symptoms, can result in inappropriate treatment and in some cases, the damage is permanent, destroys the quality of life and leads to permanent disability. One can ask, how many patients are fully informed prior to starting on statins. Some would say almost none. Instead, they are given relative risk reductions which are deceptive in the extreme.

For more information of statin side effects, see the review by Dr. B. A. Golomb (45 pages, 800 references)¹⁷ and the book by Dr. Duane Graveline, *The Statin damage Crisis*.¹⁸ A transcript of a roundtable discussion of appropriate clinical use of statins involving three prominent physicians is also recommended and is in the public domain.¹⁹ Google the combination of the three names in the citation.

THE BOTTOM LINE

For diabetics without cardiovascular disease, the very small absolute benefits of statin treatment are just slightly larger than for non-diabetics. From an individual point of view, the probability of no benefit which is between 98 and 99% needs to be carefully considered in the light of the serious side effects which appear to be associated with statins when considering accepting treatment recommended by the new guidelines.

MOST CARDIOVASCULAR RISK CALCULATORS APPEAR INACCURATE

Guidelines for interventions to prevent cardiovascular events such as heart attacks and stroke have for many years used algorithms that yielded simple calculation schemes which used data such as age, gender, cholesterol levels, blood pressure information, smoking, family history and preexistence of cardiovascular disease. With the advent of the internet, online calculators were available and physicians even had them on their iPads. For example, the calculators provided the 10-year risk of a heart attack or a cardiovascular event as a percentage. This allowed guideline writers to organize their recommendations according to the calculated risk, perhaps with added conditions. The validation of these calculators depended on comparison with databases involving large diverse populations. These results were then applied to individuals.

Concern regarding the validity of these calculators mushroomed when the American Heart Association and the American College of Cardiology came out with new guidelines for the management of cardiovascular risk when they introduced a new calculator which was immediately attacked as being inaccurate and potentially resulting in statin overtreatment. Within days of the calculator details becoming available, Paul Ridker and Nancy Cook of Brigham and Woman's Hospital had published an analysis suggesting that the new tool overestimated the risk of heart attack and stroke by 75% to 150%. However,

the creators of the new tool stood by their work, claiming that the databases used by Ridker and Cook were not representative of the US population.

The results of a study and an accompanying editorial just published in the *Annals of Internal Medicine* will no doubt heat up the controversy considerably.^{20,21} Andrew DeFilippis from the University of Louisville, KY and colleagues used the Multi-ethnic Study of Atherosclerosis (MESA), a community based, sex-balanced multiethnic US cohort. They found the AHA/AAC calculator overestimated risk by 86% in men and 67% in women. They found that those with a risk score of 7.5% to 10% had an actual rate of heart attacks and strokes of only 3% in men and 5% in women. The risk of 7.5% was the threshold that served as the foundation of the new guidelines. In addition, three older Framingham-based risk scores overestimated events by 37% to 154% for men and 8% to 67% in women. In the accompanying editorial, Ridker and Cook suggest that one probable explanation for the failure of the new AHA/ACC calculator was that it was developed using data that was too old.

Thus the criticism that the new AHA/ACC guidelines would result in significant overtreatment appear to have just been considerably strengthened.

TIGHT GLYCEMIC CONTROL AND OVER-TREATMENT OF OLDER ADULTS WITH DIABETES

Tight glycemic control is defined as an HbA1c level < 7% or < 6.5% depending on the source of the guidelines. The American Diabetes Association (ADA) adds the qualification that this applies to younger healthy adults. However, diabetes is most prevalent among older persons (≥ 65 years of age), and for these individuals, optimum glucose management is ill-defined, but ADA recommendations suggest higher glycemic targets for older patients with multiple comorbidities, functional impairments, established diabetic complications or limited life expectancy. The rationale for this position is that intensive glycemic control is unlikely to result in benefit, but is associated with a risk of harm. Thus if adults over 65 have HbA1c levels of less than 7%, they can be viewed as over-treated and exposed to unnecessary risk. An important adverse effect is hypoglycemia (very low blood sugar. Hypoglycemic can cause one to pass out, fall and it even increases the risk of death.

In a just published paper in *JAMA Internal Medicine*. Lipska *et al* address this issue with data from the National Health and Nutrition Examination Survey for the years 2001 through 2010.²² In a nationally representative sample of noninstitutionalized adults, a total of 62% of older individuals (age ≥ 65) with diabetes had HbA1c < 7%. This corresponded to about 3.8 million US persons. For individuals with complex or very complex medical problems, 60% were treated to achieve tight glycemic targets. This corresponds to about 1 million individuals. These findings were found to be relatively constant over time. The conclusion: a substantial portion of older adults with diabetes are potentially over-treated. The authors cite a study which found the same situation where 50% of individuals at high risk or hypoglycemia or cognitive impairment had HbA1c levels < 7%. They conclude that “*Recognition of both the harms and benefits of glycemic control is critical for patients and physicians and other health care professionals to make informed decisions about glucose-lowering treatment.*” Note that Lipska *et al* introduce their study by commenting that “*intensive glycemic control is unlikely to result in a benefit....*”. This comment refers to the older persons and especially those with comorbidities, something most diabetics have.

The evidence of elevated risk of cardiovascular events associated with hypoglycemic episodes is controversial. However, it was confirmed in a recent meta-analysis (study of studies with pooling of results) involving 6 studies selected for high quality, all of which individually showed statistically significant elevated risk. The meta-analysis found severe hypoglycemia increased the risk of cardiovascular events by a factor of two.²³ Severe hypoglycemia is generally defined as a blood glucose level < 2.8 mmol/L (50 mg/dL)

REFERENCES

- (1) Danilov YKV. Emerging Noninvasive Neurostimulation Technologies: CN-NINM and SYMPATOCORRECTION. *Journal of Behavioral and Brain Sciences* 2014;4:105-113.
- (2) Wildenberg JC, Tyler ME, Danilov YP, Kaczmarek KA, Meyerand ME. Sustained cortical and subcortical neuromodulation induced by electrical tongue stimulation. *Brain Imaging Behav* 2010;4:199-211.
- (3) Tyler ME, Kaczmarek KA, Rust KL, Subbotin AM, Skinner KL, Danilov YP. Non-invasive neuromodulation to improve gait in chronic multiple sclerosis: a randomized double blind controlled pilot trial. *J Neuroeng Rehabil* 2014;11:79.
- (4) Wildenberg JC, Tyler ME, Danilov YP, Kaczmarek KA, Meyerand ME. High-resolution fMRI detects neuromodulation of individual brainstem nuclei by electrical tongue stimulation in balance-impaired individuals. *Neuroimage* 2011;56:2129-2137.
- (5) Wildenberg JC, Tyler ME, Danilov YP, Kaczmarek KA, Meyerand ME. Altered connectivity of the balance processing network after tongue stimulation in balance-impaired individuals. *Brain Connect* 2013;3:87-97.
- (6) Wildenberg JC, Tyler ME, Danilov YP, Kaczmarek KA, Meyerand ME. Electrical tongue stimulation normalizes activity within the motion-sensitive brain network in balance-impaired subjects as revealed by group independent component analysis. *Brain Connect* 2011;1:255-265.
- (7) American Diabetes Association. Standards of medical care in diabetes--2011. *Diabetes Care* 2011;34 Suppl 1:S11-S61.
- (8) Sever PS, Poulter NR, Dahlof B et al. Reduction in cardiovascular events with atorvastatin in 2,532 patients with type 2 diabetes: Anglo-Scandinavian Cardiac Outcomes Trial--lipid-lowering arm (ASCOT-LLA). *Diabetes Care* 2005;28:1151-1157.
- (9) Knopp RH, d'Emden M, Smilde JG, Pocock SJ. Efficacy and safety of atorvastatin in the prevention of cardiovascular end points in subjects with type 2 diabetes: the Atorvastatin Study for Prevention of Coronary Heart Disease Endpoints in non-insulin-dependent diabetes mellitus (ASPEN). *Diabetes Care* 2006;29:1478-1485.
- (10) Colhoun HM, Betteridge DJ, Durrington PN et al. Primary prevention of cardiovascular disease with atorvastatin in type 2 diabetes in the Collaborative Atorvastatin Diabetes Study (CARDS): multicentre randomised placebo-controlled trial. *Lancet* 2004;364:685-696.
- (11) Wright J. Do statins have a role in primary prevention? An update. *Theraeutics Initiative (Therapeutics Letter)* 2010;77.
- (12) Cholesterol Treatment Trialists' (CTT) Collaborators. Efficacy of cholesterol-lowering therapy in 18,686 people with diabetes in 14 randomised trials of statins: a meta-analysis. *The Lancet* 2008;371:117-125.
- (13) Liao JK, Laufs U. Pleiotropic effects of statins. *Annu Rev Pharmacol Toxicol* 2005;45:89-118.
- (14) Sadowitz B, Maier KG, Gahtan V. Basic science review: Statin therapy--Part I: The pleiotropic effects of statins in cardiovascular disease. *Vasc Endovascular Surg* 2010;44:241-251.
- (15) Mihos CG, Salas MJ, Santana O. The pleiotropic effects of the hydroxy-methyl-glutaryl-CoA reductase inhibitors in cardiovascular disease: a comprehensive review. *Cardiol Rev* 2010;18:298-304.
- (16) Hippisley-Cox J, Coupland C. Individualising the risks of statins in men and women in England and Wales: population-based cohort study. *Heart* 2010;96:939-947.
- (17) Golomb BA, Evans MA. Statin adverse effects : a review of the literature and evidence for a mitochondrial mechanism. *Am J Cardiovasc Drugs* 2008;8:373-418.
- (18) Graveline D. *The statin damage crisis*. Duane Graveline, M.D., MPH., 2009.
- (19) Perlmutter D, Golomb B, Sinatra S, Campbell AW. Appropriate clinical use of statins: a discussion of the evidence, scope, benefits, and risk. *Altern Ther Health Med* 2013;19 Suppl 1:14-25.
- (20) Defilippis AP, Young R, Carrubba CJ et al. An Analysis of Calibration and Discrimination Among Multiple Cardiovascular Risk Scores in a Modern Multiethnic Cohort. *Ann Intern Med* 2015;162:266-275.
- (21) Ridker PM, Cook NR. Comparing Cardiovascular Risk Prediction Scores. *Ann Intern Med* 2015;162:313-314.
- (22) Lipska KJ, Ross JS, Miao Y, Shah ND, Lee SJ, Steinman MA. Potential Overtreatment of Diabetes Mellitus in Older Adults With Tight Glycemic Control. *JAMA Intern Med* 2015.
- (23) Goto A, Arah OA, Goto M, Terauchi Y, Noda M. Severe hypoglycaemia and cardiovascular disease: systematic review and meta-analysis with bias analysis. *BMJ* 2013;347:f4533.

International Health News has an arrangement with iHerb to facilitate subscribers ordering supplements from a reliable source as well as assisting the newsletter in meeting its expenses. Dr. Ware, the editor, is not involved with this aspect of *IHN*, receives no financial benefit from these sales, and is only concerned with the scientific content of the newsletter.

Please use the link below to access the Vitamin Store.

Please Visit Our Vitamin Store



<http://www.yourhealthbase.com/vitamins.htm>

FREE subscription

<http://www.yourhealthbase.com/subscribe.htm>

Editor: William R. Ware, PhD

INTERNATIONAL HEALTH NEWS is published 10 times a year by
Hans R. Larsen MSc ChE, 1320 Point Street, Victoria, BC, Canada, V8S 1A5
E-mail: editor@yourhealthbase.com World Wide Web: <http://www.yourhealthbase.com>

ISSN 1203-1933 Copyright 2015 by Hans R. Larsen

INTERNATIONAL HEALTH NEWS does not provide medical advice. Do not attempt self-diagnosis or self-medication based on our reports. Please consult your healthcare provider if you are interested in following up on the information presented.