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Osteopathic Family Physician

THE OFFICIAL PEER-REVIEWED
PUBLICATION OF THE AMERICAN
COLLEGE OF OSTEOPATHIC
FAMILY PHYSICIANS

January/February, 2015
Volume 7 | Number 1
ofpjournal.com

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Osteopathic Family Physician (ISSN 1877-573X) is published bimonthly by the American College of Osteopathic Family Physicians, 330 E. Algonquin Rd, Suite 1, Arlington Heights, IL 60005. Periodicals postage paid at Arlington Heights, IL and additional mailing offices.

USA POSTMASTER: Send address changes to *Osteopathic Family Physician*, Membership Department, Suite 1, 330 E. Algonquin Rd, Arlington Heights, IL, 60005.

CUSTOMER SERVICE (orders, claims, online, change of address): Membership Department, 330 E. Algonquin Rd, Suite 1, Arlington Heights, IL 60005. 800-323-0794, membership@acofp.org

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EXAM	DATES AND EXAM LOCATION	POSTMARK APPLICATION DEADLINE
Family Medicine/OMT Certification Performance Evaluation ONLY	ACOFPP Conference March 12-15, 2015; Las Vegas, NV March 10-11, 2015	October 1, 2014; filing with late fee thru December 1, 2014
Family Medicine/OMT OCC/Recertification Exam - Performance Evaluation ONLY	ACOFPP Conference March 12-15, 2015; Las Vegas, NV March 12-13, 2015	November 1, 2014; filing with late fee thru December 15, 2014
Undersea & Hyperbaric Medicine Conjoint CAQ	March 14, 2015; Ft. Lauderdale, FL	November 25, 2014; filing with late fee December 30, 2014
Correctional Medicine Conjoint CAQ	March 14, 2015; Ft. Lauderdale, FL	November 25, 2014; filing with late fee December 30, 2014
Family Medicine/OMT Certification - Cognitive Exam	Electronic Testing; Regional Sites April 25, 2015	October 1, 2014; filing with late fee thru December 1, 2014
Family Medicine/OMT OCC/Recertification - Cognitive Exam	Electronic Testing; Regional Sites May 16, 2015	November 1, 2014; filing with late fee thru December 15, 2014
Geriatric Medicine CAQ Certification - Cognitive Exam	Electronic Testing; Regional Sites April 25, 2015	October 1, 2014; filing with late fee thru December 1, 2014
Geriatric Medicine CAQ OCC/ Recertification - Cognitive Exam	Electronic Testing; Regional Sites April 25, 2015	October 1, 2014; filing with late fee thru December 1, 2014
Sleep Medicine CAQ Certification Cognitive Exam	Lombard, IL August 22, 2015	
Sleep Medicine CAQ - Recertification Cognitive Exam	Lombard, IL August 22, 2015	
Family Medicine/OMT Certification - Cognitive Exam	Electronic Testing; Regional Sites September 26, 2015	April 1, 2015; filing with late fee thru June 1, 2015
Family Medicine/OMT OCC/Recertification - Cognitive Exam	Electronic Testing; Regional Sites September 26, 2015	April 1, 2015; filing with late fee thru June 1, 2015
Family Medicine/OMT Certification - Performance Evaluation ONLY	AOA OMED Conference October 17-21, 2015; Orlando, FL October 16, 2015	April 1, 2015; filing with late fee thru June 1, 2015
Family Medicine/OMT OCC/Recertification - Performance Evaluation ONLY	AOA OMED Conference October 17-21, 2015; Orlando, FL October 17-18, 2015	April 1, 2015; filing with late fee thru June 1, 2015
Hospice & Palliative Medicine Conjoint CAQ	October 18, 2015; Orlando, FL	July 1, 2014; filing with late fee July 15, 2015

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Editor's Message

Lies, Damn Lies, and Statistics

Merideth C. Norris, DO, FACOFP
Editor, Osteopathic Family Physician

I used to call them the Left Brain and the Right Brain. They were my two roommates at the student housing during one of my remote rotations. Lars, the Right Brain, was in med school as his second career and although he was quite bright, stunningly talented at OMM and a great listener, he resisted rote memorization of pathogens and algorithms so much that although it was our fourth year, he had yet to pass Step 2 of the boards. Tim, the Left Brain, was a delightful and friendly person who listened to Audio Digest for fun and would joyfully jump in and do the blood draws at the clinic if the MA was too busy. It was from Tim that I first heard about the JNC. Specifically, he came back to our shared apartment upset because his attending was not adhering to JNC-6 guidelines about spironolactone in CHF.

While I was trying to play it off as though I even knew what "guidelines" Tim was talking about, Lars hurtled in to the discussion defending the attending: "Patients are human beings! Not numbers! We practice according to what is best for the patient, not according to what some committee tells us! One size does not fit all!" Tim, also a patient-centered kind of guy, nodded in agreement, but added, "We do need to practice according to the evidence, not just according to what the guy before us always did. Isn't that a better way to provide care?"

Both are great people and neither was wrong. And all of us experience an internal battle of the brain hemispheres when practicing medicine. After JNC-7, we followed the guidelines, got all our patients' blood pressure to target, and felt great about it until our preload-dependent seniors started hitting the floor. That's "left brain" medicine gone awry. On the flip side, how many of us ignore the large body of evidence in support of amiodarone for certain dysrhythmias because we are haunted by that one patient whose nose turned purple and stayed that way? Our intuitive, gestalt-driven right brain can reactively put us on the wrong path as well.

Guidelines do a great job of predicting what an intervention will do to a population, but not to an individual. As my pulmonology attending used to point out, "Even if it's a rare

side effect, if it happens to you, it's 100%." Another mentor, however, would assert, "The plural of 'anecdote' is not 'data.'" Yet this same mentor was also fond of quoting Mark Twain on the three kinds of lies: "Lies, damn lies, and statistics."

We do have a responsibility to practice according to evidence, not intuition, and however some of us may flinch at the notion of applying a treatment algorithm to a human being, we are really fortunate to have review bodies like the JNC and the US Preventative Services Task Force to sift through the enormous amount of evolving data so we don't have to. We also need to understand the way the conclusions are drawn and know their limitations as applied to certain individuals. To quote yet another mentor, "this is why medicine is hard."

In this issue of OFP, we offer an update of the JNC-8 recommendations on blood pressure. You may be happy to notice that the targets for seniors have relaxed a bit. Inevitably when new guidelines are released, someone points to the change as proof that they were "wrong" the last time, and some will take it a step further and bemoan the uselessness of these committees because "they keep changing their mind so what good are they? I'm just going to keep doing what I know works." I disagree. Guidelines are not the Ten Commandments or the Magna Carta, static instructions to be followed no matter what new information comes through. They were never intended to replace good judgment. Guidelines are a tool, and just like any tool, it's important use the best one you can find, but to use it appropriately and within its scope: no matter how terrific your new screwdriver is, you don't use it to make an omelet. And if you try to anyway, the ruined breakfast will be your failure, not evidence that it was a lousy screwdriver.

Almost 15 years later, I periodically run into both Lars and Tim. They both remain intelligent, kind people and both seem happy with their lives and their choices. It is worth noting, however, that Tim is a beloved Associate Dean who just received a national award for excellence in education. But although he did eventually pass his boards, Lars no longer practices medicine at all.

Osteopathic Family Physician 2015 Call for Papers

Editor-in-Chief—Merideth C. Norris, DO, FACOFP

Associate Editor—Amy Keenum, DO, PharmD

Call for Papers

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- » Anemia
- » Chest Pain (Request OMT component in this paper)
- » Constipation (Request OMT component in this paper)
- » Dysuria
- » Hemorrhoids
- » Monetary Incentives in Care - Both the Ethics, and How Do I Calculate my RVU Bonus?
- » Nausea with Vomiting
- » Otitis Media, Acute
- » Sprain/Strain Neck (Request OMT component in this paper)

Didactic Images

We are seeking clinical images from the wards that covers essential concepts or subject matter to the primary care physician. Please provide a brief synopsis of how the case presented along with 1-4 questions and approximately 1 page of education with reference to the image and questions.

The JNC 8 Guidelines: A Clinical Review

Gary Rivard, DO; Erik Seth Kramer, DO, MPH; Sean Tyler O'Sullivan, DO

Central Maine Family Medicine Residency Program

KEYWORDS:

Hypertension
Review
Diagnosis
Treatment
Guidelines

Hypertension remains a significant cause of mortality and morbidity in the United States and is seen routinely in the primary care setting. Family physicians are frequently encountering individuals with hypertension and are primarily responsible for the initial diagnosis and initiation of treatment. The last review of this condition with a summary of definitions and recommendations for both diagnostic criteria and treatment came in the form of the guideline by Seventh Joint National Committee on the management of hypertension (JNC 7) in 2003. In the last decade research has placed direct questioning of the recommendations put forth in that document. Now the Eighth Joint National Commission (JNC 8) review has been made available with changes in diagnostic criteria and treatment options.

Three questions guiding the most recent review of literature were put forth. 1) Does initiating treatment at a particular threshold improve outcomes, 2) Does treatment to a particular systolic or diastolic goal improve outcomes, and 3) Do the various classes of medication confer different benefits and harms relative to specific outcomes. Key changes from JNC 7 include an increase in the systolic threshold to 150mmHg prior to initiation of pharmacologic treatment in those aged 60 and older and specific pharmacologic options based on racial differences and the presence of diabetes and/or chronic kidney disease.

INTRODUCTION

The National Lung, Heart, and Blood Institute (NHLBI) has long been the administrating organization for the National High Blood Pressure Education Program (NHBPEP) Coordinating Committee and subsequently the organization responsible for the formation of the Joint National Committee (JNC) on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. This group is charged with evaluating the evidence and submitting periodic reports with recommendations for the evaluation and management of hypertension.

In 2003, the JNC 7 was released. It was the first review of this topic since the JNC 6 report in 1997. When released, it was the most comprehensive review of the management of hypertension to date and was universally adopted as a reference. The goal was to synthesize the evidence available at the time and put forth patient centered recommendations for the management of hypertension. Examples of these recommendations include the formal adoption of the “DASH” diet and the use of concise resources for both patients and clinicians for use to educate and guide both groups in evaluation and treatment in the form of pocket cards and

electronic resources. Key messages included systolic blood pressure goals and a summary of both non-pharmacologic and medication options for the treatment of hypertension.¹

In 2013, an updated review of current literature was performed by the Eighth Joint National Committee (JNC8). A multi-disciplinary team assembled to review all recent literature on this topic. The 50-plus member team consisted of those from primary care; geriatrics, cardiology, nephrology, pharmacology, nursing, epidemiology, informatics, as well as specialists in review of evidence based medicine and the development and implementation of clinical guidelines. The guideline was then submitted through a peer review process between January and June of 2013. The reviewers were those with expertise in the treatment of hypertension. The guideline was also sent for review by federal agencies and those with primary interests to include primary care physicians, cardiologists, nephrologists, and pharmacologists. At the completion of this vigorous process the JNC 8 report was released in December 2013.

Only randomized controlled trials (RCT's) were included in the most recent literature review. This was a departure from the prior processes used to form the recommendations. In the JNC 7 report, a “less than systematic” approach to a review of the literature was used. Therefore, the choice to use only RCT's was based on a “true” evidence review and led to a more systematic approach.² A database search spanning 1966-1996 was done initially with an ongoing literature search performed as the document was being drafted.

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Four criteria were used to determine the adequacy of data and overall study selection for review to include in the summary of recommendations. These were 1) The primary focus of the study was hypertension; 2) the study had at least 2,000 participants, 3) multicentered, and 4) met other inclusion/exclusion criteria. The data were synthesized into tables of evidenced based “statements” that were then voted on. The panel was also asked to assign a grade based on the quality of evidence for each statement. For recommendations and statements based on reviewed evidence, a 2/3-majority vote was necessary for inclusion into the guideline. For those recommendations based on expert opinion only, a 75% majority agreement was required.

In stark contrast to the JNC 7 document, this review and its recommendations are based largely on expert opinion and are not endorsed by any public or professional organization. The JNC 7 report had been reviewed by multiple professional organizations to include federal agencies and the NHBPEP which was a primarily driver for the formation of the JNC 7 as noted above.

EPIDEMIOLOGY

Hypertension remains an important risk factor for cardiovascular disease including stroke, the development of arrhythmia, and myocardial infarction. The prevalence of hypertension has seen little change from 2000 to 2010, remaining at approximately 30%.³ In the 2007–2010 Morbidity and Mortality Weekly Report Supplement, the prevalence of hypertension was found to be higher in persons aged 65 and older (71.6%) and among non-Hispanic blacks (41.3%).³ These two groups remain an important focus of the new JNC 8 guidelines.

Healthy People 2020, a science-based 10-year national objectives initiative, set goals to both reduce the prevalence of hypertension among adults to 26.9% and to increase the prevalence of blood pressure control among adults “with” hypertension to 61.2%.⁴ According to the National Health Examination Surveys (NHANES) 2011-2012 study, the age adjusted total percentage of adults aged 20 and over with hypertension has decreased from 32.1% in 2003-2004 since the JNC 7 report was first published to 30.0% in 2011-2012⁵ (Figure 1). While the percentage of uncontrolled hypertension (defined as an average systolic blood pressure of 140 mm Hg or higher, or an average diastolic pressure of 90 mm Hg or higher among those with hypertension) has decreased for all age groups with high blood pressure, nearly 54.6% of adults continue to have uncontrolled high blood pressure in 2011-2012.⁵ The age-specific prevalence was 11.2% in males (22-44 years old). This rate has increased to 41.2% in the group ages

45-64 old; further increasing to 61.7% in the group aged 65-74 years old, and 75.1% in the group aged 75 years and over.

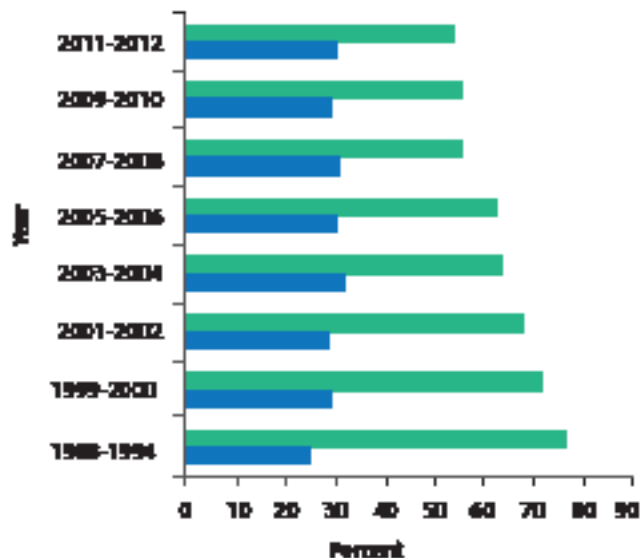
Prevalence of Hypertension by Race and Ethnicity

Black individuals have shown a higher prevalence and incidence of hypertension than white persons⁵ with rates, 38.8% (male) and 42.8% (female). In addition to higher prevalence, this population has experienced a much lower awareness of hypertension, affecting control of resultant comorbidities such as stroke, coronary heart disease, and chronic renal failure.⁶ These increases are likely due to the increased incidence of hypertension and diabetes in this population. In general, Mexican Americans are similar to or lower than those in non-Hispanic whites⁵ with rates of 27.3% (male) and 29.3% (female), showing a lower prevalence than black individuals.

Cardiovascular Risk

The Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7), the older population greater than 50 years, SBP > 140 was a more important cardiovascular disease risk factor than DBP. The risk doubled with each increment of 20/10 mm Hg.¹ Limited control of blood pressure has led to increased morbidity and mortality, primarily in cardiovascular disease and stroke. From 2000-2010, the age-adjusted mortality rate among males decreased by 37% and females by 32% for stroke, and 30% and 12% for heart disease.⁵

Figure 1: Total Hypertension and Uncontrolled Hypertension in > 20 years old.



■ Total age-adjusted % uncontrolled high blood pressure in patients with hypertension > 20 years old
 ■ Total age-adjusted % patients with hypertension > 20 years old

Source: CDC/NCHS, National Health and Nutrition Examination Survey, 2013.

Table 1: Recommendations

1	For individuals aged 60 or older, goal systolic blood pressure is ≥ 150 mmHg and diastolic blood pressure is ≥ 90 mmHg. These values should be used as the threshold for diagnosis and goals for treatment. Do not change treatment in those aged greater than 60 if current treatment is adequate for prior goals and the individual is not experiencing adverse side effects.	Strong Recommendation – Grade A evidence
2	For individuals aged 30-59 use a diastolic blood pressure goal of < 90 mmHg for diagnosis and initiation of treatment.	Strong Recommendation – Grade A evidence
2a	The diastolic goal of < 90 mmHg is also reasonable in those aged of 18-29	Expert Opinion – Grade E evidence
3	Start medication treatment of hypertension in those < 60 to achieve a systolic blood pressure of less than 140mmHg	Expert Opinion – Grade E evidence
4	For individuals with chronic kidney disease older than 18, start medication with a goal of less than 140mmHg/90mmHg	Expert Opinion – Grade E evidence
5	For individuals with diabetes disease older than 18, start medication with a goal of less than 140mmHg/90mmHg	Expert Opinion – Grade E evidence
6	For the nonblack individuals, including those with diabetes, initiation of medication treatment of hypertension should begin with either a thiazide diuretic, calcium channel blocker (CCB), angiotensin converting enzyme inhibitor (ACE-I), or angiotensin receptor blocker (ARB).	Moderate Recommendations – Grade B evidence
7	For black individuals, including those with diabetes, initiation of medication treatment of hypertension should begin with either a thiazide diuretic or CCB*	Weak Recommendation – Grade C evidence
8	For all individuals diagnosed with chronic kidney disease over the age of 18, the initial choice or add-on treatment should include an ACE-I or ARB	Moderate Recommendation – Grade B evidence
9	<ul style="list-style-type: none"> • Evaluate effectiveness of treatment after one month • Titrate to a maximum dose or consider “add on” treatment with additional first line agents • Do not use an ACE-I and ARB together • If unable to achieve optimal control with a combination of 3 first line agents, consider other classes loop diuretics, alpha blocking agents, aldosterone agonists, combination alpha and beta blocker agents (ie. carvedilol or labetalol) 	Expert Opinion – Grade E evidence

JNC 8 REPORT RECOMMENDATIONS

A summary of the literature review answering the questions facing the JNC 8 panel comes in the form of 9 recommendations. These are listed in Table 1. The first set of recommendations address the questions of what threshold to use for the diagnosis of hypertension and the subsequent goals in treatment and the remaining recommendations provide a concise framework for the choice of pharmacologic agents in the treatment of hypertension.

DIAGNOSIS OF HYPERTENSION AND WHEN TO INITIATE TREATMENT

The first set of recommendations address the issue of what threshold to use for the diagnosis of hypertension and the subsequent goals in treatment for older individuals and those with diabetes, chronic kidney disease, or both. In patients aged 60 years old or greater, a systolic threshold of 150mmHg and diastolic threshold of 90 mmHg is recommended. This is as a result of literature review suggesting improved outcomes in stroke and coronary heart disease.⁷⁻⁹ However, if an individual is optimized on current treatment and not experiencing adverse side effects, their medication should not be changed despite having a more tightly controlled blood pressure.

In those aged 30-59, a diastolic threshold for initiation of treatment and subsequent goal of less than 90mmHg is

supported by grade A evidence (strong recommendation). The recommended systolic goal, however, of 140mmHg in all persons > 18 years of age has been proposed but the evidence supporting this is a less robust and based on expert opinion.¹⁰⁻¹³

In all persons aged 18 years and older with a diagnosis of diabetes or chronic kidney disease the recommendation is a systolic threshold for treatment initiation and subsequent goal of 140mmHg and a diastolic value of 90mmHg. There is no evidence suggesting improved preservation of renal function with blood pressure goals less than 140/90.^{14,15} There are conflicting recommendations however with the last comprehensive guideline established by the American College of Clinical Endocrinologists suggesting 130/80 remain the goal and threshold for treatment.¹⁶

PHARMACOLOGIC MANAGEMENT

In addition to the diagnostic changes, a major focus of the current update involves how to approach the initiation of anti-hypertensive pharmacologic treatment.

Previously, the JNC 7 proposed thiazide diuretics as initial therapy for nearly all patients. The JNC 8 report still recognizes thiazide diuretics as useful first-line agents, however angiotensin converting enzyme or ACE inhibitors,

angiotensin receptor blocker agents or ARBs, and calcium channel blockers or CCBs are also reasonable first line choices. The JNC 8 makes treatment plans more flexible by allowing providers to choose from three or four broad classes of medications. In essence, there is not a single class of medications that are considered first-line, but most classes are considered reasonable choices.¹⁷

JNC 7 also supported ACE inhibitors, ARBs, and CCBs in addition to thiazide-diuretics, but numerous other medications were utilized early, such as beta-blockers, alpha-blockers, loop diuretics, and many more. It is no longer recommended that beta-blockers or alpha-blockers be used as first-line therapy as beta-blockers were associated with higher rate of adverse cardiovascular events and alpha-blockers showed inferior cardiovascular outcomes respectively.^{18,19} Using combination treatment strategies with a thiazide diuretic, CCB, and either an ACE inhibitor or ARB is preferred before initiation of a beta-blocker, alpha-blocker, aldosterone agonist, or loop diuretics.¹⁷

Patients already demonstrating adequate control, regardless of therapy, need not have their treatment regimen changed. For example, if a patient is well controlled on beta-blocker therapy, this should be continued.

African-American individuals should not be started on ACE inhibitors or an ARB as initial therapy due to worse cardiovascular outcomes based on the ALLHAT trial, however comorbidities must be taken into account.²⁰ If an African-American patient has underlying renal disease or diabetes, ACE-inhibitors or ARBs are beneficial for renal protection and may be an acceptable initial option.^{15,17}

CHOICE OF PHARMACOLOGIC AGENT

Thiazide Diuretics

Thiazide Diuretics work at the distal tubule of the nephron to inhibit sodium and chloride reabsorption creating diuresis. Thiazide diuretics are not as effective as loop diuretics for edema, but can be very effective in hypertension. They are appropriate for initial therapy in all ethnicities, however as discussed in the ALLHAT trial, potassium should be carefully monitored with use of thiazide diuretics due to risk of inducing new-onset diabetes. Chlorthalidone carries a higher risk for subclinical hypokalemia²¹ but has been shown to produce a more effective decrease in systolic blood pressure and has a longer lasting effects on blood pressure than hydrochlorothiazide.²⁰

Calcium Channel Blockers (CCB)

Calcium channel blockers act in lowering blood pressure by lowering contractility of vascular smooth muscle thus leading

to systemic vasodilation. The most studied and effective of these is amlodipine. It is generally well tolerated, effective for managing hypertension, and has good compliance with once daily dosing.²⁰

Angiotensin Converting Enzyme Inhibitors (ACEIs)/ Angiotensin Receptor Blockers (ARBs)

Both ACEIs and ARBs act on the renin-angiotensin system to promote vasodilation and decrease vascular resistance to promote lowered blood pressure. Both ACEIs and ARBs are generally well tolerated and are recommended in diabetics due to renal protective effect.¹⁵ Also of note, ACEIs and ARBs are indicated in patients with chronic heart failure and history of myocardial infarction.¹

Table 2: Pharmacologic options for the treatment of hypertension in certain populations

Population	Initial Therapy	Add On Therapy	Other Considerations
18-75	Thiazide, CCB, or ACE-I/ARB	Triple therapy before other agents	
>75 years old	Thiazide or CCB	Thiazide or CCB	Do not use ACE-I or ARB
Diabetics	Thiazide, ACE/ARB, or CCB	Triple therapy before other agents	
Chronic Kidney Disease	ACE-I/ARB	Thiazide or CCB	ACE-I or ARB first-line for CKD regardless of race or diabetes status
African-American	Thiazide or CCB	Thiazide or CCB	ACE/ARB contraindicated

Table 3: Comparison of potential “first line” medication classes for the treatment of hypertension

Medication Class	Benefits	Risks	Other Considerations
Thiazide Diuretics	May also improve edema	May cause hypokalemia or hypomagnesemia	
CCB	May also control irregular heart rate	Lightheadedness/ dizziness -> possible gait instability	
ACE-I/ARB	Renal protection	Worse cardiovascular outcomes in African-American patients	Do not combine ACE-I and ARB. No benefit from combination therapy.

CONCERNS REGARDING THE UPDATED RECOMMENDATIONS:

This is not an official updated guideline sanctioned by the NHLBI, as was the case in the prior JNC reports. There is

no plan to further release JNC type guidelines. This updated set of recommendations was designed to help the practicing clinician and to offer the most recent review of the literature with several key questions to be addressed. Only randomized clinical trials were included in this review. Other organizations have produced evidence based guidelines as well, particularly those from specialty organizations reviewing the clinical impact of hypertension on cardiovascular outcomes to include those individuals with diabetes and chronic kidney disease.

Issues surrounding the validity of these current recommendations as “stand alone” points should be questioned. Much of what is discussed in this update is reflective of evidence-based discussion from other groups who have the support of more extensive research for the basis of their recommendations.

SUMMARY

In stark contrast to the JNC 7 document, this review and its recommendations are based largely on expert opinion and are not endorsed by any public or professional organization. The JNC7 report had been reviewed by multiple professional organizations to include federal agencies and the NHBPEP, which was a primary driver for the formation of the widely accepted JNC7 as noted above. The more liberal thresholds for diagnosis and treatment should be evaluated relative to co-morbid conditions and in discussion with the patient.

There may never be another update of JNC recommendations like those seen last in the JNC 7 report. This is evidenced by the fact that no recommendations continuing to support lifestyle modification were included. The basis for those recommendations remains without question. The (Dietary Approach to Stop Hypertension) DASH diet, exercise recommendations, and smoking cessation continue to be the cornerstone of prevention.¹ In the future we will likely be offered recommendations from multiple work groups representing different organizations coming together for more “consensus” type work. This will certainly eliminate repetitive work and will decrease the degree of conflicting recommendations.

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Dietary Supplements: Navigating the Pharmacologic Influences of Nature's Medicine

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KEYWORDS:

Dietary supplements
Supplement label
Vitamin D
Omega 3
Glucosamine/Chondroitin

The use of dietary supplements occurs in the majority of American adults >20 years old and has been reported to be on the rise by the National Health and Nutrition Examination Survey. People are not only taking more dietary supplements, but taking them without the advice of a health care provider. With the lack of education time and focus on this topic, physicians need to know some evidence regarding the most common supplements used, how to understand dietary supplement labels, and where to find reputable information about dietary supplements. Vitamin D, Omega-3, and Glucosamine/Chondroitin are reviewed here. Also, a description of the various components of a dietary supplement label is explained. Finally, a brief description of independent companies (Consumerlabs.com®, US Pharmacopiedial Convention, Natural Medicine Comprehensive Database, and Natural Standard) as well as the federally run Office of Dietary Supplements are presented.

DIETARY SUPPLEMENTS

Dietary supplements (referred to as “supplements” throughout this article), as defined by the Dietary Supplement Health and Education Act (DSHEA) of 1994, are:

“Products (other than tobacco) that are intended to supplement the diet; contain one or more dietary ingredients (including vitamins, minerals, herbs or other botanicals, amino acids, and other substances) or their constituents; are intended to be taken by mouth as a pill, capsule, tablet, or liquid; and are labeled on the front panel as being a dietary supplement.”¹

The United States Food and Drug Administration regulates supplements differently than food and drug products. Companies producing supplements must register their manufacturing plant, provide their own safety testing prior to bringing a product to market, and keep records of the adverse events of a supplement.¹ Because supplements are not strictly regulated, they can be marketed and purchased directly by consumers. This makes it imperative that family physicians have an understanding of supplements. The goal of this review is to provide information on who uses supplements,

what supplements are used, the evidence of some popular supplements, an explanation of supplement labels, and where to go to find reputable information regarding supplements and their ingredients.

USE

The National Health and Nutrition Examination Surveys (NHANES) began gathering data on supplement use in the United States in the early 1970s when the prevalence of use was 28% among adult males and 38% among adult females.² With subsequent reports, there has been an increase in the percent of Americans who were taking at least one supplement.³ Since 1999, data continues to be collected every two years and this trend of use does not appear to be slowing down. The last analyzed data from 2007-2010 showed almost half of the U.S. population used at least one supplement.⁴ The reports indicate that more women use supplements than men (54% vs. 43%) and their use is highest among non-Hispanic whites (54%), adults >60 years old (67%), and those with more than a high school education (61%).^{4,5} Children use supplements less, but there is a positive relationship with their parents' level of education and household income.⁶ Another striking fact is that 77% of adults surveyed were taking supplements without a prescription from a health care provider.⁴ Among the top reasons why adults older than 20 take supplements are to “improve” (45%) or “maintain” (32.8) overall health.⁴

Data from the 2007-2010 NHANES shows people choose to take multivitamin and mineral supplements more than any other supplement (31.9%), followed by calcium (11.6%),

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omega-3 (9.8%), botanicals (7.5%), vitamin C (7.1%), vitamin D (4.9%), vitamin E (3.7%), and joint supplements (4%), along with other supplements without as much prevalence of use⁴. Other data from a survey of adults who used natural products in the last 30 days showed omega-3 to be the most used at 37.4%, next glucosamine (19.9%), then echinacea (19.8%), along with others including chondroitin (11.2%).⁷

EVIDENCE

Figure 1: Summary of the evidence for commonly used supplements.

<p>Vitamin D</p> <ul style="list-style-type: none"> • Doses of Vitamin D3 1000-2000IU PO daily up to 10,000IU have been shown to be safe and effective • Keep levels between 40-60nmol/L • No consensus on routine screening for Vitamin D deficiency in asymptomatic, healthy adults • Vitamin D receptor on a majority of cells in the body, checking vitamin D levels can be considered helpful especially in an area where the population does not receive adequate sunlight.
<p>Omega-3 (DHA/EPA)</p> <ul style="list-style-type: none"> • SMASH (Salmon [wild pacific], Mackrel [spanish], Anchovies, Sardines, and Herring) • 1-2g PO daily for cardiovascular benefits • 2-4g PO daily anti-inflammatory benefits • 4g PO daily for elevated triglycerides
<p>Glucosamine/Chondroitin</p> <ul style="list-style-type: none"> • 1500mg Glucosamine Hydrochloride (500mg PO TID) combined with 1200mg Chondroitin Sulfate (400mg PO TID) can help with moderate-severe knee arthritis pain (GAIT) • 1500mg Glucosamine sulfate (1500mg PO daily) can help with knee arthritis pain (GUIDE)
<p>Multivitamin/mineral</p> <ul style="list-style-type: none"> • Do not use unless known deficiency • Correct specific deficiency • Do not have health benefit

The evidence of some of these supplements has been reviewed, while consensus about others still needs to be hashed out. For example, 400-800 micrograms of folic acid daily for women of childbearing age have been shown to decrease neural tube defects by 50-70%⁸. With data like that, you would expect more than 1.5% of American's to be using it.⁵ On the other end of the spectrum are multivitamins. They are the most commonly used supplement, but recently a consensus statement by the United States Preventive Services Task Force (USPSTF) recommended against their daily use unless a patient has a known vitamin or mineral deficiency.⁹ Currently, some of the most commonly studied dietary supplements in the literature are: vitamin D, omega-3, and glucosamine/chondroitin.

Vitamin D

Vitamin D is a fat-soluble vitamin that is thought to be a hormone since a vitamin D receptor was discovered to be

universally expressed in nucleated cells.¹⁰ Vitamin D is rarely found in unfortified foods, so the major source is synthesis from sunlight exposure. Whether ingested or dermally synthesized, vitamin D requires enzymatic conversion in the liver to 25-hydroxyvitamin D (25[OH]D; the major circulating form) and further conversion in the kidney into 1,25-dihydroxyvitamin D (active form). The form that is usually evaluated by venous blood testing is 25[OH]D. There is a major initiative through the Office of Dietary Supplements, as well as other researchers, to get a better understanding of vitamin D. In the NHANES 2005-2006, 42% of adults greater than 20 years old had 25[OH]D levels that were considered vitamin D deficient.¹¹ A committee from the Institute of Medicine (IOM) reviewed the data and concluded that serum levels of 25[OH]D > 50nmol/L would cover the vitamin D requirements for 97.5% of the population and serum concentrations > 125nmol/L are associated with potential adverse effects.¹² Therapeutic levels of 25[OH]D are targeted between 40-60 nmol/L. This can be achieved through daily dosing with a supplement containing 1000-2000 IUs of vitamin D3 with dosing dependent on the adiposity of the patient, sequestered more with increased adiposity.¹³ Doses as high as 10,000 IUs per day have not been shown to cause hypercalcemia or acute intoxication¹² and can be indicated in adults who are vitamin D deficient.¹⁴

The USPSTF had released a draft document regarding its recommendation for the screening for vitamin D deficiency in asymptomatic individuals at the time of this manuscript preparation. Its conclusion was that screening for vitamin D deficiency is not necessary for healthy, asymptomatic adults.¹⁵ It is difficult to say who is "asymptomatic" since vitamin D deficiency has been associated with a variety of pathologic conditions. Vitamin D deficiency has been shown to have an influence on cardiovascular disease, cognition, bone mineral density, falls, development of diabetes, cancer, the immune system and chronic pain.¹⁶

Omega-3

Omega-3 is a type of fatty acid that exists in the phospholipid membrane of every cell in our body. It is the counterpart to omega-6, which is also present in our cells. The biggest difference between these two fatty acids is that omega-6 is pro-inflammatory and omega-3 are anti-inflammatory. The omega-3s are found in the diet as alpha-linolenic acid (ALA; 18:3 omega-3) and eicosapentaenoic acid (EPA; 20:5 omega-3) as well as docosahexaenoic acid (DHA; 22:6 omega-3) with different functions of each of the omega-3s in different cells. ALA is considered an essential fatty acid (EFA) because humans cannot produce it in vivo; both EPA and DHA may be obtained either directly through foods, supplements, or by the enzymatic conversion of ALA.

These fatty acids are known to have pleiotropic effects, including effects against inflammation, platelet aggregation, hypertension, and hyperlipidemia.¹⁷ These effects may be mediated through several distinct mechanisms, including alterations in cell membrane composition and function, gene expression, and eicosanoid production.¹⁷ The standard American diet has a ratio of 10:1 to 25:1 omega-6 to omega-3. The optimal ratio is considered to be 2:118. The IOM has set a recommended macronutrient dose of 0.6 - 1.2 g/day for people > 1 year of age. The best way to get omega-3s is through your diet. You can achieve the minimal needs with two servings of fatty, cold-water fish per week. For the best sources of omega-3 - EPA and DHA, remember the acronym SMASH: Salmon (wild Pacific), mackerel (Spanish), anchovies, sardines, and herring. If you do not reach the recommended dose with your diet, you can take a supplement. Most 1g supplements contain 30% of the active ingredients EPA and DHA, so you must choose wisely. Most experts recommend 1-2 g/day for cardiovascular benefits, 2-4 g/day for anti-inflammatory benefits, and 4 g/day for elevated triglycerides.

Glucosamine/Chondroitin

Glucosamine and chondroitin are in the body and are used to make cartilage that protects intra-articular bones from compressive forces. One cannot obtain glucosamine or chondroitin from a dietary source. Most glucosamine supplements are made from chitin, which is found in the hard shells of shellfish, while chondroitin is made from shark cartilage, bovine cartilage, or synthetically.

There have been two major studies of glucosamine and chondroitin for treatment of pain from knee osteoarthritis: the Glucosamine/Chondroitin Arthritis Intervention Trial (GAIT) and the Glucosamine Unum In Die [Once a day] Efficacy (GUIDE) trials. In the GAIT trial, a large, randomized controlled, multi-center population in America was given either 500 mg of glucosamine hydrochloride three times per day, 400 mg of chondroitin sulfate three times per day, both glucosamine and chondroitin, celecoxib 200 mg daily, or placebo for 24 months. There were no significant differences among the groups overall, but a sub-group analysis showed that the combination of glucosamine hydrochloride and chondroitin sulfate helped relieve moderate to severe pain.¹⁹ In the GUIDE trial, a group of patients in Europe was randomized to receive 1500 mg of glucosamine sulfate once daily, acetaminophen 3 g daily, or placebo for six months. The results showed that once daily dosing of glucosamine sulfate was safe and effective for the relief of pain associated with knee osteoarthritis.²⁰

LABELS

Besides knowing the evidence backing the use of a specific supplement, it is just as important, if not more important, to know the contents of that supplement. If patients bring in their supplement bottles for you to read, then you will be able to start deciphering their choices. Understanding the different parts of a supplement label will be the first step in this analysis.



Image 1: How to Read a Vitamin Label²¹
(Printed with permission from the AAFP)

There are key aspects to the label that can help the provider understand the supplement:

1. Suggested Use

A supplement will contain this group of statements to inform the user of what the company considers the appropriate amount to take and any special instructions on how it should be taken.

2. Serving Size

This unit will be the basis of how one can determine the dosage of the ingredients within the supplement. The serving size will tell the user how much they need to take to reach the amounts listed per serving. An example from this label would be if you wanted someone to take 1000 mg of calcium, they would have to take two tablets because each tablet will have 500 mg.

3. Percent Daily Value

The percent daily value indicates how the dose of an ingredient in the dietary supplement covers the Daily Recommended Intake (DRI) established by the IOM. These differ among ages and genders. An example from this label would be that the DRI of calcium is 1000 mg per day. Because this dietary supplement only contains 500 mg of calcium per serving, it

has a percent daily value of 50%. The DRI of an ingredient is constant, but the amount per serving of an ingredient can vary.

4. No Percent Daily Value

There are still some ingredients that may offer health benefits and are put into supplements without a DRI having been established by the IOM.

5. Lot Number

A lot number is used with any manufactured product in order to track when and how it was produced as well as what ingredients and equipment may have been used to produce that specific product.

6. Expiration Date

The expiration date is put on the supplement to let the user know how long until the product will not be as potent. Supplements, like most products made of nondurable goods, may not be as effective after they have passed their expiration dates.

7. Ingredients

The ingredients are listed in descending order by weight. Something to watch out for with ingredients is what type of a specific ingredient manufacturers are using to produce the supplement. For example, with the label, the calcium is being provided by calcium citrate. This type of calcium ingredient has different absorption and percent of elemental calcium than the more common form of calcium carbonate. Calcium can also be supplemented with calcium phosphate and calcium lactate, but these are less common due to cost and lower concentration of calcium.²²

8. Manufacturer's Facility and Contact Information

These pieces of information should be included on all supplements to be used to report adverse events.

9. Quality Marks and Statements

Not all supplements will bear this specific USP seal displayed here, but if it does, then you know it has passed rigorous standards.

10. Cautions and Warnings Statement:

Statements may be included on a supplement that warn specific groups of people with certain medical conditions, allergies, pregnant or lactating, or taking other prescription drugs who should avoid using this supplement. It could also include precautions before taking the supplement or potential side effects of its use.

There are also other important details that can be seen on a supplement label that should not be overlooked.

Health Claims

A product can place a health claim on its label but it must be reported to the FDA within 30 days. Most supplements will have a blanket statement to cover liability such as:

"These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure or prevent any disease."

Amount Per Serving

The amount per serving is closely tied to the serving size and percent daily value listed above. This value will tell you how much of a specific ingredient is in one serving of the dietary supplement. Depending on the dose one wishes to take, the serving size can be adjusted based on the amount per serving. You can help patients see if their supplement choice will be cost effective based on the dose they may need.

Allergens

As with any product that is ingested, there needs to be disclosures about allergens.

INGREDIENTS

Figure 3: Resources for verifying ingredients

<p>NIH Office of Dietary Supplements (https://myds.nih.gov/) <i>Director: Paul M. Coates, Ph.D.</i></p> <ul style="list-style-type: none"> • Searchable databases of federally funded projects, fact sheets, supplement ingredients, supplement labels • Vitamin D Initiative • Evidence-based reviews • Research support • Training and career development
<p>Natural Standard (https://naturalmedicines.therapeuticresearch.com/) <i>Co-Founders: Catherine Ulbricht, PharmD, MBA[c] and Ethan Basch, MD, MSc, MPhil</i></p> <ul style="list-style-type: none"> • Indexed databases on a variety of topics including Food, Herbs, and Supplements; Health and Wellness; Medical Conditions; Commercial Products; and Manufacturers • Advanced and Basic Interactions Checker • Continuing Education
<p>Consumer Lab (http://consumerlabs.com/) <i>President: Tod Cooperman, MD</i></p> <ul style="list-style-type: none"> • Membership = \$36 for 12 months or \$59 for 24 months • Independent reviews of products (membership required) • Recalls and Warnings (membership required)
<p>Natural Medicine Comprehensive Database (http://naturaldatabase.therapeuticresearch.com/home.aspx?cs=&s=ND) <i>Editor-in-Chief: Jeff M. Jellin, Pharm.D</i></p> <ul style="list-style-type: none"> • Membership = single user subscription 1 year: \$299, 2 year: \$525, and 3 year: \$725 • Daily website updates with evidence-based monographs, interactions, brand product reports, and special reports
<p>United State Pharmacopeial Convention (http://www.usp.org/)</p> <ul style="list-style-type: none"> • Sets worldwide standards for medicines, food, and supplements • Scientifically tests: 1) consistent quality between batches, 2) consistent quality of ingredients, 3) proper manufacturing practices, and 4) tolerable levels of contamination • Teamed with the Natural Medicines Comprehensive Database

Once you have read the label, you can then begin to critically analyze the ingredients used. All supplement ingredients are not created equal. The different types of glucosamine and chondroitin used during the GAIT and GUIDE trials highlights the importance of understanding which ingredients are used to make a supplement and how they actually work within the body. In this regard, active ingredients of supplements should be thought about as if they were prescription drugs. Pharmacokinetics, pharmacodynamics, safety, efficacy, potency, bioavailability of an ingredient are important and should be understood in order to direct your patients toward appropriate and intelligent use of supplements.

The underlying pharmacology, physiology, chemistry, and biochemistry of some ingredients are well known while others are less studied. This can be a challenging point in understanding the benefit of different supplements. Family physicians need to know where to go to get the most up-to-date information regarding supplement ingredients. There are a few websites we recommend using as references.

The Office of Dietary Supplements

The Office of Dietary Supplements was established in 1995 within the Office of Disease Prevention at the National Institutes of Health after the passing of the Dietary Supplement Health and Education Act of 1994. Its purpose is to lead the national understanding of supplements by promoting scientific investigation, reviewing the available literature worldwide, compiling databases, and coordinating funding for the NIH.²³ It principally acts as a funding source, with 69% of its 2008 budget going toward grants, but also operates a large database of information for consumers and professionals on common supplements, including a searchable database of federally funded supplement research projects, fact sheets, ingredients, and labels.²³

Natural Standard

Natural Standard was founded by healthcare providers and researchers in order to analyze scientific data on complementary and alternative medicine. It has numerous senior editors, authors, peer reviewers, and contributors with a wide range of clinical and research expertise. They take a systematic approach to reviewing the literature to provide their databases and interaction checkers. Within the databases, you can find general information about a complementary and alternative medicine modality as well as an in-depth review of articles about it. The interaction checker includes complementary and alternative medicines as well as some common generics used by many patients (eg: Lisinopril).²⁴

ConsumerLab.com

ConsumerLab.com® was started in 1999 as an independent tester of health and nutritional products. The results are published on its website and available to members. It also conducts an annual Survey of Vitamin and Supplement Users. Its product testing procedure is detailed on the webpage and includes a random sample purchased in the open market; tests for identity, strength, purity, and disintegration; and retests the product every 12 months to keep the “CL Seal of Approval on the product.”²⁵

Natural Medicines Comprehensive Database

The Natural Medicines Comprehensive Database is an independent organization that was established in the fall of 1999 by a group of researchers from the Therapeutic Research Center. This group originally began to write evidence-based, unbiased recommendations in 1985 for pharmacy and prescribing health professionals when it began to receive a large volume of questions regarding natural medicines. It researched the evidence and found that there were no solid studies. The goal was to produce highly objective, evidence-based resources for health professionals. The researchers for this database update their website daily with evidence-based monographs, interactions, brand product reports, and special reports. This information is available with a subscription.²⁶

United States Pharmacopeial Convention

The U.S. Pharmacopeial Convention (USP) is a nonprofit organization that has been around since 1820. Since then, the USP has set the standards for the identity, strength, quality, and purity of medicines, food ingredients, and supplements manufactured, distributed, and consumed worldwide. Specific to supplements, the USP has been putting their mark on the labels of companies that have volunteered their products to be evaluated based on the USP’s rigorous scientific standards. If a supplement bears this mark then it has passed testing for consistent quality between batches, consistent quality of ingredients, proper manufacturing practices, and tolerable levels of contamination.²⁷ The USP has even teamed with the Natural Medicines Comprehensive Database to have its mark appear next to supplements that have passed the USP standards and have been reviewed by its team.

CONCLUSION

Over 100,000 patients die each year from pharmacologic treatments, which is leading to disenchantment with the medical profession and its traditional treatment modalities.²⁸ This article was prepared to give family physicians a resource from which to propel their understanding of supplements. First and foremost, we should take note that a majority of patients are taking supplements⁵ and most patients are taking

them without consulting a healthcare provider.⁴ We need to be sure to ask patients what supplements they are taking, how much, how often, what brand, and why?

It is commonly stated:

“Let your health care providers (including doctors, pharmacists, and dietitians) know which dietary supplements you’re taking so that you can discuss what’s best for your overall health. Your health care provider can help you determine which supplements, if any, might be valuable for you.”²⁹

We need to be armed with knowledge of supplements so we can be an active participant in this discussion with them.

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The Current Role of Long-Term Benzodiazepines for the Treatment of Generalized Anxiety

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KEYWORDS:

Benzodiazepines
 Long-term treatment
 Generalized anxiety
 Current role

Benzodiazepines are one of the most widely used medications for the treatment of generalized anxiety. Due to their quick onset of action, efficacy and tolerability, benzodiazepines are widely prescribed by clinicians and utilized by patients. Although benzodiazepines have been beneficial and effective for the short-term management of anxiety, they have not been shown to be effective in producing long-term improvement. Chronic use of benzodiazepines has demonstrated multiple side effects including cognitive impairment, decreased motor coordination, concentration, social phobia, and depression. The development of tolerance, dependence and withdrawal are some of most significant problems associated with the long-term use of benzodiazepines. Withdrawal associated with the use of benzodiazepines includes insomnia, agitation, anxiety, seizures and coma.

INTRODUCTION

Generalized anxiety disorder (GAD) may be treated with different classes of medications such as selective serotonin reuptake inhibitors (SSRIs), serotonin-norepinephrine reuptake inhibitors (SNRIs), tricyclic antidepressants, antihistamines, barbiturates, and benzodiazepines. Prescribed for a multitude of medical conditions (anxiety, agitation, panic disorder, alcohol withdrawal, dystonia, insomnia, etc.) benzodiazepines have been approved for many indications.¹ While much is known about the safety and efficacy of benzodiazepines for the short-term treatment of GAD, there is limited data to guide decisions for the extended duration of benzodiazepine therapy for this medical condition.²

GENERALIZED ANXIETY DISORDER

According to the Diagnostic and Statistical Manual of Mental Disorders (DSM V), the diagnosis of GAD involves tension, worries, and fears about everyday events and problems on most days of the week for at least six months. The inclusion of the following criteria must also be met: anxiety or worry that interferes with daily life, anxiety that isn't related to another mental disorder (post traumatic stress disorder, substance abuse, etc.) and difficulty controlling worry. Additionally, at least three of the following must be present in adults or one of the following in children to contribute to the diagnosis of GAD: difficulty with concentration, problems falling or staying asleep, irritability, muscle tension, feeling of restlessness and unusual fatigue. Other generalized symptoms may also occur.³

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FINDING A ROLE FOR LONG TERM BENZODIAZEPINES

There is controversy regarding the long-term use of benzodiazepines due to the adverse physical and psychological effects, tolerance, physical dependence and eventually withdrawal symptoms that can occur with cessation of treatment with this category of medication. Known for their rapid onset of action and clinical effectiveness over the short term, benzodiazepines can be used during the initiating phase of an SSRI or SNRI.⁴ In the decision tree below, note the role of benzodiazepines in the management of anxiety.

Table 1: Generalized Anxiety Disorder⁵

Target Symptoms:	Subjective with anxiety/tension, excessive worry, and a variety of physiological complaints (GI, musculoskeletal, neurological)
Medication Treatment:	<p>Start with SSRIs in doses higher than for depression.</p> <ul style="list-style-type: none"> • Escitalopram (Lexapro) 10-25 mg Once Daily • Sertraline (Zoloft) 50-150 mg Once Daily • SNRIs in usual doses <p>Or</p> <p>VenlafaxineXR (EffexorXR) 75-225 mg Daily</p> <p>Or</p> <p>Buspirone (Buspar) 5-15 mg TID Alone or adjunct to above.</p> <p><i>Note: often 6-8 weeks before evident response.</i></p> <p>Or</p> <p>Benzodiazepines may be used alone or in combination for ongoing treatment or in management of periods of exacerbation</p> <p>Clonazepam (Klonopin) 1-2 mg up to TID</p>
Psychotherapy:	Referral to outside or co-located professional for cognitive behavioral psychotherapy may be effective as adjunct or in lieu of medication.

In the short term, benzodiazepines can be used with antidepressants in a combined effort since antidepressants take weeks to work. During the first several weeks of antidepressant therapy, benzodiazepines can help alleviate the nervousness with starting antidepressants. When the effect of an antidepressant begins to take effect, the benzodiazepine can be tapered off. In certain instances, benzodiazepines may be continued for the long term in patients who cannot tolerate tapering. Additionally, intermittent therapy may be needed in patients who have periodic symptoms initiated by identifiable anxiety provoking situations.

Long-term use of benzodiazepines is defined as use for two months or more at therapeutic dose. As most clinical trials on anxiolytic therapy are four weeks or less, few placebo-controlled trials exist to extrapolate the long-term effects of benzodiazepines in anxiety. Long term placebo-controlled trials are difficult from an ethical standpoint as they put a patient with psychiatric needs in the uncomfortable position of using a placebo or ineffective medication.⁶ To ask if there is a role of long term benzodiazepines for anxiety begins with appreciating the spectrum of benzodiazepine half-lives and their pharmacokinetics.

PHARMACOKINETICS

When looking at the potential of their clinical effectiveness, the pharmacokinetics of benzodiazepines should always play a role in defining an appropriate therapeutic regime. The lipid solubility of benzodiazepines determines the speed of entry into lipid tissue of the brain, followed by their redistribution into adipose tissue. Known to depress the central nervous system at the levels of the limbic system and the brain-stem reticular formation, as well as through their binding to the GABA-chloride receptor complex, benzodiazepines facilitate the action of GABA, an inhibitory neurotransmitter on CNS excitability. Benzodiazepines enhance the effect of GABA resulting in hypnotic, sedative, anxiolytic, anticonvulsant, amnestic and muscle relaxant properties.

The lipid solubility of benzodiazepines creates a high volume of distribution, resulting in the tissue drug concentration at a higher level than the blood drug concentration. Metabolized primarily through hepatic microsomal oxidation and demethylation, benzodiazepines are excreted by conjugation. Following conjugation, benzodiazepines become the more polar, water-soluble glucuronide derivatives. Patient age, smoking, liver disease, and concurrent use of other drugs may change the volume of distribution and the elimination half-life of benzodiazepines.

As we consider the differences in the short versus the long-term use of benzodiazepines for the treatment of GAD, we

note that generally the longer the half-life of the drug, the greater the likelihood the compound will have on daytime functioning. In shorter half-life drugs, withdrawal and anxiety between doses along with anterograde amnesia are more common. Short acting agents are generally used as hypnotics and for acute anxiety. Agents in this category include diazepam, lorazepam, alprazolam, triazolam, and estazolam. Triazolam's half-life of two to three hours is the shortest in this category, with the others ranging from eight to thirty hours. As a result of their short acting half-lives, the absorption, attainment of peak concentrations and onset of action are quickest. For long acting agents such as diazepam, chlordiazepoxide, clonazepam, clonazepam, flurazepam, prazepam, quazepam, and halazepam, half-lives are 30 to more than 100 hours in duration.⁷ See Chart A for an overview of the pharmacokinetics of benzodiazepines.⁸

CAUTIONS WITH LONG TERM USE OF BENZODIAZEPINES

Benzodiazepines have been shown to be effective in the short-term management of anxiety, but have not been effective in producing long-term improvement.⁹ According to the National Institute for Health and Clinical Excellence (NICE), benzodiazepines can be used in the acute setting of anxiety, however they should not be used for longer than two to four weeks.¹⁰

Several cautions should not be overlooked in order to consider benzodiazepines for long-term anxiety therapy. Since the medication is metabolized by the liver, elderly and liver disease patients may need to be closely monitored through liver function testing. Caution should also be used in the treatment of obstetric patients. As there is potential for habit formation, benzodiazepines can be misused by polysubstance abusers who prefer agents with rapid peak drug effects such as diazepam, lorazepam, and alprazolam. And, since benzodiazepines have more of a sedating effect with longer half-lives, methadone users may take a benzodiazepine to augment a high while users of opiates may use benzodiazepines to self-medicate withdrawal symptoms. By raising the seizure threshold, benzodiazepines can also diminish the therapeutic effects of electroconvulsive therapy. Finally, considerable attention should be given to patient education of benzodiazepines leading to excessive sedation and respiratory depression when given with other CNS depressants such as alcohol, barbiturates, tricyclic and tetracyclic drugs, dopamine receptor antagonists, opioids, and antihistamines.

USE IN PEDIATRICS

The role of long-term treatment with benzodiazepine category medications needs to be looked at from a patient perspective in

order to minimize complications. In the pediatric population, the drug is metabolized faster than in adults, thus children may require small divided doses to maintain blood level.¹¹ Adverse effects include sedation, cognitive, and motor effects, while disinhibition and agitation are reported in up to 30% of children.¹²

USE IN GERIATRICS

In the geriatric population, specific caution should be used as drugs metabolized by oxidation can accumulate, while benzodiazepines combined with other drugs that affect the CNS may affect gait, memory, balance, cognition, behavior, fall risk, and motor vehicle collision risk.¹³

Benzodiazepines are often prescribed for the elderly population to treat symptoms of generalized anxiety disorder (GAD), agitation, alcohol withdrawal and insomnia. However, associated side effects are frequent and include intellectual, cognitive and psychomotor impairment, as well as an increased for falls and automobile accidents. Additionally, several studies indicated an association between benzodiazepine use with recurrent falls and hip fracture.

The risk of falls has been linked with sudden increases in dosage, as well as with continuous use of benzodiazepines. Consequently, benzodiazepines with shorter half-lives are recommended for the elderly to prevent accumulation of active metabolites in the blood. However, this approach brings with it a greater potential for abuse and dependence. A meta-analysis revealed the use of benzodiazepines in the elderly was associated with a 2.45 greater risk of developing adverse effects compared with placebo. In fact, for every seven elderly patients treated with a benzodiazepine, one will have an adverse event. Consequently, the use and potential side effects of benzodiazepine category medications in the elderly need to be closely monitored.¹⁴⁻¹⁸

USE DURING PREGNANCY

The United States Food and Drug Administration (FDA) classifies benzodiazepines as pregnancy category “D”. Yet, in spite of these risks, the incidence of the use of benzodiazepines during pregnancy ranges from 1-40%. Animal studies demonstrate that benzodiazepines can interfere with fetal development, including neurodevelopment. The potential side effects during pregnancy include low birth weight, respirator and feeding difficulty, irritability, convulsions, floppy baby syndrome, neonatal drowsiness, hypotonia and withdrawal symptoms.¹⁹⁻²²

Finally, in pregnant patients, benzodiazepines may cross the placenta and accumulate in the fetal circulation. In the third trimester, high doses may lead to fetal benzodiazepine

syndrome including floppy infant syndrome, impaired temperature regulation, and withdrawal symptoms. The threat to newborns in the benzodiazepine-dependent mother includes sedation, lethargy, and poor temperature regulation as benzodiazepines are excreted into breast milk in sufficient levels.²³ Longer acting agents can also accumulate in infants as the metabolism of benzodiazepines is slower in this population.²⁴

CAUTIONS WITH CHRONIC USE OF BENZODIAZEPINES

Chronic use of benzodiazepines has been associated with cognitive impairment, decreased motor coordination, impaired concentration, poor reaction time, and slower speed of information processing and verbal learning.²⁵ Patients on long-term benzodiazepines experience agoraphobia, loss of sex drive, social phobia, increased anxiety and depression, as well as various other problems. Learning impairment with benzodiazepines decreases the effect of psychotherapy.²⁶ In patients who have taken benzodiazepines regularly for one year, deficits in visual-spatial ability and sustained attention have been reported.²⁷ Excessive parenteral dosage can result in respiratory distress and apnea, along with a tranquilizing effect on the central nervous system.

Long-term benzodiazepine use puts patients at risk for dependence and withdrawal.²⁸ The most significant problems with chronic use of benzodiazepines are the development of tolerance and dependence. After four to eight months of treatment, as many as 40% of patients become dependent which explains why patients with substance abuse histories should not be prescribed benzodiazepines.²⁹ Additionally, withdrawal symptoms are possible after only one month of daily use, with up to 30% of patients suggested to experience withdrawal after eight weeks of benzodiazepine treatment.³⁰ In a meta-analysis study looking at withdrawal from an average of 17 mg per day of diazepam, the long term use of benzodiazepines has been shown to lead to substantial cognitive decline that did not resolve after three months of discontinuation.³¹

GOALS OF BENZODIAZEPINE THERAPY

While benzodiazepines may be effective for the short-term treatment of generalized anxiety, more research is needed to better understand the effects of long term benzodiazepine therapy. As previously mentioned, placebo controlled trials of long term benzodiazepine therapy are not common due to their ethical concerns. If there is to be a role for long-term benzodiazepine therapy, patients and clinicians should be aware of the clinical effects due to the differences between long half-life and short half-life drugs. Advantages of long half-life benzodiazepines include less frequent dosing, less

variation in plasma concentration, and less severe withdrawal phenomena. Disadvantages of long half-life benzodiazepines include drug accumulation, increased risk of daytime psychomotor impairment and increased daytime sedation. For short half-life benzodiazepines, advantages include no drug accumulation and less daytime sedation. Disadvantages of short half-life benzodiazepines include more frequent dosing as well as earlier and more severe withdrawal syndromes, in addition to the more common symptoms of rebound insomnia and anterograde amnesia.³²

DISCONTINUATION OF BENZODIAZEPINE THERAPY:

As patients may become accustomed to using benzodiazepines for two months or more at a therapeutic dose, understanding withdrawal symptoms helps to optimize patient outcome. Benzodiazepines are known to produce withdrawal symptoms within one to two days following discontinuation of short acting drugs and within five to 10 days after discontinuation of long acting drugs.³³ Symptoms such as insomnia, agitation, anxiety, perceptual changes, dysphoria, headache, muscle aches, twitches, tremors, loss of appetite, gastrointestinal distress, and severe reactions such as seizures, coma, and psychotic states may prompt a clinician to suspect withdrawal.³⁴

Current recommendations to discontinue benzodiazepine therapy to eliminate the potential for withdrawal symptoms includes substituting the current benzodiazepine with an equivalent dose of diazepam as well as:

1. Reduction of the total daily dosage of diazepam by 10 mg daily until a total dose of 20 mg is reached, then reducing the dose by five mg daily to an end point of abstinence, while possibly using propranolol to aid with withdrawal symptoms or
2. Reduction of the diazepam dosage by 25% per week, or
3. Reduction of the diazepam dosage by 50% over four to eight weeks, then tapering the final 50% of the dose more gradually. Notably, this protocol should not be used for alprazolam which must be decreased by 0.5 mg weekly as quicker discontinuation may lead to delirium and seizures.

Additionally, the use of carbamazepine (Tegretol) during benzodiazepine discontinuation has been reported to allow a better tolerated discontinuation when used at 400 to 500mg per day.³⁵

THE FUTURE ROLE OF LONG TERM BENZODIAZEPINES FOR ANXIETY:

With little data to support the long term use of benzodiazepines for anxiety, along with clinical studies that indicate cognitive impairment from prolonged use, a closer look should be taken to better understand why patients are prescribed benzodiazepines for greater than two months duration of treatment. Are patients being prescribed benzodiazepines as a result of poor clinical judgment, patient addiction, fear of withdrawal symptoms, or because clinicians don't understand how to best discontinue long term therapy?

As the diagnosis of generalized anxiety disorder requires a period of symptoms lasting greater than six months in duration, the clinician needs to take particular precaution not to overprescribe benzodiazepines as a short-term solution to an often long term problem. This is especially important as the most successful treatment solutions to GAD requires additional modalities that include lifestyle modifications, counseling, and/or psychotherapy.³⁶ As benzodiazepines have addiction potential and may be taken with other drugs of abuse to cause life-threatening complications or withdrawal symptoms, antidepressants may be the better pharmacologic option for the initial medical treatment of GAD.

Addendum: Chart A

Generic Benzodiazepine	Brand Equivalent	Equiv Dose (mg)	Peak Plasma Level (PO)	Lipid Solubility	Elimination Half-Life	Metabolites	Comments	Use in Renal and Hepatic Disorders
Alprazolam	Xanax; Kalma; Apo-Alpraz; Novo-Aloprazol; Nu-Alprax; Tafil	0.5	1-2 h	Moderate	6-27 h	Metabolized by oxidation: principal metabolites are α-hydroxyalprazolam, desmethylalprazolam, 4-hydroxyalprazolam; Metabolized by CYP3A4 and 1A2	Rapidly and completely absorbed. Clearance in elderly only 50-80% that of young adults	Renal – increased plasma level of free unbound form and possible decreased clearance Hepatic – half-life increased
Bromazepam	Lexotan; Lexomil	3.0	0.5-4 h (2-12 h in elderly)	Low	8-30 h	Metabolized by oxidation: 3-hydroxybromazepam Metabolized by CYP3A4 In elderly peak plasma level and half-life increased	In elderly peak plasma level and half-life increased	?
Chlor-diazepoxide	Librium; Nova-Pam; Apo-chlordiazepoxide; Corax; Medilium; Novo-Poxide; Solium	25.0	1-4 h	Moderate	4-29 h (parent drug), 28-100 h (metabolites)	Metabolized by oxidation: desmethylchlordiazepoxide, oxazepam, desmethyldiazepam	Metabolites accumulate on chronic dosing	Renal – decrease dose by 50% in patients with creatinine clearance less than 10 mL/min Hepatic – half-life increased (2-3 fold) in patients with cirrhosis
Clonazepam	Klonopin; Rivotril	0.25	1-4 h	Low	19-60 h	Metabolized by oxidation: no active metabolite Metabolized primarily by CYP2B4, 2E1, and 3A4	Quickly and completely absorbed; slow onset of activity	Renal – no change Hepatic – increase in unbound clonazepam in patients with cirrhosis
Clorazepate Dipotassium	Gen-Xene; Tranxene; Apo-Clorazepate; Novo-Cloplate	10.0	0.5-2 h	High	1.3-120 h (metabolites)	Metabolized by oxidation: N-desmethyldiazepam	Metabolites accumulate on chronic dosing	Renal – clearance of metabolite impaired Hepatic - ?
Diazepam	Valium; Ducene; Antenex; D-Pam; Pro-Pam; Apo-Diazepam; Diazemuls; E Pam; Meval; Novo-Dipam; PMS-Diazepam; Vivol	5	1-2 h	High	14-80 h (parent drug) 30-200 h metabolites	Metabolized by oxidation: N-desmethyldiazepam, oxazepam, 3-hydroxydiazepam, temazepam Metabolized by CYP3A4, 2C9, 2C19, and 2B6 Inhibitor of UGT2B7	Less protein bound in elderly, attains higher serum levels; Rapid onset of action followed by re-distribution in adipose tissue; accumulation on chronic dosing	Renal – increased plasma level of unbound diazepam and decreased clearance Hepatic – 2-3 fold increase in half-life in patients with cirrhosis
Estazolam	ProSom; Tasedan	1	0.5-6 h	Low	8-24 h	Metabolized by oxidation: 4-hydroxyestazolam, 1-oxoestazolam Metabolized by CYP3A4	Metabolites inactive Metabolites impaired in the elderly and in hepatic disease	Renal - ? Hepatic – metabolism impaired
Flurazepam	Dalmane; Apo-Flurazepam; Novo-Flupam; PMS-Flupam; Somnol; Som Pam	15	0.5-1 h	High	0.3-3 h (parent drug) 40-250 h (metabolites)	Metabolized by oxidation: N-desalkylflurazepam, OH-ethylflurazepam, flurazepam aldehyde Metabolized by CYP2C and 2D6	Rapidly metabolized to active metabolite Elderly males accumulate metabolite more than young males on chronic dosing	Renal - ? Hepatic – metabolism impaired
Lorazepam	Ativan; Apo-Lorazepam; Novo-Lorazepam; Nu-Loraz; PMS-Lorazepam; Pro-Lorazepam	1	PO: 1-6h IM: 45-75 min IV: 5-10 min SL: 60 min	Moderate	8-24 h	Conjugated to form lorazepam glucuronide by UGT2B7	Metabolite not pharmacologically active	Renal – half-life of metabolite Increased Hepatic – half-life and volume of distribution doubled in patients with cirrhosis

Generic Benzodiazepine	Brand Equivalent	Equip Dose (mg)	Peak Plasma Level (PO)	Lipid Solubility	Elimination Half-Life	Metabolites	Comments	Use in Renal and Hepatic Disorders
Midazolam	Versed; Hypnovel; Dormicum	Acute use only	0.5-1 min	High	1-4 h (parent) 1-20 h metabolites	Metabolized by oxidation: 1-OH-methylmidazolam Metabolized primarily by CYP3A4	Metabolites active	Renal – decrease dose by 50% in patients with creatinine clearance less than 10 mL/min Hepatic – metabolism significantly impaired in patients with cirrhosis
Nitrazepam	Mogadon; Alodorm; Insoma; Nitrados	2.5	0.5-7 h	Low	15-48 h	Metabolized by nitroreduction by CYP2E1 No active metabolites	Metabolism impaired in elderly Accumulates with chronic use	Renal - ? Hepatic – metabolism impaired
Oxazepam	Serax; Serepax; Murelax; Aleпам; Serenid; Benzotran; Apo-Oxazepam; Novo-Oxazepam; Oxпам; PMS-Oxazepam; Zapex	15	1-4 h	Low	3-25 h	Conjugated to oxazepam glucuronide by UGT2B7	Metabolites not pharmacologically active Half-life and plasma clearance not affected much by age or sex	Renal – prolonged half-life Hepatic – no effect
Quazepam	Doral	7.5	1.5 h	High	15-40 h (parent) 39-120 h (metabolites)	Metabolized by oxidation: 2-oxoquazepam, Desalkylflurazepam Metabolized primarily by CYP2D6	Rapidly absorbed and metabolized Accumulation on chronic dosing	?
Temazepam	Restoril; Euhypnos; Normison; Temaze; Euhypnos; Nocturne; Normison; Temaze; Temtabs; Sompam	10	2.5 h	Moderate	3-25 h	Conjugated by UGT2B7	No accumulation with chronic use	Renal - ? Hepatic – no effect
Triazolam	Halcion; Apo-Triazo; Gen-Triazolam; Novo-Triolam; Nu-Triazo; Hypam; Tricam	0.25	1-2 h	Moderate	1.5-5 h	Metabolized by oxidation: 7- α -hydroxyderivative Metabolized by CYP3A4	Metabolite inactive; Clearance in elderly only 50-80% that of young adults	Renal – no change Hepatic – reduced clearance

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How Crowdsourcing & Crowdfunding Are Fueling Health Care Innovation

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KEYWORDS:

Crowdsourcing
Crowdfunding
Knowledge sharing
Open intellectual exchange

Informational and financial exchanges, which take place among groups of like-minded people with a specific directive or purpose, are referred to as crowdsourcing and crowdfunding, respectively. Crowdsourcing is an open call for intellectual contributions; it is a means by which individuals can brainstorm, assess, evaluate and consult on projects and research. Crowdfunding facilitates direct, financial contributions to projects, charities, individuals, etc. For-profit and non-profit organizations use crowdsourcing and crowdfunding to obtain expert-level help, solve complex problems, broaden their support networks, advertise products or services, solicit feedback, and reach entirely new groups of prospective investors or consumers.

The health care community is also benefiting from crowdsourcing and crowdfunding: Medical researchers are accessing broad, qualified sample groups; physicians are consulting providers from all backgrounds whose experiences lend unique perspectives; and, consumers with mounting medical expenses are requesting and receiving financial help from friends, family and strangers. Crowdsourcing and crowdfunding prove that the power of many is greater than the power of one.

Smartphones, computer tablets and other devices provide for the near-instantaneous exchange of information and ideas at virtually any time of day and from virtually any location. A study by the communications technology firm Ericsson found that 35 percent of U.S. Android and iPhone users regularly check a variety of mobile apps even before getting out of bed.¹ As a result of this growing compulsion to stay connected, organizations have begun creating online communities and using electronic messaging media to notify individuals of meetings, events, news items and more.

The Texas Medical Association (TMA) reports that its members use iPhone, Android and BlackBerry devices to access its private 24/7 mobile app – which allows them to: browse through a real-time, 45,000 member directory; locate, contact, and connect with peers; make appointments; refer patients; and, receive related alerts.² Similarly, public social media venues (i.e., LinkedIn, Facebook) encourage open and ongoing commentary between groups of friends and associates, their friends and their associates, and so on. When those types of informational exchanges take place among like-minded people with a specific directive or purpose, they are collectively referred to as crowdsourcing.

What's more, the Internet is also a vehicle for commerce. Total e-commerce sales for 2013 were recently estimated at \$263.3 Billion.³ But not all online transactions are limited to the traditional purchase of goods. From large corporations to small non-profits, organizations have begun soliciting funds via the Internet in order to gain financial backing for special projects and/or to secure a greater number of charitable donations. When those types of financial exchanges take place among like-minded people with a specific directive or purpose, the phenomenon is referred to as crowdfunding.

CROWDSOURCING: AN OPEN INTELLECTUAL EXCHANGE

What crowdsourcing amounts to is an open call for intellectual contributions that is pitched to a largely undefined group within the greater community. It is a means by which experts in their respective fields or areas of specialization can receive an invitation to brainstorm, assess, evaluate and consult on specific projects, and/or participate in research endeavors. It is by using this technique that the individuals who are best suited to perform a task, solve a complex problem or generate innovative ideas can be accessed and their intellectual acumen applied—regardless of where they are located geographically and in relation to the origin of the request.

Crowdsourcing has become an effective tool, or method, for mass collaboration via the Internet with the intention of achieving business, personal, and/or creative goals. It is a means through which businesses are able to: enlist the talents

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of individuals who are employed or otherwise work outside of their own companies; learn more about what interests consumers (en masse) so that products and/or services can be tailored accordingly; and establish a sense of kinship and brand loyalty with sympathetic supporters prior to the launch of new ideas, campaigns, etc. In short, establishing a crowdsourcing presence online allows companies to quickly and inexpensively mine for valuable talent, data and ideas.

Crowdsourcing and crowdfunding are now taking hold in the health care sector, helping fuel health care innovation in ways that produce notable outcomes.

Proctor & Gamble uses what it calls “open innovation, also known as crowdsourcing or co-creation, (to) harness the ideas and strength of people outside their organization to make improvements to internal processes or products.” Through its P&G Connect + Develop program, individuals and companies external to the organization submit ideas for new or improved products, technologies, business models, methods, trademarks, packaging, and/or design. The way contributors do that is by logging on to a dedicated P&G crowdsourcing website, browsing a list of the company’s identified needs and submitting their proposals for consideration. In return, P&G-approved innovation partners are said to gain access to its “innovation, distribution and marketing assets.”^{5,6}

P&G’s CEO A. G. Lafley spearheaded the Connect + Develop strategy as a way to “broaden the horizon by looking at external sources for innovation (and to use) technology and networks to seek out new ideas for future products” after company estimates identified a pool of nearly 1.5 million creative-thinking inventors and individuals who might serve as potential innovation sources. Lafley estimates that “through Connect + Develop—along with improvements in other aspects of innovation related to product cost, design, and marketing—the company’s R&D productivity has increased by nearly 60 percent. In addition, its innovation success rate has more than doubled, while the cost of innovation has fallen and, within a two-year period, P&G launched more than 100 new products for which some aspect of execution came from outside the company.”⁷

CROWDFUNDING: DIRECT FINANCIAL SUPPORT

While crowdsourcing enables the exchange of intellectual assets (i.e., ideas, information, and talent), crowdfunding facilitates direct financial investment in the form of contributions to projects, charities, etc.—enabling individuals to support related initiatives. More specifically, crowdfunding occurs when groups of people pool their money and/or other resources in support of a wide range of endeavors. Crowdfunding helps bankroll disaster relief efforts, non-profit

organizations, and creative/other endeavors (i.e., musical careers, film production, enterprise startups). Indiegogo is an international crowdfunding platform which operates under the premise that anyone anywhere can raise money, noting that “people contribute to campaigns for many reasons, but usually it is because they want to be involved in what the campaign is doing or because they want (access to perks which) are part of the campaign.”⁸

However, crowdfunding is not necessarily a 21st century phenomenon. In 1885, Joseph Pulitzer led one of the earliest-recorded crowdfunding efforts, urging readers of his newspapers to help finance the construction of the pedestal on which the Statue of Liberty rests.⁹ Political campaigns may have always employed some version of the technique, whether in the form of passing a hat in town meetings or using direct mail and phone solicitations to request donations. Yet, technology makes those transactions easier, more immediate and more potentially viral.

A crowdfunding call for contributions is often spread through email, online community notices and social network postings. These forms of communication encourage a ripple effect—with recipients forwarding alerts about the project or cause of interest to other people in their online social networks, who then forward them throughout their own networks. Online crowdfunding news travels faster and farther than traditional calls for fundraising ever could. In addition, individual contributors find the ability to make secure online donations convenient.

DISEASE SURVEILLANCE: CROWD HELP FOR HEALTH CARE

The success of crowdsourcing and crowdfunding in the business world has spurred other industries such as the health care sector to adopt similar practices aimed at addressing their own unique needs. What if instead of encouraging competition between physicians, research labs, and other health care-related entities we invested our energy and intellectual property in the pursuit of collective intelligence? After all, crowdsourcing makes it possible to tap into a wealth of intelligence from around the world in as little as a few keystrokes.

One highly practical health care application involves the collection of data about diseases that are known to affect various populations but is difficult to track and/or collect large amounts of sample-group data on. Crowdsourcing, in this instance, is a timelier and less expensive means for collecting relevant data than traditional research methodology. HealthMap and Health Tracking Network are two related programs worth taking a closer look at.

HealthMap.org

HealthMap was created, in 2006, by a team of researchers, epidemiologists, and software developers at Boston Children's Hospital to utilize informal online sources for disease-outbreak monitoring and real-time surveillance of emerging public health threats. The HealthMap website, along with its companion mobile app Outbreaks Near Me, delivers real-time intelligence on a broad range of emerging infectious diseases. Its typical audience includes local libraries, health departments, government agencies and even international travelers. HealthMap taps into a variety of data sources (i.e., eyewitness reports, expert-curated discussions and validated official reports) to present comprehensive assessments of the state of a given infectious disease and the potential effects it may have on human and animal health.¹⁰

HealthTracking.net

Health Tracking Network's (HTN) creators are said to have devised this crowdsourcing site with four primary goals in mind: 1) To uncover factors related to common conditions; 2) To promote participant wellness by tracking health, fitness and other variables; 3) To help fundraise for related charities; and, 4) To provide physicians and researchers with access to quality samples for surveying potential. HTN engages both patients and health care providers over long periods of time, eliciting health information from individuals whose responses then help physicians' track trends, developments, and responses to treatment or medication. Participating patients provide "Symptom Updates" on a regular basis and respond to researcher-issued prompts that are related to specific conditions. This data collection method carries a low operational cost and promotes quality samples thanks to its prolonged timeframe and active patient participation.¹¹

CROWDSOURCING INVITES INNOVATION

Crowdsourcing is particularly well suited to enabling medical providers, organizations, and other influential figures in health care to pool their intellectual resources, expand their collective knowledge base, and—thereby—deliver higher quality care. Crowdsourcing platforms which facilitate a meeting of medical minds include: CrowdMed, MEDTING, Webicina, and B-a-MedFounder and angelMD.

CrowdMed.com

Physicians are trained to assess and identify common causes behind symptoms and then develop treatment plans. However, there are cases that defy common causes. At that point, specialists are called in to lend their expertise. Still, there are some cases so rare that both health care providers and patients wind up spending extraordinary amounts of time and money trying to secure a correct diagnosis and develop an

effective treatment strategy—with 7,000 currently known rare and/or difficult-to-diagnose diseases. Such was the case for Jared Heyman's sister, whose family invested three years and more than \$100,000 before receiving an appropriate diagnosis, prognosis and course of action.¹²

Frustration inspired Heyman to create CrowdMed, which he launched in April 2013. Utilizing prediction market technology, CrowdMed helps health care providers narrow down diagnostic possibilities for difficult-to-diagnose cases. A broad pool of providers (including physicians) is invited to review patients' symptoms, medical histories, and other pertinent data—with 100 to 200 "Medical Detectives" reviewing and researching case specifics before recommending their diagnoses and expert opinions. CrowdMed aggregates that feedback and sends patients the top diagnostic recommendations, noting the estimated probability of accuracy for each one. Patients can then discuss those findings with their personal physicians and health/or care teams. To date, CrowdMed reports an accuracy rate of more than 90 percent.¹²

Medting.com

MedicalExchange's MEDTING is a crowdsourcing site which corrals information from a wide array of physicians. It is a closed-community forum through which health care providers can engage in collaboration, solicit advice, and/or share their experiences with one another. Integrated with PubMed, MEDTING invites physicians to post medical images and videos that other medical experts can review and evaluate in order to help them build stronger clinical cases. Individual physicians can register with MEDTING as independent users, as members of clinical collaborative groups with their own virtual meeting space, or as members of an enterprise that is able to customize its own information-exchange environment.¹³

Webicina.com

An Internet search can result in thousands of recommended links that are smattered with select keywords, but not always ones that are highly relevant. Sifting through page upon page of search results to find the most relevant sources can be quite time consuming. Webicina.com is a free online service that helps focus individual medical literature and information searches to produce highly pertinent results. It does this by curating information from the most relevant, quality, and reliable medical social media resources through crowdsourcing with medical professionals and e-patients to cover more than 140 topics in 20 languages.¹⁴

B-a-MedFounder.com

Due to their extensive experience with a wide range of medical tools and equipment, physicians possess a valuable perspective for product design—and sometimes hatch their own ideas for new devices or modifications to existing tools. Physicians may not be prepared, however, to travel the road from concept to prototype and then on to testing and production. B-a-MedFounder is a crowdsourcing site that specifically caters to the physician-turned-inventor. Its network of inventors, technical experts, and medical-device-manufacturer representatives review physicians' medical device ideas for viability. Approved projects are then promoted online where others can learn about their uses/potential impact and where interested parties can invest in their production.¹⁵

AngelMD.com

The medical investment crowdfunding platform, angelMD, is a crowdfunding platform that connects physicians and leading medical startups. The parameters for the startups approved to list on the site are those that have a medical product or product enabled service, are an legal entity and prepared to share their story. Darci Moreau VP of Startup Relations for angelMD said, "Getting startups on the site is just the first step in allowing us to help them share their story and progress milestones. This often leads to making valuable connections such as landing key advisors, early product adopters and capital investments. In March 2014, the 100th medical startup company went live on angelMD, Constellation from Cambridge, Massachusetts. Constellation is a MIT incubated startup aiming to prevent skin cancer. The service processes images of the entire body and alerts if any moles change."¹⁶

CROWDFUNDING CLOSES THE FINANCIAL GAP

Medical expenses continue to climb. In 2011, Americans spent an average of \$8,508 per person on expenses related to medical care, including insurance premiums and out-of-pocket costs.¹⁷ In addition, medical debt is now identified as the number one cause of personal bankruptcy in the United States, with NerdWallet Health estimating that more than 20 percent of Americans aged 19 to 64 struggled to pay their health care-related bills in 2013.¹⁸ Yet, this is an area in which crowdfunding has proven to be highly effective. In 2012, more than \$2.8 Billion was raised through medically-oriented crowdfunding efforts.¹⁹ Three organizations which are paving the way in medical crowdfunding are Give Forward, Human Tribe Project and You Caring.

GiveForward.com

Give Forward reports show that, since 2008, it has helped generate more than \$95.5 Million through individual fundraisers set up to assist people in need of help paying their

medical bills. In some cases, a few thousand dollars helps fill the void between insurance coverage and actual treatment costs incurred. In other cases, hundreds-of-thousands of dollars have helped cover recipients' long-term care needs. In excess of \$880,000 was donated, at GiveForward.com, on behalf of two 2013 Boston Marathon bombing victims who will have lifelong implications from their injuries. Other donations are circumstance-specific (i.e., cost of organ transplant, disaster relief, funeral expenses).²⁰

HumanTribeProject.com

The cost of cancer treatment frequently exceeds insurance coverage levels, leaving patients liable for the difference. The Human Tribe Project (HTP) was designed to aid cancer patients in covering their out-of-pocket costs. In recent years, HTP has expanded its services to provide crowdfunding opportunities for anyone who is struggling with overwhelming costs related to necessary medical care. Beneficiaries—the term HTP attributes to individuals receiving funds—create Tribe Pages where they or their family members can post blog updates about their condition(s). Guests can also sign in and post messages of support.²¹

YouCaring.com

You Caring identifies itself as "the first truly free website of its kind," explaining that—despite the amount of money raised—fundraisers are not charged a fee to use the encrypted crowdfunding site. This crowdfunding source allows people to raise money to defray a wide range of costs that they or their family members may have incurred, including medical, memorial, and funeral expenses. Additional donation categories include: Education and tuition assistance, adoption expenses, funding for mission trips, pet/animal rescue expenses, and quite simply "helping another in need." Funds are paid directly to recipients via their own private PayPal or WePay accounts.²²

CONCLUSION

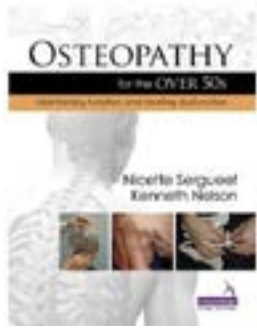
Technological advances have made information more accessible and staying connected more affordable. That, in turn, has allowed for-profit businesses, non-profit organizations and individuals to benefit from myriad talents and treasures made available by peers, other professionals and the general public in open-ended networks which provide access to greater depths of knowledge, broader ranges of experience and diverse perspectives—otherwise known as collective intelligence. And collective intelligence knows no limitations.

Health care professionals, organizations, and consumers can all benefit from crowdsourcing and crowdfunding—whether the intent is to share information, generate funds to support

special projects/research, or provide support for individuals who are struggling to maintain costly health care regimens or cover the most basic health care expenses. Crowdsourcing and crowdfunding have the power to elevate the level of care provided by physicians, other medical professionals, and entire health care organizations—or anyone who desires to increase the probability of positive outcomes. After all, the power of many truly is greater than the power of one.

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Osteopathy for the Over 50s

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This is a welcome addition to our Osteopathic literature and the library of any Osteopathic student or physician. This husband and wife team are both professors at the Chicago College of Osteopathic Medicine, are internationally known educators and speakers, as well as prolific researchers and writers, individually and collaboratively counting over 100 papers and several textbooks published so far. The subtitle for *Osteopathy for the Over 50s* sums it up: “maintaining function and treating dysfunction” by applying Osteopathic principles within the total healthcare of our aging patients.

This easy-to-read textbook begins with a logical progression of an up-to-date review of relevant anatomy and physiology, with a special emphasis on the Osteopathic highlight and importance of the fascia, true to Dr. A.T. Still’s holistic vision. This is followed by a masterful description of our distinctive Osteopathic palpatory diagnostic and treatment perspectives and skills, leading the reader, with photographs and illustrations, through the steps of diagnosis and treatment emphasizing the aging patient.

The second half of the book is devoted to clinical considerations. Somatic dysfunctions cover major areas of the older patient: neuromusculoskeletal, postural imbalance, cardiovascular, respiratory, gastrointestinal, urogenital, autonomic, auditory and visual. Each chapter provides the interested reader

with a concise, scientific explanation, and a generous list of references, of various conditions within each of the above-mentioned systems, with a detailed description of the relevant autonomic contributions to the specific condition, such as hypertension, pneumonia, irritable bowel syndrome, etc. The Osteopathic physical examination and treatment is carefully described and reasoned from a holistic perspective, providing both the physician and patient with a thorough and satisfying experience. Each chapter then ends with “Advice to the patient”, always including the patient in the complete treatment prescription. Advice ranges from self-treatment modalities to diet, exercise, and addressing the always-important stressors in one’s life, physically, emotionally and spiritually.

The authors wisely emphasize the more gentle Osteopathic treatment techniques for the aging patient. These diagnostic and therapeutic treatment methods can be integrated into any treatment session, style, or specialty, giving them value to any physician who practices hands-on modalities. Drs. Sergueef and Nelson are a unique and highly respected team, combining the best of Osteopathic medicine, science, research, writing, and educating, and have left a lasting impact and legacy to students and physicians around the world. I highly recommend this book to Osteopathic physicians of all kinds who care to advance and enhance the science and art of hands-on healing and manual medicine.

CME RESOURCE: OSTEOPATHIC FAMILY PHYSICIAN OFFERS 2 HOURS OF 1-B CME

ACOFPP members who read *Osteopathic Family Physician* can receive two hours of Category 1-B continuing medical education credit for completing quizzes in the journal. Visit the eLearning Center at www.acofp.org to access the quizzes.

Nov/Dec 2014 Answers:

1. b 2. d 3. a 4. d 5. d 6. b 7. b 8. a 9. c 10. d

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OFP Patient Education Handout

Peter Zajac, DO, FACP, Author • Merileth C. Norris, DO, FACP, Editor
Amy J. Keenan, DO, PhD, Health Literacy Editor

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New High Blood Pressure Treatment Guidelines



High Blood Pressure is a common medical condition. If it is not checked or treated, it can damage body organs such as the brain, heart, and kidneys. A number of problems such as heart disease and stroke are caused by high blood pressure. Blood pressure is measured by taking the systolic pressure (the upper number) followed by the diastolic pressure (the lower number). High blood pressure occurs when either of these numbers is too high which can happen with no symptoms. Signs and symptoms in instances of severe High Blood Pressure may include headache, feeling weak and tired, dizzy or light headed, chest pain or tightness, fast heart rate, visual or hearing problems, and shortness of breath.

Recommendations in the New Treatment Guidelines Include:

New US guidelines for the treatment of high blood pressure were released in 2013. The guidelines address when and which drugs should be used to treat high blood pressure in patients. The guidelines also state the need to follow a healthy lifestyle along with taking medications to help prevent the problems of high blood pressure as mentioned above. Among the recommendations:

1. In patients aged 60 years or over, drugs should be started when systolic blood pressure is 150 mm Hg or higher or diastolic blood pressure is 90 mm Hg or higher.
2. In patients under 60 years of age, medicine should be started when systolic blood pressure is 140 mm Hg or higher or diastolic blood pressure is 90 mm Hg or higher.
3. If the blood pressure goal is not reached within 1 month of starting treatment, the dose of the first drug should be increased or another drug should be added.

Healthy Lifestyle Changes Include:

Eat a healthy diet (a low salt and fat diet with fruits and vegetables.) Exercise regularly. If you are overweight or obese (defined by a Body Mass Index (BMI) of 25 or higher), this can increase your risk of high blood pressure. Lose some weight. If you smoke, please stop! Limit alcohol use. Reduce your stress. Stress can make your heart beat faster and your blood vessels contract which may be harmful over time.

Medical Care and Treatment Options:

If you have any questions about your blood pressure please contact your osteopathic family physician. High blood pressure can be lowered with the right treatment plan and regular visits with your doctor. Your family doctor will help you choose which drugs and treatments will work best for you. In case of any emergency, you should call your doctor or 911 right away.



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Source(s): American Heart Association, Medscape, National Heart, Lung, and Blood Institute, and Prescriber's Letter.

The Osteopathic Family Physician Patient Education Handout is a public service of the ACOFP. The information and recommendations appearing on this page are appropriate in many instances; however, they are not a substitute for the advice of your physician. For specific information concerning your own medical condition, ACOFP suggests that you consult your family physician. This page may be reproduced non-commercially by physicians and other health care professionals to share with their patients. For additional patient-related educational material please visit www.acofp.org.

2015 Calendar of Events

January 17-19, 2015

Iowa ACOFP Midwinter Osteopathic Family Practice Conference
Embassy Suites
Des Moines, Iowa
<http://www.ioma.org>

January 22-25, 2015

MAOFP Mid-Winter Family Medicine Update Conference
Shanty Creek Resort
Bellaire, Michigan
www.maofp.org/cme

January 23-25, 2015

Ohio ACOFP January Seminar
Renaissance Cleveland
Cleveland, OH
www.ohioacofp.org

January 23-25, 2015

ACOFP Future Leaders Conference
Loews Madison Hotel
Washington, DC
www.acofp.org

January 28-31, 2015

26th Annual Osteopathic Winter Seminar and National Clinic Update
Sand Pearl Resort Hotel
Clearwater Beach, Florida
www.pcomsociety.com

January 29-February 1, 2015

Missouri Winter Scientific Seminar
The Westin Kansas City Hotel at Crown Center
Kansas City, Missouri
www.msacofp.org

February 6-8, 2015

Maine Osteopathic Association
Mid-Winter Symposium: CME by the Bay
Holiday Inn by the Bay
Portland, Maine
www.mainedo.org

February 20-22, 2015

Ohio ACOFP 20th Annual Family Practice Review and Reunion
Sinclair Community College
Dayton, OH
www.ohioacofp.org

March 5, 2015

DO Day on the Hill
Washington, DC
www.acofp.org

March 12-15, 2015

ACOFP Annual Convention & Scientific Seminars
The Cosmopolitan Hotel
Las Vegas, Nevada
www.acofp.org

April 16-19, 2015

Virginia Osteopathic Medical Association Spring CME Conference
The Great Wolf Lodge
Williamsburg, VA
www.voma-net.org

April 18, 2015

MAOFP Spring Family Medicine Update Conference
Okemos, MI
www.maofp.org/cme

April 30-May 3, 2015

Oklahoma ACOFP
Norman, OK
www.okosteo.org

June 4-7, 2015

Maine ACOFP
www.mainedo.org

July 30-August 2, 2015

MAOFP Summer Family Medicine Update Conference
Grand Traverse Resort
Acme, MI
www.maofp.org/cme

August 6-9, 2015

CA-ACOFPC 39th Annual Scientific Medical Seminar
Disneyland Hotel
Anaheim, CA
31 1-A AOA CME Hours Anticipated
www.acofpca.org

August 7-9, 2015

Pennsylvania ACOFP
Hershey Lodge
Hershey, PA
www.poma.org

Official Notice to the ACOFP Membership

Proposed Amendments to the ACOFP Constitution & Bylaws

CONSTITUTION

According to the Constitution of the American College of Osteopathic Family Physicians, Inc. Article IX – Amendments Section 1. This Constitution may be amended at any annual meeting of the Congress of Delegates by a two-thirds vote of the total number of delegates or authorized for voting, provided that the proposed amendments shall have been filed with the Executive Director of the College at least 60 days before the first day of the meeting of the Congress of Delegates and that the Executive Director shall have notified the membership of the College in writing of the proposed amendment at least 30 days preceding the first day of the meeting of the Congress of Delegates.

Section 2. All amendments to the Constitution shall not be effective until they are submitted to and approved by the Board of Trustees of the ACFP.

The ACOFP Board proposes the following amendments to the Constitution. Approval of the amendments will be voted on at the ACOFP Congress of Delegates at its March 12, 2015 meeting. If adopted by the ACOFP Congress of Delegates, approval will be sent to the American Osteopathic Association Board of Trustees for approval. (New material in all caps and old material in strike out.)

JULY, 2007-2015

CONSTITUTION OF THE AMERICAN COLLEGE OF OSTEOPATHIC FAMILY PHYSICIANS, INC.

ARTICLE II – MISSION AND OBJECTIVES

Section 2. The objectives of the College are:

1. To encourage and improve the educational opportunities for the training of osteopathic family physicians in all branches of osteopathic medicine and surgery, including the osteopathic family practice MEDICINE training programs.

ARTICLE VI – OFFICERS

The elected officers of this College shall be the President, President-Elect, the Past Presidents for the preceding two years, Vice President, AND Secretary/Treasurer, six (6) Governors-at-large, and Speaker and Vice-Speaker of the Congress of Delegates.

ARTICLE VII – BOARD OF GOVERNORS

Section 1. The Board of Governors shall be composed of the President, President-Elect, the Past Presidents for the preceding two years, Vice President, Secretary/Treasurer, six (6) Governors-at-large, one osteopathic family medicine/Resident GOVERNOR, and one osteopathic medical student GOVERNOR, and the Speaker of the Congress of Delegates, all to be selected as provided in the Bylaws. The Speaker has voice but no vote.

BYLAWS

According to the Bylaws of the American College of Osteopathic Family Physicians, Inc. Article XXI – Amendments Section 1. Modifications. These Bylaws may be amended at any annual meeting of the Congress of Delegates by a two-thirds vote of the total number of delegates or authorized for voting, provided that the proposed amendments shall have been filed with the Executive Director of the College at least 60 days before the first day of the meeting of the Congress of Delegates and that the Executive Director shall have notified the membership of the College in writing of the proposed amendment at least 30 days preceding the first day of the meeting of the Congress of Delegates.

Section 2. Approval. An amendment to these Bylaws shall not be effective until they are submitted to and approved by the Board of Trustees of the ACFP.

The ACOFP Board proposes the following amendments to the Bylaws. Approval of the amendments will be voted on at the ACOFP Congress of Delegates at its March 12, 2015 meeting. If adopted by the ACOFP Congress of Delegates, approval will be sent to the American Osteopathic Association Board of Trustees for approval. (New material in all caps and old material in strike out.)

BYLAWS OF THE AMERICAN COLLEGE OF OSTEOPTHIC FAMILY PHYSICIANS, INC.

ARTICLE III – AFFILIATE SOCIETIES

A group of osteopathic family physicians desiring a charter as an affiliate society of ACOFP in a state, A DESIGNATED GEOGRAPHIC AREA WHICH INCLUDES TERRITORY WITHIN MORE THAN ONE STATE IN WHICH THERE IS NO EXISTING AFFILIATE SOCIETY WITHIN ANY PORTION OF THE DESIGNATED GEOGRAPHIC AREA, the District of Columbia, or a foreign territory or an organization of osteopathic family physicians serving in the uniformed services of the United States shall submit its request to the Board of Governors of ACOFP for its approval. Following authorization to form a society, the group may organize and then submit its Constitution and Bylaws to the Congress of Delegates for approval before the society may be granted a charter. At any time thereafter, upon demand of this organization, evidence that the approved society's Constitution, Bylaws, Code of Ethics and policies conform to those of this organization while said charter is in force shall be furnished to the Board of Governors. Affiliates may be dissolved upon recommendation of the Board of Governors and approval of the Congress of Delegates.

ARTICLE III – MEMBERSHIP

Section 2. Membership Classifications

The membership of this College shall consist of the following classes: Active, Academic, and Associates.

A. Active members shall have completed AOA-approved post-doctoral training IN FAMILY MEDICINE or Accreditation Council of Graduate Medical Education (ACGME) approved post-doctoral training or have been in active family medicine for greater than six years. The Committee on Membership may recommend to the Board of Governors a waiver of these requirements based on individual considerations. Active members are entitled to serve as delegates to the ACOFP Congress of Delegates, hold office, hold committee appointments, and THEY MAY BE included IN ONE OF the following categories:

BYLAWS CONTINUED

- (2) Life membership may be granted by the Board of Governors to any active member who has reached the age of 70 years, or who has completed 50 years of osteopathic family medicine, whichever comes first, and who has been a member in good standing for 25 consecutive years immediately preceding. The Committee on Membership may recommend waiver of these requirements on individual consideration. Life members shall not pay dues or assessments. Life members shall be deemed not have the privileges of active members.
- (3) Retired membership may be granted by the Board of Governors to active members in good standing in this organization who, because of age or through disability, have discontinued practice. These members shall have the same privileges as active members except they shall not hold office or vote.

B. Academic members shall be students in pre-doctoral COLLEGES OF osteopathic MEDICINE training programs accredited by AOA THE COMMISSION ON OSTEOPATHIC COLLEGE ACCREDITATION who are also members of their local osteopods chapter located within the geographic boundary served by the ACOFP affiliate society or interns in post-doctoral programs accredited by AOA or ACGME, or residents in family medicine post-doctoral programs accredited by AOA or ACGME. Academic members shall be entitled to serve as committee members, board members and delegates, and shall have voting privileges as set forth in Article V-Congress of Delegates.

C. Associate members shall be those persons whose professional activities involve cooperation with osteopathic family physicians through their specialty, or who contribute to some phase of the special field of osteopathic family medicine, such as education and research in scientific fields, or others interested in supporting this College. Associate members may not vote as delegates or hold office. Associate members shall include the following categories:

- (1) **PROFESSIONAL.** Associate members whose professional activities involve cooperation with osteopathic family physicians, or who contribute to some phase of the special field of osteopathic family medicine, such as education and research in scientific fields, may serve on committees and may vote on committees, but may not vote as a delegate or hold office.

ARTICLE V – CONGRESS OF DELEGATES

Section 1. Composition

A. The ACOFP Executive Director shall provide to the Secretary of each ACOFP affiliate society in writing the number of delegates to which that Society is entitled at least 60 days before the first day of the annual meeting of the Congress of Delegates.

- (1) Each affiliate society shall be entitled to at least one voting delegate whose national/state dues are current and, in addition, WHO IS SHALL BE A MEMBER IN GOOD STANDING, AND shall be entitled to at least one AN ADDITIONAL voting delegate for every 25 MEMBERS THEREAFTER, or the majority fraction thereof, active members, plus one voting delegate from each approved osteopods chapter located within the geographic boundaries served by the ACOFP affiliate society.

ARTICLE VI – BOARD OF GOVERNORS

Section 2. Composition

A. The Board of Governors shall consist of the President, President-Elect, the Past Presidents for the preceding two years, Vice President, Secretary/Treasurer, six (6) Governors-at-large, ONE OSTEOPATHIC RESIDENT GOVERNOR and ONE OSTEOPATHIC STUDENT GOVERNOR two Academic members, as provided for in the Bylaws.

ARTICLE VII – OFFICERS

Section 1. Composition

The elected officers of the College shall be the President, President-Elect, the Past Presidents from the preceding two years, Vice President, AND Secretary/Treasurer, six (6) Governors-at-large, and Speaker and Vice Speaker of the Congress of Delegates.

Section 5. Duties of Officers

A. The President:

- (N) Shall discharge such duties as may be required by the Family Practice MEDICINE Resident Training Program and the American Osteopathic Board of Family Physicians.

E. IMMEDIATE PAST PRESIDENT AND PAST PRESIDENT: THE IMMEDIATE PAST PRESIDENT AND PAST PRESIDENT SHALL PERFORM DUTIES AND PROVIDE ADVICE AND COUNSEL AS REQUESTED BY THE PRESIDENT.

ARTICLE IX – ELECTIONS

Section 2. Terms

D. The RESIDENT AND STUDENT Governors representing the Academic members of the College shall be elected annually for a one-year term.

ARTICLE X – DEPARTMENTS AND COMMITTEES

Section 4. General Duties

The duties of the departments and committees shall be outlined in the OPERATING Policy Manual and shall be reviewed annually for revisions by the Executive Director, who will make recommendations for modification to the Board of Governors.

ARTICLE XVII – GENDER DISCLAIMER

The American College of Osteopathic Family Physicians is open to persons of both ALL genders and does not discriminate against any persons because of gender IDENTITY, SEXUAL ORIENTATION OR CHOICE; therefore, the wording herein reporting the masculine or feminine gender includes the other genders and reports no such discrimination.



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