What about the evidence for functional medicine?

For many years, the conventional medical establishment has promoted a narrow view of clinical research—that without randomized, double-blind, placebo-controlled (RDBPC) clinical trials we cannot know what works. Such trials do indeed tell us which agents *among those measured* have the most overall success across many patients. But the more accurate statement would be that without RDBPC trials we cannot know whether agent X has a greater impact than agent Y *on the particular populations studied*. The data are grouped, analyzed, and interpreted with this goal in mind.

RDBPC studies play a significant role in evaluating and comparing efficacy of new pharmaceutical treatments, especially when it is important to rule out placebo effects, but they have many inherent limitations which constrain their ability to inform medical decision making.[1,2]

- The subjects in clinical trials are usually screened to exclude patients with multiple conditions. That means research subjects rarely resemble the patients actually treated in physicians' offices.
- The decision about which interventions to study is extremely biased: 70% of U.S. research dollars is provided by pharmaceutical companies.[3] That means that many potentially effective approaches are never formally studied and those that are published are frequently shown later on to have faulty and even biased findings.[4,5]
- Therapies that do not involve drugs but that do involve multiple individualized interventions (e.g., diet and exercise) do not fit the RDBPC research model.[6,7,8]
- Most important, what such trials do NOT tell us is how to create an individualized, patient-centered therapeutic plan that will work for a person with a unique combination of existing conditions, genetic influences, environmental exposures, and lifestyle choices.[9]

When people ask to see "the evidence for functional medicine," they often mean, "Where are your RDBPC trials, comparing functional medicine to conventional medicine in a clinical setting?" We'd like to see those also; for many of the reasons summarized above, they do not exist. To advance the goal of collecting useful data in clinical settings on real patients (not carefully selected research subjects without co-morbidities), IFM has begun developing pilot projects in collaboration with institutions that provide care to patients. At the same time, we are exploring research models that can address individualized, multifaceted, whole-systems care.[10,11] And we are working with leaders in academic medicine to help transform medical education so that doctors of the future will have functional medicine skills. Does that mean there is not yet any evidence for functional medicine? Not at all. There is a vast array of evidence to consider:

- Understanding the causes of disease requires extensive knowledge about the physiology and biochemistry of the human body. The scientific community has made incredible strides in helping practitioners understand not only the most basic of biological functions (assimilation, defense and repair, energy production, biotransformation and elimination,

communication, transport, and structural integrity) but also how environment and lifestyle influences, moving continuously through an individual's genetic heritage, psychosocial experiences, and personal beliefs, can impair those functions. Using that knowledge to find the sources of each patient's problems is powerful science!

- Scientific support for the functional medicine approach to treatment can be found in a large and rapidly expanding evidence base about the therapeutic effects of ***nutrition*** (including both dietary choices and the clinical use of vitamins, minerals, and other nutrients such as fish oils)[12,13,14]; ***botanicals***[15,16,17]; ***exercise***[18] (aerobics, strength training, flexibility); ***stress management***[19]; ***detoxification***[20,21,22]; ***acupuncture***[23,24,25]; ***manual medicine*** (massage, manipulation)[26,27,28]; and ***mind/body techniques***[29,30,31] such as meditation, guided imagery, and biofeedback.

IFM invests considerable resources in reviewing, analyzing, and presenting the scientific foundation of functional medicine to health practitioners:

- The *Textbook of Functional Medicine* explores the evidence underlying biochemical individuality, the weblike interactivity of physiological factors, the influences on healthy aging, the effects of genetics, environment, and lifestyle on individual health, and the common dysfunctions that, if left untended, drive us toward disease. It is extensively researched (thousands of citations) and carefully explains how this evidence can be applied to clinical practice.
- Three in-depth Monographs, comprising many hundreds of references, comprehensively explore the evidence supporting functional medicine approaches to managing conditions associated with mood disorders, GI dysfunction, and pain.
- All speakers at IFM continuing medical education activities are asked to provide the most recent and relevant citations supporting the topics they discuss.

Making healthcare choices—and making sure they are effective—involves the functional medicine clinician and patient in a relationship where science and art, information and belief, attention and insight, communication and trust all have value. Functional medicine practitioners are taught to integrate what they know from their previous education and clinical experience with what they learn about functional medicine—how to seek the underlying causes of disease and how to craft a personalized, systems-oriented therapeutic plan for each unique patient using evidence and insight, art and science.

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[1] Kaplan, et al. BMC. Medical Research Methodology. 2011;11:65. http:/www.biomedcentral.com/1471-2288/11/65
[2] Ames BN, et al. Evidence-based decision making on micronutrients and chronic disease: long-term randomized controlled trials are not enough. Am J Clin Nutr. 2007;86:522-5.
[3] Overholt A. Health and the profit motive. FastCompany.com. http://www.fastcompany.com/node/46025/print.
[4] Ioannidis, J.P.A. Why most published research findings are false. PLOS Medicine. www.plosmedicine.org. 2005;2(8). E124. 0696-701.
[5] Abramson J, Wright JM. Are Lipid-lowering guidelines evidence-based? The Lancet. 2007;369:168-9.
[6] Heaney RP. Nutrition, chronic disease, and the problem of proof. Am J Clin Nutr. 2006;84:471-2.

[7] Cerutti S. et al. Non-linear algorithms for processing biological signals. Computer Methods and Programs in Biomedicine. 1996;51:51-73.
[8] Chen Y, et al. Variations in DNA elucidate molecular networks that cause disease. Nature. 2008;452(27):429-35.
[9] Genuis SL, Genuis SJ. Exploring the continuum: medical information to effective clinical practice. Paper I: the translation of knowledge into clinical practice. J of Evaluation in Clinical Practice. 2006;12(1):49-62.
[10] Bell IR, Koithan M. Models for the study of whole systems. Integr Cancer Ther. 2006;5(4):293-307.
[11] Genuis S L, Genuis S J. Op cit.
[12] Ames BN, et al. High-dose vitamin therapy stimulates variant enzymes with decreased coenzyme binding affinity (increased K_m. Am J Clin Nutr. 2002;75:616-58
[13] Lands B. Prevent the cause, not just the symptoms. Prostaglandins Other Lipid Mediat. 2011 Jul 30. [Epub ahead of print]
[14] Sofi F, Abbate R, Gensini GF, Casini A. Accruing evidence on benefits of adherence to the Mediterranean diet on health:
an updated systematic review and meta-analysis. Am J Clin Nutr. 2010 Nov;92(5):1189-96. Epub 2010 Sep 1.
[15] Agency for Healthcare Research and Quality. *Milk Thistle: Effects on Liver Disease and Cirrhosis and Clinical Adverse Effects*. Evidence Report/Technology Assessment no. 21. Rockville, MD: Agency for Healthcare Research and Quality; 2000. AHRQ publication no. 01-E025.
[16] http://nccam.nih.gov/health/greentea/
[17] http://nccam.nih.gov/health/stjohnswort/ataglance.htm
[18] McArdle WD, Katch EI, Katch VL. Exercise Physiology: Energy, Nutrition, and Human Performance. Philadelphia: Lippincott Williams and Wilkins, 2001.
[19] McCraty R. Coherence: Bridging personal, social and global health. Altern Therapies. 2010;16(4): 10-24.
[20] Yi B, Kasai H, Lee HS, Kang Y, Park JY, Yang M. Inhibition by wheat sprout (Triticum aestivum) juice of bisphenol A-induced oxidative stress in young women. Mutat Res. 2011 Sep 18;724(1-2):64-8. Epub 2011 Jun 28.
[21] Johnson CH, Patterson AD, Idle JR, Gonzalez FJ. Xenobiotic Metabolomics: Major Impact on the Metabolome. Annu Rev Pharmacol Toxicol. 2011 Jul 6. [Epub ahead of print]
[22] Scapagnini G, Caruso C, Calabrese V. Therapeutic Potential of Dietary Polyphenols against Brain Ageing and Neurodegenerative Disorders. Adv Exp Med Biol. 2011;698:27-35.
[23] Colak MC, Kavakli A, Kilinç A, Rahman A. Postoperative pain and respiratory function in patients treated with electroacupuncture following coronary surgery. Neurosciences (Riyadh). 2010 Jan;15(1):7-10.
[24] Cao H, Pan X, Li H, Liu J. Acupuncture for treatment of insomnia: a systematic review of randomized controlled trials. J Altern Complement Med. 2009 Nov;15(11):1171-86.
[25] Lee A, Fan LT. Stimulation of the wrist acupuncture point P6 for preventing postoperative nausea and vomiting. Cochrane Database Syst Rev. 2009 Apr 15;(2):CD003281.
[26] Rubinstein SM, Leboeuf-Yde C, Knol DL, de Koekkoek TE, Pfeifle CE, van Tulder MW. The benefits outweigh the risks for patients undergoing chiropractic care for
neck pain: a prospective, multicenter, cohort study. J Manipulative Physiol Ther. 2007 Jul-Aug;30(6):408-18.
[27] Beyerman KL, Palmerino MB, Zohn LE, Kane GM, Foster KA. Efficacy of treating low back pain and dysfunction secondary to osteoarthritis:
chiropractic care compared with moist heat alone. J Manipulative Physiol Ther. 2006 Feb;29(2):107-14.
[28] Kshettry VR, Carole LF, Henly SJ, Sendelbach S, Kummer B. Complementary alternative medical therapies for heart surgery patients:
feasibility, safety, and impact. Ann Thorac Surg. 2006 Jan;81(1):201-5.
[29] Ornish D. et al. Changes in prostate gene expression in men undergoing an intensive nutrition and lifestyle intervention. PNAS. 2008;105(24):8369–8374 www.pnas.org_cgi_doi_10.1073_pnas.0803080105
[30] Xiong GL, Doraiswamy PM. Does meditation enhance cognition and brain plasticity? Ann N Y Acad Sci. 2009;1172:63-9.
[31] Hölzel BK, et al. Mindfulness practice leads to increases in regional brain gray matter density. Psychiatry 2011; 30;191(1):36-43. Epub 2010 Nov 10.