

Module 4 - Diet and Nutrition

With more than two-thirds of Americans overweight and more than one-third obese, every physician will confront patients with nutritional problems in everyday practice, no matter what their specialty. Physicians are the key opinion leaders in matters of health and are frequently called on to advise on how communities should address health problems; with the current crisis in rising childhood obesity, many LSU graduates may play a role in shaping community approaches to healthy environments for children. Furthermore, physicians will certainly encounter patients who use (and abuse) supplements and botanical products, since their use is on the rise, partly due to the different standards that govern their marketing. All of these issues are important ones for consideration in a course on Diet and Nutrition. Thus, the overarching objective of this module is to prepare physician graduates of LSU to address the common nutritional problems they are likely to encounter in their future careers.

Four topics have been chosen for exploration.

- The first, *“Genetic, Epigenetic and Environmental Influences on Risk for Obesity”* explores current understanding of the factors which contribute to the risk for obesity and its associated metabolic co morbidities.
- The second, *“Prevention of Diabetes and development of cardiovascular risk factors”*, looks at diet as a form of primary prevention for these major causes of morbidity and mortality.
- The third, *“Management of the Medically Obese Patient – Diet, Drugs and Surgery,”* looks at current approaches to weight reduction for the obese patient.
- The fourth topic, *“Botanicals and Supplements”* looks at some over the counter supplements that may or may not have a role in controlling diabetes. It also addresses the larger concern about the use, regulation, and potential benefits and harms of supplements in general.

Corresponding to the four topics, the learning objectives for the Diet and Nutrition Module are as follows:

- To promote understanding of obesity as a complex interaction of biology (genetic factors), early life influences (epigenetic) and environmental influences (i.e., food supply and pricing, neighborhood design, social networks and many others factors);
- To understand the specific role of diet as a method of primary prevention for common diseases and the current recommendations for optimal lipid levels;
- To understand the current recommendations for treating obesity – when to employ diet, drugs and surgery – and the potential benefits and limitations of these approaches;
- To know the widespread usage of botanicals and supplements by Americans and to recognize the potential that these products have for harm and for benefit.

Prior to your small group meeting:

All physicians should have some fundamental understanding of good nutrition, food labels, and energy requirements. Please review the following prior to your small group session:

1) **Review some fundamental principles** in the Stanford Nutrition Curriculum on-line. Go to the following web site: http://www.medschool.lsuhsu.edu/medical_education/undergraduate/Nutrition/index.html

Click on Nutrition Principles, and then review *Unit 1 Nutrition Basics*. In particular, pay attention to the sections on balance and adaptation and on regulation of dietary supplements by the FDA.

2) **Access the website for The Obesity Society.** www.obesity.org and access their Education activities. The online course, *Office Management of Obesity* was rated the best online CME by the Robert Wood Johnson Foundation.

3) Think about the following questions

1. What are your attitudes to people who are obese or overweight? Do you have a close friend or family member who is overweight or obese? Do you think that managing obesity is simply a matter of eating less and exercising more?
2. What role does food play in your life? Biochemical? Physiological? Psychological? Why do you eat? Do you eat too much? How much is enough? How many calories a day do you eat and how are they broken down? Do you know the answer to these questions? Do you know how to find these answers?
3. Do you ever think about the plethora of calories in this country, its uneven distribution and what it has done to our health?
4. Have you ever considered at your age that unhealthy eating might eventually result in your own chronic disease?
5. Our society is one where taking supplements to improve health is mostly accepted, even when the efficacy of those products is not really supported by strong efficacy evidence, as long as they are generally regarded as safe. How many different supplements or over-the-counter “natural” products have you taken or do you take regularly? What is the evidence to support the claims made about these products’ effects?
6. Do you eat with health in mind? Do you ever look at food labels? Do you understand how to read them? Look at the following sites:

How to Use the Nutrition Facts Label-

<http://www.fda.gov/Food/ResourcesForYou/Consumers/NFLPM/ucm274593.htm>

Figuring Out Food Labels- www.kidshealth.org/kid/stay_healthy/food/labels.html

My Pyramid.Gov- www.mypyramid.gov

Finding calorie content of foods- www.my-calorie-counter.com

Instructions for the Small Group Meeting

A. Discuss the following as a group: How much food intake do you need to maintain your current body weight? How much is your actual food intake? Several equations can be used to calculate energy needs.

1. Harris Benedict Equations

Daily energy requirements (kcal) = BMR X Activity Factor

- **BMR from the Harris Benedict Equation**

(Harris Benedict equations obtained from AACE/ACE Position Statement on Prevention, Diagnosis, and Treatment of Obesity, 1998.)

Men :

$BMR (Kcal) = 66 + (13.8 \times \text{weight in kg}) + (5 \times \text{height in cm}) - (6.8 \times \text{age})$

Women :

$BMR (Kcal) = 655 + (9.6 \times \text{weight in kg}) + (1.8 \times \text{height in cm}) - (4.7 \times \text{age})$

- Activity Factor

Examples of status :

Examples of Factors :

Sleeping	1
Sedentary	1.3 *
Slightly active	1.5
Moderately active	1.6
Active	2
Athlete	2.5

2. World Health Organization Formula

WHO Formula:

- Women aged 31-60: $BMR = (0.016 \times \text{weight} + 3.5) \times 240$
- Men aged 31-60: $BMR = (0.022 \times \text{weight} + 3.7) \times 240$
- Add activity factor of 1.3* for sedentary or 1.5 for regular exercisers (*recommend 1.3)

3. "Rule of Thumb" estimate of energy requirements: 10 calories per pound (no corrections for exercise).

Exercise #1: Calculate your energy requirements by each of the three methods listed above.

Harris Benedict Equation: _____Kcal/day
WHO Formula _____Kcal/day
Rule of thumb _____Kcal/day

Exercise #2: Write down your food intake for the last 24 hours. Start by writing down all the foods you consumed in the last 24 hours and be sure to include quantity. Go to www.my-calorie-counter.com and calculate the energy intake from those foods.

Exercise #3: Formulate a diet for yourself that would enable you to lose 4 pounds in 4 weeks; this is an energy deficit of 500 Kcal/day. Structure your personal diet around the following principles that represent the best available recommendations for dieting: Eat breakfast and structure at least three meals per day. Since our appetites are driven by food weight, avoid energy dense and high fat foods. At least five servings of fruits and vegetables should be part of every daily diet. Portion-controlled options (frozen entrees, pre-measured servings) may help in keeping within caloric limits.

Discuss your personalized diet with a colleague. How closely does this dietary pattern follow your usual dietary intake? Would increasing your physical activity by moderate activity for one hour on a treadmill be “worth it” in terms of allowing you to increase intake by 450 Kcal? What foods (and how much) would you add back to the diet to compensate for one hour of physical activity?

B. Plan your group project and presentation

Your group has been asked to research one of the following topics for a symposium to be held in several weeks. At that symposium, one or two members of the group will be expected to give a 15-minute presentation on this topic using PowerPoint. Each member of the group should help research the questions and provide information for the presentation.

Look over your assigned topic and the guidelines that have been provided. A librarian will help you conduct a proper literature search, but suggested references are also provided. As a group, begin to discuss how you will gather the information and put it together into a presentation.

Contact Dr. DiCarlo if you have any questions about your presentation. Finally, email a copy of your PowerPoint presentation to Dr. DiCarlo (rdicar@lsuhsc.edu) at least one day prior to your presentation.

Small Groups 1, 5, 9 and 13

Study Topic #1 “Genetic, Epigenetic and Environmental Influences on Risk for Obesity”

Obesity, like Type 2 Diabetes, is clearly determined by both genetic and environmental factors. For obesity, twin studies have shown a heritability of up to 75% whereas sibling and family studies provide a number closer to 35-50%. The strongest experimental paradigm to disentangle the contribution of environmental and genetics factors has been the study of monozygotic twin pairs adopted together or separately. Choose one of the case studies below and build a 15 minute PowerPoint presentation around the case discussion as a teaching method. Build the references below (and additional references) into the presentation to buttress your efforts. **Instructions:** Give a 15-minute PowerPoint presentation on *one* of the above topics. Send Dr. DiCarlo a copy of the PowerPoint prior to the presentation.

Case Study #1

Pima Indians living in Arizona have the highest prevalence of Type 2 Diabetes and obesity in the world. More than 75% of the population is frankly obese whereas more than 40% have Type 2 Diabetes at age 35 and above. A population of genetically related Pima Indians lives in a very remote area in the mountains of North Mexico in Maycoba at the border between the States of Sonora and Chihuahua. Recently, the 2 populations decided to have an exchange of 20 people moving from Maycoba (average BMI of 24 ± 2 kg/m² and fasting glucose of 95 ± 8 mg/dl) to Arizona; 20 individuals moved from Arizona (average BMI of 35 ± 5 kg/m² and fasting glucose of 126 ± 15 mg/dl) to Maycoba in Mexico.

Question #1: Ten years later, what has happened to these 20 people in terms of

- Average and SD of BMI?
- Average and SD of fasting blood glucose and type 2 diabetes?
- Average and SD of % body fat?
- Physical activity and diet?

Case Study #2

Epigenetics is the impact of environmental factors especially early in life, and is believed to be mediated through modifications to gene expression via DNA methylation and histone modification. Offspring from mothers with gestational diabetes mellitus are more likely to develop obesity and/or Type 2 Diabetes than offspring from non-diabetic mothers.

Question #2 What would be the perfect experimental setting to show that the impact of in utero development can be impacted by factors independent of parental genes? Design and discuss your experiment, its expected outcome and the pitfalls that might occur in executing the experiment.

Case Study #3

Research has been done to measure the prevalence of obesity in mainland Japan, in Hawaii among migrants and finally on the west coast of the United States among Japanese migrants.

Question #3 What are the expected BMI and % body fat of Japanese from these three areas, assuming that the genetic pool of these Japanese migrants are similar? What are the likely changes from first to second generations?

Suggested References to start the work:

- Stunkard AJ, Sorensen TI, Hanis C, Teasdale TW, Chakraborty R, Schull WJ, Schulsinger F: An adoption study of human obesity. *N Engl J Med* 314:193-198, 1986
- Bouchard C, Tremblay A, Despres JP, Nadeau A, Lupien PJ, Theriault G, Dussault J, Moorjani S, Pinault S, Fournier G: The response to long-term overfeeding in identical twins. *N Engl J Med*:1477-1482, 1990

3. Christakis NA, Fowler JH: The spread of obesity in a large social network over 32 years. *N Engl J Med* 357:370-379, 2007
 4. Schulz LO, Bennett PH, Ravussin E, Kidd JR, Kidd KK, Esparza J, Valencia ME: Effects of traditional and western environments on prevalence of type 2 diabetes in Pima Indians in Mexico and the U.S. *Diabetes Care* 29:1866-1871, 2006
 5. Ravussin E, Valencia ME, Esparza J, Bennett PH, Schulz LO: Effects of a traditional lifestyle on obesity in Pima Indians. *Diabetes Care*:1067-1074, 1994
 6. Ravussin E, Bogardus C: Energy balance and weight regulation: genetics versus environment. *Br J Nutr*:S17-20, 2000
 7. Willer CJ, Speliotes EK, Loos RJ, Li S, et al.: Six new loci associated with body mass index highlight a neuronal influence on body weight regulation. *Nat Genet* 41:25-34, 2009
 8. Pettitt DJ, Forman MR, Hanson RL, Knowler WC, Bennett PH: Breastfeeding and incidence of non-insulin-dependent diabetes mellitus in Pima Indians. *Lancet* 350:166-168, 1997
 9. Pettitt DJ, Lawrence JM, Beyer J, Hillier TA, Liese AD, Mayer-Davis B, Loots B, Imperatore G, Liu L, Dolan LM, Linder B, Dabelea D: Association between maternal diabetes in utero and age at offspring's diagnosis of type 2 diabetes. *Diabetes Care* 31:2126-2130, 2008
 10. Sayer AA, Syddall HE, Dennison EM, Gilbody HJ, Duggleby SL, Cooper C, Barker DJ, Phillips DI: Birth weight, weight at 1 y of age, and body composition in older men: findings from the Hertfordshire Cohort Study. *Am J Clin Nutr* 80:199-203, 2004
-

Small Groups 2, 6, 10 and 14

Study Topic #2 "Prevention of Diabetes and development of cardiovascular risk factors"

Patient Visit: During a routine physical, a 45 yo WM patient is concerned about future medical problems

"I found out recently during a health screening that my blood sugar was somewhat elevated. They did a finger-stick glucose value and it was 105 mg/dl. They wrote it down on this piece of paper. Also, they told me my blood pressure was a little high at 142/93. They also did a finger-stick cholesterol and my total cholesterol was 240 mg/dl. I am worried because my father developed diabetes in his 50s and had his first heart attack at 59 years of age. Of course, I never worried about it because I thought it was because he never exercised much and I didn't think his diet was very good. But, my brother also told me recently that he had developed diabetes last year....for some reason, he didn't want me to know about it. Now, I am concerned about this problem....what can I do about it"

On Physical and laboratory exam, you confirm the following:

BMI = 33.2; BP = 143/85

Total Cholesterol = 220 mg/dl, Triglycerides = 350, HDL-C = 35, LDL C = 135 mg/dl. Fasting blood glucose was 106 mg/dl; HbA1c = 6.4 %

Instructions: Using the best available scientific evidence, develop a plan of action to address all the questions on this patient and design a plan of action to delay or prevent future disease states? During a 15-minute PowerPoint presentation on this topic, the following should be addressed:

- 1) What is the natural history of this patient's condition?
- 2) What is considered the major pathophysiologic abnormality to be altered?
- 3) What instructions would you provide as far a nutritional counseling?
- 4) What guidelines would you provides as far as exercise?
- 5) What is the reality that if he adheres to your plan that changes can actually be made?

Provide your classmates with some basic information and evidence that diet can play an important role in preventing one of the common causes of morbidity and mortality in the U.S. 1) Briefly provide some data demonstrating the increasing rate of diabetes in this country. What is pre-diabetes? Several studies have been done to examine whether or not diabetes can be prevented through a healthy lifestyle. Briefly outline the common preventive measures and briefly discuss one primary study that has shown some benefit. How should this be integrated into physician practices? 2) Briefly review the current guidelines for optimal lipid levels based on other cardiovascular risk factors. Briefly summarize the key principles of a heart healthy diet according to the American Heart Association. Discuss one primary study demonstrating the efficacy of diet in improving cholesterol levels.

Instructions: Give a 15-minute PowerPoint presentation that incorporates both of the above topics. Send Dr. DiCarlo a copy of the PowerPoint prior to the presentation.

Suggested References to start the work:

Review the National Heart, Lung, and Blood Institute ATP III Guidelines regarding evaluation and treatment of high blood cholesterol. (Note, ATP IV guidelines are due to be released next year.)

Review the 'DASH' diet or other diet recommendations of the American Heart Association

Review diabetes statistics and information of prevention trials from the National Institute of Diabetes and Digestive and Kidney Diseases.

- 1) *Diabetes Prevention Program Research Group: Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. N Engl J Med 346: 393– 403, 2002*
 - 2) *Diabetes Prevention Program Research Group: Impact of intensive lifestyle and metformin therapy on cardiovascular (CVD) risk factors in the Diabetes Prevention Program. Diabetes Care 28: 888– 894, 2005*
 - 3) Haffner SM, Mykkanen L, Festa A, Burke JP, Stern MP *Insulin-resistant prediabetic subjects have more atherogenic risk factors than insulin-sensitive prediabetic subjects: implications for preventing coronary heart disease during the prediabetic state. Circulation 101: 975– 980, 2000*
 - 4) [Goldberg RB](#), [Temprosa M](#), [Haffner S](#), [Orchard TJ](#), [Ratner RE](#), [Fowler SE](#), [Mather K](#), [Marcovina S](#), [Saudek C](#), [Matulik MJ](#), [Price D](#); [Diabetes Prevention Program Research Group](#) Effect of progression from impaired glucose tolerance to diabetes on cardiovascular risk factors and its amelioration by lifestyle and metformin intervention: the Diabetes Prevention Program randomized trial by the Diabetes Prevention Program Research Group. [Diabetes Care](#). 2009 Apr;32(4):726-32.
 - 5) Tuomilehto J, Lindström J, Eriksson JG, Valle TT, Hämäläinen H, Ilanne-Parikka P, Keinänen-Kiukaanniemi S, Laakso M, Louheranta A, Rastas M, Salminen V, Uusitupa M; Finnish Diabetes Prevention Study Group. *Prevention N Engl J Med. 2001 May 3;344(18):1343-50.*
-

Small Groups 3, 7, 11 and 15

Study Topic #3: "Management of the Medically Obese Patient – Diet, Drugs and Surgery."

Case Study: You receive the following email:

I've always had a weight problem with being 20 or so lbs overweight, but the last few years it's gotten out of control- some medical issues and medicines helped me gain more weight.

I'm 5'4" tall, 45 years old, and I weigh 230 lbs. I feel like I'm 144 years old. I've got sleep apnea, high cholesterol, diabetes, high blood pressure, migraines, fibromyalgia, diabetic neuropathy, depression and several other issues. When I was 18 I had a breast reduction, and had about 3lbs removed from each breast according to my doctor. I now have the nightmare again-with gaining in my breasts when I was pregnant and the weight gain they are back. And they hurt.

I have tried Xenical when it was prescription.. I lost a total of about 10lbs-and gained about 12lbs. I've tried Atkins-lost about 13 lbs and gained it all back and then some when I couldn't afford to eat the expensive foods that go hand-in-hand with this diet. I've tried moderating this and that through all the confusing hype of which foods are good today that might change and be a bad food tomorrow. I've tried Slim Fast, fasting, and other types of diets. I have tried everything I can to lose weight. I'd stand on my head if I thought it would help.

I have researched weight loss surgeries for over 2 years. I've learned the pros and cons, risks and benefits. I've made the decision to go forward with the surgery to save my life. The problem that I've run up on is that I'm a single mom, relying on Medicaid. There is not ONE DOCTOR in this state that accepts Medicaid, even though they pay for the surgery. If I could afford the approximately 24,000 to self-pay then WHY would I need Medicaid?

This patient represents several issues that are important in obesity management. Discuss the following topics and prepare a PowerPoint presentation to your classmates.

Diets and weight loss.

There are a number of popular nutrition programs which are directed either at losing weight or maintaining an optimum state of health. The publishing industry is delighted with each new idea or diet. It means more book sales and a visit to the local bookstore bears this out. The obvious question is, do these diets really help?

In order to prepare yourself for the many questions you will be asked by patients, review the diets from the list below. Prepare a PowerPoint that gives a **brief** analysis of each diet's content and the rationale behind it. Briefly present one **primary study** which demonstrates efficacy for one of these diets or that compares one diet to another.

1. Low fat diet
2. Atkins Diet
3. Weight Watchers Program
4. The South Beach Diet
5. The Zone Diet
6. The Mediterranean diet.

Medical and Surgical Management for weight loss.

Primary Care Physicians and many specialists as well will be called upon to manage obesity as an underlying cause of patient disease. As discussed above, diets may have limited long term efficacy. Review the Guidelines for Evaluation and Treatment of Obesity (or The Practical Guide) http://www.nhlbi.nih.gov/guidelines/obesity/ob_home.htm . Briefly summarize the current indications for pharmacologic management of obesity and the current indications for surgical management. Discuss one **primary study** that demonstrates efficacy of management of obese patients in an office environment with pharmacologic treatment, **or** discuss one primary study that demonstrates the improved mortality

after one of the current surgical approaches to obesity management. What are the long term complications or the surgical procedure you discussed.

Instructions: Give a 15-minute PowerPoint presentation on these topics. Send Dr. DiCarlo a copy of the PowerPoint and the primary study you will discuss prior to the presentation.

Suggested References to start the work:

1. Dansinger et al JAMA Dansinger M I et al. Comparison of the Atkins, Ornish, weight watchers, and zone diets for weight loss and heart disease risk reduction. JAMA 2005; 293: 43-53.
2. Gardner CD, Kiazand A, Alhassan S, Kim S, Stafford RS, Balise RR, Kraemer HC, King AC. Comparison of the Atkins, Zone, Ornish, and LEARN Diets for Change in Weight and Related Risk Factors among Overweight Premenopausal Women JAMA. 2007;297:969-977
3. Shai I, Schwarzfuchs D, Henkin Y, Shahar DR, Witkow S, Ilana Greenberg I, Golan R, Fraser D, Bolotin A, Hilel Vardi H, Osnat Tangi-Rozental O, Zuk-Ramot R, Sarusi B, Brickner D, Schwartz Z, Sheiner E, Marko R, Katorza E, Thiery J, Fiedler GM, Blucher M, Michael Stumvoll M, Stampfer MJ. Weight Loss with a Low-Carbohydrate, Mediterranean, or Low-Fat Diet. N Engl J Med 2008;359:229-41.
4. Sacks FM, Bray GA, Carey VJ, Smith SR, Ryan DH, Anton SD, McManus K, Champagne CM, Bishop LM, Laranjo N, Leboff MS, Rood JC, de Jonge L, Greenway FL, Loria CM, Obarzanek E, Williamson DA. Comparison of Weight-Loss Diets with Different Compositions of Fat, Protein, and Carbohydrates. N Engl J Med 2009;360:859-73.
5. Tsai AG and Wadden TA. Treatment of obesity in primary care practice in the United States: a systematic review. JGIM 24(9):1073-9.
6. Yanovski S Z. Pharmacotherapy for obesity-promise and uncertainty. NEJM 2005; 353: 2187-2189.
7. Buchwald, H Am J Med Buchwald H, Estok R, Fahrenbach K, Banel D, Jensen MD, Pories WJ, Bantle JP, Sledge I. Weight and type 2 diabetes after bariatric surgery: systematic review and meta-analysis. Am J Med. 2009 Mar;122(3):248-256.Review.
8. Dixon JB, O'Brien PE, Playfair J, Chapman L, Schachter LM, Skinner S, Proietto J, Bailey M, Anderson M. Adjustable gastric banding and conventional therapy for type 2 diabetes: a randomized controlled trial. JAMA. 2008 Jan 23;299(3):316-23
9. Nestle M. Food marketing and childhood obesity-a matter of policy. NEJM 2006; 354:2527-2529.
10. Wing R et al. A self-regulating program for maintenance of weight loss. NEJM 2006; 355: 1563-1571.
11. Mello M et al. Obesity- the new frontier of public health law. NEJM 2006; 354:2601-2601.
12. Sjostrom L, Narbro K, Sjostrom D, et al. Effects of bariatric surgery on mortality in Swedish obese subjects. NEJM 2007; 357:741-52.
13. Adams TD, Gress RE, Smith SC, et al. Long-term mortality after gastric bypass surgery. NEJM 2007; 357:753-61.
14. Executive Summary of the Recommendations of the American Association of Clinical Endocrinologists, the Obesity Society, and American Society for Metabolic and Bariatric Surgery Medical Guidelines for Clinical Practice for the Perioperative Nutritional, Metabolic and Nonsurgical Support of the Bariatric Surgery Patient. <http://www.obesity.org/news/BariatricExcSum.pdf>

Small Groups 4, 8, 12 and 16

Study Topic #4: “Clinical Use and Efficacy of Nutritional Supplements”

Patient Visit: During an initial physician visit to you, the patient discloses the following information;

“I have had adult onset diabetes for over ten years. Initially, I was treated with diet and exercise and did well. My A1c at diagnosis was 9.5 %, but after some initial weight loss and exercise, I maintained my A1c at around 6.5-7.0% for years. However, beginning at around 5 years ago, the sugars started going up again. My A1c was over 7% and my doctor put me on metformin. Since that time, I’ve had to increase my metformin to over 2 grams a day, and a year ago, he put me on another drug called glipizide along with the metformin. That dose has also increased to 10 mg a day. My primary doctor recently obtained another A1c and it was close to 8%. He suggested I go on another drug or add insulin, but isn’t there anything I can do with something more natural? I am tired of taking drugs and I have gained 10 pounds over two years. My friend told me about some over the counter supplement she was taking, I think it was chromium. It seemed to help her. Also, she was also taking this other natural product to lose weight. So, I have a couple of questions...Is there something over the counter I can take that is safe, cheap and effective? Is there a natural product I can take to help with this weight loss? If I do take these over the counter products, are they safe? Can they interfere with my other medications? I am really at the end of my rope!”

Instructions: Using the best available scientific evidence, develop a plan of action to address all the questions on this patient? During a 15-minute PowerPoint presentation on this topic, the following should be addressed:

- 1) What is the natural history of this patient’s diabetes? What should she expect now and in a few years as far as additional medication?
- 2) What is the role of “over the counter” products in controlling her diabetes and weight loss now?
- 3) Describe possible concerns of “supplements” and how the regulation, preparation and testing of supplements differs from pharmaceutical products.

Suggested References to start the work:

1. Gibson JE, Taylor DA. Can claims, misleading information and manufacturing issues regulating dietary supplements be improved in the United States of America? *J Pharmacol Exp Ther* 314:939–944, 2005
2. Neuhouser ML. Dietary supplement use by American women: challenges in assessing patterns of use, motives and costs (Review). *J Nutr* 133:1992S–1996S, 2003
3. Cefalu WT, Hu FB. Role of chromium in human health and in diabetes. *Diabetes Care* 27:2742–2751, 2004
4. Balk EM, Tatsioni A, Lichtenstein AH, Lau J, Pittas AG. Effect of chromium supplementation on glucose metabolism and lipids: a systematic review of randomized controlled trials. *Diabetes Care* 30(8):2154-63, 2007
5. Albarracin CA, Fuqua BC, Evans JL, Goldfine ID. Chromium picolinate and biotin combination improves glucose metabolism in treated, uncontrolled overweight to obese patients with type 2 diabetes. *Diabetes Metab Res Rev* 24(1):41-51, Jan-Feb 2008
6. Schmidt, B.M., D.M. Ribnicky, P.E. Lipsky, I. Raskin. Botanical therapeutics: New life for the old concept. *Nature Chemical Biology* 3: 360-366, 2007
7. Riddle MC Glycemic management of type 2 diabetes: an emerging strategy with oral agents, insulins and combinations.. *Endocrinol Metab Clin North Am* 34:77–98, 2005
8. Cefalu WT, Ye J, Zuberi A, Ribnicky DM, Raskin I, Liu Z, Wang ZQ, Brantley PJ, Howard L, Lefevre Botanicals and the metabolic syndrome. *Am J Clin Nutr.* 87(2):481S-7S, 2008
9. Ribnicky DM, Poulev A, Schmidt B, Cefalu WT, Raskin I. *Am J Clin Nutr* Evaluation of botanicals for improving human health.. 87(2):472S-5S, 2008
10. Schmidt B, Ribnicky DM, Poulev A, Logendra S, Cefalu WT, Raskin I.A Natural History of Botanical Therapeutics. *Metabolism.* 57(7 Suppl 1):S3-9, Jul 2008
11. Liu Z Preparation of botanical samples for biomedical research. In the "Hot Topics" issue on “Botanical Treatments for Diabetes and Obesity”. *The Journal “Endocrine, Metabolic & Immune Disorders - Drug Targets.”* *Endocr Metab Immune Disord Drug Targets.* 8(2):112-121, Jun 2008