Leveraging the Power of Lifestyle Medicine:
Nutrigenomics and Beyond.

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What is wrong with this numbers?

>75%

• The Chronic Disease Burden due to Poor Lifestyle Choices and Environmental exposure?

• Physician Office visits that involve a prescription medication?

http://www.cdc.gov/nchs/fastats/drugs.htm

The Irony of Modern Medicine

“If [greater than 75%] of the chronic metabolic diseases plaguing mankind today are preventable, why do we spend most of our money on solutions that avoid addressing the root cause? Science hasn’t failed to give us the answers; scientists have just moved on to find answers that they think we will like better. Since we have failed to act by changing our lifestyle habits, we are paying them to discover the magic bullet, one that will allow us to somehow become healthy, while ignoring our unhealthy habits.”

The Original Prescription- pg22-Guilliams
The Type of Medicine you Practice is influenced by How you Measure Risk?

Risk Management and Defensive Medicine.

Based on current biomarkers, age, sex etc.- patient has 30% chance of an event in the next 10 years.

Where is the patient along the risk continuum and what is there momentum?
How to influence outcomes based on Risk

A single point in time

Manage the Numbers

Manage The Patient

RISK TRAJECTORY

Numbers driven therapies....

A Functional/Medical View Of Risk
A Lifestyle View of Risk

• Risky person life
• EtOH/drugs
• Addictive foods

• Glycemic Insulin
• Meal Timing & Energy
• Phytonutrients
• Ins. Sensitizing nutrients

• Risky person life
• EtOH/drugs
• Addictive foods

• Sense of Belonging
• Group dynamics
• Life purpose

• Sedentary Time
• Energy Expenditure
• Cell-Signaling from Ex

• Obesogenic Toxins
• Sunlight-Vit D
• Microflora

• Circadian HPA axis control
• Sleep patterns
• Seasonal patterns
• Phase-shifters

• Cortisol Signaling
• Stress-induced eating
• HPA-axis sensitivity

What do you see?

The definition(s) of lifestyle medicine

• The use of lifestyle as an intervention strategy in the treatment and management of disease.
• The integration of lifestyle practices into conventional medicine to lower the risk for chronic disease and, if disease is already present, to serve as an adjunct to therapy.
• The study and practice of how to help individuals understand that their daily habits and practices have a profound impact on their short and long term health and quality of life.
Prevention-Intervention Hierarchy

All Therapies Begin with Lifestyle!

A Different Approach

Conventional | Lifestyle
---|---
Treats individual risk factors | Treats lifestyle causes

A Different Approach

Conventional | Lifestyle
---|---
Patient is passive recipient of care | Patient is empowered & active partner of care
A Different Approach

Conventional
Patient is often not required to make big changes

Lifestyle
Patient is often required to make big changes

A Different Approach

Conventional
Treatment is often short term

Lifestyle
Treatment is ongoing - Life

A Different Approach

Conventional
Responsibility falls mostly on the clinician or system

Lifestyle
Responsibility falls mostly on the patient
Conventional Lifestyle

A Different Approach

Treatment relies almost exclusively on prescription medications.

Meds (when needed) are an adjunct to lifestyle change.

Emphasis on diagnosis and naming the condition.

Emphasis on motivation to see change.

Environment is designed to facilitate the medical system.

Attempt to create a daily healing environment.
Is there hope to change the future?

• We must think differently about “diseases” and their cause(s)
• We must view prevention as part of our every day life

The Germ Theory of Disease

• Identified each disease as being caused by one organism or cause
  – Bacteria
  – Virus
• Diseases were linked to Symptoms
• Treating Symptoms was thought to “treat” the disease

Yes...but

• We must think differently about “diseases” and their cause(s)
• We must view prevention as part of our every day life
When Cures seemed like Magic Bullets

- If you could identify the germ causing the disease (Germ Theory)
- You could then find something to make the disease go away by killing the cause!

Could our solutions be part of the problem?

“We are quickly running out of therapies to treat some of these infections that previously had been eminently treatable. There are bacteria that we encounter, particularly in health-care settings, that are resistant to nearly all — or, in some cases, all — the antibiotics that we have available to us, and we are thus entering an era that people have talked about for a long time.”

The Risk-Reward of Rescue Medicine

- How much of the past 100 year shift in human metabolic function might have been caused by a massive shift in our microbiome due to the rampant use of antibiotics?
What is the lifetime health consequence from repeated childhood use of antibiotics?

Failure Rate (need for new antibiotic within 2-18 days of first prescription) was ~10%

**C. Diff and antibiotics**

- Taking antibiotics is the top risk factor for developing *C. difficile* infections for both children and adults.
- Researchers found that 71 percent of cases of *Clostridium difficile* infection among American children aged 1 to 17 occurred shortly after they took antibiotics that were prescribed in doctors’ offices to treat other conditions.
- Most of the children received antibiotics for problems such as ear, sinus or upper respiratory infections. Previous research has shown that at least 50 percent of antibiotics prescribed to children in doctors’ offices are for respiratory infections, most of which do not require antibiotics, the U.S. Centers for Disease Control and Prevention researchers said in an agency news release.

U.S. Centers for Disease Control and Prevention, news release, March 7, 2014
Look into the mirror—not the microscope

**chronic diseases**
associated with overweight and obesity

- HIGH BLOOD PRESSURE
- HIGH CHOLESTEROL
- TYPE 2 DIABETES
- CORONARY HEART DISEASE
- STROKE
- GALLBLADDER DISEASE
- OSTEOARTHRITIS
- SLEEP APNEA
- RESPIRATORY PROBLEMS
- ENDOMETRIAL CANCER
- BREAST CANCER
- PROSTATE CANCER
- COLORECTAL CANCER

Disturbing Trends of the Recent Past

**Obesity Trends in the United States 1960-2008**

- Overweight (BMI ≥ 25)
- Obese (BMI ≥ 30)
- Extremely Obese (BMI ≥ 40)

Graph showing increasing obesity rates from 1960 to 2008.

**U.S. Prevalence of Diabetes**

- **4.2 million** in 1976-1980
- **18.2 million** in 2000-2004
- **21.1 million** in 2009-2014

Graph showing increasing diabetes prevalence over time.
Our Children are getting heavier

The “Gene” Theory of Disease

- Since modern technology has allowed us to sequence the human genome and
- Since we know that some diseases are genetically determined…
- Therefore we should be able to find the “gene” for each “disease” and a develop a “cure” which corrects that gene or gene outcome!
Doesn't our increasing Life Expectancy tell us we are healthier?

Life-Expectancy – the phantom of improving health

Health & Science

Boomers in worse health than their parents at the same life stage, study says

Boomers in bad health?
Can we reverse this trend?

A single Point- Doesn’t Predict the outcome!
The Power of Lifestyle Medicine

Leveraging small changes over a long period of time.

A prospective cohort study of 81,722 US women in the Nurses’ Health Study from June 1984 to June 2010. Lifestyle factors were assessed via questionnaires every 2 to 4 years.

- Sudden cardiac death (SCD) accounts for more than half of all cardiac deaths; the majority of SCD events occur as the first manifestation of heart disease, especially among women.

Nurses’ Health Study—Measurement

- Mediterranean Diet Score
- Smoking Status
- Amount of Exercise
- Body Mass Index
Sudden Cardiac Death (SCD) by the Binary Lifestyle Score

The number of “top scores” in any lifestyle categories↓
- 40%
- 68%
- 92%

Relative Risk of SCD

“Residual Risk”
- 2/3 of patients given statins still have “residual risk”
- Statins add risk for:
  - Diabetes
  - Cataracts
  - Mental Confusion
  - Muscle pain
  - CoQ10 depletion
Onset of Diabetes Diagnosis

Cumulative Incidence of Diabetes (%) by Year:
- Placebo
- Metformin: 31% drop
- Lifestyle: 58% drop

Number of diagnoses per 100 person years by age:

- Placebo
- Metformin
- Lifestyle

10-year follow up on DPP:

- All
- 25-44 y
- 45-59 y
- >60 y
Compared with the placebo intervention, the cost per quality adjusted life years was approximately $1100 for the lifestyle intervention and $31,300 for the metformin intervention...the lifestyle intervention dominated the metformin intervention.

DPP- Model for Real World Setting

For every additional session attended, subjects reduced weight by an additional 0.26%.
The Power of Lifestyle Medicine

- Overpowers the Influence of Aging
- Overpowers the influence of Genetic Risk
- Overpowers the influence of ethnicity
- Works in both men and women
- Improves nearly every outcome measure
- Is recommended in nearly every guideline for cardiovascular or metabolic disease intervention
TLC from ATPIII

Evidence-Based Recommendations
Four TLC Goals
1. Reduced intake of saturated fat and cholesterol (macronutrient changes)
2. Dietary and therapeutic options for enhancing LDL-C lowering
3. Weight reduction
   - BMI 18.5-24.9 kg/m²
   - Waist circumference (35” women / 40” men)
4. Increase regular physical activity

For diabetics with A1C over 7%

Hypertension Guidelines (JNC8)
“For all persons with hypertension, the potential benefits of a healthy diet, weight control, and regular exercise cannot be overemphasized. These lifestyle treatments have the potential to improve BP control and even reduce medication needs. Although the authors of this hypertension guideline did not conduct an evidence review of lifestyle treatments in patients taking and not taking antihypertensive medication, we support the recommendations of the 2013 Lifestyle Work Group.”

But they can be systematically underemphasized.

The Obstacles to Implementing Lifestyle Medicine

How much time and money is used to educate clinicians and patients on:

- The mechanisms and benefits of Rx and OTC pharmaceutical products?
- The mechanisms and benefits of Lifestyle-related interventions?
To make Lifestyle Medicine work

• Must understand How “Life” signals are interpreted by our bodies and converted into health
• Must be able to understand these signals in the form of actionable events in which to engage or avoid.
• Must be able to create achievable goals which are related to real health outcomes
• Must have a plan which allows person to make progress toward goals
• Must have a plan to overcome obstacles and setbacks
• Must purpose to make the plan a new lifestyle—rather than an intervention which ceases when “the goal” is reached.

Leveraging Lifestyle Medicine

How a Lifetime of Decisions Turns into Healthy Outcomes

What Has Changed?
According to the Institutes of Medicine:

“There has been no real change in the human gene pool in this period of increasing obesity, the root of the problem must lie in the social and cultural forces that promote an energy-rich diet and a sedentary lifestyle.”

How did we get here?

- 150 years of radical changes in our lifestyles.
- Changes in eating patterns
  - Increase in energy intake
  - Decreased biodiversity (phytonutrients)
  - Changes in food preparation and eating patterns
- Changes in physical activity
- Changes in work habits/labor
- Environmental stresses on tissues and detoxification systems
- Increased lifestyle stress (mental/emotional)
  - Loss of normal rhythms which permit restoration of body systems (social, sleep, seasons)

Progress?

What we have deemed as the “progress” that currently defines civilized Western society may actually be slowly destroying human physiology.
How does “Lifestyle” work?

Lifestyle Synergy: Key Principle

• Our bodies are designed to take the appropriate messages from our “lifestyle” and turn them into “health.” Since the most powerful remedy is the intrinsic healing mechanism within our bodies, therapies will work best when they are targeted toward triggering these mechanisms rather than circumventing them.

Vis medicatrix naturae

• Healing mechanism(s) are intrinsic to capacity of each living cell, organ and organism.

• Lifestyle medicine, ultimately, is building, restoring and leveraging this capacity!

• “Life” or “Vitality” was at one point, a part of every healing tradition...

“It is highly dishonorable for a reasonable soul to live in so divinely built a mansion as the body she resides in - altogether unacquainted with the exquisite structure of it.” - Robert Boyle (1627-91)
A Steady State?

Is this a good model to describe The systems managing our body?

Rhythmic fluctuations...

Lifestyle Synergy: Key Principle

- Lifestyle medicine is not about doing the same exact thing every day but about understanding the rhythms and responses that our body uses to keep us healthy. When our actions mirror this understanding, we create a synergistic force that unlocks the healing power within each cell. We must work with our body, not impose a solution upon it.
To Bend Without Breaking

- Physiological Resilience: The ability of nearly every important function in the body to be pushed away from its ideal function and still return to normal function.

Loss of Physiological Resilience

- Lifestyle Synergy: Key Principle
  - Our bodies are designed with a series of overlapping buffering mechanisms that give us an amazing resilience against poor lifestyle decisions. Every lifestyle decision we make strengthens or weakens the capacity of this system a little bit at a time. It may take months, years, or even decades to notice, but both good and bad decisions have a cumulative effect on our ability to create a healthy outcome.
The Metabolic Continuum

Metabolic Reserve
- The long-term (reserve) capacity to rebuild our resilience when it is challenged.

Fat Mass- The Ultimate Buffer
- Nearly every metabolic buffering system uses fat mass as a buffer against immediate crisis
  - Energy imbalance
  - Hormone imbalance
  - Toxin dilution
  - Stress and emotional
  - Sleep imbalances
When beta cells lose their reserve

- Nearly all of those who develop diabetes have insulin resistance.
- Not all who have insulin resistance will develop diabetes.
- Beta cell function is critical in determining which persons will develop diabetes (lose their control of blood glucose).

Lifestyle Synergy: Key Principle

- Building metabolic reserve through Lifestyle Synergy expands and even strengthens the buffers we will later rely upon to maintain our health. While it's never too late to begin building metabolic reserve, the earlier you start, the better.
Definition of Chronic Disease:

- The depletion of an organ system's metabolic reserve, such that it cannot no longer buffer the consequences of poor signals, eventually decreasing both the structure and function of the organ system.
- Most chronic disease mechanisms are identical (inflammation, oxidative damage, etc.).
- They differ by which tissue is the weakest link.

The Burden and Causes of Chronic Disease

[Graph showing leading and actual causes of death in the United States.]

Changing the outcome one signal at a time
Different Genomes-w/Similar Function

- **Human**
  - 46 Chromosomes (23 pairs)
  - 3.2 Billion base pairs of DNA
- **Mouse**
  - 40 Chromosomes (20 pairs)
  - 2.7 Billion base pairs of DNA
- **Frog (species differ)**
  - 26 Chromosomes (13 pairs)
  - 1.7 Billion base pairs
- **Rainbow Trout**
  - 58-64 Chromosomes (28-32 pairs)
  - 2.4 Billion base pairs of DNA

Liver Cells

Identical DNA- Different Functions

- 23 Pairs (46 total)
- Only 1 of each chromosome in germ cells

Chromosome as Cookbooks

- Each chromosome has thousands of different DNA sequences (genes) which have the potential to be expressed.
- Just like a cookbook of thousands of recipes, each with the potential to become supper.
Genes are the recipes of life!

- When a gene is “turned on” a RNA copy is made and is “translated” into a protein.
- Why are some genes turned on and some turned off?

Turning Genes on or off!

1. Find the right Chromosome
2. Unpack Chromatin fiber
3. Expose DNA between histones
4. Bind the promoter region of the gene and make mRNA

The Signals of Life

- Corn Syrup-Fructose
- Sunlight
- Sleep Time
- Sitting
- Noises
- Exercise
- Water
- Vitamin D
- Bisphenol-A
- Broccoli
- Stress
- Anger & Guilt
- Love
- Resveratrol
- Walking
- Skipping Meals
The "Lifestyle" signals creating oxygen radicals

ORAC value of some foods:

- ORAC measures chemical antioxidant capacity
- Measures one aspect of the oxygen radical protection of plants or foods
Nutrigenomics: How Nutrients Signal Gene Expression

Basic Inflammatory Signaling

NRF-2 – pathway to cellular "stress management"
Known Nrf2 modulators

Pleomorphic effects of NRF2

Stilbene Derivatives

- Pterostilbene
- Resveratrol
Sirtuin 1-related effects

Vitamin D: One Signal—many effects!
- Vitamin D (VD) triggers gene expression by binding to its receptor (VDR) and together they recruit the machinery to activate genes with a Vitamin D response element (VDRE) gene sequence.

Probiotics and dendritic cell signaling
Can the dose of probiotic change the immunological signal?

Changes in Dendritic cell gene expression

qRT-PCR analysis of target genes expression in DCs after contact with the probiotic Lcr35.
Maturation of human monocytes after exposure to a range of *L. rhamnosus* Lcr35 concentrations.

- A: Markers of high density surface molecules
- B: Markers of low density surface molecules

Everything is a signal to our cells

- Corn Syrup-Fructose
- Stress
- Broccoli
- Sunlight
- Sitting
- Noises
- Exercise
- Water
- Vitamin D
-爱
- Anger & Guilt
- Resveratrol
- Walking
- EMFs
- Bisphenol-A
- Skipping Meals

Epigenetics

- Choices you make everyday determine your gene expression
- Some of these choices put "tags" on your DNA
- Some of these tags can be passed along to future generations
Epigenetics- Bookmarks in your Cookbook

- Like bookmarks along our DNA, chemical tags can mark favorite gene “recipes”
- Or like syrup sticking two pages together-prevent us from even seeing those gene recipes

The Agouti Mouse Model

- These mice are genetically identical
- Both susceptible to obesity, diabetes and a yellow coat color
- The susceptible gene is turned off through methylation (epigenetics) by feeding supplements to the mother.
The Pima Indians

- US Pimas: “Westernized” after WWII
- Adopted American Diet and habits

- Mexican Pimas: Genetically identical
- Maintained historical diet and habits

Nurture Trumping Nature

Your DNA is not your Destiny

- Your genes determine only your health potential - they don’t dictate its outcome
- Gene expression (not sequence) determines most cell functions
- Thousands of signals you provide every day influence your gene expression and health
- Genetic “tags” (epigenetics) can follow influence multiple generations
- Healthy Choices can improve or even trump a poor genetic background.
Lifestyle Synergy: Key Principle

• We set our lifestyle habits long before those habits influence our health, causing us to miss the "cause and effect" of those decisions. The habit becomes fixed- making it difficult to break.

• Our body is forced to compensate (adapt), developing biological coping mechanisms- while our DNA becomes tagged with epigenetic markers; both of which prevents easy reversal of the habit's consequences- even when they are eventually stopped.

Leveraging Lifestyle as Intervention

• The Lifestyle Synergy Model

How to influence outcomes based on Risk Management

RISK TRAJECTORY
A single Point- Doesn’t Predict the outcome!

Lifestyle Medicine
It Must Be Personal before it can be Personalized!
(For Both Patient and Clinician)

The Power of the Patient
Arthur Boorman's Story
Basic Principles of the LS Model

• You can’t obtain good health by overdoing one sphere of Intervention while neglecting the others. The sum is greater than the parts!

Basic Principles of the LS Model

• When it comes to prevention, the earlier the better; but it’s never too late to leverage lifestyle intervention.

Basic Principles of the LS Model

• A healthy lifestyle pattern reduces ALL chronic disease risk. The side effect of Lifestyle Synergy is more health.
Basic Principles of the LS Model

- Give lifestyle intervention enough time to work - you didn't get here overnight.

- Everything in moderation, even lifestyle intervention. You can get too much of a good thing.

- Find a companion for your journey; life is meant to be shared. With Lifestyle medicine there is strength in numbers.
A Different Approach

Conventional  Lifestyle

Patients most often are alone in their healing journey
Patients often join groups to facilitate their health journey

Prevention-Intervention Hierarchy

All Therapies, especially dietary supplements, Begin with Lifestyle!

The Prevention to Intervention Hierarchy
Everyone has a physician inside him or her; we just have to help it in its work. The natural healing force within each one of us is the greatest force in getting well.

Lifestyle Medicine is Real Medicine

Relax- We are Done!