



Introduction to Functional Medicine

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Functional Medicine is a personalized, systems-oriented model that empowers patients and practitioners to achieve the highest expression of health by working in collaboration to address the underlying causes of disease. It is an evolution in the practice of medicine that better addresses the healthcare needs of the 21st century. By shifting the traditional disease-centered focus of medical practice to a more patient-centered approach, Functional Medicine addresses the whole person, not just an isolated set of symptoms. Functional Medicine practitioners spend time with their patients, listening to their histories and looking at the interactions among genetic, environmental, and lifestyle factors that can influence long-term health and complex, chronic disease. In this way, Functional Medicine supports the unique expression of health and vitality for each individual.

“Disease is neither the starting point nor the end point of illness. It is a pathological process that may not be discovered until decades after the identification of an illness.”¹ This insight has been the impetus for many of the new approaches to disease prevention and treatment that have emerged over the last 30–40 years. Most of us—scientists and physicians alike—would rather not wait until we have a diagnosable disease to address the underlying problems that, over time, cause the signs and symptoms that influence the development of illness and disease.

A major premise of Functional Medicine is that, using science, clinical wisdom, and innovative tools, we can identify many of the underlying causes of chronic disease and intervene to remediate the dysfunctions, both before and after frank disease is present. People may wonder (quite reasonably) why preventing and treating chronic disease effectively requires something different than is usually available in our very expensive healthcare system.² Perhaps the most urgent reason is that a rapidly spreading epidemic of chronic disease has compromised the effectiveness of our healthcare system and threatens to bankrupt both national and global economies. Alarming projections suggest future generations may have shorter, less healthy lives if current trends continue unchecked.³ Our current healthcare model fails to confront both the causes of and solutions for chronic disease and must be replaced with a model of comprehensive, personalized care geared to effectively treating and reversing this escalating crisis.

Consider the Facts

Over the last century, there has been a dramatic shift in prevalence from acute to chronic diseases. By 2020, worldwide deaths from chronic disease are projected to total more than twice the number of deaths from infectious disease (50 million vs. 20 million). It is estimated that more than half of all Americans suffer from one or more chronic diseases,⁴ and that the 8 million Medicare beneficiaries who have five or more chronic conditions accounted for over two-thirds of the program’s \$302 billion in spending in 2004.⁵

Of total healthcare costs in the United States, more than 75% is due to chronic conditions.⁶ In 2008, the U.S. spent 16.2% of its GDP (\$2.3 trillion) on health care.⁷ This exceeded the **combined** federal expenditures for national defense, homeland security, education, and welfare. By 2023, if we don’t change how we confront this challenge, **annual** healthcare costs in the U.S. will rise to over \$4 trillion,^{8,9} the equivalent—in a single year—of four Iraq wars, making the cost of care using the current model economically unsustainable. If our health outcomes were commensurate with such costs, we might decide they were worth it. Unfortunately, the U.S. spends twice the median per-capita costs of other industrialized countries, as calculated by the Organization for Economic Cooperation and Development (OECD),¹⁰ but has extraordinarily poor outcomes for such a massive investment.¹¹

In the United States, about 133 million Americans—nearly 1 in 2 adults—live with at least one chronic illness, and chronic diseases already cause 7 in 10 deaths each year:

- **Heart disease:** 81 million people¹²
- **Cancer:** 11 million people¹³
- **Depression:** More than 1 in 20 Americans, 12+ years old¹⁴
- **Diabetes:** “In the past 20 years [in the U.S.], the prevalence of diabetes has doubled and will do so again in the next 16 years.”¹⁵ “One in every 3 children born [in the U.S.] today will develop diabetes during his/her lifetime.”¹⁶

Chronic Disease is a Global Problem

The challenge of chronic disease falls on all nations today, regardless of national wealth or health system models. “By 2020, it is predicted that **noncommunicable diseases** will account for 80% of the **global burden** of disease, causing 7 out of every 10 deaths in developing countries, compared with less than half today.”¹⁷ From 1983 to 2009, the number of people in the world with diabetes increased seven-fold, from 35 million to 225 million.¹⁸ In 2010, 92 million diabetics and 148 million pre-diabetics were identified in China alone.¹⁹ The World Health Organization reports that, “Chronic diseases are the leading cause of death and disease burden worldwide. Some 45% of chronic disease deaths and 86% of the burden of chronic diseases occur in people under 70 years of age.”²⁰ “[W]ith the exception of the African Region, NCD [noncommunicable disease] mortality exceeds that of communicable, maternal, perinatal, and nutritional conditions combined. For men in the European Region, deaths from NCDs are estimated to be 13 times higher than these other causes combined, and for men in the Western Pacific Region they are estimated to be eight times higher.”²¹

Outdated Clinical Models

Despite notable advances in treating and preventing infectious disease and trauma, the acute-care model that dominated 20th century medicine is not effective in treating and preventing chronic disease.²² **The primary driver of chronic disease is the interaction among genes, activities of daily living (lifestyle), and the environment.**^{23,24,25} Adopting a **new operating system** for 21st century medicine requires that we:

- Recognize and validate more appropriate and successful clinical models
- Re-shape the education and clinical practices of health professionals to help them achieve proficiency in the assessment, treatment, and prevention of chronic disease
- Reimburse equitably for lifestyle medicine and expanded preventive strategies, acknowledging that the greatest health threats now arise from how we live, work, eat, play, and move

Given the prevailing evidence, there can be little doubt that 21st century health care demands a different approach than the acute-care, specialist-driven model that emerged during the 20th century. During the last 100 years, such significant advances were made in conquering or controlling scourges such as tuberculosis and pneumonia, and in the treatment of trauma, that life expectancy and quality of life both increased dramatically. However, over the last 50 years, other influences (see Figure 1) have fueled the current epidemic of chronic disease,^{26,27} including heart disease, diabetes, cancer, asthma, multiple sclerosis, Alzheimer’s and other dementias, stroke, irritable bowel syndrome (IBS), and inflammatory bowel disease (IBD), to name some of the most common. Assessment, treatment, and prevention of these chronic conditions are not well served by an acute-care, organ-specialty medical model.²⁸

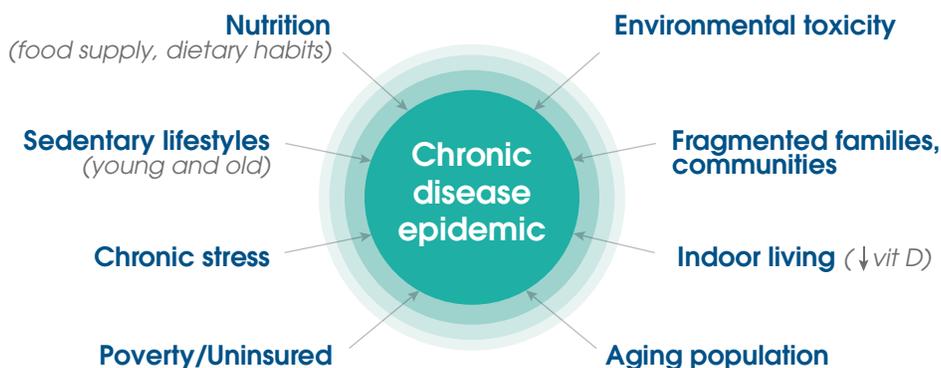


Figure 1. Major Influences Contributing to the Epidemic of Chronic Disease

Why doesn't the old model work? Because chronic disease is a food- and lifestyle-driven, environment- and genetics-influenced phenomenon. It won't be conquered with drugs and surgery, however helpful those tools may be in managing acute signs and symptoms. It won't be conquered by adding new or unconventional tools (e.g., botanical medicine, acupuncture) to a failing model. It won't be conquered by pharmacogenomics (although advances in that discipline should help reduce deaths from appropriately prescribed medication—estimated to be the 4th leading cause of hospital deaths²⁹). It can be conquered by integrating what we know about how the human body works with individualized, patient-centered, science-based care that addresses the causes of complex, chronic disease, which are rooted in lifestyle choices, environmental exposures, and genetic influences.

The transformation of 21st century medicine from the prevailing acute-care model to a far more effective chronic-disease model will succeed only if we attack the underlying drivers of the epidemic—the complex, lifelong interactions among lifestyle, environment, and genetics.³⁰ In order to be successful, clinicians must pay much closer attention to etiology; taxonomy alone—naming the disease—and prescribing drugs or surgery are no longer sufficient strategies. Achieving a systems-oriented approach to health care requires new concepts, tools, and interventions. We must integrate the science of medicine with the art of clinical practice:

- Take what we know from clinical research about the causes of complex, chronic disease, and change what we do in patient care
- Learn to restore balance in the complex adaptive system that is a human being
- Develop effective therapeutic partnerships between practitioners and patients
- Identify the causes of and remedies for each individual's unique expression of chronic disease

Functional Medicine exemplifies just the kind of systems-oriented, personalized medicine that is needed to transform clinical practice. The Functional Medicine model of comprehensive care and primary prevention for complex, chronic illnesses is grounded in both science (evidence about common underlying mechanisms and pathways of disease; evidence about the contributions of environmental and lifestyle factors to disease) and art (the healing partnership and the search for insight in the therapeutic encounter).

What is Functional Medicine?

Functional Medicine is a personalized, systems-oriented model that empowers patients and practitioners to achieve the highest expression of health by working in collaboration to address the underlying causes of disease. By actively listening to a patient's history and mapping their personal story to a timeline, the Functional Medicine provider seeks to identify predisposing factors, triggers, and events that shift the set-point from health to illness. This process is deeply affected by genomic predispositions, dietary patterns, nutritional influences, and foundational lifestyle behaviors. By changing the disease-centered focus of medical practice to a patient-centered approach, Functional Medicine addresses the whole person, not just an isolated set of symptoms. When a patient's clinical history, signs, symptoms, and story are viewed through the Functional Medicine matrix, the systems view illuminates the root causes of illness and practitioners can support the healing process. As diet and lifestyle are major contributors to chronic diseases, a personalized approach to nutrition, provided through therapeutic dietary interventions, is considered to be essential. A food-first approach, with focused therapeutic interventions that address underlying physiological concerns, provides the foundational plan to be implemented by the practitioner.

Functional Medicine conceptualizes health and illness as part of a continuum in which all components of the human biological system interact dynamically with the environment, producing patterns and effects that change over time. Functional Medicine helps clinicians identify and ameliorate dysfunctions in the physiology and biochemistry of the human body as a primary method of improving patient health. Functional Medicine is often described as the clinical application of systems biology.

In this model of practice, chronic disease is almost always preceded by a period of declining function in one or more of the body's systems. Returning patients to health requires reversing (or substantially improving) the specific dysfunctions that have contributed to the disease state. Those dysfunctions are, for each of us, the result of lifelong interactions among our environmental exposures, our lifestyle influences, and our genetic predispositions. Each patient, therefore, represents a unique, complex, and interwoven set of influences on intrinsic functionality that have set the stage for the development of disease or the maintenance of health.

To manage the complexity inherent in this approach, Functional Medicine has adopted practical models for obtaining and evaluating clinical information that leads to individualized, patient-centered therapies. Functional Medicine concepts, practices, and tools have evolved considerably over a thirty-year period, reflecting the dramatic growth in the evidence base concerning the key common pathways to disease (e.g., inflammation, GI dysfunction, oxidative stress), the role of diet, stress, and physical activity, and the effects of environmental degradation (air, water, soil) on health.

In addition, new concepts that emerged from the prolific research literature are altering our view of disease, patients, and all types of health care, including Functional Medicine:

- **Emergence:** How genes are translated into patterns of health and disease
- **Exposome:** How internal metabolic factors and environment influence gene expression
- **Epigenetics:** The study of heritable changes in gene expression or cellular phenotype caused by mechanisms other than changes in the underlying DNA sequence
- **Nutritional genomics or nutrigenomics:** How different foods may interact with specific genes to increase the risk of common chronic diseases such as type 2 diabetes, obesity, heart disease, stroke, and certain cancers
- **Pharmacogenomics:** Prediction of drug response and clinical outcomes, reduction in adverse events, and selection and dosing of drugs based on genotype

- **Proteomics:** The study of the proteome, the complete set of proteins produced by a species, using the technologies of large-scale protein separation and identification
- **Metabolomics or metabonomics:** The study of metabolic responses to drugs, environmental changes, and diseases—an extension of genomics (concerned with DNA) and proteomics (concerned with proteins)
- **Sociomics:** How social networks influence health and disease

Elements of Functional Medicine

The knowledge base—or “footprint”—of Functional Medicine is shaped by seven core principles:

- Acknowledging the **biochemical individuality** of each human being, based on concepts of genetic and environmental uniqueness
- Incorporating a **patient-centered** rather than a disease-centered approach to treatment
- Seeking a **dynamic balance** among the internal and external factors in a patient’s body, mind, and spirit
- Addressing the **web-like** interconnections of internal physiological factors
- Identifying **health as a positive vitality**—not merely the absence of disease—and emphasizing those factors that encourage a vigorous physiology
- **Promoting organ reserve** as a means of enhancing the health span, not just the life span, of each patient
- Functional Medicine is a **science-using profession**

These foundational principles of how the human organism functions—and how its systems communicate and interact—are essential to the process of linking ideas about multifactorial causation with the perceptible effects we call disease or dysfunction. To assist clinicians in understanding and applying this information, Functional Medicine has adapted, organized, and labeled a set of seven biological systems in which core clinical imbalances are found; these function as the intellectual bridge between the rich basic science literature concerning physiological mechanisms of disease (first two years of medical training) and the clinical studies, clinical experience, and clinical diagnoses of the second two years of medical training. The core clinical imbalances serve to marry the mechanisms of disease with the manifestations and diagnoses of disease. Many common underlying pathways of disease are reflected in a few basic clinical imbalances:

- **Assimilation:** digestion, absorption, microbiota/GI, respiration
- **Defense and repair:** immune, inflammation, infection/microbiota
- **Energy:** energy regulation, mitochondrial function
- **Biotransformation and elimination:** toxicity, detoxification
- **Transport:** cardiovascular and lymphatic systems
- **Communication:** endocrine, neurotransmitters, immune messengers
- **Structural integrity:** subcellular membranes to musculoskeletal integrity

Using this construct, it is possible to see that one disease/condition may have multiple causes (i.e., multiple clinical imbalances), just as one fundamental imbalance may be at the root of many seemingly disparate conditions (see Figure 2 on following page).

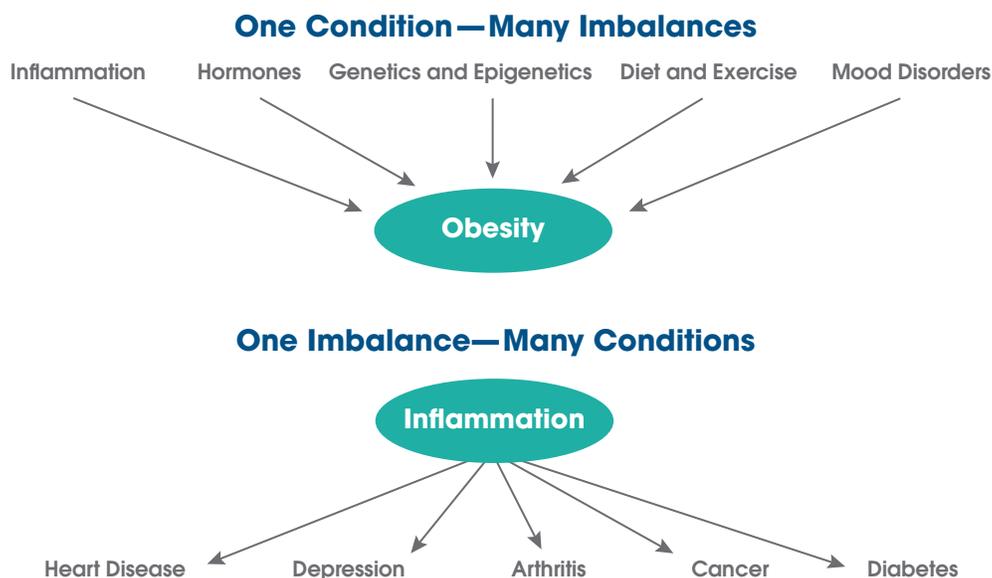


Figure 2. Core Clinical Imbalances—Multiple Influences

The most important precept to remember about Functional Medicine is that restoring balance—in the patient’s environmental inputs and in the body’s fundamental physiological processes—is the key to restoring health.

Constructing the Model and Putting it into Practice

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, interacting 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.

Distilling the data from an expanded history, physical exam, and laboratory tests into a narrative story line that includes antecedents, triggers, and mediators^a of disease can be challenging. Key to developing a thorough narrative is organizing the patient’s story according to the seven clinical imbalances, as shown on the Functional Medicine Matrix Form (Figure 3). Using this Matrix, Functional Medicine practitioners evaluate and map the patient’s history, signs and symptoms, physical exam findings, and laboratory results in each of the seven functional systems to identify the underlying clinical imbalances (disturbances in physiology and biochemistry). The patient’s lifestyle influences are entered across the bottom of the matrix, and the antecedents, triggers, and mediators of disease/dysfunction are entered in the upper left corner. The centrality of the patient’s mind, spirit, and emotions, with which all other elements interact, is clearly shown in the figure. When the matrix is complete, the clinician has—on a single form—all the key elements of the patient’s story.

^aAntecedents are factors, genetic or acquired, that predispose to illness; triggers are factors that provoke the symptoms and signs of illness; and mediators are factors, biochemical or psychosocial, that contribute to pathological changes and dysfunctional responses. Understanding the antecedents, triggers, and mediators that underlie illness or dysfunction in each patient permits therapy to be targeted to the needs of the individual.” (Galland L. Patient-centered care: antecedents, triggers, and mediators. *Altern Ther Health Med*. 2006;12(4):62-70.)

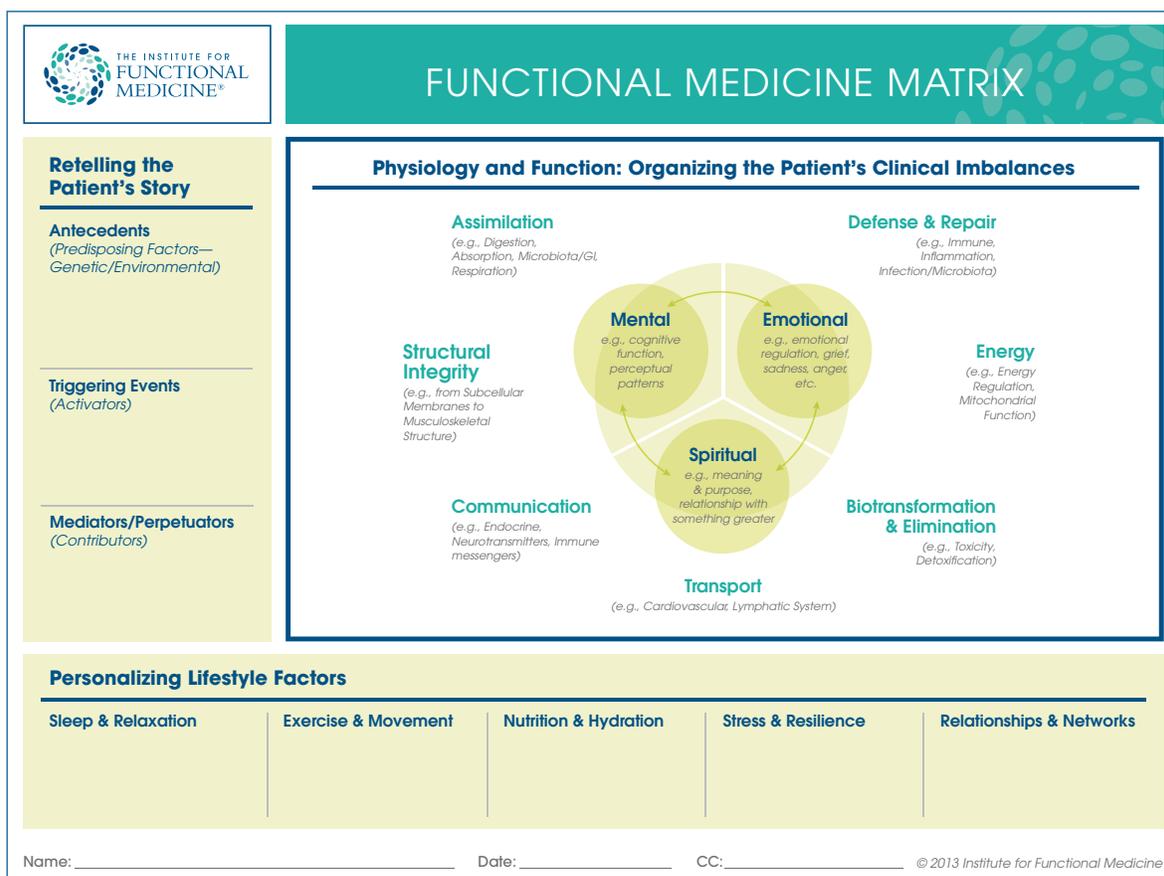


Figure 3. The Functional Medicine Matrix

Within this single, complex figure the most important elements of Functional Medicine can be seen:

- Identifying each patient's antecedents, triggers, and mediators of disease and dysfunction
- Discovering the factors in the patient's lifestyle and environment that influence the expression of health or disease
- Applying all the data collected about a patient to a matrix of biological systems, within which disturbances in function originate and are expressed
- Integrating all this information to create a comprehensive picture of what is causing the patient's problems, where they are originating, what has influenced their development, and—as a result of this critical analysis—where to intervene to begin reversing the disease process

Thus, the Matrix form helps organize and prioritize information, and also clarifies where further investigation is needed. For example, indicators of inflammation on the matrix might lead the clinician to request tests for specific inflammatory markers (such as hsCRP, interleukin levels, and/or homocysteine). Essential fatty acid levels, methylation pathway abnormalities, and organic acid metabolites help determine adequacy of dietary and nutrient intakes. Markers of detoxification (glucuronidation and sulfation, cytochrome P450 enzyme heterogeneity) can determine functional capacity for molecular biotransformation. Neurotransmitters and their metabolites (vanilmandelate, homo vanillate, 5-hydroxyindoleacetate, quinolinate) and hormone cascades (gonadal and adrenal) have obvious utility in exploring messenger molecule balance. CT scans, MRIs, or plain x-rays extend our view

of the patient's structural dysfunctions. The use of bone scans, DEXA scans, or bone reabsorption markers, can be useful in further exploring the web-like interactions of the matrix. Technologies such as functional MRIs, SPECT, or PET scans offer more comprehensive assessment of metabolic function within organ systems. It is the process of completing a comprehensive history and physical and then charting these findings on the matrix that best directs the choice of laboratory work and helps to identify successful treatments.

Using all the information obtained from patient questionnaires and the initial interview, Functional Medicine practitioners plot what they know about the patient's history on a specially designed Timeline—a device that helps to clarify what preceded a decline in function and what factors in the patient's history may still be influencing his/her health today. Next, the Functional Medicine practitioner utilizes a system of sequencing clinical activity (called GOTOIT) that describes both the process of care and the phases of care. After a comprehensive assessment has been made, and initial laboratory results have been obtained, the GOTOIT system helps the Functional Medicine practitioner develop a treatment plan that focuses on the areas where the greatest leverage can be found—those sections of the matrix which appear to have the largest concentration of dysfunctions and which are connected to the most important of the patient's signs and symptoms.

A therapeutic plan may involve one or more of a broad range of therapies, including dietary interventions (e.g., elimination diet, anti-inflammation diet, low glycemic-index diet), nutraceuticals (e.g., vitamins, minerals, essential fatty acids, botanicals), lifestyle changes (e.g., improving sleep quality/quantity, increasing physical activity, decreasing stress and learning stress management techniques, quitting smoking), acupuncture, physical medicine (e.g., massage, manipulation), and counseling. Where the clinician does not have the requisite expertise in the prescribed therapy, the patient should be referred to a practitioner who does. Follow-up is done regularly and the patient's progress is tracked and evaluated.

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)^{33,34,35}; **botanicals**^{36,37,38}; **exercise**³⁹ (aerobics, strength training, flexibility); **stress management**⁴⁰; **detoxification**^{41,42,43}; **acupuncture**^{44,45,46}; **manual medicine** (massage, manipulation)^{47,48,49}; and **mind/body techniques**^{50,51,52} such as meditation, guided imagery, and biofeedback.

All of this work is done within the context of a therapeutic partnership. The practitioner engages the patient in a collaborative relationship, respecting the patient's role and knowledge of self, and ensuring that the patient learns to take responsibility for his/her own choices and for complying with the recommended interventions. Learning to assess a patient's readiness to change and then providing the necessary guidance, training, and support are just as important as ordering the right lab tests and prescribing the right therapies.

To summarize, the practice of Functional Medicine involves four essential components: (1) eliciting the **patient's complete story** during the Functional Medicine intake; (2) identifying and addressing the challenges of the patient's **modifiable lifestyle factors and environmental exposures**; (3) organizing the patient's clinical imbalances by underlying causes of disease in a **systems biology matrix framework** and using the timeline and GOTOIT system to develop a comprehensive assessment and plan, and (4) establishing an **effective therapeutic partnership** between practitioner and patient.

Functional Medicine and Integrated Health Care and Integrative Medicine

Even using the Functional Medicine model that has been reviewed here, no single practitioner—and no single discipline—can cover all the viable therapeutic options. Interventions will differ by training, licensure, specialty focus, and even by beliefs and ethnic heritage. However, all healthcare disciplines (and all medical specialties) can—to the degree allowed by their training and licensure—use a Functional Medicine approach, including integrating the matrix as a basic template for organizing and coupling knowledge and data. Functional Medicine can provide a common language and a unified model to facilitate integrated care. Regardless of which discipline the primary care provider has been trained in, developing a network of capable, collaborative clinicians with whom to co-manage challenging patients and to whom referrals can be made for therapies outside the primary clinician’s own expertise will enrich patient care and strengthen the clinician-patient relationship.



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