

# **The Population-Based Medical Model Should No Longer Be Used as An Exclusive Model in Medicine**

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## **INTRODUCTION**

In this article, we will review the history of medical model development, examine the quality and reliability of medical knowledge existing when the functional approach was legally adopted by the U.S. Food and Drug and Cosmetic Act, enacted in 1938 and amended, and further indirectly promoted by U.S. patent law. This functional approach plays an important role in the formation of the population-based medical model (“the deduction model”).

Deduction model was primarily based on reductionism and dualism. Reductionism views the entire systems in terms of their individual, constituent parts and their interactions, and dualism views mind and body as two separate entities. Every medical study can be done by following deduction logic reasoning. After examining medical knowledge and later advances, we found that the validity of dualism and reductionism, as applied to chronic diseases, has been refuted by recent discoveries in neuron-sciences and cancer research.

We examine common research tools used in the deduction model including the population-based approach, randomization, double blinds experimental design, variable controlling method, statistical analysis, binary disease definitions, categorization method, etc. in light of the optimization approach used in the competing holistic model. On the basis of multiple ways analysis, we concluded that the deduction model is good only for studying strong and fast health properties or treatments, but introduce massive errors and inaccuracies making it unfit for studying weak and slow health properties or treatment effects. It tends to systematically fail to recognize weak and slow treatment benefits. We further find that the deduction model is primarily responsible for the inability to find cure for chronic diseases and cancer.

We urge medical researchers to consider the holistic model as the primary model for conquering chronic diseases and cancer. We also urge the U.S. Congress to amend the FD&C, patent law, tax law, and health regulations, and leaders of all nations to steer medical research to a right track. To find cure for chronic diseases, the holistic model with mind being included as an essential component for treating chronic and life-threatening health

problems must be used.

## **A. Adoption of The Deduction Medical Model**

In modern medicine (commonly known as western medicine or traditional medicine in Western nations), doctors and other healthcare professionals treat symptoms and diseases using drugs, radiation, or surgery by using what we call as a population-based model or deduction model.

The FD&C enacted in 1938 and amended subsequently, provides a legal definition for drug, which includes four separate definitions. The second and third definition is “(B) articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals; (C) articles (other than food) intended to affect the structure or any function of the body of man or other animals.” The first definition is “articles recognized in the official U.S. Pharmacopoeia, official Homoeopathic Pharmacopoeia, or official National Formulary. Only articles that meet the second definition would be qualified under the first definition. The last definition is a component for a drug which thus also includes this requirement. To meet the legal definition of a drug, an article must satisfy the second and third definition.

Before the FD&C was enacted, the holistic model, which treats the body and mind as an integrated whole, was well known. Every system of medicine throughout the world treated the mind and body as a whole. Using natural products to cure diseases were widely accepted practices throughout the world. Herbs were used in China for more than 4000 thousands of years. The holistic mind-body model is reflected in Emperor Nejin.

When the FD&C was enacted, medicine has been heavily influenced by reductionism and dualism. This is evidenced by the functional definition used in the FD&C. This functional definition is based on methodological reductionism, attempting explanation of entire systems in terms of their individual, constituent parts and their interactions. Descartes (1596-1650) saw the man comprising two separate parts: mind and body. Per this theory, the body could affect the mind, but mind simply could not affect the body. This Reductionism school of thought considered the mind as merely part of the body “machine.”

Medicine was influenced by Rene Descartes’ reductionism and dualism. Those two theories allow doctors to focus on diseases but not patients (so the model may also be referred as diseased-focused model). The reduction approach turns any complex health problem into relevant body functions and allows for use of deductive reasoning in medical research. In deductive reasoning, if all premises are clear and true, and the rules of deductive logic are followed, the conclusion reached is necessarily true. Thus, the medical model can be characterized by function reduction, deduction reasoning,

mind separation, and disease-focused treatment.

Under reductionism and dualism, any health problem can be simplified by ignoring genetics differences, environmental influences, organ-organ interactions, emotions and mind, etc. Any disease, such as alcoholic liver, swollen spleen, high blood pressure and even cancer, can be studied like a simple property like body size. Even a biological function can be studied by examining the function without paying attention to differences in people. It is natural to assume that any treatment is good for all people with the same disease. It is inevitable to use population trials to study diseases. The deduction model requires conclusion in every medical study. Therefore, we will refer the medical model as the “deduction model” or “population-based model.”

The adoption of the deduction model was influenced by then new technologies such as microscopy, the stethoscope, the blood-pressure cuff, and refined surgical techniques. Those technologies allowed doctors to see the functions of the body as if mind were separated from the body and disease could be isolated from mind and body. The discovery of bacteria and later antibiotics further dispelled the role of mind, environment and culture. When the body is treated as a machine, curing a disease is same as identifying and fixing the parts with functional and structural faults.

When the legal definition in the FD&C is read in combination with the implied purpose of using drugs, one would find several presumptions: (1) diseases are caused by structural and functional changes in the body, (2) altering structures and functions of the body could cure diseases; (3) drugs are capable of altering structures and functions of the body, and (4) synthetic drugs and natural drugs are same.

The first implied presumption seems right because structural and functional changes can be found for a vast majority of diseases. Whether the second presumption is valid depends on how to alter structures. If a treatment can restore the body's structure and function to a health state, the disease could be cured. The third presumption is troublesome because whether mind controls structure and functions was not fully understood. If mind plays a role in controlling structures and functions, then administering drugs alone cannot cure diseases. The fourth presumption, that synthetic drugs and natural compounds are treated as same, seems to be fail, too.

The functional approach seems not intend to exclude the holistic model because the third definition of the FD&C could read on any articles which may affect diseases through mind. The definition may be used to prevent the FDA to exercise jurisdiction over old treatments. However, the FD&C plays an important role in separating mind from body and abandoning the holistic model. The functional approach is similar to that used to address physical systems such as cars. When any component in a car is damaged or its function is abnormal, the car can be restored by replacing the affected compo-

nent.

While the FD&C did not reject the holistic model literally, dualism has influenced every law in the U.S. The U.S. patent law excludes any invention directed to mind by several court doctrines such as abstract ideas, laws of nature, natural phenomena, mental processes, methods of organizing human activity, etc. [See *Alice Corp. v. CLS Bank International*, 573 U.S. 208, 134 S. Ct. 2347 (2014)]. Any drug, treatment, or device is ineligible for a patent if its patent claim is directed to mind, emotion, mental steps, or physical activities. Due to lack of financial rewards, few studies have ever been directed to understanding the roles of mind for a bulk part of medical histories. Due to lack financial rewards, few serious studies were ever been done to understand how exercises modulate mind. Federal tax law recognizes only drugs and treatments meeting the FD&C definitions as qualified medical treatments. Thus, the U.S. quickly established an environment for abandoning the holistic model.

## **B. Medicinal Landscape Created by the Deduction Model**

We will consider how the deduction model departs from the old holistic model, and how it acquires necessary research tools.

We present the oldest concepts in old medicine. The health of a life system such as human beings depends on the balance of all biological processes and cellular activities, the balance among all body parts and organs, and the harmony between the physical part and the spiritual part. Under the holistic model, a healthy state can be achieved only by focusing on the balances within an individual person. For energy metabolism, what is important is that a perfect dynamic balance between glucose intake and its consumption. No more is consumed and no more is stored in wrong places. Absolute numbers such as glucose levels, metabolites concentrations, activities of enzymes, or white blood cell counts, the immune cell count, etc. are not controlling. The is important is the overall balance, and mind and body are in harmony.

The deduction model promoted by U.S. laws has played a critical role in establishing the current medical landscape. This law recognizes the idea of using drugs to correct the structures and functions of the body. It can focus on components or parts. It implies that if a disease is on the liver, the focus is on the liver and there is no need to pay attention to the rest part of the body and mind. Heart disease can be treated without paying attention to the liver and kidneys. The deduction model allows researchers to select any factors in a drug study, control variables in any manner, and ignore variables that are inconvenient or unknown. It allows researchers to ignore variable interactions in studies. It discourages researchers from using mind as part of

a treatment. It encourages researchers to use oversimplified animal models and even tissue cell cultures to understand disease mechanisms.

The deduction model allows for focusing on important part in the body. It is natural to reduce variables in studies. It is natural to extend the idea of treating all machine units in the same way to human persons. If a drug works on a person, it must work on other persons by presumption (even the chance is less than 10%) and all persons in the population. This notion gained acceptance even though Mendel's Laws of Inheritance were understood in 1900 because its implications were poorly understood in medicine.

The deduction model is responsible for the common research practices such as selecting a single variable for study, double-blinds experimental design, randomization of test subjects, variables controlled experimental design, objective diagnosis methods, evidence-based approach, and use of statistical methods. Those research tools rely on several data manipulation methods including converting continuous health properties into a binary scale, categorizing health concepts, and using binary disease definitions, etc. Medicine slowly establishes a legal framework as it stands today and have never examined how those tools impair medical merits and its ability to find cures.

Due to the influences of dualism, medicine has formed a convention that mind must not be the part of any cure and nor in drug trials. Medicine slowly become an art which eliminates any distinction between the highest form of life and a physical object. Medicine pays little attention to mind and fails to direct enough resources to studying the roles of mind in treating diseases a most of its histories. It is well reflected in how medicine approaches the Central Nervous System. For a very long time, medicine focuses primarily on motor functions and sensory functions. Even motivation to study is based on perceived functions such as motions and sensory functions. Dualism profoundly influenced how medical research projects are selected and how diseases are treated.

The functional definition used in the FD&A act reflects an unwarranted extension of drugs. In the prior human history, humans could not synthesize compounds and drugs were all from natural sources. Without understanding the big differences between natural compounds and man-made compounds, the drug definition was automatically extended to man-made compounds. Even more strangely, due to the discrimination by patent laws, man made drugs become preferred drugs. One big problem is found that man-made drugs have never worked as selection pressure in evolution and must infringe a large number of gene-encoded proteins and metabolites.

The success of medicine lies in treating acute diseases including bodily injures, infections, poisons, pains, and trauma, etc. In each of those cases, drugs are not used to restore impaired or lost balance in the body. Research methods cannot deliver required accuracy and reliability for

studying chronic diseases, and treatments cannot cure chronic diseases. Despite the obvious failure, the deduction model has achieved a status as the only medical model as scientific valid. Medicine's influences are further enhanced by the FDA regulations, its drugs approval protocols, massive research funds distributed by the U.S., state laws, and similar laws enacted in other nations.

Dualism was a theory by early philosophers when valid medical evidence was lacking, and its validity, as applied to chronic diseases, was never proved thereafter. The medical model based on this presumption has never been evaluated as a model. The validity of the research methods used under the deduction model has never been examined independently from teachings of the model. Its scientific validity is based on deduction reasoning with all key assumptions being treated as unfailing. Its acceptance in the world was promoted by political influences, fund distribution, and media influences. Its acceptance by citizens have been promoted by FD&C, patent laws, tax policies, health regulations, and financial influences. Its credibility is raised by commercial advocacy. Its unique status has been maintained by peer review practices which discourage research in mind and mind-body interactions.

Two fatal problems in reductionism as relevant to chronic diseases is that if a study selects only one or a few factors, it introduces excessive errors and inaccuracies for characterizing chronic diseases; and most medical findings acquired by using the reductionist approach cannot be probably combined in the human body in the treatment phase. Attempts to use multiple drugs with each being based on a population study will not be able to restore lost balance. This is at least one of the reasons no cure can be found for chronic diseases.

Systematic study of the deduction model is long overdue. If mind is a required component for curing chronic diseases and cancer, treatments developed under the deduction model will not yield cures, and will continue frustrating every human life in the world.

### **C. Model Flaws Revealed by Later-Developed Medical Discoveries**

We will evaluate the merit of the deduction model in following aspects: (1) the soundness of the presumption and their proof after its adoption; (2) the accuracy and reliability of medical knowledge necessary for establishing the deduction model as revealed by medical discoveries in neuron-science research and cancer research; (3) assessment of accuracy and reliability for the model, (4) overall performance of the model; (5) the extension of nature-made drugs to synthetic drugs.

#### **1. Core Presumption Is Unproved and Has Not Been Validated**

The core presumptions in the medical model include dualism, reduc-

tionism, and population approach. A flawed medical model was built on those wrong presumptions.

Revolved around the flawed medical model is the legal framework for medicine. This legal framework is loosely defined by U.S. FD&C, U.S. patent law, U.S. tax law, FDA regulations, states professional regulations, state health laws, etc. The large number of laws and regulations in this legal framework jointly recognizes and promote only the deduction medical model with an effect of barring the holistic model. This legal framework has fostered a very bad medical landscape with all chronic diseases as incurable diseases and with cancer being worldwide panic. All wrong presumptions together with related research tools have found their ways to medical theories, medical practices, human lifestyles, cultural understanding, science practices, human belief, etc.

Such a medical system is utilized by commercial interests to promote anti-evolution and useless but harmful medical options such as surgeries, radiation, and synthetic drugs. The dominance of surgeries, drugs and radiation is reflected in literature, culture, novels, movies, etc. Those options are viewed as only medicine in modern people's minds. The so-called medical merits are presumed to exist just like "irrefutable" legal presumptions. The core presumptions have been proved to be wrong by thousands of studies, and are responsible for ruining medicine. Legal framework, medical model, and deeply-rooted wrong medicinal practices cannot be corrected easily because people from both medicine and non-medicine fields have accepted them in their entire lives, are used to the same thinking to accept them, and lack vigilance against their problems.

The flawed medicine is aggressively defended at three levels: politicians and governmental officials protect the flawed legal framework by using federal and state laws, and federal and state enforcement agency, and controlling financial incentives such as policies on medical expenses. Medical researchers promote the flawed medical research model by conducting studies which can generate findings but no cures. Medical practicing professionals promote the practicing model by using established practicing guidelines and standards of care, all of which are from the same flawed medical models. Media journal editors rely on the legal framework, the medical model, and core presumptions to make their decisions. Most medical journals use article review system as a censorship system in evaluating medical studies. Such a medical system is capable of inflicting perpetual damages to human civilization even though the failure of medicine in finding cures for chronic diseases has been known for more than a century.

Overthrowing the legal presumptions do not require high level evidence because those presumptions were never proved before. Mind and body separation and functional reduction are based on theories in philosophy. We could not find any proof that those presumptions can be validly used

in medicine or any systematic validation studies from outside the medical field. Besides, justification of dualism in chronic diseases, if any, is most probably based on acquired from observing physical systems. In repairing physical devices such as cars, it is obvious to examine the structures and functions of damaged components. It is an unanswered question whether deduction model can be used to model the most complex form of life on the Planet. The two presumptions have never been validated to be correct after its adoption in medicine. To show this fact is enough to reject those presumptions. Moreover, we can find no proof that those assumptions in the reduction model are able to support required research accuracy for finding cures for chronic diseases. Population approach, which prevents using mind as part of cure, must be rejected if dualism is rejected.

We believe that using common sense to solve complex problems is unreliable, as reflected in human history. The miasma theory (the miasmatic theory) once held that diseases, such as cholera, chlamydia, or the Black Death were caused by a miasma (e.g., "pollution"), a noxious form of "bad air", also known as night air. In the 1st century BC, the Roman architectural writer Vitruvius described the potential effects of miasma. The theory remained popular in the Middle Ages. It influenced the world for almost two thousand years. It was not until 1876 that the theory was definitively overthrown [Koch, 2019].

Another human civilization tragedy is that "Xiandan" ("the longevity pills") hurt people for more than two thousand years. The pills, which were believed to promote longevity, were made from mercury, sulfur, carbon, tin, lead, copper, gold and silver. If people took the pills, they would not only fail to extend life, but be poisoned. Twelve Chinese emperors from Qin to Qing dynasty suffered mercury and lead poisoning from taking the pills. When a bad practice was favorably accepted by political powers and become a culture, it inflicted long-lasting harms to human civilization. The total deaths in the two thousand years is presumed to be substantial.

Miasma theory and the longevity pills abuse histories show how wrong medical practices resisted changes. In the long histories of using longevity pills, many articles vividly described how the pills killed people, yet people still were willing to ingest them in more than two thousand of years, people in the early twenties still used them in attempts to achieve "longevity".

When a medical model is accepted by laws or has permeated into every fiber of the medical culture, the ability to correct such a model problem does not lie in human knowledge advances. The wrong presumptions, the flawed deduction models and the legal framework are integrated as whole, no body can change it from any part. Thus, humans choose death without knowing how it can inflict harms to their follow human being and themselves. In chronic diseases, medicine has harmed several generations of people. If it is not corrected, it will continue affecting every person for years to



come.

## **2. No Support for the Deduction Model at Time of Adoption**

Dualism was accepted as core presumption by law. We will determine whether medicine had sufficiently reliable knowledge to guarantee an established medical model is error free.

We can show that medical science is an incremental sciences marked with abundant unknown, inaccuracies, and mistakes in its development history. Moreover, a century of medical research reveals abundant problems which can be traced to the core presumption. We will examine medical science development history in neuron-science, and cancer research as only examples.

We will show that neuron-science knowledge developed very slowly and just started picking up speed. Although neuron-science could be traced to 2700 B.C. when Shen Nung originated acupuncture or ca. 1700 B.C. when Edwin Smith wrote surgical record about the nervous system, its early knowledge was revolved around a few human functions that would be perceived directly. Due to the negative influences of dualism, the bulky knowledge of the CNS is about motor functions and sensory functions. Very little important knowledge was acquired for a long period of time. Due to the influences of dualism, medicine failed to focus on the CNS's role on biochemical, metabolic and cellular processes in a big part of its histories. Recent discoveries, which undermine the meaning of past neuroscience knowledge, include G-protein coupled receptors and their role in signal transduction (1994), prions as a new biological principle of infection (1997), signal transduction in the nervous system (2000), odorant receptors and the organization of the olfactory system (2004), the machinery regulating vesicle traffic (2013), and cells that constitute a positioning system in the brain (2014), discoveries of molecular mechanisms controlling the circadian rhythm (2017).

The year 2013 was just the start of the Human Brain Project and Advancing Innovative Neurotechnologies Initiative. Moreover, old knowledge is rapidly being updated. The privileged-immune site concept of the CNS has changed dramatically [Limanaqi et al, 2019]. The rapidly changing history shows that a medical model legally adopted from 1938 to post world war II is not entitled to the presumption of unfailing correctness. A fair inference is that people at that time lacked required knowledge and intuition to correctly set up unfailing presumptions for a perpetual medical landscape.

Now, we will show how the knowledge of cancer has changed since it being described in the first time and particularly since 1938. Cancer was once viewed as a “milk clot” in a mammary duct by German professor Wilhelm Fabry, then as “acidic lymph fluid” by the Dutch professor Francois de la Boe Sylvius, then as “slowly spreading poison” by Nicolaes Tulp. Nose

cancer was considered as having been caused by “tobacco snuff” (John Hill de in 1761). With the widespread use of the microscope in the 18th century, it was discovered that the “cancer poison” spreads from the primary tumor through the lymph nodes to other sites (“metastasis”). The cancer poison view was first formulated by the English surgeon Campbell De Morgan between 1871 and 1874. Later arriving molecular biological technologies enabled cancer researchers to find evidence that genetic mutations play an important role.

Then clonal selection and clonal expansion theory gained acceptance since 1976. Before this theory was accepted, surgeries had been used routinely on the basis of the assumption that cancer can be removed like a docked bullet; and chemotherapy started gaining acceptance after 1940. However, later developed knowledge shows that many categories of changes in large numbers are revolved around cancer: the immune system, growth signals, anti-growth signals, apoptosis, altered cell adhesive molecules, and blood vessels development and nerve networks. The later developed knowledge show that cancer cannot be removed like a foreign object or killed like invading microbes.

Since 1938, twenty four Nobel prizes have been awarded to discoveries in neuron-science with seven being awarded from 2000 and 2017.

### **3. Later Medical Discoveries Refute Dualism**

The deduction model is based on the presumption of separation of mind from the body. It is based on a wrong belief that mind cannot affect the body.

#### **(1) Mind and Body Connection**

We note that dualism as a philosophical concept is a different thing. We do not care that mind and body as to classes of concepts are separate.

We will discuss new evidence found in cancer research and Central Nervous System. Due to the influences of dualism, medicine failed to pay attention to the role of mind in cancer initiation, progression and metastasis for a bulk part of the medical history. Later, medicine has acquired mountains of evidence which is sufficient to reject dualism.

The emotional roles in causing cancer were not studied until later 1970's or the early 1980's [Cross, 1989]. Cited eighteen studies support a consensus that emotional expression may be directly implicated in cancer onset and progression. Social isolation was associated with higher tumor intratumoral norepinephrine among ovarian cancer patients. Psychosocial factors, such as social support and distress, are associated with changes in the cellular immune response, not only in peripheral blood, but also at the tumor level, and distress was related to lower Natural Killer Cells' cytotoxicity in tumor-infiltrating lymphocytes [Lutgendorf et al, 2005].

Growing amount of evidence from clinical studies shows that stress-

related processes impact pathways implicated in cancer progression, including immunoregulation, angiogenesis, and invasion [Lutgendorf, 2010]. A variety of stressors, including severe trauma, marital discord and bereavement, as well as depression and social isolation, have been associated with dysregulation or alterations in various neuroendocrine hormones, particularly catecholamines and cortisol [Moreno-Smith, 2010]. Contributions of systemic factors, such as stress hormones, to the crosstalk between tumor and stromal cells appear to be critical in modulating downstream signaling pathways with important implications for progression.

Chronic stress plays a role in cancer proliferation and affects immune system in a potentially detrimental way [Segerstrom et al, 2004]. Stress management can modify neuroendocrine dysregulation and immunologic functions that potentially influence tumor development and progression [McDonald, 2005].

Stress also plays a much bigger role in metastasis in orthotopic mouse model. Cancer diagnosis can elicit strong and varied emotions [Claire, 2016]. Stress-induced neuroendocrine activation induced more than 30-fold increase in metastasis to distant tissues including the lymph nodes and lungs. These effects were mediated by  $\beta$ -adrenergic signaling, which increased the infiltration of CD11b + F4/80 + macrophages into primary tumor and thereby induced a prometastatic gene expression signature accompanied by indications of M2 macrophage differentiation [Sloan et al, 2010]. As  $\beta$ -adrenergic signaling may affect cancer outcomes in ovarian cancer [Lutgendorf et al, 2011].

Stress is found to have overwhelming impacts on health. Recent research showed that acute and chronic psychological stress, related to low socio-economic status, can increase the risk of heart attack by increasing circulating levels of platelet-leukocyte aggregates [Brydon et al, 2006]. Several studies show it to be an emerging risk factor for heart disease [Sundquist et al, 2005; Nemeroff et al, 1998]. It was found that stress made medical students susceptible to infection, and short-term stress negatively affects wound healing by disrupting the production of proinflammatory cytokines [Kiecolt-Glaser et al, 1995]. More recently, they showed that stress increases the pro-inflammatory response in caretakers of Alzheimers' patients [Kiecolt-Glaser et al, 2003].

Recent discoveries allow us to see several sensitive regions in the brain by which mind and body interacts. The fundamental hypothalamic system was found to control metabolism, circulation and the immune system [Buijs et al, 2006]. The central and peripheral nervous systems play important roles in controlling liver cytochrome P450 (CYP) [Wójcikowski et al, 2011], hypothalamus, which lies at the intersection of the neuroendocrine and autonomic systems, is a central component in the regulation of glucose and blood pressure homeostasis [Han et al, 2016]. Hypothalamus lies at the

intersection of the neuroendocrine and autonomic systems. When a variety of stressors influence neuroendocrine, it is predictably affect the functions of hypothalamus, and thus the body.

It is well known that fears and emotional distress work through the amygdala. The amygdalae, part of the limbic system, performs a primary role in the processing of memory, decision-making and emotional responses (including fear, anxiety, and aggression). Neuroscientists have made significant findings concerning the amygdala in the human brain. A variety of data shows that the amygdala plays a substantial role in mental states, and is related to many psychological disorders. The amygdala sends projections to the hypothalamus, the dorsomedial thalamus, the thalamic reticular nucleus, the nuclei of the trigeminal nerve and the facial nerve, the ventral tegmental area, the locus coeruleus, and the laterodorsal tegmental nucleus [Best, 2004]. When the structure and function of the amygdala is changed by any emotional factors, it is anticipated to affect all of those connected regions of the brain.

Dualism was validated by observing fast and strong medical treatments such as pain killers, antibiotics, surgeries, and sedative drugs. A strong treatment has an overwhelming power to override the total effects that could be caused by individual persons. A study of a strong treatment does not require a high degree of accuracy. Antibiotics must kill bacteria in short times notwithstanding personal differences, and surgery must remove diseased tissues or foreign objects. In those cases, dualism remains to be valid as an approximation. However, most chronic diseases are caused by small departures from balanced biochemical and cellular processes, and mind can alter the balance by infinitesimal amounts in sufficiently long times. The disease state is resulted from the long term-impacts of small deviations. Deviations from balanced biochemical and cellular processes are often less than one tenth percent to a few percents. Past medical experts were unable to see such slow and weak changes, and reached an oversimplified conclusion that the body and mind are separated.

## (2) The Body Cannot Be Treated As Independent Parts.

Each human body is a system running at a nearly steady-stead condition with a very long lifespan. Most measurements of health properties do not have much utilities. By using the deduction model, medicine often treats individual organs and parts without paying sufficient attention to the whole body. This approach ignores the obvious fact that all biochemical and cellular processes are in balance within a person. Medicine has to use objective diagnostic data. Those data are defined by using population means plus or minus more than 50% deviations. In reality, a disease can arise when only a tiny imbalance exists.

While the deduction model helps medical researchers establish a great amount of knowledge in basic medical research in the past century, the

knowledge of the CNS role in controlling chronic diseases were nearly nonexistent when the deduction model was forming. The worst problem is reflected in how doctor treat patients: There is no way to apply hundreds to thousands of medical findings to any patient. A vast number of medical findings from the reduction model have no real utility in treatments. We note that multiple simplified factual findings can be applied independently to a machine in fixing its functions, but multiple findings concerning health properties cannot be applied to the human body. It is impossible that such findings can be applied separately to restore the balance.

No argument can be made that early political leaders and scientists could set up a flawless medical model that is immune from challenging. Given all obvious problems, dualism should be rejected as far as chronic diseases are concerned.

#### **D. Inaccuracies and Errors in Population-Based Medicine Under the Deduction Model**

We will prove how the deduction model introduced massive inaccuracies and errors into medical research findings and treatment methods. We first show that the functional approach and population approach is incompatible, and then show that the degree of required balance among biochemical processes in a person is not any less than the degree of matches among individual components in any complex machine.

##### **1. Mismatch of Health Properties Between a Population and a Person**

By focusing on functions, repairing an individual machine is like identifying and fixing fault parts. A workable method for repairing a machine can be used to fix another machine make of the same blueprint.

##### **(a) Population-Individual Mismatch Implied In Physical Systems**

Medicine makes a presumption that a treatment for one person must be useful to another person if the treatment is valid. Thus, the validity of a treatment can be established by proving the treatment's validity in a population of persons. Over years, it has become the golden standard in medicine.

To see flaws of the population-based model, we will use an auto repair model as an analog. The functional approach does not suggest that a method for repairing a car is good for repairing any other cars. The functional approach is expected to work in repairing physical objects such as cars, TV sets, computers, airplanes, etc. Our experiences tell us that the population approach is good for repairing only individual units made according to the same blueprint, but cannot be used to repair all units of different models and makes.

We could not find real examples of using population data to repair machines. We believe that functional approach is inherently incompatible to

the population approach. In auto repair, mechanics focus on structures and functions of individual cars, but never mind other cars. If cars were repaired by using a population approach like the one used in medicine, what could happen?

To explore an answer, we establish two hypothetical models to be used to show whether population-based research method is sound. In the first one, all cars made by Honda will be diagnosed and repaired by using the performance data which is acquired from all cars of Honda such as Accord, Civic, Honda Fit, Honda CR-V, and Honda Pilot, etc. In the second hypothetical model, car performance and repairing data is acquired from all makes and models of cars in the world. Such population data is then used as guidance in repairing any car from any makes. In the first hypothetical model, even though most parts are similar in structure and function, they vary in size, shape and capacity. Most repair attempts would be predicted to fail. If a lucky attempt makes a broken car to run, it most probably would not restore the car's optimum performance.

In the second hypothetical model, the performance data acquired from all cars would be summed and averaged for makes, models, mileages, mechanical conditions, accident histories, etc. We anticipate that few or no problems in cars can ever be fixed. What we have shown is that the functional approach is inherently incompatible with the population approach even in mechanical industries.

Even a moderately complex machine such as a car requires balance among individual components. Each component must match other components. The component must be able to mount in an exact location, have a required installation space, and be sufficiently strong or use a correct amount of power or energy. All key components must maintain balances among fuel flow rate, heat exchange speed, lubricant usage, etc. In addition, even parts age and conditions may influence final performance.

The two hypothetical models show the same kind of flaws existing in the population-based medical research and treatment paradigm. The mismatch between a population and an individual person can be traced to the unique genetic composition of the person. Due to genetic recombination, even siblings from the same parents have different genetics. Human genetic diversity is much more than minor production variations of cars made according to the same blueprint. We infer that people within the same family differ in the pattern of all biochemical and cellular processes. Observed differences may be reflected in chemical diagnostic data, imagine data, health condition, disease histories, etc. Those differences are enough to defeat imagined presumption that all human beings are equal.

### **(b) High Degree Balance Required for Maintaining Personal Health**

We show the level of balance required in a human body is not any less than the balances required in any machine. We will explore several health

properties below.

(1) The glucose “normal range” is said to be 3.89-5.50 mmol/L. In a hypothetical person, the optimum level of 4.0 mmol/L will not result in fat accumulation. Assuming that the glucose level is raised by 25% or 1.0 mmol/L (still within the normal range), we want to see what will happen (ignoring daily fluctuations). The concentration of 1.0 mmol/L would be  $0.001 \text{ mol/L} \times 180 \text{ g/mol} = 0.18 \text{ g/L}$ . Each liter of blood contains additional 0.18 grams glucose. If the person has an average heart output of 6 liters per minute, the total heart output volume each year, is  $6 \times 60 \times 24 \times 365 = 3,153,600$  Liters. So, the total extra glucose that could be available for storage as fats is  $3,153,600 \text{ L} \times 0.18 \text{ g/L} = 567,648 \text{ g} = 567.6 \text{ kg}$ . If only 1% (e.g., 0.01 mmol/L) of the extra glucose is actually deposited on blood vessels and the body, the person will gain  $567.6 \times 1/100 = 5.676$  (fats) kg each year. A serious vascular problem is caused by drawing and depositing glucose at the rate of 0.01 mmol/L from the heart output. The population-based reference, 5.50 mmol/L, is meaningless. What is far important is by what degree the glucose level is deviated from the ideal number for the person and how much of deviated glucose is being deposited in a long time.

(2) Capillaries, the important component of micro-vascular network, comprise small blood vessels from 5 to 10 micrometers ( $\mu\text{m}$ ) in inner diameter. Disk-like red blood cells can pass through capillaries only by deforming themselves. The capillary density in tissues and capillary inner diameters determine blood flow resistance. Flow resistance for any blood vessel segment can be computed by using  $R = 8\eta l / \pi r^4$ , where,  $\eta$  is viscosity of blood,  $l$  is the length of blood vessel, and  $r$  is the inner radius of the blood vessel. If  $r$  is expanded by 10% and 25%, the flow resistance is reduced respectively by 32% and 59%. Assuming that a capillary of 10  $\mu\text{m}$  has been coated with 1  $\mu\text{m}$  fats in its inner wall, and a one-year exercise helps remove the coated fats, the radius of each capillary is increased by  $(5-4)/4 \times 100 = 25\%$ . So, the exercise reduces the flow resistance of the capillary by 59%. This indicates that the ability to remove fats at the rate of  $1/365 = 0.0027 \mu\text{m}$  per day will help the body to restore healthy micro-vascular network.

(3) A person with 10 cancer cells that grow at 0.1% (increase one cell for one thousand cancer cells), the total cancer cell number is estimated to 32.4 billion after sixty years. A 10% increase in the growth rate constant from 0.01 to 0.011 for a tumor of 500 cells will increase the final cancer cell number from 42 billion to 261 billion in five years. A 1% increase in the apparent rate constant, 0.01, will increase the final cancer cell number by a multiplication factor of 1.2 in a five year time; and a mere 0.5% increase in the rate constant, 0.05, will increase the final cancer cell number by a multiplication factor of 1.6 in five years. Regardless of cancer causes and mechanisms, cancer outcome depends on the imbalance between cancer cell death rate and cell division rate. This tiny rate imbalance will result in a big tumor.

Similar results can be found by using the first order kinetic equation or numeric simulation of cell population on a daily basis.

(4) Most human physical properties must be maintained in narrow ranges. The "normal" body temperature can have a range from 97°F (36.1°C) to 99°F (37.2°C). However, for a given person, a fever at half a degree temperature elevation can cause noticeable discomfort. The pH of the human body must be maintained in a tight range between 7.35 and 7.45, and any minor deviation from the personal optimal number can have health implications.

(5) In vertebral body replacement, shape and size of a placement vertebral body structure must match exactly the original one to be replaced. If the replacement part has one millimeter extra, it may cause great discomfort and pain. In using artificial teeth, the mounting base of the denture must match mouth's mounting member exactly. Even a small degree of misfit can cause pain. The structural imbalance can found in all joint diseases.

Those examples show that health problems arise from a tiny imbalance among all biochemical pathways, structural changes, shape changes, capacity changes, etc. Disturbing structural imbalances can be caused by the long term effects of small deviations from balanced rates of biochemical and cellular processes. Deviations causing chronic diseases are often "infinitesimally small" (e.g. a tenth percent to a few percents of ideal personal numbers).

### **(c) Population Studies Are Useful Only in Limited Situations**

To understand the misuse of the population approach, we explore under what conditions the population approach could be used in research.

One class of properties suitable for a population study is those with all contributions of all included parts. Suitable properties include body height, body weight, daily food consumption, etc. Those properties can be attributed to individual parts of the body, but not functions of individual parts. If one studies body weight, weight is always a result of the whole body. Another class of properties suitable for population study include things like personal spending, personal allowances, etc, which depend on personal use or control. This class of things cannot be used to understand health conditions or disease treatments, but can be used in maintaining social order and managing societal resources. In such a study, it is impossible to attribute part of a whole thing to one or more inner components. If one attempts to assign body weight to various health problems such as liver, kidneys, the digestive track, cancer, and spleen, such assignments must be arbitrary.

Whether a health problem can be studied by a population approach depends on the purpose of the study. A threshold requirement is that the health property or treatment's effect can be detected in sufficient accuracy and reliability so that such a trial will satisfy the purpose of the study. To



study the strong pain-stopping effect of a pain killer, one may concern only pain-stopping effect. The purpose is that the painkiller can stop pains for all people. In this case, a treatment-for-all people presumption is sound. Similarly, in studying surgery, antibiotic drugs, sedative drugs, etc., differences among persons and organ-organ interactions will not defeat the study purpose.

In contrast, the presumption that a treatment is good for all people with same diseases is wrong if it concerns chronic diseases. Patients suffering liver cancer differ in their personal health properties that affect cancer progression and reversal. Personal differences are enough to defeat this presumption because, like an auto repair case, differences among persons can generate too large errors and inaccuracies so that acquired data and conclusions drawn from the data are meaningless. The treatment for cancer may work on some patients, and fail on most other patients.

Findings from population trials concerning chronic diseases is like summing performance data for a Honda Accord, a Nisan Altima and a Lincoln Town car, applying their average to each of them, an anticipated result is that all three cars will be crippled.

#### **(d) Population Approach Is Extended to Studying Chronic Diseases By a Mistake.**

After the success in using population trials to study strong and fast treatments, the same method is extended to all areas of medicine. We will show that it is a mistake.

##### **1. Population data lacks required accuracy for studying chronic diseases.**

Medicine fails to pay attention to differences between acute diseases and chronic diseases and have not paid attention to accuracy requirements. The validity of the same-treatment-for-all-persons presumption, as applied to chronic diseases, has not been evaluated. Based on mountains of evidence, this presumption must be rejected as far as it is applied to chronic diseases.

As we have shown, chronic diseases arise when health properties in a person depart from optimal values by a tenth percent to a few percents. A cure to such diseases would require correcting such tiny departures. However, health properties that are derived from a population depart from any personal optimal values by huge margins. To show one example, "normal" cholesterol level in blood is believed to be 1.3 to 5.2 mmol/L. This can be expressed as  $3.25 \text{ mmol/L} \pm 60\%$ . The huge deviations are unable to meet the required accuracy. Moreover, such a large number range does not reflect cholesterol accumulation rate. The variance ( $h$ ,  $\sigma_h$ ) of any health property deducted from a population depends on three sources of variances. The biggest source ( $p$ ,  $\sigma_p$ ) is caused by personal genetics and phenotypes, the second source, ( $d$ ,  $\sigma_d$ ), is caused by fluctuations in 24 hours, and the third source, ( $m$ ,  $\sigma_m$ ), is caused by fluctuations attributable to measurement

technology, measurement skills and measurement conditions. We can expect what is really important is the actual profile ( $d_i, \sigma_{d_i}$ ) for the person, rather than a single numeric number. We must conclude that population data cannot meet accuracy requirements.

We assume the this kind of accuracy is not required in dealing with strong and fast treatments. It is long overdue to study fundamental differences between acute diseases and chronic diseases and differences in required accuracy for studying them. A household scale is useful for common weighing needs, but cannot be used to weigh chemical reagents in a laboratory. For studying chronic diseases, one cannot rely upon population studies simply because they were working in studying acute diseases. We will show in next section, population trials can introduce massive errors and inaccuracies relative to the accuracy and reliability required for studying chronic diseases.

## 2. Mismatch between a population and a person

When a population trial is conducted to study diseases or drugs, the findings are for the average person of the population. We call the average person as an “abstract person.” This idea was originally used at the common law court, but is adopted in medicine by an unwarranted extension. There are a large number of health properties ( $H_1, H_2, \dots, H_n$ ), with some examples being body height, body weight, body temperature, glucose level in blood, blood pressure, etc. If a disease mechanism or a treatment protocol is developed from the population, an assumption is that population can be represented by an “abstract person” like the fiction of legal representation. The health properties of the abstract person are defined by a matrix of population means. However, we know that no person has all his health properties falling on all population's means. We attribute the differences to genetic differences between the person and the population's means. Any differences in genetics, environment, and mind would cause most health properties to depart from the population's means.

We assume that the departures are necessary to maintain body balance. If a person's genetics reflects weakness in generating capillaries in tissues, the person will have reduced density of capillaries. This will result in poor blood circulation in terminal tissues. In an attempt to improve blood supply to tissues, the body will raise blood pressure. All kinds of similar adjustments must be made for all related health properties. Various health properties are thus depart from all means of the abstract person. Even organ size such as the heart size must be a factor responsible for departures of health properties from the population's means. The genetics is only one factor. Genetic recombination can cause more differences than what we can see from height, weight, looks, etc. Personal genetic differences are further influenced by environmental factors and opportunistic and elusive role of mind. An expected result is that no person would have all of his health prop-

erties match the population's means. Each of his health properties may fall a distinctive position of in the population range ( $\bar{X} \pm \text{departure\%}$ ).

In medical studies, health properties are selected arbitrarily, real health properties that must be considered include all health properties that could and might affect the diseases even if many of them are currently not measured or used in medicine. If we include all potentially important but neglected health properties for the population, we predict that the chance of a match between the population's average and an individual person's is nearly zero.

We have shown that chronic diseases are caused by tiny deviations from balanced chemical and cellular processes, and that damages are realized by long term-impacts often in a time scale from several years to several decades. The time scales imply that deviations are "infinitesimally small." If the ideal value of a particular health property for a person is 21% below the population's mean, a change from -21% to +31% would be disastrous. We must conclude that if all population means are forcefully applied to each person in the world, no one can live for their expected lifespans. For this reason, we must reject the idea of using population data as guidance for personal health and longevity except that they are used to acute acute diseases and medical emergence.

All departures from population's means are necessary to correct genetic weakness and fault, and thus are presumed to be important in maintaining good health. If all departures were eliminated, the person could not live healthy life because his health properties would infringe his genetic functions. The only people who can use population data is those whose health property match all those of the abstract person. The chance of match between a person and the abstract person would be same as that of a DNA match (1 in 113 billion based on 9 loci; 1 in 400 trillion in 13 loci) between two unrelated persons. We predict that it is zero. This fact implies that a person's health properties cannot match a population's means unless the person's genetics were changed to be same as that of the abstract person.

Differences in health properties between a population and a particular person are explained by differences in three dimensions. A lucky genetic match between two unrelated persons may happen at lower odds of finding a match in a DNA test. Moreover, the diversity of health properties among human individuals are further increased by an unlimited number of possible human phenotypes. The number of phenotypes depends on long lifespans, different lifestyles, different cultures and different environments. Due to the massive number of phenotypes, even a genetically identical twin are predicted to have very different health properties. The number of phenotypes of human beings is further enlarged by differences in mind or the Central Nerve System. A successful cure for a patient may instantly defeated by a sudden change of mental status as a result of shocks, fears, or

emotional trauma.

We have shown any cures for chronic diseases established from population trials will not work for any person due to the mismatch of health properties between the population and any person.

(3) Many health properties may not predict chronic diseases.

Considering functional aspects, health properties references derived from a population are ballpark numbers, that are further complicated by measurement conditions. They cannot be used to predict chronic diseases. Many health properties cannot be correlated to conversion rates of metabolites and net impacts to tissue structures. Health properties may fluctuate in daily basis or other cycles. Such health properties must be determined dynamically. What are important are the highest values, the lowest values, and the mean over a long period of time. For example, periodic high glucose levels in some time intervals may be balanced by lower levels in other time intervals to prevent excessive fat storage. A number like less than 90 mg/dL may signify that the person does not have a disastrous glucose imbalance, but does not guarantee that the glucose usage is in a dynamic balance. Population-based number lack accuracy as the guidance for achieving personal optimal health.

### **(e) Misusing Population Study Findings to Individual Patients in Treatment**

We will show that findings from population trials cannot be correctly applied to patients in treating patients.

Basic medical research has yielded a large number of new discoveries that are related to disease causes and treatments for major diseases such as heart disease and cancers. However, when a doctor treats a specific patient, the doctor cannot determine what are particular causes and what are suitable treatments for this patient. In practice, only few diagnosis tests can be done, which cannot be sufficient to identify disease mechanisms (if it is understood). As a common practice, the doctor runs mini-drug trials on this patient: try this drug, try that procedure, try this dosage, and try that chemo protocol. Each drug, procedure, dosage, and protocol have been developed from population trials. All attempted treatments are based on abstract persons in drug trials. If a similar approach is used in auto repairs, a five percent of success rate might be the maximum. Only a small number of patients may be close to an "abstract person." Most treatments fail, and those succeed, the drug can improve only symptoms but not cure. Cancer's complete responsive rate is centered around 7.4% [Ashdown et al, 2015], which does not cure cancer.

If findings in population studies are established with variables controlled, such findings cannot match any real person because no one lives his life with variables controlled. If a treatment established in a population study

is used to treat patients without controlling the same variables, the treatment fails. This impossibility in treatments is another reason that medicine has not succeeded in finding cures for chronic diseases. The application is worse than an experience-based medicine because this application step implicates a systematic failure: it totally disregards all conditions that have been used in population studies.

For all those reasons we have provided, medical professionals should systematically examine population based approach, and limits its application to only suitable medical problems.

## 2. False Results from Focusing Only a Single Disease Mechanism in a Population Study

A drug is normally designed to work on a particular mechanism M1, but patients suffering the same disease involve different mechanisms M1, M2..., Mn. A treatment by using a single drug most probably fail at a high chance. A disease mechanism may mean a cause factor at different detail levels.

If a drug is used to a population of patients, the drug will work only on the patients who have a matched mechanism M1. If only a small percent of the patients involve M1, the theoretical maximum response rate is the portion of patients whose disease is caused only by M1. In reality, whether the effectiveness of the drug in this portion of patients can be recognized in a population trial still depends on many other factors such as the experimental design, the size of experimental error and factors that can interfere with the mechanism, M1.

This one-out-of-many disease causes model shows that combining different people without understanding all disease mechanisms for the population can result in false results. We will use hypothetical data to show how a plurality of factors contribute to high blood pressure. The following table shows a list of main disease mechanisms and reasons for causing high blood pressure, and some exemplar influencing factors.

Table 1. Disease Mechanisms and Influencing Factors for High Blood Pressure

Main Disease Mechanisms	Reasons for Causing High Blood Pressure	References	Exemplar Influencing Factors
Narrowed and reduced capillaries.	$R=8\eta l/\pi r^4$	Common knowledge.	Lack of exercises, sedative lifestyle, calories imbalance, over intake of carbohydrates, fats and proteins.
Blood vessel	Damaged blood	Pollutants, high	Heavy metal, pollution,

damages.	inner walls, and plaque formation from repairs.	oxidative potential, etc.	contaminants, harmful food additives, transit excessive high blood pressure, etc.
Systemic inflammation.	Swelling tissues.	Through C-reactive protein, high glucose level, etc.	Uncured infections. intake fried food, refined starch, sugars and beverage resulting in too high glucose spikes.
Impaired kidney functions.	Failure to remove all toxic by products in time.	Elevating renin that makes small arteries narrow; salt excretion, leads to volume overload. [Tedla et al, 2011]	Damaged caused by prescription drugs, long term fatigue, toxic damages, shock, fears, and chronic stress, etc.
Impaired liver functions.	Liver is involved in fat distribution and energy balance.		Alcohol use, excessive fatigue, poor emotion, stress, all kinds of liver infections.
Fat plaques in certain locations.	$R=8\eta l/\pi r^4$ plus location effects in moving and activities.		Lack of exercise and calories imbalance, more due to imbalance of exercises. Fats are less likely be accumulated in active area of the body.
Faulty CNS regulation.	The CNS controls the blood pressure.		Poor cerebral blood circulation, stroke of all types, damaged brain tissue, lack of essential nutrition.
Emotional health.	Shock, fears, nervousness triggers excessive hormonal actions.	Common sense	Emotional health habits, frequent shocks and fears, and chronic exposures to emotional distress.
Straining or relaxation habits.	$R=8\eta l/\pi r^4$ ; Blood vessels contract in re-		This class of factors is hard to notice. A bad habit can form slowly

	sponse to fight-or-flight.		without conscience knowledge. The only way is to learn relaxation by frequent attention to the problem.
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The massive number of influencing factors play their roles at different degrees. We deduce that each person has its own unique profile of contributions of the influencing factors. An infinite number of anticipated profiles is another proof that any treatment protocol derived from a population must fail in certainty.

The mechanisms and influencing factors listed in the above table are symbolic representations. The actual number of variations under the capillaries in the first row must have an infinite differences. Capillaries conditions can differ in capillaries density, fats and cholesterol compositions in deposits, and other chemical compounds in the deposits, and distribution patterns of different narrowing patterns in different parts of the body and organs. The variations in human vascular condition implied in the above table are an example of the massive variations that are caused by genetics, phenotypes and mind.

All main mechanisms, which are expressed in function, could be expressed by differences in genetics, phenotypes and mind. The roles of genetics and phenotypes in each of the main mechanism are self-evident. Mind plays its roles through relaxation which affects the inner pass-through holes of capillaries (by  $R=8\eta l/\pi r^4$ ). Shocks, fears, nervousness, and chronic stress can influence blood pressures by triggering the releasing of hormones. They can also affect blood pressures by impaired functions of kidneys which are damaged by excessive blood pressures triggered by released hormones. The hypothetical case implies that patient vascular systems differ in main mechanisms and their differences can be traced to differences in genes, environment and mind. This also shows the person and a population must mismatch.

If one attempts to correct high blood pressures by using one or a few of the influencing factors, the chance of success is low or non-existent. However, if one utilizes a large number of those factors covering all main mechanisms as well as rare factors not listed, the chance of success will be higher, or very high, and eventually is a certain. Success or failure does not depend upon statistical analysis.

This hypothetical disease cause model is another way to prove that the single factor or a single drug is expected to fail. There is no way the health problem involving so many aspects can be fixed by action of a single drug. This example shows that the holistic model that is directed to all of those potential problems can achieve the best result.

We will make another hypothetical disease cause model for cancer. We will discuss some known mechanisms below.

Table 2. Main Mechanisms Affecting Cancer and Their Influencing Factors

Cancer Main Mechanisms	Reasons for Promoting Cancer	References	Exemplar Influencing Factors
Certain types of mutations.	Oncogene and tumor suppress genes/ clonal expansion.	Nowell, 1976; Wang, 2002; Wood, 2007; Jones, 2008;	Exposure to carcinogens, radiation, and toxins which can cause genetic damages and affects DNA repair mechanisms.
Immune system change (Inhibit anti-tumor immunity).	TAMs by receptors ligands, and suppress cytotoxic functions of T-cell, NKT cells and NK cells, and apoptosis.	Noy and Pol-lard, 2014.	Diet can have a massive influences on immune system state, exercise is a key influencing factor. Both affect T-cells, B-cells, macrophage, natural killer cells, etc.
Growth signals.	Tumor must get sufficient signals for growth.	Hanahan & Weinberg, 2000.	Although signals working on the tissues, but tissue is controlled and influenced by the CNS. [Afsar et al, 2017].
Anti-growth signals.	Tumor must cripple anti-growth signals.	Hanahan & Weinberg, 2000.	
Metabolic pathways.	Favor glycolysis, but disfavor oxidative metabolism.	Wangburg Effect (disregard disputes).	Glucose levels in the blood; deep breath exercise; fat, protein, and carbohydrates ratios, etc. affect pathways.
Apoptosis and cell necrosis.	Promote apoptosis rate.	Hanahan & Weinberg, 2000.	Natural compounds influence apoptosis. [Safarzadeh et al, 2014], Aung, 2017].
Altered cell adhesive molecules.	This is a required change for cancer metastasis.	Hanahan & Weinberg, 2000.	



Limitless replicative potential.	The number of cell division will not be limited.	Hanahan & Weinberg, 2000.	
Angiogenesis.	Required for solid tumor of 2 mm.	Hanahan & Weinberg, 2000.	Some drugs can affect angiogenesis. [Sagar et al, 2015].
Neurogenesis.	Neurogenesis takes place in all solid tumors.		Some nutrition may help nerve development. [Poulose et al, 2017]
Mind and CNS roles.	Affect initiation, development and Metastasis.	Many references.	Herbs, drugs, and exercises, entertainment, environment setting, etc.
Cell Cycle Arrest.	Stop cell cycles.	[Bailon-Moscoso, 2017].	Natural compounds inhibit the cell cycles.
Physical properties (T, pH, & vibration)	Cancer cells are sensitive to temperature, and may be to mechanical vibrations.	[Levine & Robins, 1970]; [Yeung & Wang, 2003].	Exercises raise temperature, increase mechanical vibration, alter pH.

The main mechanisms listed in the above table are intended to cover only those that are common for solid cancers. Although one would predict that if any of main mechanisms is blocked, cancer proliferation will be stopped. That is never the case. The cancer can quickly beat drug action directed to a single mechanism.

While a vast number of facts are the consensuses of cancer researchers, we expand things related to exercises as it is a neglected area of research. Since population model is unable to recognize weak and slow factors, we include them in the model.

The effects of physical properties are inferred from findings in basic research. Cancer cells are more sensitive to temperature [Levine and Robbins, 1970] and cell division can be slowed down by mechanical disruption of cell division apparatus [Yeung and Wang, 2003]. Doubt in their roles can be resolved by examining the potential effects of physical activities on cancer prevalence. Other properties are yet to be discovered by using more sensitive research methods.

We note that each mechanism listed in the Table 2 can be affected or influenced by a large number of natural compounds. For example, herbs with

angiogenic activity includes Chinese wormwood, European mistletoe, curcumin, Chinese skullcap, grape seed extract, Chinese magnolia tree, green tea, *Ginkgo biloba*, quercetin, *Poria cocos*, ginger, panax ginseng, etc. Activator protein 1 (AP-1). In contrast, angiogenesis can be promoted by a more than twenty endogenous angiogenic polypeptides such as angiogenin (AG) and angiotropin (AT), angiopoietin (APN). Natural health products also have direct and indirect anti-angiogenic activity. In practice, it would be hard to achieve a right balance between anti-angiogenic and angiogenic activities. Each of those factors influence the property in a quantitative manner.

While nature provides a massive number of weapons for fighting cancer, medicine could not use them. It attempts to extract one from natural products or use synthetic drugs, expect them work like a painkiller, and have their effectiveness confirmed by a statistic analysis. This medical practice cannot achieve scientific validity, but appear to be driven by the need to comply with the accepted research standard. We will prove that a fast acting single drug cannot cure cancer or any other chronic diseases for a large number of reasons.

#### **(a) Implications of a Train Braking Model**

When a train comprising twenty cars runs with a huge momentum, applying brake to only one car or only two wheels can stop the train in theory, but will most probably fail in reality. Failure of brake, insufficient braking power, and any unexpected reason will result in failure to stop the train. A moving train has a huge momenta.

#### **(b) Implications of a Tissue Structure Reconstruction Model**

To reverse a diseased structure, a large number of chemical bond structures must be changed. Those bond structures include different molecular ratios, arranged in different ways and different attraction forces. Ignoring biochemical processes, a conversion from a cancer-residing tissue structure to a normal structure requires a massive number of small structural changes at molecular and atomic levels. Assuming that this change can be achieved by micro-engineering work, force is required to break existing chemical bonds and move molecules apart, and energy may be necessary to create new structure. From this structural reconstruction model, we hypothesize that positive efforts are required to change all points in the structure. However, it would be much harder to make such a change only by making effort to change only one or two points.

#### **(c) Implications of A Chemical Chain Reaction Model**

Biochemical reactions are not same as a solid state. It has been assumed that cancer can be cured by using one single drug, as reflected in routine attempts in finding cure. Assuming this presumption were correct, a complete change in the tissue structure must take more time. As implied by

the train braking model, if brake is applied to only one car or a pair of wheels, it would take an extended time to bring the moving train to a stop. As implied by the structural reconstruction model, it would take more time to have all points changed back to a non-diseased state.

#### **(d) Drugs Resistance Consideration**

In cancer treatment, cancer can use a variety of mechanisms to defeat drug actions. A method of using a single drug for a long term is predicted to fail because its effectiveness will be defeated before the cancer is cured. Thus, we predict that a single fast and strong drug cannot cure cancer; and if a single drug is used at a slow working speed, it is most probably defeated by cancer's resistance to the drug.

#### **(e) Disruption of State by Excessive Disturbances**

Using a single drug intended at a fast speed can cause massive disturbances to an established balance in the body. In other words, a cancer developed in forty years is better be reversed at a slower speed (e.g., one or more years).

#### **(f) Risk Analysis for Multiple Factors Approach**

When a drug is used in a high concentration, its risk is much higher than using natural products, many of which can be used as foods. If a matrix of natural compounds are used, the odds of creating serious drugs side effect is lower, but the chance to hit sufficiently number of points to cause structural changes will be higher. For those reasons, a successful cure for cancer should be based on applications of multiple factors approach.

#### **(g) Chances of Match Between a Cure And a Cancer**

Cancers come with all colors and shapes. The potential number of variations caused by differences in those factors must be comparable to the variations caused by genetics, phenotype, and mind. For example, if angiogenesis is poor in a particular patient, the cancer may be limited by size. In treating cancer, a definite match can be found only by using multiple factors. We will show in next section, statistical method is an improper method for evaluating treatment effects.

On the basis of the train braking model, the structural reconstruct model, the chain reaction model, drug resistance consideration, and risk-benefit analysis, using a single or a limited limited number of drugs is not a best strategy for curing cancer, and multiple variables optimization is superior to population based treatment methods.

A cure to cancer is predicted to be straightforward by using system optimization method under the holistic model. One single factor, chronic stress, is reported to increase metastasis size by more than 30 folds [Sloan, 2010]. From cancer latent times from 5 to 70 years, we infer that cancer proliferation rate can be manipulated by great margins. The rate constant, which is defined as % increase in cancer cells on each day is very small. If

tens to hundreds of factors are correctly used, there is no reason to hold against reversal. A large number of cancer miracles can be found and should be studied.

### **3. Inability to Detect Single Slow and Weak Cause or Treatment Factor**

The development of chronic diseases depends on many weak cause factors  $C_1, C_2, \dots, C_n$ . Similarly, a successful treatment may comprise many treatment components,  $F_1, F_2, \dots, F_n$ , and overall health of a person may depends a large number of health factors. We will consider whether or not the reduction model can enable researchers to determine a variety of such weak factors.

In current research paradigm, researchers can only look into one or a limited number of cause factors. They cannot tell whether a finding of specific cause factor is reliable. It is desirable to include a yardstick of experimental errors so that they can judge how reliable the findings are in comparison with experimental errors. Thus, more test subjects are used in the study. In a population study, researchers focus on one or a few factors while keeping the rest of factors constant.

We will show below that if contributions of a cause factor is small relative to the contributions of experimental errors, such a study always tends to fail to recognize the weak and slow factor. We will explore how their ratios will affect the outcomes of conducting hypothesis tests.

#### **(a) Hypothesis Test Comparing Two Populations' Means (Two Means Test)**

In a typical population trial, the objective is to determine if a treatment is different from a control, the trial acquires two sets of measures  $X=X_1, X_2, \dots, X_n$  and  $Y=Y_1, Y_2, \dots, Y_n$  (as a control). We assign a start patient survival data in Table 3 below, and assume that the treatment can be adjusted by strengthening or weakening its curative effects, we will get following data sets.

Table 3. A Hypothetical Test Data Using Two Means

Ctrl Srvl. (days)	$Y_i - \bar{Y}$	$(Y_i - \bar{Y})^2$	Treat (days)	TX Srvl. (days)	$X_i - \bar{X}$	$(X_i - \bar{X})^2$
130	-75	5625	57	187	-75	5625
160	-45	2025	57	217	-45	2025
190	-15	225	57	247	-15	225
220	15	225	57	277	15	225
250	-45	2025	57	307	45	2025
280	75	5625	57	337	75	5625

From the hypothetical data, we get following statistical parameters:

Control:  $n_1$  is sample number,  $\bar{Y}$  is survival mean for the control,  $S_y^2$  is the variance of the control.

Treatment:  $n_2$  is sample number,  $\bar{X}$  is survival mean for the treatment,  $S_x^2$  is the variance of the treatment. Assuming that all design and condition are met (which is NOT possible due to the nature of this simulation). We will conduct the hypothesis test below:

$$S_y^2 = \frac{1}{n_1 - 1} \sum (Y_i - \bar{Y})^2 \quad (1)$$

$$S_x^2 = \frac{1}{n_2 - 1} \sum (X_i - \bar{X})^2$$

$$S_w^2 = \frac{(n_1 - 1)S_y^2 + (n_2 - 1)S_x^2}{n_1 + n_2 - 2} \quad (2)$$

$t_{0.05}(n_1 + n_2 - 2)$  is a found from a t distribution table.

$$\text{If } \bar{X} - \bar{Y} \geq t_{0.05}(10) S_w * \sqrt{\left(\frac{1}{n_1} + \frac{1}{n_2}\right)}, \text{ reject the null hypothesis. (3)}$$

We compute to get the following statistical parameters (S means sample variance):

For the control:  $|\bar{Y}|=205$ ,  $s_y^2=3150$

For the treatment:  $|\bar{X}|=262$ ,  $s_x^2=3150$

$$S_w^2 = \frac{(6-1)3150 + (6-1)3150}{6+6-2} = 3150$$

Find t value with 0.05 as the rejection probability:  $t_{0.05}(10)=1.81$ .

$$t_{0.05}(10) S_w * \sqrt{\left(\frac{1}{n_1} + \frac{1}{n_2}\right)} = 1.81 * \sqrt{3150} \sqrt{\frac{1}{n_1} + \frac{1}{n_2}} = 58.65.$$

Since  $\bar{X} - \bar{Y} = 57 < 58.7$ , accept the null hypothesis and the treatment is not significant. This results in a result which is against the hypothetical data. In this hypothetical question, the treatment is assumed to extend 57 days. In conducting the hypothesis test, the significance or probability by which the treatment extends survival time is determined by comparing the treatment effectiveness  $\bar{X} - \bar{Y}$  with variances ( $s_x^2$ ,  $s_y^2$ ) or standard errors attributable to differences among individual patients. When the survival time is widely dispersed among patients, the treatment's effect is hidden in the experimental errors so that the true benefits of the treatment would be viewed as the experimental errors.

By looking at the mathematical operations in the statistical analysis,

we note that a hypothesis test outcome depends on treatment's mean,  $\bar{X}-\bar{Y}$ , and  $S_y^2$  and  $S_x^2$ . The test outcome depends on standard deviations  $S_y$  and  $S_x$  because  $S_w$  can be computed from  $S_y^2$  and  $S_x^2$ . We construct a spreadsheet data set which allow us to change the data in the first column so that we can explore how the hypothesis test results would change with data being manipulated.

(1) If the data dispersion is changed, the chance of rejection entirely depends on the effect of the treatment. When  $S_y^2=3150$ ,  $S_x^2=3150$ , and  $S_w^2=3150$  are held constant, the point of rejection is a constant. When the treatment's effect is increased to 59 days, the true effect is confirmed at 0.05 probability. True effect of extending life by 1-58 days is not recognized and extension of life from 59 to any reasonable days will be recognized at the probability of 0.05.

(2) If data dispersion is held as zero. All random variables become ordinary variables. Even the effect of one day extension of survival time can be found by common sense. To extrapolate the limit, this hypothetical model can be viewed as an imagined case, where the same patient is tested in  $n1$  times assuming that each test will not affect the result of subsequent trials. To avoid the density distribution vanishes, we will add several hours noise to the control data set so that  $S_x^2=0.035$ ,  $S_y^2=0.035$ , and  $S_w^2=0.035$ . In this case, a treatment with 1 day of extension is found to be significant at 0.05 probability (ignoring difficult in setting up  $H_0$  and  $H_1$ ). So, we get the following result.

Table 4. Rejection ( $\bar{X}-\bar{Y}$ ) Increase with Control's and Treatment's Variances.

$S_y^2$ for Baseline	0.035	350	3150	12655	35000
$S_x^2$ for Treatment	0.035	350	3150	12655	35000
$S_w^2$	0.035	350	3150	12655	35000
Rejection regions (at $\alpha=0.05$ )	>0.19	>19.6	>58.7	>117.3	>195.5
Min $\bar{X}-\bar{Y}$ accepting $H_1$ (days)	1	20	59	118	196

The above table shows when data dispersion increases, the rejection point for the same probability dramatically increases. Even one day extension of survival time can be detected if the patients are strictly same. This is like a limit which is same as non-random variable cases. However, if a patient population is selected with great differences in their baseline survival times, even 195 days survival extension cannot be recognized due to type II mistake (false acceptance of the null hypothesis). This trends is a well known fact, but what is shown is that in most, if not all, population trials, the expected variances are sufficiently large to result a consistent failure to

recognize weak treatment effects. Here the survival time differences are very reasonable numbers found in cancer research studies.

(3) In both simulation cases, we assume that the variances in the control and treatment are consistent. For a small population trial,  $S_x^2$  may be larger than  $S_y^2$ . However, for large population trials, we expect that  $S_x^2$  and  $S_y^2$  are close. When the patient numbers in the control and the treatment are sufficiently large, the acceptance region for  $H_0$  are determined by the following range:

$$\bar{X}-\bar{Y} \pm Z_{0.05} * \sqrt{\left(\frac{S_y^2}{n_1} + \frac{S_x^2}{n_2}\right)}$$

In this case, the sample's variances may be used as the population's variances and the cutting-off value is determined by using the normal distribution rather than the t-student distribution.

(4) If the treatment comprises more factors and have actually more effects of extending survival time for each of the patients, it will result in a larger  $\bar{X}-\bar{Y}$ , which is directly compared with a value defining the rejection region. While the multiple factors may increase data dispersion of the control and the treatment, it tends to move into the region for rejecting the null hypothesis faster, resulting in recognizing overall effects of the treatment.

### **(b) Hypothesis Test Comparing the Paired Differences (Paired Difference Test)**

In this hypothetical test using bogus data, variables controlled trials tend to fail to recognize single factor and weak factor, as a result of type II error (failure to reject null hypothesis).

There are N persons with a health property X being observed before a treatment and after a treatment. If the treatment is too long, it is assumed that the health property before the treatment and after the treatment can be accurately measured. A treatment may comprise one treatment component or factor F selected from F1, F2...., Fn. For each person, this trial would produce paired data,  $x'_i-x_i$ . For all patients, the trial would result in a series of paired data:  $X_i=x'_1-x_1, x'_2-x_2, x'_3-x_3, \dots, x'_n-x_n$ , where  $x'$  is a health property after a treatment and X is the value of the property before the treatment.

In this test model, the health property is a systolic blood pressure. The treatment is a weak single factor, which can alter blood pressure by only 1.5 mm Hg. We first tried six data points with blood pressure range from 145 to 180 mm Hg, and then added some random noises to the data in an arbitrary way. We want to see whether the true effect of the treatment could be confirmed in the hypothesis test. We generated following data:

Table 5. Blood Pressure Data In a Hypothetical Trial

Assumed Sys. BP mm Hg	Treatment Real Effect (mg Hg)	Fluctuations (mm Hg)	Predicted Change $X_i=(x'_i-x_i)$	Mean changes $\bar{X}$	$(X_i-\bar{X})^2$
161	-1.5	2	+0.5	-1.5	4
180	-1.5	-2	-3.5	-1.5	4
130	-1.5	2	+0.5	-1.5	4
150	-1.5	-2	-3.5	-1.5	4
145	-1.5	2	+0.5	-1.5	4
179	-1.5	-2	-3.5	-1.5	4

By following statistical steps, it is assumed (against assumed true effects) that the treatment had no real affect and all measurements were caused by random errors. Their distribution would be a distribution centered at zero. So, the task is to determine if  $x'_i-x_i$  is belong to the distribution  $N(0, \sigma^2)$ . Now, we have the null hypothesis:  $E(X)=0$ .

$$|\bar{X}| = \frac{1}{n} \sum X_i; \quad (4)$$

$$S^2 = \frac{\sum (X_i - \bar{X})^2}{n-1} \quad (5)$$

$$\text{If } |\bar{X}| > t_{\alpha/2} \frac{s}{\sqrt{n}}, \text{ reject the null hypothesis.} \quad (6)$$

From the data, one can find  $s^2 = 4.9$ ,  $s = 2.19$ , and find from a t-distribution table,  $t_{0.05}(5) = 2.01$ .

$$t_{\alpha} \frac{s}{\sqrt{n}} = 1.79$$

Since the mean  $|\bar{X}| = |-1.5| < 1.79$ , the hypothesis test accepts the null hypothesis. The finding that the treatment is ineffective is contrary to the presumed effect that the treatment has 1.5 mm Hg reduction. Here, the treatment may be viewed as a very weak treatment factor. This outcome implies, as expected, that when errors attributable to measurements and daily fluctuations are larger than the true effect, such small effect cannot be recognized.

We set up a spreadsheet data set with variables that can be changed. We could repeat the same simulations by using a much larger data set. Measurement errors may be much larger than 2 mm Hg, but this does not change the general trend: weak factor will not be recognized due to type II error (False acceptance of the null hypothesis).

Assuming that the same treatment is optimized by using several factors to treat blood pressure, and the treatment could contain following components:



(1) Jog one hour each morning, which is assumed to generate an effect of lowering 10 mm Hg by removing fats from inner walls of blood vessels.

(2) Administrate a heavy metal deduction program, which helps the patient remove heavy metals from the body. It is assumed to result in a 5 mm Hg reduction by stopping and reversing damages to blood vessels.

(3) Practice meditation daily to help blood vessels to achieve relaxation state. It is assumed to reduce blood pressure by 5 mm Hg.

(4) Reduce and avoid refined foods, fast foods, fried foods, etc. for one year. It is assumed to reduce the blood pressure by 5 mm Hg by reducing systemic inflammation.

(5) Correct vitamin deficiency to improve the brain's function so that the brain will improve its ability to regulate and control blood pressures. It is assumed to lower blood pressure by 5 mm Hg.

(6) Reduce life stress, job stress, and emotional stress, etc. to improve the hormonal regulations. It is assumed to reduce the blood pressure by 5 mm Hg.

(7) Improve the kidney functions to improve the efficiency of removing metabolic toxins. It is assumed to reduce blood pressure by 5 mm Hg.

(8) Adjust fat compositions for omega 3/6 fatty acids ratio in diet to near 1 so that the body fat compositions are changed. It is assumed that this factor can lower blood pressure by 5 mm Hg.

It is further assumed that those weak effects are delivered slowly. If the treatment is not longer enough, the treatment may be deliver only part of the respective maximum effects.

The above factors are assumed to interact with each other. If blood vessels are enlarged, the brain's regulation of the vascular system is improved, damages to blood vessels are cured, toxic compounds are removed, and inflammation is reduced, total effect in blood pressure reduction will be more than the sum of all assumed individual effects. If we conduct similar simulations by using various combination factors, the chances of rejecting the null hypothesis rapidly increase to affirm the treatment's true health benefits.

In conducting a hypothetical test, the error term, as reflected in S, does not increase as the measured blood pressure. Thus, if more factors are used in a treatment, the data set will happen in more extreme cases, with a practical effect of rejecting the null hypothesis. This implies that optimization using as many factors can yield a result of recognizing weak and slow treatment. If the treatment comprises factors 1 and 2, it could result in  $X=15 > 1.79$ . A combination, making up of factors 2, 3, 4, 5, would result in 20 mm Hg reduction. If all factors are used, the treatment might reach 45 mm Hg as the potential maximum. However, blood pressure cannot go lower than threshold numbers for patients.

Looking at the logic, we should note the variance is caused by  $(X_i - \bar{X})^2$ . If the treatment has same total net effect, the variance depends upon how the treatment effects are dispersed among individual patients. If all patients are very consistent, and their net treatment effects are all close to the mean, the test would be able to recognize small treatment effects. If some patients show big treatment effects, but others show little effects, the large differences will result in large variances and the value for defining the rejection region for rejecting the null hypothesis will increase per the equation (6).

Whether a true treatment effect can be detected by a hypothesis test depends on whether all patients respond to the treatment in a similar quantitative amount. This would require that all patients have very similar health conditions, very similar disease mechanisms, and have the ability to have their health condition restored. Their health properties must be close to one type among the infinite number of variations defined by the genetics, phenotypes and mind. In reality, the population can introduce massive variances, and the treatment adds additional variances, use of population trials is clearly a wrong approach. If 3 out of 6 patients are cured, there is no point to use the three failed cases to refute the extraordinary treatment benefits of the treatment. This example shows that population approach is fundamentally wrong.

This trend is well known in statistics, but what is shown is that in most, if not all, population trials, the expected variances are sufficiently large to result a consistent failure to recognize weak treatment effects. Due to the similar statistical logic behind all hypothesis tests or confidence intervals, the same trend can be found for hypothesis tests using other distributions.

### **(c) Grossly Inaccurate Results Caused by Population Trials**

P-value does not tell whether the hypothesis targeted for testing is true or not, and says absolute nothing specifically related to that hypothesis unless every other assumption used for its computation is correct—an assurance that is completely lacking in population studies.

One big problem for studying multiple weak treatment effects under optimization method is that weak effects are not the type that can be determined in population trials. The validity of such trials depends on whether the true weak treatment effect can be detected accurately and reliably relative to true experimental errors. The first type of design is completely unfit for studying weak treatment effects. The second trial method also has limited utility for studying treatments under the holistic model.

Variable controlled methods cannot find treatment effect caused by synergistic interactions among individual factors. The simulation results also reveal that if a health property is influenced by more variables, an attempt to select one single variable with other variables controlled would achieve the

false result. If the health property such as cancer risk is influenced by hundreds of factors, a study focusing on one single factor a time would result in failure to recognize each factor. Hundreds of independent studies will result in failure to find all the factors. We must find that misuse of controlled variable methods is most probably responsible for creating a false notion that none of lifestyle factors can cure diseases. Since most treatment protocols have been developed by using population trials, it is natural that such treatment protocols cannot cure chronic diseases.

Medical studies attempted to understand the roles of diets, nutrition, exercises, mind regulation, emotional stress, fears, etc. routinely focus on a single factor often with insufficient duration. In such studies, massive errors are introduced by races, personal genetics, age, sex, diet, exercise, lifestyle, health conditions, and prior treatment histories, mental state, etc. The current trial methods are able to affirm only strong factors that stand out over experimental error and all interference factors, but routinely fail to recognize weak and slow-acting factors whether or not statistical analysis is used or not. Misuse of population trials is the most probable reason why medicine could not find cure for chronic diseases.

Two mean test is suitable for randomized population trials and is very bad if patients have large differences in baseline health properties because any variances caused by all sources not attributable to the treatment will become the error term. Due to large variances which are caused by personal differences. Such a statistical analysis is greatly bias and capable of detecting only very strong treatment effects. It should be presumed to be incapable of recognizing any weak and slow treatment or cause effect. Although in some population studies, adjustment is made to correct variances for a well established factor such as sex, it is impossible to take out all known variances from the error term. Such a statistical analysis, as well any existing data analysis methods, can never do away with the population-and-person mismatch that can be traced to massive variations created by genetics, phenotypes and mind. This methodological error is rooted in a wrong presumption that a treatment derived from a population can be applied to a person.

Paired differences mean test is able to detect the difference by observing changes in health properties before the treatment and after the treatment. It provides a chance to show up net treatment effects. However, many health properties such as death rate, survival time, hazard rate, etc cannot be acquired in a paired manner. It is not a tool for randomized population trials. It is a better test for a system optimization process. Like car repair, the car owner can tell if his car has been properly repaired by observing changes to the car. However, one difficulty is that if a patient has accepted multiple treatments, some of which are ineffective, it is hard to tell which of the treatments have contributed to final success.

A worse problem is toxic effects of environmental pollutants, contaminants, food additives, pesticide residues, herbicides, industrial chemicals, etc. By focusing on a single toxic agent in each trial, a vast number of weak and slow toxic agents will escape from being caught. Since multiple toxic agents always work together in reality, negative findings by focusing single toxic agent a time does not represent reality in the human body. Variable controlling and statistical method cannot correctly predict lack of toxic damages to the body when thousands of them work together.

In studying adverse health effects of trace amounts of toxic compounds, even the paired difference test is not good enough because the interactions among thousands of synthetic/natural compounds cannot be examined in reality. Before better research strategy is developed, it is better to rely upon wisdom rather than findings from population studies.

The societal reliance of such study findings is most probably responsible for bringing down the health of the world population, and there is a clear sign that national and worldwide health problems will eventually nullify economic benefits that humans can ever achieve.

Our simulation results in both two means test and paired-difference test indicate that the variables controlled trial method is inherently bias against weak health factors, weak treatments, and slow working treatments. The failure can be traced to the irreconcilable conflicts among the huge population variances, required high experimental accuracy, and weak effects of treatment effects.

#### **4. Inability to Deal with Interference Variables**

Assuming that a disease can be caused only by a mechanism. So a drug is indented to work on the mechanism. However, a large number of other factors such as race, personal genetics, age, sex, diet, lifestyles, drug use histories, interactive compounds, health condition, mental state, etc. can interfere with the drug's effects on the disease. "Interference" means more broader than it may mean in other medical research contexts and works like random variables in an unpredictable manner. Whether the drug works depends on individual person and all influencing factors. When the population approach is used to study the drug, researchers cannot study so many interference variables and thus must control those variables. In conducting a drug trial with a placebo as control, the effects will depend on whether the interference factors affect both the drug and the placebo in the same way.

We will examine if randomization can cancel out all interference effect of variables. Randomization is based upon an unrealistic presumption that a disease can be cured by using one single drug. A typical trial contains one or more treatment groups and a control group. To make the true effects of the treatments show up, all interference factors that are not studied must be constant or affect both the treatments and the control in the same way. An

implied requirement is that the effects of randomized variables are small relative to treatment effects, and must fall on both side in a random fashion. For example, two sides should have a similar age pattern, a similar race mixture, similar genetic types, similar sexes, etc. It is hoped that the effects of all controlled variables will cancel each other. If the drug under the investigation can improve outcome, the finding is believed to be real.

While the logic sounds great. A deep analysis of this approach reveals many flaws. Based upon the hypothesis test mathematical operations, we deduce that that the validity of a randomized trial depends on the following five assumptions: (1) the contribution from each of the variables can be measured in the same scale, (2) contribution of each variable follows the same linear relationship, (3) every factor can be defined in a reasonable accuracy and consistency, (4) all interference factors interact in the same ways, (5) all interference variables can be randomized.

We believe that in dealing with health properties, there is no common comparative basis and there is no common scales for measuring them among all people. For examples, a negative contribution from some old men might be much more than that of other men at similar ages. This means that the effects of randomized variables cannot by canceled by themselves. Contributions of some variables to drug effects do not follow the same linear relationship. If a chemical analysis reading is used to define a variable, the contribution of this variable may be linear in some situations and nonlinear in other situations. Many variables such as drug-use histories and health conditions cannot be defined in a meaningful way. Health properties such as health condition, feeling, and pain cannot be compared because there is no common comparative basis. There is no way to compare those qualities across persons due to a lack of a comparative basis. The worst problem is that most variables interact with each other to generate synergistic impacts. For example, young age and no-prior-drug-use history may work together to dramatically increase the drug's effectiveness.

Departures from the five requirements are insignificant in studying fast and strong factors like surgery and pain killers. However, when the treatment effect is comparable to or even weaker than the true experiment error, the validity of findings in any study would depend on everything including experimental design, measurement quality, data processing method, and hypothesis test. The data processing method used in most hypothesis tests indicates that all data are treated in a linear model. Ultimately, a hypothesis test depends on a comparison, which indicates that data used in the test can be compared in a way of not comparing an apple against an orange.

For the above reasons, small population trials will not work at high probability, so researchers come up with an idea of conducting large randomized trials. The idea is that when the number of test subjects are so

large, the effects from those randomized variables are most probably canceled. The reasons are that both sides will have similar contributions, similar erratic effects, similar non-linear effects, similar interaction patterns, etc. However, this approach has a different problem: the large number of patients will bring in all potential different causes. It will bring in all variances caused by three dimensions. The drug may work only on a small percent of matched patients. Moreover, it will have another problem: when the trial is so big, only a small number of variables can be controlled. In certain cases, corrections can be made against certain factors such as age, sex, etc. It is impossible to control everything including diet, exercises, emotional adjustment, etc. In most cases, most of those interference factors are widely open.

There are thousands of things that could not be controlled, those variables are entirely up to patients. It is possible that environment, culture, weather, etc. might affect trial outcomes. To correct this problem, the trial will be done in multiple nations and multiple locations in different times, etc. By escalating trials in population size, one may hope that all interference effects are canceled. However, it also further expands the size of variations to more dimensions. The chance of match between a person and population's may reduced to one of a billion. So, population trials cannot solve the problem. When the fundamental presumption is wrong, nothing can solve the population-and-person mismatch.

System optimization can achieve the best results by optimizing a large number of variables. All weak variables that are ordinarily present at the same time must be considered at the same time. If an important variable is omitted, system cannot be optimized to achieve the optimum state. Reductionism plays an important role in the failure of medicine.

## **5. Double Blinds Design Precludes Optimization Method and Mind Cooperation**

Double blinds design is often regarded as a required feature of population trials. The first recorded double-blind study was conducted in 1907 by W. H. R. Rivers and H. N. Webber to investigate the effects of caffeine. Double-blind methods came into prominence in the mid-20th century.

When double blinds requirement is used in a population trial, a patient does not know whether the patient gets a treatment or a placebo, and researchers do not know whether a patient receives the treatment or the placebo.

The patient blind component removes mind component from being part of the cure and thus prevents the CNS from cooperating in curing diseases. As ancient people knew, mind is a critical component for curing chronic diseases including cancer. Per the holistic model, mind and body are connected and interlocked. No healing is allowed if mind does not cooperate for healing. It is well known that fears and emotion distress work through

the amygdala, which is the most vulnerable part in the brain, chronic stress works through neuroendocrine regulation, and emotion distress can interfere with the CNS by impairing the hypothalamus to pituitary path and competing for the attention of the CNS.

More, recent findings reveal that chronic stress can increase cancer cell population at metastasis sites by more than 30 folds, emotional factors can affect cancer by many mechanisms, and fears can have adverse impacts on cancer outcomes. When patients are blind to their treatment status, patients are forced to deal with high levels of stress and fears. Thus, such trials generate more emotional force to defeat the benefits of the treatment. Under the double blinds protocol, a drug can have its effectiveness affirmed by a statistical analysis only if the drug's effect can trump the effects of mind. Such trials will less likely affirm the effects of slow-working healing factors such as lifestyle factors, exercises, diets, herbs, natural products, etc.

The double blinds requirement is intended to avoid bias from both researcher and patients. It is placed on a wrong benefit-risk analysis. It stresses drug credibility by making sure that no weak and slow acting drugs will be recognized. However, by precluding optimization method, it discourages and prevents researchers from using multiple treatment factors to cure diseases. The researcher's blind has an effect of forcing researchers to treat patients as an abstract "diseases." This blind component plays a big role in promoting the reductionist idea: any disease can be studies like statistical figures.

By removing mind cooperation and multiple factors optimization methods from experimental designs, the requirement allow the population trials to detect only "pure" treatment effects over massive experimental errors. Naturally, the requirement helps reach extreme bias: rejecting weak and slow treatments, but recognizing strong and fast treatments. Naturally, treatments developed under the double blinds can only control symptoms, but do not cure.

## **6. Inaccuracies Caused by the Binary and Arbitrary Scales**

By using population trials, medical researchers must use a binary system to define diseases: any health property can be classified into Yes and No states; and any properties can be categorized by fitting into arbitrarily set ranges like good or bad; and any abstract concepts can be compared and counted like physical objects. Those practices are routinely used in designing treatments, selecting patients for the control, and defining diseases, etc.

(1) A binary system with yes and no status is misapplied to all health properties except death and living states. A vast majority of health properties are continuous. In the gray world which is often defined by continuous properties, every health question has been attempted with yes or no answer solely due to the reduction reasoning convention. In reality, under the holistic model, everything in the body must be in balance. Even in a machine, cer-

tain level of balance must be maintained among components such as cooling and combustion systems.

Similarly, all biochemical processes in the human body must be in balance in a quantitative manner. Lungs must be in harmony with the heart; the heart must be in harmony with the kidneys; and the kidneys must be in harmony with both the lungs and the heart, etc. The performance of each organ may take one of an infinitely large number of states. Optimal health cannot be achieved by using two binary states because forcing performance into two states can introduce enormous errors. As we have shown, chronic diseases are caused by tiny departures in the rate balance among biochemical processes, and such imbalanced rates result in structural changes by long term effects. Modeling health properties in a binary scale must introduce massive errors. When the binary scale is used in defining health properties for controls, treatments, diseases, or research conditions, etc. it induces massive errors.

(2) Categorization method is misused in medicine. Categorization is often used in courts to put descriptive properties into one or more categories such as good, bad, fair, improved, slightly improved, etc. This method can be arbitrarily used against natural laws. However, categorizing any health properties in an arbitrary manner is against natural laws which control human physiology. Categorization method may be used to compel humans to comply with laws, it cannot force the human body to change physiology and biochemistry. We must assume that modeling any continuous health property by fitting abstract properties into arbitrarily set ranges introduce massive errors.

(3) Objective references. Health property parameters deduced from a population are routinely used as references for individual persons, they reflect too much inaccuracies. Most such health parameters introduce huge departures like 50% while in reality, one percent departure from the personal ideal number in any of biochemical processes in balance can result in serious health consequences as a result of long-term effects.

## **7. Statistical Analysis Cannot Fix Population Method's Flaws**

All statistical analysis methods and interpretations are premised on the model assumptions; that is the model provides a valid representation of the variation we would expect to see across data sets, faithfully reflecting the circumstances surrounding the study and phenomena occurring within it. In other words, every model assumption including the test hypothesis must be correct [Greenland et al, 2016].

Statistical analysis has been widely abused in a long history [Campbell, 1974]. In our view, even flawed and misused statistical analysis can provide great incremental benefits for studying social and political problems if the findings, notwithstanding all formality flaws, actually make society better. However, this necessity-based approach cannot be used in medicine because



finding cure requires highest research accuracy. The use of statistical approach in medicine results in a massive portion of flawed studies. For example, 47 potential statistical errors and shortcomings, differentiated for the distinct phases of medical research are presented and discussed [Strasak et al, 2007]. A review concluded that nearly 50% of the clinical research publications contain at least one statistical error, some of which may have meaningful impacts on results and interpretation [Gore et al, 1977; Kim et al, 2011; White, 1979]. In an Australia analysis of surgical literature, 71 out of 91 analytical papers (78%) contained errors in the usage of non-descriptive statistics [Hall et al, 1982].

When the population-based method is used, it automatically incorporates unrealistic or unjustified assumptions.

#### **(a) Population Trials Lack Required Accuracy for Studying Chronic Diseases**

In any studies, one most basic assumption that detection method must be sufficiently sensitive relative to experimental errors. In a study, if an insensitive household scale is used to measure reagents in a chemical analysis, such a study would be meaningless no matter how the experiment is designed and how data is processed. In a traditional population study, the purpose is to identify a useful treatment or actual disease causes. To satisfy this requirement, a population study must be able to affirmatively detect treatment effects. Whether this requirement is satisfied depends on the nature of the study. A population trial seems working fine if the purpose is to study the effects of strong and fast treatments such as surgery and strong/fast medicines. In such a case, the treatment can “stand out” among all interference factors.

In dealing with chronic diseases, the purpose of conducting a population is to find disease causes and treatments for a disease. As we have found that chronic health conditions are caused by multiple weak causes and may respond to multiple weak and slow treatment factors. We have also shown that chronic diseases are a result of long-term effects of tiny deviated imbalance among involved biochemical and cellular processes. We also found that a best treatment must include multiple factors to correct imbalances. We have also shown that there are a large number of disease cause factor profiles and correspondent treatment factor profiles for different people. To cure the chronic disease, one must use the best matched treatment factor profile for a specific person. Therefore, the traditional presumption, a single treatment for all people, fails. The failure of this core presumption is catastrophic because degrees of mismatch between the population (e.g., an abstract person) and a specific person can be traced to the differences caused by genetics, phenotype, and mind. Using statistical analysis is like an attempt to improve study validity by making a massive number of measurements where a household scale is used to measure reagents in a chemical

analysis project.

Having shown the core flaws in the population study, we will explore several specific problems.

### **(b) Errors Caused by The Binary Scale and Other Statistical Flaws**

Three common practices that further distort results are the binary disease definition, disease binary classification methods, and selection of control groups. When a control in a study is faulty, finding in the study will be wrong. In a cancer research, surgery has been viewed as standard of care. All present chemotherapy trials are conducted by comparing a new drug with other drugs. However, the first treatment was developed on a presumption that cancer could be killed like a bacteria. Diseases are defined by the binary system like defining contractual consideration. However, all health properties (except death and living) are continuous and any infinitesimally small changes must be presumed to have health significance, chronic diseases are a result of tiny rate imbalance in health properties that are continuous. The binary system is used to "digitize" such health properties and thus must introduce massive inaccuracies and errors. A yes and no scale just cannot have the accuracy for measuring a tiny departure from a balance. As a result of this conversion of data defining disease properties and treatment benefits, the population study is unable to support high accuracy and reliability necessary to correctly characterize subtle imbalances. Arbitrary categorization methods also routinely introduce massive errors in studying chronic diseases. Digitizing health properties violates natural laws. In this respect, we must find that the holistic model does not rely on controlled studies and thus can avoid massive data distortions. When those sources of errors are not removed, whatever a researcher does will not change results.

Errors introduced by data binary conversion are further compounded by additional errors attributable to race, genetics, age, sex, diet, life styles, drug use histories, other interactive compounds, and health condition, mental state, etc, the findings in most studies do not reflect reality. This is why that medical research has produced a large number of statistically significant findings, but could not yield cures for chronic diseases. The "science" characterized in medical publications is not consistent with the working in the human body.

### **(c) Conflicting Promises In Statistical Analysis**

We also show that statistical method is misapplied to many health properties. To see a problem, we first review a classical physical model for statistical applications. One purpose is to improve production volume  $P$  of cellular phones by using two production methods,  $T_1$ ,  $T_2$ .

$P_1$  produced by method  $T_1$

$P_2$  produced by method  $T_2$

In this hypothetical model,  $P_1$  and  $P_2$  are not two points on a

continuous cure. Due to random fluctuations, both P1 and P2 will appear as different profiles. Whether the difference between P1 and P2 is significant can be determined by a statistical hypothesis test. If their difference falls within the acceptance region of the distribution, the null hypothesis is accepted. In this case, the null hypothesis is used without against a known indication, and acceptance of the null hypothesis does not clash with known knowledge. If the two distributions are very close, it happen purely by chance.

Most health properties are different from properties like production volume. A health property is most probably continuous, and many natural variables such as glucose concentrations in blood are continuous.

$$H=f(V_1,V_2,\dots,V_n)$$

The value of H is continuous in concerned ranges. This property depends on a large number of factors  $V_1, V_2, V_3, \dots, V_n$ . When a disease happens, some or all of those dependent values departs from the optimum values. To restore the health property H to a normal condition, all of those values will be changed by  $\Delta V_a, \Delta V_b, \Delta V_m$  to achieve the optimum H value.

The glucose level from 100 to 170 mg/dL is expected to change continuously. We now, use  $V_1$  to denote glucose level and H to denote stored fats. If  $V_1$  is changed in a given time intervals by an infinitesimally small amount, H will change according to the expected effect of  $V_1$ . H must be infinitesimally different. Since we know they are different from independent medical knowledge (as well as common sense) before the study, the statistical hypothesis - whether changed H is different from original H - is logically absurd. For any change in  $V_1$ , there must be a correspondent change in H. While the change is infinitesimally small, that change is known, predictable and significant in curing chronic diseases. When one makes a null hypothesis, one actually assumes that two H values corresponding to two methods are same, which is against the knowledge of “infinitesimally small” change. The problem is especially serious when a treatment  $V_i$  can affect the body in long-terms and can work by interacting with many other weak factors.

Medical studies ignore differences between two known infinitesimally changing properties and two distinctive populations. The rationale of using statistical analysis can be justified only for practical utilities. One reason might be that statistical analysis will provide an error yardstick, allowing researchers to determine whether an outcome was caused by an experimental error. Thus, the statistical method has a practical utility in situations where accuracy is not important or misused statistical analysis can still provide desirable benefits.

Focusing on hypothesis test results is never the interest of patients. What is important is the infinitesimal chances that actually cure diseases. Patients' interest is not which one is significant and which one is not, but

that factors actually work. If a hundred variables in a treatment can be simultaneously optimized to achieve the best H, which is equivalent to dissolution of a health problem, the treatment is a cure. If a one-year treatment using the hundred variables does not cure the disease, two years of the treatment resolving the problem is still a cure. There is no point to ignore weak and slow curative variables. In optimization, uncertainty attributable to experimental errors will appear only once because H is not measured for hundreds of times, the true curative benefits of all variables will not be shadowed by experimental errors.

In contrast, by using the controlled variable method, one can find a treatment's contribution to H in each individual trial,  $\Delta H_i = f(\Delta V_i)$ . Randomization can make the contributions of some random variables uniform across the treatment and the control, but is effectively reduce variances attributed to differences among people in the population. Most of those variances will end up as experimental errors. When the treatment effect on H is weak relative to experimental error, it will result in a failure to recognize the weak and slow variables.

### **(b) Multiple Trials Cannot Resolve Variables Interactions**

The outcome of a controlled study depends on ratio of the treatment variable's effect on the health property and the effects of random errors. If change in health property,  $\Delta H$ , attributable to the treatment variable is small relative to the experimental error, even a true curative effect will be hidden as an experimental error. We believe that the large experimental errors caused by interference factors result in failure to recognize infinitesimally small curative effects. Even assuming that  $\Delta H_i$  would be found for each of variables by several independent trials, the controlled variables method does not allow for determining contributions from interactions between any two variables.

The inability to determine interaction terms is also fatal because any biochemical process requires several steps, and proper functioning of a biochemical process depends on simultaneous effects of reactants, enzymes catalysts, mediators, reaction conditions, etc. Moreover, the same biochemical process may be interfered or prohibited by metabolites or products, mediators, regulators, etc. Any variables that can overcome the limiting effects of bottlenecks of biochemical reactions may dramatically increase the curative effects of other variables. Some variables can impact many points. The idea of solving health problems by using the controlled variable method is unrealistic.

Our analysis shows that statistical analysis and variable controlled method will result in systematic failure to recognize treatment effects. This is why an overwhelming number of medical studies could not affirmatively detect weak variable benefits, and is a main reason for failure to find cures for chronic diseases.

### **(e) Other Forms of Statistical Error**

Statistical abuse is an unavoidable consequence of the population-based medical model as it is used for studying chronic diseases. The deduction model provides great incentives for abuse. In the current medical research culture, when a research problem is unfit for a statistical analysis, it must be transformed to one that can be analyzed statistically (e.g., sham needle). When a research design is motivated to meet publication requirements, such a study loses scientific merits.

Statistical analysis is often used to create a misleading scientific validity. P-value used in statistical analysis often has little meanings but mislead ordinary readers and patients. For example, suppose 50,000 patients showed an average improvement in symptoms that was statistically significant compared with another 50,000 who used placebos. If the improvement is only a trivial health property, the statistical significance derived from the p-value would likely have no practical value. A massive trial is not worth one complete cure in a paired comparison. In comparison, a treatment that can cure 20% cancer are far more valuable even if statistical analysis is missing or impractical.

### **8. A Challenge to Drugs as Cure for Chronic Diseases.**

Medicine has made an unwarranted extension that any synthetic drug can cure diseases. This presumption has been proved to be true and reliable in two circumstances: drugs from natural sources can cure diseases including chronic diseases; and both synthetic and some nature-made drugs can cure acute diseases including physical injuries, infections, poisoning, pains, etc.

The unwarranted extension of synthetic drugs can be seen from the synthetic drugs development history. In 1832, chemist Justus Von Liebig began the synthesis of chloral hydrate, a sleeping drug, marking the start of using synthetic drugs. The ability to make synthetic drugs in the early twentieth century was very limited. Among about 18 drugs made from 1901 to 1940 [N1, Sup], most are natural hormones, painkillers, antibiotic drugs, and anti-seizure drugs. Most of them were intended for brief uses.

It was not understood until decades later that synthetic drugs are different from natural compounds. Synthetic compounds were never a selection pressure in evolution and thus clash with gene-encoded products and metabolites at higher chances. When the drug definition was extended to include synthetic drugs, there were few court reports on drug-induced personal injuries and little knowledge about drug resistance. The human body has more than 20,000 genes which have been evaluated, it is impossible to bet that a man-made synthetic drug will not infringe any of gene-encoded proteins/enzymes and their metabolites. No one can prove that such a drug will not affect massive biochemical reactions and will not affect any of a large number of tissue structures in the body. Thus, the side effects of synthetic drugs are

inherent.

We also question whether synthetic drugs can ever help restore lost balance in the body. In treating acute disease such as killing bacteria and stopping pain, any treatment can go in one way to the end (like killing all bacteria and removing all poison, etc.). In treating chronic diseases, a cure cannot be completely disable biochemical and cellular processes, but must slow down or speed up certain biochemical processes. It is about correcting one tenth percents to a few percents deviations from an ideal balance. Whether the body state can be restored would depend on how well the treatment can control the rates of the biochemical and cellular processes. Drugs developed under the reductionist concept work at short time windows. In comparison, herbal, dietary, and exercise remedies can change rates of the biochemical and cellular processes. They do not have the power to seriously affect biochemical process as synthetic drugs. From medical publications, we see few attempts that are ever directed to achieving right rates for the biochemical and cellular processes. Rather, the drug concept is heavily influenced by a yes and no thinking used in deduction reasoning.

We have shown that when drugs were used in early human history, they were intended to restore lost balance. When drugs are extended to synthetic drugs and used in a way they are used now, they cannot cure chronic diseases, but only control symptoms.

## **9. Health Risks from Evidence-based Approach**

Due to influences of common law, medicine also accepts the idea that medical decisions are based on evidence.

One big problem with evidence-based approach is that medicine is incremental science, medical knowledge has progressed slowly with significant inaccuracies and errors in the past. The histories of cancer research and neuron-science research, discussed above, reveal that humans understood very little about cancer and the CNS in the early time. No one can bet that all correct medical knowledge has been discovered in those areas. There is no guarantee that all current medical knowledge is correct. If all medical decisions are made on basis of knowledge and understanding, a massive number of medical decisions would be wrong or poor. It is still an open question whether medicine has acquired sufficient knowledge so that patients can trust their lives to existing evidence.

The knowledge of the CNS is still very limited. It is unwise policy to refuse to recognize anything that has not been proved or could not be proved. Substantive meanings of neural signals are completely unknown. No one can preclude that neural signals exchanges may be far important than hormonal regulations. When a vast among of disease mechanisms are unknown, a sound approach is developing hypotheses on suspected functions, and then testing the hypotheses in a proper manner. Otherwise, no cure will ever be found until substantive nature of neural signals is understood. If a

evidence-based medical decision is made, which is actually contrary to natural laws governing the human body, the medical decision may have severe adverse impacts.

We suspect that the CNS plays a critical role in regulating the health of the body. If this is proved to be true, a disease or health condition is not simply functional and structural changes and cannot be cured by using a single or a few drugs. This hypothesis would have widespread impacts on strategies for treating diseases.

#### **D. Poor Performance of The Medical Model in Chronic Diseases**

We consider the last question, whether medicine has achieved reasonable performance so that a world's lives can be entrusted to the deduction model.

Medicine started emerging after the Industrial Revolution in the 18th century. Although medicine has dominated for several hundred years, it has failed to find cures for essentially all chronic diseases. Even if some people experience disease reversals, such reversals cannot be attributed to medical treatments in most cases. In the last 80 years, it yielded only medical discoveries but not real cures. Main evidence for its failure includes:

(1) The progressing poor national population health in the U.S. and the world. People cannot live their lives with full enjoyment in a predictable way. It is too often, people can suddenly die from incurable and terminal diseases and leave the world abruptly.

(2) Nearly all chronic disease are officially listed as incurable diseases in medical references. At the best, chronic diseases are labeled as “treatable.” See the long list of incurable diseases [Note 1, Sup]. In addition, cancer is still considered as incurable and terminal.

(3) Drug working mechanisms for a vast number of drugs are “unknown” or “poorly understood.” Synthetic drugs cannot cure diseases but often cause serious incurable diseases. Most autoimmune diseases are actually caused by synthetic drugs.

(4) The total number of premature deaths from chronic diseases is estimated to be 30 millions each year.

The poor performance of medicine can be found in cancer treatment. A systematic review [Ashdown et al, 2015] concluded the complete response of rates of chemotherapy to cancer have remained essentially static and locked at about 7.4%.” The complete response does not prevent relapse. A systematic review [Albero et al, 2016] of thyroid cancer treatment performance concluded: “Response rate was 22.1% (0-57%) for 13 studies, 25% for the 176 patients and 27.1% for the 70 patients, with 2.5, 3.4 and 2.8% complete responses respectively. A retrospective cohort study [Davis et al, 2017] found

that this systematic evaluation of oncology approvals by EMA (the European Medicines Agency) in 2009-13 shows that most drugs entered the market without evidence of benefit on survival or quality of life. At a minimum of 3.3 years after market entry, there was still no conclusive evidence that these drugs either extended or improved life for most cancer indications. A study which systematically examines the most promising cancer treatment methods concluded: "The claimed 'targeted' therapies that may or may not extend remission of cancer for a few months should not be accepted any longer as 'cure' by oncologists, scientist or patients...." [Maeda and Khatami, 2018].

The complete response rate of 7.4% is very high compared with match probability of health properties between two persons. An obvious reason is that cancer drugs are developed by focusing on only a few properties that affect cancer cells numbers.

The inability to find cure for chronic diseases has resulted in huge burden on each nation and the world. In a study released by the Milken Institute, the annual economic impact on the U.S. economy of the most common chronic diseases is calculated to be more than \$1 trillion, which could balloon to nearly \$6 trillion by the middle of the century.

This poor performance is a factual finding that does not depend on any theory. We predict that any treatment which is based on dualism, reductionism, and population-based medicine is destined to fail. The lack of progress in finding cure is strong evidence that the deduction model is to blame. Chronic diseases must be addressed in a holistic way with mind as essential curative component.

## **E. Comparative Analysis Of Holistic Model**

The reduction model is not objectionable in all use applications. It could be a tool for studying disease mechanisms and acute health problems. We will show how the deduction model has been used as a weapon to invalidate medical research and treatment methods under the holistic model.

### **1. The Holistic Model Is Criticized By the Current Standard**

The reduction model not only affects medical research designs and medical treatment methods, but powerfully constrain thinking in medical research. The FD&C does not intend to preclude other cures. When the FD&C was enacted in 1938, legislation did not intend to use the functional approach as the sole approach to curing diseases. It did not define the double blinds experiment designs in the text. However, the impacts of this legislature has become uncontrolled with the help of other laws. It has become a powerful tool to invalidate any remedies or treatments that do not meet the requirements of the deduction model. One example shows how the medical community evaluates acupuncture and Chinese Medicine.



Acupuncture is not a drug and the treatment is intended to affect the nerve system. When needles are inserted into the tissue, it must generate nerve stimulation. Yet, such a treatment has been evaluated under randomized double blind trial protocol. Turning acupuncture into a blind treatment requires creative thinking. On article states: “No clear definition of placebo acupuncture exists, so we accepted the placebo interventions used by the authors of the trial reports, such as insertion of needles into non-acupuncture points or use of non-penetrating needles” [Madsen et al, 2009]. This definition makes the study meaningless. First, acupuncture does not require accurate points, and second non-penetrating needles still have the effects of acupuncture. Massaging in the nearby places would have similar effects. While design logic of those trials seems irrational, we note the population method is flawed on multiple grounds.

Another study concludes “...The evidence for the effectiveness of acupuncture for the treatment of primary dysmenorrhoea is not convincing compared with sham acupuncture. Further rigorous nonpenetrating placebo-controlled RCTs are warranted.” The authors accept the unproved and clearly wrong presumption that mind must not be the part of cure. In acupuncture, the needle stimulates the CNS and thus diffuses the focus of the pain. The experimental design dismantles this mechanism and the sham acupuncture has a similar effect of a needle treatment. It is natural to find nothing between a sham needle/off-point needle and acupuncture.

A study attempted to evaluate Chinese Herbal Medicine found: “An assessment of the research found that 41 of 70 systematic reviews of the scientific evidence (including 19 of 26 reviews on acupuncture for a variety of conditions and 22 of 42 reviews on Chinese herbal medicine) were unable to reach conclusions about whether the technique worked for the condition under investigation because they could not find enough good-quality evidence. The other 29 systematic reviews (including 7 of 26 reviews on acupuncture and 20 of 42 reviews on Chinese herbal medicine) suggested possible benefits but could not reach definite conclusions because of the small quantity or poor quality of the studies.” [Manheimer et al, 2009]

The flaw in this study is that it is based upon a presumption that population trial is only proof and statistical analysis can remedy flaws of population trials. Chinese medicine was focused on the whole body like system optimization method. In most cases, a full treatment for any serious health condition normally comes with food restrictions, lifestyle adjustments, massage, required avoidance, etc. Herbs are prescribed with different species and radios according to personal conditions. This personalized treatment model cannot be randomized. It is like a system optimization process intended to work on the whole body or on multiple organs. The study failed to note that most traditional treatments work at

magnitudes more slowly than surgeries and painkillers. Naturally, controlled trials are wrong methods for performance evaluation. If herb prescriptions were evaluated as synthetic drugs, their curative effects would naturally be hidden among the massive number of interference factors.

Most conclusions were based on “evidence quality” which is judged according to flawed deduction model. There is no way to find two persons which can be prescribed exact same herb species in the same ratios. Duplication of trials is impossible, and “poor data quality”, is an inherent characteristics of any system optimization methods, which are superior to any population-based methods.

Such critique articles show how medical professionals used the deduction model, which misuses population trial concept, to downgrade a the competing model, which has stood the longest time test in multiple cultures. If medicine accepts the balance theory, it cannot insist producing statistical data, but must look into each person and determine whether the disease is improved or cured for each individual case. Like car repair, any car owner can instantly know if a car has been properly repaired. There is no point to look at a population of cars.

We have noted different problems with the holistic model. Such model depends on the doctor’s experiences. So, selecting doctors will be important. This factor determines that the performance of quack doctors and renowned doctors may not be combined and averaged. A good mechanic can repair car but a bogus technician may just rip off car owners. Another problem is that, some modern herb doctors have turned the holistic model into a half of deduction model to yield to pressure of quality critiques. They used identical prescriptions for all patients like a standard of care. Thus, such a treatment naturally defeats system optimization benefits and transports all flaws from the reduction model into the holistic model. To pursue fast results, such a commingled model ends up with controlling symptoms only. Still another problem is the risk of the toxic effects of pollutants on natural products. Herbs and animal products are often used on a long term basis. If herbs are contaminated by pesticides and herbicides while animal products contain abnormal fatty acids, hormones, and antibiotics, the use of herb formulations on a long-term basis may result in accumulated toxic effects. When correcting a disease and making a new disease take place on the same time scale, one must be careful with selecting herbal sources. Those reviews did not pay attention to those real issues that are critically important to patients.

## **2. No Medical Model Should Serve as a Super Standard.**

The practice of using the deduction model to invalidate other medical research and treatment methods is not intended by law. Both models can be used to improve overall medical performance.

The mankind's common interest is not in resolving which medical

model is right or wrong, but finding cures for diseases or improving public health. The sole judgment standard for evaluating a medical model is the ability to find disease causes and the ability to deliver cures. The ability of a medical model depends upon what specific diseases are concerned. bloms and delivering cures in their own competent areas.

Assuming, we have two medical models. The first is the deduction model as it stands, which is developed from the functional approach. The second one is based on the holistic model, which is based on required balance among multiple organs in the body. The holistic view requires consideration of mind. We will compare those two medical models.

To make our arguments, we further assume that the CNS orchestrates the whole body and thus protects disease state like a mind-and-body interlock. Thus, chronic diseases cannot be cured by working on the body only. We further assume that to cure diseases, changes must be made to the CNS regulatory functions. If the law had legalized nature-made drug formations for improving the balance of multiple organs and treatments to alter mind or the CNS, we would see a completely different medical landscape now.

Under the holistic model, all studies have to be made on individual basis. Each study will look at a variable pattern - five things or tens things - are combined to cure a disease. The validity of such a study cannot be determined by using statistical methods. The credibility can be established only by repeating the same or similar pattern by one or more times. If the same results were found in two or more times, the finding could be presumed to be good. This medicine would require considerable experiences to be successful. This method would reject evidence-based approach, binary disease definitions, statistic analysis, double blind requirement, randomization, etc. The holistic model is like the car repair model currently used in auto shops. It focuses on the whole body and mind.

If the holistic model controlled the medical landscape, it would invalidate each of research findings and each treatment method that have been developed under the deduction model. It even can rely on a portion of valid medical discoveries acquired from the reduction model to invalidate the reduction model as far as the model is used to study and treat chronic diseases. Since the reduction model controls medicine, it is not strange that everything developed under the holistic model can be criticized or even invalidated under the standard of the deduction model. When the two medical models are so different, one cannot use one of the models to evaluate the merits of research findings achieved according to the other model.

The deduction model cannot be viewed as an absolute standard. It has some advantages in establishing disease causes and mechanisms, discovering potential treatments for acute diseases, and promoting technologies in surgeries and pain management, etc. The deduction model is simple to use in studying and treating acute diseases. However, the deduction model has

failed to deliver satisfactory results in treating chronic diseases and terminal diseases, and revealed many fatal model flaws. By introducing massive errors and inaccuracies, the deduction model has failed to catch a massive number of health injuring agents and weak treatment factors, and will put human civilization at peril, unless a firm brake can be applied to stop the adverse impacts of massive pollutant chemicals and chronic diseases.

The deduction reasoning used in the reduction model is not unfailing. This process is based on simple logic reasoning for a simple system. Potential flaws can be found in promises, application of rules and conclusion. Promises such as using a population to represent a person in a vast number of health properties is wrong. Use of such a premise could preclude finding cures for chronic diseases. Imposing such a premise will make the holistic model fail. Most research tools used in the reduction model introduce massive errors and inaccuracies. By insisting that the using of such tools is required, it forces other medical models to introduce inaccuracies and errors.

Even the practice of getting a single conclusion in reduction model should be questioned. This practice was essential in common law court because judges must settle each case only in one way. Findings in reduction model are too often expressed in yes and no outcomes (e.g., whether acupuncture is valid). Conclusions on health properties and treatments cannot be expressed in yes or no outcomes. Beside a few health properties, most health properties do exist in a spectrum of continuous properties. Most of them interact with other health properties plus an unlimited number of other factors including genetics, environment, culture, etc. In addition, such health properties interact with mind. The gigantic number of body-and-mind interactions and body-and-external factors interactions cannot be accurately predicted by simple logic reasoning. When the reduction model is used as a standard to judge the merits of the holistic model, it will constrain the medical development. Therefore, the merit of a medical model must be evaluated by examining the benefits of its treatments, without regarding any standard used by other medical models.

The judgment for model merits should be flexible and should not be limited by mechanical application of devices. In evaluating medical models, one should be aware that the merits of a medical model can change. A medical model may be poor or useless due to inability to implement an essential component. The weakness may disappear when later medical discoveries can find the missing component. Organ-organ interactions and mind-and-body interactions were not provable in the past, but knowledge for proving both types of interactions are forthcoming rapidly. Both types of interactions are indisputable facts now.

If a medical model can cure diseases, society must recognize the model. It is very unwise to freeze the medical model as the only a judgment model by law. Due to the inflexible nature of law, freezing medical landscape

by laws will result in massive damages to public welfare and such harm can befall on any person and frustrate anyone's life in an unpredictable way. The deduction model promoted by laws have in part impaired at least several generations of people by precluding cures that would have been found long ago under the holistic model.

### **3. Advantages of The Holistic Model**

Now we will briefly show main merits of the holistic model.

(1) The holistic model has withstood for the longest time test. It is found in multiple cultures as China, India, etc. This is particularly important when this model was developed by multiple cultures. This implies that massive efforts were made in discovering this health model. The holistic model is based on wisdom of generations of early medical practitioners and the amount of time for formulating it is predicted to be many magnitudes more than the time used in developing the deduction model. Given current knowledge in cancer, the CNS and autoimmune diseases, we cannot rely upon the unproved presumption used in the deduction model. There is much strong reason to believe the holistic model than the reduction model.

(2) The holistic model can be practiced by using only partial or full system optimization methods, which are superior to the population-based method. In using the holistic model, treatment must be based on individual patients, but not on a population. The holistic model will have a similar advantage of the auto repairing model. In addition, it does not need to use controlled variables, double blinds, statistical analysis, etc, all of which are irrelevant to patients' interests in having diseases cured, and thus do not introduce too many and too large errors. It is capable of accumulating all slow and weak treatment effects. If the method is used to study toxins, it can show accumulative effects on the person, but not clear-cut conclusions in publications. We predict that full optimization can increase curative effects of treatments by one or more orders of magnitudes.

(3) The optimization method requires use of multiple corrective factors to treat diseases. The idea is completely different from the idea of controlling variable method from reductionism and dualism. The purpose of optimization is not to find which treatment factors can correct imbalance. Potential treatment factors are dietary adjustments, lifestyle changes, mind regulation, massages, herb formations, etc. A large number of the factors may be used simultaneously for a long time. When the treatment involves multiple treatment factors, some patients may respond to most of the factors, some may respond to several of the factors, some may respond to one or a few. It clearly avoids a total missing or lost in the forest as discussed in two statistical cases. The chances for a mismatch between all treatment factors and a person's is thus very low. The "weakness" of the optimization method is that patients may never know which of the factors cure the disease. However, this is not the interest of patients because they do not resell cures to others.

(4) Treatments under the holistic model reduce the time needed to hit a match between treatment factors and a patient. Under any medical model, disease causes and personal health are difficult to study, it is inherently difficult to tailor prescriptions for individual patients. Precise treatments are generally impossible under any medical model. Under the reduction model, a doctor has to keep trying drugs one by one. Treatments under the deduction model can spend too much time. If all drugs have obvious side effects, the attempt to find a matched drug slowly harms the patient's health. Generally, a large number of man-made drugs cannot be used in optimization method under the holistic model, but only lifestyles, diet, exercises, natural products and massages, etc. are safe candidates for use. Holistic model can save time for trying out a large number of low risk treatment factors.

(5) Optimization method is to find an optimal health point. The optimization treatment can utilize knowledge acquired by experiences and knowledge acquired from the deduction model. It is not constrained by professional formality, experimental designs, personal bias, etc. It has its own way to judge treatments. It does not require that a treatment trial affirmatively answer a medical question with a statistic reliability. It is an open model to accommodate new knowledge. It will not have a problem of freezing medical landscape like what the deduction model has done.

(6) The holistic model does not have a record of failure. While its performance in human histories cannot be judged by using statistical method due to its unique nature. Statistical analysis is not and should never be the sole standard for judging scientific validity. As we have demonstrated, statistical analysis can be disastrously misleading and incompetent. As indicated by the car repair model, lack of statistical analysis is never be a real problem. In healing art, people know whether their health conditions are improved or whether their diseases are cured. The first-hand experience in feeling health improvement or disease reversals has the same reliability as inspecting a repaired car. The ability to judge medical merit by ancient people is not any poorer but much better due to their great reliance on experienced-based medicine. Only perceived "problem" is that patients would not correctly attribute their successes to any particular factor, which should never be a thing of significance, and is actually improper question in the first place. The legally promoted practice of treating statistical data as the sole proof is responsible for creating the strange world where abundant healing miracles happen contrary to the claim of lack of cure in medicine. Lack of cure is clearly a result of using the reduction model to chronic diseases.

(7) After the basic medical knowledge has increased, much more variables can be included as optimization factors. Thus, the holistic model can take advantage of new medical knowledge to conquer medical problems. This is like combining a best model with the portions of right knowledge to achieve the best results.

(8) By restoring true power of the holistic model, medicine can quickly expand its research to understand the roles of exercises and deep secrets of mind. It will open up a new field for studying the roles of a large varieties of exercises invented and accumulated in multiple civilizations in more than 4000 years. Due to dualism influences, modern people have failed to appreciated the role of exercises. While we cannot overstate the potentially vital roles of exercises in healing diseases, we hope that the future research will rediscovery the most variable assets that modern humans could ever reinvent in our times.

(9) We believe that the holistic model will be essential to conquer cancer. All evidence we have seen points to the fact that multiple factors and mind are part of the disease and also part of the cure. Exclusion of the holistic model and other alternative model is same as betting the entire medical research future on a deduction model. Two hundreds of failure to find cures is too big human life price to be ignored.

(10) We assume the Central Nervous System (CNS) plays a controlling role in chronic diseases. Based on evidence, mind is clearly component for holding up diseases. It is possible that nothing can ever cure chronic diseases unless mind is altered to cooperate with the body. If we call it as a bet, it is biggest bet in the human history. Each year's delay would result in massive more premature deaths. We invite the medical community to explore new medical research and treatment strategies so that cures for terminal diseases will be found rapidly.

Given the failure to find cures for chronic diseases in the medical history, the world cannot continue entrusting human lives to the deduction model. The deduction model must be limited in application because it was adopted without careful deliberation, has never been validated thereafter, and is clearly against mountains of new medical discoveries. After the model is added with new research tools such as population trials, controlling variables, randomization, statistical analysis, etc, it induces massive errors and inaccuracies. This model cannot produce accurate and reliable results required for studying and finding cures for chronic diseases including cancer.

## **CONCLUSION**

Chronic diseases can randomly terminate human lives by very high chances, and make human life journeys unpredictable. Chronic diseases caused about 30 million annual premature deaths globally. In this incurable era, medical professionals must search for causes of the failure of medicine in finding cures for chronic diseases. Based on overwhelming evidence, performance data, and hypothetical model simulations, we found that the medical model is unfit for studying and treating chronic diseases even though it is

useful for studying fast and strong health properties or treatments. We summarize our findings in the following table.

Table 6. Itemized Flaws of Research Methods in the Reduction Model

Deduction model Elements	Potential Basis	Valid on What Condition	Rejected on Evidence or Flaws
Function- or disease-focused approach.	Machines.	Individual unit made of the same blueprint.	When it is used in a population study: there is a mismatch between population and a person.
Dualism	Machines.	Strong and fast health properties or treatments like surgeries.	Discoveries in neuroscience, cancer and other medical research, and poor performance of medicine.
Reductionism	Machines.	Strong and fast health properties or treatment like surgeries.	Multiple findings cannot be applied to human body separately to restore lost balance, the body cannot reconstruct reduced “parts” in the body.
Population trial with focus on one single or few factors.	Presumed to be valid and appear to work well in studying fast and strong effects.	If the factor is stronger than all interference effects (e.g., surgeries, antibiotics, poisons, pains, etc.	Rejection is based on: population-and-person mismatch; hypothetical blood pressure case; hypothetical cancer case, two statistical simulations; massive inaccuracies (the binary scale, categorization, and control selection); the poor performance of the model; etc.
Population trial for studying a weak and slow factors in each trial.	Unproved, misused, and invalid.	Unable to recognize any weak and slow factor as a treatment factor or a disease cause.	Same as the above.



Population trial for studying diseases with too many interference factors.	Unproved, misused, and invalid.	It is valid only for studying a super strong factor that can stand out of all interference factors.	Same as the above.
Statistical analysis.	Empirical utilities for improving reliability.	If the variable or treatment to be studied is much stronger than combined effects of all other variables.	Population trial, human 3-ways of variances, the binary scale, and categorization, etc. introduce massive errors relative to the treatment.
Synthetic drugs as cure.	Based on natural products as cure.	For fast and strong effects such as bacteria, poison, injuries, pain, etc.	Latent drug side effects, and lack of thinking for restoring lost balance.
Double blinds design.	To avoid research bias.	If mind is really not a required component.	Mind plays roles in cancer, other chronic diseases.
Evidence based approach.	Common law court: No evidence is same as not existent.	If a decision affects human life, lack of knowledge of something is not a basis for assuming it does not exist.	Medicine is an incremental science reflecting massive errors and inaccuracies. Must exercise wisdom when knowledge is unavailable.
Treatment model.	Apply population derived treatment protocols.	Valid for strong and fast treatments.	Mismatch between a population and a person; Findings under the deduction model cannot be reconstructed in the body to achieve balance.

By studying model properties, we found that population-based research method is extended by mistake to studying chronic diseases because it is attempted to match health properties of a population with those of an individual person by ignoring massive number of differences generated by genetic differences, phenotype differences and mind differences. The chance of finding a match between a set of population-derived properties and those of a specific person is practically zero. By studying medical discoveries, we rejected dualism as far as it is used to study chronic diseases. We also found

that the functional approach and population-based research combination was adopted in medicine without being unproved, has not been validated as the model after its adoption, but has long be refuted by mountains of medical evidence.

By creating hypothetical data and examining model performance, we found that the one-treatment-for-a-population presumption is clearly wrong. because it clashes with the massive variations in health properties that can be traced to personal genetics, phenotype and mind. The massive variations are demonstrated by a high blood pressure model and a cancer mechanism model. We further found that statistical analysis method cannot remedy all fatal problems in population trials, and that statistical analysis cannot fix inaccuracies problems.

We further found that other associated research tools including evidence-based approach, binary disease definitions, variables-controlled method, and patient-treating method are unable to correct any of those identified model problems. Those methods actually introduce additional errors and inaccuracies; that the deduction model is good only for studying fast and strong health properties or treatment, that the findings from the deduction model cannot be reconstructed in the treatment phase to help restore lost balance and that the misuse of deduction model together with the population trial is primarily responsible for the failure of medicine in finding cure for chronic diseases.

The population study approach and randomized population trials should be abandoned because it is impossible to resolve the conflicts among the massive population variances, the high accuracy requirement, and weak effect of useful treatments or health properties. After conducting comparative analysis, we found that the holistic model should be used as the primary model for finding cures for chronic diseases including cancer.

To end the incurable era, Food and Drug and Cosmetic Act, the U.S. patent law, and U.S. federal tax laws and state health care laws should be reformed to provide sufficient incentives for developing treatment protocols based on system optimization methodology. Leaders of all nations are urged to reform their laws to avoid providing incentives to further misuse of population trial designs in studying chronic diseases and provide incentives to use lifestyle factors such as diet, exercise, mind regulation, etc. that could actually cure diseases.

## **SUPPLEMENT**

1. Per List of drugs by year of discovery: wikipedia: the drugs made before 1940 include: adrenaline(natural hormone, 1901);oxytocin (natural hormone, 1906); arsphenamine (antibiotic for syphilis, 1907); phenytoin (synthetic drug, 1908); vitamin C (Natural compound, 1912); phenobarbital (for seizures, 1912); thyroxine(natural hormone, 1915); ergotamine (for migraine, 1918); metamizole (a painkiller, 1920); insulin (natural hormone, 1921); levothyroxine (synthetic hormone, 1927); penicillin (antibiotics, 1928); sulfanilamide (antibiotics, 1932); prontosil (antibiotics, 1932); cortisone (natural hormone, 1935); Tetracaine (a local anesthetic, 1935); methylphenobarbital (an anticonvulsant, 1935); dapsone (an antibiotics, 1928).

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