Population-Based Reductionist Measures Cannot Prevent SARS-CoV-2 Induced Global Health Crisis

A Compelling Need To Improve Personal Resistance to the Virus

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ABSTRACT

To predict how the COVID-19 pandemic progresses, we developed a systematic method for predicting disease outcomes. In the method, we evaluate how personal disease outcomes are mainly affected by viral concentration and exposure time and four defense mechanisms: human innate immunity/host response, acquired immune response, inflammation resolution and micro circulation, and the available space in the thorax cage. By considering how pandemic measures affect viral exposure and those mechanisms, we found many pandemic measures are misused or abused to deliver long-term adverse impacts. We noted that lifestyles have been changed as a result of movement restriction measures. By using the method, we found that altered lifestyles are predicted to raise infection rate, disability and death risks in the future. We show that a person can use personal, environmental, emotional factors to reduce infection rate and death risk. To prove the validity of this finding, we extensively examined medical research models, holistic and reductionist models, epidemiological models, disease risk factors, etc, and found that population methods are unfit for studying holistic health, statistical population does not exist in most clinical trials, mathematical models were misused for studying disease properties for a population, mathematical equations for modeling personal diseases are beyond human ability to solve, statistical models are misused, population-derived treatments are inherently dangerous to patients, vaccines have limited benefits due to unique lung structure and rapid RNA mutation, and immune system damage is caused by fast viral replication rate. We found that altering biological properties to improve the defense mechanisms could prevent a super majority of deaths and prevent the virus from reaching a point to damage the immune system. For vulnerable persons, such measure is a viable strategy for surviving from the pandemic. As a whole, holistic personalized medicine is more powerful than

population-based reductionist treatment by one to several orders of magnitudes. We urge people do their parts to force the medical establishment to abandon population treatment models that are responsible for failure of medicine and dissemination of misleading and factually wrong information on the effectiveness of medical treatments.

INTRODUCTION

After five months of global efforts in all nations, the pandemic has not been bright under control. Starting from middle of June, the case number has rapidly increased. By the hottest season, the daily reported cases have reached 75,000 on July 17, 2020 in the U.S. It is twice of the highest daily cases of 35,930 on April 24, 2020 [1]. The second wave of reported cases results in a second lockdown in some cities. The movement restriction measures have failed to stop the spreading of the virus. Our concern is adverse effects of the measures and their long-term impacts on population health. All movement restriction measures severely disrupt personal life, education, business and economical activities. From reading personal stories on blogs, we noted that those measures have driven people to crazy. This is very similar to the experimental biosphere 2 where eight hippies spent two years inside a dome [2]. They ended up starving and gasping for breath, and become crazy. The experiment was dismissed as non-scientific, and it does indicate how lockdown can adversely affect people in a long run. We believe that movement restriction measures are expected to have severe adverse effects on personal disease outcomes but their adverse effects could not be studied in medicine [3]. Recently, Dr. Fauci pointed out that stay-at-home orders could cause 'irreparable damage' if imposed for too long [4]. From reading personal stories about staying at home, it is possible to identify several classes of health properties that can affect personal health. It is well known that disease incidences and death rates are highly associated with certain risk factors [5]. It is possible to determine how movement restriction measures alter those known risk factors by long term effects. From those two lines of evidence, it is expected that home isolation, stay-at-home practice and lockdown, etc. adversely affect human ability to resist the virus. To find best strategy for reducing personal risk of infection and risk of death, it is essential to explore all factors explanatory of higher incidence and reduced death rate in the U.S. and the factors that are predicted to have definite adverse impacts on pandemic outcome.

One of the biggest unanswered questions is why some patients develop severe disease, whilst others do not [5]. The conventional wisdom based on overall immunity of the infected persons cannot explain this disparity [6]. Personal disease outcome must depend on rate competition between viral replication speed and immune response [7], and must also depend on lung structural characteristics [8]. Lack of durable immunity is similar to what is seen for influenza. Vaccine effectiveness can vary; studies show that flu vaccination reduces the risk of flu illness by between 40% and 60% among the overall population during seasons when most circulating flu viruses are well-matched to the flu vaccine [9]. Those studies imply that vaccines do not work on all cases, and vaccine effectiveness depends on personal health factors.

It has been found that controlled trials are improper methods for studying weak health factors when there are many interfering factors [10] and most of results of controlled trials are biased [11]. A large number of personal stories reveal repeated (2 to 5) infections within several months. Immunization by vaccines does not work in at least on substantial portion of people. The

effectiveness of vaccines depends on personal biological properties. Based on all those facts, secrets controlling personal disease outcomes are hidden in personal biological properties. Unfortunately, the population-based research model is not a proper method for exploring a large number of health factors. To avoid continuous failure in the war against the disease, it is necessary to study assumptions used in research models from biological aspects, and develop a method for identifying a matrix of biological properties that can be altered to improve personal ability to survive from the virus.

MATERIALS AND METHODS

This study uses all available data which tend to show the effects of health factors on viral infection and death risk. When the world population's lives are at risk, we must explore new research approach. We rely on data from four sources: one of the sources is research findings that establish how lifestyle factors affect human immune system and human resistance to the COVID-19 virus or other related viruses. Due to an extremely large set of study findings, we will cite only selected references, and treat others as common knowledge. The second source of data we rely on is media stories, reports from health care providers, personal stories, and our own observations. Due to noted flaws and biases of controlled trials, we give more weights to those sources of evidence. Moreover, we will ignore negative findings from controlled trials directed to weak factors. We take this approach because controlled trials are proved to be unfit methods for determining weak factors on theoretical basis, mathematical modeling (for the purpose of refuting the use of mathematical model), and overwhelming biological properties. If our analysis is based on a personal story, the point to be taken must be corroborated by similar stories, biochemical, cellular or structural mechanisms, or other rational explanations. We use them if facts in the stories cannot be evaluated by controlled trials and stories reflect the best evidence that we could find. The third source of data is data from simple mathematical models to refute or support a point of view. The fourth source of data is the performance data in disease incidence and death rates. As justification of this unique research method, we extensively discuss flaws in using clinical trials and mathematical models in medicine. No statistical analysis is used.

ANALYSIS OF EXISTING DATA AND FINDINGS

A. Failure of Current Pandemic Measures and Practical Problems That Pose Risks to Population Health

In the U.S. and other nations, major public intervention measures are personal isolation, quarantining infected persons, staying at home, social distancing in public places, wearing of masks, limiting people density in public areas. In the U.S., lockdown and personal isolation have been used by all states for different lengths. Personal, social and business activities have been severed disrupted. Countries and territories around the world have enforced lockdowns of varying degrees.

Some countries impose complete movement restriction while others have used partial restrictions [12]. In many countries, only essential businesses are allowed to remain open. Schools, universities and colleges have closed either on a nationwide or local basis in 161 countries, affecting approximately 98.6 per cent of the world's student population [13].

The failure in controlling this pandemic can be in part attributed to a variety of bad practices.

(1) In the old winter and raining days, customers were required to stand in long lineup in an attempt to control the total number of customers inside stories. When a customer is in chilly temperature or under rain for half an hour, their innate immune will be temporally depressed [8, 14-16]. This practice is expected to make people more susceptible to the virus and raise death rate [7] within reasonable time window of infection.

(2) In order to control customer number, some stores closed all doors except one for both entries and exits. This is a smart way to comply with administrative order without assigning more than one door attendant. However, this change results in poor ventilation. Exposure to viral load actually depends on more on the air volume per person than the static volume or space per person. If wind blow from two or more doors can cause rapid changeover of air, the concentration of the virus in unit of gene copies per unit volume must be lower. Many stores ceased controlling customer number but continue to have door closed. This one store with one door might be to raise viral concentration by one or more folds.

(3) Merge customers in one single lineup is another wrong practice. It is natural to use one line to enforce social distancing. So, all customers are forced to stand in a single long lineup. To compliance with the letter of social distancing, they even do not allow a customer to load goods before the front customer has left. This practice dramatically increases the time for making payments. Customers may have to stand for half an hour to complete payments. This doubted or tripled shopping time increase exposure to viral amount. In the summer, the chilling temperature in some stores would make people sick.

(4) Some stories have placed marks on the floor for each customer positions. Some lines may be arranged to pass by frozen foods sections (which are not closed in the hot summer). When customers have grilled at early 100 F outside the store, then suddenly chilled to various lower temperatures depending on where they stand, and then have to stand for several minutes next to freezing temperatures with only T short, this is the most effective way to make people capture cold and influenza. We found that the triple combos bad air, extended shopping time and hot-warning temperature cycling are consistent experienced in groceries stores. This triple combination cannot help stop the pandemic but make the situation worst then doing nothing.

(5) Lock-down everything is another unwise thing we have seen personally in Maryland. We like to exercise outside the door. However, the problem is we cannot go outside any more. Although most parks in Maryland are “open”, the restrooms were locked. Perhaps, those in charge might think that bathrooms pose risks of transmitting the virus and so shutting down both rooms is simple solution. They did not think about providing precaution to users, but simply shut them down as sure solution. What they actually achieved is to force people stay at home.

(6) Masks are misused or abused. Masks are the most powerful protective measure for avoiding exposure. Most people do not know the doubt roles of wearing masks [17]. We have seen people are wearing masks in wrong situations such as running in open spaces, driving cars in

limited-access highways, riding bicycles, jogging in very early morning (with no conceivable chance to get close to other people). Some people even wear masks in widely open spaces, private yards, private door ways, etc. While most people do not understand how particles in air move, but governments do not provide right instructions.

(7) Over use of disinfectants. Personal hygiene habits are important part of measures against the disease. However, some people are not taught to strike a balance. We have seen reports that people have used disinfectants excessively so that they have broke skin and cause skin infection and inflammation. If tissues are exposed, the body loses the strongest protection against the virus.

(8) To avoid risks of getting the diseases, people have completely changed their lifestyles. Most changes we have observed are staying at home, spending more time on watching TV, using cellular phones for more time, doing less exercises, eating more convenient foods (processed foods and junk foods), exposing more toxic substances, etc. Some self reported stories reflect that they gained ten to twenty pounds of weights.

(9) Death rates of chronic diseases are increasing. Due to the pandemic, people with chronic diseases are unable to take regular medical treatments. Some patients died from failure to receive necessary dialysis for end stage kidney disease. Some died sooner from existing diseases aggravated by severe emotional distress and worries. When movement is restricted, most people use worst lifestyles. While their activities do not show their adverse effects immediately, it is a matter of time to see their adverse effects materialized on the population in the long run.

Wrong measures, wrong practices, unwise options have been seen in all over places. They, directly or by their adverse impacts, depress human immune system, extend time to expose to the virus, raise viral concentration in the air, or ruin personal health. When long-term adverse effects start showing up, they most probably inflict more harm and good. Each of measures plays its role by multiple variables. When a measure is used to just control one variable, with all other variables uncontrolled, such a measure could be worse than doing nothing.

B. Known Factors That Affect Human Ability to Resist the Virus and Disease Outcome

The pandemic causes a good portion of persons to develop new lifestyles. We have identified inactivity and lack of exercise, emotional distress, monotonic activities, imbalanced nutrition, increased exposures to toxic substances, and excessive TV and cellular use as the most persistent adverse factors. Since temperature is an important factor in the coming winter, we will discuss it as well.

1. Temperature and fluctuating temperatures

Temperature is the most important factor affecting cold and influenza [14-16]. It would be surprising to rising disease incidence rate in the hot summer. Based on our observations, we attribute the rising incidence rate in the U.S. to temperature fluctuations to which people are exposed to. When a person in hot environment is subject to low temperatures, the body temperature is rapidly decreasing. This results in contract of the blood vessels. The degraded blood circulation is reflected in blue veins, blue lips, etc. It is expected that the micro-circulation conditions in the

respiratory tracks suddenly deteriorate. The lowered temperature temporarily reduces the body's immune system to fight the invading virus because white blood cells, which are much larger than capillary pores, have to squeeze through capillaries [8]. Normally, white blood cells (including those differentiated resident macrophages) have to squeeze through capillaries and tissues. Even through exact mechanisms for white blood cells mobility are not understood, we found that suddenly lowered temperature reduces capillary holes, but increase blood viscosity and tissue rigidity. Thus, temperature-induced impaired mobility of white blood cells impairs innate immunity and host responses against the virus. That is why cold, influenza and lung infections are facilitated by lower temperatures. The high incident rates in Florida, Texas, Georgia, Louisiana, Arizona, Alabama, South Carolina, Nebraska and Idaho can be explained by this extreme temperature cycling effect.

We also noted that nominal death rate in the U.S. has been dramatically reduced from round 20% in the cold season to lower than 10% in the summer. We attribute it to the benefits of higher temperature in patient recovery time. However, when temperature goes down in the winter, this protective benefit will disappear. Thus, death rate is expected to rise in the winter.

2. Overwhelming emotional distress and chronic stress

This is most serious negative factor to most world population. When people have to stay at home and cease all activities that are essential for the emotional health, this adverse effect will be realized by accumulative effects. Staying at home for two weeks can be a huge stress to most people. However, if people must stay home for several months to a year, the isolated lifestyle is expected to have severe adverse impacts on human emotional health. A body of evidence has shown that depression, chronic stress, and emotional problems can suppress human immune system [18-24].

In addition to the direct adverse impacts of a variety of emotional problems, the pandemic has created all kinds of additional life stress that can harm mental health. Various pandemic measures have caused business closures, disrupted normal education, disrupted professional services, disrupted necessary personal health care, stopped economic activities, and lost important life opportunities. A largest number of people live miserable lives and is under attacks of various sources of stress and emotional distress. The adverse effects will be realized by influencing other diseases and health properties such as wound healing [25-26] and chronic diseases. Those adverse impacts have been neglected in the U.S. If time is long enough, they can cause severe irreparable damages to population health.

3. Lack of exercise and inactivity, and increased degree of obesity

Exercise has been used as medicine in the entire human history [27]. Inactivity and lack of exercise has been causes of most chronic diseases [28]. Exercises have great survival benefits for all cancer types on nearly all kinds of patients [29-40]. Obesity is known to impair the immune system [41-48] and exercises are the most effect measures for curing obesity and improving the immune system. While isolation is an essential measure for controlling viral spreading in various situations, a good health and strong immune system are more important than just avoiding the virus. The importance of personal health is well reflected in completely different outcomes between two similarly aged persons. An infection can end up with no illness on some persons, but cause severe lung damages and even deaths on others [5]. The great differences in disease outcomes cannot be explained by personal genes alone.

All movement restriction measures have caused people to do less exercise. Based on online personal stories, we found that some people do not do exercise because they are afraid of being exposed to the virus; some do not do exercise because they hate wearing masks which are required; some live much static lifestyle because they are ordered to stay at home, etc. As a result of lack of exercise, a considerable number of people have reported weight gains. A gain of 10 to 20 lbs is a serious sign of compromised anti-virus capacity.

4. Reduced food choices and wrong food combination

Nutritional balance is essential for good health and strong immunity [49-59], but malnutrition can impair the immune system [51-52], and increase lung infection [58-59]. The need to avoid exposure to virus has forced some people to change their eating and shopping habits. They may shop foods at reduced frequencies, select fewer food varieties, reduce food quality, and pay less attention to nutritional balance. Some people buy more processed foods, junk foods, or packaged foods. The changed diet may result in nutritional imbalance and increased intake of heavy metals, additives, contaminants, etc. The diet affects the immune system by long term effects.

5. Misuse of face masks

Use of masks is the most important measure to prevent infection. However, mask can be a double-edged sword [17]. When there is no external virus source, wearing masks can be harmful. It can prevent or reduce the virus from entering the respiratory track, but the mask also prevents any internally generated virus and harmful by-product from exiting the respiratory track. One single judgment is which way the virus travels. Although, it is hard to make a call in some cases, it is a simple decision in many situations. A person should not wear a mask when driving in an open high way, running in a widely open space with no chance to get closer to another person, or is at home with healthy family persons. Some regulation imposing fine for failure to wear masks is too extreme because such rule discourages people from doing exercises in widely open fields.

6. Excessive time on using cellular phones and watching TV

When people are ordered to stay at home, they more likely than not spend more time on cellular phones and TV. Inactivity for as short as four hours can have adverse health effects [28]. Cellular phones and internet access can relieve stress from lack of communication with the world, they have their own problems. It is found in a Berkley study that those who used wireless phones for more than 25 years were at greatest risk—300% greater risk of brain cancer than those who used wireless phones for a year or less [60] and this finding was partially corroborated by a Danish study [61]. A contrary opinion was made by Scientific Committee on Emerging and Newly Identified Health Risks [62]. Given the severe limitations of randomized controlled trials [10, 11] and flaws of clinical trials and mathematical models, the no-harm option should not be trusted. Ignoring cancer data, the lack of personal interactions can have negative health impacts on personal emotion, and long-time use of cellular phones can hurt the neck and upper back. Excessive use of cellar phones with poor posture can hurt hands, the back and neck [a common experience]. Injuries in the neck and upper back could affect other parts through affected spinal cord. The lack of in-personal interactions can also raise the risks of developing mental diseases such as Alzheimer's disease. Excessive use of cell phones is predicted to reduce exercises, thus increase the risk of getting chronic diseases [28] and cancer risk [28-40]. This indirect adverse effect (via the immune system) cannot be refuted regardless of the effects of electronic waves on brain cells. Since the population trials are unable to resolve weak effects, we urge people to error on the side of caution.

7. Over use and abuse of disinfectants

The media has reported a number of stories reflecting overuse and abusive use of disinfectants. It was reported some people have damaged skin by over washing hands. The Environmental Protection Agency (EPA) has developed a mobile app that allows users to search an online database of more than 400 disinfectant products that can help prevent and reduce the spread of COVID-19 virus [63]. The virus has a crown-like spikes on their surfaces, known as envelope protein, and can be deactivated by disinfectants. Many brands may contain various chemicals such as alcohol, isopropyl alcohol, hydrogen peroxide, phenolics, quaternary ammonium compounds, chlorine and chlorine compounds, formaldehyde, lutaraldehyde, iodophors, ortho-phthalaldehyde (OPA), peracetic acid, etc [63-63.1]. It is possible wrong disinfectants are used in work places and homes. Most active ingredients are toxic, oxidative, and some are carcinogens.

Exposure to common quaternary ammonium compounds significantly impaired reproductive health in mice [64-65]. The harm should be extrapolated to adults by considering weak and long-term effects that cannot be determined by current research model. Some active compounds are known to have toxic and hazardous impacts on environment when released by evaporation [66]. In early five months of 2020, American Association of Poison Control Center reported 9504 alcoholic hand sanitizer exposure cases in children under the age of 12 years. Hydrogen peroxide causes toxicity via three main mechanisms: corrosive damage, oxygen gas formation and lipid peroxidation [67]. Concentrated hydrogen peroxide is caustic and exposure may result in local tissue damage; ingestion of concentrated (>35%) hydrogen peroxide can also result in the generation of substantial volumes of oxygen; and when the amount of oxygen evolved exceeds its maximum solubility in blood, venous or arterial gas embolism may occur.

The harmful compounds in disinfectants can get into the human body through cuts, contaminated foods, and air vapor. When disinfectants are spread in air, they get into the respiratory tracks by vapors. Absorption by skin and vapors cannot be easily prevented. The harmful compounds can be absorbed on skin and can enter the body through skin pores and sweat grands. Since the molecular sizes of most harmful compounds are much smaller than the pores and inter-cellular spaces, they can easily get into to bloodstream by diffusion. The amounts of harmful compounds entering the body depend on totol contact times, but cannot be determined and nor evaluated in any accuracy. Over exposure to disinfectants may not deliver benefits on each application instance, but can have adverse effects if too much of them have gotten into the body.

In the last five months, people have over-exposed to a variety of disinfectants; and some active compounds from disinfectants might have reached sufficiently high blood concentrations to damage health. Moreover, compounds from different disinfectants may find themselves into the person's body at different places and affect the same person by combination effects. For example, a person may be exposed to one disinfectant from a shop, another disinfectant from a fast food store, another one at a work place, and get another one from contaminated meals at home. Some disinfectants may be misused. None of the combination effects can be studied by known method.

We expressed an opinion that risk from contacting the virus is small [68]. Our findings are based our observation of China pandemic measures, where disinfectants and gloves were not widely used as they are in the U.S. Based on a recent review, the chance of transmission through inanimate surfaces is very small [69]. Moreover, the virus loses its potency with time, and viral amount is reduced by successive contacts.

8. Monotonic activities (related to inactivity and lack of exercise)

While movement restriction is essential for containing local outbreaks, personal isolation, lock-down, and staying home can have additional adverse effects through monotonic activities. People lose their normal life activities and varieties, and monotonic activities have adverse impacts on health. One reason is that all mental and physical activities require use of different neurons because all activities are controlled by the brain. If a person's life activities are very monotonic, only a certain portion of the neurons are actively and repeatedly in use. The inevitable result is that neuron usage is out of balance. Some neurons overwork while some neurons are in disused state for an extended time. The overused neurons or brain tissues are hurt like hand's carpal tunnel syndrome. The disused neurons slowly lose their functions for disuse. Monotonic activities are like doing too little exercises for some part of the body.

9. Unknown risks and poor ventilation

239 scientists across 32 countries published an open letter to the World Health Organization, showing evidence that the new virus can spread through the air and infect humans [179]. Their concern is relevant to an elevated risk in closed buildings. In a closed door environment with poor air ventilation, the required 6 feet distancing may have little protection. We provide a descriptive model to show how viral particles are accumulated in a poorly ventilated building and how the virus may infect persons inside. It is believed that the virus in very small particles may stay in air for about ten minutes [179]. It is safe to assume that the smallest viral particles would stay in the air for half an hour (use additional time as a safety margin). If an infected person periodically discharges the virus into air, the ventilation will spread the viral particles in the air. If multiple infected persons inside the building periodically discharge viral particles into the air, the viral concentration rises by cumulative effects even though viral particles also fall onto the ground from time to time.

The ventilation system accompanied by human activities may stir up the dusts and bring some dusts into air, but cannot to bring them out of the buildings due to design problems of old ventilation systems. It is possible that some viral particles on the dusts on the ground may be brought back to the air before the virus has lost infectious power. The building is like a chamber from which viral particles are added to and removed from. Viral concentration may reach a steady state (at any time, there is some level of viral gene copies). Even though the virus cannot stay active very longer in the air or on the ground, the virus may maintain infectious power much longer after they have landed on human respiratory tracks. Thus, the viral copies inhaled into the respiratory tracks in the morning may still have infectious power when more viral particles are inhaled in the afternoon. In this way, active viral particles can be accumulated in the respiratory tracks for much longer time. Large amount of viruses have stronger infectious power according to collective infection theory. Even masks cannot completely eliminate this infection risk for those with compromised immune systems.

While the collective adverse impacts of those factors cannot be determined by any controlled trial, their combination efforts are expected to be very large. If society continues allowing those adverse effects to be materialized, we expect to see the worse global health crisis in the future. We predict that death rates for most chronic diseases, and death rate and disability rate for the COVID-19 disease will rise dramatically in the coming winter. The overall war will end up with higher death rate, disability rate, and disastrous economic downturn.

C. Adverse Effects of Pandemic Measures Cannot Be Accurately Determined By Using Existing Medical Research Models

When there is a clear sign that the current population-based measures have made humans more vulnerable to the virus, we will appraise those effects even though population medicine could not. We will examine why the population-based medicine fails.

1. Flaws and limitations of current research model

The long-term adverse effects of personal isolation cannot be determined by using existing research methods [10]. Randomized controlled trials, or any kind of well controlled trails, are incompetent for determining any of those individual adverse effects. This is a scenario that each weak factor cannot be revolved because it is interfered by hundreds to thousands of other factors that have similar levels of effects. Each of the interfering or co-causal factors cannot be determined or rejected as errors. Their combination effects are beyond human ability to assess by direct evidence. Implied by biological pathways and multiple disease-controlling mechanisms, it is reasonable to expect that the factors interact in a complex manner and no mathematical model is able to characterize their interactions. Randomized controlled trials do not have the power to overcome sensitivity limits [10].

2. Flaws and limitations in early statistical studies

Past studies done by Altman, Senn, Zhao and Berger have made a predetermined assumption that human beings can be treated as a statistical population for any health and disease properties [70-75], without exploring the effects of all interfering and co-causal factors in human bodies. This presumption had existed for several centuries and become well accepted. It had been beyond challenge. By using this presumption, all extremely complex health and disease properties can be treated as random events like rolling a dice or blowing colored balls from a lottery machine. After examining disease mechanisms and existing data, we found that no disease happens like flipping a coin and blowing colored balls. In addition, the unit additivity assumption and an implied random error assumption fail to hold in nearly all trials for studying chronic diseases. In addition, mathematical models used in statistics are far too simple to represent health properties that control disease outcomes. We found that no mathematical model that we can conceive in our widest imagination is able to meaningfully characterize the extremely complex biological pathways and their interactions, the multiple interactive disease mechanisms, factor-factor interactions, and the structural features of tissues and organs. The statistical models used in their studies may be good enough to study crop yields and reactor production volume.

Due to a historical development reason, they could not pay attention to biological properties. Flaws in those studies can be summarized as follows: first they made a presumption that disease and health properties can be studied like drawing events and that all human beings in a treatment group can be treated as a statistical population. They then made an assumption that disease or health properties can be mathematically added up and divided to yield a mean for the presumed population. In doing so, they actually made another assumption that health properties are fungible and exchangeable, and all uncontrollable interfering factors do not exist or can be neglected as random errors, and failed to examine how interfering factors affect health properties under investigation and how their plus and minus effects distort analysis outcome. In the process, they did not have the

vantage to see an irrefutable evidence that most so-called errors are not true random errors that have been seen in statistical trials, but a combination effects of hundreds to thousands of interfering or co-casual factors. Without seeing external evidence, they were not in a position to compare the effects of a treatment with effects of interfering factors, and naturally found there is no need to be concerned with baseline balance for making valid statistical inference. By ignoring the distinctiveness of personal biological properties, massive interfering factors and their complex interactions, the relative size of uncontrollable interfering factors and true measurement errors, and relative sizes of treatment effects and combined effects of interfering factors and measurement errors, they never proved that disease properties can be treated as statistical populations.

Past studies share several common errors: They treated human beings as all apples while they are like sesames, apples, oranges, watermelons, etc. as far as their health and disease properties are concerned. They assumed the errors happen like those in statistical sampling in conflict with abundant evidence that the treatment has different levels of effects on different persons, that magnitude of measured errors can be larger than treatment effects; and that interfering factors often have plus and minus effects, with sufficient magnitudes to distort trial results. If this statistical fix were correct, we could reach absurd conclusions that controlled trials have the power to resolve contributory effects of any weak factors; valid scientific research did not depend on separation method and detection technologies; and research sensitivity limits could be overcome by running bigger clinical trials followed by doing a statistical analysis. Each of those conclusions must fall automatically.

3. Flaws and errors reflected in development history of clinical trials

The development history of clinical trials reveals that clinical trials were developed by adding components piece by piece by different contributors in several centuries [76]. When clinical trial was first used, there was no need to examine statistical population because statistical analysis was not a part of analysis methods for clinical trials. Population used in the early human history just means a collection of members, and early medical researchers naturally used population to study diseases because it always created a false impression: a treatment capable of curing more persons must be better than one that does not. This is still a reason for convincing researchers. In the early days, there was never a need to examine the population of biological properties or health and disease properties. Before about 1980s, medical researchers could not see differences in personal genomes, environmental factors, emotional states, etc. and the overwhelming evidence on effects of a large number of health factors on disease initiation and outcomes. The 1747 scurvy trial conducted by James Lind contained most elements of a controlled trial. By 1946, all components of randomized controlled trials have been added. It is fair to infer the clinical trials have gained general acceptance in the 60's [76] without using statistical analysis. By that time, much of the huge amounts of biological properties were unknown. Decades after clinical trials gained general acceptance, a large number of researchers started looking into human genome, biochemical pathways, environmental factors, and lifestyle factors, emotional problems, etc. The effects of a large number primitive factors on diseases have been established by tens of thousands of studies mainly after 1980 [One could find all references after 1980]. Even though, a good portion of studies are based on population approach, affirmative findings in those studies suffer inaccuracy by various degrees. Nevertheless, those positive findings have firmly established that differences in health and disease properties cannot be treated as random errors, and there is no statistical population as far as health and disease properties are concerned. Unfortunately, the massive evidence has not caused medical researchers to revisit the core presumption of population in the last a few decades. We have

shown that effects of massive interfering factors are responsible for trial outcome uncertainty. When the nature of interfering factors was not understood, it was natural to attribute the trial outcome uncertainty and conflicting findings to experimental errors. It is natural to try to solve this problem by using misapplied statistical analysis.

Statistical analysis was added to clinical trails as one of final a few last components. Misusing statistical analysis of data from clinical trials is clearly reflected in the development history of statistics. The origins of statistical theory lie in the 18th-century, but improved experimental design, hypothesis testing methods, etc. were developed in the 1910s and 20s by William Sealy Gosset, and Ronald Fisher, and further refinement was made in the 1930s [77]. Hypothesis tests are used to determine whether experimental positive outcomes are really caused by the treatment effect or due to uncontrollable experimental error. Use of hypothesis tests in clinical trials started centuries after the initial use of clinical trials and more than a decade after the formation of modern clinical trials. Major development for adding statistical analysis to clinical trials took place from the 30s to about 60s. At that time, medical researchers still did not have the vantage to see and understand the nature of hundreds to thousands of interfering factors in human body and naturally expected statistical analysis to solve outcome uncertainty.

The use of hypothesis tests is a futile attempt to address experimental uncertainty. This time line demonstrates that the “population” presumption was made for lack of knowledge, statistical analysis was misapplied as a wrong fix for clinical trial outcome uncertainty caused by interfering factors, and nobody knew about the effect degrees and nature of interfering factors when hypothesis was first introduced. While hypothesis tests are not wrong in theory, they can address only experimental uncertainty that are truly caused by uncontrollable random errors that happen like flipping a coin, blowing colored balls out of a chamber of a lottery machine, or rolling a dice. The random errors must be ones that cannot be altered by conscious human action.

An implied requirement for classical drawing trials is the coin must have identical weights on two sides to have the unbiased chance to produce each outcome, all balls in the chamber must have same weight, same shape, same size, and uniform internal density, and the dice must be a cubic with same area on all six faces, and has same density at every inner locality within the dice. The rim or density near two surfaces of a coin can be altered to result in spinning outcomes by a ratio other than 1:1. The ball sizes and densities among different balls can be changed to result in different probabilities to be drawn. Compared with the supposed classical probability outcomes, the altered coin or balls introduce systematic errors that will make the classical probability trials fail. Systematic biases cannot be corrected without understanding the nature of the biases. The evidence of systematic biases must be established by evidence other trial results. All interfering factors can cause systematical impacts on trial outcomes. Present inability to control interfering factors is not the reason to ignore their existence.

Moreover, a vast of the primitive factors such as nutrition, toxins, heavy metals, exercise, emotion issues are not really uncontrollable. Most intermediate factors such as glucose level can be controlled by lifestyle adjustments. None of those factors work like an uncontrollable driving force that makes a spinning coin to take one particular outcome and make the readings of an electronic balance to fluctuate. Given the easiness to change interfering factors, continuing treating interfering factors as errors is same as refusing to find cures.

Misuse of statistical analysis could not remove the trial outcome uncertainty. Great uncertainty in trial outcomes provides a great room for manipulation of experiments. Instead

investigating the inherent flaws, medicine has tried to address this uncertainty problem by controlling selection biases and conflict interests as remedies. Thus, we see massive ethical regulations. While selection biases can cure uncertainty caused by identifiable health properties such as age, sex, overall health, but cannot do away with outcome uncertainty caused by a large number of other uncontrolled interfering factors. Conflict-of-interest measures can never do away with outcome uncertainty except that it is has become a scapegoat for the flaws of clinical trials and failure of medicine. Such measures create massive administrative burdens which are rarely seen in other fields such as industrial designs, aviation, automobile, etc. Such measures cannot stop research fraud, and nor research outcome uncertainty.

4. Statistical populations of health properties do not exist for most research purposes in medicine

While human population concept can be used for various purposes, the population as used in statistical analysis in medicine can be refuted by relying on observed health properties and known analytical data. People comprise boys, girls, men, women, healthy persons, and persons with unidentified diseases, etc, are expected to have different baselines. For example, a healthy young person may have a baseline survival time of five thousand days while an old patient may have a baseline survival time of fifty days. Among the persons in a trial, besides the term "person", they are different in biological age, physical strength, shape and look, size and weight, etc. They differ in physical check-up data and laboratory analysis data [181]. Differences in intermediate compound concentrations in tissues between two persons could be more striking even though few studies were done to understand such differences. Even if assuming that diseases were realized in a manner like blowing human physical entities out of a lottery chamber, some persons might be "drawn" at much higher probabilities. There is no population which would meet statistical distribution except by approximation in limited situations. In most trials, the baseline health property for each person cannot be determined. This present inability is not a valid basis for treating them as random errors. The core assumption "population" does not exit.

As a general rule, when a treatment in a trial is sufficiently strong while experimental errors are relatively small, two experiments with two measurements in each would be enough without using statistical analysis. In a drug trial with endpoint being patient survival time, experimental errors are small because survival time, treatment dates, and drug doses can be determined and recorded accurately. But for the interfering or co-causal factors, the trial is expected to produce consistent results without need to use statistical analysis. In a trial involving a poorly defined treatment such as a stress-relieving method, part of outcome uncertainty is caused by the poor definition of treatment; and part of the outcome uncertainty is caused by interfering factors. Based on classical drawing models that different outcomes are driven by errors that are beyond control, statistics is not a correct method for taking care of interfering factors and definition uncertainty of treatments.

The flaw in clinical trials cannot be corrected by achieving baseline balance between the treatment group and the control group. A partial remedy is to determine baseline for each person so that net treatment effect can be determined for each person. This paired test can correct only part of the baseline problem. However, effects of interactions between the treatment and other interfering factors cannot be removed. Assuming that treatment T is under the influences of uncontrollable interfering factors (H_1, H_2..., H_n), the detectable treatment value for a person is $AT_i=\Sigma(T_i+T_i-H_{j=1}+T_i-H_{j=2}+\ldots,T_i-H_{j=n}$. Each interfering factor H_j causes plus and minus affects ($T-H_j$) over an imagined treatment T_i. Some interfering factor may raise treatment effect by various degrees while

other interfering factors may depress treatment effect by various degrees. The net effect of the treatment on a person depends on the treatment and all interaction effects. Thus, net treatment effect on each person must be different from the net treatment on another person. The total treatment's effect for the treatment group is the sum of all treatment effects on all persons (Ignoring the problem in additivity for the time being). When a large number of interfering factors interact with the treatment, the average of treatment effect is meaningless. We point out that the mathematical model for describing interactions cannot represent reality and the flaw in clinical trials cannot be remedied. The utility of clinical trials can be justified only for approximation, but not on a theoretical ground. Its utilities are limited to investigate strong treatment for limited research purposes.

As we have also shown that all assumptions used in epidemiological models fail to hold [3, 78-79]. Moreover, there is no way to design a clinical trial with all interfering factors controlled due to practical difficulties. This difficulty does not justify ignoring their existence. Furthermore, even if future researchers can develop a reasonable method for making a quantitative assessment, such a method cannot benefit people in our time.

5. The flaws of reductionist treatment approach

Most medical treatments are developed according to reductionist thinking. If a treatment is to alter a single process attribute, the treatment fails because it is intended to alter only one attribute in the biological pathways network. One well known example is the alteration of biochemical and cellular pathways in cancer patients: attributes of six categories of biological properties (growth signaling, cell apoptosis, anti-growth signaling, angiogenesis, tissue invasion and metastasis, and cell replication limits) are changed in cancer patients [97.1]. A treatment targeted to one attribute of one pathway cannot achieve the purpose without disturbing the attributes of all other pathways. If a treatment is to alter the rate of one pathway, it is impossible to tell how the treatment might alter other pathways. Besides, the responses in other pathways might depend on personal variations. Thus, one must find that diseases cannot be cured by correcting one seemingly fault pathway. It is possible some unexpected changes in other pathway attributes may make personal health or disease worse. We can safely assume (99% chance of correctness) that all attributes in one person's biological pathway network are different from those in another person's network. If the treatment is used on different persons, changes caused by the treatment in all attributes in one person's network must be different from changes in other persons networks. Even if the treatment is derived from a population, it cannot be matched to any person's network. Thus, such a treatment most probably show side effects if it is used for a long time. In addition, the role of mind and other biological pathways prevent the body from making changes that are sought. This is like a gearbox containing two gears. One gear cannot be freely altered without making correspondent adjustment to the other.

6. Inherent limitations of mathematical models

Mathematics is useful tools for studying health properties. We found that it cannot be used to find best treatments or preclude what would be cure. We first show that mathematical operations have all kinds of problems to make population medicine fail.

Mathematical operation is attempted to transfer health properties from a person to another person. If all persons in a population are truly same, differences in the measured values are caused by random measurement errors. Thus, one unit extra value in John Doe's measurement would be similar to one minus unit of value on Jack Doe's measurement. In reality, health properties cannot be transferred. This is shown in an example where John Doe suffers Vitamin A deficiency while

Jack Doe suffers Vitamin A poisoning. Both may be terribly sick even though their average is perfect. In population medicine, the minus effect on one person and plus effect on another person can have no effect on the mean. Similarly, two treatments with 5% curative rates are considered as same even if one treatment cures only female while another cures only men. The population model makes an assumption that health properties are as transferable, but in reality, they cannot be transferred from one person to another. What is really important is who will survive and who will die. The above examples show mathematical model is insensitive to personal differences and cannot be used to formulate the best treatment for each person.

The assumption of linear effect of treatment fails in nearly all situations. Most interfering factors influence health properties by complex manner. For example, nutritional intake, physical activities, sleep duration, thinking activities, environmental factors such as temperature, atmospheric pressure, and humidity, etc. affect personal health often by quadratic functions (if we do not resolve precise effects at a finer scale). A low nutrient intake has negative effects, its beneficial effect increases with intake amount, and hits an imagined optimal point; after this point, further increased intake causes a reduced beneficial effect, and results in progressively increasing toxic effects. The point of the optimal value for any factor is not static. The effect depends on personal genome, health condition, age, physical activities, lifestyle, diets, and emotional states, etc. This rough quadratic pattern is true even for physical activities. Too little sleep can hurt due to insufficient rest time and too much sleep time may result in excessive fat accumulation. It is even true for things like usage levels of body parts such as hands, feet or joints. Long inactivity hurts, and overuse also hurts.

Mathematical models cannot address complex interactions of health properties and primitive factors. Health properties such as glucose level, triglycerides levels, oxygen saturation, etc. may work like influencing factors for other health and disease properties. Such properties are further influenced by other primitive lifestyle factors, but also affect other health properties such as disease risk, death rate, etc. Due to complex interactions, we found there is no best nutritional profile, no best diet, no best copper intake, no best environment, etc. because the effect of each factor also depends on other factors and personal activities. There are no objective criteria for determine what is best. There is no best amount of exercise, and nor best kind of exercises for all people in a population. Even for a given person, there is no static best value. An imagined best value may exist only under certain conditions with respect to arbitrary evaluation criteria, and must change with age, health condition, activity levels, emotional health and other personal, environmental and lifestyle factors. The notion of good numbers for a population is flawed. Current mathematical model used in statistics can model only simple properties like crop weights and production yields.

Mathematical average of health properties generally has no meaning. The notion of regarding average of a population as the best value was formed by false perception of trail outcomes. By using comparison, clinical trials always produce a false impression that the positively determined treatment must be good for population. Thus, treatments developed from clinical trials have been regarded as the best for centuries. The validity of controlled trails becomes a presumption for centuries. This presumption was never challenged before. The purpose of a clinical trial is determining whether a treatment is better than a control often by using statistical analysis. In conducting statistical analysis, measurement values from all persons in the treatment group are added up to yield an average. There is no scientific proof that such an average can represent all persons in the treatment population. This presumption holds only if all persons in the population actually had mean, and the averaging operation is to remove true random experimental errors. We have shown there is no such statistical mean because there is no statistical population.

If there is no statistical population of a health property in the treatment group, averaged value acquired by mathematical averaging can represent none of the members in the treatment group. If a treatment is found to have positive effects over a control group, what is proved is that the treatment has sufficiently positive effects on the members of the treatment group over the control. Such a positive finding can be detected if the treatment effect is stronger than the sum of all interfering factors in the treatment group, the treatment produces beneficial effects on more persons than it produces adverse effects of same degrees on others within the treatment group, or the treatment has a net beneficial effects on the treatment group over the control for whatever reasons. It does not prove that the treatment is effective for the treatment group, is effective for treating the disease, or is the best for all persons with the disease.

The notion that "an average represents a population" is generally wrong unless a statistical population can be established by independent evidence. In a statistical population, the members must share enough similarity so that the members can be used to investigate something such as a treatment. This is entirely relative. Computed average can represent a population only if a statistical population actually exists. The existence of a statistical population cannot be proved by mathematical operation itself, reasonable data pattern or a computed averaged value. Mathematics can be used to determine average weight of a sesame seed and a fighter carrier or the average heart output of an elephant and a bird. Such averages can represent neither the weight of the sesame or the carrier, and nor the heart output of the elephant or the bird. While the values in those two examples are extreme, similar data values do not provide a basis for finding a population. The same reaction conversion rates at nearly 1 gram per minute for tigers and similar numbers for turtles do not make the data points become a population (even though turtle data may be used to estimate the tiger's mean). It is possible that apple data might nicely fit into human data purely by accident. Existence of a statistical population must be established by examining individual members and the purpose of investigation. If an identical nutrient intake has a beneficial effect on one person but a toxic effect on another person, the average value, which has the same value, does not represent a beneficial effect for both, and nor a toxic effect for both. On the contrary, apple, orange, and plum in a compartment mixture could be treated as a reasonable population if the investigation purpose is to estimate packaging volume. Even abstract concepts become a statistical population if their differences do not defeat the investigation purpose. Similarly, deformed coin, irregular balls, and non-cubic dice with varying inner densities cannot be used in drawing sampling for classical statistical trials.

To see show the flaw of mathematical operation in medicine, we present a mini trial comprising four persons: a 90-year old man, a 40-year old man, a 40-year female, and a 10-year old boy. We must presume there is no statistical population for health and disease properties. We first acquired data and find an averaged value in a health property for this population. If we apply the averaged value to all of them by any treatment or measure, we should anticipate that measure most probably will kill all of them in a long run (because they are very different). Obviously, to develop a treatment by the population approach, attempts are made to balance age effect and sex effects. Treatment of the old man is balanced by the need to offer benefits to the young boy. A treatment for the man is balanced by the need to offer benefits to the female. This mathematical averaging violates our observed principle that health property cannot be altered arbitrarily and cannot be transferred from a person to another person. Any treatment based on the representation principle must be detrimental to all persons if the treatment is used for a long time. This flaw cannot be cured by increasing the number of participants in the trial.

The permissible use of mathematical operations for population study depends mainly on the purpose of research. Grain weights may be added and divided if research purpose is to study the grain supply and demand. In this situation, grain weight is fungible: mathematics does not differentiate sources just like market demand. However, if the research purpose is to increase individual seed weights by using a new treatment, grain weight is not a fungible property. We must consider if the treatment has the same effect on each individual seed. If the same treatment can have different effects on different seeds with different genetic compositions, a mathematical model that regards the treatment having the same effect must fail. If a mathematical model takes care of plus and minus effects by experimental errors, the errors must be sufficiently smaller than the treatment effect so that study validity can be justified by approximation. Based on this rational, mathematical operations cannot be used to find best treatments for persons who have distinctive biological properties.

An averaging of a larger number of trial subjects cannot turn disjointed members into a statistical population. Many large-scale clinical trials such as TAILORx trial [102] reveal misuse of representation principle. It attempted to get better "representation" from people by running a multiple national trial. Since findings from clinical trials always had some kind of average of personal numbers, they cannot represent a super majority of the persons other than lucky persons whose numbers luckily fall on the average (which may happen by the chance of winning a lottery). The average is not the optimal value of any person in the trial subjects. Since health property data derived from a population cannot represent individual persons, treatments on the basis of such health properties cannot be valid for any of participant persons except an abstract person that does not exist in the world. There is no basis to find such a treatment is best for other patients outside the trial. Clinical trials have been misused for centuries by the false impression that they are capable of finding valid or best treatments.

We can find no proof from theories to practice in medical literature that clinical trials are valid. Many assumptions are questioned [11]. We can find overwhelming indications to refute assumptions used in clinical trials. The linear additivity assumption is used in regression and variance analysis. An overwhelming number of uncontrollable factors defeat the presumptions by plus and minus effects. Suppose that exercise is good for heart health, but exercise may have negative effects on some people whose blood vessels are severely damaged. In those individuals, the rapid rising blood pressure caused by exercises can damage the vascular system. The plus and minus effects of a large number of nutrients, physical properties, environmental factors can make the assumption fail.

All assumptions used in simple mathematical models cannot hold in light of the complex biochemical processes. Health properties depend on complex interactions of hundreds of biological pathways, and this implies, although most people are loathe to look into, that there is no simple additive relationship. Moreover, the interactions between disease initiation and multiple layers of disease defense mechanisms also refute this assumption completely. Disease mechanisms are further influenced by a large number of primitive lifestyle and environmental factors. Clinical trials can produce unpredictable and inconsistent results due to effects of influencing factors at different layers. In one trial, influencing factors for diseases may be found to have no effect if a strong defensive mechanism in most subjects can overcome initiated diseases; and in another trial, a factor effecting disease initiation may be found to be strong controlling factor if the defensive mechanism in most subjects is compromised.

We will consider how mathematical model might be used to predict disease outcome for a distinctive person. Infection diseases are mainly controlled by (1) exposures to the virus, (2) viral reproduction ability, (3) innate immune responses and host responses, (4) acquired immune response [169-173], and (5) the capacity to withstand tissue swelling. Thus, the disease severity such as risk of death could be expressed as multiple functions of a large number of factors under various conditions. To write an approximation, if the virus exposure is well controlled, the contribution from (2) to (5) will appear to have no role to the disease outcome. If acquired immune response is fast and powerful, all of the effects from (1) to (3) and (5) may appear to have no role. From those large contributory ranges, we expect to establish a mathematical model having multiple component equations with various conditions. Each of the component equations may include linear equation, polynomial equation, power law, etc, which has tens to thousands primitive lifestyle, personal, dietary, emotional, and environmental factors. The disease severity also depends on aging or development stage, information in neurons, hormonal regulation, eptigetic changes in cells, menopause, activities nature, etc. Many of the factors are random variables so the mathematical model can provide several conditional density distribution functions. For a population, the disease severity is just viewed as the totality of all individual persons. There is no solution.

Even if we can use the world computing resources to solve this model, it can only predict disease severity for the single person we have intended. This model cannot be used to predict disease severity for another person. The model may tell how to change dependent variables to achieve a better outcome. We must find that current epidemiological models are remotely irrelevant to the disease and human being. An articulation like “temperature or oxygen can cure the disease” has far more science than a mathematical model. Epidemiological models contain almost none of the biological factors. Manipulation of twenties to a hundred factors, most of which are conceived out of arbitrary imagination, will not help solve the pandemic. Medicine needs to focus on each patient’s biology but do not play coins, dices, lotteries, etc. When each patient is cured, the population must be safe and sound. It is wrong strategy to junk onto the population while forgetting the very basics of disease biology.

We have shown that the population model cannot be used to study weak effects. The problems in clinical trials are found by studying its theory, basic assumptions, biological pathways, disease initiation and defense mechanisms, factor-factor interactions, body structure, etc. Treatments developed by using population approach are inherently invalid except by accident and inherently dangerous if they are used in long term.

D. Distinctive Personal Biological Properties Determine Personal Resistances to the Virus

1. Holistic model, unique disease principle and integrative medicine

Decades after the acceptance of clinical trials, details about human genome was known [81]. As of 2015, the typical difference between the genomes of two individuals was estimated at 20 million base pairs (or 0.6% of the total of 3.2 billion base pairs) [81.5]. This proves that each person is a unique biological being like a specific car model. Moreover, difference genetic information can be found beyond the DNA sequence [82-83]; and epigenetic changes can have an effect of turning on or off gene expressions. The large number of studies of health factors in cancer research lead to

the finding that each cancer is distinctive and a result of personal genome, living environment, etc. [84-85]. This unique disease principle implies that best treatments must be tailored to persons. Moreover, we can find that information written on the CNS neurons must be different, and it, like computer programs, affects emotional health and CNS regulatory functions over the body. The cancer unique disease principle reinforces the long-held personalized medicine principle used in nearly all ancient medical systems [86]. The CNS affects nearly many aspects of the body [87-95] "There is no real division between mind and body because of networks of communication that exist between the brain and neurological, endocrine and immune systems" [86]. The ancient holistic model [104] and integrative medicine [21, 85, 86.1, 111-119] all require that treatments are focused on the whole persons.

2. Personal biological properties

Based on the evidence we have cited above plus common experience and observed facts, we found unique disease unique biological properties. There are more than hundred biochemical and metabolic pathways in human cells [96-97]. Personal distinctive chemical data signatures routinely observed implies the reactant concentrations, product concentrations and intermediate concentrations in different biochemical pathways are distinctive and unique. Even though the total number of pathways may be same among different persons, all pathways must run at distinctive turnover rates with different concentrations of intermediate compounds. The net rate of each pathway must be constrained by the rates of upper stream pathways, influenced by coupled pathways, and promoted by downstream pathways. In addition, the net pathway rates are controlled or influenced by gene expressions, affected by blood flow rates, and structural features, etc. To compensate for personal differences in the pathways, each person must maintain intermediate concentrations at different levels. Those biological features explain why chemical analysis values for one person are always different from those for another person. The concentrations of intermediates in cells in different tissues are expected to vary even though data are not available. Moreover, personal biological properties are influenced by and interact with nutrients, toxic substances, vascular system, CNS function, information in neurons, tissue structure, body structure, organ structures, organ reserve, etc. Health is run by massively multifactorial system networks.

Personal biological properties determine personal ability to resist the diseases by mainly influencing innate immunity, host anti-viral responses, acquired immunity, overall inflammation potential, free space in the thorax cage, etc. We show several sub classes of personal biological properties are particularly relevant to personal resistance to COVID-19.

1. Genetic signatures. Personal genome is equivalent to the blueprint for a distinctive product. To some extend, genetic signatures determine predisposition to diseases. It can put some persons at high risks for acquiring unique diseases. However, since personal genome is not what we can change, we will not consider it further in this article.

2. Nutritional signatures. All nutrients exist in various concentrations in different parts of the body and organs. For example, vitamin C level (or oxidative and reduction potential), vitamin A, mineral concentrations, etc. exist in different levels in different parts of the body. Considering the large number of conceptual points in the body and all essential and non-essential nutrients, the nutritional profile must be distinctive and unique for each person. Nutritional signatures affect biological properties.

3. Toxic substance signatures. External toxic substances including heavy metals (such as mercury and lead), gases, inorganic compounds and organic compounds. Those substances may get into the body as food and water contaminants, air pollutants, and medicine. They exist in different parts of the body in different concentrations. Metabolic by-products also exist in different concentrations in different parts of the body. The natures of the substances and their concentrations in different parts or organs determine where damages take place. It affects personal biological properties.

4. Chemical data signatures. More than potentially 500 chemical analysis items could be used in medical laboratories. Each person's data profile is distinctive. Different persons have completely different chemical data patterns. Each chemical analysis item can have plus and minus 50% among human population. Most personal values can be anywhere in the ranges recognized in medicine. The distinctive personal chemical data signatures are a result of human genes, environment, and emotional state.

5. Vascular property signatures. Due to genetic, dietary, environmental effects and emotional effects, each person develops distinctive vascular signatures. Distinctiveness of the vascular system may be found in blood vessel distribution in the body, blood vessels' surface characteristics, blood flow rates in tissues in different parts of organs, capillary densities in different parts of organs, blood pressures at different locations, etc. In addition, the cells compositions, the concentrations of nutrients, concentrations of metabolic products, and concentrations of toxic substances at any location of the body are also distinctive.

6. Organ micro-circulation signatures. Micro-circulation signatures are related to the vascular signatures. We stress them because micro-circulation is very important to resolution of inflammation, and elimination of toxic substances. Those signatures are also defined by personal genome, environmental factors, and emotional state.

7. CNS function signatures. The CNS functions depend on condition of neurons and other brain cells, cerebral circulation (including micro circulation in brain tissues), scars and voids, etc. In addition, one important factor is information written on neurons. It is common knowledge that people differ in their thinking and reasoning logic. People react differently to similar personal events, similar external signals, and similar natural events such as thunderstorm, flooding, heavy rain, earthquake, etc. The overall health of the CNS affects innate and acquired immunity, hormonal actions, sleep quality, etc. It affects a disease severity and disease outcomes.

8. Physical structural signatures. Each person has different physical structures. Physical structure signatures are a result of biochemical pathways signatures, nutritional signatures, CNS functions signatures, etc. It affects personal resistance to the virus by two critical factors: First, an obese body structure will demand more of the organ functions. If a person body weight is increased from 100 lb to 150 lb, the body requires more functions of all major organs including the heart, lungs, liver and kidneys. Excessive structure caused by obese is equivalent to reduced organ usable functional capacities. An obese person will experience shortness of breath more easily due to relatively lower organ usable functional capacities. Second, excessive structure has an effect of reducing the available space that can accommodate tissue swelling inside the thorax cage. When the body develops extra structure, the extra structure can increase tissue rigidity. When excessive tissue is built inside abdomen, the tissue can force the belly to expand. However, excessive tissues developed inside thorax cage cannot force the ribs to expand. Thus, it must take up available space including alveolar spaces. The third problem is that excessive fat deposits aggravate micro

circulation in all organs. So, obesity has triple-combination adverse effects: depressing all organ usable functional capacities, reducing available spaces for accommodating swelling volumes caused by inflammation, and impairing the body ability to control inflammation. This is why obesity is the biggest risk factor for lung infections. When an infection causes the lungs to swell, the thorax cage has little or no space to accommodate swelled tissue. The swelled tissue must take alveolar spaces and destroy the lungs [8]. It was found that the risk of getting infection is related to body height. We reinterpret this risk as vascular structural disadvantage. Compared with a short person, terminal blood flow resistances of a tall person is higher. Overall blood vessel lengths are longer and a tall person has higher static pressure. It would require further higher blood pressure to maintain the same level of blood circulation in the brain.

9. Organ usable functional capacities signatures. As a result of influences of the above personal signatures, each person has distinctive organ usable functional capacities. Poor nutrition may impair organ's normal function; toxic substances may interfere with the biochemical pathways; faulty CNS functions may cause fault regulations; excessive body weight would demand more of organ function capacities to maintain body's baseline functions; and poor vascular system diminishes organ usable functional capacities. Age is one important factor because a ninety years old person roughly has lost 30% of organ reserve [98-100].

10. Physical endurance signatures. Each person has unique physical endurance signatures. Some person has poor physical endurance in the initial phase of physical activity. With time passing, they can do better and better. In contrast, some persons have better endurance in early stage of physical activities, but quickly get exhausted. Moreover, people have different abilities and strengths in doing different things. Physical endurance patterns can be important in preventing damage to major organs. In most cases, physical activities are the most dynamic demand that can compete for the organ usable functional capacities of heart, lungs and kidneys. Damage to organs take place when the demand of the body for maintaining baseline functions and the demand caused by physical activities exceed what the organ can provide. Excessive activities by infected persons with limited usable organ functions can pose great risk to damage heart, lungs, and kidneys.

11. Personal overall resistance to COVID-19. We use overall resistance to mean both a person's ability to resist infection and the ability to withstand damages in the event of infection. Personal overall resistance to the virus depends on all above biological signatures. The most important factors are the vascular condition, lung micro-circulation, age, and obesity. Personal, environmental, and lifestyle factors influence personal overall resistance by influencing multiple biological properties signatures. Distinctiveness of personal biological signatures implies that population-based treatments are poor.

E. Altering Personal Biological Properties to Improve Personal Overall Resistance to the COVID-19 Disease.

Based on the above analysis, the overall ability of persons to survive from the pandemic depends on personal biological properties. Ignoring viral concentration and exposure time, a person's overall ability to survive by great extent depends on (1) present innate immunity and host responses, (2) subsequent acquired immune responses, (3) capacity to sustain inflammation, (4)

organ usable functional capacities, and (5) available space for accommodating tissue swelling in the thorax cage. The first three mechanisms serve as three layers of defenses against the virus and the last two features mainly affect the person's ability withstand damages. Those mechanisms further interact with the CNS function, the vascular system, cerebral circulation, lung micro circulation, etc. Each of those sub level properties is further influenced by a large number of personal, environmental, lifestyle, dietary, and emotional factors. If any one or several of those defenses are strong enough, a person can defeat the disease. A worst outcome is expected if viral load is large, all three defenses fail, and the last two capacities are small.

1. Good personal biological signatures

Based on forgoing discussion, vascular signatures are most important. Favorable vascular signatures are characterized by: good blood vessel structures, large inner hole sizes of arteries and veins in all branches or locations, high elasticity of blood vessels, good structure of blood vessels, undamaged cells in blood vessels, higher capillaries density in tissues, shorter capillary lengths, larger capillaries inner diameters, higher elasticity of capillary walls, sufficient number of white blood cells in blood (this one factor can be further divided into a large number of parameters), normal blood pressure, proper nutritional concentrations in blood, lower toxic substances in blood, lower toxic metabolic byproduct concentrations in blood, etc.

Fault biological pathways do not always directly hurt health, but deliver their adverse effects by altering affected tissue ecosystems in organs. Nutritional intakes and toxic substance exposures are biggest influences of the biological properties. Malnutrition and toxin accumulation slowly alter tissue ecosystems. Good tissue ecosystem is characterized by good blood circulation condition, good nutritional profiles in tissue, lower toxic substance concentrations in tissue, healthy tissue cells composition, strong cell functions, lower tissue rigidity, etc. The tissues has healthy nerve network so that it can exchange neuronal signals with the CNS and nearby tissues. Healthy ecosystem insures that the body has strong innate immunity and host responses, fast immune response, efficient clearance of toxic by-products, and strong ability to resist inflammation caused by viral activities and immune responses.

The vascular system, tissue ecosystem, and CNS function jointly determine the efficiency of innate immunity, acquired immunity, the ability to resist inflammation, and ability clear up metabolic substances. The vascular system affects immune cells mobility and waste removal and thus affects immune responses and the ability to resist inflammation.

The last line of properties are related to human structures: a low tissue rigidity favors the pass-through of immunity cells from inflamed tissues, low body mass index generally mean lower fat deposits on blood vessel walls and lower demand for organ functions and more organ usable functional capacity for fighting against viral damages. Particularly, larger usable organ capacities of the lungs, heart, and kidneys mean better ability to sustain virus-induced damages to organs. Large available space in the thorax cage means that the lungs accommodate welling volume of lungs. The vascular system and CNS affect organ usable functional capacities and body structure by long term effects.

2. Poor biological signatures (am example)

Poor biological properties are characterized by poor innate immunity, delayed or compromised immune response, a reduced organ capacity to withstand viral damages and reduced

free space to accommodate tissue swelling. While certain biological properties involving molecular specificity must be addressed for specific persons, most poor biological properties can be found in obese persons.

Obesity is found to be a high risk factor for COVID-19 disease [101] and other virus infections [41-48]. An obese person has more fat deposited on blood vessels or smaller holes of blood vessels, longer mean capillary paths, poorer tissue micro-circulation, reduced circulation efficiency, etc. Those features impair white blood cells mobility and thus compromise innate immunity against the virus. Poor micro-circulation efficiency also results in a diminished capacity to clear up metabolic by-products from immune response. Poor micro-circulation efficiency impairs acquired immune responses [8]. Impaired micro-circulation is a critical risk factor because all white blood cells (including immune cells) must move through tissues by squeezing through congested capillaries. Excessive obesity forces the heart to maintain blood circulation in larger body mass and thus reduces organ usable function necessary to fight virus-caused inflammation. Reduced heart capacity and reduced lung usable capacity diminish the person's capacity to withstand the damages to the lungs.

Obesity increases lung tissue rigidity, reduce available space for tissue expansion in the thorax cage (reduced tidal volume, inspiratory reserve volume, expiratory reserve volume). A healthy person may have 3000 ml inspiratory volume over above 500 ml tidal/breath volume. When a healthy person is infected, the lung can accommodate 2500 ml of volume expansion caused by tissue swelling without infringing lung alveolar sacks. If an obese person has an inspiration volume reduced to 1000 ml, it has only about 500 ml to accommodate tissue swelling which is about one fifth of a normal person's free volume. In normal persons, most of white blood cells pass capillaries by squeezing and deforming themselves. In an obese person, the narrowing of capillaries by fat deposits results in reduced white blood cells mobility, increased tissue rigidity, and reduced free space for accommodating swelling. When tissue swells in lungs without available space, the compression force caused by tissue swelling increases the friction of white blood cells [11] against capillary walls. The increased friction results in accumulation of white blood cells in capillaries, which quickly blocks capillaries, and raise pulmonary blood pressure. When the local blood pressure is sufficiently high, it forces blood to squeeze out of capillaries and destroy lung alveoli. It is expected to a self-aggravating rapidly degrading process that can be prevented only long before it happens. When the free space in the thorax cage is almost used up, there is no conceivable way to resolve this problem. This mechanism explains why young obese people can be vulnerable to the disease. In addition, those obese biological property features simultaneously affect innate function, adaptive immune function, and the capacity to control inflammation. Those biological properties also affect other diseases and other viral infections [41-48].

While obese persons share most of those common features by different degrees, each of them still has unique signatures in vascular properties, toxic substances, tissue structures, cellular biochemistry, CNS functions, organ usable functional capacities, organ micro circulation, etc. Best protective measures should be tailored to their specific signatures to achieve best outcomes. Weak factors cannot be studied by clinical trials. Most population studies may be used as ballpark guidance. However, they cannot be used to all persons. For example, mercury toxicity must be a universal property, but the exact tolerable levels are different among persons. A level that may raise a concern for an infant may be tolerable to old adult. Most health properties are influenced by personal genome, age, health condition, lifestyle, activities, stress, diets and environment factors, etc.

In formulating health factors such as exercise and activities, the most reliable guidance is their roles in evolution: how the factor affects people in revolution. Extreme and excessive exercise can have negative health effects, but a suitable amount of exercise is beneficial to health for all persons because exercise is part of human activities in revolution. Moderate social interactions are presumed to be essential because personal interactions are part of human lifestyles in evolution; bodily contacts are presumed to be good because those things are part of activities among young animals. Processed foods, refined foods, food additives, artificial flavors are presumed to be harmful, regardless the findings of controlled trials. Raw foods are presumed to have some benefits because eating raw foods was the dominant form of evolutionary diets. Long hours TV watching and excessive cellular phone use should be presumed to be bad, regardless of the findings in controlled studies. Ingesting tens to hundreds synthetic additives should be presumed to bad because controlled trails are incapable of producing accurate data.

F. Reductionist Measures Expected to Raise COVID-19 Death Rates and Death Rates of Other Diseases in the Long Run

We have shown that both controlled trials and mathematical models cannot be used to appraise the full effects of treatments in most situations, and reductionist approach is incapable of curing diseases, we try to find a different method for finding treatments for diseases. The effects of measures and treatments must be judged by following holistic approach. In evaluating the benefits of pandemic measures, we consider their effects on viral concentration (VC), exposure duration (ET), effect on innate immunity/host responses (II), effect on adaptive immune responses (AI), effects on micro circulation (MC), and free space in thorax cage to accommodate tissue swelling (FS). This is absolutely the minimum to consider under the holistic model. Some public intervention measures are deemed to fail, as shown in the below table.

Table 1. Public intervention measures in the U.S. cause long-term irreparable injuries to public health.

Measures	Useful Cases	Uncontrolled Factors	Overall assessment
Social distancing	When all other factors are fixed	VC, ET may be doubled or tripped.	It may have little benefit in enclosed buildings, and can inflict massive harm when C, T are increased by many folds, and ruin II, AI, and FS.
Limit human density in stores.	If exposure time and viral density are same.	Double or triple VC, ET. and fails to improve ventilation.	It is generally negative. Human density is NOT a controlling factor because it depends on ventilation; and viral density in the air and exposure time are important.
Personal	Avoid present	Reduce exercise	This measure can cause overwhelming

isolation (PI)	exposure.	and create the most susceptible biological signatures.	adverse impacts in long term. Its long term effects are realized by ruining mental health, vascular system, and structure (II, AI, and FS).
Stay at home order	Same as IP	Same as IP	Same as IP
Lockdown city.	Same as IP	Same as IP	It is the worst among the worst. It may be used as emergency measure, but cannot be used as a long term solution. It ruins II, AI, and FS.
Forced quarantine	To stop a seed pandemic, as a must-measure.	It is not effective after the disease has spread to the area to protect.	Forced quarantine can shut down human immune system and make people insane. Increase the number of cross-infections.
Poor lifestyles under movement restriction	It may be used as a short-term fix.	People develop depression, obesity, and mental diseases, etc	Prolonged bad lifestyles can ruin II, AI, MC and FS. It takes time to have the adverse effects materialized.
Over used disinfectants	Disinfectants are used to prevent an infection.	The risk of harm depends on use frequencies, amounts, locations, and time.	The harm is not observed in a short time. There are too many sources that users are unaware of. Most people do not know their adverse effects.
Other unintended abuse and wrong practice	Expose people to chilly temperature, fluctuating temperatures, and chilly rains.	Impair present health, innate immunity, and anti-viral responses.	It can comprise the immune system, and provide higher risk of getting infections in later exposures.

Most public intervention measures used in the U.S. are taken by focusing on one single parameter such as social distancing, head count in a store, isolation, etc. Such measures reflect extremely reductionist approach. Measures taken with strict compliance with one single parameter are meaningless because the net benefits depend on other parameters such as viral concentration, exposure time, viral activity level, human innate immunity and host responses, subsequent adaptive immune response, micro-circulation, fee space in the thorax cage, etc. When a measure is taken by following one single parameter, one or more of other parameters may be enlarged by one to several folds. For example, 6 feet distancing may be achieved by doubling viral concentration in the air, doubling exposure time in a store, and, in the worse case, total crippling innate immunity. Good pandemic outcome cannot be achieved by making people sick. Worse adverse effects of movement restriction measures are realized by emotional distress, degraded vascular systems, and routine exposure to temperature fluctuation. Several months staying at home is believed to be one of the

main reasons for rising infection rate in the U.S. in the summer. The disease cannot be controlled by reductionist approach. Governments should provide guidelines that all measures are not taken at the costs of ruining people health and inflicting emotional distress.

G. A Method for Determining Health Factors and Treatment Measures on Infection Risk and Death Risk

To improve over current treatments, we develop a systemic method for determining the effects of preventive measures and primitive factors on infection risk and death risk. The method comprises (1) analyzing the most relevant biological properties for the diseases, (2) from the personal biological signatures identifying the values that are known to raise infection risk and death risk, (3) identifying primitive personal, environmental, and emotional factors that could be used to alter the offending health property values, and (4) using those identified factors to mitigate infection risk and death risk. One must note that each factor works by slowly delivering its effect, and such an effect cannot be determined by clinical trials.

The diagram in FIG. 1 is intended to be used in both ways. While it is worded to show adverse effects, it can be used to show beneficial effects of factors simply by altering the value, sign or direction of each factor. If a factor affects multiple health properties, we need to consider how the factor affects other affected properties.

1. Using all existing knowledge in medicine

The diagram in FIG. 1 is based on the holistic approach. The merit of holistic model was well known [86], is implied in the model study [10] and further supported by a large number of studies [103-119]. FIG. 1 is intended to cover all known factors and unknown factors. A number of emotional factors can affect the immune system. They include emotional sock, chronic disease, monotonic lifestyle and social isolation. They can cause the immune system suppressed [18-26, 89-95]. Since the brain controls hormonal actions and biological processes, whatever disorder in the brain affects correspondent tissue ecosystem as well as the lung micro circulation condition. The critical roles of the CNS were observed in 1875 [103]. Nutritional biases are expected to have adverse impacts on tissue ecosystem, and vitamins can boost immunity while heavy metals, toxic substances, pollutants, etc. can suppress human immunity. Lack of exercise and physical inactivity are found to the substantial causes of chronic diseases [28]. From the great benefits of exercises on cancer survival times [29-40], it is expected that reduced exercise and increased inactivity has adverse impacts on survival among cancer patients.

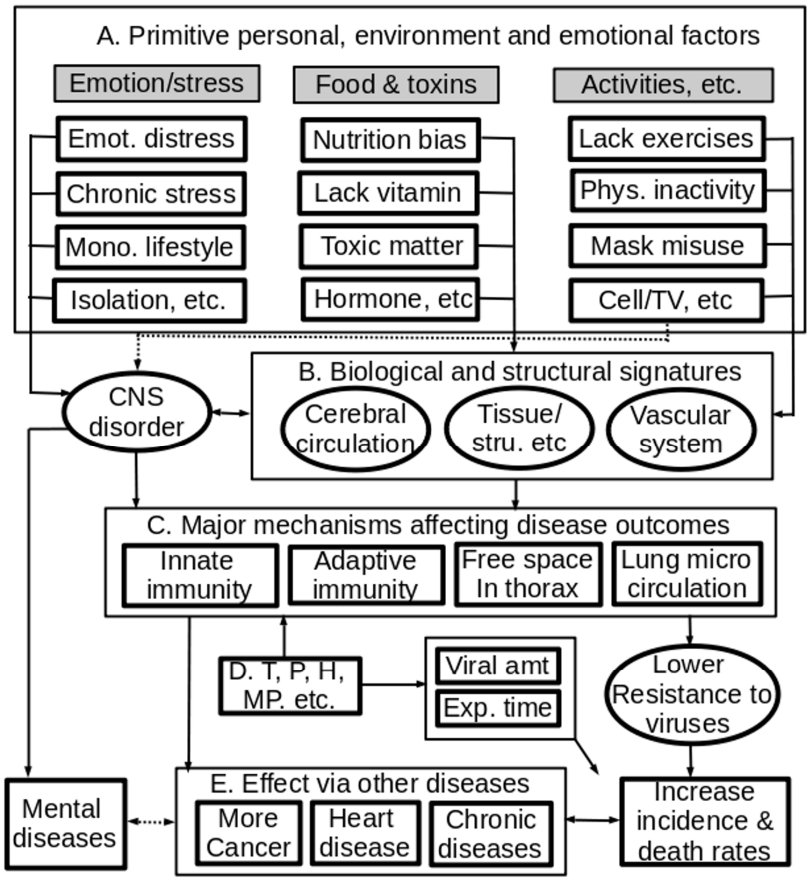

FIG. 1. A systematic diagram shows how primitive personal, environmental, and emotional factors affect disease outcomes by altering biological signatures which affect disease mechanisms and other chronic diseases.

2. Determine the adverse effects of misused pandemic measures.

By looking at the diagram, we can visually see the following exemplar impacts.

(1) Unnecessary use of masks can reduce oxygen exchanging efficiency and is predicted to have adverse affects on the lung functions and the vascular system on the long run.

(2) Chronic stress can suppress both innate and acquired immunity and thus favor bacterial and viral attacks.

(3) Low levels of vitamins A and C reduce protection against cell damages by free radicals while heavy metals may initiate damages to blood vessels and cells.

(4) High intake of processed foods promotes accumulation of contaminants, which can damage the immune system, blood vessels, etc.

(5) Lack of exercise and excessive calories result in increased flow resistance due to formation of fat plaques on blood vessel walls.

(6) Obesity reduces the organ usable function of major organs. Increased lung rigidity and reduced available space in the thorax cage. When the available space has been taken by tissue

swelling, further swelling can quickly destroy the lungs. When pulmonary pressure is too high, blood is exuded into lung alvoeli, destroying the lungs quickly.

(7) Severe adverse effects are realized by combination effects. Chemical damages caused initially by imbalanced nutrients, toxic substances, and excessive calories will work in a synergistic way to increase blood flow resistance. The narrowed blood vessels and increased flow resistance result in starvation in the tissue of organs, which will demand improvement in blood supply. The heart raises heart out and thus raises blood pressure. Increased blood pressure causes mechanical damages to blood vessels. Now, the narrowed blood vessels are further damaged by mechanical force to further ruin the vascular system, celebrate circulation, and lung micro circulation. When blood micro-circulation in organs is severely impaired, the innate immunity, adaptive immunity, and tissue repairing functions are compromised.

(8) Hundreds to thousands of primitive factors affect personal biological properties. While the magnitudes of all factors cannot be determined by simple mathematical models, the factors are ultimately responsible for infection susceptibility and death risk.

(9) An inactive and fault lifestyle formed while staying at home is a perfect way of creating personal biological signatures in favor of getting infection and severe disease. It can include all of the adverse effects discussed from items 1 to 8 above. Most adverse effects are slowly realized in long time, especially when people lack of sense to do anything to prevent adverse effects. If the bad lifestyle goes on from days to years, it is difficult to reverse or neutralize materialized adverse effects.

3. Using the diagram to improve personal resistance to the virus

The diagram can be used to identify primitive factors to improve personal biological properties to resist against and survive from the disease. To reduce risk of infection and risk of death, the first thing is to get rid all chronic diseases (E in FIG. 1) and avoid exposures to high viral concentration for long time. However, such measures do not provide reliable and definite protection in all exposure opportunities, and thus a better measure is improving those four major mechanisms for fighting the disease: innate immunity and host responses, adaptive immunity, lung micro-circulation, and available space in the thorax cage. Those mechanisms depend on the vascular system, cerebral circulation, tissue ecosystem and body structure, all of which can be altered by using personal, environmental and emotional factors (A). While the method is similar, each person has distinctive biological signatures for his vascular system, cerebral circulation, tissue ecosystem, and body structure. Even if two persons have similar vascular damages, their precise causes are different: the vascular system in one person might be caused by heavy metal damages as the primary cause while that in the other might be caused by inactivity. Even though, the total number of factors to be considered is same, each person may find a unique set of primitive factors to be used to correct the fault biological signatures (B).

FIG. 1 represents a systematic method. Each of the black boxes in A denotes a large number of primitive factors. For example, toxic matters include heavy metals, pollutants, food contaminants, food additives, prescription drugs, toxic minerals, antibiotics, foreign hormones, disinfectants, microorganism's metabolic byproducts, etc. Similarly, the box for vitamins denotes essential and non-essential nutrients (including those that are not understood). Nutritional biases mean that nutrients are not in good proportion to maintain health. Similarly, emotional factors denote all emotional factors that could affect human health. FIG. 1 is intended to cover potentially hundreds to

thousands of factors that are important to personal ability to withstand infection and death risks. This diagram in combination of knowledge of primitive factors can help a person find a matrix of specific factors to be used.

H. Need to Improve Personal Biological Properties as a Viable Surviving Strategy

Death rates of COVID-19 patients depend on personal health and certain risk factors [5]. The affect of personal health in other viruses can be extended to this disease because those factors are not used by relying on chemical specificity. Based on great disparity in death rate among infected persons, personal health condition is the most important factor influencing disease outcome. It implies that improving personal health in certain ways is a reliable measure.

Movement restriction measures are effective only against present risks. A successful prevention of infection in one instance does not guarantee future success. Improvement in personal health can have long-term protective effects. Exposure-preventing measures can also fail because even infected persons get negative viral test results for one to eight times before their infections are finally confirmed [176]. Due to a large number of false negative test results, measures based on test results are not reliable. This is a disease that few people can successfully avoid in life time.

A compelling reason for improving personal health as surviving measures is the failure of population-based treatments. We have proved that treatments derived from clinical trials are deemed to be poor or inherently dangerous due to mismatched application [10]. Besides the mismatch of treatment, the poor performance of population-based treatments can be attributed to reductionist approach, which is found to be poor or unworkable in nutrition [105-106], lower back pain [107], neuroscience and brain research [108-109], diagnostics [110], exercise [111], patient care [112-114], public health programs [115], and holistic medicine [116-118]. The evidence, taken as whole, has firmly established the holistic model is superior and safer.

Lack performance of medical treatments is anticipated from its model problem: health and disease outcome for a person must be highly complex polynomial or complex functions of hundreds to thousands factors, and some of which are random variables with various distributions. Thus, a treatment focusing on one or few factors must be inferior or even grossly inadequate. “The health benefits of mind-body [holistic] medicine have barely touched the surface of what it offers for future health and well-being.”[104]. Use of personalized medicine is what persons must consider. The validity of population-based treatments is limited to strong treatments such as antiviral drugs and vaccine, and the use of clinical trials is justified on the ground of approximation. With that narrow exception, treatments developed by clinical trials and mathematical model may be used on short term. Population-based treatments have failed in cancer, heart diseases, mental disease, etc [119-124].

The mistaken expectation of clinical trials as best research method has prevented medical researchers to investigate subtle factors such as disease event timings and phases, factor-factor interactions, etc. for individual cases. Such subtle factors often have decisive impacts on disease outcomes. One strategy for treating an infection is promoting the immune system in the early stage, but suppressing the immune system in a later stage. The reason for suppressing immune system is avoiding excessive damages by viral action and immune response [7]. The changing point in the

timing depends on infection timing, personal organ usable function, immune system, vascular system, etc. We suspect that the available space for accommodating swelling volume is a critical factor to withstand damages [8]. In addition, the timing is expected to depend on how fast prior treatments can change the immune system. Suppressing immunity in the early stage is same as inflicting more damages to the lungs; however, promoting immune response in a later stage on certain patients may speed up death. A population-based treatment protocol could not address such critical issue.

All movement restriction measures can deliver present benefits but have adverse effects, which are realized in the long run. Due to lack of public attention to those adverse effects, current measures are brewing catastrophic global health crisis. If effective vaccines or antiviral drugs are found, the slowly realizing adverse effects will ruin population health in a long run.

Based on a large number of personal stories and research findings [5, 125], a large number of COVID-19 survivals suffer a variety of long-term health problems and disabilities. We saw a large number of reported stories that survival is the start of pain and suffering. Some survivals have lost substantial lung functions and others have lost organ usable functional capacities. Persistent symptoms include extreme weakness or lack strength to walk, rigid and inflexible joints, muscle ache, throat inflammation, fatigues, muscle withering, breath difficulties, chest pain, headache, stomach ache, acute cerebrovascular disease, sleep disorders, disturbance of consciousness, delirium, epilepsy, PTSD, loss of taste sense, loss of smell sense, loss of appetite, neuralgia, lost vision, etc. The virus is believed to damage pancreas, heart, liver, brain, kidneys, etc.

Long-term disabilities are associated with severe disease. The survivals whose lungs have been in severe distress state tend to sustain permanent lung damages. While viral damages are blamed for damages of organs, it is possible that severely impaired blood circulation has contributed to the unrecoverable damages to affected organs. Some survivals die from other causes soon after their discharges from hospitals. If we add other deaths, the real death rate of the disease is higher than the nominal rate. Since most deaths are associated with underlying chronic diseases, personal biological signatures are clearly differentiating factors that can affect infection risk of the disease and death risks for all associated diseases.

Although the virus may attack the whole body and many organs, most deaths are caused by heart failure triggered by lung failure [8]. We have attributed the pulmonary circulation blockage to accumulation of white blood cells in lungs [8]. Infection-induced inflammation causes tissue swelling and alters surface characteristic of blood vessels. The swelling of tissue increases flow friction of traveling white blood cells against the walls. The aggravated blood circulation further promotes swelling of lung tissues. The swelling forces blood to occupy the available space in the lungs. When the available space is used up by swelling tissues, the patient cannot breathe; and a further accumulation of white blood cells will destroy capillaries. Bad disease outcomes are attributed to the long phase lag between viral replication curve and immune response curve (more precisely the area between the two curves), small available space in the thorax cage, and low organ usable capacities. A survival strategy is to shorten the phase lag [7], enlarge organ usable capacity [98-100], and increase the available space in the thorax cage [8].

Some studies revealed that the disease can damage the human immune system like HIV virus. Virus was found in T lymphocytes [126], macrophages 127-129] and monocyte-derived dendritic cells [130]. Direct virus killing of lymphocytes could contribute to the observed lymphopenia in patients [127]. This finding implies a grave risk. We hypothesize how the disease

get into this situation: the fight between the virus and the immune system is like a military battle which is always controlled by the supremacy side. If viral concentration rises slowly, the virus does not have a decisive power to kill substantially all T and B cells in the bloodstream. If the immune response rapidly, it can produce enough antibodies to clear up the virus. However, if viral concentration rises rapidly while immune system is activated with a long delay or respond slowly, the virus might reach a concentration to kill substantially all T and B cells that are moving into the bloodstream. We suspect that viral infection of T and B cells may be not uncommon, and what is unique in this disease viral replication has better chance gain supremacy over the underdog immune response. Thus, what is important is how to prevent the virus to gain its supremacy to suppress the immune system so that the immune system has no chance reverse its unfavorable position. This hypothesis should be understood in light the retention of white blood cells in the lungs. Immune cells are affected by metabolic toxins and nutrition condition. The death of immune cells in the lungs does not prove that the virus is particularly lethal to immunity cells. The outcome could be changed by altering this speed competition.

To slow down viral replication speed and improve immune responsive speed, four lines of measures could be used to prevent delayed immune response: early use of effective antivirus drug, avoiding exposure to a large amount of viral gene copies, using favorable environmental factors, and developing personal antiviral biological signatures.

Vaccines may provide partial protection against the virus based on influenza vaccination performance [9, 177, 180]. Survivals of a prior COVID-19 infection may still get severe infection in future. After an infection is brought under control, antibodies concentration in the blood declines to an undetectable level. B cells against the infection will remain, and due to irreversible change in the DNA by somatic hypermutation, their progeny offspring inherit genes that encode the same receptor specificity and become memory B and memory T cells, which is expected to shorten the time required to raise antibody concentration in a future infection [131, 172, 173].

The existence of memory B and T cells for this virus does not provide full immunity. Since the lungs are exposed to internal airways, the virus can attack alveolar epithelial cells from air sacks of the alveoli without traveling through blood [68]. Lung infections are often initiated by viral attack of the respiratory tracks [17] and this has been firmly established by the effectiveness of using masks. Airborne virus can quickly directly get onto lung cells or virus generated from the upper respiratory track may quickly get into the lung cells by large amount. This infection routes deprives a chance to interact with existing B cells in the early stage. Strong acquired immune response is triggered only after a meaningful amount of viral particles has been released to the bloodstream [172-173]. Extrafollicular fast antibody response requires antigens; but the virus is not immediately sensed by the immune system. This delay serves as a time window for the virus to damage the lungs and is one reason that influenza vaccines do not perform well [180]. The shortest time windows inferred from exposure to the virus to onset of disease signs can be one to two days, while smallest time window based on model viral properties could be several hours. This time window may give the virus an opportunity to completely destroy the lung tissue before the immune system is able to raise antibody concentration in extreme cases.

The time for the virus in an infected person to reach its peak is an indicator of relative viral development speed. It takes 5–6 days for the SARS-CoV-2 virus from symptom onset to reach its peak — significantly earlier than 10 days of he related SARS-CoV after symptom onset [132-135]. The fact does not tell absolute viral concentration or cell destruction speed. It still implies the

importance of comparative speeds of viral development and immune response. Considering personal differences, we infer that the risk of death must be higher among people whose the innate system is compromised [169-171] and the lungs are exposed to a large amount of viral particles through inhalation in a short time like synchronized viral attacks on multiple cells on alveolar inner surfaces. The viable strategy for overcoming this kinetic disadvantage is improving personal resistance to the virus, improving innate immunity and increasing adaptive immune response rate.

Vaccine is not a preventive measure without costs to personal immunity. COVID-19 is not the type of disease that immunization can offer a reliable protection. We suspect that only a limited number of B cells can exist in the body based on observed B cells count (50-500 per cubic mm). If B cells exceed certain volume fraction, they must raise blood flow resistance. Each type of B cells is differentiated for a type of antigen. B cells against fatal diseases remain in the body. When a person is vaccinated against a mild disease, the portion of B cells against the mild disease can be raised to reach up to 30% of the total B cells. It is natural that memory B cells against fatal diseases are reduced and "replaced" by new B cells against the mild disease. The immunity developed in the past is replaced by immunity against recent infections. Moreover, immunity interference was observed by released substance. IL-10-producing B cells induced in microbial infections can inhibit concurrent immune responses directed towards unrelated antigens in a bystander manner [136]. In addition, SARS-CoV-2 virus can mutate rapidly, thereby defeating a vaccine [137]. Personal variations also affect disease spreading [178].

Among the well known worldwide pandemics, influenza is among the most deadly ones [174]. The worst influenza, Spanish flu, caused by virus H1N1, killed 17-100 million people in 1918. In addition, a flu pandemic killed 1 million from 1889 to 1890; Asian flu, caused by virus H2N2 killed 1–4 million from 1957 to 1958; and Hong Kong flu caused by virus H3N2 killed 1–4 million from 1968 to 1970. The COVID-19 disease is related to bubonic plague and HIV. Two biggest bubonic plague pandemics, respectively occurred from 541 to 542 and from 1346 to 1353, killed 100 million to 300 million people. It is hypothesized that the pneumonic version of the plague was mainly responsible for the Black Death that resulted in approximately 50 million deaths in the 1300s. HIV/AIDS kills about 23.6–43.8 million people. Unfortunately, COVID-19 disease shares two lethal features: attacking lungs and destroying the immune system. While medicine has advanced medical knowledge and art for treating acute diseases, it has not failed to find cures for influenza and HIV. Given all uncorrected flaws in research models, the world cannot bet on vaccines with its entire population lives.

For all reasons stated above, it is highly unlikely to find for this disease a reliable treatment or cure that can protect all people in all circumstances. For most people, developing anti-viral biological signatures is a reliable strategy for survival from the pandemic.

I. Medicine Lacks Incentives and Channel for Improving

The merit of clinical trials can be exaggerated by producing convincing results: a treatment is better than a control. The outcome uncertainty has been fixed by conducting statistical analysis. Randomized clinical trial has gained general acceptance in medicine, become a crone jewel of medicine, and used as the final arbiter for controversial research findings. After clinical trials are

used for more than a century, they have found their ways into research culture, business practice, laws and regulations, legislative standard, etc. People are foreclosed to question their validity. Challenges to assumptions were raised in 2018 [11] with findings that ten big controlled trials are biased. After the publication of our study [10], clinical trials are still widely used in medicine for several reasons.

One reason for continuous use of controlled trials is the strong desire to see that research findings can be repeated by others. Although research findings could be confirmed by any method without relying on clinical trials, medicine takes the position that repeatability must be achieved by objective evidence and only clinical trials can produce objective evidence of repeatability. The passion for demanding research repeatability is reflected in the funding policies of NIAID Data Sharing Guideline at https://www.niaid.nih.gov/research/data-sharing-and-release-guidelines. When research activities become professional livelihood, an objective standard must be used, allowing researchers to complete for research funds on an equal footing. While this research standard promotes research repeatability, it fails the mission of finding cures. Medicine has failed to produce cures for cancer, heart diseases, infection diseases and mental diseases [104-124]. Failure of medicine was observed in 1875 [103], and 145 years later, it continues repeating the same failure. In reality, repeatability in controlled trials is perceived by imagination with no substances.

The second reason is that population-based medicine can be practiced much more easily than personalized medicine. The oldest epidemiological model [138-141], second reproduction number R0, was based on an oversimplified reproduction model which is remote from reality of infectious diseases. We examined all key assumptions and found they all of them fail to hold [3]. Two things are particularly striking: the model fails to address any aspect of disease-developing speed, a determinant factor for disease outcomes; and lack utility for telling which health factor works and which does not except strong measures like quarantine. While some epidemiological models use nearly hundreds of model parameters, they do not use any of personal biological properties. Such models could not predict the adverse effects of intervention measures [3] and nor personal health factors on infection and death risks.

The epidemiological model cannot be used to tailor a single factor to all people. For example, a heavy metal cleanser, a nutrient or a particular vitamin cannot be applied to all persons because of personal plus and minus effects of uncontrollable factors. Since all persons differ in their biological properties and are influenced by different factors in different degrees, such a model cannot determine true effect of a target factor because it is affected by plus and minus effects of interfering factors. One obvious strategy for utilizing weak factors is tailoring a matrix of personal influencing factors to each specific person. The concentration, amount, or effect level of each of the factors must be tailored to each person according to his specific condition. Obviously, personalized treatments and influencing factors cannot be used as model parameters of epidemiological models [78]. Indeed, the true effects of social, economical and environmental factors go into the resultant R0, which is hidden as part of disease agent [141]. Such factors are explanatory of several folds differences (3.7–203.3) in R0 for measles [142]. The epidemiological models should not be read to prove lack of benefits of personalized measures and weak factors.

Medical research and treatment options are driven by financial interests [143], and medicine has emerged as a medical enterprise driven by mainly financial interest [144-146, 153]: that doctors and drug companies lack financial incentives to promote personalized medicine and health lifestyle; medical journals promote only narrow types of research articles in exchange for publication

revenues [143,147-148, 150]; and peer review precludes publication of articles contrary to what is generally accepted [144-160]. NIH continues funding research projects that cannot lead to cures [143], While NIH does not have power to review outside research articles, it can only award research fund to the same studies which cannot produce predictable treatments [143]. The reductionist approach is supported by media portrayal of medical advances that can fix the human like a machine. Public campaigns reinforce this by highlighting medicalization: the message to the public seems to be that if you have a symptom, it can and should be diagnosed, treated, and ultimately cured. [116, 145]. The changes must be made by government [116,150].

As a result of influences and control by interest groups at multiple billions scale, the medical literature is full of flawed, obsolete and useless medical theories and practices [143]. The somatic mutation theory is clearly wrong for decades [161], but continues being used as the basis for cutting off tumors and killing cancer cells [119]. Randomized controlled trials and a vast number of treatments, epidemiological models, etc. are remotely from reality. Treatment-developing articles reflect great theories, high technicalities, and elegant language, but the treatments cannot cure diseases because they are developed by wrong models. Most medical treatments can only control symptoms with responsive rates of a few percents [119], which we found, have been exaggerated by ignoring damages to an unused part of organ reserve [98-100]. Drug side effects often cannot be detected by clinical trials [162-168]. All national governments fail to do their parts to correct flaws in medical research, and fail to promote personalized health [143].

After centuries of influences by population-based reductionist treatment model, public health wisdom has been ruined. The public has been misled to believing that chronic diseases are incurable and only FDA-approved treatments are safe. Population-based treatments are dangerous due to the flaws in the research model. Reductionist method can detect only a fraction of total benefits of a large number of health factors as the treatment. Inaccurate and misleading research findings continue misleading the public. Medicine continues failing to acknowledge the extraordinary benefits of personalized measures of using health factors as cures. By continuing relying on flawed research methods, medicine discriminates against holistic personalized medicine by restricting funding, rejecting articles for publication, refusing to recognize alternative treatments as legally reimbursable treatments. Medicine continues discouraging the public from using personal, environmental, lifestyle, and emotional factors as cures. This pandemic is predicted to become a worst global health crisis for which medicine has no cure.

DISCUSSION

The subject of this study is not what could be done by controlled trials. We have shown that controlled trials are not a suitable method for studying weak effects and may not be used to develop treatments for individual persons, and mathematical models are incapable of appraising the benefits of holistic model and personalized medicine. Same of main flaws are shown in the table below:

Table 2. Summary of Key Flaws in Research and Knowledge Sencership

Grounds	Reasons	Degrees of Departure from Reality	References

A. Lack of statistical population	1. Distinctive personal genome; 2. Distinctive epigenetic changes; 3. Distinctive environment substances/nutrition/toxins; 4. Distinctive emotional state 5. Distinctive chemical analysis data values; 6. Distinctive tissue/body structure; 7. Unique time in development; 8. Distinctive information on neurons; 9. Distinctive vascular system/circulation condition; 10. Distinctive disease mechanism attributes. ….	Such treatments may endanger life; However, statistical population may exist for social, political, and other purposes.	5,7, 9, 81-85-101; distinctive personal lab. data; Personal variations are implied in 175, 176, 178.
B. Reduction approach as cure	1. Interfering factors hide the effects of a single factor; 2. Mind-body interlock; 3. Systematic, cascading and chain constraints prevent changes in single point in gene, structure, biological network, etc.	Interfering factors prevent accurate assessment of a single factor; mind-body interlock prevents cure; systematic, cascading chain constraints prevent diseases from being reversed.	Indirect evidence: 86, 103-118
C. Statistical analysis and mathematical model	1. A health property in a person has a distinctive value and cannot be changed due to biological network constraints; 2. Most health factors have non-linear complex effects; 3. Plus and minus effects of a treatment factor (e.g. a nutrient) on different persons; 4. Complex interactions at multiple layers of disease mechanisms; 5. A large number of uncontrolled interfering factors have effects more than true measurement errors; 6. Treatment inaccuracies caused by treatment definition; 7. Observation error (e.g., side effects are recognized only after they have depleted organ surplus functional capacities)	Cannot be used to model population, and cannot be used to finding cures; No mathematical model can be valid in dealing with single weak factor; mathematical equation for modeling personal health/disease is far too complex to be useful.	10, 11, 70-80, Sect C, D
D. Use of control	1. Use the binary scale to arbitrarily turn continuous properties into two values (e.g., normal and diseased);	The conversion from continuous property to the binary scale makes the finding	10, 119

	2. Select a control from a narrow set of options (surgeries and chemo therapies).	meaningless; if a treatment is developed by using a chain comparison, it is poor (even though it is the best among the few options).	
Traditional medical publication practice	Publication is a business driven and run by money or revenue optimization, but has been misused to determine the merit of research.	It is natural that merit is decided by evaluating revenue-generating potential for the publishers. Medical knowledge pool is full of incorrect and obsolete theories and practices.	143-151
Lack of attention to rate balance	1. Heath state is determined by balance in biological and cellular processes in a network; 2. Disease outcomes depend on rates of various biological and cellular processes.	Due to influences of clinical trials, a vast number of studies are focused on diseases outcomes, but fail to focus rate issues.	119; Rates role implied in 169-173, but RCTs are not good.
Peer review	1. It is based on a wrong assumption a peer could determine the merit of medical discoveries at the time of publication; 2. Finding 3 favorable reviewers out of potentially millions is absurd proof of scientific merits; 2. Review is used by publishers as a device to conceal the realty that articles are selected and published for revenues.	Some medical discoveries are thrown out after 100 to 2000 years; If this approach had been used to evaluate inventions, none of the current technologies could exist. Medicine is an art that any of three randomly selected reviewers can appreciate by a scan.	157-160
General acceptance	Every wrong theory and practice has been gained general acceptance.	General acceptance is a bad standard for discoveries merits; this is the main reason for seeing massive flawed theories, useless treatments, and profitable practices in medical literature.	Common facts; 161 (cancer); 166-168 (drug side eff.); 119 (surgery) 78-80,138-142 (R0)

Statistical population for biological properties do not exist for the most intended research purposes of finding cures, and this flaw alone makes treatments invalid or even dangerous if they are used for long term. Statistical analysis cannot solve outcome uncertainty but has an effect of raising the rejection threshold for null hypothesis [10]. The mathematical models may not be used to model population because it attempts to transfer health properties from persons to persons as if they are fungible and transferable and non-distinctive. The values of an attribute of a biological pathway

for a population are scattered like a distribution. The computed average of such scattered data is different from the value of each of the persons. Moreover, each person's value cannot be freely changed into the average because the person's value is constrained by upper-stream, coupled and downstream biological pathways in the biological pathways network. In other words, departures from the perceived mean is not caused by random errors, but intended by biological law. So mathematical models can be used only as empirical predictors.

Assuming that the measured values of persons have no statistical population, the use of population-based treatment implies that the measured and averaged value is forced on each person. This would lead to an absurd conclusion that any attribute in the biological network in a person can be freely changed. This is against the known fact that every person's measured chemical data are distinctive. The unit additivity implies that for a same amount of change (e.g., 100 days survival), the biological network can be changed to support the incremental change. This is also against the constraint of the biological network.

Personal disease outcome depends on multiple layers of mechanisms concerning disease initiation, progression, innate immune response, adoptive immune response, and resolution of damages; and the disease cannot be modeled by a simple mathematical model that has been used in statistics and epidemiology. Mathematical equations for modeling a personal infection disease are too complex to be useful in the near future. It is better to use the common sense approach or use approximate models to evaluate personal health measures.

The assumptions used in statistical analysis and epidemiological models cannot hold in view of the interactions of biochemical pathways, human disease-controlling mechanisms, factor-factor-interactions, human body structural features, etc. Epidemiological models may not be used to prove the lack of the effects of personalized medicine. In the last half a year, medicine has shown its failure in the fight against COVID-19. This failure can be attributed to population and reductionist approach. By focusing on one single parameter such as customer distancing or customer density, such measures can harm the population by raising viral concentration in the air inside buildings, make customers to expose filthy air for much longer time, force them to stand lineups in chilly rain, or otherwise subject them to temperature fluctuation cycles. Such measures have effects of raising viral load and temporarily cripple human innate immunity, thereby increasing infection risk and death risk.

When society was in a lockdown state, main transmission risks are found in limited social activities. The sharp rise in infection incidents in the U.S. in this summer are attributed to prevalent wrong practices, adverse impacts of temperature fluctuations, and slowly degrading population health. By using simple reductionist public measures, people are not taught to understand how locking up doors, crippling ventilation, exposing people to freezing temperatures, rains, and severe temperature fluctuations, restraining people in extended duration, consuming imbalanced foods, exposing to more toxic substances, etc. can diminish their abilities to survive from the pandemic. Medicine lacks useful methods to detect and predict the adverse effects of movement restriction measures and associated poor lifestyles.

Governments should formulate better regulations other than one-parameter rules. Banning social events based on head counts may be used as emergence measures, but cannot be used as long-term solution. Head count is not definitely associated with viral infection rate and death risk, but provides only a possibility that a larger number of people could be exposed to the virus. Banning all social activities has long-term adverse impacts on personal antiviral biological signatures. The

measures should be formulated in favor of promoting human long-term health. Instead banning social activities by head count, focus should be the use of protective measures in each situation.

Personal biological signatures affect human infection risk and death risk. This fact has been firmly established by a large number of studies, risk factor analysis, biological signatures among died patients, transmission studies, etc. This fact is strongly corroborated by correlation between certain biological signatures and infection and death risks. Most important personal biological properties and influencing factors include organ usable functional capacities [175], exposure route and severity, innate immunity and host responses, adaptive immune response, micro circulation in lungs, and available volume in the thorax cage. People differ in heart output by 2 folds?, organ usable functional capacities by more than one fold, and in available space in the thorax by five times. We conservatively estimate that as much as 90% of deaths and disabilities could be prevented or mitigated by altering those biological and structural properties.

Most biological properties (except genes and age) can be altered by using lifestyles, foods, exercise, emotion management, and avoidance of toxic substances. Even certain genetic properties can be altered to limited extent by changing epigentics. The effects of many primitive factors have been found in studies; and effects of weak factors such as activity habits, cellular phone use, etc. cannot be determined under current research models but may be established by studying disease mechanisms or disease risks. There is no valid basis to argue that findings from controlled trails are valid or better. The adverse effects of lack of exercise and inactivity can be seen in elevated disease risks among obese people, people having vascular diseases, people who are sedentary. However, negative findings in clinical trials should not be read to preclude potential benefits of weak factors on specific persons.

Medicine actually uses a democratic representation principle in research. Treatments developed in clinical trials can have severer adverse impacts on minorities. The genetics are more similar between persons within a race than between members in different races. The computed average health property for a population of a majority race is expected to be different from that for a population of a minority race. If a treatment is developed by a clinical trial containing persons of both races according to their population ratio, the average will be more closer to the average of the majority race. This implies that the treatment for the minority race is poorer or more dangerous than it is for the majority race. This is a big political question.

Medicine is controlled and maintained by interest groups as an enterprise [143-148]. Medical subjects are selectively disseminated by medical journal publishers, peer reviewers, research funds, and laws and regulations (medical expenses reimbursement policies) to advance the enterprise interest. Medicine has become a dysfunctional profession that lacks channels and incentives for self improvement. Even journal article specifications are designed to promote articles addressing a narrow topic under the reductionist paradigm. Massive research findings on lifestyle factors, reductionist approach's limitations and the performance failure could not generate momentum for correcting the flawed foundation of medicine. By using the same flawed research model, medicine repeats its failure in finding cures for chronic diseases, but keep producing treatments for controlling symptoms. The flaws in its foundation are responsible for failure to prevent billions of premature deaths in its history. Now, it is failing mankind in the war against the pandemic.

The medical paradigm has been developed for flawed population-based reductionist research and treatment models. Even knowledge dissemination practices are custom-made for reductionist

articles. Word count limitation, article structures, evidence standard, reference requirements, peer review, etc. are set up for an experiment intended to address a single narrow issue. Under the reductionist model, medical researchers can address any single issue out of context, and a supper majority of findings in treatments are grossly inaccurate and completely wrong. When every key assumption fails, there is no point to argue that treatments so established somehow could cure diseases. Among the large number of model inputs used in epidemiological models, few of them even touch biological properties, and yet, thousands of such articles are published as science, but articles that focus on hundreds of disease-controlled factors are rejected for failure to comply with discriminatory review standards, absurd conventions or affect its financial interests. We need to see a revolution to end this gross injustice that hurts every human life in the world. Nature does give mercy to the crime of the injustice.

Gross health injustice will continue as usual, and medicine will repeat its perpetual failure unless it is forced to examine its model flaws, acknowledge the inherent risks of existing treatments, and stop propagating factually wrong messages that diseases are incurable and that only FDA proved treatments are safe. Public must get the message that FDA-proved treatments are inherently dangerous and best cures lie in personalized health. We urge governments, public organizations, patients, and private citizens to initiate legal processes to dismantle all barriers that have maintained the medical paradigm, and provide financial incentives and legal obligations to acknowledge and disuse dangerous treatments.

CONFLICT OF INTERESTS

None.

ADDITIONAL INFORMATION

Additional information is provided in a supplemental document and some information will be stored in igoosa.com online database.

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