Surgery, Chemotherapy and Radiotherapy Promote Cancer Growth Speeds and Shorten Patient Lives

Jianqing Wu[1], Ph.D., J.D. and Ping Zha[2], M.D. (Chi. Med.)

Correspondence: tempaddr2@atozpatent.com

1. End the Incurable Era (Independent researcher for cause), P.O. Box 689, Beltsville, MD 20704. www.igoosa.com.

2. Independent Researcher (Not affiliated with any entity), can be reached by using the above address.

ABSTRACT

After reviewing cancer theories, cancer treatment development histories, randomized clinical trial's performance, cancer treatment strategy, trial follow-up times, and conducting numerous simulations using existing data, the authors found: (1) medical treatments come with three to four lethal factors: treatment side-effects, emotional distress and chronic dress, lack of exercises or physical inactivity, and excessive nutrition in some cases; (2) clinical trial exaggerates the benefits of fast-acting treatments and underestimates the slow-delivering adverse side effects as a result of statistical averaging, interfering effects of personal lifestyle factors, and insufficient follow-up times; (3) the benefits of medical treatments are limited by chain comparison, where surgery sets up a negative standard relative to the best way for resolving cancer; (4) the strategy of destroying the tumor is unworkable; (5) medical treatments can turn natural cancer growth curve into approximately doubly exponential curve; (6) multiple factor non-medical measures are much more powerful than medical treatments in controlling cancer growth and metastasis rates; and (7) cancer early diagnosis and over treatments are bad strategies that have great adverse impacts on cancer patients. Based on huge increases in cancer growth rate constants, substantial of loss of organ functional capacity, and severe systemic aging-like cellular damages, the authors concluded that medical treatments promote cancer growth and metastasis rates and shorten patient lives in most cases, and the claimed benefits are caused by triple biases of clinical trials. The authors believe that the better strategy for ending the global cancer epidemic is abandoning clinical trails as the research model, changing caner treatment strategy from killing cancer cells to slowing down cancer growth rates by using multiple factors optimization approach in personalized medicine.

INTRODUCTION

15   President Nixon declared a war on cancer in 1971 with his signing of The National Cancer Act. Half a century later, no cure has been found.

We have heard time and again about "ground-breaking cancer research." One thing that has never changed is the approach used in cancer research and the cancer treatment model. A recent meta review shows that the complete re-
20 sponse rates for remission of later stage cancer are around 7.4% [1]. The complete response does not preclude cancer from returning, implying the actual performance is much worse. Chemotherapy has severe drug side-effects and causes cancer relapses at much faster speeds. A systematic review of thyroid cancer treatment performance found that response rate was 22.1% to 27.1%, with com-
25 plete response rates being 2.5% to 3.4% [2]. A retrospective cohort study conducted a systematic evaluation of cancer approvals by the European Medicines Agency in 2009-13 and found that most drugs entered the market without evidence of benefit on survival or quality of life [3]. At a minimum of 3.3 years after market entry, there was still no conclusive evidence that these drugs either ex-
30 tended or improved life for most cancer patients. This is similar to another finding: "The overall contribution of curative and adjuvant cytotoxic chemotherapy to 5-year survival in adults was estimated to be 2.3% in Australia and 2.1% in the USA [4].

Cancer researchers started seeking target drugs since around 1980. A can-
35 cer drug like beta-blocker was thought to block cancer growth, but inevitably interferes with normal biological functions including blood glucose uptake by skeletal muscle. Half or more of people who start taking a beta blocker stop within a year [5]. The latest meta-study involving 319,006 patients shows that beta blockers have nearly no benefits [6]. Another meta review similarly found
40 dubious benefits or marginal benefits and small negative impacts, depending on cancer types [7]. A meta review on the effects of angiogenesis blockade for the treatment of gastric cancer show mixed benefits [8]. Small benefits are found for only certain types of cancers and certain types of patients.

Another meta review also found that such drugs do not extend overall sur-
45 vival for biliary tract cancer [9]. The use of target therapy with radiotherapy compared to standard therapy increased the chance of severe adverse events while yielded comparable survival in glioblastoma multiforme patients [10]. The addition of targeted drugs to a chemotherapy (TEM + RAD) did not improve the overall survival of patients with glioblastoma multiforme; however, it had some
50 effect of stopping cancer progression for patients treated by cilengitide and the rate of adverse effects was higher in the experimental group than in the placebo group [11].

The general picture is that a vast number of patients do not fully respond to cancer drugs; none of chemotherapy, adjuvant drugs, and target drugs can

55 cure cancer in a predictable manner; and no drugs can reduce the risk of cancer returns. "The claimed 'targeted' therapies that may or may not extend remission of cancer for a few months should not be accepted any longer as 'cure' by oncologists, scientist or patients...." and designer drugs cost between $100,000–$1000,000. [12]. Numerous surveys show that few doctors would consider using
60 radiotherapy on themselves because it can cause new cancer, and that 75% of doctors would not consider using chemotherapy on themselves (N1, Sup.).

Those little benefits are under challenge here.

METHODS

65 The author assumes that "killing cancer cells" is a wrong strategy, and tried to evaluate treatment effects by using cancer growth rate constant -- daily cell net gain from the balance between cell dividing rate and cell dying rate. Our assumption is that cancer cannot be cured by killing all cancer cells, but is presumably cured by decreasing cancer cell daily net gain to negative.
70 Therefore, we wanted to develop a methodology for comparing medical treatments with non-medical measures.

We systematically evaluated the performance of medical treatments from many angles such as treatment history, cancer theories, treatment performance data, medical model, recent studies and meta reviews. We will evaluate
75 treatment benefits by focusing on how they affect cancer growth rates.

To analyze the adverse impacts of medical treatments, we extracted important elements such as systemic inflamation, tissue loss, cell damages, chornic stress, physical inactivity, exericses, exessive nutrition, etc. from each of the medical treatments. From cancer research literature, we extracted data that
80 show how each of such elements affects cancer growth rates. We then analyzed how the elements of each medical treatment or a combination of treatment collectively affects cancer growth rate.

To determine how lifestyle factors affect cancer growth rates, we reviewed the findings from a large number of studies, and estimated the effects of non-ki-
85 netic data on cancer growth rates. The non kinetic data we used include incidence data, hazard ratios, and survival times, etc. In estimating their impacts on cancer growth rates, we will show how clinical trial outcomes are biased and how to estimate their true effects.

90 **RESULTS**

3   A preprint for discussion only

A. Medical Treatments Were Guided By Obsolete Cancer Theories And Were Never Compared With Non Medical Measures

One fatal flaw in medical treatment development is revealed in Figure 1. The figure shows the times for various cancer theories (from pre-1800 to 2019), the start times of increasing uses of surgeries (1846), the start time for using radiotherapy (about 1900) and the start time for using chemotherapy (1946), the start time of discovering cancer cause-related factors and influencing factors (mainly after 1980), and the start time for discovering exercises effects (mostly after 2000). A large number of factors can affect cancer outcomes. The factors, including risk factors, cause factors, and influencing factors, fall within six large classes: the side-effects of medical treatments, emotional distress and chronic stress, exercises and inactivity, diet and nutrition, cancer fighting natural compounds, and certain other lifestyle factors. Those factors are shown in the top box in Figure 1.

The cancer theory history reflects how cancer treatments were developed. It was believed that cancer is caused by a milk clot in a mammary duct, acidic lymph fluid, cancer poison, hormone, chronic irritation, infections, tobacco snuff, etc. [13]. Some theories include homoral theory (Hippocrates's belief), lymph theory (Stahl and Hoffman), blastema theory (Johannes Muller, 1838), chronic irritation theory (Virchow), trauma theory (widely accepted belief from the late 1800s until the 1920s), infectious disease theory (Zacutus Lusitani, 1575-1642, and Nicholas Tulp, 1593-1674) [14]. All old cancer theories are clearly wrong or inaccurate, but are presumed to have influenced the developments of cancer treatments.
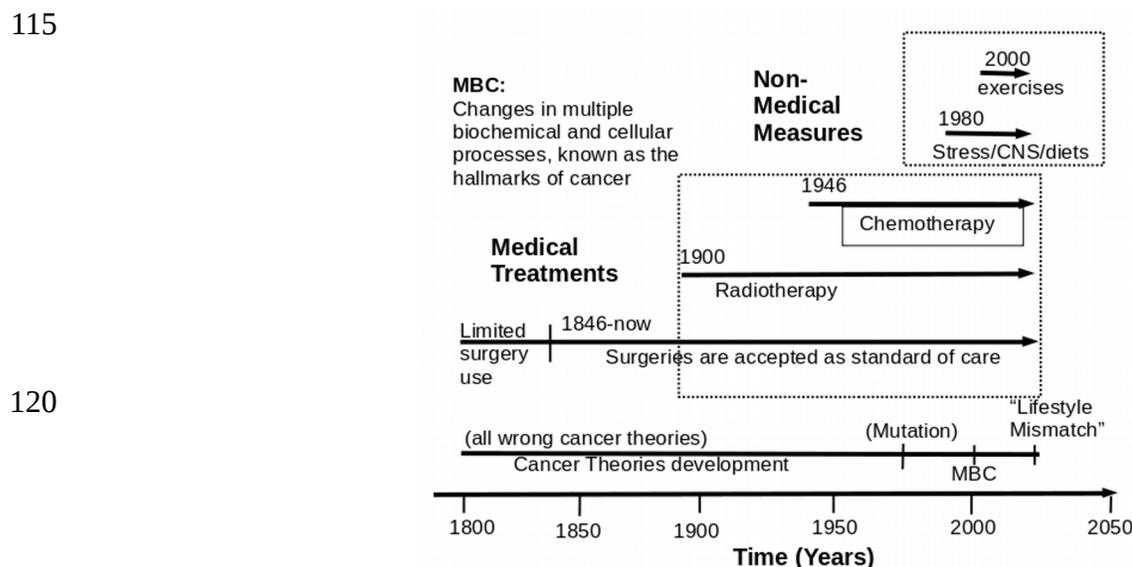

Figure 1 Time Lines of Cancer Theories, Medical Treatments, and Causal Factors Such As Stress, Inactivity, Diets, Lifestyle Factors, Etc.

4   A preprint for discussion only

125   Most influential cancer theories include somatic mutation theory (SMT) [15 Brücher and Jamall, 2016], somatic evolution theory [16] and revolutionary cancer theory [17]. None of modern cancer theories can explain all causal factors, risk factors and influencing factors. The SMT theory cannot explain the most striking fact that most mutations take place at the birth and new mutations are
130   added in a similar pace in each year, cancer incidences strike mainly people above 60. It does not explain the roles of emotion, personal lifestyles, and personal habits.

        In the last half century, cancer research slowly discovered that cancer is accompanied with changes in a large number of biochemical and cellular pro-
135   cesses. Some of such changes are well reflected in "The Hallmarks of Cancer" by Hanahan & Weinberg [18]. Cancer is considered to be also caused by the mismatch between modern lifestyles and what human genes were adapted to [19]. Inferring from known causal factors, risk factors, and influencing factors, cancer is a result of changed biochemical and cellular processes associated with misfit-
140   ted lifestyles. Changed biochemical and cellular process patterns further imply that cancer cannot be cured by cutting off the detected tumor or killing all cancer cells. Thus, surgery, chemotherapy and radiotherapy developed by relying on old and obsolete cancer theories are deemed to fail in one or many aspects.

        The unsettled performance of surgery can be explained by examining its
145   development history. The "benefits" of surgery for "curative" treatment of breast cancer was "recognized" by the Greek physician Galen of Pergamum (130–200 A.D.) and Scottish surgeon John Hunter (1728-1793). A century later, matured anesthesia art (e.g., diethyl ether in 1846) promoted its use. It later became a standard treatment. This standard gained wide acceptance long before any re-
150   motely right cancer theory was developed. Its use in treating rectal cancer was prompted by anaesthesiological techniques. In 1908, William Ernest Miles introduced the basis of modern rectal cancer surgery with improved surgical options [20]. Thus, the rationale of using surgery is based on an unproved "notion" that a tumor can be cut off and killed and a cure is to remove the tumor. It is like an
155   attempt to change biochemical and cellular processes by cutting reactant media. An obvious reason for its continuous use is that surgery can reduce cancer burden and patients can survive for several months to several years. This notion might have been right in the ancient time when cancer patients were not enabled to fight cancer. All cancer patients could do were taking more rest, eating better,
160   and doing everything incorrectly.

        Chemotherapy started gaining momentum around 1946 when Gustaf Lindskog's study on non–Hodgkin's lymphoma was published. It had been heavily influenced by old cancer theories on infection. The "chemotherapy" was a term used for treating infectious diseases in the early 1900s. Penicillin was initially
165   thought to have anti-tumor properties. The antibiotic, actinomycin D, had significant anti-tumor properties and enjoyed considerable use in pediatric tumors in the 1950s and 1960s. Medicine has slowly developed clinical trials as a standard

for evaluating effectiveness of drugs [21, 22]. A key requirement is that human subjects are randomly assigned to a control group or a treatment group. How-
170 ever, a large number of factors relating to lifestyles cannot be controlled. When clinical trials are used as the standard, medicine essentially excludes as cure anything that cannot be controlled and anything that require patients' active involvement. What is excluded include mind regulation (changing emotional state, reducing stress, avoiding fears, changing faith, being happy, etc.), changing life-
175 styles, getting rid of bad habits, using special diets, doing exercise, raising body temperature, altering body mechanical properties, etc. Moreover, using placebos in cancer is improper because cancer can cause deaths, and controls are thus selected by using best-available-therapy [23]. The generally accepted strategy is to kill all cancer cells. Since it was impossible to show that non-medical measures
180 can kill cancer cells, they cannot be used as treatments for cancer.

        Accepting clinical trials and the best-available-therapy as controls essentially narrows treatment options to only things that can be swallowed without distinctive tastes and anything that does not grab the attention of the human subjects. Best candidates are naturally synthetic drugs, radiation, and things that
185 can be wrapped in small sizes for easy administration.

        The misplaced trust in clinical trials naturally leads to this current drug-evaluating practices. A review of drug approval history reveals a chain comparison scheme: the benefits of each drug are determined by comparing the drug with surgery or an old previously approved drug, and the newest drug is com-
190 pared with a previously approved drug or equivalent. This comparison pattern can be seen in any clinical trials [24, 25, 26, 27]. Most experimental designs of clinical trials can be found in the online database www.clinictrial.gov. The treatments in both control and treatment arms include surgery and one or more drugs. A common randomized trial is to compare a new drug with old drug on pa-
195 tients who have some type of cancer. The FDA approved panitumumab for extending mean time to disease progression or death by 36 days over the best available drugs (fluoropyrimidine, oxaliplatin and irinotecan). To save resources, the control arm can be shared among different clinical trials [28].

        All cancer treatment studies focus on the treatment's ability to remove or
200 kill cancer cells. A cure must have power to kill cancer cells. This long treatment convention leads to an unspoken presumption that risk factors can cause cancer or influence cancer growth, but cannot be used to cure cancer. After tens of thousands of studies have been published to show the effects of a large number of lifestyle and environmental factors on cancer, the factors can be used only to pre-
205 vent cancer but not cure cancer. This presumption has frozen medical research mindset to selecting "tallest dwarf" from a room full of dwarfs in treatment of cancer.

        Surgery has escaped from being validated in the entire medical history. Since surgery has been used as the standard treatment, the true benefits of surg-

210 eries are unknown. Before 1980, most cancer causal factors, risk factors, and in-
fluencing factors, and self-healing were largely unknown. The roles of lifestyles,
life habits, hundreds of factors such as omega 3, vitamins, antioxidants, free radi-
cals, apoptosis-inducing compounds, exercise, emotional distress and chronic
disease, etc. were unknown. Thus, the true benefits of surgeries could not be as-
215 sessed against measures for correcting causal and risk effects. From 1980 to
present, more of knowledge of cancer has been found, but medical researchers
could not overcome the presumption that a treatment must have a sufficient
power to destroy the tumor. With that presumption, ethical consideration further
prevents anyone from using any unapproved non-medical measures as cancer
220 treatments. Thus, potentially tens of thousands of non-medical measures are au-
tomatically precluded as potential cures. Medicine has not evaluated surgical ab-
solute performance, which must be made against everything under the Sun.

Surgeries were used as standard treatments [29]. When surgeries were
used as controls for chemotherapy and radiotherapy, determined performance of
225 chemotherapy and radiotherapy is relative to that of surgeries. All drugs and
other treatments are evaluated by comparing them against surgeries directly or
indirectly. If surgeries have large negative benefits over best references, the "de-
termined" performance of drugs or other treatments can be still on the negative
side. If surgeries do shorten lives dramatically, drugs or other treatments may
230 similarly shorten lives. Moreover, surgeries may set upper limits on the patient
lives by their strong adverse effects. Whatever benefits of chemotherapy and ra-
diotherapy exhibit in clinical trials are only some improvements over life-shorten-
ing treatments.

B. Four Big Lethal Factors Associated with Medical Treatments

235 Cancer treatments are often associated with four lethal factors: their side
effects, emotional distress and chronic stress, lack of exercises and physical inac-
tivity, and excessive nutrition that is often seen on some cancer patients. Radical
or invasive medical treatments exert adverse effects by causing systemic dam-
ages and tissue loss and raising systemic inflammation. Emotional factors exert
240 their adverse impacts by shocks, emotional distress, chronic stress, angry, etc.
Long-term physical inactivity exerts its adverse impacts by speeding up aging-
like health deterioration. Excessive nutrition improves nutritional supply to can-
cer cells inside a tumor.

1. Kinetic methods for characterizing cancer growth rates

245 The purpose of this study is establishing a method for evaluating every po-
tentially relevant factor on cancer growth rates. It is necessary to use a kinetic
method to characterize cancer growth. Tumors often exhibit Gompertzian
growth, but their growth rates depend on cell numbers. Thus, the first order law
must be the main characteristic of kinetics [30, 31, 32]. Cell divisions among all
250 cells are initially synchronized, once the clock control is off, their division timings

will become out of phrases after a number of division cycles, and the fractions in each phase of the cell cycle reach a steady state. After that, cells divide in an asynchronous manner with different number of cells dividing in different times. For convenience, daily gain or loss of cancer cells can be evaluated by cell cycles (or every 24 hours). The exponential growth curve of solid tumors will level off due to resource limits. The fraction of cancer cells that are dividing vary from day to day. Net growth rate constant (1/day) is equivalent to a fraction of cancer cells in the tumor that actually completes cell division in each day, and will be referred to as an apparent rate constant. In fighting cancer, what is important is the daily cell changes (the differential equation). The integrated equation can be used to only show general cancer cell number changing pattern.

2. Surgery raises cancer growth rates

Until Halsted (1908), the general consensus was clearly that, unless forced by the circumstances, surgical resection should be avoided for disease much more advanced than very early stage tumors (the cacoethesis of Celsus) [33].

Obvious evidence against use of surgery is that cancer is not a single tumor. Cancer may often come with different tumors of different sizes, with different detection times. After a primary tumor is removed or destroyed, the body does not stop any cancer cells or even normal cells from growing into new tumors. Cancer metastasis is not about one tumor in one site. Surgeries with or without drugs and radiotherapy cannot stop micro-tumors in pipeline.

Surgery often removes tumors with large tissue margins or remove a significant part of organ. It reduces organ functional capacity. Organ reserve correlates with the outcomes of surgical treatments or chemotherapy as implied by a treatment-accelerated aging process [34]. It can safely be assumed that death occurs when a vital organ's functional capacity is reduced to below a threshold of death. When cancer burden progressively reduces a vital organ's functional capacity, further reduction of the organ functional capacity by removing margin tissues shift time of death to an earlier day. Surgeries also exert adverse impacts by creating emotional distress. Patients may be disabled physically, lose dignities, and sustain emotional pain from abandoning their life plans and hopes. Physical and emotional impacts in various degrees have not been used to appraise surgeries' performance against "best reference" performance.

Since patients do not immediately die, it creates an impression that a radical operation is the correct way to extend life. No attempt has been made to understand how surgery actually shortens patients lives over "best reference" lifespans that patients would live if their cancers naturally resolve OR are held in check by using non-medical measures.

We show that the notion that "tumor must be cut off with all cancer cells killed" is like an attempt to halt somatic cell revolution and human aging

process. To a reasonable person, killing all cancer cells is impossible. This presumption is clearly incorrect but forces medical professionals to accept only invasive and harmful treatment methods and reject everything else. No valid evidence exists to show that approved medical treatments are better than tens of thousands of other non medical measures. No existing evidence can show that non-medical measures cannot safely slow down cancer growth rates. There is no basis to believe that medical treatments are best, can extend lives or improve life quality. The "scientific validity" of the cancer treatments cannot pass the weakest challenge.

Recent studies started to cast serious doubt on surgery. One adverse effect of surgery is that it raises cancer growth rates of return cancer. Although some cancers recur many years after tumor surgical removal, a substantial fraction of patients develop overt metastases relatively soon after removal of their primary tumors [36, 37, 38]. A prior surgery dramatically alters the body's ability to resist future cancer [36, 37, 39, 40]. Surgically operated patients experience a sharp rise in the risk of distant recurrence that begins 6 months after surgery and peaks between 12 and 18 months.

A study by Krall et al. provides conclusive evidence that surgical tumor removal triggers the outgrowth of otherwise-dormant metastases, leading to the synchronous pattern of relapse. The tumor incidence rate and tumor size are related to the severity of wound. The study further found that the systemic wound-healing response triggers tumor outgrowth at distance sites. The study pinpoints the wound of surgery as at least one cause of fast cancer returns and cancer metastasis. This is consistent with the finding that inflammation promotes invasion and metastasis [41]. This finding also supports the fact that surgery can paradoxically augment development of metastases [42].

Cancer growth time from tumor initiation to the time that a tumor is or could be detected is particularly important in practice. For many types of cancers, cancer growth rates start picking up at about 50 to 55. The incidence rate of cancer at an age is proportional to probabilities of occurrence of each mutation per unit time and the sixth power of the age [43]. Most patients are diagnosed at ages after menopause [27, 29] while dormant cancer was frequently found from 80 to 85. The total growth times for most types of cancer is about 5 to 25 years while some types of cancer could take 50 to 70 years to reach a detectable size. A median growth time is about 15 years. One surgical operation will shorten next tumor's growth time to one and half a year. This implies that surgery raises the cancer apparent growth rate constant by as much as ten folds.

For a tumor of an initial size to reach a detectable size, the product of the rate constant k and time t is fixed. When k is raised by 10 times, the growth time for achieving the same final tumor size will be reduced by 1/10 folds. The rise in the growth rate constant by one order of magnitude is a game-ending adverse effect for cancer patients.

3. Chemotherapy and radiotherapy promote cancer growth rates

335   Chemotherapy and radiotherapy have been known for raising cancer growth rates for decades. One well known old puzzle is the rapid return of cancer after administration of chemotherapy and radiotherapy. A rapid regrowth of cutaneous or pulmonary metastases has been observed [30, 31] and in non-small cell lung cancer [44]. The change is characterized by a much shorter doubling
340   time ("DT") which is the time required to double cancer cells. In 31 human metastases in which it was measured, the value of this ratio ranged from 2.5 to 5. Since DT*K=Ln(2), the reductions of DT are equivalent to 2.5 to 5 times increase in the apparent rate constant. Similarly, untreated and unresponsive patients had a growth fraction of less than 4% for myeloma, but relapsing patients
345   had growth fraction ranging from 14% to 83% [45]. Growth fraction is closely related to DT, it is estimated that the rate constant increases by about 3.5 to 20.75 times.

    Cancer growth rate depends on existing cancer cell number. This is true even if a large number of other factors such as geometry, nutrition, daily food in-
350   take, daily physical activity, etc. affect cancer dividing rates. Assuming that a cancerous aggregate of 100 cells becomes a detectable tumor of 1 billion cells in 10 years, it would be equivalent to a daily net addition rate of 0.004416 (1/day). This is equivalent to a kinetic process where about 4.4 cells per 1000 cells in the tumor divide (ignoring the cells that die). The times for 100 cells to reach 1 bil-
355   lion cells under various rate constants are shown in Table 1 below.

Table 1 The Impacts of 2.5-5 Times Increase in Growth Rate Constants

Change in (k)	Start Cells (No.)	Final Cells (Billion)	Rate Const. (k)	Time (Years)	Comments
Pri. Tumor	100	1.0	0.004416	10	Slow
2.5X	100	1.0	0.01104	4	Faster
5.0X	100	1.0	0.02208	2	Very fast

    If the rate constant rises, the final cancer cell number from an initial number in a given time will be increased by a multiplier M. This multiplier M can be estimated by M=Exp((n-1)*kt), assuming that the tumor grows in the same pace
360   (N2, Sup.). For example, by raising the rate constant by 2.5 times, a returned or a secondary tumor could generate 1413 times more final cancer cells within the same 3 years (N3, Sup.). This is why returned cancer is often terminal if no measures can stop the cancer from growing. While cancer division rate can vary from day to day and true rate constants fluctuate from day to day, its daily values are
365   critically important.

    The final cancer cell numbers depend on cell dividing cycles and rate constants. An increased apparent rate constant or reduced doubling time can lead to much larger final cell numbers. The tumor will become much larger with each day passing. This problem should be viewed in light of another problem that mul-
370   tiple tumors may erupt in various organs at dramatically increased rates (even though they are not detected). Due to differences in tissue ecosystem, one year

difference in detection time is natural. The adverse effects of increased rate constants lie in compounding effects. It is like multiple mortgage loans compounded at variable daily interest rates. A slight rise in the daily rates for a loan may bankrupt the debtor because the increased loan balance can affect each of thousands of subsequent compounding cycles.

Most administrative protocols of chemotherapy cannot kill all cancer cells by batch applications; the half lives of a super majority of cancer drugs are short [N4, Sup.]. We estimate that they lose 90% concentrations in just 1 to 3 days. In each hiatus between two administrations, cancer cells could generate new cells even though the new cells cannot be accurately detected by any known method.

The scope of side effects of cancer drugs were underestimated. If the drug causes any symptoms in any part of the body, a proper presumption should be that the drug affects every part of the body because the same drug is circulated in every part of the body. However, some parts of the body can tolerate the drug side effects better and thus need more time to realize damages. If the drug is slowly diminishing an organ's functional capacity, its side effects will not be felt until the subject's health has deteriorated to a point that the organ functional capacity is insufficient to support life. The scope of adverse effects is reflected in cancer survivors' aging-like cellular damages and lost lifespans [34, 46, 47, 48].

Our findings refute findings that chemotherapy and radiotherapy have a few percents contribution to the 5 years survivals. Cancer treatments were driven by the presumption of "killing cancer cells." That strategy is clearly obsolete. All prior studies are based on chain comparisons using surgery as a starting reference. If surgery shortens patient lives by various big margins, a few percents improvements over such a bad control as determined by 5 years survival rate cannot turn their net effects to the positive sides. Clinical trials are unfit for studying slow-delivering side effects; and statistical analysis of clinical data is meaningless when controls are improper. After those flaws are corrected, we predict that the true effects of chemotherapy and radiotherapy are negative.

4. Adverse emotional factors promote cancer growth rates

Emotional distress, chronic stress and other emotional factors speed up cancer initiation, growth and spread [49, 50, 51, 52, 53]. The evidence, taken as whole, is conclusive. Adverse emotional factors also dramatically speed up cancer metastasis.

The study of Sloan *et al.* sheds light on the magnitude of effects of chronic stress on cancer growth and metastasis. Chronic stress applied to mice for 20 days increased the metastasis of the primary breast tumor cells to distant tissues by 38-fold versus controls [50]. The rate constant was raised by 0.182 (1/day) (N5, Sup.), which is equivalent to the doubling time of 3.81 days. Even assume that the apparent growth constant k for the control is zero (e.g., the cancer would be in a dormant state), this rate constant would drive cancer growth at the

speed equivalent to that for 100 cancer cells to reach 1 billion in about 89 days (23.35 days doubling time). While the mice model in the study cannot be directly applied to humans and the kinetic model provides only a ballpark estimate, this finding supports a point that stress can dramatically raise metastasis rates. We personally heard stories where a shock and extreme fears can inflict extreme emotional pain.

5. Physical inactivity promotes cancer growth rates

Physical inactivity is an important cause of a large number of chronic diseases [54, 55]. They found: "The comprehensive evidence herein clearly establishes that lack of physical activity affects almost every cell, organ, and system in the body causing sedentary dysfunction and accelerated death." Some cited studies show that inactivity can produce adverse impacts in as short as 3 days. Although this study doses not concern cancer, the finding is applicable to cancer because exercise can reduce inflammation and inflammation is a central promoting factor for cancer. By making an inference, exercises can have large beneficial effects.

The magnitude of adverse impacts of lack of exercises on cancer outcomes cannot be found from cancer literature, but the beneficial impacts of exercises are well documented. Exercise is found to be an important adjunct therapy in the management of cancer [56]. In this review, a total of 100 studies were reviewed involving thousands of individual patients whose exercise behavior was assessed following the diagnosis of any type of cancer. They concluded: "[s]pecifically, superior levels of exercise following a cancer diagnosis were associated with a 28%–44% reduced risk of cancer-specific mortality, a 21%–35% lower risk of cancer recurrence, and a 25%–48% decreased risk of all-cause mortality." The role of exercise in reducing cancer return is outstanding.

Exercises, like any other lifestyle factors, work by altering cell division on a daily basis. They work not by killing cancer cells like medical treatments. Naturally, they could not deliver instantaneous beneficial effects on cancer growth, but deliver beneficial effects by influencing cell compounding speeds on a long-term basis. Each new cancer cell reduced in an early day is equivalent to killing a potential seed which would be compounded for thousands of cycles like a home mortgage loan. Thus, the benefits of exercises cannot be detected by using randomized clinical trials, but their accumulated effects are substantial. The magnitude of benefits and the scope of effects are conclusively established by a large number of studies [57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68].

Exercise is presumed to be the best measure for slowing down and stopping cancer metastasis. It reduces systemic inflammation and mitigates chronic stress, both of which are known to speed up cancer metastasis speeds. Many exercise parameters relevant to its performance were not explored in cited studies.

6. Excessive nutrition promotes cancer growth rates

Most cancer patients lose weights as a result of cancer's natural effects. This leads to a belief that better nutrition is necessary. Over nutrition is often seen among patients in early stages of cancer. Since most cancer patients die while they are progressively losing weights, it is counter-intuitive to advise nutritional restriction in cancer care. Cancer cells are in an unfavorable condition to compete for nutrition because more of them need nutrition for uncontrolled cell proliferation. Cancer cells cannot grow to become more than 1-2 mm in diameter if blood vessels are not generated [69]. Even if partial blood vessel networks are created, at least some cancer cells cannot get enough nutrition. The need for more nutrition is not entirely based on nutritional amounts actually used by cancer cells, but is more based on required delivery capability. Since nutrients get into most cancer cells inside tumors by diffusion, a concentration gradient is a thermal force to push more of nutrient molecules into the inner cells of the tumor, thereby preventing them from dying from lack of nutrition. There must be a concentration at which normal cells could get enough nutrients, but some cancer cells could not. It is generally agreed that obese and high glucose levels increase cancer risks.

7. Medical treatments combination accelerates cancer growth and shorten patient lives

The four lethal factors are often associated with or aggravated by cancer treatments. When those lethal factors are combined, their total adverse impacts are expected to be extremely large.

Figure 2 shows how all medical treatments exert instantaneous impacts and long-term impacts. Surgery is extremely powerful in removing the tumor as shown in (A) in Figure 2. Cancer drugs lose their effectiveness in killing cancer cells by developing drug resistance by many mechanisms [70]. While the efficacy of killing cancer cells rapidly decrease with time, severe adverse effects are accumulated with time (B). Surgery reduces organ functional capacity by removing margins tissues and organ tissues, and raises systemic inflammation; and chemotherapy and radiotherapy increases the degree of damages to body cells and organ tissues with time (B). Emotional distress and chronic stress further promote cancer growth and metastasis. Lack of exercises also encourage systemic inflammation like an adverse effect. Excessive nutrition may be an additional lethal factor for some cancer patients. When all of those lethal factors work on the same patient, the tissue's ability to resist cancer cell division is progressively reduced so that cancer daily dividing rates progressively rise with time (C). As a result of those impacts, medical treatments speed up cancer growth rates, cancer return rates and metastasis rates. Surgery dramatically raises cancer growth rates by raising systemic inflammation and diminishing organ functional capacity; and chemotherapy and radiotherapy raise 2.5 to 5.0 times of original rate constants.
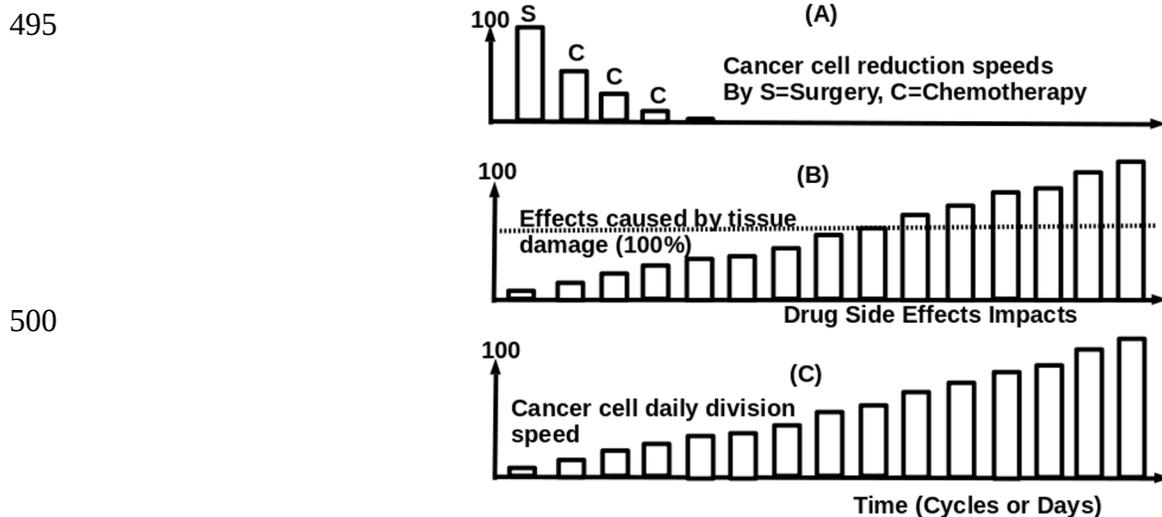
495

Figure 2 Instant and Accumulated Effects of Medical Treatments on Cancer Rate Constants.

500

505

The adverse effects of cancer treatments could not be fully revealed in clinical trials. The side effects result in cellular damages to the body. The cellular damages influence cancer outcomes by affecting cancer cell division cycles on a daily basis, and their adverse effects are expected to have enhanced uprising exponential characteristics. While the degree of cellular damages caused by drug side effects is expected to increase with time, the tissue's ability to resist or inhibit cancer cell division is presumed to deterioate with time. This progressive diminishing tissue ability favors more cancer cells to divide in each of the cell cycles in the patient's life time. An extra number of cancer cells on any day over a natural baseline will undergo cell division in each of later cell cycles with increasing higher chances in the future. If the patient life time has N cell cycles, it has N series of extra cells gains, compared with the natural reference without side effects. The total number of cancer cells which are from all those series is expected to be very large. Each series of extra cells divide at increasing rate constants as shown in (C). Even if cancer cells divide at a constant rate constant, the cancer cell growth cure exhibits exponential characteristics. When the rate constants have uprising characters like slow exponential curve, the cancer cell growth curve exhits nearly doubly exponential characteristics with increased uprising degree. To determine the full side effect including the later effects, a clincial trial must be sufficiently long and interfering factors must be controlled. This later-realized side effects will nullify the benefits from the strong effects of killing cancer cells in the early times.

The effects of side effects of medical treatments on cancer growth rates can be established by examining the role of aging. It has been established that cancer incidence rate is proportional to the sixth power of the age [43]. This high incidence rate implies that natural aging is responsible for greatly accelerated

cancer growth rates as a whole. Cancer treatments can collectively speed up a range of aging-liking changes, which include genomic instability, telomere attrition, epigenetic alterations, mitochondrial dysfunction, loss of proteostasis, chronic low-grade inflammation and cellular senescence [46]. Aging like cellular damages can be found in all organs and all body cells in cancer patients.

By combining those two pieces of evidence, we have to find that the accelerated cellular aging in cancer patients is mainly responsible for observed rapidly reduced growth times. A normal median 15 years growth time is shortened to one-and-half a year for a second or returned cancer, and further shortened to several months for a third cancer. The accelerated aging caused by medical treatments is responsible for rapidly increased cancer growth rates. The combined adverse impact of all lethal factors is reflected by change in cancer growth rate constants by one to more orders of magnitude plus greatly increased chances of metastasis.

Medical treatments driven by "killing cancer cells" shorten patient lives in several ways. In a first scenario, patients of advanced stage cancers have lost some organ functional capacity as a result of damages of invastive cancer cells. Any additional adverse effects on the patients would depress organ functional capacity below the treshhold of death. In a second scenario, medical treatments shorten lives of cancer survivors by raising cancer growth rates. Cancer's natural growth time is often more than ten years, an advanced stage cancer's growth rates level off due to resources limits. Such patients may be often attacked by adverse events, but do not lose their lives quickly. Their natural development course depends on his or her efforts of fighting cancer. Any aggressive measures that cause severe tissue loss and systemic inflimation naturally make death happen earlier.

In a third scenarios, when the first tumor is removed, a second cancer or return cancer appears in about one year or so. The tissue loss, systemic inflammation, and overwholeing aging-like cellular damages cause the body to raise cancer growth rate constants by one to several orders of magnitude. Even though medical treatments have lowered cancer burden to nearly zero, it results in much faster cancer return. A returned cancer is deadly that we must question whether medical treatments are a unworthiwhile trade. This question can be answered only by comparing patients' lifespans with correspendant reference lifespans that patients could achieve without using the treatments. The finding will depend on selection of the reference. In a long history when cancer causal factors and risk factors were unknown, patients would do everything incorectly to shorten lives, medical treatments could give one to several years additinal lives. This out-of-date analysis does not reflect reality anyone. As we know that cancer growth rates are highly sensitive to a large number of lifestyle and environment factors, their lives can be extended by beneficially using those factors. Consistent with this fact is a large number of cancer miracles.

In the last senario, the primary tumor is destoryed by medical treaments, cancer patients die from a different cancer or other cause. However, the patients

lose a part of lifespans due to the severe damages caused by the side effects. Whether the side effects are a fair cost depends on alternative measures for controling cancer growth. Base on the above analysis and poor outcomes, we must conclude that medical treatments are no longer good options unless forced by the circumstances. The general view against surgery before William Stewart Halsted (1908) is correct.

Clinical trials are unable to detect slowly accumulated side effects due to a large of interfering factors, averaging effect within a treatments, and short follow up time. The some accumulated adverse impacts may be revealed only in long term studies. Lifespans of cancer survivors are cut shorter by estimaited 30% [45, 46] for certain type of cancer.

Whether or not medical treatments extend lives should be based on human inherent ability to survive from cancer. That ability is abundantly reflected in a large number of cancer miracles, where cancer resolves or heals naturally (N6, Sup.). True merit of medical treatments should be established by comparing with them with everything that is known to have beneficial effects on controlling cancer growth by using an unbiased method.

C. Non-medical Measures Can Control Cancer Growth Rates

1. A large number of non-medical factors can slow down cancer growth rates

A body of evidence acquired after 1980 shows that cancer is highly sensitive to hundreds of factors. Emotional distress, chronic stress, lack of exercises and inactivity have been discussed above. Other factors include omega-3 fatty [48], pollutants and toxins [72], unhealthy diets and nutritional imbalance [73], i nflammation causing factors [41], chemical carcinogens [74], other chornic disea ses such diabetes [75], natural products and natural apotosis-inducing compound s [76, 77, 78], etc. Those and other similar measures are referred as non-medical measures. They include exercises, emotional management, diets and nutrition, changing lifestyles, natural anti-cancer products, etc. They can influence apparent rate constants for cancer growth. Such measures do not have lethal side effects, but influence cancer growth or outcomes. After the roles of the cancer cause factors, risk factors, and influencing factors were discovered, they have never been used as treatments in cancer care. They can be used in a beneficial way to slow down cancer grow rates.

2. Accumulated beneficial effects of non-medical measures dramatically slow down cancer growth rates

Current medical research model is capable of detecting strong and fast treatment effect, but unable to detect any effects that are realized slowly. Wu and

Zha found that randomized clinical trials are inherently biased in studying weak and slow treatment benefits [35] (N7, Sup.).

620   For the same reason, the adverse effects of each medical treatment cannot be accurately determined because the adverse effects are materially interfered by other factors. Thus, the medical research model is biased in favor of hiding adverse effects and against finding true benefits of non-medical measures. Past findings from clinical trials exaggerate the merit of medical treatments, underes-
625   timate adverse effects of medical treatments, and underrates the true benefits of non-medical measures. This three-way of biases caused by randomized clinical trials make past findings meaningless.

Figure 3 below shows that the beneficial effects are accumulated over time and thus bring down cancer cell dividing rates progressively over time with a potential to reach negative values.
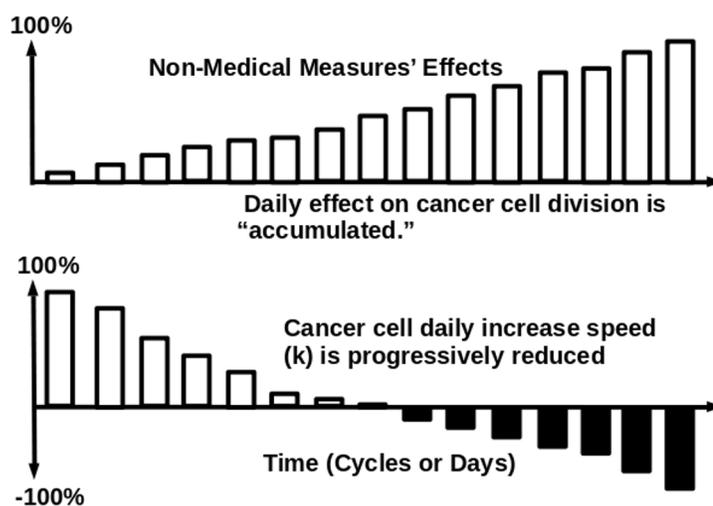
630

Figure 3 Instant and Accumulated Effects of Non-Medical Measures on Cancer Rate Constants.

645   Their beneficial effects of non-medical measures cannot be appreciated without understanding the compounding effects. A reduction in the daily growth rate on any day will result in a small reduction of cancer cells in that given day. The reduction is like removing a few "seeds" which could compound in more than a thousand cycles in the person's life time. When the apparent rate constant is negative, the cancer is in a process of healing. A presumed cure for cancer is "a negative rate constant." Considering rate constant's daily fluctuations, a presumed cure for cancer is to reach "overall negative rate constants."

650   Different effects of different rate constants caused by medical treatments and non-medical measures are shown in Figure 4. Cancer burden is at the joint

point at time zero. If the rate constant is a constant zero, the cancer size will not change as shown in line (A). If the cancer grows naturally (B), the total cancer cell number exponentially increases. Due to resource limits, the growth curve
655   will level off. If the cancer is treated by medical treatments (C), the cancer burden is rapidly reduced in the early time; but cancer cells repopulate as a result of increasingly enlarged k values. Surgery can instantly get most cancer cells, but cancer can repopulate much faster. Because medical treatments promote cancer metastasis, resource limits can no longer effectively control growth of wide-
660   spread tumors. If the cancer is controlled by non-medical measures only, cancer cell number continues increasing (D). However, the apparent rate constants gradually go down so that the cancer growth curve shows a leveling off point followed by a downward trend. Whether medical treatments can extend lives over the natural growth curve depends on cancer types and patient conditions. If the
665   patient attempts to use non-medical measures, it is also possible that cancer burden hits the threshold of death if the measures are insufficient to slow down cancer growth in the early time.
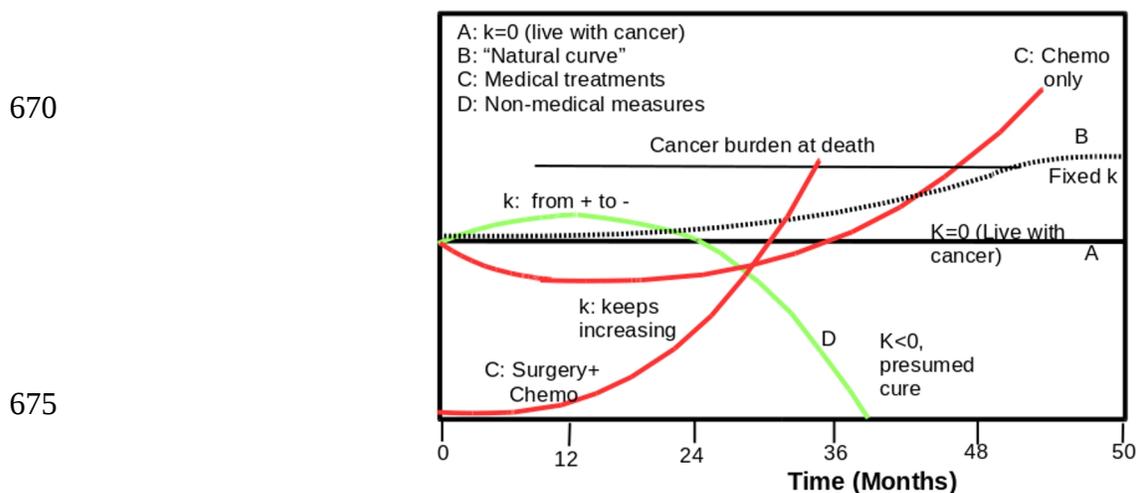
670

Figure 4 Projected Cancer Burdens for Medical Treatments, Non-medical Measures, a "Natural Course" and Living with Cancer

675

680   Figure 5 shows cumulative effects of medical treatments and non-medical measures. If a medical treatment is used, its beneficial effect is delivered quickly. Medical treatments are more powerful than non-medical measures in destroying cancer cells (A). However, the side-effects of the treatment is accumulated slowly, and the slowly realized side effects will gradually nullify its beneficial ef-
685   fects in a long run. The performances of each drug or treatment will follow the similar pattern. If a treatment is applied to a second cancer or a third cancer, accumulated net effects will become progressively worse. The adverse effects such as lost tissues, damaged cells and increased systemic inflammation, etc. raise cancer growth rate constants and slowly bring down the beneficial effects to zero

690 or negative values in a long run. For the reason found by Wu and Zha [35], the weak beneficial effects can be nullified by adverse effects of side effects of medical treatments.
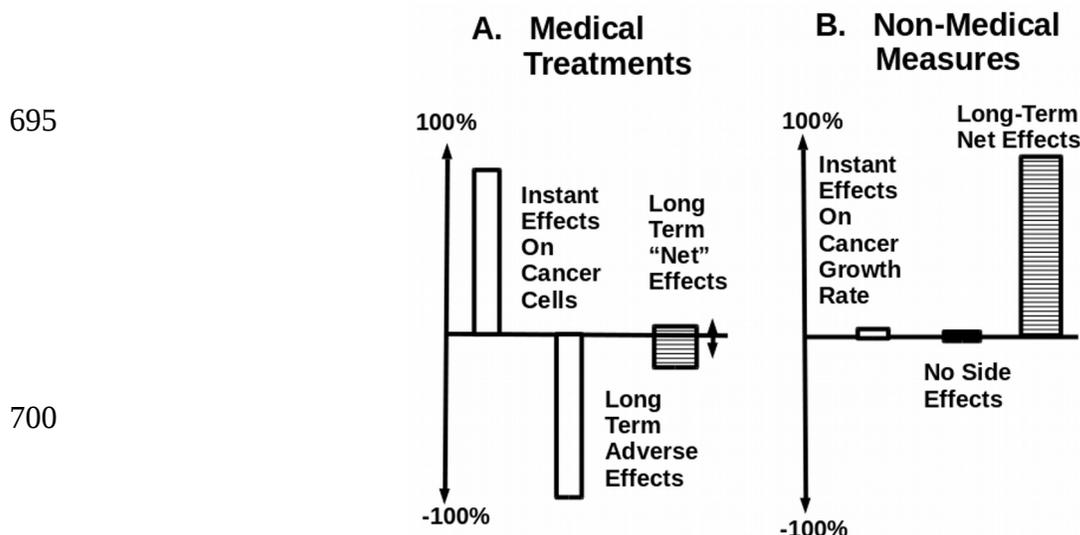
695

Figure 5 Instant and Accumulated Effects of Medical Treatments and Non-Medical Measures Such as Exercises, Diets, and Lifestyles, Etc.

700

705

As shown in above figure (B), non-medical measures do not have inherent side effects when they are correctly used to matched patients. They produce a small amount of often-undetectable beneficial effects in each day. Since no adverse side effects are accumulated, small beneficial effects are added up to be-
710 come larger and larger. The instantaneous daily effect can cause the tissue to reduce cancer cells in each day, which has the effects of removing "seeds" for later cancer cell division. The accumulated beneficial effects will become larger and larger with time, and thus have more power to slow down cancer cell division rates on later days. All of those effects can change cancer cell numbers by alter-
715 ing compounding effects (e.g., a downward bending curve). Their net accumulated beneficial effects are much more powerful than medical treatments in a long run.

Non-medical measures can alter cancer outcomes not by destroying tumor and killing cancer cells, but alter the rates balance between cancer cell division
720 rate and cancer cell death rate. Cancer will be stabilized or cured if the apparent rate constant is reduced to zero or negative. Final cancer cell numbers are very sensitive to rate constants, and rate constants expressed as percent of cancer cells that divide is rather small. This overall slow growth process is the basis that non-medical measures can be cures to cancer as long as they are used properly
725 to right patients.

3. Exercises can dramatically slow down cancer growth rates

Some factors such as exercises, emotion management, diets and nutrients, body temperature, physical activity levels, etc. have universal impacts on all patients of all types of cancer, they could be used reliably to fight all types of fully developed cancer. The impacts of lifestyle factors on cancer growth rates are extremely large when viewed on a long run. Significantly lower risk of cancer recurrence was observed for patients with higher exercise levels in studies [79, 80, 81,82]. Both exercise intensity and duration are important parameters. Three MET-hours is equivalent to walking at average pace of 2 to 2.9 mph for 1 hour. Compared with women who engaged in less than 3 MET-hours per week of physical activity, the adjusted relative risk (RR) of death from breast cancer was 0.80 for 3 to 8.9 MET-hours exercise per week, 0.50 for 9 to 14.9 MET-hours exercise per week, 0.56 for 15 to 23.9 MET-hours per week, and 0.60 for 24 or more MET-hours per week [79]. Compared with patients engaged in less than three metabolic equivalent task (MET)-hours per week of physical activity, the adjusted hazard ratio for disease-free survival was 0.51 for 18 to 26.9 MET-hours per week and 0.55 for 27 or more MET-hours per week [80]. Men who walked briskly for 3 h/wk or more had a 57% lower rate of progression than men who walked at an easy pace for less than 3 h/wk. Walking pace was associated with decreased risk of progression. There was a suggestive inverse association between risk of progression and intensity of activity. The author also noted that exercise intensity is an important factor for eradicating actively expanding moles (N8, Sup.).

Cancer cells have poor ability to tolerate moderately raised temperature [83], and thus exercises can slow down cancer growth rate by raising body temperature. Exercise also increases the degree of mechanical vibrations, which can inhibit cell division by disrupting cell division apparatuses [84]. Exercise causes working muscles to deplete glucose level in blood and thus makes less glucose available to cancer cells. Exericses, diets and lifestyle factors affect the vascular system, the renal system, the respiratory system and Central Nervous System, the body's systemic inflammation level, and the body's physical conditions on a daily basis.

Non-medical factors include any lifestyle factors that would influence cancer growth rates. They even include eating habit, working habit, thinking habits, and activity patterns. Among causal factors, risk factors, and influencing factors, only some of the factors may be relevant to a specific patient. While the scope of applicability of the factors depends on patients' lifestyle, potentially, a large number of sub sets of known factors may be relevant to the patient. The effects of the factors are additive in unknown ways. When a risk factor causes cancer relapse incidence to reduce by 50%, the effect can be viewed as causing all relapse incidence to a wider time window so that half of them are not observed within the trial follow-up time. A conclusion is they slow down cancer growth rate. Exercise alone can have an enough power to alter cancer outcomes for a large portion of patients. If several, tens, hundreds relevant factors are used beneficially, they can alter cancer outcomes predictably.

770   **4. Feasibility of using non-medical measures to slow down cancer growth rates**

Some cancer experts exert that any non-approved methods other the legalized few cannot cure cancer. Their belief is based on the assumption that destroying the tumor is the only right approach, and this can be achieved only by
775   surgery, chemotherapy and radiotherapy. The notion to cut tumors and kill "all cancer cells" was slowly formed under the influences of obsolete cancer theories developed from 1500 to 1946 and is incorrect. This approach should be rejected now.

We have shown that clinical trials have triple biases and cannot produce
780   correct results. All post findings on this point are incorrect. They are not the only biased devices against weak treatments. Most studies use five-year (few with ten years) follow-up time. Both adverse effects of medical treatments and beneficial effects of lifestyle factors (such as exercises and changed diets) are realized by long term effects. Their true effects cannot realized in short times. A short time
785   window allows surgery and drugs to fully realize their effects of killing cancer cells, but also effectively hide their side effects. When patients are still healthy in the early years, their side effects are unable to depress the organ's functional capacity below the threshold of death. However, the side effects are accumulated with time; and start affecting a patient only when the cancer burden has de-
790   pressed the organ functional capacity to near the threshold of death. If the trial lasts sufficiently long, the adverse effects of surgery and cancer drugs also influence cancer growth curve by altering the compounding characteristics. They affect cell division on each cycle. The short follow-up time is also a reason for further underrating beneficial benefits of lifestyle factors.

795   Risk factors, lifestyle factors and environment factors affect cancer growth rates. Cancer initiation and growth take place at varying speeds. If a factor is found to reduce cancer incidence rate, the factor actually slows down cancer initiation and growth speeds so that the detection times of the tumor will shift to later times. The degrees of shifts depends on individual patients. Thus, tumor de-
800   tection times for some patients fall outside follow-up times, and thus exhibit as a reduced cancer incidence rates. A significant reduction in the incidence rate means a slowed down cancer growth rates. Nearly all factors discovered after 1980 actually speed up or slow down cancer initiation and growth speeds. They can be used in a beneficially way to cure cancer.

805   The feasibility of using lifestyle factors to slow down cancer growth or metastasis rates can be seen from the high sensitivity of changing rate constants on growth rates. Tiny or small changes in growth rate constants significantly reduce the final tumor sizes in a long run (N9, Sup.). If the rate constant is reduced by 10% from 0.01 to 0.009 (1/day), the total tumor size would be only 2.6% of the
810   reference tumor in ten years. The tumor size would differ by 38 times. Assuming that a tumor of 1 billion cells grows at the rate of 0.001 or 0.1%, if the tumor is

held in check, the tumor cannot produce more cancer cells. However, if in a cycle, the body condition allows the tumor to produce a million new cancer cells, those extra cancer cells would become 1.4, 3.0, and 6.2 million in 1, 3 and 5 years if they grew at the same rate. Those new cancer cells continue dividing by the same fraction for more than a thousand cycles. This is the basis why multiple slow-working non-medical factors can alter cancer outcomes. Those examples explain why correct exercise can reduce cancer morbidity by as high as 50%.

The predicted feasibility of using lifestyle factors does not guarantee success. Failure can be attributed to patient's failure to understand cancer growth kinetics. Cancer compounding is similar to loan compounding by a daily interest rate except that cancer has the fast compounding pace and increasing daily rate. A good strategy is to use sufficient measures with sufficient fire intensity to hold daily cell division in check. If the measures are insufficient, cancer will progress and expand. Fighting cancer must be aimed to change tissue ecosystem in each day. When the body is in intense exercise, the tissue ecosystem is unfavorable to cancer cell division and potentially hold dividing cancer cells in check. When the patient stops doing exercise, the tissue ecosystem will slowly go back to the condition that favors cancer cell division. Therefore, one important criterion is the time averaged MET value per each day must be sufficiently high. Reasonably intense exercises are performed in three to six sections in each day. Most cancer patients do not understand that strict discipline is the key to success.

Cancer cell number is like the final loan balance of a mortgage compounding at a variable daily rate. A debtor cannot pay off the balance if he skips payments on some payment cycles and makes partial payments in other cycles. Exercise is the best tool for manipulating cancer division. Simulations can show that three-day exercises and two-day breaks will achieve very little. To win a fight against cancer, the patient needs to understand how to control cancer daily compounding rates.

5. The notion against using non-medical measures to cure cancer is a product of using flawed research model and obsolete cancer treatment strategy

Our findings refute the notion that non-medical measures cannot be used to cure cancer.

Medicine not only confines its treatment options to the very few options that clash with evolution. FDA outlaws doctors from suggesting or prescribing vitamins, supplements, herbs and super-foods, and legally endorses surgery and approved "treatments". American Cancer Society and FDA often made propagation to preclude true cures in a long history. Medicine frequently criticizes alternative options for fighting cancer [85]. Publicity is made to discredit non-medical measures as unproven and disapproved cancer treatments. A common statement is like: "no evidence supports claims that X is effective in preventing or treating cancer" [85, 86]. Some of them are clearly best cancer fighting measures if they

855   are used correctly to right patients. One article states: "Some alternative thera-
pies are harmful, and their promoters may be fraudulent."

The medical system creates a catch-22 for non-medical treatments. It
never looks into options as cures beyond surgery, chemotherapy and radiother-
apy, etc, but discourages the public from exploring non-medical options. By using
randomized clinical trials, medicine favors fast-acting and strong measures.
860   Patent law bars patenting on anything that is from nature and made of nature.
Tax law and medicare provide a legal basis for discouraging the public from ex-
ploring non-medical measures. Under such a legal framework, nobody would
study the true benefits of non-medical options. Then, medicine discredits any
non-medical measures for "lack of evidence."

865   The flaws in clinical trials and misplaced propagation ruin public health
wisdom, prevents researchers from finding cures for cancer, and makes cancer
much worse than it really is. Influenced by such propagation in several decades,
a vast majority of cancer patients have not realized the importance of lifestyle
factors and the super strong combination effects of non-medical measures. Be-
870   lieving nothing can kill cell cancer cells, cancer patients choose invasive surg-
eries, accept toxic drugs, and harmful radiotherapy, etc. to do more violence to
organs than cancer. Cancer patients are willing to get onto deadly palliative
tracks. When patients are treated by medical treatments, cancer patients survive
only by miracles or survive by withstanding dramatically increased cancer
875   growth rates or by miraculously overcoming severe adverse effects.

6. Multiple factors optimization can dramatically decrease cancer growth rates

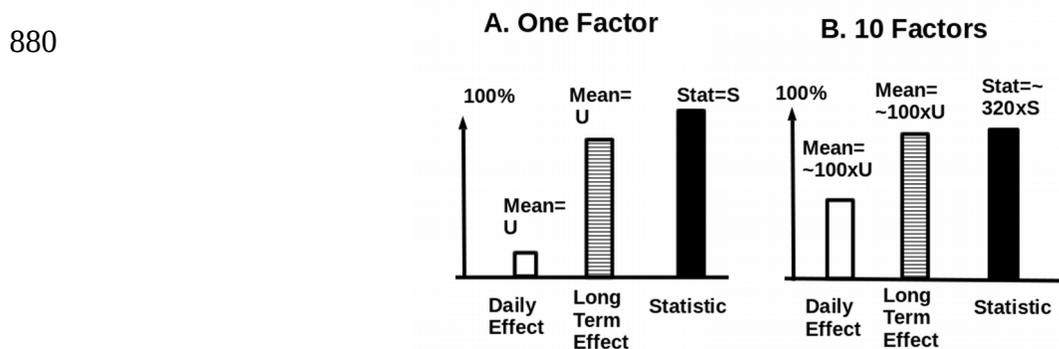Figure 6 shows the importance of using multiple factors in fighting cancer.

880

**Figure 6 Effects of 10 Similar Factors on Treatment
Mean and Test Statistic Compared with Treatment
Mean and Test Statistic for a Single Factor.**

885

In a randomized trial, beneficial effects on some subjects are negated by ad-
verse effects on other patients due to statistical averaging. Based on an assump-

890 tion that a factor works on about 10% of the patient population, an optimization would avoid adverse effects in the 90% mismatched patients. If a single factor is used in an optimization trial, its negating effects that normally existed in a randomized trial can be avoided. Assuming that one factor would deliver 10% response rate in a randomized trial, if 10 similar-strength factors are used in an op-
895 timization trial, the combined treatment effect will be raised by nearly 100 times, and hypothesis statistic for affirming true treatment benefits will be raised by about 320 times relative to a randomized trail focusing on a single factor with the other 9 factors be treated as interfering factors. This estimated impacts imply that a right strategy for fighting cancer is correctly utilizing as many factors
900 as possible.

D. Adverse Effects of Early Diagnosis of Cancer

When medicine can cure few cancer patients, medicine tries to combat cancer by using early diagnosis strategy. Due to the liability law, doctors have no option but diagnose cancer at the earliest times. It was estimated that among 70-
905 79 year old people, more than one-third of Caucasian men and half of African American men have indolent prostate cancer that would not cause harm if not diagnosed and untreated [87]. The detection of indolent prostate cancer has obvious adverse consequences [88]. It has been estimated that 42-66% of diagnosed prostate cancers would have caused no clinical harm had they remained unde-
910 tected [89]. One study estimated that the magnitude of over-diagnosis from randomized trials: about 25% of mammographically detected breast cancers, 50% of chest x-ray and/or sputum-detected lung cancers, and 60% of prostate-specific antigen-detected prostate cancers [90].

Early diagnosis is a wrong strategy for several reasons. The latent times of
915 naturally occurring cancers can be from 5 to 70 years. Growth from a large adenoma to cancer was estimated to require about 17 years, and generally the same mutations are present in primary tumors and their metastases [91, 92, 93]. The time scale implies that cancer could be easily controlled by any of a large number of non-medical measures. Second, it is a well known fact that many cancers
920 are dormant and inactive and can remain in that state for patient lives [94]. Histologically advanced microscopic tumors are detected in many tissues of adult humans [95, 96], but appear to be mostly held in check by unknown mechanisms. This line of evidence together with cancer self-healing cases shows that cancer could be cured or held in check by using non-medical measures.

925 An early cancer diagnosis will have overwhelming adverse impacts on patients. The biggest adverse effect of the strategy is a shift of cancer diagnostic ages from old ages or post-death ages to younger ages. The strategy could have an effect of labeling more people with cancer at the ages of 50, 60, 70, etc. rather finding cancer after their deaths or have the undetected tumors self re-
930 solved. A diagnosis of cancer always triggers the on-set of the adverse effects of three or four lethal factors. Early detection of cancer means starting affecting

patients lives in earlier ages. In addition, early diagnosis also inflicts routine emotional distress. Annual screening using embarrassing procedures such as colonoscopy can inflict great pains and sufferings. Each time when a growth, a
935   polyp, bleeding or whatever is found, the person will be tormented for a few days until a biopsy can rule out malignancy.

Early diagnosis will generate a big cancer patient population. Cancer statistical data shows that maximum cancer occurring ages are above 70 years (1 in 3) and 85 above (nearly a unit). Now, men have a 39.66% probability, or approxi-
940   mately a one in three risk, of developing cancer in their lifetime. Men have a 22.05% lifetime risk of dying from cancer, while the risk for women is around 18.75%. Cancer in a good portion of old people is not diagnosed [97]. The prevalence rate is close to 50% among US White and European men aged 80 or above. If this prevalence rate is added with the clinically diagnosed prevalence rate, one
945   would expect to see a unity for those of 85 or above. Projected based on the age and racial distribution, life expectancy and total U.S. population in 2015, these data suggest roughly 45 million cases of potentially detectable prostate cancer in the US [87].

The above data is about only one type of cancer. If all types of dormant and
950   micro tumors were diagnosed and their incidence rates are added together for elderly people, the total chances could be 90% to 100% for the people who have lived above 80. Medicine will never solve the cancer problem by cutting off tumors and killing cancer cells. Early diagnosis and treatment of indolent, small, and/or slowly developing cancer has adverse impacts on patients, society and na-
955   tion. Even for highly malignant cancer, the incidental benefits brought by changes to lifestyles are not enough to neutralize the adverse effects of the four lethal factors. The early diagnosis will deprive chances for tumors to self resolve and invite unnecessary emotional battles against dormant, harmless tumors or tumors. Early diagnosis may be good for only extremely aggressive rare cancers
960   that medical treatments can control while non-medical measures cannot.

Perceived benefits of cancer early diagnosis are most probably false. The reduced incidence rate for cancer is mainly attributed to a reduced population of smokers in the population, a big reduction in the lung cancer cases, and indirect benefits from anti-cancer efforts such as healthy diet, lifestyles and exercises.
965   Moreover, improved cancer survival rates among early diagnosed cancer patients are inaccurate because the 5-year survival rate is an improper measure of the survivals for early diagnosed cancer. Making diagnosis by 10 years earlier but losing the life 7 years later is not a winning strategy. Some might die in the same time window if they had not been diagnosed with cancer earlier. In addition,
970   some patients would heal their cancers naturally if they had not been inflicted with the four lethal factors. Some benefits of early diagnosis is a temporary trend seen for some types of cancer, and the true disastrous picture will appear only when those early diagnosed patients start dying.

975 Most of apparent benefits on cancer patients cannot be attributed to the medical treatments. If a cancer is cured while the patient accepts medical treatments (we call it as "type A miracle"), the true cures cannot be attributed to drugs, surgery and radiotherapy, each which is not used in evolution. Cancer is a result of cancer cell growth driven by changed biochemical and cellular processes. Current medical treatments cannot permanently restore altered biochem-

980 ical and cellular process patterns. Cancer is not like a lodged bullet, poison, traumatic injuries, and bacteria that can be removed. What actually cure cancer are things that are used in parallel to medical treatments.

Based on above reasons, a wiser strategy is to delay detection times to post-death and encourage people to use cancer-risk reduction programs to stop

985 cancer from growing without triggering the onset of the four lethal factors.

E. Adverse Impacts of Over Treatments of Cancer Care

In 2019, there is an estimated 1,762,450 new cancer cases diagnosed and

990 606,880 cancer deaths in the U.S. We estimate (based on 50/(100+50)=33% rate) that, 200,000 annual deaths in the U.S. could be attributed to unnecessary treatments. Among the remaining 400,000 deaths, medical treatments have shortened lives by various margins. The number of cancer survivors in the U.S. is between 15 to 20 millions now. Those people will lose lifespans by large margins.

995 In China, there are 4.51 million cases and 3.04 million deaths for 2020. We estimate that medical treatments may cause about 1 million annual deaths. In the world, about 9 million people are dying from cancer. A large number of deaths are acellerated by medical treatments while the remaining survivors lose considerable parts of livespans or will die from future cancer.

1000 To save life from terminal diseases, patients naturally want to accept as many treatments. Patients' trust in medicine, doctors' financial incentive to earn medical service revenues, and doctors' desire to avoid malpractice lawsuits for failure to diagnose or treat cancer become a driving force for creating the over-treatment landscape. When all interests are aligned to promote over treatments,

1005 over treatments become the hall-marks of cancer care industry.

Patients' trust in medicine becomes a negative factor in the area where medicine is incompetent. Medicine is viewed as the only science-based medicine, and its performance in treating acute diseases is not questioned. Even in treating cancer, patients still depend on medicine in treating emergency problems as

1010 bleeding, blockages, fracture, stroke, heart attack, organ failure, etc. The patient's trust has impaired their judgment in cancer care. Patient stories reflect a common understanding that best care are equivalent to more drugs, newest drugs, more treatments, and more hospital stays, etc. and most patients do not appreciate the magnitudes of harmful risks of medical treatments. It is well

1015 known that, unlike normal people, cancer patients are more willing to use treatments with small benefits and major toxicity [98].

Over treatments are in part caused by conflicting findings in cancer re-
1020 search. The population-based medicine has molded a popular belief that every disease could be cured by the same treatment protocol. However, cancer research has generated a massive number of conflicting, confusing and even incorrect findings. In selecting treatment options, doctors are often not in a position to make a final decision and thus have to let patients make final calls. Medical science has produced a large number of complex issues that few patients can un-
1025 derstand. They are unable to understand complex cancer knowledge and would not evaluate statistical analysis and experimental designs. We note that most patients cannot tell differences between a 2% reduction in a hazard ratio at $p=0.001$ and a 20% reduction in death rate at $p=0.09$. When they are in doubt, they often err on the side of getting more treatments.

When patients' desire for getting over treatments is consonant with doc-
1030 tors' desire to avoid liability from withholding treatments, over treatment is very common. Patients tend to accept over treatments with unrealistic expectation that a tiny good chance like 1% will happen to them but major risks like 60% will not. Palliative care studies reflect that patients hope that "something will be done, a wonder drug will be available", a patient "….struggles on and fights be-
1035 cause he/she clings to a hope which is probably 99% unrealistic," and patients "still maintain their expectations despite all evidence to the contrary" [99]. Patients often are on chemo even just a few days before their deaths. Over treatments are clearly driven by patients. The only way to stop such tragedies is educating patients with right knowledge.

1040 Studies show that a cancer drug may extend life by a few months at high significant level but also has any combination of around 30 to 50 specific side effects. Cancer drugs can often damage nerves, liver, kidneys, ears, heart, etc, and can cause nausea, vomiting, hair loss, cognitive dysfunction, fatigues, and changes in sexual functioning and reduced quality of life. Most studies underesti-
1045 mate true side effects. Medicine has a convention to characterize drug side effects as localized symptoms, but not as systemic damages. They do not study lost functional capacity of vital organs. Some damages are revealed in obvious changes in patient's intellectual capacity, darkened blood vessels, impaired nerve functions, etc, but are neglected in studies. The aging-like adverse effects can be
1050 found only in long-term studies [46].

Over treatments are also driven by the belief that a cure to cancer is killing "every cancer cell." If patients want to achieve zero levels, doctors could meet patients' demands. Science cancer adverse outcomes happen at high chances, a refusal to meet a patient's demand may be a ground for a malpractice suit if the
1055 patient later dies, but shortening the patient's life by medical treatments will not. Honoring the patients' demands is consistent with established treatment proto-

cols, liability law, and doctors' financial gains. From published diseased patients' stories on blogs, one can see the same pattern that patients are driving for over treatments.

1060   From discussions with cancer patients and posted case reports, we found that a good patient population cannot understand the real purpose of palliative care, the magnitudes of the risks of drugs, and the precluding effects of medical treatments.

1065   Palliative care, which is always accompanied by three to four lethal factors, shortens patients lives. Final outcomes of palliative care are well understood in cancer literature. Use of this option is based on a presumption that absolutely no other options can save life. However, medicine has no basis to assert that none of the tens of thousands of non-medical options can save lives. Any assertion that cancer cannot be cured cannot stand in front of a large number of cancer mira-
1070 cles. Thus, "terminal" is factually incorrect; and patients' consents to palliative care are acquired with a legal flaw.

      Leaving the "incurable" notion aside, patients are not properly informed of the nature of the palliative care. In one study, one third of patients being treated palliatively thought that their therapy was curative [100]. In another study of 149
1075 patients with incurable cancer, 45 (31%) believed their cancer was incurable, 61 (42%) were uncertain, and 39 (27%) believed their cancer was curable [101]. We estimate that a super majority of patients never think that cancer drugs can potentially preclude future cures. Medicine has not considered and has not studied methods of using a right combination of lifestyle factors to slow down cancer
1080 growth rates or reverse cancer progression direction as a far better strategy for curing cancer.

      Most patients cannot conduct risk-and-benefit analysis in the context of palliative care. Patients do not understand the long lasting adverse impacts of cancer treatments. Most patients hope that medical treatments can save their
1085 lives for a few years, with a wishful thinking to further extend life. They never understand palliative care most probably set the maximum limit on their survival times: when they get on this track, they give up the hope and accept the worst outcomes as known in medicine.

      Another problem is that cancer patients are exposed to regular risks from
1090 medical treatments such as surgeries, drugs, and radiotherapy and from diagnosis procedure such as CT scans and invasive sampling procedures. The risks from CT scans are known [102, 103]. If the risks from all sources are added up, some of them may hit 100%, and some are exposed to different categories of risks with each being close to a unity. They may get secondary cancer by certainty, ruin
1095 their kidneys by certainty, destroy the liver by certainty, and cripple their immune systems by certainty. However, since each risk cannot be materialized without a time course, they appear to be well. So, they keep taking more and

more risks. If all risks are viewed on a long term basis, they would die in one of several ways. They do not know that abusive treatments and procedures forever cut their lives short and nothing can help except miracles.

DISCUSSIONS

1. A Summary of Flaws in the Medical Model

The presumed cure for cancer is "achieving overall negative cancer growth constants." A right strategy is to beneficially use multiple factors to slow down cancer growth rates. This strategy requires a completely different analysis of available options and measures. All cancer treatments driven by the notion of destroying the tumor or killing cancer cells have been poor, did not work, and will never work.

Cancer cell daily gain or loss depends on cancer dividing rate and total death rate; and the final cancer cell number is the sum of net gains or losses of cancer cells over the entire patient lifespan. The death rates depend on cancer cell necrosis, natural death, cell programmed death or apoptosis, cell destruction caused by immune responses and possibly cell reformation (like stem cells change their differentiation behaviors). Cancer net growth rate constants are generally very small, and adverse cancer outcomes are due to the unique compounding effects of cell division cycles. Both the cancer cell division rates and cancer cell death rates are highly sensitive to a huge number of lifestyle factors and environmental factors, a right approach to fighting cancer is to slow down cancer net growth rates. Cancer could be cured by beneficially using any of a combination of non-medical measures to reverse cancer growth direction. This approach does not depend on molecular specificity although activation of anti-tumor immunity by luck may rapidly shorten the entire healing process.

The inability to find curative benefits of non-medical measures are attributed to (1) selecting improper controls by precluding all non-medical measures, (2) grossly underestimating the role of tissue loss and cell damages, (3) the use of too short follow-up times in clinical trials, (4) the averaging effects of between treatment and interfering factors in randomized trials, (5) failing to use multiple factors approach, and (6) failing to understand the compounding effects of cancer cells division. The research model with those flaws exaggerates strong treatment effects, but consistently undermines weak treatment effects and slowly damaging side effects.

The research model has triple biases in favor of confirming strong effects of medical treatments. The biases collectively reduce treatment effects of non-medical measures by one or more orders of magnitude. Moreover, under the obsolete legal framework, factually wrong propagation has been used to discourage

cancer patients from using best, safest, and most powerful cures which are built in human genes or can be readily found from nature. The terminal and incurable labels are just inadvertent products of the flawed research model and the wrong cancer treatment strategy. All of biased effects of the medical treatments are shown in the following table.

1140

Table 2 Medical Treatment Performance Are Greatly Overrated While the Beneficial Effects of Lifestyle Factors Are Greatly Underrated

Treatments	Effect Element Name	Impacts	Mechanisms	How it Changes True Benefits	Degree of Bias
Surgery	Systemic inflammation	Adverse	Premature death; alter immune resp; promote metastasis	Not recognized until recently.	+++
	Loss of organ tissues by 10%-90%	Adverse	Premature death; Shorten lifespans; (10% to 90%).	Patients are not informed generally.	++++
	Control/historical reason.	Adverse	Select controls from "little dwarfs".	Benefits grossly exaggerated.	+++
Chemotherapy	Alter Rate Constants.	Adverse	Increase cancer growth rate constants by 2 to 5 times.	Not officially recognized in clinics.	+++
	Damage cells and organs.	Adverse	Favor cancer growth; promote metastasis.	Not fully recognized; follow-up is insufficient.	+++
	Damage CNS	Adverse	Promote cancer initiation, growth, metastasis.	Not recognized or used in cancer care.	+++
radiotherapy	Damage cells and organs.	Adverse	Promote cancer growth; promote metastasis.	Not recognized fully; follow-up is insufficient.	++
	Cause mutations and cell damages	Adverse	Get new type cancer.	Well known; 5-year follow-up is too short.	+

| Lifestyle factors (work by known causal factors) | Improve tissue ecosystem; Improve vascular system; Improve CNS; Reduce toxins, etc. | All are beneficial effects; Some are optional; all with week adverse action. | Reduce cancer growth speed; improve organ capacity; strength Immune Response; Inhibit cancer metastasis; Prevent cancer return. | (1) Not known before 1980; (2) Unable to detect benefits by randomized clinical trials; (3) Compounding effects not understood. | - - - - - -
 - - - - - -
 (off by one to several orders of magnitude) |

2. Adverse effects of medical treatments

1145   Claimed benefits of medical treatments for cancer is refuted for all of the following reasons:

All medical treatments were developed on the "notion" to remove the tumor or kill cancer cells. This notion was formed long before 1846, was based on obsolete wrong cancer theories, and clashes with latest discoveries of the
1150   changes in biochemical and cellular processes and the latest evolutionary cancer theory. The latest knowledge and cancer theories implicate that cancer cannot be cured by cutting, radiating and drugging because they can make cancer grow faster. Autopsy cancer incidence, evolutionary cancer theory, a massive number of cause-relating studies, and our kinetic simulations show that a real cure for
1155   cancer is to slow down cancer growth rates or reverse its course. Lack of cure should be attributed to this ancient wrong notion.

Medical treatments were confined by the flawed legal framework and commercial interests. All performance data of medical treatments are acquired by making chain comparisons among surgeries, drugs, and radiotherapy, all of
1160   which are similarly ineffective and harmful. Each of medical treatments may clash with other compounds or cell apparatuses in the human body because they were not exposed to human body in evolution. Medicine did not explore how a comprehensive program comprising multiple lifestyle factors would perform. Thus, medicine does not know how medical treatments perform on an absolute
1165   scale, as compared with best references which would be achieved by any combinations of ten of thousands of lifestyle factors.

All medical treatments are associated with three to four deadly lethal factors. Surgery increases cancer apparent growth rate constants by as much as 10 times; and chemotherapy and radiotherapy can raise cancer growth rate con-
1170   stants by 2.5 to 5 or more times. Emotional distress and chronic stress could increase cancer growth rate constants for metastasis by adding 0.182 (1/day) to corespondent values. Surgery, chronic stress and physical activity can jointly promote cancer metastasis. When adverse impacts from surgery, chemotherapy, radiotherapy, and emotional distress are added up, medical treatments cannot de-

1175 liver benefits in a conceivable way. Surgery shortens lives by reducing the vital organ's functional capacity. The complete response rates of 7.4% and overall performance of chemotherapy reflect the heights of "the tallest dwarfs" selected from a narrow number of options. Those facts explain why cancer growth times rapidly reduce from about 15 years to several months for tumors erupted in dif-
1180 ferent times.

Clinical trials are biased in favor of detecting strong effects but are incapable of detecting slowly-working beneficial effects and slowly-damaging drug side effects. In a randomized trial, a treatment is indiscriminately used on patients, thus some beneficial effects and some adverse effects are evened out by
1185 statistical averaging. Also, the beneficial effects of a single factor is too small when multiple other interfering factors affect the same measured health properties like the treatment. Such a randomized trial reduces statistical mean of the treatment and raises error variance, thus resulting in failure to affirm true treatment effect. Due to interference of other factors and short follow up times, clini-
1190 cal trails are unable to detect the later-delivered side effects that realized in later times. Compared with an optimization trial, the treatment effect is underestimated by one to several orders of magnitudes, depending on the number of interfering factors and trial duration.

Some studies found that cancer global survival rate is steadily improved
1195 over the years and have given this credit to use of surgery, drugs, and early diagnosis of cancer. The real reason of the improvement is the increased use of cancer-fighting measures by cancer patients. Cancer patients know the importance to improve diets, adjust lifestyles, do more exercise as a result of influences by studies published after 1980. When those lifestyle factors are used beneficially
1200 by a substantial portion of patients, overall death cancer rates are reduced, and more cancer miracles naturally arise. However, no single study has proven how a diminished organ functional capacity, raised systemic inflammation, and damaged cells and tissues can improve cancer survival rates. The one-time tumor destruction cannot explain any success. Adverse effects of surgeries, drugs and ra-
1205 diation may nullify whatever benefits alternative non-medical treatments may offer. Any cure based on the notion of killing cancer cells clashes with the presumed cure of slowing down cancer growth rates.

3. True curative benefits of non-medical measures

Hundreds of well-documented cases and estimated millions of undocu-
1210 mented cancer miracles conclusively prove that cancer can self resolve or heal naturally, with the fastest time scale from 1 month to 6 months. The incurable notion is false. Cancer self-healing becomes miracles (we call type B miracles) because medicine does not explore the cause self healing and has not explored as cure exercises, diets and nutrition, natural products containing any of tens of
1215 thousands of anti-cancer compounds, and other lifestyle factors. Those factors

were never used as comparisons in evaluating medical treatments. Thus, "lack of scientific valid" evidence is a result of flawed clinical trials.

Cancer self-healing is not a miracle. Behind cancer miracles are thousands of basic discoveries, which could explain the mysteries of each cancer miracle. Difference between "cancer patients" and "normal people" are cancer growth rates. A body of evidence show that potential benefits of exercises are one or more magnitudes larger than medical treatments if their respective effects are evaluated for a long term. Well designed and well executed exercise programs can be cures for most types of naturally occurring cancers. Some cancer miracles happened when the tumor is inoperable or patients do not accept medical treatments. We attribute the miracles in a main part to avoidance of three or four lethal effects, and avoidance of raised apparent growth rate constants. Some cancer miracles can be attributed to improvements in emotional state. Since emotional distress, chronic stress, and emotional state have huge impacts on metastasis processes, successful control of emotional problems and abasement of chronic stress could be enough to change cancer outcomes in some cases. Right dietary adjustments and nutritional programs can alter cancer outcomes by reducing cancer growth rate constants. Any of other lifestyle factors or natural anti-cancer compounds from natural products may be able to alter cancer outcomes by slowing down tumor growth rates. We estimate that a good cancer fighting program is one to several magnitudes more powerful than any of radical medical treatments.

Medical researchers lack incentives to study weak treatment effects of lifestyle and environmental factors because they focus on things that can kill cancer cells and rely on flawed misused clinical trials. A change in future research requires abandoning the old strategy and using optimization trials that are capable of determining weak and slow treatment effects.

4. Adverse effects of early cancer diagnosis

Early diagnosis of cancer is a wrong strategy because cancer is always a part of human life and somatic evolution. Early diagnosis is accompanied by three to four lethal factors and the total destruction of life hopes. Incidental benefits from early diagnosis is marginal. Declined cancer death rates are an "artifact" caused by the flawed five-year survival measure and cannot be attributed to early diagnosis. Cancer screening torments fragile people by inflicting serious emotional pains. A better strategy is to using cancer risk reduction programs to slow down cancer growth, or reverse cancer development direction to avoid labeling the patients with "incurable" cancer.

5. Issues in palliative cancer care

The analysis above implicates multiple issues for palliative care.

Given the fact that cancer can resolve by itself and naturally heal under influences of a large number of lifestyle factors, the incurable notion is untrue.

Medical failure is due to the treatment wrong strategy, misuse of clinical trials, and chain comparison in evaluating medical treatments. If patients understand poor medical treatment performance, insufficiently disclosed risks, and numerous flaws in the research model, most patients could not accept palliative treatments. Also, if cure exists, few patients would accept palliative care. Thus, palliative treatments are often used without getting informed consent.

Patients are generally not informed of one or more severe adverse impacts of medical treatments, nor the four associated lethal factors. They generally are not told how cancer drugs raise future cancer growth rates and dramatically cut short their lifespans. Research articles do not fully disclose drug side effects. Most patients are unable to appraise accumulated risks from operations, drugs, radiation, CT scans, invasive tissue sampling, etc. Most patients are not informed that medical treatments have precluding effects on future cures. Few patients understand that the use of such drugs may completely diminish the body's ability to fight cancer in the future.

6. Limitations of this study

Due to the nature of issues, some evidence is approximate. However, the validity of the findings does not depend on high data accuracy because the conclusion is not based on percent differences. Most findings are based on orders of magnitude or consistent patterns that have been observed by multiple groups. The gain from using an optimization trial over the randomized trial would be one to more orders of magnitude. Most studies are backed up by multiple reliable findings in cancer research. It is understood that the kinetic data have little utility in population medicine, and cannot be used to make comparison between one person and another, but is used to predict changes within the same person in personalized medicine. Simulation data are used to show growth trends, treatments' effect patterns, and relative tumor sizes. It is irrefutable that a huge number of factors affect cancer growth rates, and can be used in practice to alter cancer outcomes. From cancer miracles, we note that chances of success depend on how to use them. Unfortunately, modern people are not enabled to use such measures. To turn this treatment model into a predictable cure, medical researchers should develop practicing details.

Since the three research model biases and cancer treatment strategical change require a new analytic framework, citations in part of the article are limited. We cannot cite negative findings due to inherent inaccuracies and errors.

1295   The author(s) declared that no grants were involved in support-
ing this work.

REFERENCES

1300   1. Ashdown ML, Robinson AP, Yatomi-Clarke SL, Ashdown ML, Allison A, Abbott D, Markovic SN, and Coventry BJ, Chemotherapy for Late-Stage Cancer Patients: Meta-Analysis of Complete Response Rates, Version 1. F1000Res. 2015; 4: 232.

2. Albero A, Lopéz JE, Torres A, de la Cruz L, Martín T. Effectiveness of chemotherapy in advanced differentiated thyroid cancer: a systematic review. Endocr Relat Cancer. 2016 Feb;23(2):R71-84.
1305

3. Davis C, Naci H, Gurpinar E, Poplavska E, Pinto A, Aggarwal A, Availability of evidence of benefits on overall survival and quality of life of cancer drugs approved by European Medicines Agency: retrospective cohort study of drug approvals 2009-13, BMJ 2017;359:j4530.

1310   4. Morgan G, Ward R & Barton M. The contribution of cytotoxic chemotherapy to 5-year survival in adult malignancies. Clin. Oncol. (R. Coll. Radiol.) 2004: 16, 549–560.

5. Harv Letter. A second look at beta blockers and blood pressure. A beta blocker alone isn't usually the best choice for simple, uncomplicated high blood
1315   pressure. Harv Heart Lett. 2008 Jun;18(10):4-5.

6. Na Z, Qiao X, Hao X, Fan L, Xiao Y, Shao Y, et. al. The effects of beta-blocker use on cancer prognosis: a meta-analysis based on 319,006 patients. OncoTargets and Therapy 2018:11 4913–4944.

7. Yap A, Lopez-Olivo MA, Dubowitz J, Pratt G, Hiller J, Gottumukkala V, Slo
1320   an E, Riedel B, Schier R. Effect of beta-blockers on cancer recurrence and survival: a meta-analysis of epidemiological and perioperative studies. Br J Anaesth. 2018 Jul; 121(1):45-57.

8. Bai ZG, Zhang ZT. A systematic review and meta-analysis on the effect of angiogenesis blockade for the treatment of gastric cancer. Onco Targets Ther. 2018 Oct 17;11:7077-7087.
1325

9. Li Y, Zhou Y, Hong Y, He M, Wei S, Yang C, Zheng D and Liu F. The Efficacy of Different Chemotherapy Regimens for Advanced Biliary Tract Cancer: A Systematic Review and Network Meta-Analysis. Frontiers in Oncology. May 2019,Volume 9,Article 441.

1330   10. Dos Santos MA, Pignon JP, Blanchard P, Lefeuvre D, Levy A, Touat M, Louvel G, Dhermain F, Soria JC, Deutsch E, Le Teuff G. Systematic review and meta-analysis of phase I/II targeted therapy combined with radiotherapy in patients with glioblastoma multiforme: quality of report, toxicity, and survival. J Neurooncol. 2015 Jun;123(2):307-14.

1335   11. Su J, Cai M, Li W, Hou B, He H, Ling C, Huang T, Liu H, Guo Y. Molecularly Targeted Drugs Plus Radiotherapy and Temozolomide Treatment for Newly Diagnosed Glioblastoma: A Meta-Analysis and Systematic Review. Oncol Res. 2016; 24(2):117-28.

    12. Maeda H and Khatami M. Analyses of repeated failures in cancer therapy for solid tumors: poor tumor-selective drug delivery, low therapeutic efficacy and unsustainable costs, Clin Transl Med. 2018; 7: 11.

1340

    13. Wikipedia, cancer. Accessed at https://en.wikipedia.org/wiki/Cancer#History. Last Accessed on November 8, 2019.

1345   14. American Cancer Society. Early Theories about Cancer Causes. Accessed at https://www.cancer.org/cancer/cancer-basics/history-of-cancer/cancer-causes-theories-throughout-history.html. Last Accessed on November 8, 2019.

    15. Brücher B, Jamall IS. Somatic Mutation Theory - Why it's Wrong for Most Cancers. Cell Physiol Biochem 2016;38:1663-1680.

1350   16. Nowell, P. C. "The clonal evolution of tumor cell populations". Science. 1976:194 (4260): 23–28.

    17. Attolini CS, Michor F. Evolutionary Theory of Cancer. The Year in Evolutionary Biology 2009: Ann. N.Y. Acad. Sci.2009:1168: 23–51.

    18. Hanahan D. & Weinberg R. The Hallmarks of Cancer. Cell, 2000 January; Vol. 100, 57–70.

1355

    19. Hochberg, ME & Noble RJ. A framework for how environment contributes to cancer risk. Ecology Letters. 2017:20, 117–134.

    20. Lange MM, Rutten HJ, van de Velde CJ. One hundred years of curative surgery for rectal cancer: 1908-2008. Eur J Surg Oncol. 2009 May;35(5):456-63.

1360   21. Twyman RA. A brief history of clinical trials. The Human Genome. 2004. Sep, http://genome.wellcome.ac.uk/doc_WTD020948.html. Accessed on Oct 2009.

    22. Legumes C.R. lemons and streptomycin: A short history of the clinical

trial. CMAJ. 2009;180:23–24.

23. Au DH, Castro M, and Krishnan JA. Selection of Controls in Clinical Trials, Introduction and Conference Summary. Proceedings of The American Thoracic Society Vol 4 2007.

24. Tournigand C, André T, Achille E, et al., FOLFIRI Followed by FOLFOX6 or the Reverse Sequence in Advanced Colorectal Cancer: A Randomized GERCOR Study. J Clin Oncol. 2004; 22:229-237.

25. DeVita VT Jr, Chu E. A history of cancer chemotherapy. Cancer Res. 2008 Nov 1;68(21):8643-53.

26. Chang SC, Liu KH, Hung CY et al. Adjuvant Chemotherapy Improves Survival in Stage III Gastric Cancer after D2 Surgery. Journal of Cancer 2018; 9(1): 81-91.

27. Sparano JA, Gray RJ, Makower DF, Pritchard KI, Albain KS, Hayes DF, et al. Adjuvant chemotherapy guided by a 21-gene expression assay in breast cancer. N Engl J Med 2018;379(2):111–121.

28. Gee AW, Balogh E, Patlak M, Nass SJ (reportors), The Drug Development Paradigm in Oncology: Proceedings of a Workshop. National Academies of Sciences; National Cancer Policy Forum. Washington (DC): National Academies Press (US); 2017 Jul 24.

29. Verkooijen HM, Fioretta GM, Rapiti E, Bonnefoi H, Vlastos G, Kurtz J, Schaefer P, Sappino A, Schubert H. and Bouchardy C. Patients' Refusal of Surgery Strongly Impairs Breast Cancer Survival. Ann Surg 2005;242: 276 –280.

30. Tubiana M. Repopulation in human tumors. A biological background for fractionation in radiotherapy. Acta Oncol 1988; 27: 83-8.

31. Tubiana M. Tumor Cell Proliferation Kinetics and Tumor Growth Rate, Acta Oncologica, 1989;28:1, 113-121.

32. Mehrara E, Forssell-Aronsson E, Ahlman H, and Bernhardt P. Specific Growth Rate versus Doubling Time for Quantitative Characterization of Tumor Growth Rate. Cancer Res. 2007; 67: (8). April 15, 2007.

33. Baum M, Demicheli R, Hrushesky W, Retsky M. Does surgery unfavourably perturb the ''natural history'' of early breast cancer by accelerating the appearance of distant metastases? European Journal of Cancer. 2005; 41 508–515.

34. Ahles TA, Root JC, Ryan EL. Cancer- and cancer treatment-associated cognitive change: An update on the state of the science. J Clin Oncol. 2012;30:3675–86.

35. Wu J. and Zha P. Randomized Clinical Trial Is Biased and Invalid In Studying Chronic Diseases, Compared with Multiple Factors Optimization Trial (November 4, 2019). Available at SSRN: https://ssrn.com/abstract=3480523.

36. Colleoni M, Sun Z, Price KN, Karlsson, Forbes JF, Thürlimann B, Gianni L, Castiglione M, Gelber RD, Coates AS, Goldhirsch A. Annual hazard rates of recurrence for breast cancer during 24 years of follow-up: Results from the international breast cancer study group trials I to V. J. Clin. Oncol. 2016;34, 927–935.

37.Cheng L, Swartz MD, Zhao H, Kapadia AS, Lai D, Rowan PJ, Buchholz TA, Giordano SH. Hazard of recurrence among women after primary breast cancer treatment—A 10-year follow-up using data from SEER-medicare. Cancer Epidemiol. Biomarkers Prev. 21, 800–809 (2012).

38. Hüsemann Y, Geigl JB, Schubert F, Musiani P, Meyer M, Burghart E, Forni G, EilsR, Fehm T, Riethmüller G, Klein CA. Systemic spread is an early step in breast cancer. Cancer Cell 2008;13,58–68.

39. Krall JA, Ferenc R, Mercury OA, Pattabiraman DR, Brooks MW, Dougan M, Lambert AW, Bierie B, Ploegh HL, Dougan SK, Weinberg RA. The systemic response to surgery triggers the outgrowth of distant immune-controlled tumors in mouse models of dormancy. Sci. Transl. Med. 10, eaan3464 (2018).

40.Demicheli R, Retsky MW, W. Hrushesky JM, Baum M. Tumor dormancy and surgery-driven interruption of dormancy in breast cancer: Learning from failures. Nat. Clin. Pract. Oncol. 2007; 4,699–710.

41. Solinas G, Marchesi F, Garlanda C, Mantovani A, Allavena P. Inflammation-mediated promotion of invasion and metastasis. Cancer Metastasis Rev. 2010; 29:243–248.

42. Tohme S, Simmons RL, Tsung A. Surgery for Cancer: a trigger for metastases. Cancer Res. 2017;77:1548–1552.

43. Armitage P, Doll R. The age distribution of cancer and a multi-stage theory of carcinogenesis. Br J Cancer. 1954;8(1):1–12.

44. Chen CP, Weinberg VK, Jahan TM, Jablons DM, and Yom SS. Implications of Delayed Initiation of Radiotherapy Accelerated Repopulation after Induction Chemotherapy for Stage III Non-small Cell Lung Cancer. Journal of Thoracic Oncology Volume 6, Number 11, November 2011.

45. Drewinko B, Alexanian R, Boyer H, Barlogie B, Rubinow SI. The growth fraction of human myeloma cells. Blood. 1981 Feb;57(2):333-8.

46. Cupit-Link MC, Kirkland JL, Ness KK, et al. Biology of premature ageing in survivors of cancer. ESMO Open. 2017 December 18.

47. López-Otín C, Blasco MA, Partridge L, et al. The hallmarks of aging. Cell 2013;153:1194–217.

48. Navarro SL, Kantor ED, Song X, Milne GL, Lampe JW, Kratz M, White E. Factors associated with multiple biomarkers of systemic inflammation. Cancer Epidemiology Biomarkers and Prevention. 2016;25(3), 521 10.1158/1055-9965.EPI-15-0956.

49. Segerstrom SC, Miller GE. Psychological stress and the human immune system: a meta-analytic study of 30 years of inquiry. Psychological Bulletin 2004;130(4):601-630.

50. Sloan EK, Priceman SJ, Cox BF, et al. The sympathetic nervous system induces a metastatic switch in primary breast cancer. Cancer Research 2010;70(18):7042-7052.

51. Moreno-Smith M, Lutgendorf SK, Sood AK. Impact of stress on cancer metastasis. Future Oncology 2010;6(12):1863-1881.

52. Lutgendorf SK, Sood AK, Anderson B, et al. Social support, psychological distress, and natural killer cell activity in ovarian cancer. Journal of Clinical Oncology 2005;23(28):7105-7113.

53. Lutgendorf SK, DeGeest K, Dahmoush L, et al. Social isolation is associated with elevated tumor norepinephrine in ovarian carcinoma patients. Brain, Behavior, and Immunity 2011;25(2):250-255.

54. Booth FW, Roberts CK, Laye MJ. Lack of exercise is a major cause of chronic diseases. Compr Physiol. 2012;2:1143–1211.

55. Carlsson S, Andersson T, Lichtenstein P, Michaelsson K, Ahlbom A. Physical activity and mortality: is the association explained by genetic selection? Am J Epidemiol. 2007; 166:255–259.

56. Cormie P, Zopf EM, Zhang X, Schmitz KH. The Impact of Exercise on Cancer Mortality, Recurrence, and Treatment-Related Adverse Effects. Epidemiologic Reviews, Volume 39, Issue 1, January 2017, Pages 71–92.

57. Des Guetz G, Uzzan B, Bouillet T, et al. Impact of physical activity on cancer-specific and overall survival of patients with colorectal cancer. Gastroenterol Res Pract. 2013;2013: 340851.

58. Friedenreich CM, Neilson HK, Farris MS, et al. Physical activity and cancer outcomes: a precision medicine approach. Clin Cancer Res. 2016;22(19):4766–4775.

59. Ibrahim EM, Al-Homaidh A. Physical activity and survival after breast cancer diagnosis: meta-analysis of published studies. Med Oncol. 2011;28(3):753–765.

60. Je Y, Jeon JY, Giovannucci EL, et al. Association between physical activity and mortality in colorectal cancer: a meta-analysis of prospective cohort studies. Int J Cancer. 2013; 133(8):1905–1913.

61. Lahart IM, Metsios GS, Nevill AM, et al. Physical activity, risk of death and recurrence in breast cancer survivors: a systematic review and meta-analysis of epidemiological studies. Acta Oncol. 2015;54(5):635–654.

62. Li T, Wei S, Shi Y, et al. The dose-response effect of physical activity on cancer mortality: findings from 71 prospective cohort studies. Br J Sports Med. 2016;50(6):339–345.

63. O'Keefe JH, Vogel R, Lavie CJ, Cordain L. Achieving Hunter-gatherer Fitness in the 21(st) Century: Back to the Future. Am J Med. 2010; 123:1082–1086.

64. Otto SJ, Korfage IJ, Polinder S, et al. Association of change in physical activity and body weight with quality of life and mortality in colorectal cancer: a systematic review and meta-analysis. Support Care Cancer. 2015;23(5):1237–1250.

65. Schmid D, Leitzmann MF. Association between physical activity and mortality among breast cancer and colorectal cancer survivors: a systematic review and meta-analysis. Ann Oncol. 2014;25(7):1293–1311.

66. Tipton CM. The history of "Exercise Is Medicine" in ancient civilizations. Adv Physiol Educ. 2014;38(2):109–117.

67. Wu W, Guo F, Ye J, et al. Pre- and post-diagnosis physical activity is associated with survival benefits of colorectal cancer patients: a systematic review and meta-analysis. Oncotarget. 2016;7(32):52095–52103.

68. Zhong S, Jiang T, Ma T, et al. Association between physical activity and mortality in breast cancer: a meta-analysis of cohort studies. Eur J Epidemiol. 2014;29(6):391–404.

69. Gimbrone MA, Jr, Leapman SB, Cotran RS, Folkman J. Tumor dormancy in vivo by prevention of neovascularization. J Exp Med. 1972;136(2):261–276.

70. Housman G., Byler S., Heerboth S.h, Lapinska K, Longacre M., Snyder

N. and Sarkar S., Drug Resistance in Cancer: An Overview. Cancers 2014, 6, 176 9-1792

71. Zhou Y, Li C, Huijbregts MAJ., Mumtaz MM, Carcinogenic Air Toxics Exposure and Their Cancer-Related Health Impacts in the United States. PLOS ONE DOI:10.1371/journal.pone.0140013

72. Donaldson MS. Nutrition and cancer: A review of the evidence for an anti-cancer diet. Nutr J. 2004; 3: 19.

73. Grosso G, Bella F, Godos J, Sciacca S, Del Rio D, Ray S, Galvano F, Giovannucci EL. Possible role of diet in cancer: systematic review and multiple meta-analyses of dietary patterns, lifestyle factors, and cancer risk. Nutrition Reviews, 2017; 75 (6):405–419.

74. Stratton MR. Exploring the genomes of cancer cells: progress and promise. Science. 2011;331:1553–1558.

75. Giovannucci E, Harlan DM, Archer MC, Bergenstal RM, Gapstur SM, H abel LA, Pollak M, Regensteiner JG, and Yee D. Diabetes Care. 2010 Jul; 33(7):1 674–1685.

76. Bailon-Moscoso N, Cevallos-Solorzano G, Romero-Benavides JC, and Or ellana MIR. Natural Compounds as Modulators of Cell Cycle Arrest: Application for Anticancer Chemotherapies. Current Genomics, 2017, 18, 106-131.

77. Sagar S.M., Yance D., and Wong R.K. Natural health products that inhib it angiogenesis: a potential source for investigational new agents to treat cancer —Part 1, CURRENT ONCOLOGY — VOLUME 13, NUMBER 1.

78. Millimouno FM, Dong J, Yang L, Li J, and Li X. Targeting Apoptosis Path ways in Cancer and Perspectives with Natural Compounds from Mother Nature. Cancer Prev Res; 2014; 7(11); 1081–107.

79. Holmes MD, Chen WY, Feskanich D, et al. Physical activity and survival after breast cancer diagnosis. JAMA. 2005;293(20):2479–2486.

80. Meyerhardt JA, Heseltine D, Niedzwiecki D, et al. Impact of physical act ivity on cancer recurrence and survival in patients with stage III colon cancer: fin dings from CALGB 89803. J Clin Oncol. 2006;24(22):3535–3541.

81. Richman EL, Kenfield SA, Stampfer MJ, et al. Physical activity after di agnosis and risk of prostate cancer progression: data from the cancer of the prostate strategic urologic research endeavor. Cancer Res. 2011;71(11): 3889–3895.

82. Sternfeld B, Weltzien E, Quesenberry CP Jr, et al. Physical activity and r isk of recurrence and mortality in breast cancer survivors: findings from the LAC

E Study. Cancer Epidemiol Biomarkers Prev. 2009;18(1):87–95.

83. Levine EM & Robins EB. Differential temperature sensitivity of normal and cancer cells in culture. Journal of Cellular Physiology. 1970;76(3):373–379·

84. Yeung PK, Wong JT. Inhibition of cell proliferation by mechanical agitati on involves transient cell cycle arrest at G1 phase in dinoflagellates. Protoplasma. 2003 Mar;220(3-4):173-8.

85. Wikipedia, List of unproven and disproven cancer treatments https://en.wikipedia.org/wiki/List_of_unproven_and_disproven_cancer_treatments Cancer.

86. Brigden ML. Unproven (questionable) cancer therapies. West J Med. 19 95 Nov; 163(5): 463–469.

87. Jahn J.L., Giovannucci E.L., Stampfer M.J. The high prevalence of undia gnosed prostate cancer at autopsy: Implications for epidemiology and treatment of prostate cancer in the prostate-specific antigen-era. Int. J. Cancer. 2015;137:2 795–2802.

88. Hoffman KE, Niu J, Shen Y, Jiang J, Davis JW, Kim J, Kuban DA, Perkins GH, Shah JB, Smith GL, Volk RJ, Buchholz TA, et al. Physician Variation in Manag ement of Low-Risk Prostate Cancer: A Population-Based Cohort Study. JAMA Inte rn Med. 2014.

89. Draisma G, Etzioni R, Tsodikov A, Mariotto A, Wever E, Gulati R, Feuer E, de Koning H. Lead time and overdiagnosis in prostate-specific antigen screeni ng: importance of methods and context. Journal of the National Cancer Institute. 2009; 101:374–83.

90. Welch HG, Black WC. Overdiagnosis in cancer. J Natl Cancer Inst. 2010 May 5;102(9):605-13.

91. Wang TL, et al. (2002) Prevalence of somatic alterations in the colorect al cancer cell genome. Proc Natl Acad Sci USA 99:3076–3080.

92. Wood LD, et al. (2007) The genomic landscapes of human breast and co lorectal cancers. Science 318:1108–1113.

93. Jones S, et al. (2008) Comparative lesion sequencing provides insights i nto tumor evolution. Proc Natl Acad Sci USA 105:4283–4288.

94. Aguirre-Ghiso JA. Models, mechanisms and clinical evidence for cancer dormancy. Nat Rev Cancer. 2007;7:834–846.

95. Greaves M, Maley CC. Clonal evolution in cancer. Nature. 2012;481(7381):306–13.

96. Naumov GN, Akslen LA, Folkman J. Role of angiogenesis in human tumor dormancy: animal models of the angiogenic switch. Cell Cycle. 2006;5(16):1779–87.

97. Stemmermann GN. Unsuspected cancer in elderly Hawaiian Japanese: an autopsy study. Hum Pathol. 1982 Nov;13(11):1039–1044.

98. Matsuyama R, Reddy S, Smith TJ. Why do patients choose chemotherapy near the end of life? A review of the perspective of those facing death from cancer. J Clin Oncol. 2006;24:3490-3496.

99. Pfeil TA, Laryionava K, Reiter-Theil, S., Hiddemann W, Winkler EC. What Keeps Oncologists From Addressing Palliative Care Early on With Incurable Cancer Patients? An Active Stance Seems Key. The Oncologist 2015;20:56–61.

100. Mackillop WJ, Stewart WE, Ginsburg AD, Stewart SS. Cancer patients' perceptions of their disease and its treatment. Br J Cancer. 1988;58:355-358.

101. Beadle GF, Yates PM, Najman JM, et al. Beliefs and practices of patients with advanced cancer: implications for communication. Br J Cancer. 2004;91:254-257.

102. Mathews JD, Forsythe AV, Brady Z, et al. Cancer risk in 680000 people exposed to computed tomography scans in childhood or adolescence: data linkage study of 11 million Australians. BMJ 2013;346:f2360.

103. Zondervan RL, Hahn PF, Sadow CA, Liu B, Lee SI. Body CT scanning in young adults: examination indications, patient outcomes, and risk of radiation-induced cancer. Radiology. 2013;267(2):460-9.

Supplement to Jianqing Wu and Ping Zha, Sugery, Chemotherapy and Radiatherapy Promote Cancer Growth Speeds and Shorten Patient Lives

N1. Most Doctors Would Refuse to use Chemotherapy

USA August 16, 2018, 75% of Physicians in the World Refuse Chemotherapy for Themselves. (because the FDA outlaws doctors from suggesting or prescribing vitamins, supplements, herbs and super-foods, chemical therapy is still "recommended.")

Slack Jen Dec 11 2017. 75 Percent of Doctors Would Refuse Chemotherapy - The Same PercentageRecommend It To Patients. EmaxHealth, Last Accessed at https://www.emaxhealth.com/13781/75-percent-doctors-would-refuse-chemotherapy-same-percentage-recommend-it-patients

Innes ME. Most doctors who were terminally ill would AVOID aggressive treatments such as chemotherapy - despite recommending it to their patients. 30 May 2014. Access at ://www.dailymail.co.uk/health/article-2643751/Most-doctors-terminally-ill-AVOID-aggressive-treatments-chemotherapy-despite-recommending-patients.html

LaCapria Kim, Chemotherapy Doesn't Work, Doctor Blows the Whistle. 28 June 2016 "Hardin B. Jones recently revealed that chemotherapy doesn't work 97% of the time, and doctors only recommend it to get kickbacks." This article reflect long dispute on the validity of chemotherapy.

N2. Effects of Rate Constants' Multiplier N on the Multiplier M of Final Cancer Cells Numbers

To see the adverse impacts of raised rate constants, a primary tumor with K=0.004416 (1/day) is used, when k is changed by a multiplier N, the final cancer cell number will be changed by a multiplier M. Multiplier M are computed for 1, 3 and 10 years and different rate constants (with N being 2.5X, 5X and 10X) and shown in Table S1 below.

Table S1. Effects of Rate Constants' Multiplier N on the Multiplier M of Final Cancer Cells Numbers

A preprint for discussion only

Rate Const. Multiplier (N)	Rate Const. (k)	Time (Years)	Cycles No.	Final Cells No Multiplier (M)
2.5	0.01104	1	365	11
2.5	0.01104	3	1095	1413
2.5	0.01104	10	3650	31637216440
5	0.02208	1	365	631
5	0.02208	3	1095	251280398
5	0.02208	10	3650	1.00E+28
10	0.04416	1	365	1995809
10	0.04416	3	1095	7.94E+18
10	0.04416	10	3650	1.00E+63
15	0.06624	1	365	6312262455
15	0.06624	3	1095	2.51E+29
15	0.06624	10	3650	1.00E+98

1620 **N3. The Final Cancer Cell Numbers Depend On Cell Dividing Cycles And Rate Constants**

Table S2. Effects of 2.5 to 5 Times Increases in Rate Constants on the Final Cancer Cell Numbers in 3, 5 and 10 Years

Rate Const. Multiplier N	Start Cell No	Rate Constants (K)	Time (Years)	Final Cell Number (Million)	Comments
(NA)	100	0.004416	10	1.0E+9	Primary Tumor
2.5	100	0.01104	3	1.8E+7	
2.5	100	0.01104	5	5.2E+11	
2.5	100	0.01104	10	3.2E+19	
5	100	0.02208	3	3.2E+12	
5	100	0.02208	5	3.2E+19	
5	100	0.02208	10	1.0E+37	

1625

N4. Some Common Cancer Drugs' Half Lives

Table S3 Some Cancer Drugs and Their Half Lives

Cancer type	Short Name	Drugs and Half Lives	Comments
Breast cancer	CMF	Cyclophosphamide: 3–12 hours Methotrexate: 3–10 hs or 8–15 hs	Eliminated in 2-3 days.

		5-Fluorouracil: 16 min Vinorelbine: 27.7-43.6 hours	
	AC	Doxorubicin: 12 m/3.3 h/30 h/Mn: 1-3 hs Cyclophosphamide: 3–12 hours	Eliminated in 2-3 days.
Hodgkin's lymphoma	TAC	Docetaxel: 86 hours Doxorubicin: 12 m/3.3 h/30 h/Mn: 1–3 h Cyclophosphamide: 3–12 hours	Docetaxel stays for several days.
	ABVD	Doxorubicin:12 m/3.3 h/30 h/Mn: 1–3 h Bleomycin: 2 hours Vinblastine: 24.8 hours (terminal) Dacarbazine: 5 hours	Vinblastine stays for several days.
	MOPP	Mustine: Vincristine: 19-155 hs (mn: 85 hs) Procarbazine: 10 min Prednisolone: 2–3 hours	Vincristine stays for several days.
Non-Hodgkin's lymphoma	CHOP	Cyclophosphamide: 3–12 hours Doxorubicin: 12 m/3.3 h/30 h/Mn: 1–3 h Vincristine: 19-155 hs (mn: 85 hs) Prednisolone: 2–3 hours	Vincristine stays for several days.
Germ cell tumor	BEP	Bleomycin: 2 hours Etoposide: oral: 6 hs., IV: 6-12 hs. Cisplatin: 38–45 min	Eliminated in 2-3 days.
Stomach cancer	ECF	Epirubicin: 30–100 hours Cisplatin: 38–45 min 5-Fluorouracil: 16 min	Epirubicin stays for several days.
	ECX	Epirubicin: 30–100 hours Cisplatin: 38–45 min Capecitabine: 33 to 54 min	Epirubicin stays for several days. Two drug rapidly disappears
Bladder cancer	MVAC	Methotrexate: 3–10 hs or 8–15 hs Vincristine: 19-155 hs (mn: 85 hs) Doxorubicin: 12 m/3.3 h/30 h/Mn: 1–3 h Cisplatin:38–45 min	Vincristine stays for several days.
Lung cancer	CAV	Cyclophosphamide: 3–12 hours Doxorubicin: 12 m/3.3 h/30 h/Mn: 1–3 h Vincristine: 19-155 hs (mn: 85 hs) Vinorelbine: 27.7-43.6 hours	Vincristine stays for several days.
Colorectal cancer	FOLFOX	5-Fluorouracil: 16 min Folinic acid: 6.2 hours Oxaliplatin: 10–25 min	Cancer drug rapidly eliminated.

The data is used only for the purpose to show their short term effects of killing cancer cells. Half life is the time needed to have half of the drug concentration or

1630

amount eliminated by biological processes.

Other drugs with short half lives include Chlormethine (1 min), Carboplatin (1.1–2 hours and 2.6–5.9 hours), Dacarbazine (5 hours), and Paclitaxel (5.8 hours). Drugs that have long half lives include Vinblastine (24.8 hours), Vinorelbine (27.7 to 43.6 hours), Vincristine: (19 to 155 hours; mean: 85 hours), Epirubicin (30–100 hours), and Docetaxel (86 hours).

N5. Impacts of Chronic Stress on Cancer Growth Rate Constants

1. Experimental Design of Sloan et al (2010)

They employed an in vivo metastasis model where six-week-old female mice was used. Tumor cells (100,000) were injected into the 4th mammary fat pad or into the tail vein. Chronic stress was induced by restraining mice, which has been shown to induce chronic stress as shown by neuroendocrine activation. Induced stress was applied to mice for 2 hours per day for 20 days commencing 5 days before tumor cell inoculation or for 14 days commencing 2 days after surgical removal of the primary tumor. Metastasis was measured by measuring total bioluminescence in distance sites such as chest region and brachial lymph nodes. Cancer cells were estimated by measuring tumor-specific luciferase activity using an in-vivo imagine system. The mice were sacrificed on day 28 for later microscopic study. Chronic stress applied for 20 days increased the metastasis of the primary breast tumor cells to distant tissues by 38-fold versus controls in 28 days.

Assuming that the metastasis starts with one single cancer cell and the migration step is sufficiently faster and frequent that it is ignored, the rate constants for the stress-applied group is ks=kc+LN(38)/20, where kc is the rate constant for the control that was not exposed to stress.

N6. Several Exemplar Cancer Miracles

One well known cancer miraculous survivor is Guolin. She had her uterus removed in 1949 for uterus cancer. A return cancer spread to her bladder. She was operated six times, but nothing could stop her cancer from engulfing her. When the returned cancer became terminal, she started developing special exercises known as Qigong to combat her cancer, she not only got rid of her cancer completely, but also got rid of chronic diseases such as heart disease, arthritis, and high blood pressure. She spent her remaining life to teach her exercises until she died from other cause in 1983. Her exercises are immensely popular. Now, her Qigong is practiced in the U.S., Canada, Japan, Singapore, Philippines, Malaysia and Indonesia et al.

By using Quolin exercises, many patients with terminal cancer miracu-
lously survived. One patient, Gao, had his thorax opened to remove a tumor. Due
to the widespread tumors, the surgeon had to stitch the thorax back without
touching any tumor. He started using Quolin exercise by struggles: walking a
step, taking a break, often spitting up blood. The exercise helped him survive. In
another case, a patient, Zhu, had his eye ball pushed out by a stage 4 pharyngeal
cancer with metastasis to the brain. The exercise in combination of herbs helped
eliminate symptoms in two months, which is incredible.

A 50 years old man, one Mr. Liu, was diagnosed with a stomach cancer.
When he was operated, the surgeon found that the cancer had spread to the liver
and many organs in his abdomen. Abdomen was stitched back because nothing
could be done. To avoid unnecessary emotional distress, the surgeon told the pa-
tient that the cancer had been completely removed (this practice was common at
that time in China). After the patient was discharged, he retired from his job,
made a plan for recovery and changed his lifestyles. He is now around 80 and
still alive. Stories like this are frequently heard. In early years when CT was not
available, doctors could not accurately determine cancer conditions for opera-
tion. Thus, aborting operations was rather common, and some of patients sur-
vived for decades or their remaining lives.

Forbes reported several cancer miracles under "Cancer Miracles" on Feb
12, 2009. In one case, one Burrows was diagnosed with an inoperable liver can-
cer in November 2005. He was told to live for 30 to 60 days. In February 2006,
Burrows developed abdominal bloating, shaking, chills and nausea. Soon after
that he noticed that the lump on his stomach was gone. In another case, one
Schou suffered a melanoma, which had spread to his liver, abdomen, lungs,
bones and ten spots in his brain. He made changes to his diets. Four months
later, 90% of his tumors had disappeared.

Another well documented cancer miracle is described in "Cancer: the mys-
terious miracle cases inspiring doctors", by one Robson on March 6, 2015, BBC,
Future. A 74-year-old woman was diagnosed with carcinoma, a form of skin can-
cer. Given his tumor condition and his age, her treating doctors were debating
what could be done. Despite receiving no treatment at all, the tumor was shrink-
ing and shrivelling under the doctors' eyes. The tumor just disappeared. After 20
weeks, the patient was cancer-free, based on the biopsies and the scans.

There are about several hundred cases that can be considered well docu-
mented in literature. I estimate that the total number of cancer miracles is in mil-
lions. Most cancer miracles in developing nations were not documented or re-
ported. Sometimes, cancer patients refused to accept medical treatments but
lived for deceases or experienced cancer healed naturally. Some cancer miracles
happened decades ago when surgery was attempted but aborted.

The time scales of resolving fully developed metastasis tumors in the above cases are from 2 to 5 months. The shortest times for resolving a tumor of an infant head size was reported to be about 40 days (Dr. Lee Ke's book). We am compelled to find that human healing power is many magnitudes larger than the effects of medical treatments.

Those cited miracle cases, together with several hundreds of documented cases and potentially million of cancer miracles, are conclusive and irrefutable evidence that cancer can resolve on its own, or can be cured by adjusting lifestyles. Any claim of terminal and incurable is factually false. Medicine confines its treatment options mainly to surgeries, drugs and radiation because the legal framework, professional regulations, and most research funding sources are tailored for them. Medicine does not explore any of a vast number of lifestyle factors such as diets, exercises, mind regulation, natural anti-cancer compounds, and life habits as cures.

N7. Flaws in Clinical Trial

They found that when a non medical measure can work with both beneficial and negating effects and when it is indiscriminately used against human subjects, its statistical mean is massively reduced or reaches zero. They show that randomized clinical trials are unable to correctly determine beneficial benefits for any weak effect like lifestyle factor as long at least one other similar factor interferes with the factor. Their study shows that lifestyle factors must be studied by well controlled optimization trials but not a randomized trail. Based on a multiple interfering factor model, a treatment package using k factors has much strong effect than a single treatment. If each of the k factors has a same treatment effect, an optimization trial to evaluate a heath property by using all k factors will raise the total treatment effect by $(1/g)*k$ times than a randomized trial (where g is a degrading factor caused by misapplication of a treatment to patients, with its value from 0 to 1), and raises T statistic, Z statistic or F statistic by about $(1/g)*k*\sqrt{k}$. If the total number of factors is increased from 1 to 5, 10, T statistic, Z statistic and F statistic will increase by approximately 11.2 or 32 times. Moreover, by avoiding negating effects, an optimization trial using k factors as a treatment package can raise treatment effect potentially by one to several orders of magnitude.

N8. Personal Observation

The author personally noted that an actively growing mole of 10 mm in diameter on chest was not held in check by regular walking, but was completely eradicated by jogging accompanied by six song uttering at one hour per day (about 42 MET per week) for about 2 years. Similarly, a flatten circular mass of about 6 mm in diameter on a hand was eradicated by the same jogging for about 1.5 years.

1755

N9. Small Reductions in Rate Constants Significantly Reduce Tumor Sizes

Table S4 The Effects of Small Reductions in Rate Constants on Tumor Sizes

Original k (1/day)	Reduction in k (%)	Rate Constant (K)	Time (Years)	Cycles or Days	Multipliers M
0.01	-1	0.0099	1	365	0.96
0.01	-1	0.0099	3	1095	0.89
0.01	-1	0.0099	5	1825	0.83
0.01	-1	0.0099	10	3650	0.69
0.01	-5	0.0095	1	365	0.83
0.01	-5	0.0095	3	1095	0.58
0.01	-5	0.0095	5	1825	0.40
0.01	-5	0.0095	10	3650	0.16
0.01	-10	0.009	1	365	0.69
0.01	-10	0.009	3	1095	0.33
0.01	-10	0.009	5	1825	0.16
0.01	-10	0.009	10	3650	0.026
0.01	-30	0.007	1	365	0.33
0.01	-30	0.007	3	1095	0.037
0.01	-30	0.007	5	1825	0.0042
0.01	-30	0.007	10	3650	1.7E-05
0.01	-50	0.005	1	365	0.16
0.01	-50	0.005	3	1095	0.0042
0.01	-50	0.005	5	1825	0.00011
0.01	-50	0.005	10	3650	1.18E-08

1760

1765