The RECLAIM system

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RECLAIM

Regenerative Cloud AI Multiprocessing

Preface

The world is now five decades into the 1970s Information Age and the possibilities seems endless with high-speed internet right in the palm of our hands. Much more people have access to information, and the shear amount of information itself has increased tremendously but one question still occupies the mind of people since the dawn of civilization: Health. I believe more people have the opportunity to be healthy today than for thousands for years ago, yet lifestyle complications are booming at high-speed as well. Paradoxically, The Information Age also bought exposure to misinformation from self-proclaimed health gurus, fitness geeks and experts. The vast amount of myths, fad diets and fearmongering leaves people confused in this health-jungle with ever-changing opinions coming from all opposing sides. Others simply chose to ignore every advice and thus, leaves them uninformed. This book aim for a clear-cut through the jungle and the intention is to not leave anyone misinformed or uninformed. My personal motivation for writing this book is two-fold. First, I am a trained medical doctor which reflected my natural interest in health but seeing how my colleagues struggle with one lifestyle complication after another I knew something had to be done. Second, becoming a father was the greatest eye-opener for me and I intend to make the world a better place for her. The statistics are definitely not in our favor and therefore I see no better time to start improving our health than now. My fortunate journey has luckily brought me in close proximity with great people and their impeccable knowledge in a field so simple but yet very complex as health. I have allied myself with these people as they have proven themselves more than once in both academia and sports with outstanding results. People with this mixture of a pragmatic researcher are extremely rare as it encompasses not only those who practice what they preach but also the opposite way around: Preach what you practice. The latter is often overlooked but is at least as important and if not more important than following your own philosophy of health. Thanks to the Information Age nearly every person knows about health to some degree but to actually implement this knowledge into their busy and often unforeseeable lives remains unclear for the majority. Healthy living can simply be boiled down to eating your vegetables, stay active and no smoking or drinking but how this translates into superior health is a whole different ball-game. Thankfully, we developed a completely new system named “RECLAIM” to focus on every aspect of health because nothing works in isolation and we emphasize two learnings: 1) The right knowledge and 2) The right mindset. This is essentially our system to utilize the right information from the Information Age for your specific needs and not anybody else. This book uses a cocktail of biology, biochemistry, physics, chemistry and mathematics to give you the right tools at first. Afterwards, we take a deep-dive into philosophy, psychology and sports performance to modulate your introspective thoughts about why you do what you do. Health is not about feeling healthy or good but about actually being healthy even if it means cutting through the BS of strong marketing and “feel-good” products. Our hope is to bring an end to unhealthy lifestyle and give people more control over their lives which ultimately materializes into improvement of life quality. Improvement of life quality essentially means more quality time with family, friends and colleagues. Nothing beats a group of people with common vision at the right place and right time which is why I want to thank all my contributors to this book; I acknowledge the hard work you had to put in this book, dealing with my crazy high ambitions and sacrificing family time but ultimately we can all hope it was a greater cause.

Introduction

According to WHO the definition of health is as follows: “Health is a state of complete physical, mental and social well-being and not merely the absence of disease or infirmy”[1], and despite their ambitious endeavor health has occupied the minds of humans for thousands for years. In fact, there are sources dating back 4000 years to the ancient Mesopotamians who diagnosed and prescribed medication in the search for optimal health[2]. Whether this was the first attempt in human history to perform modern medicine remains unclear but the focus on health was ever present as well in Chinese history, the Islamic civilization and during Greece with famous physician Hippocrates[3–5]. Thus, health has transcended both time and space in our history. It may seem counter-intuitive how such an old discipline as health still holds its high degree of complexity and controversy. On one hand, every human is unique in both their biological mark-up, lifestyle and history which provides a plethora of levers to manipulate. If only these levers would reproduce the specific outcome in others as we anticipated there would less controversy but we have all heard about the 100-year-old war veteran who smoked cigars every day or the 100+ grandma who never touched a vegetable, let alone a superfood. On the other hand, we know for sure there are things detrimental to our health such as poison and radiation but nowadays we rarely find ourselves in these extreme situations. This leaves the majority of people in an everlasting search for optimal health, the fountain of youth, and only to left with speculative results. Take for example, the popular debate about whether carbohydrates or fats are detrimental for health and has spiked the well-known LCHF (Low Carb High Fat) diet in recent years. While LCHF may be a new term the story actually dates back to 1863 with William Banting banning bread, butter, milk, sugar, beer and potatoes in his “Banting diet”[6]. A similar dispute has reigned in sports about whether endurance training or resistance training is superior for healthy aging[7,8]. Confusion is eminent when science itself fuels this bonfire of controversy by pulling in different directions which has no sure path for people to follow. Regardless, the truth is often somewhere in the middle but if so, this provides little to no guidance for a person who wants to improve his or her health. When everything is right and wrong at the same time we tend to rely on intuition or emotions, thereby empowering those self-proclaimed gurus who relates ourselves. While there is nothing inherently wrong with being emotionally involved in own health it should always be sedimented in concrete results rather than “gut-feelings”. However, there is no easy way to forecast what interventions are most effective given the long lag-time of 10–30 years and thus, one must trust the system while remaining patient. We would to propose a new system to address health which, in our humble opinion, provides a much more personalized and intuitive understanding. This system, RECLAIM, is based on scientific disciplines within biology, biochemistry and medicine. In addition, AI and healthy people from “blue zone” serves as the template which the system is built upon. While AI acts as the glue between different disciplines people from blue zone are well-known living examples of what can be humanly possible in terms of optimal health. The latter is especially important since many systems, approaches and even scientific articles have no merits to real-life examples other than those produced with surrogate markers of health. In 2014, Dan Buettner lead a National Geographic expedition to find place where a high proportion of centenarians were seen in the population[9]. These places were uncovered as “blue zones” in five places around the world: Loma Linda (USA), Nicoya (Costa Rica), Sardinia (Italy), Ikaria (Greece) and Okinawa (Japan). The latter place, Okinawa, wins over the others in longevity at 68 centenarians per 100K people[10]. In centenarian hotspots people reach age 100 years at 10 times greater than in the United States. It is tempting to think that one must win the genetic lottery to live pass 100 years but nothing could

further from the truth as evidenced by the presented arguments. First, the famous Danish study on 2872 twin pairs from 1870 – 2000 showed only a modest effect of genes on longevity of 20% while 80% is dictated by lifestyle. Second, more and more blue zones are losing their edge in longevity such as Okinawa in Japan is now declining to the countries average life expectancy[11]. This has largely been attributed to the adoption of a Western diet. Third, the advantages in health enjoyed by blue zones are more or less lost when they migrate to other countries and the earlier they migrate the more they tend to lose[12,13]. This is true even when adjusted for socio-economic status as Asians with type 2 diabetes were younger, had higher education and less likely to be smokers or drinkers than U.S.-born Caucasians. What makes blue zones rise above special is not confined to only their longevity but also the extremely high life quality they enjoy and share with each other. Many have hypothesized diet, exercise or low pollution as the main contributor to superior health in blue zones but the reality is multifaceted with no single cause. Although many other blue zones exists[14,15] the following are well-described and documented as we will go through each one of them. Loma Linda in CA and especially the Seventh-Day Adventists live on average 5 years longer than the general population[16–18] but the most probably the most intriguing fact is their vegetarian diet and low rates of cancer[19]. Most Seventh-Day Adventists follow a vegetarian diet and very few eat meat or follow a strict vegan diet. The low mortality from cancer has been attributed to their high consumption of healthy fats from nuts and fish[20–22]. Another interesting fact is they follow a faith of holistic understanding of the person, conservative principles and lifestyle. However, vegetarians in Britain have not gained the same benefits[23] which may indicate other factors than diet is involved as well. Saturdays are reserved for charitable work and social gatherings with accompanied activity such as nature walks or lunch outside. Seventh-day Adventists also show superior health in other countries outside the US as those who live in Denmark have a lower risk of cardiovascular disease than the of rest of the country[24]. Seventh-Day Adventists outperform others in longevity, and to understand why it must be seen through the perception of life by whole communities rather than confined to them being vegetarian or nature-loving. Their religion has been under criticism because of rigid rules and exclusion but at the same time serves as a powerful catalyzer for health since strong feelings of belonging are reserved for those who embrace their way of life. Nicoya is a North-western region of Costa Rica with around 161,000 inhabitants and economic underdevelopment but have 20% lower mortality compared to the rest of the country[25,26]. The elderly, particularly males, have the lowest mortality in the world and the health expenditure per capita is one-tenth of that in United States[27,28]. The Nicoya advantage is mainly in the low risk of cardiovascular diseases[29] despite a higher intake of calories, proteins and carbohydrates along with fibers than traditional Costa Ricans. In addition, they also exhibit similar smoking habits as the rest of the country and the quality of their soil is also similar[30]. There is one main distinctive characteristic unique to Nicoya is their high level of physical activity in agriculture for planting, harvesting and handling crops. Due to their state of enforced self-sustainable lifestyle many daily chores must be handled manually and thus; their quotidian food is minimally processed compared to more industrialized foods such as cookies or hamburgers. However, the elderly and especially centenarians in Nicoya are disappearing at alarming rate which is caused by multiple factors such as migration and industrialization. Elderly Nicoyans are living proof of the effectiveness in constant natural movement by physical activity from A to B and “working for your food” from seedling to table. The effects of physical activity on health is well-documented and once it diminishes, we expect the health advantages of Nicoya will disappear along with its status a *bona fide* blue zone. Meanwhile Sardinia in Italy takes a different

approach to achieve longevity. Older adults from Sardinian Zone live in a low socioeconomic status of this region but surprisingly have high perceived well-being and low mental ill-health[31–33]. Depressive symptoms are the lowest in Sardinia and this has spiked various hypothesis about maintaining mental health, among them the term “resilience” is well-explained in the literature for healthy aging. There are as many meanings of resilience in the literature but a common agreement often refers to showing positive adaptation in the face of adversity. This is not to be mistaken with positivity or happy thinking as positive adaptation emphasize a strong sense of accept or acknowledgement. It may be achieved as an individual personality trait, through interpersonal/social relations or external sources (e.g., health and education services) from childhood to adulthood[34,35]. No matter when or how resilience occurs the elderly in Sardinia achieve superior cognitive abilities with little to no external sources (limited education and healthcare). Also, very noticeable is the social support across age-groups, family and friends to provide for each other which especially the older adults in Sardinia utilize to a higher degree compared to a matched control sample from Northern Italy[36–38]. Italy is generally well-known in the world for their tight-knit communities across all ages but people in Sardinia elevates it even more due to their sparse environment. The ability to absorb stress with a high coping capacity and recover quickly is interestingly more related to cultural disposition rather than socioeconomic status. This may be a key player for other OECD countries to combat the uprising cases of depression and neurodegenerative diseases. The next blue zone is Greece with the people in Ikaria Island centralized in the eastern part of Aegean Sea. The small population of 8,000 people lives on the Island with eight super-hot radioactive saline springs[39], making it a rather hostile place with one radioactive spring per 1000 inhabitants. Interestingly, very few are current smokers but the majority have smoked before and this is somewhat indicative of why smoking cessation is never too late. Besides napping and daily activity Ikaria is perhaps best known for the Mediterranean diet as their main secret to longevity[40–43]. The Mediterranean diet involves a large quantity of olive-oil, fish and whole grains[44] to prevent numerous lifestyle complications ranging from depression to cardiovascular diseases. Poultry and wine are consumed as well but consumption of meat, especially red meat, is relatively scarce at under 10 grams per day. Outside Greece, the Mediterranean diet has also proven to be effective in mitigating risk of lifestyle complications and many European countries have adopted the diet to improve survival among older people[45]. Ikaria is perhaps the most intriguing of all blue zones as radioactive springs and smoking would impose a tremendous threat to health but there seems to be a counter in their lifestyle albeit genes may play a significant role. Nevertheless, people who seek out to change their lifestyle should never speculate whether dropping bad habits such as smoking is too late, and instead focus on how malleable the human body is to the environment. The last blue zone, Okinawa in Japan, is the most spectacular place as evidenced by the highest number of scientific articles on longevity. Japan already has the highest life expectancy in the world but the prefecture (state) Okinawa has 20 more centenarians per 100,000 inhabitants than the rest of Japan with the increasing number of centenarians despite uprising lifestyle-related diseases mostly among males[10,46–48]. Okinawa has been praised because of the highly independent centenarians and especially the females lead the way with an impressive 16.46 years remaining at age 75. Thus, there is no other place on earth to quite match the life-quantity and quality of Okinawa. The typical middle-aged Okinawan is lean, physically active and works in farming or fishing but the main secret to their superior longevity has been hypothesized as calorie restriction[49–51]. In fact, the principle of calorie restriction or low-calorie diets might apply to all other blue zones of two reasons: i) Physical activity is often

underreported in studies as daily chores are not included[52] and ii) Calorie restriction has been linked to longevity[53–56]. However, Okinawans do not achieve caloric restriction on purpose but as part of their mantra by saying "hara hachi bu" before every meal which means to eat only until they are 80% full. This truly reflects their disciplined culture by practicing mindful eating. The centenarians in Okinawa have a high degree of independent functioning equivalent to what is seen in a normal healthy 90 years old and avoid age-related diseases until very late in age[57,58]. Ongoing extensive research on Okinawans shows, along with low levels of inflammation, data consistent with younger biological age in older Okinawans than their chronological age[59]. Within Okinawa there are even smaller communities divided into "Moai", social support groups, formed by the closest friends who helps each other in everything from financial to spiritual guidance[60]. Taken together, we believe the blue zones can all teach us something about health: Loma Linda thrive on a plant-based diet, Nicoya's continuous natural activity as farmers, Sardinia's social inclusion, Ikaria is all about second chances given their hostile environment and Okinawa teaches us about mindful eating. The blue zones might have more in common with each other than their country of residence and definitely vastly different from traditional OECD countries. This is perhaps the reasons behind our declining health: i) The heterogeneity nature of health as "many roads lead to Rom" and ii) The lack of execution as blue zones are extremely to replicate in other areas. Especially the latter seems almost impossible to implement given our modern society with lifestyle and cultural differences which is far away from the traditional life of a farmer. Our health is still declining despite billions of US dollars in research, governmental guidelines and national campaigns. Although life expectancy is increasing, we have to bring the question of life quality into the equation. Thus, health encompasses more than just life expectancy and the true measurement of health on a national level would be [health expenditure per capita] divided by [life expectancy]. This ratio gives a much clearer view of how much each person will cost society per living year and grouping or stratifying by age (e.g. $/age 1, $/age 2… $/age 80) shows an even more melancholic picture. Aging does indeed hurt unless aging occurs healthy and the RECLAIM system aims to do exactly one thing: Healthy aging. First, we want to redefine health as we respectfully disagree with WHOs definition of health and instead emphasize our own: "Health is a state of transcendence purpose, social belonging and free from lifestyle complications or diseases". This is less ambitious than WHOs definition but gives a person more self-control and takes into consideration if a person suffers from genetic diseases or accidents. Second, we want to build a community with the RECLAIM system. We believe this is the sole reason why blue zones thrive and why previous efforts to increase health in a population has failed. Simply delivering the message of eating healthy and to exercise more brings no value other than what people already know from their grandparents. The community we are build has to be open to everyone and all-inclusive which means having as many touch points as possible with people. This include but is not limited to: Culture, beliefs, diet, activity, friends, family, work and spirituality. Overall, we are trying to trigger a paradigm-shift without interfering or demanding anything from people and we believe this can achieved through the creation of our own "moais". Third, we need to uphold consensus on how to measure health as there is no universal agreement on how health should be measured or monitored. The field of diagnostics is growing at fast pace as technology mature but we are more concerned with giving people a measurement of health for usage of personal guidance. Health is not the absence of disease or infirmity as being healthy has nothing to do with being sick. Being healthy and sick gives you the ability to overcome the disease faster than a person who is unhealthy and sick. Therefore, we want to introduce AI into the RECLAIM system as we believe the

technology is ready for commercial use and is an essential tool for us when we consider many variables towards achieving personal health. In order to utilize the full functionality of AI we need to quantify any variable essential to human health and thus, we propose a mechanistic approach to such. The foundation of health is composed of three subcomponents: i) Body, ii) Mental and iii) Exposure. Body is how the body responds to exposure and follows Cricks central dogma of going from DNA to mRNA to protein[61] but also includes nuances such as retro flow from protein to DNA modulation and DNA methylation in epigenetics[62]. However, the latter is a new field and still controversial on how retro flow can be achieved by influencing our genes through our actions. Our genes are in large part fixed and not much can be done to change our phenotypic manifestations like height, eye color and color pigmentation. The point being central dogma is very static and thus, only depends on the interaction with our environment. This interaction is interpreted by your mind and your body through electricity or chemicals. If the flow in central dogma totals to zero it means the body no longer responds to outside stimulus and you are by definition dead. Your body will slowly disintegrate, still through interaction with the environment, but you are no longer in control of the processes and they appear somewhat chaotic. The mental component refers to the job demands-resources model which is a balance between demands on the individual and the resources he or she has to deal with those demands[63,64]. To finalize the component, we add additional layers such as perception and interpretation along with tools such as mental resilience for easing out the readers process from understanding to execution. Lastly, exposure refers to how our physical body interacts with its environment. There are multiple ways through which we can accomplish interaction with our environment: Our five senses, intake, physical activity, pollution, contamination, etc. Basically, we use the principles of physics and see our body as a three-dimensional box interacting with matter around us in the form of electrical or chemical substance. Food is chemically divided into protein, carbohydrates and fat with some nutrients while our five senses are electrical signals from nerves firing “0” or “1” to our brain for interpretation. For example, the simplest box we can imagine is a person who lives a normal life. The person consumes food as building blocks for the body, and to produce energy for movement. Under normal circumstances the body burns a mixture of fat and carbohydrate to convert chemical energy into mechanical energy measured as joule and as heat to the surrounding tissue. Like an engine, fat and carbohydrate needs oxygen to be burned for production of joule which occurs in the mitochondria. This is a complete combustion of fat and carbohydrate into carbon dioxide while oxygen is incorporated into water. To simplify our model, we measure the interaction between body and environment with three parameters: Frequency, volume and intensity. For example, when we ask about smoking: “How often do you smoke?”, “how much do smoke each session?” and “What kind of tobacco do you smoke?”. Following the same principle of quantification, we can start to map out a box for each exposure relevant to the person. We can actually start to map the whole person as one big box: Genetic mark-up under body, job demands-resources model under mental and environmental interaction under exposure. This big box has sub compartments with components and sub components all connected to each other. This connection occurs in time and space as well — The spatiotemporal distribution. For example, eating a banana in the morning is not the same as eating a banana in the evening even though they contain the same amount of energy because your level of cortisol spikes in the morning which mobilizes sugar to your bloodstream. The overall result could be two different physiological responses in your body, neglecting the fact if you may feel the same or not. On top of this there a genetic component and the best example is how likely Asians develops diabetes type 2 when

compared to Caucasians with similar BMI. Thus, the only way to solve such a complex problem and aggregate it into something meaningful would be approached from AI. We suggest to use the framework Pytorch[65] or Tensorflow[66,67] as both have been proven excellent in personalized medicine and screening but what matters more is the use of a graph database like Neo4j over traditional SQL databases[68]. We believe this may the missing link in implementing AI as a powerful tool in healthcare and with the help of cognitive networks such as Neo4j we are taking a quantum-leap towards real value for patients. There are many other methods but in the RECLAIM system we chose TensorFlow together with Neo4j although the future may bring otherwise. The following will briefly explain what TensorFlow and Neo4j is. TensorFlow is a free and open-source software developed by Google for internal use in the beginning but later in 2015 they released it to the public[69]. TensorFlow offers a software library for machine learning and thus, gives the ability to make prediction algorithms by feeding it with data. There are two ways to learn, supervised or unsupervised, but we only consider the former for now as unsupervised learning is used when the outcome is uncertain. We already know the outcome of medical history or scientific articles and therefore, use supervised learning to predict their risk of lifestyle complications. As we feed our algorithm with data it will become better to forecast the risk of each and every individual because 80% of our data is used for training the algorithm to become better while the remaining 20% is for cross-validation to make sure the right outcome is produced. It should be noted how inaccuracy any system is in its initial phase with data being a very scarce resource but, to our knowledge, the RECLAIM system still provides a deeper understanding of health than any other schemes or flowchart currently available. We add an additional layer of understanding by using Neo4j as our main database and while it seems more labor intensive to implement the benefits downstream are outstanding. Basically, Neo4j is another way to store data by looking at relationships between datapoints (called nodes) but the real power comes in visualization and exploration with Neo4j Bloom. In fact, Neo4j was used in The Panama Papers[68] to establish connections between 11.5 million documents or 2.6 TB of data worth of data which ultimately resulted in the largest financial fraud in history by involving over 140 politicians from 40 countries. The ability to immediately see data clusters and step into helicopter-view makes Neo4j extremely relevant in sorting out signal from noise in any given dataset and coupled with TensorFlow gives makes it a perfect symbiose. Some data scientists and programmers have emphasized how an algorithm or AI is only as good as the data it receives but with Neo4j we believe much data tidying and cleaning is done optimally. However, this should never stand alone as we strive to hire the world's best and brightest minds to manage the flow from raw data to pure insights. The technology we use is relatively new and our approach has never been before but similar projects have used TensorFlow with Neo4j to predict how existing customers review other products with 97% accuracy[70]. To summarize, we have three important major levers in our system: i) Healthy lives from blue zones, ii) Quantification of health and iii) AI acting as the glue to combine everything together. With this in mind we are in a very good position to give an example on how everything can work together for personalized health, and most importantly give unique advices to an individual what must he or she must do to achieve optimum health. The goal is not to embrace all interventions at once but rather tell exactly how a person can stay as healthy as possible with the bare minimum amount of effort. The example we use is this synthetic case about a 47-year-old woman, BMI: 50 kg/m^2 and non-smoker. At first sight we might want to reduce her weight through diet and exercise. She is from Denmark and thus, according to demographics (2017) her risk of death from cancer is 32.1% or 26.8% from cardiovascular disease (CVD)[71] which are the two main leading causes of death in

Denmark. From research we know obesity is correlated with those two diseases and her BMI is above normal, giving her an additional risk compared to the average Danish person. The relative risk of elevated BMI to kg/m^2 is 1.10 given no other diseases (comorbidity) or unhealthy predispositions[72]. From the scientific literature we find different relative risk of cancer and cardiovascular disease depending on the persons BMI from 18 – 50 kg/m^2 which we plot on a graph. We arrive at the formula by fitting a line:

$$Risk_{Cancer}^{CVD} = \left(\frac{\sqrt{BMI}}{14} - 0.3\right)$$

For simplicity we assume the relative risk of elevated BMI is similar for CVD and cancer. The formula does match the relative risk we find from the literature as setting BMI to 50 gives

$$Risk_{Cancer}^{CVD} = \frac{\sqrt{50}}{14} - 0.3 = \underline{0.10}$$

There is an additional 10% "penalty" on top of each risk and thus, this elevates her risk of cancer to 42.1% and CVD to 36.8%. We also measure her fat around internal organs (visceral fat) through bioelectrical impedance analysis to be 3000 g and since this is the dangerous fat the relative risk is further elevated[73–75]. The normal amount of visceral fat is 300 g but scaling to 3000 g gives her an additional risk:

$$Risk_{Cancer}^{CVD} = \left(\frac{\sqrt{Visceral\ fat}}{230} - 0.138\right) = \left(\frac{\sqrt{3000}}{230} - 0.138\right) = \underline{0.10}$$

If the relative risk from visceral fat is additive there is an additional 10% risk on top of her BMI to give her a 52.1% risk of cancer and 46.8% of CVD. For simplicity we assume there are only two risk factors, BMI and visceral, which are equally weighted in contribution to health. However, if her visceral fat was only 76 g it would offset the penalty from her increased BMI as

$$Risk_{Cancer}^{CVD} = \left(\frac{\sqrt{76}}{230} - 0.138\right) = -\underline{0.10}$$

And thus, there is an 10% gain to zero out the 10% penalty from her BMI. Her risk of cancer will again be 32.1% and 26.8% for CVD like the background population. The opposite is also true as someone with BMI 17.6 kg/m^2 and 3000 g of visceral fat would have the same risk of cancer and CVD as the background population. However, it is very unlikely for a person to have only 76 g of visceral fat at BMI 50 kg/m^2 but some bodybuilders or people with fluid accumulation might achieve this. The full formula:

$$Risk_{Cancer}^{CVD} = Risk_{Background}^{CVD} + \left(\frac{\sqrt{BMI}}{14} - 0.3\right) + Risk_{Background}^{CVD} + \left(\frac{\sqrt{Visceral\ fat}}{230} - 0.138\right) + Risk_{Background}^{Cancer} + \left(\frac{\sqrt{BMI}}{14} - 0.3\right) + Risk_{Background}^{Cancer} + \left(\frac{\sqrt{Visceral\ fat}}{230} - 0.138\right)$$

The full algorithm requires to factor in all demographic data, all measurements and how they are weighted which can only be achieved through the use of supervised learning in AI. To finish the case, we want to propose an intervention for our 47-year-old woman with BMI 50 kg/m^2 and 3000 g of visceral fat but otherwise healthy. Instead of "boiling the ocean" and advise her multiple interventions at once we want to give her the most efficient way to become healthy: Exercise. Exercise, especially of aerobic type such as endurance running, has been proved to be superior in improving health among people with increased visceral fat when compared to a hypocaloric diet[76]. Not only can we tell her to do aerobic exercise but also advise her to perform at medium intensity for at least 30 minutes each day which is twice as efficient as a hypocaloric diet. Of course, the final solution always relies on the decision-maker but if she wants to gain the most health out of a tight schedule and with constrained resources this would be it. After adjusting to her new routine, we can schedule for health checks every three months to monitor her progress and identify any

pain-points in our intervention as we also measure her stress-levels. The important part is not whether our algorithms give her 25 % or 26 % risk of CVD death, the overarching factor for RECLAIM to succeed is based on supportive social groups. Thus, the moias she creates with her closest 5–10 people who understands the journey she is about to undertake as changing lifelong habits can be nearly impossible without the understanding of your surroundings. We emphasize a very high degree of personal development in process of transformation, not only for oneself but to everyone around the person as well. We believe in full-scale changes as nothing works in isolation which is true for both psychology and biology.

The end result will be what we proposed initially: A safe shortcut to longevity with tranquility, omitting the noise and misguidance.

Blue Reference

Our system choose to rely on sound scientific evidence, but it must also be pragmatic. Therefore, we draw our attention towards the blue zones as explained earlier. The questionnaires, blood values and anthropometric data we extract from these place are referred to as our 'blue reference'. The most recent well-documented explanations is their low inflammation through either Okinawan caloric restriction[77,78], the Mediterranean diet of Ikaria and Sardinia[79–83], Nicoyas physical performance (despite low Vitamin D levels)[25,84] and Loma Linda vegetarians[85]. There are multiple ways to obtain low-grade inflammation. However, we emphasize how all these factors are highly malleable and can be achieved by anyone. To our knowledge, no studies have found any clear link between genes, body composition or vitamins with longevity. It is plausible all these factors converge to one or more inflammatory pathways. The earliest and most well-studied marker for inflammation is C-Reactive Protein (CRP). It was discovered for nearly 100 years ago (1930)[86], but has recently exploded in popularity with over 28,000 articles the last 5 years[87]. The underlying reason for this is how well CRP can predict future risk of disease and current health status. In addition, CRP is easily measured and relatively stable[88–90]. CRP contributes greatly to our blue reference and is weighted heavily in our algorithms. Normal levels among young adults is under 1 mg/L, but may increase 10,000-fold to more than 500 mg/L during infection[91]. For example, patients with COVID-19 can have CRP levels well above 100 mg/L and show poor outcome[92]. CRP is a ring-shaped pentameric protein produced mainly by hepatocytes under transcriptional control by IL-6 in response to an infection. However, the plasma concentration of CRP can quickly rise after a single stimulus to 5 mg/L after 6 h and peaks at 48 h while the half-life is relatively constant at 19 h[93]. Thus, the severity of any pathological process is reflected by its CRP levels through *de novo* synthesis from hepatocytes. No other acute-phase reactants show same stability as a marker for inflammation as CRP due to three factors: i) No seasonal changes in baseline CRP[94], ii) No diurnal variation and iii) Unaffected by intake[95,96]. A plethora of conditions give rise to elevation of baseline CRP, ranging from inflammatory diseases (e.g. rheumatoid arthritis, Crohn disease and systemic vasculitis) to malignancy (e.g. lymphoma). However, some inflammatory diseases such as SLE (systemic lupus erythematosus) may not increase baseline CRP at all. The mechanism behind normal levels of CRP in SLE is currently unknown, but could be limited by the detection limit of modern instruments. Recently, high-sensitivity C-reactive protein (hsCRP) have gained attention, and is basically measurements of CRP under 1 mg/L. The range of 0.1 mg/L – 1 mg/L or lower requires specialized equipment, but provides extremely valuable information for the clinician. hsCRP predicts risk independently of traditional factors, and is now a

validated measure of cardiovascular inflammation[97–106]. There are two noticeable studies worth mentioning: CANTOS[103] and MONICA[100]. The first, CANTOS, was a proof-of-concept on how lowering inflammation could reduce the risk of cardiovascular events independent of lipid levels[98,107–109] while MONICA showed the role of hsCRP in early pathogenesis of atherosclerosis. The latter study followed nearly 1000 men over 9 years, but the hypothesis of hsCRPs involvement in the pathogenesis of atherosclerosis was presented over a decade before the study[110]. Another study, JUPITER[111], showed a clear cardiovascular benefit from Simvastatin in individuals without hyperlipidaemia. In addition, MONICA successfully predicted future risk of cardio heart disease even when adjusted smoking and age. hsCRP levels were measured as low as 0.05 mg/L, which is significantly lower than what our instruments can measure (0.1 mg/L). A single-measurement of baseline hsCRP > 2.4 mg/L showed a relative risk of 2.0 in future cardiovascular event when compared to hsCRP < 1.0 mg/L[112]. The Reykjavik Icelandic Heart Study included 19,000 individuals (2,459 coronary events) and underwent almost 20 years follow-up is currently in preparation for more robust interpretation of hsCRP. Another hot topic is the use of LDL cholesterol in evaluating coronary health.

Low-density lipoprotein (LDL), denoted 'the bad cholesterol', still remain a debatable topic on cardiovascular health[113–116]. The Framingham Offspring Study[114], a prospective cohort study, showed no association between cardiovascular events and serum cholesterol. The correlation seems more tight in type II diabetic people with higher than average cholesterol intake[117,118]. In addition, low levels of LDL have been associated with an increased risk of diabetes mellitus[119–121] as well as neurodegenerative conditions[122,123]. We speculate whether LDL cholesterol follows a U-shaped curve with too little being as unhealthy as too much. The optimal level of LDL is still to be determined. The effects on cardiovascular health are even more pronounced when LDL and hsCRP is lowered altogether as evidenced by the FOURIER[124] and SPIRE[125] trials. The mechanisms behind the very early phase of atherosclerosis is yet to be determined, but does involve inflammatory processes. One possible explanation may involve hsCRP with LDL particles, thereby depositing proinflammatory plaques in a cascade-like series of events. Thus, LDL particles are merely the patches to dampen local inflammation and also why a high baseline hsCRP precedes LDL in the formation of plaque. In light of this we did not include LDL cholesterol in our measurements nor algorithms.

hsCRP has a role in cancer-related predictions, but the case is more pronounced in men than women[126–128]. The underlying reason is still unknown although estrogen may attenuate chronic inflammation. However, more evidence is now favoring hsCRP in cancer prediction[127,129–141] although it remain less strong to predict cancer-mortality[142–147]. The types of cancer related to elevated baseline hsCRP are probably more site-specific as previously thought[148] there has not been any association between hsCRP and prediction of cancer in general[149,150]. Some cancers are strongly associated with elevated levels of hsCRP: Prostate cancer[151–153], endometrial cancer[154,155], lung cancer[156], colorectal cancer[157–159] and breast cancer[130,133,160]. However, predictions are not tight-knit since other studies found no association as well[161,162]. Inflammation is known to be involved in the pathogenesis of colorectal cancer[163] and lung cancer[164]. The controversy in cancer prediction and cancer-mortality may arise from several factors involved in the association between hsCRP and cancer. First, the probability of a cancer to raise baseline hsCRP relates to the communication with systemic blood vessels. Since hsCRP is measured from whole blood there

would be little to no elevation of hsCRP in case of carcinoma in situ (CIS). Thus, hsCRP is only elevated in cases where the communication between local and systemic inflammation is facilitated my mediators of the immune system. Second, the cancerous tumor must favor an inflammatory milieu or at least elicit an immune response from cells of the adaptive or innate immune system. Whether this involve a *bona fide* inflammatory reaction from the cancer cells themselves or in conjunction with other cells remain unclear, but does not change the outcome of systemic inflammation. Third, the baseline hsCRP of individuals must be measured prospectively in order to determine whether there is an actual increase in hsCRP. This must be done under the assumptions of stable production, half-life and clearance of hsCRP. Cancer has been known to trigger systemic responses such as cachexia and other related degenerative conditions including inflammation itself. Some of these altered systemic processes may interfere with overall hsCRP levels including the treatment for cancer. The overarching question is whether elevations in hsCRP precede carcinogenesis (causality) or is concomitant increased with carcinogenesis. Regardless, hsCRP is a strong prognostic marker for monitoring cancer patients in combination with other substances such as albumin (Glasgow Prognostic Score)[165,166]. Many site-specific cancers are associated with elevated hsCRP, and is summarized in numerous meta-analysis[167]: Breast cancer[168], colorectal cancer[169,170], osteosarcoma[171], nasopharyngeal cancer[172], lung cancer[173,174], esophageal cancer[175,176], urological cancer[177], bladder cancer[178,179], renal cancer[180,181] and prostate cancer[182,183]. In addition, hsCRP has been associated with severe conditions in cancer patients such as cachexia[184–188] and even metastasis[189] although more studies are needed to confirm this hypothesis. Systemic inflammation is known to attenuate the immune system by keeping it busy while other processes such as metastasis and ectopic neoplasm takes place. The inflamed blood vessels are also more prone to metastasis, thereby providing a double whammy for cancer patients. It has now become apparent to others how many diseases and medical conditions are associated with hsCRP. The list continues as more links are found, but those worth mentioning are cardiovascular events and cancer since they make up the majority of fatality cases in OECD-countries. However, hsCRP have also been linked to other non-communicable diseases/conditions such Neurodegeneration[190–193], diabetes[194–204] and respiratory diseases[205,206].

The instrument we use, a portable fluorescent immunoassay (Standard F100 Analyzer, SD-Biosensor), offer much faster measurements while still maintaining clinical relevance. Within three minutes the F100 can measure hsCRP down to 0.1 mg/L on whole blood with a coefficient of variance (CV) of <10%, which is considered acceptable. Below are the method comparison of F100 Analyzer with current golden standards (ELISA, Roche Cobas).

» Method comparison Reference : Internal evaluation

Reference method vs STANDARD F hs-CRP	
Correlation vs ECLIA Method	y=0.9994x-0.01, R=0.9989, n=120
CV%	QCL=7.6% / QCM=9.7% / QCH=9.8%
Differ(%)	within 15%

Actually, the F100 Analyzer showed the least CV in lower regions. We believe the F100 Analyzer is sensitive enough to identify people with potential health risk although measurements in the 0.01 mg/l would be considered ideal. Extremely low levels of hsCRP (<0.01 mg/L) may be of interest for

research purposes and/or high-performance people who requires a tight control. Especially when hsCRP is involved in ageing[207], lifestyle choices[208,209] (e.g. smoking, physical activity, BMI, etc) and is even elevated in preterm infants[210]. Thus, baseline levels of hsCRP follow a U-formed curve from cradle to grave. The elevation of hsCRP in ageing may be caused by subclinical conditions while preterm infants spike hsCRP due to an extreme change in environment from their mother's womb to the outside would. During this process the infants lungs expand, water evaporates and body temperature drops. A real nadir must be established before the full benefit and effect of monitoring hsCRP make sense. The best way to achieve this is to have clients in a cohort with regularly measurements from 3–6 times a year, and the sooner in life the better. In addition, interpretation of nadir hsCRP must be taken cautiously given the multiple factors involved in elevation of hsCRP in certain situations: Vigorous exercise, infections and pregnancy. These conditions either spike hsCRP acutely and/or give a natural elevated level of hsCRP, but is expected with an intact immune system. Thus, the timing of hsCRP is extremely important to take into account when a true nadir is established. We speculate whether the studies who showed a low association with hsCRP had taken these precautions when hsCRP was measured since not all studies specified the condition of their participants. If nadir hsCRP was naturally elevated in some individuals then they would not *per se* be unhealthy, and influence the statistics towards a type 1 error. Although the immune system and inflammation are often coupled processes then we must consider one without the other, which indicate two processes with mutually exclusive properties. This raise a very important questions about the source of hsCRP if the immune system does not precede or is involved at all in the elevation of hsCRP. Other hepatoectopic sources have been suggested such as visceral fat and leaky gut, but no studies have confirmed this. Regardless, if hsCRP is elevated without involvement of the immune system then we consider this as chronic inflammation. Perhaps the most intriguing prove-of-concept are studies on the relations between hsCRP, immune system and aging known as 'inflammaging'. Inflammaging represents a reverse causality on how hsCRP triggers the immune system although the immune system is known to decline in performance over time[211–214]. We find the hypothesis very eligible given how well it fits with increasing of nadir hsCRP in ageing while the immune system declines.

Although many external factors are involved in raising nadir hsCRP then HbA1c is most interesting of several reasons. First, the dose makes the poison[215] as Homo Sapiens will most likely consume macronutrients: Carbohydrate, protein and fats. Laboratory models of nutritional overload such as blood-sucking insects leads to degeneration of their system[216]. Second, the underlying mechanisms behind an immediate increase in postprandial reactive oxygen species (ROS) may be caused by harmful byproducts from breakdown of proteins and formation of new molecules[216]. Third, persistent high glucose concentrations cause superoxide radicals in mitochondria[217] while transient high glucose spikes cause epigenetic alterations[218]. The superoxide radicals and epigenetic alterations cause a high level of systemic oxidative stress[219,220], leading to a higher nadir hsCRP. Interestingly, transient hypoglycemia has a stronger effect on endothelial dysfunction than glucose variability[221], and even more detrimental when hypoglycemia was followed by hyperglycemia[222]. Patients with type I and type II diabetes with dysregulated blood glucose deviate from euglycemia, and provide a model for the isolated effects. Thus, the latter is also a systemic inflammatory condition while diabetes type I is believed to be more local. Two conditions with elevated blood glucose levels if not treated, but with different emphasis on clinical manifestations. For example, glucose variability (long-term and short-term) seems to be more

severe in T1DM than T2DM when considering retinopathy[223–226] and neuropathy[227–230]. In contrast, T2DM suffers more than microangiopathic complications than T1DM when levels of chronic blood glucose is increasing as measured by HbA1c. This emphasize the acute destruction of beta-cells in T1DM while T2DM is a slow degeneration of systemic functions. Thus, the difference in pathophysiological mechanisms between T1DM and T2DM is acute and chronic inflammation, respectively. In T1DM the autoimmune disorder is selective and targets insulin-producing pancreatic beta cells without involvement of Langerhans cells[231]. Especially, CD8+ T cells and CD4+ of the immune system is engaged in the destruction of beta cells though peri-islet inflammation[232–235]. The main mediators of inflammation in T1DM are interferon gamma (IFN-gamma), tumor necrosis factors (TNF-alpha) and interleukin 1 (IL-1beta)[236]. T2DM usually show hypersecretion of insulin in beta cells, but the pancreatic reserve is unable to cope with the required insulin secretion[237–239]. In addition, fat accumulation in the liver (steatosis) often precedes T2DM[240,241], and leads to insulin insensitivity up to 15 years before onset[242]. The fat accumulation starts in the subcutaneous tissue, but if excessive caloric intake is continued then a 'spillover' effect occurs in the internal organs as visceral fat. This condition from the double-whammy effect of lipotoxicity and glucotoxicity is referred to as metabolic syndrome. Metabolic syndrome is accompanied by systemic inflammation by raising levels of crp, TNF-alpha, IL-1, IL-6, IL-10, leptin and adiponectin just to name a few[243–245]. The main source of chronic low-grade inflammation appears to be the visceral fat, and is easily measured around the trunk at the thickest place in anterior-posterior dimensions. In addition, pancreatic cell failure is also seen in T2DM, and is further worsened by systemic inflammation. The insulitis is a result of local inflammation from stressed beta cells. Macrophages are attracted to the islets of Langerhans through inflammasome/IL-1 beta signalling[246–250], and thus further escalates the inflammatory processes. It occurs systemically as macrophages become primed towards a pro-inflammatory status through systemic inflammation, and this has been shown to affect multiple organs such as liver[251], neural system[252], blood vessels[253] and kidneys[254]. Regardless of aetiopathophysiology, we believe the two models of diabetes, T1DM and T2DM, provide tremendous insight of local versus systemic inflammation. Especially in the early phase as T1DM might progress to systemic inflammation if blood sugar levels are dysregulated. HbA1c is not only used for estimation of blood glucose. HbA1c or glycated hemoglobin is a surrogate marker of glycated organic matter in the body of which many will become altered. This is the sole reason why HbA1c stabilize over the last three months: Glucose is irreversibly bound to the surface of hemoglobin, and the average lifespan of erythrocytes in healthy individuals are 120 days[255]. Thus, the only way to alter HbA1c would be through the turnover of erythrocytes. We speculate whether this explains why T2DM suffers more clinical manifestations than T1DM with increasing HbA1c. As the level of glycated matter increases so does e.g. ROS from free and non-free radicals, which promotes further metabolic damage. However, the redox potential of T2DM is lower than T1DM due to chronic inflammation. This lowers the threshold for T2DM to tolerate metabolic insults, and cause severe clinical manifestations. Another detrimental effect is the altered proteins from systemic hyper-glycation, and the attenuated immune system of T2DM. Taken together, chronic inflammation is detrimental of two reasons: 1) Inability to tolerate ROS or metabolic damage, because the redox potential is lowered and 2) Inability to counter altered proteins due to an attenuated immune system.

Deriving clinical practice from hsCRP and HbA1c is the levels of Blue Zones, which we refer to as 'blue reference'. Thus, hsCRP and HbA1c serve as a surrogate marker for chronic inflammation and metabolic health, respectively. We recommend nadir levels of hsCRP below 0.5 mg/L based on the healthiest population and strongest blue zone: Japan[256]. Although genes might be involved in nadir hsCRP[257] we prefer to take a safe stand on achieving optimum health. The country with the world's highest life expectancy, Japan, has a prefecture with even healthier individuals: Okinawa. In Okinawa, the average person has a BMI of 21 (kg/m^2) with low waist circumference and they have extremely healthy metabolic profiles[10]. The optimal level of HbA1c is yet to be determined, but the general population of Japan has a HbA1c of 4.8 – 5 % or 29 – 31 mmol/mol[258]. We recommend a HbA1c of 30 mmol/mol, and is equivalent to an estimated blood glucose of 5.2 mmol/L. This is significantly lower than WHOs guidelines of 6% for healthy individuals[259], but is considered close to the upper blood sugar level of 5.5 mmol/L in fasted state[260,261]. The level of 5.5 mmol/L is also under the threshold for the hyperglycemia-induced inflammation of 6.1 mmol/L[262]. Above 6.1 mmol/L there are significant increase in glutathione (GSH), glutathione:glutathione disulpide (GSH:GSSG) ratio, 8OHdG, 8-hydroxy-20-deoxyguanosine (8OHDG) and IL-1beta. Glutathione is a ubiquitous antioxidant towards free radicals, and is readily oxidized to GSSG as the main physiological redox reaction. 8OHDG is a surrogate marker of DNA and RNA damage from free hydroxy radicals as it reacts with DNA nucleobase guanine to form C8-hydroxyguanine (8-OHGua) or 8OHDG. Blood glucose levels above 6.1 mmol/L significantly reduced GSH, increased GSSG, reduced GSH:GSSG ratio, increased 8OHDG and increased IL-1beta when compared to 4.1 mmol/L.

The overall theme for our 'blue reference' is best understood from the opposite end of the scale: Metabolic syndrome (MetS) or syndrome X. Metabolic syndrome encompasses everything we have discussed so far into a coherent and well-studied context with an easy-to-understand concept. Mets has a strong global prevalence of around 40 – 50% of the population, and is steadily increasing[263–266]. Basically, there are four components in metabolic syndrome: Central obesity, systemic hypertension, insulin resistance and atherogenic dyslipidemia[267]. The molecular pathogenesis is not yet understood, but several hypothesis are emerging: Mitochondrial dysfunction[268], iron overload[269] and gut dysbiosis[270] to name a few. Regardless of origin, we take notice of the nutritional overload in our Western world compared to the Blue Zones. Also, this is independent of BMI as metabolic syndrome can occur in normal-weight people, and is denoted metabolically obese, normal-weight (MONW)[271] or thin outside, fat inside (TOFI)[272]. It is simply not sufficient to 'judge a book by its cover', and therefore we emphasize to measure at least hsCRP and HbA1c.

The wear and tear on organic matter is guided by perturbation of homeostasis with inflammation as the key-player. Without inflammation there would be no perturbation, and only status quo or eventually breakdown is favored.

Intervention

While there is nothing new about healthy lifestyle choices then the focus is now shifted into execution, and how new habits can maintained in the long-term. We know blue zones have a superior diet from mostly plant-based sources, and have incorporated natural movements into their daily life. However, this is far-stretched from the Western world we currently live in with

millions of calories just around the corner, sedentary lifestyle and tremendously stress. We emphasize a diet resembling the blue zones on a grading scale: Flexitar->Pescatar->vegetarian based on hsCRP and HCLF->MCMF->LCHF based on HbA1c. In addition, we value 1 – 2 hours of aerobic exercise everyday with supplementary strength-training. Many people will find this exaggerated, but we must remember how our bodies are built for metabolically flexibility[273,274]. This comes from several hours of hunting (i.e. aerobic exercise) each day and being natural fasted during these strenuous long-lasting events. Being metabolic flexible is the ability to switch emphasis between carbohydrate or fat-burning, but carbohydrate is always being utilized to some degree. People have tried to trick this system by living on a diet of HFLC, but end up sacrificing enzymes for efficient carbohydrate utilization—They become metabolic inflexible. To date, the only way to stay metabolic flexible is through exercise although many interventions can 'kickstart' metabolic flexibility. It is basic knowledge how excessive calorie intake leads to obesity, but metabolic flexibility can hamper the retrograde flow of how obesity leads to excessive calorie intake. Thus, we want to break the viscous cycle of high calories in, low calories out.

Before we lay the foundation of our intervention then we emphasize the following approach:

1) Evidence-based approach with structural analysis and disaggregation of scientific articles. i) For whether there is an effect of substance x: Randomized double blind placebo control (RDBPC)[275], ii) Whether if we want to use in special occasions: Systematic review[276] and iii) If it's something we want to recommend to everyone then there must be evidence on the highest level: Meta-analysis[277].
2) We use standardized Tensorflow algorithms with a combination of biostatistics, Fourier transformation and quantitative psychology. A full explanation is beyond the scope of this paper, but essentially we derive from the maximum number of years in a human lifespan (~120 years) to each person. This is done by factoring in demographics, cognitive abilities, physical performance, lifestyle choices, body measurements and blood sample values. Again, we use our blue reference to essentially have three points in our dataset: Birth, average person and death. A simplified version of cardiovascular risk is given as example in the following:

$$Risk_{Person\ X}^{CVD} = Risk_{Denmark}^{CVD} * Risk_{Denmark}^{CVD} * \left(0.1 - \left(\frac{Smoking\ Score}{60}\right)\right) * 1.25 + \left(0.1 - \left(\frac{TrainingScore}{150}\right)\right) * 0.75 + (0.1 - \frac{MentalScore}{135})) * 1 + \left(0.1 - \left(\frac{BodyScore}{75}\right)\right) * 0.75 + (0.1 - \frac{AlcoholScore}{60})) * 1 + (0.1 - \frac{FoodScore}{135})) * 0.25 + ((\frac{\sqrt{age}}{25}) - 0.27) * 1.75 + ((\frac{\sqrt{bmi}}{14}) - 0.4) * 0 + (0.19 - (\frac{\left(\sqrt{\frac{\sqrt{MuscleMass}}{BodyFat}}\right)}{11})) * 0.25 + (\frac{\sqrt{VisceralFat}}{230}) * 0.50 + (1.9 - (\frac{\sqrt{Saturation}}{5})) * 1 + ((\frac{\sqrt{hsCRP}}{16}) - 0.12) * 1 + ((\frac{\sqrt{hsCRP}}{10}) - 0.6) * 0.5 = Risk_{Person\ X}^{CVD}$$

Please take notice of how the example represent a concrete situation without forward and backpropagation. The formula is derived from logistic regression to obtain the odds ratio of person X dyeing from cardiovascular events. The cost function resemble logistic regression, but is applied to a neural network. Taken together, the relative risk is given as: $Risk_{Person\ X}^{CVD}$

3) We use our network and experience for the remaining 10 – 20% of our foundation. This enable us to work closely with our clients, and extrapolate the last mile to accommodate their needs. Clients working with us will have to quantify their end-goal although this may be more challenging with qualitative values. However, we are normally able to deduce what is essentially the main driver for their approach whether it may be weight loss, increased performance, superior cognitive abilities, etc.

First line of intervention will always be lifestyle-modifying factors, and reduce exposure to chronic stress. However, we want to emphasize the beneficial effects of exercise to reduce visceral fat[278], and especially aerobic exercise is the most effective method[279–282]. In fact, aerobic exercise is superior to a hypocaloric diet[283]. Therefore, we suggest moderate aerobic exercise for 1 – 2 hours per day with an anti-inflammatory diet of plenty omega-3 polyunsaturated fat[284,285] and low consumption of meat[286,287]. We may supplement with garlic[288,289], L-carnitine[290], circumin[291] and green tea[292–294] although the evidence is not completely solidified. The effect may be minuscule in these supplements, but the side effects are close to non-existent so their usage should pose no additional risk to the client. According to internal statistics then 90 – 95% of our clients will not adhere to these lifestyle modifications on the long term, and we acknowledge the hardship of incorporating exercise regimes. On the other hand, there is simply no other way around exercise. Sometimes, a gentle push or nudge is needed to avoid spiraling down on health. When all lifestyle interventions are exhausted there is a need for medication to kickstart the 'escape velocity' although we are always very reluctant to prescribe medication.

The medication we use are extremely have a well-proven record, are highly sophisticated and always at the frontier of medical research. We always use specifically targeted drugs, and each drug is uniquely fitted to our clients. Often the drugs we use are monoclonal antibodies such as Anakinra (IL-1 receptor blockade)[295–297], Gevokinumab (IL-1beta antagonism)[298–301] and Ro 45-2081/Etanercept (TNF antagonism)[302–304]. However, we may even expand our range of drugs to include engineered DNA plasmid encoding proinsulin (BHT-3021)[305] to mitigate loss of function or GSH to counter attenuation of redox potential. The list is incomplete, but our repertoire span over 100 drugs with classes and subclasses. These are delivered to each client at a specific spatiotemporal distribution based on both genotype and phenotype so nothing is by coincidence. In addition, every client is in daily dialogue with our staff and under constant biomonitoring for potential side-effects. We always take a safety-first approach, and will immediately terminate any drug if any anomality are detected or if symptoms are experienced by the client. Every client must also understand how each drug is only a temporary boost to support new the new habits, and cannot stand alone without lifestyle interventions. This would further invalidate our approach of minimal principal for the safety of our clients. Last solution will be surgery such as gastric bypass, but is deemed beyond the scope of our expertise and overall approach in general.

We have often wondered why health is so complicated, but yet easy to understand. Perhaps what seems like suffering for a Westerner is normal for a blue zone centenarian and vice versa. What comes easy for one person may seem like a struggle for another, and if health is not approached multidisciplinary then the battle is lost beforehand. Sometimes the push may be entirely mental, medicinally or self-driven. Proactive or reactive. Regardless, talking about health without execution is just hot air. Humanum est.

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