A vastly revised and updated version of this preprint is available as a chapter in a book titled: Reorientation of activities and self-environment integration: A new theory of activities. The book is available from <https://www.amazon.com/dp/9357738096>.

Perspectives on targeting cardiovascular diseases through reorientation of activities

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1. Abstract

Cardiovascular diseases (CVD) include coronary artery, cerebrovascular, renovascular, and peripheral vascular diseases. These vascular diseases are known to present with many serious conditions—which include angina and acute coronary syndromes, strokes, cognitive impairment and dementia,^{1, 2} epilepsy,³ parkinsonism,⁴ claudication, erectile dysfunction, renal failure, and hypertension. The underlying pathology for these ailments is atherosclerosis. Since 1950s, we have become increasingly focused on causation and management of cardiovascular diseases, which have strong behavioural components. Primary and secondary prevention remains our long-term goal. This paper discusses a new perspective on targeting CVD through reorientation of activities (ROA).

2. Reorientation of activities to target cardio-vascular diseases

I have proposed a new theory of our activities: reorientation of activities and self-environment integration (ROA-

SEI).⁵⁻⁷ In that theory we “take a broadest possible view of activities, and for our purpose, whatever little action we undertook—during previous 24 hours, or during last week or month—every bit can be included in our activities like sleeping, breathing, eating, drinking, thinking, walking, worrying, getting angry, watching TV, and rest of the mundane things including sex”⁵. These activities have been classified as restoration related (RR), growth related (GR) activities, and adjustment related (AR) activities⁶—and they are quantitatively represented through pie charts called activities-circles^{6, 7}. Each activities-circle (AC) has three pie slices representing three types of activities—RR, GR, and AR. In order to fulfil her needs, a normal (and even an abnormal) person would continuously manipulate her activities, with innumerable strategies, both intuitive and formal. These strategies can be collectively called ROA.⁷ Such reorientation can be reversible, minor, short-term, or routine that we carry out during the course of the day. Reorientation can also be longer term or major that is in response to a threat or imbalance of activities (Figure-1). For example, chronic cough may force a person to stop smoking, and detection of diabetes may force a person to change her dietary habits. When a person successfully stops smoking or changes her dietary habits, many other activities have long-term changes—often characterized by reduction in RR and increase in GR and AR activities, such broader change can be considered a major reorientation.

2-1. Is coronary artery disease caused by an imbalance of activities?

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Figure-1. Longer-term or major reorientation of activities can be our response to imbalanced activities. Shorter-term or minor reorientation can be in either direction.

“Loss of control or imbalance of activities leads to unwanted, unexpected, and relatively rapid changes in AC of an individual. For example, COVID-19 pandemic led to sudden and massive disruption of normal activities, as billions were confined to their homes.”⁷ Resulting anxiety and depression^{8,9} was in many cases leading to imbalance of activities and shift of activities-circle towards the left (Figure-1, X). “A casual view of three circles would tell us that three groups of activities are equal in Y. RR activities are dominant in X, and GR and AR activities are dominant in Z. This means that X is likely to indulge more in RR activities such as sleeping, watching television, using tobacco, worrying etc., while Z would be more adjusted and growth oriented.”⁶

During COVID-19 lockdown, imbalance and resulting dominance of restoration related activities can be understood, as people become more anxious and depressed. They are more likely to use television and social media. They are more likely to indulge in food, tobacco, and alcohol. And due to lockdown, they are less likely to do any physical activity. These are all risk factors, and we can see that such imbalance of activities if it persists can lead to coronary artery disease. I will discuss historical and other evidence of such imbalance causing coronary artery disease. I will also discuss that reorientation of activities can be used for reducing the burden of CVD.

3. Current treatment options for cardiovascular diseases

Angina and acute myocardial infarction are two prominent symptoms of cardio-vascular diseases (CVD). Angina occurs because of narrowing of coronary arteries. During physical activity such as going upstairs or during emotional distress, the cardiac activity increases leading to increased demand for oxygen to the heart. However, due to narrowing of the coronary arteries the blood supply to the heart cannot be increased. This leads to demand-supply mismatch, which clinically manifests as symptoms of an-

gina. Synthesis of nitroglycerin¹⁰ in 1847 was an important milestone in the management of angina. The drug dilated the coronary arteries leading to increased blood flow and relief from angina symptoms. For next one hundred years the nitrates reigned supreme, as anti-anginal drugs. During the middle of twentieth century, the efforts for new and more effective drugs for angina intensified, as the epidemic of coronary artery disease reached near its peak in the western world.

Discovery of Verapamil and propranolol during 1960s is illustrative of how important drug discoveries may occur through intensive and targeted molecular and receptor level research.¹¹ Verapamil a calcium antagonist was first to come on the scene in 1960. Like nitrates, it also acted as a coronary vasodilator. The essential aim of anti-anginal drugs till that time remained achieving coronary vasodilation to increase blood flow and oxygen supply to the heart. Around the same time, however, Black and his team at Imperial Chemical Industries were busy developing a drug that would reduce myocardial oxygen demand. The outcome was discovery of beta blockers, for which Black was awarded a Nobel Prize. Strategy of reducing myocardial oxygen demand and increasing blood supply to the heart to relieve the symptoms of angina is relevant for our purpose, as myocardial oxygen mismatch can also be reduced through reorientation of activities aimed at stress management.

Verapamil and propranolol were developed under tight schedules. Unlike them low dose aspirin as a clinically useful antiplatelet agent was getting established at a leisurely pace during 1970s and 80s.¹² All antiplatelet agents work by reducing platelet adhesiveness and aggregation—processes responsible for progress of atherosclerosis and its adverse consequences. During the same period, cholesterol lowering drugs were also being developed, as high levels of cholesterol were found to be linked with increased risk of atherosclerosis and cardiovascular diseases.^{13, 14}

The Framingham Heart Study was established in 1948, much before our quest for more drugs had started. The

purpose was to understand how cardiovascular disease developed by studying the lifestyles of the residents of Framingham, Massachusetts. The first findings of the study published in 1961 indicted hypertension and hypercholesterolemia for increased incidence of coronary artery disease and acute myocardial infarction.¹⁵ The Framingham study opened the flood gates for further exploration of risk factors and related interventions across all major disease conditions. Management of multiple behavioural and psychosocial factors, such as sedentary habits, smoking, and diet are recommended today for reducing the incidence of CVD. Other recommended measures are control of body weight, hypertension, diabetes, and lipids—and use of antiplatelet drugs.^{16, 17}

Evidence has been building that atherosclerosis is reversible.^{18, 19} Lifestyle measures including physical activity, low fat vegetarian diet, smoking cessation, and stress reduction have been found to relieve symptoms, reduce the risk of acute cardiac syndromes, and reverse coronary artery disease.²⁰⁻²² As I will discuss, many of these measures require reorientation of our activities.

3-1. Managing obstructed segments of coronary arteries

Three treatment strategies that we have already discussed are:

1. Coronary vasodilators (nitrates and calcium antagonists) increase blood flow through the affected arteries—providing relief from symptoms of angina, without survival benefits.
2. Beta blockers reduce myocardial oxygen demand—providing symptomatic relief, without survival benefits^{23, 24}.
3. Lifestyle measures and drugs (mainly lipid lowering and antiplatelet agents) provide symptomatic relief, survival benefit, and reversal of atherosclerosis.

I will now come to the fourth strategy of managing severely obstructed segments of coronary arteries through coronary artery bypass graft (CABG) and coronary angioplasty (CA). This strategy was born in Cleveland Clinic in 1958, with Mason Sones's accidental discovery of selective coronary angiography, when the tip of his ventricular catheter slipped into a coronary artery.²⁵ That visualization of coronary arteries by his team irrevocably transformed our understanding of coronary artery disease. "Instead of seeing the expected diffuse obstructions from coronary atherosclerosis, Sones found "remarkable localization" of the disease process."²⁶ Thus the idea arose to fix the focal obstructions of the coronary arteries—leading to development of CABG²⁷ and CA²⁸.

A rationalization for CABG came from none other than Favaloro and his team. "Atherosclerotic obstructions that produce major myocardial perfusion deficits constitute a

threat to the myocardium and, thereby, to the life of the patient. Any surgical procedure that could remove, or circumvent, a significant arterial occlusion and relieve a myocardial perfusion deficit would have theoretic value."²⁷ Half a century later, this mis-conceptual model continues to persist that regards coronary artery disease as clogged pipes.²⁹ For a long time, demands for subjecting CABG to scientific scrutiny were being met with resistance and hostility²⁶—and finally we felt a sense of déjà vu, when the story of COURAGE³⁰ trial was repeated and much awaited results of ISCHEMIA trial were out³¹. The mandate became clear that CA and CABG did not provide survival benefits in stable-angina.^{30, 31}

I have tried to give a perspective of current treatment options for CVD. Only very few strategies are capable of reversing atherosclerosis and/ or delaying complications—and they have the potential to cure CVD. The rest are only palliative strategies aiming at reducing symptoms. My argument is that all or most of the reversal strategies can be classified as ROA, making ROA an important tool for targeting CVD.

4. The eighteenth-century origins of angina pectoris

In 1768 William Heberden made a presentation to the Royal College of Physicians of London in which he reported a score of individuals having typical clinical features of angina pectoris. The number of similar patients that he saw rapidly rose in the next decade, during which reports of angina by many other English medical writers appeared for the first time. This is in striking contrast to the paucity of earlier accounts of angina pectoris.³² The inference made was that the incidence of angina pectoris was low, so as a clinical entity it was non-existent till Heberden's presentation. As its incidence increased, angina began to be noticed by the physicians, as if a new disease 'originated' in eighteenth century England.

To support that inference, Michaels has described the rapid changes that were occurring in eighteenth century England, as a result of agricultural and industrial revolutions. Food particularly animal food consumption amongst the affluent classes was showing a rapid accent. At the same time amount of physical activity was showing a marked decline. Consumption of tobacco, coffee, and sugar was also going up. And the stress levels in the society were increasing. To convey the gravity of these changes, I am quoting a few paragraphs from his book here:

"Meals taken by the affluent during the late eighteenth century frequently included a late breakfast and a substantial midday meal, possibly accompanied by some entertainment. After this there was often a dinner at four in the afternoon that would usually last a couple of hours or more and be followed by some late evening refreshment to

conclude the day. The length of time spent at table contributed to excessive consumption.”

“Eating on the scale described was not confined to the nobility, but also became a part of the way of life of the affluent among the growing eighteenth-century middle classes. Successful shopkeepers’ tables were as well served as those of rich merchants. The physician and the man of law ate as well as the archbishop, and the landowning gentry as well as the nobleman with his broad acres.”

“The multitude of activities associated with the coffee houses resulted in their being patronized, especially in London, by large numbers of men whose visits were frequent and often extended for a great part of the day. The coffee was continuously on the boil in eight to ten gallon pots and the cups or mugs of the patrons were constantly replenished. As a result, consumption was very much higher than is customary nowadays, ten or even more cups a day being not infrequent. Dr Johnson would drink a dozen cups of coffee at a time, and in this respect he was by no means exceptional. The coffee that was drunk was almost invariably black, very strong and taken with large amounts of sugar cut from a loaf. Coffee houses were associated with the smoking of pipes and the atmosphere was usually laden with tobacco smoke.”

“Net imports of sugar [to England] rose from 15,771 tons in 1713 to 43,103 tons by 1739”, and it “reached 69,146 tons by 1768”. It is assumed that the upper and middle classes were consuming many times more sugar than this over 4 times rise in imports over these 55 years would suggest. “Sugar was used in baking, in desserts and above all to sweeten the coffee and tea which were being drunk in ever greater amounts.”

The economic changes were leading to stresses in the society because of upward mobility and a rising middle class, as well as financial insecurity. The anxieties associated with foreign wars were persistent and involved more people. The emotional consequences of bereavement and illness became more intense as people were becoming more rational. So, faith in religion and medicine was declining and becoming diminished source of consolation for the people.

“In an era in which servants were both readily available and easily affordable, physical activity in connection with either work or home was virtually unknown even among people whose means were only moderate.” Roads were getting better and horse drawn coaches were becoming more comfortable. This was resulting in middle and upper-class travelling in carriages more and walking or riding on horseback less as the century progressed. “These changes had a possible impact on levels of physical activity comparable to those which resulted from rising car ownership during the twentieth century.”

During eighteenth century England many changes were occurring involving the activities of the people, particularly the upper and middle classes. These changes in human activities are being held responsible for the origin of angina. If that is true, reversing those changes at the level of the individual by reorientation of her activities should be considered a valid strategy for managing CVD.

5. Modifying currently identified risk factors

Stress at work or in family life, social isolation or lack of social support, depression, hostility, anxiety, and other mental disorders are psychosocial factors contributing to the risk of developing CVD and a worse prognosis of CVD, with the absence of these items being associated with a lower risk of developing CVD and a better prognosis of CVD. Type D or distressed personality is a combination of two personality traits: negative affectivity (the tendency to experience negative emotions) and social inhibition (the tendency to inhibit the expression of emotions). Such personality is also associated with enhanced CVD risk, its poor prognosis, and poor health related quality of life.^{16, 33-35}

Lack of leisure time physical activity, unhealthy dietary practices, and tobacco use are some behaviours—and uncontrolled diabetes, obesity, hypertension, and lipid abnormalities are clinical conditions that contribute to incidence and adverse outcomes of CVD.¹⁶ The clinical conditions mentioned here too have the same activities as risk factors: lack of leisure time physical activity, unhealthy dietary practices, stress, and depression. Moreover, our activities are responsible for keeping these clinical conditions under control. Thus, from multiple angles our activities matter for both preventing and controlling CVD—and activities that need to be reduced or controlled are invariably RR activities. Thus for a long time, most people with CVD may be safely assumed to be living with dominant RR activities (X in Figure-1), as CVD has considerable incubation period³⁶.

Managing these risk factors should be considered the most desirable aspect of CVD management. However, every risk factor needs to be addressed separately¹⁶—making it nearly impractical to follow the guidelines. To overcome these difficulties, some researchers are focusing on multiple health behaviour change. But the challenges exist “to make such interventions more effective, cost effective and less demanding.”³⁷

However, this whole risk factor approach has been considered too narrow. Friedman wanted us to have a capacious all-inclusive focus—and introduced two antithetical personality constructs termed disease-prone and self-healing personalities.³⁸ In his view more than a hundred years of personality research has given us a general verdict that

“a person who is chronically irritated, depressed, hostile, impulsive, bored, frustrated, lonely, or powerless is indeed more likely to develop illnesses and to die prematurely than is someone who generally feels emotionally balanced and effective, is in a satisfying job, has stable and supportive social relationships, and is well integrated into the community”. Friedman was describing disease prone personality, but we might use the same description for the risk factors of CVD—or even for diabetes. This seems to validate Friedman’s contention. Through his constructs, Friedman’s aim was to “direct theory and research away from associations between single predictors and single outcomes, focusing instead on multiple-predictor, multiple-outcome developments over long periods of time”.

How are Friedman’s constructs useful for our discussion? Our overall activities must be having a strong correlation with our personality. So, the constructs of Friedman can be paraphrased as—*activities of a disease-prone person* and *activities of a self-healing person*. From the perspective of AC, activities of a disease-prone person have dominance of RR activities. While the activities of self-healing person have dominance of GR and AR activities.⁵⁻⁷ ROA leads to increasing the dominance of GR and AR activities (Figure-1). Thus, a single intervention based on ROA can lead to very strong control of currently identified risk factors. I am using the words ‘very strong control’ because all the activities of a person (and not just a few risk factors) are getting changed. This creates a new perspective for targeting CVD.

6. The special case of obesity

We often look down upon the obese, without realizing that it is not easy to lose weight. Scientific explanation for the difficulty is known. “Obesity is not a personal failing. In trying to lose weight, the obese are fighting a difficult battle. It is a battle against biology, a battle that only the intrepid take on and one in which only a few prevail.”³⁹ This is biological or genetic view. But a powerful ecological view of the obesity also exists. This view agrees that the individual susceptibility may be decided by biology. However, our behaviour and the existing ecosystem is responsible for the epidemic of obesity that is raging our society.⁴⁰⁻⁴²

“To reverse the obesity epidemic, we must address fundamental causes. Overweight comes from consuming more food energy than is expended in activity. The cause of this imbalance also is ironic: improved prosperity. People use extra income to eat more and be less active. Market economies encourage this. They turn people with expendable income into consumers of aggressively marketed foods that are high in energy but low in nutritional value, and of cars, television sets, and computers that promote

sedentary behavior. Gaining weight is good for business. Food is particularly big business because everyone eats.”⁴¹

“The U.S. food supply provides 3800 kilocalories per person per day, nearly twice as much as required by many adults. Overabundant food forces companies to compete for sales through advertising, health claims, new products, larger portions, and campaigns directed toward children. Food marketing promotes weight gain. Indeed, it is difficult to think of any major industry that might benefit if people ate less food; certainly not the agriculture, food product, grocery, restaurant, diet, or drug industries. All flourish when people eat more, and all employ armies of lobbyists to discourage governments from doing anything to inhibit overeating.”⁴¹

The ecosystem that is promoting weight gain seems here to stay. Hence cognitive control of body weight becomes a necessity.⁴³ “We should consider how to make sure that everyone has the information and tools needed to cognitively manage energy balance. This might involve, for example, providing better information about appropriate portion size, the energy value of food, and physical activity energy equivalent of food. It might also involve cognitive skill building, probably beginning early in school, for how to achieve a balance between intake and expenditure.” The problem of obesity is often defined as imbalance between energy intake and expenditure, and therefore the authors are looking for population level training beginning early in school.⁴³ Many of their assumptions may not be true or implementable. We already know that the notion of obesity as energy imbalance is too simplistic.

Contemporary obesity epidemic has also been attributed to a variety of emerging pressures, behaviours and physical factors—collectively called as the obesogenic niche. This niche has resulted from numerous secular trends, having an extensive history. These trends have intensified recently through technological innovation and Western economic model of capitalism.⁴⁰ So far we have failed to fight these trends, both individually and collectively, as our behaviour is constantly being manipulated, rendering us passive to ecological challenges.⁴¹ “These exposures constitute both ‘push’ and ‘pull’ factors, impacting at a variety of different levels of biology. Reflecting this complexity, we might think of the obesity epidemic as a number of upward steps in prevalence, as each new obesogenic factor is added to the overall scenario and adds to the intensity of the niche.”⁴⁰

Where does the theory of activities fit in this perspective? The obesity epidemic can be seen as a great ecological challenge to us. Reorientation of activities (Figure-1) can help us in selective consolidation of activities and self-environment integration⁷, and this may be possibly the only integrated strategy to fight that challenge at multiple ecological levels.⁵

7. Stress, psychological conditions and CVD

Stress, depression, anxiety, posttraumatic stress disorder, and other psychosocial factors are risk factors for increased incidence and adverse prognosis of CVD.¹⁶ Large, prospective, epidemiological studies have found that “depression predicts the development of CHD in initially healthy people. The stronger effect size for clinical depression compared to depressive mood points out that there might be a dose–response relationship between depression and CHD.”⁴⁴ Reviews indicate that depression is highly prevalent in patients with CVD—with 20 percent suffering from major depressive disorder, and another 20 percent evidence lesser but clinically meaningful levels of depressive symptoms, each of which increases risk for cardiac recurrence and mortality. More than half have depressive symptoms prior to their acute coronary syndrome.⁴⁵ CVD has similar associations with psychosocial stress^{46, 47} and anxiety⁴⁸

Psychosocial factors mediate widespread changes in nervous, circulatory, endocrine, and immune systems leading to enhanced risk and adverse prognosis of CVD. Psychosocial factors also mediate reduced social support and unhealthy behaviours, further contributing to allostatic load and CVD.⁴⁵ Acute psychological stress is associated with an increased risk for acute cardiovascular complications such as myocardial infarction, left ventricular dysfunction, and arrhythmias.⁴⁷

“[The] ultimate test of an underlying unidirectional relation between acute stress induced psychiatric disorders and cardiovascular disease will be through intervention studies to treat these disorders. If the association is causal then effective treatment of the psychiatric disorder should reduce the risk of future cardiovascular disease events. Psychiatric intervention studies have so far been disappointing in relation to reductions in cardiovascular disease events, although some people suggest that the null findings had more to do with the limitations of the interventions than a true failure of the hypothesis.”⁴⁹

“Most practice guidelines do not recognize the importance of screening for stress in primary and secondary CVD prevention. There is a paucity of large, scalable, and cost-effective approaches for stress intervention. Two potential strategies are required for reducing stress: strategies that are population-based, and narrower targeted strategies for clinical practice.”⁵⁰ The core components of cardiac rehabilitation today remain limited to aerobic exercise and medical management of CVD risk factors.⁵¹

Around 1960, coronary vasodilators were the only drugs for angina. However, Black and his team at Imperial Chemical Industries were busy developing a drug that would reduce myocardial oxygen demand.¹¹ The outcome

Figure-2. Three conceptual models to define interrelationships between stress, depression, and CVD.

was discovery of beta blockers, for which Black was awarded a Nobel Prize. Strategy of reducing myocardial oxygen demand and increasing blood supply to the heart to relieve the symptoms of angina is relevant for our purpose, as myocardial oxygen mismatch can also be reduced through reorientation of activities aimed at stress management. In a recent study, addition of Transcendental Meditation to cardiac rehabilitation led to substantial improvements in myocardial flow reserve that is the ratio of maximum flow during stress to flow at rest.⁵² Such improvement has been found to depend on twin mechanisms of lowering resting blood flow and increasing coronary vasodilatory capacity.⁵³

The significance of dealing with psychosocial factors for secondary prevention of CVD has been emphasized.^{16, 50, 52} “Unlike other risk factors, psychosocial stress is heterogenous in nature and is related to numerous factors such as interpersonal relationships, previous trauma, financial constraints, employment-related issues, neighborhood,

community, and society related, political policies that directly or indirectly affect one's lifestyle, discrimination based on race, and sex and other perceived disparities."⁵⁰ We "should adopt an inclusive approach in our interventions, targeting negative emotions and psychosocial conditions generally, rather than trying to isolate and focus on a single "risk" emotion or condition"⁵⁴. A general disposition toward negative affectivity may be more important for CVD risk than any specific negative affect.⁵⁵ It can be concluded that we need wider and simpler (yet effective) approaches for their integration into cardiac rehabilitation programs and for primary prevention at population levels.

AC of depressive illness has dominance of RR activities.⁷ It can also be argued that negative affectivity in general would mean dominance of RR activities in the AC. So far, I have discussed that CVD is caused, when RR activities gain dominance in the AC. Thus, ROA to reduce the dominance of RR activities becomes a logical choice for cardiac rehabilitation. Numerous heterogeneous factors related to psychological stress and cited in the paragraph above can be dealt with by reorientation and selective consolidation of activities. Reorientation and selective consolidation of activities will lead to dominance of GR and AR activities.⁶ ⁷ When growth and adjustment is improved, in medium to long term this would result in a happier person. Subjective well-being significantly predict longevity in the general population.⁵⁶

Two conceptual models linking stress with depression and CVD have been suggested (Figure-2, Panels A and B).⁴⁵ In first model (Panel A), environmental stress causes depression—and depression in turn causes physiological perturbations in the circulatory system that lead to atherosclerosis. The corollary model depicted in Panel B means that stress can independently lead to both depression and atherosclerosis.⁴⁵

Here I am suggesting a third conceptual model (Panel C) conceiving imbalance of activities at the centre, with stress, depression, and CVD making a triangle. Bidirectional arrows connect all four. Imbalance of activities leads to dominance of RR activities. The dominance of RR activities, once established, can independently lead to stress, depression, and CVD. Once clinical symptoms of CVD are established, CVD can contribute to imbalance, stress, and depression. Depression contributes to imbalance, stress, and CVD. Stress also contributes to remaining three. According to this model, ROA (Figure-1) can help in controlling stress, depression, and CVD simultaneously. I have reported that severe drug resistant depression were helped with a ROASEI based intervention.⁵⁷ Epidemiological studies confirm a temporal relationship between depression and CVD, with depression being a marker of CVD^{45, 58} (Panel A). However, longer incubation period of CVD³⁶ could be plausible explanation for this phenomenon that depression becomes detectable before CVD. *General informent dysregulation* has been held ac-

countable for both depression and physical diseases.⁵⁹ Imbalance of activities and general informent dysregulation are parallel phenomenon. Dysregulation occurs at the level of brain, endocrine, and immune systems—while imbalance occurs at the level of our activities.⁶⁰

8. Conclusions

In our context, ROA means expanding GR and AR activities, while reducing RR activities. During imbalance of activities the opposite happens (Figure-1). Historically population level imbalance of activities occurred leading to origin of angina in eighteenth century England. Current risk factors of CVD can be explained as imbalance of activities. Current obesity epidemic can also be described as an ecological disaster entailing imbalance of activities. CVD epidemic has links with worsening state of stress, depression, and other psychological factors. We cannot reverse the ecological universe. ROA with selective consolidation of healthful activities can prove to be the only answer to the current CVD epidemic.

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