Perspective

Novel strategies halt cardiovascular, diabetes, and cancer strips

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Abstract

In this article, we introduce briefly several strategies for preventing atherosclerotic cardiovascular disease and promoting healthcare for non-communicable diseases (NCDs). These novel strategies include four core elements of health − sleep, emotion, exercise, and diet − and consist of SEED intervention (SEEDi) and E(e)SEEDi due to supplementation of the environment as a core element, and Hu's healthy lifestyles intervention (HHLi) which originates from E(e)SEED-BasED healthy lifestyles. They are suitable for the early evaluation of risk factors, and play a key role in the prevention and management of human NCDs when combined with the RT-ABCDEF strategy and the Grade 210 prevention, which include obesity-OSA-hypertension syndrome and C-type hypertension, especially in halting cardiovascular, diabetes and cancer (CDC) strips we first discovered. After successful clinical practice, we may expect our novel strategies for controlling these chronic diseases according to the conception of mass prevention and treatment.

Introduction of novel strategies

Since we first discovered cardiovascular, diabetes and cancers (CDC) strips[1] and further disclosed their mechanisms, classifications, and clinical significances, attention has increased on how to prevent and halt them. We already developed a series of new strategies for the prevention and management of hypertension[2] and atherosclerotic cardiovascular disease (ASCVD)[3] as well as for healthcare.[3−5] These novel strategies, which are based on sleep, emotion, exercise and diet (SEED) intervention (SEEDi), were also called "Chinese vaccine" or "hero for human health (HHH)." As important strategies of "Grade 210 prevention" which is a new synthetic strategy for delivering policy prevention (grade-zero prevention) as well as primary and

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secondary prevention,[6] they play a key role in the prevention and management of human chronic non-communicable diseases (NCD) when combined with the RT-ABCDEF strategy.[3−5] For example, the authors observed and named obesity-OSA-hypertension (OOH) syndrome[4−7] and C-type hypertension (CtH). In this article, considering several conceptual and technical breakthroughs, we briefly introduce these novel strategies.

After the healthy "SEED" rulers were developed in 2005,[3,8,9] we actively used and conducted these novel strategies in the clinical setting for the primary and secondary preventions of ASCVD as well as for healthcare, and cited them in the related literature. SEED rulers were further developed into the E(e) SEED rules in 2007 due to the important role of the environment.[4] These new strategies were further developed into the more novel "E(e)SEED-BasED" rules and renamed "Hu's healthy lifestyles (HHL)" in 2009 (Table 1).[3]

Novel strategies for the early evaluation of risk factors

ASCVD is worldwide, it causes 17.5 million deaths every year, which creates a substantial global public health burden. Moreover, it plays a key role in the development of CDC strips. Single gene defects and target diseases have now come to include multi-genetic and multi-factorial diseases, such as ASCVD, neuro-degenerative diseases such as Parkinson's disease, type 1 or type 2 diabetes mellitus (T1DM or T2DM), and cancer, especially CDC strips. Therefore, screening and evaluating early cardiovascular status is very important for predicting and preventing cardiovascular events and CDC strips. Both previous experimental and clinical studies confirmed the role of single factors in the development of human disease. However, little is known about the detailed role of a series of risk factors or multi-risk factors, especially 5 to 10 or more, although there are some related studies.[10,11]

We developed the Chinese E(e)SEED-BasED score (CEBS) according to our "E(e)SEED-BasED" healthy lifestyles. These healthy elements and related risk factors play a very important roles in human health. If people intervene early with these risk factors, they can effectively avoid CDC strips. As shown in Table 1, we have already developed these new strategies for improving healthcare. We even developed a novel strategy that was based on our Q&A list and CEBS (Table 2). According to CEBS, people can determine their hazard levels of CDC strips from low to moderate to high, and accordingly adopt effective measures including follow-up and intervention with SEED, E(e) SEED, or HHL (i.e. SEEDi, E(e)SEEDi, or HHLi). We believe that CEBS will be better for the early evaluation of NCDs, especially CDC strips based on previous work and this innovative idea.

Here we may easily compare with other scores such as QRISK a new CVD risk score for the United Kingdom, Framingham CVD algorithm (FA) and Scottish score (ASSIGN) (Table 2). These scores focus on standard, common, classic, multiple modifiable or non-modifiable (e.g. positive family history) risk factors, but we think that CEBS is advantageous, validated, and global with 15 classifications of risk factors due to its comprehensive and systematical way of controlling the CDC strips, generally by early evaluation and intervention of major risk factors. Of course, regarding degree of improvement, the population in question, and other questions, we must perform the analysis in a real cohort population.

Table 1
Core elements and contents of related healthy lifestyles.

Core elements	SEED (version 1.0)	E(e)SEED (SEED version 1.5)	Hu's healthy lifestyle (HHL) [E(e)SEED-BasED healthy lifestyle] (SEED version 2.0)
E(e)		Environment	Environment
S	Sleep	Sleep	Sleep
E	Emotion	Emotion	Emotion
E	Exercise	Exercise	Exercise
D	Diet	Diet	Diet
B			Behavior
/a			Age
/s			Safety sex study
E			Education employment ethnic
D			Disease drug

Table 2
Four kinds of risk factor scores for estimating CVD and CDC strips.

Algorithm Names	Subjects	Risk factors	Patients	Features
QRISK	UK population	More	High risk CVD	Not include environment
FA	USA population	Common	CVD	Not include environment
ASSIGN	Scottish population	Common	CVD	Not include environment
CEBS	Global population	15 classifications (Table 1)	The whole population	To emphasize external & internal environment

Notes: CVD: cardiovascular disease; CDC: cardiovascular, diabetes, and cancer; QRISK: a cardiovascular disease risk algorithm; FA: Framingham cardiovascular disease algorithm; ASSIGN: a Scottish score algorithm; CEBS: Chinese E(e)SEED-BasED score.

However, not only is this a hugeworkload? but it is also costly.

Novel strategies for CDC strips

RT-ABCDEF strategy and Grade 210 prevention

The RT-ABCDEF strategy developed in the previous work is very suitable for the management and prevention of human disease, especially NCDs or CDC strips (Table 3).[4,5] Early prevention is the choice of treatment. Efforts to achieve the ambitious goals of Healthy China 2030 require the new synthetic "Grade 210 prevention" strategy. Due to it containing preventive and healthcare strategies for main risk factors, HHL includes the core contents of the Grade 210 prevention strategy. Therefore, its global conduct and application is worthwhile, not just that within healthcare providers and medical organizations. Of course, collaborative efforts among governments, private healthcare providers, insurers, policymakers, nonprofit organizations, and the global public are necessary for true Grade 210 prevention. It is a synthetic core

Table 3
RT-ABCDEF strategy and its Tips for human NCDs which include CDC strips.

RT-ABCDEF strategy	Tips
F(Follow-up)	To trail outcome
E (Examination)	General or specific screening
D (Disease & risk control)	See Table 1
C(Changing unhealthy lifestyle)	E(e)SEED-BasED healthy lifestyle (also named Hu's healthy lifestyle, HHL)
B(Biohazard control)	Keep biochem-physiological indexes in normal range
A (Antagonistic treatment)	To control related symptoms

Notes: RT: right, routine, and reversible treatment; NCDs: noncommunicable diseases; CDC: cardiovascular, diabetes, and cancer.

strategy of healthcare for everyone or anyone and from birth to death.

SEEDi, E(e)SEEDi, or HHLi for CDC strips

Most patients with NCDs including chronic heart failure (CHF), particularly those with more severe heart failure and T2DM or T1DM, need the option of palliative care as assessed by symptom burden, depression, and spiritual well-being similar to patients with advanced cancer, i.e. palliative care is effective for most CDC strips.

The development of CDC strips results from the numerous shared many risk factors related to lifestyles according to our "Bad SEED" +/− "bad soil" theory or doctrine.[1] Thus, synthetic strategies are needed to prevent and control the development of CDC strips. Therapeutic lifestyles interventions, such as SEEDi, E(e)SEEDi, or HHLi, all of which are based on E(e)SEED-BasED lifestyles, eg. HHLi-related rational drug interventions (Table 4), can significantly improve nutrition and physical activity behaviors and reduce many of the risk factors associated with common NCDs, especially CDC strips. We think that it was very useful and effective for most CDC strips. Therefore, people may call it the "Chinese vaccine" or HHH. This may help reduce the morbidity and mortality of CDC strips.

For example, among 74,607 men and women aged ≥60 years without coronary heart disease (CHD), stroke, or cancer at enrolment, the Mediterranean diet modified for application across Europe was associated with increased survival among older people and is associated with longer life expectancy among elderly Europeans.[12] These results also help explain the role of SEEDi, E(e)SEEDi, or HHLi. The "Rainbow diet" we conducted in HHL is also very helpful due to balanced nutrition. For example, coffee consumption was verified to be helpful for preventing NCDs, including CDC strips. Besides, green tea and grapes are useful foods for interventional diets because an increased

Table 4
Rational drugs for CVD, diabetes, cancer, and related CDC strips.

Drugs	CVD	Diabetes	Cancer	CDC strips
Asprin	−	−	−	−
ACEI/ARB	−	−	−	−
CCBs	−	−	+/−(?) or No	−
Statins (eg. atorvastatin, pravastatin, rosuvastatin, simvastatin)	−	−	−	−
CBD	−	−	−	−
Coenzyme Q-10	−	−	−	−
Antioxidants (eg. GSH, Selenium, Zinc, Vit C, Vit B, Vit D, Vit E, n-3 fatty acids)	−	−	−	−
Traditional Chinese medicine (eg. Ginseng, Barbary Wolfberry Fruit, Cordycepin, Ganoderma lucidum, SR10, Astragalus)	−	−	−	−

Notes: CVD: cardiovascular disease; CDC: cardiovascular, diabetes, and cancer; ACEI/ARB: angiotensin converting enzyme inhibitor/angiotensin receptor blocker; CCBs: calcium-channel blockers; CBD: Cannabidiol; GSH: L-Glutathione; Vit: vitamin; -: decreasing risk; +: increasing risk; ?: uncertain; No: not change.

consumption of vegetables and fruits may elevate antioxidative component levels. According to a study in *Nature*,[13] diet is the main factor which was linked with gut microbial ecology and health because unbalanced dietary nutrients can cause intestinal inflammation and induce human aging. Another clinical trial showed that both walking and vigorous exercise are associated with substantial reductions in the incidence of cardiovascular events among postmenopausal women. As characteristic physical activities, Yuga, Chinese Tai chi, and Qigong may be helpful for preventing Re-CDC strips due to their effects on chronic diseases.[14−16]

As a part of the HHLi, rational drug choice plays an important role in the initiation, progression, treatment and prevention of NCDs, especially for effectively halting the development of CDC strips. These drugs include aspirin, angiotensin-converting enzyme inhibitor/angiotensin receptor blocker, calcium channel blocker, cannabidiol[17] and coenzyme Q-10.

Several animal experiments and clinical trials showed that, as chemo-protective agents, statins (pravastatin, rosuvastatin) not only prevented and decreased ASCVD and cardiovascular events,[18,19] and indicated no increase in over all cancer risk (simvastatin, pravastatin), they also protected against the development of T2DM or T1DM and cancer, e.g. lung, pancreatic, colon, renal cell carcinoma, and polycystic ovary syndrome (atorvastatin) (Table 4). Thus, statin use may help prevent and halt CDC strips.

Glutathione (GSH) plays important roles in antioxidant defense, nutrient metabolism, and regulation of cellular events, and its deficiency contributes to oxidative stress, aging, and the pathogenesis of many

diseases,[20] including NCDs, especially CDC strips. Thus, we believe that GSH is an effective cytoprotective chemoagent for treating NCDs such as CDC strips (Table 4).

Studies indicate that selenium and zinc, essential and critical trace elements and antioxidants, indicate, may play a role in the pathogenesis of atherosclerosis and be useful for the secondary prevention of ASCVD. Their deficiency is associated with numerous diseases including CVD, T2DM or T1DM, and cancer.[21] Hence, these antioxidants may be useful as therapeutic agents for CDC strips. Vitamin D and n-3 fatty acids[22] as well as traditional Chinese medicine,[23−25] e.g. ginseng, barbary wolfberry fruit, *Cordyceps militaris, Ganoderma lucidum*, SR10, and *Astragalus* are also very helpful for preventing CDC strips (Table 4).

For reducing the morbidity and mortality of CDC strips, enhancing collaboration is critical because CDC strips share many risk factors and preventive opportunities, e.g., by assessing and regularly updating one's family history. Regarding a positive family history, e.g., patients with CHD and T2DM or cancer, just like successful gene therapies,[26,27] RNAi or knockout technology is a new choice when all strategies are of no use, but we must evaluate its early and late effects in clinical trials.[28,29] At the same time, we must ensure the protection of some genes,[30,31] not just medical hypotheses. Moreover, it is necessary to identify susceptibility loci when using RNAi or knockout technology.[32,33] An updated study showed that an intensive lifestyle intervention focusing on weight loss did not reduce the cardiovascular events rate in overweight or obese adults with T2DM.[34] This confirms the need for comprehensive strategies

such as SEEDi, E(e)SEEDi, or HHLi for CVD, T2DM, and cancers, including CDC strips rather than simple focus on weight loss. Of course, for genetic diseases, RNAi or CRISP/cas technology is required.[35–37]

Clinical practice and prospective

OOH syndrome first identified and named in 2006,[9] is a classic NCD and a synthetic killer with three independent risk factors that is characterized by "a shaped and sounded killer at night but a shaped and no sounded killer by day." According to preliminary clinical data (manuscript not published yet), there is a high risk of T2DM, CHF, and various cardiovascular events, even cancers, developing, e.g. prostate cancer in men and breast cancer in women. It is a status of pre-CDC strips, or already met a branch (Type A) of CDC strips.

We recently identified a group of patients with hypertension related to "new-type stress" due to unhealthy lifestyles and named it CtH. Its main clinical features are a temporary absolute increase or continuously slow increase in the level of human cortisol, a biomarker of CtH. It often occurs in young or middle-aged subjects and is a new ignored killer due to easy to suffer from acute myocardial infarction (AMI), CHF, stroke, or sudden cardiac death. Thus, CtH results from bad "SEED," a bad lifestyle, not bad "Soil," genetic factors.[1] Some patients with hypertension and OOH syndrome may be diagnosed with CtH because both obesity and OSA result from unhealthy lifestyles. OOH syndrome and CtH can progress to CDC strips if there are long-term lasting co-risk factors resulting in T2DM and cancer. In fact, awareness, treatment and control rates of diabetes in both Beijing and China were low,[38] thus, our comprehensive intervention strategy is needed.

SCD as an acute cardiovascular event often occurs in patients with ASCVD who are younger or older, especially those with OOH syndrome, CtH, or CDC strips (Type A or B). SCD often occurs as the endpoint event of CDC strips. Because both OOH syndrome or CtH and SCD have shared risk factors, i.e. "Bad SEED" +/− "bad soil", therefore, SEEDi, E(e)SEEDi, or HHLi is a good choice for halting the development of CDC strips in patients with OOH syndrome or CtH and for removing risk factor-induced SCD.

Conclusions

All in all, OOH syndrome, CtH, CDC strips, and SCD are closely linked. They urgently require SEEDi,

E(e)SEEDi, or HHLi to enhance quality of life and life expectancy the earlier the better. Perhaps this can be referred to as "OCS status". An updated general formula developed for the management of human disease, especially NCDs including OOH syndrome and CDC strips, is as follows: health & longevity = RT-ABCDEF + E(e)SEED-BasED + 210.[5] A detailed explanation of this formula can be found above. The most important thing is that it embodies mass prevention and treatment conducted by Prof. Da-Yi Hu.[39]

Conflicts of interest

No funding was received for this work. The authors declare that ethical approval was received but no potential conflicts of interest exist.

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