Res Exerc Epidemiol 2012; 14(1): 1-18.

【Review Article】

Physical Activity, Exercise and Non-Communicable Diseases

Edward Archer[1), Steven N. Blair[1,2)

1) Departments of Exercise Science, Arnold School of Public Health, University of South Carolina
2) Epidemiology/Biostatistics, Arnold School of Public Health, University of South Carolina

ABSTRACT The modern environment has been explicitly engineered to reduce manual labor, increase physical comfort and afford passive entertainment. As a result, physical inactivity and sedentary pastimes have become ubiquitous features of the post-industrial world. Given the fact that human metabolic, cardiovascular and musculoskeletal systems evolved in an environment in which survival necessitated extraordinary amounts of physical exertion, it is not surprising that physical inactivity has induced a host of morbidities. Epidemiological evidence has demonstrated that inactivity has significant risks and severe consequences for all individuals independent of age, genetic endowment, personal history (e.g., past lifestyle), body composition and current behavior (e.g., diet, alcohol consumption, smoking). Physical inactivity accelerates the aging process and dramatically increases the frequencies of non-communicable diseases (NCDs) such as cardiovascular disease (CVD), type-2 diabetes (T2D) and other pathologies (e.g., frailty, osteoporosis, sarcopenia, and obesity). The relative risks of physical inactivity and mortality from NCDs begin in childhood and increase with advancing age. Nevertheless, physical activity (PA) and exercise have been demonstrated to delay and/or prevent the onset of NCDs and other pathologies associated with sedentary lifestyles and aging. This review surveys data from observational studies and randomized controled trials (RCTs) that support the premise PA and exercise are essential elements in the maintenance of health as well as the prevention and treatment of age-related maladies and NCDs.

Key words: epidemiology, health, sedentary, physical activity, chronic disease, exercise

Environmental Changes, Epidemiology, and Non-communicable Disease

Humans are extremely adept at altering the environments in which they live.[1,2)] Over the past century, the evolution of the physical, social, and cultural milieus has proceeded extremely rapidly[2,3-7)] and humans are now immersed in a world explicitly engineered to reduce physical labor, increase physical comfort and afford passive entertainment. As a result, physical inactivity and sedentary pastimes (e.g., web-surfing, TV viewing) have become ubiquitous features of both developed and developing nations.[8)] The confluence of passive transportation,[9)] spectator-based entertainment,[10)] decrements in occupational energy expenditure,[11)] and household (i.e., domestic) physical activity (PA)[12-14)] has engendered an increase in hypokinetically induced non-communicable chronic diseases; NCDs (e.g., cardiovascular disease (CVD), type-2 diabetes (T2D)) and mortality.[15-17)] Given the fact that human physiology evolved within an environment that obligated remarkable amounts of energy expenditure via physical exertion,[6,18)] it is not surprising that a lack of PA has induced a host of morbidities and increased risk for mortality.[19-24)]

Over the past five decades, a substantial accumulation of empirical evidence (both epidemiological and experimental data) has established that well-known, pervasive, and yet preventable behavioral risk factors such as physical inactivity and unhealthy diets exact an enormous toll[25)] as proximal elements in the causal

Address for correspondence: Edward Archer; Departments of Exercise Science, Arnold School of Public Health, University of South Carolina; 921 Assembly Street, Suite 212 Columbia, S.C. 29208, USA; archerec@email.sc.edu

pathway of NCDs.[15,16,23,24,26-30] Fortunately, the loss of physiologic resources (e.g., strength, endurance) and increments in metabolic impediments (e.g., increased fat mass[31-35] and insulin resistance[28,36-45]) con- comitant with sedentary lifestyles and aging are not inevitable.[46-48] The evidence for the protective effects of PA and the importance of exercise in primary prevention as well as an empirically-supported treatment of NCDs is extensive and increasing.[15,28,29,49-61] Accordingly, the World Health Organization,[19,62] United Nations,[63] American Heart Association[51], American Cancer Society[64], American Diabetes Association and the European Association for the Study of Diabetes[65] have concluded that a sedentary lifestyle is a major modifiable risk factor for NCDs.

This review begins with a brief summary of the evolution of human physiology and the alterations of the socio-cultural and physical environments that have reduced the necessity of physical exertion and increased the prevalence of sedentary lifestyles. We then provide a survey of the evidence that human physiology requires a minimum amount of PA to maintain health, and that the adoption of a physically active lifestyle is now an essential component of health and wellbeing.

The Environment and the Evolution of Human Physiologic Resources

Humans evolved in an environment in which survival necessitated considerable amounts of physical exertion and energy expenditure.[66] Extremes of temperature, altitude, terrain and other environmental features regularly challenged the physiology of early humans.[15] Consequently, human metabolic, cardiovascular and musculoskeletal sys- tems (i.e., physiologic resources) evolved to meet the demands of that milieu. It has been estimated that hunter-gathers expended greater than 80 kj/kg/day (20 kcal/kg/day) in PA.[5,67] In light of this, it becomes clear that it was not only an opposable thumb that allowed early humans to gain ascendancy over other animals but the incomparable capacity to expend vast amounts of energy in sustained PA.[18,68] The ability to stalk prey (i.e., persistence hunting) and gather resources over vast distances allowed early humans to effectively utilize and eventually to dominate their natural environment. Over millions of years, the confluence of socio-cultural evolution (i.e., the development of human society) and the progression of human physiologic resources allowed humans to meet the intense demands of their environment and become the preeminent species on Earth.[1]

Nevertheless, the socio-cultural evolution (i.e., alterations of the social and natural environment) that allowed modern humans to gain preeminence now threatens human health and wellbeing. The modern environment has evolved rapidly over the last century and is now explicitly designed to reduce physical labor, and for many people physical activity energy expenditure (PAEE) is now well below that which is necessary to maintain health.[69,70] As a result, modern sedentary lifestyles have induced a host of pathologies in the form of NCDs. The evidence that humans suffer severe consequences from inactivity is extensive and increasing.[39,42,71-73]

While the medical community has only recently begun to consider PA and exercise as modalities that improve health, there is a vast evidence base that suggests that in the modern environment, PA and exercise not only improve health once it is compromised, but are essential elements in its maintenance.

The evolution of the energy demands of survival.

Humans are social animals that have evolved within the context of highly developed communal structures,[74] and while a single human is remarkably unprepared to survive in the wilds, a social milieu obviates much of the physical burden and energy demands of survival. Consequently, the evolution of human socio-cultural evolution is inversely related to PAEE[66,75] and the concomitant demands on the physiologic resources so essential to health. Early communal hierarchies allowed for the avoidance of predators and the sharing of hunting and gathering of food. By 7000 BCE, the development of agriculture facilitated the transition from foraging and persis- tence hunting (i.e., the “Neolithic revolution”)[76] to a less energetically costly way of life.[77] Attendant with this transition was a dramatic reduction in the energy costs of survival.[67] When humans toiled laboriously to survive, they expended sufficient energy in PA to tax physiologic resources and in doing so, forestall many of the NCDs that now befall modern man. In other words, the continuous and at times intense PA from hunting, farming and other 'occupational' activities was more than adequate to support health, and most people succumbed to infectious rather than chronic diseases. Nevertheless, as human societies progressed from hunting and gathering to agrarian to industrial and post-industrial (i.e., informational) economies, the PAEE obligated by the environment diminished significantly and reduced the demands on the metabolic, cardiovascular and musculoskeletal systems that are so vital to health.

The modern environment.

Despite unconvincing claims that PA has not declined over the recent past,[78] modern sedentary humans expend approximately 25-30% of the calories that hunter-gatherer populations expended in PA (~20 kj/kg/day compared to > 80 kj/kg/day respectively).[5,67] This substantial reduction in PAEE is the result of numerous anthropogenic changes in the physical, social and cultural environments,[79-87] and is one of the primary drivers of the recent increase in NCDs.[17,23,24,26,28,63,79-86]

Recent socio-cultural and environmental changes in transportation, occupation, domestic activity and entertainment have dramatically reduced PAEE. Over the past five decades, there has been a remarkable worldwide increase in the use of passive transport (e.g., private vehicles) and a concomitant substantial decline in active transport (e.g., walking, biking).[9,56,87-95] The increased availability and use of labor-saving features in the urban environment (e.g., mass-transit, elevators, escalators and moving side-walks) diminish PAEE as we move through modern cities.[87,89,92,96,97] For example, present-day Americans take significantly fewer steps than individuals in traditional agricultural lifestyles such as the Amish (i.e., < 10,000 steps/day vs. > 15,000 /steps/day).[98,99] Perhaps more importantly, there has been a substantial decrease in occupational EE as mechanization and a transition from manufacturing to informational labor have reduced the need for physical effort. The average person spends nearly 50% of their waking hours (and therefore a large portion of their PAEE) at their job. Any decrement in physical exertion and/or the time spent in occupational PA will have dramatic impacts on health and obesity. It has been estimated that the working population in the United States has experienced a decrease in occupational EE via reductions in both the number of hours spent working[13,100-102] as well as the physical effort obligated by occupation.[11] Over the past 50 years, the estimated decrement in occupational EE via decreases in the physical effort obligated by occupations in the United States is greater than 420 kj/day (> 100 kcals/day).[11] This decrement in occupational EE approximates the 'energy gap'[103] necessary for the increase in bodyweight and obesity experienced in the US over the past 50 years.[11]

In addition to decrements in transport and occupational EE, there have been substantial decreases in PAEE in almost every other component of daily life. For example, labor-saving devices have dramatically changed how housework is performed.[14,104] The physical effort necessary in the performance of domestic activity and housework have been on the decline since the middle of the 20th century and most estimates suggest that women are performing 10-15 hrs less housework per week than in the 1960s.[12-14,100,101,105] As the time spent doing housework decreased, the amount of time in sedentary behaviors (e.g., TV viewing and web surfing[13, 101, 106]) has increased dramatically. American adults now spend over 16 hours per week watching television and additional time in front of their computers.[13,100,101,106,107] The estimated change in energy expenditure from active housework (e.g., washing the dishes and sweeping the floor) to sedentary pastimes (e.g., using a dishwasher while watching TV) is the equivalent of more than 4,200 kj/week (> 1,000 kcals/week). The decrement in PAEE from these findings suggests that the recent rise in bodyweight and obesity experienced in the US is due to decreases in PA alone. Given the fact that PA is the major modifiable component of total daily energy expenditure (TDEE),[108] the substantial decrement in total PAEE from all activities (e.g., transport, occupational and housework) may be so large that current levels of obesity would be considerably higher if energy intake (EI) levels had increased. In agreement with other sources,[109-111] these PA data suggest that EI has either diminished or remained static in some groups over the recent past.

The Necessity of PA for Health

Ancient wisdom.

The importance of PA for health has been recognized for millennia and the detrimental effects of a sedentary lifestyle were observed well before the 21st century. As human societies evolved, the emergence of a leisure (i.e., sedentary) class supported by slave and/or peasant economies gave rise to the earliest instances of sedentarism and hypokinetically induced NCDs. Sushruta, the famous Indian surgeon from Kashi and father of Ayurvedic medicine (i.e., knowledge of life), practiced around 600 BCE.[112,113] His keen sense of observation led to the discovery that his most inactive/sedentary clients suffered from a number of classic hypokinetic diseases.[113,114] Sushruta chronicled numerous NCDs such as madhumeha or “honey-like urine” (i.e., diabetes); vataraka (i.e., hypertension) and medoroga (i.e., obesity) in his ancient text *The Sushruta Samhita*.[112,115]

Modern evidence.

Since the 1950s, there has been a substantial accumulation of epidemiological evidence on the primacy of PA in the maintenance of health. Some of the compelling modern evidence of the health sustaining effects of PA is provided by two classic studies: the College Alumni Study (CAS)[116] and the Aerobics Center Longitudinal Study (ACLS).[117] The CAS examined PA and all-cause mortality in over 36,500 men from their college entrance documents (1916-1950) and other public records. The work of Paffenbarger and colleagues revealed an inverse dose-response relationship between PA and all-cause mortality. Greater levels of PA were associated with a lower risk of death, and men expending > 8,400 kj per week (2000 kcal/wk) in PA had a 27% lower risk of mortality compared with men expending < 8,400 kj per week (2000 kcal/wk).

While the CAS was a seminal and landmark study, one of its greatest limitations was the use of self-reported PA. Since people tend to over-report their PA levels, there is an attenuation of relationship between PA and health.[118] As such, we have been able to extend earlier work on PA and health outcomes by objectively measuring cardiorespiratory fitness (CRF) by a maximal exercise test, which is primarily determined by a person’s PA during a few months before the test.[120] The ACLS has produced compelling evidence on the relationship between PA, CRF and health.[23,55,117,119-125] In our first report on CRF and mortality, we followed over 13,000 healthy men and women for more than 8 years of follow-up (a total of 110, 482 person-years of observation). The age-adjusted all-cause mortality rates for men increased from a low of 18.6 per 10,000 person-years in the most-fit quintile to 64.0 per 10,000 person-years in the least-fit quintile. The corresponding values for women were 8.5 per 10,000 person-years in the most fit to 39.5 per 10,000 person-years in the least fit. This strong inverse trend remained after correcting for age, smoking, systolic blood pressure (SBP), cholesterol levels, family history of CVD and fasting serum glucose levels. Higher levels of CRF delay all-cause mortality through lower rates of NCDs (e.g., CVD and cancer). Our results clearly demonstrate that a sedentary life style engenders a reduced CRF, which leads to accelerated aging, and an increased risk for NCDs and premature mortality.[28,55,117]

PA and mortality.

We recently examined the attributable fractions of deaths in the ACLS population.[24] Attributable fractions are based on the strength of a particular risk factor with mortality and on the prevalence of the risk factor in the population being examined. Figure 1 depicts the results of these analyses. The attributable fractions are the estimated number of deaths in the population that are due to a specific risk factor. Each risk factor is adjusted for possible confounding factors, including age, examination year, and each of the other risk factors in the figure. Low CRF is estimated to cause ~16% of deaths, which is far higher than any other risk factor, with the possible exception of hypertension in men, and is greater than the combined deaths due to obesity, diabetes, and smoking in both women and men.

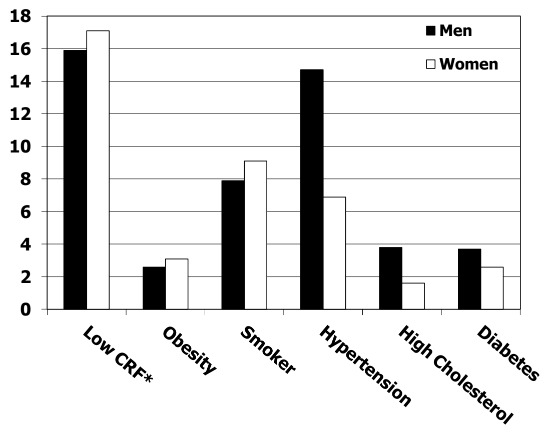

Figure 1 Attributable fractions (%) for all-cause deaths in 40,842 (3,333 deaths) men and 12,943 (491 deaths) women in the Aerobics Center Longitudinal Study. The attributable fractions are adjusted for age and each other item in the figure. *=cardiorespiratory fitness determined by a maximal exercise test o a treadmill. (Reprinted by permission of the Br J Sports Med)

Over the past 50 years, the evidence base continues to accrue via modern epidemiological studies, and it demonstrates a strong, inverse dose-response relationship between PA and NCDs, especially CVD. The health benefits of PA are irrefutable,[15,23,24,53,117,119,120,122,126,127] and even small increments in PA via reductions in sedentary behavior are beneficial, given that each is an independent risk factor for CVD.[128] The maintenance of health, reduced mortality and improvements in metabolic function, body composition, hemodynamics, musculoskeletal, and psychologic functioning are a few of the myriad benefits of PA. Active individuals have lower rates of all-cause mortality, CVD, high blood pressure, stroke, T2D, metabolic syndrome, colon cancer, breast cancer, depresssion, enhanced cognitive functioning, better quality sleep and health-related quality of life (QoL).[129]

The Economic and Societal Costs of Inactivity

Risk factors for NCDs.

In 2009, the World Health Organization (WHO) reported on the leading global risk factors for mortality.[20] More than one third of all deaths were attributed to five major risk factors (i.e., high blood pressure, tobacco use, high blood glucose, physical inactivity and overweight/obesity).[22] As global patterns of PA and consumption changed, the increasing prevalence of these well-known, pervasive and yet preventable major risk factors has exacted an enormous toll[25] as the proximal element in the causal pathway of NCDs (e.g., CVD, T2D, stroke, cancer and chronic respiratory diseases).[15,16,24,26,27] In concert with the 2009 WHO report, the United Nations General Assembly formally recognized that the spread of NCDs represents a global crisis, and that men, women, and children in all countries and in all income groups are at risk.[19,130]

Direct costs.

The confluence of physical inactivity and the aging of the global population[131] has lead to a dramatic increase in NCDs and their attendant costs.[21,26] The increasing burden of NCDs represents a significant threat to human, societal and economic development throughout the world. NCDs are currently responsible for over 65% of all deaths worldwide (i.e., > 36 million fatalities) and are projected to cause over 75% of all deaths by 2030.[22,132] In post-industrial nations, more than 85% of all deaths are due to NCDs.[21] It is important to note that in the US ~20% of the population smokes yet 40% are inactive.[21] This suggests increasing PA[108] may be the most effective solution to the global pandemics of obesity and NCDs.

The failure to reduce NCDs will result in heavy losses in terms of both human life and economic production.[16,130,133] Two of the major risk factors, obesity and physical inactivity have both direct and indirect effects on the mortality and morbidity associated with NCDs via other risk factors (e.g., high blood pressure, high blood glucose).[15,26,120,122,133,134] Globally, approximately 2.8 million adults die annually as a result of being overweight or obese, and roughly 10% of all NCD mortality is due to insufficient PA.[20,22,16,26] In the United States, obesity and physical inactivity account for nearly 20% of all deaths (i.e., > 400,000 deaths annually),[85] and a substantial portion of the burdens (i.e., disability and mortality) from certain cancers, diabetes and CVD are directly attributable to inactivity-induced low levels of

CRF and increased obesity.[22,28,55,135] Additionally, NCDs often result in slow painful deaths after extended periods of disability.[20] As such, NCDs diminish not only the quality and quantity of life, but also deprive the local community of economic production and independence.[62,63]

As the prevalence of the major risk factors increases, the costs of inaction will amplify and the failure to reduce NCDs will result in heavy losses in terms of both human life and economic production[16,130,133] while threatening health systems and economic progress in both the developed and developing world[16]. In addition to the human losses, the economic costs associated with the lifestyle-related antecedents (i.e., major risk factors) of NCDs are staggering. In the US, the cost of CVD & diabetes alone account for $750 billion annually[26] and are increasing.[22,136] In other countries the costs are equally burdensome: China $558 billion; India $237 Billion; and Britain $33 Billion.[17,26]

The Human Cost of Sedentary Lifestyles

Loss of Physiologic Resources.

It is well established that age and sedentary lifestyles diminish the physiologic resources (e.g., strength, CRF) necessary for humans to meet environmental demands (e.g., stair climbing, housework, personal care) while decreasing QoL and increasing morbidity and mortality.[26,137-139] Inactivity has significant risks for all individuals independent of age, genetic endowment, personal history (e.g., past lifestyle), body composition and current behavior (e.g., diet, alcohol consumption and/or smoking).[15,24,55,117,119,120,122,124] Sedentary lifestyles have severe consequences for all individuals since the relative risks of physical inactivity and mortality from NCDs begin in childhood and increase with advancing age.[39,79,140] A lifetime of physical inactivity attenuates peak aerobic capacity, skeletal muscle strength and bone density,[79] while predisposing individuals to a host of morbidities in later life[79,141-144] such as T2D,[28,45,145-150] osteoporosis[151,152], sarcopenia,[153-155] CVD,[156-163] frailty,[140,164] cancer,[55,64,165-169] and fatty liver disease.[171-174] Not surprisingly, the prevalence of nonalcoholic fatty liver disease (NAFLD) has increased in parallel with the rise in childhood sedentarism and hypokinetically-induced childhood obesity. NAFLD is now one of the leading global causes of chronic liver disease in children and adolescents.[85,171-174]

Premature aging.

In 2008, more than nine million of the deaths attributed to NCDs occurred before the age of 60.[21,22] These "premature" deaths are strong evidence of the acceleration of both aging and mortality from inactivity as well as other risk factors such as smoking.[21] In developing nations, the risk of premature death (< 60 yrs of age) from NCDs is 300% greater than in post-industrial nations.[21]

In elderly populations, the major inactivity-induced NCDs are often comorbid with other pathologies associated with sedentary lifestyles (e.g., osteoporosis[47,166,175-177], sarcopenia[137,154], obesity[31,33,35,178]) as well as poor nutrition.[35,178,179] The co-occurrence of these pathologies denotes a phenoltype of accelerated aging indicated by decrements in the ability to perform activities of daily living (ADL) and a reduced QoL.[138,139,176,180,181] These impairments are engendered by alterations in energy metabolism (e.g., dysglycemia),[28,36-45] body composition (e.g., loss of lean body mass,[31,32,47,137,154,182-185] bone mass,[186,187] and increments in fat mass[31-35]), musculoskeletal dysfunction (e.g., loss of muscle quality, volume, force development),[137,154] decrements in CRF[188,189] and other indices of functional capacity.[164,189,190] The relationship between age, inactivity-induced decrements in physiologic resources and morbidity are causal and not merely incidental. For example, body composition explains > 80% of the variation in energy metabolism (e.g., glucose disposal, EI expenditure and storage).[191-193] Skeletal muscle mass (SMM) is responsible for ~70-80% of insulin-mediated glucose uptake[194] and post exercise, SMM is responsible for dramatic increases in non-insulin mediated glucose uptake (NIMGU).[28,46,195-205] Low SMM from aging and inactivity is linked with insulin resistance,[204,206-208] and frailty,[47,137,140,164,176,190,209] while exercise training-induced increases in muscle volume, quality and/or function improve insulin sensitivity, sarcopenia and health.[38,53,205,210-215]

Exercise as Treatment for NCDs and other Inactivity-induced Morbidities

The loss of physiologic resources and increments in metabolic impediments (e.g., increased fat mass, insulin resistance) concomitant with sedentary lifestyles and aging are not inevitable.[46-48] Lifestyle modifications (e.g., increases in PA) have been empirically examined for over 30 years,[216-220] and have been demonstrated to improve the metabolic risk factors (e.g., inflammation, insulin resistance) for a number of NCDs: Hypertension, T2D, cancer and CVD.[15,57,120,221] A considerable accumulation of data from randomized trials suggest that exercise interventions (EXs) may prove both efficacious and cost-effective in the prevention as well as treatment of numerous NCDs.[17,28,53,57,218,222-228] EXs enhance physiologic resources (e.g., strength, CRF), ameliorate or even reverse the underlying pathologies that inhibit the ability to meet environmental demands (e.g., stair climbing) and halt progression along the continuum from inactivity to disability and death.

CVD.

In 2011, a Cochrane systematic review allowed an analysis of 47 studies which included 10,794 CVD patients randomized to either exercise-based cardiac rehabilitation or usual care.[229] With 12 months or more of follow-up, exercise-based cardiac rehabilitation reduced all-cause and CVD mortality signifycantly: RR 0.87 (95% CI 0.7 to 0.99) and 0.74 (95% CI 0.63 to 0.87), respectively. In 70% of these studies, there was evidence of a significantly higher self-reported QoL with the exercise treatment compared to usual care. Given these and other results, the prescription of PA and exercise is now an essential, but all too often underutilized component of the treatment of CVD.[15,230]

Metabolic disorders: diabetes, dysglycemia and insulin resistance.

A meta-analysis in 2006[231] demonstrated that exercise significantly improves glycemic control and reduces visceral adipose tissue and plasma triglycerides. In 2010, a meta-analysis of 13 RCTs showed that resistance training (RT) reduced glycosylated hemoglobin (HbA1c) by 0.48% (95% CI -0.76 to -0.21; p = 0.0005), total fat mass by 2.33 kg (95% CI -4.71 to 0.04; p = 0.05) and SBP by 6.19 mmHg (95% CI 1.00 to 11.38; p = 0.02). Thus, RT had both a clinically and statistically significant effect on multiple metabolic risk factors (e.g., obesity, HbA1c levels, and SBP)[232]

A more recent review and meta-analysis of 47 RCTs (duration > 12 weeks) examined a total of over 8,500 patients.[233] Structured exercise training (e.g., aerobic exercise, RT or both combined) was associated with a decline in HbA1c levels of -0.67% (95% CI, -0.84% to -0.49%) compared with control participants. The combination of both aerobic and RT was the most effective, resulting in HbA1c decrements of -0.51% (95% CI, -0.79% to -0.23%) when compared with control participants.

These results clearly support exercise as an efficacious treatment of CVD and the reduction of numerous metabolic risk factors.

Summary

Rapid and dramatic alterations of the natural and socio-cultural environments over the past century have PAEE below that which is necessary for health and wellbeing[69,70] and as a consequence, increased the prevalence of NCDs. Over the past 50 years, a substantial accumulation of epidemiological and experimental evidence has established a causal relationship between NCDs and preventable behavioral risk factors such as sedentary lifestyles and unhealthy diets.[15,16,24,26,27] As such, physical inactivity leading to low levels of fitness is a leading cause of morbidity and mortality in the world.[16,17,26,63,130] Nevertheless, there exists a lack of appreciation of the necessity of PA and exercise in the maintenance of health as well as a lack of implementation of PA interventions in the primary prevention and treatment of NCDs.

It is our hope that the vast accumulation of evidence on the relationship between the health-sustaining benefits of PA and exercise is recognized and appreciated so that future generations do not suffer the consequences of inactive lifestyles.

References

1） Vitousek PM, Mooney HA, Lubchenco J, Melillo JM. Human Domination of Earth's Ecosystems. Science. 1997; 277 :494-9.

2） Cooley CH. Human Nature and the Social Order. Transaction Publishers, Piscataway, NJ, 1983.

3） Pijl H. Obesity: evolution of a symptom of affluence. Neth J Med. 2011; 69(4): 159-66.

4） Eaton SB, Cordain L, Lindeberg S. Evolutionary health promotion: a consideration of common counterarguments. Prev Med. 2002; 34(2): 119-23.

5） Eaton SB, Strassman BI, Nesse RM, et al. Evolutionary health promotion. Prev Med. 2002; 34(2): 109-18.

6） Malina RM, Little BB. Physical activity: the present in the context of the past. Am J Hum Biol. 2008; 20(4): 373-91.

7） Alvard MS. The adaptive nature of culture. Evol Anthropol. 2003; 12(3): 136-49.

8） Berrios X, Koponen T, Huiguang T, Khaltaev N, Puska P, Nissinen A. Distribution and prevalence of major risk factors of noncommunicable diseases in selected countries: the WHO Inter-Health Programme. Bull World Health Organ. 1997; 75(2): 99-108.

9） McDonald NC. Active transportation to school: trends among US schoolchildren, 1969-2001. Am J Prev Med. 2007; 32(6): 509-16.

10） Clark BK, Sugiyama T, Healy GN, et al. Socio-demographic correlates of prolonged television viewing time in Australian men and women: the AusDiab study. J Phys Act Health. 2010; 7(5): 595-601.

11） Church TS, Thomas DM, Tudor-Locke C, et al. Trends over 5 decades in US occupation-related physical activity and their associations with obesity. PLoS One. 2011; 6(5): e19657.

12） Robinson J, Milkie M. Dances with Dust-bunnies: Housecleaning in America. Am Demogr. 1997; 19: 37-40, 59.

13） Robinson JP, Godbey G. Time for life: The surprising ways Americans use their time. 2nd ed. Pennysylvania State University Press, University Park, PA, 1999.

14） Robinson J. Time, housework, and the rest of life. J Fam Econ Issues. 1996; 17(3): 213-29.

15） Archer E, Blair SN. Physical activity and the prevention of cardiovascular disease: from evolution to epidemiology. Prog Cardiovasc Dis. 2011; 53(6): 387-96.

16） Beaglehole R, Ebrahim S, Reddy S, Voute J, Leeder S, Chronic Disease Action G. Prevention of chronic diseases: a call to action. Lancet. 2007; 370(9605): 2152-7.

17） Beaglehole R, Bonita R, Horton R, et al. Priority actions for the non-communicable disease crisis. Lancet. 2011; 377(9775): 1438-47.

18） Bramble DM, Lieberman DE. Endurance running and the evolution of Homo. Nature. 2004; 432(7015): 345-52.

19） WHO. Global Strategy on Diet, Physical Activity, and Health. World Health Organization, Geneva, 2004.

20） WHO. Mortality and burden of disease estimates for WHO Member States in 2004. Geneva World Health Organization; 2009.

21） WHO. WHO maps noncommunicable disease trends in all countries: country profiles on noncommunicable disease trends in 193 countries. Cent Eur J Public Health. 2011; 19(3): 130, 138.

22） WHO. World Health Statistics 2010. World Health Organization, Geneva, 2010.

23） Blair SN, Brodney S. Effects of physical inactivity and obesity on morbidity and mortality: current evidence and research issues. Med Sci Sports Exerc. 1999; 31(11 Suppl): S646-62.

24） Blair SN. Physical inactivity: the biggest public health problem of the 21st century. Br J Sports Med. 2009; 43(1): 1-2.

25） Manning W, Keeler E, SLoss E, Wasserman J. The Costs of Poor Health Habits. Harvard University Press, Cambridge, MA, London, 1991.

26） Cecchini M, Sassi F, Lauer JA, Lee YY, Guajardo-Barron V, Chisholm D. Tackling of unhealthy diets, physical inactivity, and obesity: health effects and cost-effectiveness.

Lancet. 2010; 376(9754): 1775-84.
27) Fisher EB, Fitzgibbon ML, Glasgow RE, et al. Behavior matters. Am J Prev Med. 2011; 40(5): e15-30.
28) LaMonte MJ, Blair SN, Church TS. Physical activity and diabetes prevention. J Appl Physiol. 2005; 99(3): 1205-13.
29) Haskell WL, Lee IM, Pate RR, et al. Physical activity and public health: updated recommendation for adults from the American College of Sports Medicine and the American Heart Association. Med Sci Sports Exerc. 2007; 39(8): 1423-34.
30) Sofi F, Capalbo A, Cesari F, Abbate R, Gensini GF. Physical activity during leisure time and primary prevention of coronary heart disease: an updated meta-analysis of cohort studies. Eur J Cardiovasc Prev Rehabil. 2008; 15(3): 247-57.
31) Villareal DT, Apovian CM, Kushner RF, Klein S. Obesity in older adults: technical review and position statement of the American Society for Nutrition and NAASO, The Obesity Society. Am J Clin Nutr. 2005; 82(5): 923-34.
32) Waters DL, Baumgartner RN. Sarcopenia and obesity. Clin Geriatr Med. 2011; 27(3): 401-21.
33) Bouchard DR, Dionne IJ, Brochu M. Sarcopenic/obesity and physical capacity in older men and women: data from the Nutrition as a Determinant of Successful Aging (NuAge)-the Quebec longitudinal Study. Obesity 2009; 17(11): 2082-8.
34) Han TS, Tajar A, Lean ME. Obesity and weight management in the elderly. Br Med Bull. 2011; 97: 169-96.
35) Going S, Williams D, Lohman T. Aging and body composition: biological changes and methodological issues. Exerc Sport Sci Rev. 1995; 23: 411-58.
36) Fink RI, Wallace P, Olefsky JM. Effects of aging on glucose-mediated glucose disposal and glucose transport. J Clin Invest. 1986; 77(6): 2034-41.
37) Bluher M. Adipose tissue dysfunction in obesity. Exp Clin Endocrinol Diabetes. 2009; 117(6): 241-50.
38) Karelis AD, Tousignant B, Nantel J, et al. Association of insulin sensitivity and muscle strength in overweight and obese sedentary postmenopausal women. Appl Physiol Nutr Metab. 2007; 32(2): 297-301.
39) Krogh-Madsen R, Thyfault JP, Broholm C, et al. A 2-wk reduction of ambulatory activity attenuates peripheral insulin sensitivity. J Appl Physiol. 2010; 108(5): 1034-40.
40) Wilkin TJ. The accelerator hypothesis: a review of the evidence for insulin resistance as the basis for type I as well as type II diabetes. Int J Obes. 2009; 33(7): 716-26.
41) Jennings CL, Lambert EV, Collins M, Joffe Y, Levitt NS, Goedecke JH. Determinants of insulin-resistant phenotypes in normal-weight and obese Black African women. Obesity. 2008; 16(7): 1602-9.
42) Thyfault JP, Krogh-Madsen R. Metabolic disruptions induced by reduced ambulatory activity in free living humans. J Appl Physiol. Jun 2, 2011.
43) Szendroedi J, Roden M. Mitochondrial fitness and insulin sensitivity in humans. Diabetologia. 2008; 51(12): 2155-67.
44) Litherland GJ, Morris NJ, Walker M, Yeaman SJ. Role of glycogen content in insulin resistance in human muscle cells. J Cell Physiol. 2007; 211(2): 344-52.
45) Ford ES, Li C, Zhao G, Pearson WS, Tsai J, Churilla JR. Sedentary behavior, physical activity, and concentrations of insulin among US adults. Metabolism. 2010; 59(9): 1268-75.
46) Lessard SJ, Rivas DA, Stephenson EJ, et al. Exercise training reverses impaired skeletal muscle metabolism induced by artificial selection for low aerobic capacity. Am J Physiol Regul Integr Comp Physiol. 2011; 300(1): R175-82.
47) Sundell J. Resistance Training Is an Effective Tool against Metabolic and Frailty Syndromes. Adv Prev Med. 2011; 2011: 984683.
48) Lemmer JT, Hurlbut DE, Martel GF, et al. Age and gender responses to strength training and detraining. Med Sci Sports Exerc. 2000; 32(8): 1505-12.

49） Johnson NA, Sachinwalla T, Walton DW, et al. Aerobic exercise training reduces hepatic and visceral lipids in obese individuals without weight loss. Hepatology. 2009; 50(4): 1105-12.

50） Thompson PD, Buchner D, Pina IL, et al. Exercise and physical activity in the prevention and treatment of atherosclerotic cardiovascular disease: a statement from the Council on Clinical Cardiology (Subcommittee on Exercise, Rehabilitation, and Prevention) and the Council on Nutrition, Physical Activity, and Metabolism (Subcommittee on Physical Activity). Circulation. 2003; 107(24): 3109-16.

51） Blair SN, Church TS. The fitness, obesity, and health equation: is physical activity the common denominator? JAMA. 2004; 292(10): 1232-4.

52） Kriska AM, Blair SN, Pereira MA. The potential role of physical activity in the prevention of non-insulin-dependent diabetes mellitus: the epidemiological evidence. Exerc Sport Sci Rev. 1994; 22: 121-43.

53） Church TS, Blair SN, Cocreham S, et al. Effects of aerobic and resistance training on hemoglobin A1c levels in patients with type 2 diabetes: a randomized controlled trial. JAMA. 2010; 304(20): 2253-62.

54） Church TS, Earnest CP, Skinner JS, Blair SN. Effects of different doses of physical activity on cardiorespiratory fitness among sedentary, overweight or obese postmenopausal women with elevated blood pressure: a randomized controlled trial. JAMA. 2007; 297(19): 2081-91.

55） Sui X, Lee DC, Matthews CE, et al. Influence of cardiorespiratory fitness on lung cancer mortality. Med Sci Sports Exerc. 2010; 42(5): 872-8.

56） Sisson SB, Camhi SM, Church TS, et al. Leisure time sedentary behavior, occupational/domestic physical activity, and metabolic syndrome in US men and women. Metab Syndr Relat Disord. 2009; 7(6): 529-36.

57） Fielding RA, Rejeski WJ, Blair S, et al. The Lifestyle Interventions and Independence for Elders Study: Design and Methods. J Gerontol A Biol Sci Med Sci. Aug 8, 2011.

58） Warren TY, Barry V, Hooker SP, Sui X, Church TS, Blair SN. Sedentary behaviors increase risk of cardiovascular disease mortality in men. Med Sci Sports Exerc. 2010; 42(5): 879-85.

59） Sigal RJ, Kenny GP. Combined Aerobic and Resistance Exercise for Patients With Type 2 Diabetes. JAMA. 2010; 304(20): 2298-9.

60） Armstrong MJ, Boulé NG, Sigal RJ. Exercise Interventions and Glycemic Control in Patients With Diabetes. JAMA. 2011; 306(6): 607.

61） Sigal RJ, Kenny GP, Wasserman DH, Castaneda-Sceppa C, White RD. Physical activity/exercise and type 2 diabetes: a consensus statement from the American Diabetes Association. Diabetes Care. 2006; 29(6): 1433-8.

62） WHO. Annual global Move for Healt hinitiative: A concept paper. 2005.

63） Beaglehole R, Bonita R, Alleyne G, et al. UN High-Level Meeting on Non-Communicable Diseases: addressing four questions. Lancet. 2011; 378(9789): 449-55.

64） Kushi LH, Doyle C, McCullough M, et al. American Cancer Society guidelines on nutrition and physical activity for cancer prevention: Reducing the risk of cancer with healthy food choices and physical activity. CA Cancer J Clin. 2012; 62(1): 30-67.

65） Nathan DM, Buse JB, Davidson MB, et al. Management of hyperglycemia in type 2 diabetes: A consensus algorithm for the initiation and adjustment of therapy: a consensus statement from the American Diabetes Association and the European Association for the Study of Diabetes. Diabetes Care. 2006; 29(8): 1963-72.

66） White LA. Energy and the Evolution of Culture. Am Anthropol. 1943; 45(3): 335-56.

67） Cordain L, Gotshall RW, Eaton SB, Eaton SB, 3rd. Physical activity, energy expenditure and fitness: an evolutionary perspective. Int J Sports Med. 1998; 19(5): 328-35.

68） Carrier DR, Kapoor AK, Kimura T, et al. The Energetic Paradox of Human Running and Hominid Evolution. Current Anthropology.

1984; 25(4): 483-95.

69） Blair SN, LaMonte MJ, Nichaman MZ. The evolution of physical activity recommendations: how much is enough? Am J Clin Nutr. 2004; 79(5): 913S-20S.

70） Blair SN, Connelly JC. How much physical activity should we do? The case for moderate amounts and intensities of physical activity. Res Q Exerc Sport. 1996; 67(2): 193-205.

71） Hamburg NM, McMackin CJ, Huang AL, et al. Physical inactivity rapidly induces insulin resistance and microvascular dysfunction in healthy volunteers. Arterioscler Thromb Vasc Biol. 2007; 27(12): 2650-6.

72） Shangraw RE, Stuart CA, Prince MJ, Peters EJ, Wolfe RR. Insulin responsiveness of protein metabolism in vivo following bedrest in humans. Am J Physiol. 1988; 255(4 Pt 1): E548-58.

73） Mujika I, Padilla S. Detraining: loss of training-induced physiological and performance adaptations. Part II: Long term insufficient training stimulus. Sports Med. 2000; 30(3): 145-54.

74） Tooby J, Cosmides L, eds. Evolutionary psychology: Foundational papersMIT Press, Cambridge, MA, 2000.

75） Passmore R, Durnin JV. Human energy expenditure. Physiol Rev. 1955;35(4):801-40.

76） Tanno K, Willcox G. How fast was wild wheat domesticated? Science. 2006; 311(5769): 1886.

77） Weisdorf JL. From Foraging to Farming: Explaining the Neolithic Revolution. J Econ Surv. 2005; 19(4): 561-86.

78） Westerterp KR, Speakman JR. Physical activity energy expenditure has not declined since the 1980s and matches energy expenditures of wild mammals. Int J Obes. 2008; 32(8): 1256-63.

79） Booth FW, Laye MJ, Roberts MD. Lifetime sedentary living accelerates some aspects of secondary aging. J Appl Physiol. 2011; 111(5): 1497-504.

80） Weinstein AR, Sesso HD, Lee IM, et al. The joint effects of physical activity and body mass index on coronary heart disease risk in women. Arch Intern Med. 2008; 168(8): 884-90.

81） Powell KE, Thompson PD, Caspersen CJ, Kendrick JS. Physical activity and the incidence of coronary heart disease. Annu Rev Public Health. 1987; 8: 253-87.

82） Shephard RJ. Exercise prescription - North American experience. Br J Sports Med. 1978; 12(4): 227-34.

83） Slentz CA, Aiken LB, Houmard JA, et al. Inactivity, exercise, and visceral fat. STRRIDE: a randomized, controlled study of exercise intensity and amount. J Appl Physiol. 2005; 99: 1613-8.

84） Pietilainen KH, Kaprio J, Borg P, et al. Physical inactivity and obesity: a vicious circle. Obesity. 2008; 16(2): 409-14.

85） Danaei G, Ding EL, Mozaffarian D, et al. The preventable causes of death in the United States: comparative risk assessment of dietary, lifestyle, and metabolic risk factors. PLoS Med. 2009; 6(4): e1000058.

86） Deshpande AD, Harris-Hayes M, Schootman M. Epidemiology of diabetes and diabetes-related complications. Phys Ther. 2008; 88(11): 1254-64.

87） TRB. Commuting in America III: The Third National Report on Commuting Patterns and Trends. Transportation Research Board: National Academy of Sciences. 2011.

88） Wen LM, Orr N, Millett C, Rissel C. Driving to work and overweight and obesity: findings from the 2003 New South Wales Health Survey, Australia. Int J Obes. 2006;30(5):782-6.

89） Svercl PV, Asin RH. Nationawide Personal Tarnsportation Study Home to Work Trips and Travel. In: Transportation UDo, ed: Federal Highway Administration; 1973.

90） Beschen DA. Nationwide Personal Transportation Study: Transportation Characteristics of School Children: US Department of Transportation, Federal Highway Administration. 1969.

91） Bell AC, Ge K, Popkin BM. The road to obesity or the path to prevention: motorized transportation and obesity in China. Obes Res. 2002; 10: 277-83.

92） Memmott M. Trends in Personal Income and Passenger Vehicle Miles Traveled: Bureau of Transportation Statistics, US Department of

Transportation. 2007.
93) Tudor-Locke C, van der Ploeg HP, Bowles HR, et al. Walking behaviours from the 1965-2003 American Heritage Time Use Study (AHTUS). Int J Behav Nutr Phys Act. 2007; 4: 45.
94) Douglas MJ, Watkins SJ, Gorman DR, Higgins M. Are cars the new tobacco? J Public Health. 2011; 33(2): 160-9.
95) Tudor-Locke C, Johnson WD, Katzmarzyk PT. Frequently reported activities by intensity for US adults: the American Time Use Survey. Am J Prev Med. 2010; 39(4): e13-20.
96) BTS. Pocket Guide to Transportation 2011: Bureau of Transportation Statistics, US Department of Transportation. 2011.
97) McGuckin SN, Nakamoto HY, Gray D, Liss S. Summary of Travel Trends 2009 Natuional Household Travel Survey. In: Transportation USDo, ed.: Federal Highway Administration. 2009.
98) Tudor-Locke C, Johnson WD, Katzmarzyk PT. Accelerometer-determined steps per day in US adults. Med Sci Sports Exerc. 2009; 41(7): 1384-91.
99) Bassett DR, Schneider PL, Huntington GE. Physical activity in an Old Order Amish community. Med Sci Sports Exerc. 2004; 36(1): 79-85.
100) Fisher K, Altintas E, Egerton M, et al. American Heritage Time Use Study. Centre for Time Use Research, Oxford, UK, 2011.
101) Robinson J, Martin S. Changes in American Daily Life: 1965–2005. Soc Indic Res. 2009; 93(1): 47-56.
102) USDOL. Occupational Employment Statistics. Accessed 08/02/2011: http://www.bls.gov/ oes/ current/oes211091.htm: US Department of Labor, 2011.
103) Schoeller DA. The energy balance equation: looking back and looking forward are two very different views. Nutr Rev. 2009; 67(5): 249-54.
104) Lanningham-Foster L, Nysse LJ, Levine JA. Labor saved, calories lost: the energetic impact of domestic labor-saving devices. Obes Res. 2003; 11(10): 1178-81.
105) Bianchi SM, Robinson JP, Milkie MA. Changing Rhythms of American Family Life. Russell Sage, New York, 2006.
106) Robinson J. IT, TV and Time Displacement: What Alexander Szalai Anticipated but Couldn't Know. Soc Indic Res. 2011; 101(2): 193-206.
107) Fisher K, Robinson J. Average Weekly Time Spent in 30 Basic Activities Across 17 Countries. Soc Indic Res. 2009; 93(1): 249-54.
108) Westerterp KR. Physical activity as determinant of daily energy expenditure. Physiol Behav. 2008; 93(4-5): 1039-43.
109) Matsumura Y. Nutrition trends in Japan. Asia Pac J Clin Nutr. 2001; 10 Suppl: S40-7.
110) Troiano RP, Briefel RR, Carroll MD, Bialostosky K. Energy and fat intakes of children and adolescents in the United States: data from the national health and nutrition examination surveys. Am J Clin Nutr. 2000; 72(5 Suppl): 1343S-53S.
111) Briefel RR, Johnson CL. Secular trends in dietary intake in the United States. Annu Rev Nutr. 2004; 24: 401-31.
112) Dwivedi G, Dwivedi S. Sushruta - the Clinician - Teacher par Ecellence. Indian J Chest Dis Allied Sci. 2007; 49: 243-4.
113) Guthrie D. India's Contribution to the History of Medicine. Nature. 1956; 178: 1079-134.
114) Guthrie D. The History of Medicine. Thomas Nelson and Sons Ltd, London, 1945.
115) Tipton CM. Susruta of India, an unrecognized contributor to the history of exercise physiology. J Appl Physiol. 2008; 104(6): 1553-6.
116) Paffenbarger RS, Jr, Hyde RT, Wing AL, Hsieh CC. Physical activity, all-cause mortality, and longevity of college alumni. N Engl J Med. 1986; 314(10): 605-13.
117) Blair SN, Kohl HW, III, Paffenbarger RS, Jr., Clark DG, Cooper KH, Gibbons LW. Physical Fitness and All-Cause Mortality: A Prospective Study of Healthy Men and Women. JAMA. 1989; 262: 2395-401.
118) Shephard RJ. Limits to the measurement of habitual physical activity by questionnaires. Br J Sports Med. 2003; 37(3): 197-206; discussion 206.

119） Blair SN, Kohl HW, 3rd, Barlow CE, Paffenbarger RS, Jr, Gibbons LW, Macera CA. Changes in physical fitness and all-cause mortality. A prospective study of healthy and unhealthy men. JAMA. 1995; 273(14): 1093-8.

120） Lee CD, Sui X, Hooker SP, Hebert JR, Blair SN. Combined impact of lifestyle factors on cancer mortality in men. Ann Epidemiol. 2011; 21(10): 749-54.

121） Blair SN, Booth M, Gyarfas I, et al. Development of public policy and physical activity initiatives internationally. Sports Med. 1996; 21(3): 157-63.

122） Blair SN, Kampert JB, Kohl HW, 3rd, et al. Influences of cardiorespiratory fitness and other precursors on cardiovascular disease and all-cause mortality in men and women. JAMA. 1996; 276(3): 205-10.

123） Blair SN, Cheng Y, Holder JS. Is physical activity or physical fitness more important in defining health benefits? Med Sci Sports Exerc. 2001; 33(6 Suppl): S379-99; discussion S419-20.

124） Lee DC, Artero EG, Sui X, Blair SN. Mortality trends in the general population: the importance of cardiorespiratory fitness. J Psychopharmacol. 2010; 24(4 Suppl): 27-35.

125） Jackson AS, Sui X, Hebert JR, Church TS, Blair SN. Role of lifestyle and aging on the longitudinal change in cardiorespiratory fitness. Arch Intern Med. 2009; 169(19): 1781-7.

126） Pedersen BK, Saltin B. Evidence for prescribe-ing exercise as therapy in chronic disease. Scand J Med Sci Sports. 2006; 16(S1): 3-63.

127） Lee DC, Sui X, Ortega FB, et al. Comparisons of leisure-time physical activity and cardio-respiratory fitness as predictors of all-cause mortality in men and women. Br J Sports Med. Apr 23, 2010.

128） Rosengren A, Wilhelmsen L. Physical activity protects against coronary death and deaths from all causes in middle-aged men. Evidence from a 20-year follow-up of the primary prevention study in Goteborg. Ann Epidemiol. 1997; 7(1): 69-75.

129） Physical Activity Guidelines Advisory Committee report, 2008. To the Secretary of Health and Human Services. Part A: executive summary. Nutr Rev. 2009; 67(2): 114-20.

130） UN. Political decalration of the High-level Meeting of the General Assembly on the Prevention and Control of Non-communicable Diseases. General Assembly; 66th Session. United Nations, New York, 2011.

131） U.N. World Population Ageing: 1950-2050. United Nations, NY, 2002.

132） Oldridge NB. Economic burden of physical inactivity: healthcare costs associated with cardiovascular disease. Eur J Cardiovasc Prev Rehabil. 2008; 15(2): 130-9.

133） Pronk NP, Goodman MJ, O'Connor PJ, Martinson BC. Relationship between modify-able health risks and short-term health care charges. JAMA. 1999; 282(23): 2235-9.

134） Stamatakis E, Hillsdon M, Primatesta P. Domestic physical activity in relationship to multiple CVD risk factors. Am J Prev Med. 2007; 32(4): 320-7.

135） WHO. Obesity: preventing and managing the global epidemic. Report of a WHO consultation. World Health Organ Tech Rep Ser. 2000; 894.

136） Abegunde DO, Mathers CD, Adam T, Ortegon M, Strong K. The burden and costs of chronic diseases in low-income and middle-income countries. Lancet. 2007; 370(9603): 1929-38.

137） Rolland Y, Dupuy C, Abellan van Kan G, Gillette S, Vellas B. Treatment strategies for sarcopenia and frailty. Med Clin North Am. 2011; 95(3): 427-38, ix.

138） Drewnowski A, Evans WJ. Nutrition, physical activity, and quality of life in older adults: summary. J Gerontol A Biol Sci Med Sci. 2001; 56(2): 89-94.

139） Rejeski WJ, Mihalko SL. Physical activity and quality of life in older adults. J Gerontol A Biol Sci Med Sci. 2001; 56(2): 23-35.

140） Charansonney OL. Physical activity and aging: a life-long story. Discov Med. 2011; 12(64): 177-85.

141） Thorp AA, Healy GN, Owen N, et al. Deleterious associations of sitting time and television viewing time with cardiometabolic risk biomarkers: Australian Diabetes, Obesity and Lifestyle (AusDiab) study 2004-2005. Diabetes Care. 2010; 33(2): 327-34.

142） Thorp AA, Owen N, Neuhaus M, Dunstan DW. Sedentary behaviors and subsequent health outcomes in adults a systematic review of longitudinal studies, 1996-2011. Am J Prev Med. 2011; 41(2): 207-15.

143） Fu MX, Requena JR, Jenkins AJ, Lyons TJ, Baynes JW, Thorpe SR. The advanced glycation end product, Nepsilon-(carboxymethyl) lysine, is a product of both lipid peroxidation and glycoxidation reactions. J Biol Chem. 1996; 271(17): 9982-6.

144） Chakravarthy MV, Booth FW. Eating, exercise, and "thrifty" genotypes: connecting the dots toward an evolutionary understanding of modern chronic diseases. J Appl Physiol. 2004; 96(1): 3-10.

145） Aman J, Skinner TC, de Beaufort CE, Swift PG, Aanstoot HJ, Cameron F. Associations between physical activity, sedentary behavior, and glycemic control in a large cohort of adolescents with type 1 diabetes: the Hvidoere Study Group on Childhood Diabetes. Pediatr Diabetes. 2009; 10(4): 234-9.

146） Dunstan DW, Salmon J, Owen N, et al. Physical activity and television viewing in relation to risk of undiagnosed abnormal glucose metabolism in adults. Diabetes Care. 2004; 27(11): 2603-9.

147） Wijndaele K, Duvigneaud N, Matton L, et al. Sedentary behaviour, physical activity and a continuous metabolic syndrome risk score in adults. Eur J Clin Nutr. 2009; 63(3): 421-9.

148） Schwartz SL. Diabetes and dyslipidaemia. Diabetes Obes Metab. 2006; 8(4): 355-64.

149） Lakka TA, Laaksonen DE, Lakka HM, et al. Sedentary lifestyle, poor cardiorespiratory fitness, and the metabolic syndrome. Med Sci Sports Exerc. 2003; 35(8): 1279-86.

150） Eriksson KF, Lindgarde F. Prevention of type 2 (non-insulin-dependent) diabetes mellitus by diet and physical exercise. The 6-year Malmo feasibility study. Diabetologia. 1991; 34(12): 891-8.

151） Stallings VA. Calcium and bone health in children: a review. Am J Ther. 1997; 4(7-8): 259-73.

152） Faulkner RA, Bailey DA. Osteoporosis: a pediatric concern? Med Sport Sci. 2007; 51: 1-12.

153） Abellan van Kan G. Epidemiology and consequences of sarcopenia. J Nutr Health Aging. 2009; 13(8): 708-12.

154） Pillard F, Laoudj-Chenivesse D, Carnac G, et al. Physical activity and sarcopenia. Clin Geriatr Med. 2011; 27(3): 449-70.

155） Berger MJ, Doherty TJ. Sarcopenia: prevalence, mechanisms, and functional consequences. Interdiscip Top Gerontol. 2010; 37: 94-114.

156） Carnethon MR, Gidding SS, Nehgme R, Sidney S, Jacobs DR, Jr, Liu K. Cardiorespiratory Fitness in Young Adulthood and the Development of Cardiovascular Disease Risk Factors. JAMA. 2003; 290(23): 3092-100.

157） Gidding SS, Lichtenstein AH, Faith MS, et al. Implementing American Heart Association pediatric and adult nutrition guidelines: a scientific statement from the American Heart Association Nutrition Committee of the Council on Nutrition, Physical Activity and Metabolism, Council on Cardiovascular Disease in the Young, Council on Arteriosclerosis, Thrombosis and Vascular Biology, Council on Cardiovascular Nursing, Council on Epidemiology and Prevention, and Council for High Blood Pressure Research. Circulation. 2009; 119(8): 1161-75.

158） Kavey RE, Daniels SR, Lauer RM, Atkins DL, Hayman LL, Taubert K. American Heart Association guidelines for primary prevention of atherosclerotic cardiovascular disease beginning in childhood. J Pediatr. 2003; 142(4): 368-72.

159） Hayman LL, Williams CL, Daniels SR, et al. Cardiovascular Health Promotion in the Schools: A Statement for Health and Education Professionals and Child Health Advocates From the Committee on Atherosclerosis, Hypertension, and Obesity in Youth (AHOY) of the Council on Cardiovascular Disease in the

Young, American Heart Association. Circulation. 2004; 110: 2266-75.

160） Hayman LL, Meininger JC, Daniels SR, et al. Primary Prevention of Cardiovascular Disease in Nursing Practice: Focus on Children and Youth: A Scientific Statement From the American Heart Association Committee on Atherosclerosis, Hypertension, and Obesity in Youth of the Council on Cardiovascular Disease in the Young, Council on Cardiovascular Nursing, Council on Epidemiology and Prevention, and Council on Nutrition, Physical Activity, and Metabolism. Circulation. 2007; 116: 344-57.

161） Daniels SR, Pratt CA, Hayman LL. Reduction of risk for cardiovascular disease in children and adolescents. Circulation. 2011; 124(15): 1673-86.

162） Kavey RE, Allada V, Daniels SR, et al. Cardiovascular risk reduction in high-risk pediatric patients: a scientific statement from the American Heart Association Expert Panel on Population and Prevention Science; the Councils on Cardiovascular Disease in the Young, Epidemiology and Prevention, Nutrition, Physical Activity and Metabolism, High Blood Pressure Research, Cardiovascular Nursing, and the Kidney in Heart Disease; and the Interdisciplinary Working Group on Quality of Care and Outcomes Research. J Cardiovasc Nurs. 2007; 22(3): 218-53.

163） McCrindle BW, Manlhiot C, Millar K, et al. Population trends toward increasing cardiovascular risk factors in Canadian adolescents. J Pediatr. 2011; 157(5): 837-43.

164） Weiss CO. Frailty and chronic diseases in older adults. Clin Geriatr Med. 2011; 27(1): 39-52.

165） Hu G, Tuomilehto J, Silventoinen K, Barengo NC, Peltonen M, Jousilahti P. The effects of physical activity and body mass index on cardiovascular, cancer and all-cause mortality among 47 212 middle-aged Finnish men and women. Int J Obes. 2005; 29: 894-902.

166） Pedersen BK, Saltin B. Evidence for prescribeing exercise as therapy in chronic disease. Scand J Med Sci Sports. 2006; 16 Suppl 1: 3-63.

167） Slattery ML, Edwards S, Curtin K, et al. Physical activity and colorectal cancer. Am J Epidemiol. 2003; 158(3): 214-24.

168） Matthews CE, Xu WH, Zheng W, et al. Physical activity and risk of endometrial cancer: a report from the Shanghai endometrial cancer study. Cancer Epidemiol Biomarkers Prev. 2005; 14: 779-85.

169） Lagerros YT, Hsieh SF, Hsieh CC. Physical activity in adolescence and young adulthood and breast cancer risk: a quantitative review. Eur J Cancer Prev. 2004; 13(1): 5-12.

170） Loomba R, Sirlin CB, Schwimmer JB, Lavine JE. Advances in pediatric nonalcoholic fatty liver disease. Hepatology. 2009; 50(4): 1282-93.

171） Nobili V, Alisi A, Raponi M. Pediatric non-alcoholic fatty liver disease: preventive and therapeutic value of lifestyle intervention. World J Gastroenterol. 2009; 15(48): 6017-22.

172） Farrell GC. Non-alcoholic steatohepatitis: what is it, and why is it important in the Asia-Pacific region? J Gastroenterol Hepatol. 2003; 18(2): 124-38.

173） Zelber-Sagi S, Ratziu V, Oren R. Nutrition and physical activity in NAFLD: an overview of the epidemiological evidence. World J Gastroenterol. 2011; 17(29): 3377-89.

174） Magkos F. Exercise and fat accumulation in the human liver. Curr Opin Lipidol. 2010; 21(6): 507-17.

175） WHO. Prevention and management of osteoporosis. World Health Organ Tech Rep Ser. 2003; 921: 1-164, back cover.

176） Morley JE. Diabetes, Sarcopenia, and Frailty. Clin Geriatr Med. 2008; 24(3): 455-69.

177） Asikainen TM, Kukkonen-Harjula K, Miilunpalo S. Exercise for health for early postmenopausal women: a systematic review of randomised controlled trials. Sports Med. 2004; 34(11): 753-78.

178） St-Onge MP, Gallagher D. Body composition changes with aging: the cause or the result of alterations in metabolic rate and macronutrient oxidation? Nutrition. 2010; 26(2): 152-5.

179) Krems C, Luhrmann PM, Strassburg A, Hartmann B, Neuhauser-Berthold M. Lower resting metabolic rate in the elderly may not be entirely due to changes in body composition. Eur J Clin Nutr. 2005; 59(2): 255-62.
180) Groessl EJ, Kaplan RM, Blair SN, et al. A cost analysis of a physical activity intervention for older adults. J Phys Act Health. 2009; 6(6): 767-74.
181) Nelson ME, Rejeski WJ, Blair SN, et al. Physical activity and public health in older adults: recommendation from the American College of Sports Medicine and the American Heart Association. Med Sci Sports Exerc. 2007; 39(8): 1435-45.
182) Hanson ED, Srivatsan SR, Agrawal S, et al. Effects of strength training on physical function: influence of power, strength, and body composition. J Strength Cond Res. 2009; 23(9): 2627-37.
183) Zinna EM, Yarasheski KE. Exercise treatment to counteract protein wasting of chronic diseases. Curr Opin Clin Nutr Metab Care. 2003; 6(1): 87-93.
184) Phillips BE, Hill DS, Atherton PJ. Regulation of muscle protein synthesis in humans. Curr Opin Clin Nutr Metab Care. Oct 27, 2011.
185) Hurley BF, Hanson ED, Sheaff AK. Strength training as a countermeasure to aging muscle and chronic disease. Sports Med. 2011; 41(4): 289-306.
186) Brandi ML. An overview of osteoporosis: from genetics to clinics. Aging Clin Exp Res. 2011; 23(2 Suppl): 3-5.
187) Dempster DW. Osteoporosis and the burden of osteoporosis-related fractures. Am J Manag Care. 2011; 17 Suppl 6: S164-9.
188) Parker BA, Kalasky MJ, Proctor DN. Evidence for sex differences in cardiovascular aging and adaptive responses to physical activity. Eur J Appl Physiol. 2011; 110(2): 235-46.
189) Hawkins S, Wiswell R. Rate and mechanism of maximal oxygen consumption decline with aging: implications for exercise training. Sports Med. 2003; 33(12): 877-88.
190) Ward SA, Parikh S, Workman B. Health perspectives: international epidemiology of ageing. Best Pract Res Clin Anaesthesiol. 2011; 25(3): 305-17.
191) Muller MJ, Bosy-Westphal A, Later W, Haas V, Heller M. Functional body composition: insights into the regulation of energy metabolism and some clinical applications. Eur J Clin Nutr. 2009; 63(9): 1045-56.
192) Müller MJ, Bosy-Westphal A, Kutzner D, Heller M. Metabolically active components of fat-free mass and resting energy expenditure in humans: recent lessons from imaging technologies. Obes Rev. 2002; 3(2): 113-22.
193) Heymsfield SB, Thomas D, Nguyen AM, et al. Voluntary weight loss: systematic review of early phase body composition changes. Obes Rev. May 30, 2010.
194) Baron AD, Brechtel G, Wallace P, Edelman SV. Rates and tissue sites of non-insulin- and insulin-mediated glucose uptake in humans. Am J Physiol. 1988; 255: E769-74.
195) Mikulski T, Ziemba A, Nazar K. Metabolic and hormonal responses to body carbohydrate store depletion followed by high or low carbohydrate meal in sedentary and physically active subjects. J Physiol Pharmacol. 2010; 61(2): 193-200.
196) King DS, Dalsky GP, Clutter WE, et al. Effects of exercise and lack of exercise on insulin sensitivity and responsiveness. J Appl Physiol. 1988; 64(5): 942-46.
197) Mikines KJ, Sonne B, Tronier B, Galbo H. Effects of acute exercise and detraining on insulin action in trained men. J Appl Physiol. 1989; 66(2): 704-11.
198) Lindegaard B, Hansen T, Hvid T, et al. The effect of strength and endurance training on insulin sensitivity and fat distribution in human immunodeficiency virus-infected patients with lipodystrophy. J Clin Endocrinol Metab. 2008; 93(10): 3860-9.
199) Ross R, Janssen I, Dawson J, et al. Exercise-induced reduction in obesity and insulin resistance in women: a randomized controlled trial. Obes Res. 2004; 12(5): 789-98.
200) Geisler JG. Targeting energy expenditure via fuel switching and beyond. Diabetologia. 2011;

54(2): 237-44.
201） Short KR, Vittone JL, Bigelow ML, et al. Impact of aerobic exercise training on age-related changes in insulin sensitivity and muscle oxidative capacity. Diabetes. 2003; 52(8): 1888-96.
202） Solomon TP, Sistrun SN, Krishnan RK, et al. Exercise and diet enhance fat oxidation and reduce insulin resistance in older obese adults. J Appl Physiol. 2008; 104(5): 1313-9.
203） Zanuso S, Jimenez A, Pugliese G, Corigliano G, Balducci S. Exercise for the management of type 2 diabetes: a review of the evidence. Acta Diabetol. 2010; 47(1): 15-22.
204） Aucouturier J, Duche P, Timmons BW. Metabolic flexibility and obesity in children and youth. Obes Rev. 2011; 12(5): e44-53.
205） Ryan AS. Insulin resistance with aging: effects of diet and exercise. Sports Med. 2000; 30(5): 327-46.
206） Ferrucci L, Studenski S. Diabetes, muscles, and the myth of Ulysses' bow. Diabetes Care. 2009; 32(11): 2136-7.
207） Park SW, Goodpaster BH, Lee JS, et al. Excessive loss of skeletal muscle mass in older adults with type 2 diabetes. Diabetes Care. 2009; 32(11): 1993-7.
208） Srikanthan P, Karlamangla AS. Relative muscle mass is inversely associated with insulin resistance and prediabetes. Findings from the third National Health and Nutrition Examination Survey. J Clin Endocrinol Metab. 2011; 96(9): 2898-903.
209） Hubbard RE, Andrew MK, Fallah N, Rockwood K. Comparison of the prognostic importance of diagnosed diabetes, co-morbidity and frailty in older people. Diabet Med. 2010; 27(5): 603-6.
210） Ryder JW, Chibalin AV, Zierath JR. Intracellular mechanisms underlying increases in glucose uptake in response to insulin or exercise in skeletal muscle. Acta Physiol Scand. 2001; 171(3): 249-57.
211） Tresierras MA, Balady GJ. Resistance training in the treatment of diabetes and obesity: mechanisms and outcomes. J Cardiopulm Rehabil Prev. 2009; 29(2): 67-75.
212） Guo T, Jou W, Chanturiya T, Portas J, Gavrilova O, McPherron AC. Myostatin Inhibition in Muscle, but Not Adipose Tissue, Decreases Fat Mass and Improves Insulin Sensitivity. PLoS ONE. 2009; 4(3): e4937.
213） Hawley JA. Exercise as a therapeutic intervention for the prevention and treatment of insulin resistance. Diabetes Metab Res Rev. 2004; 20(5): 383-93.
214） Holten MK, Zacho M, Gaster M, Juel C, Wojtaszewski JF, Dela F. Strength training increases insulin-mediated glucose uptake, GLUT4 content, and insulin signaling in skeletal muscle in patients with type 2 diabetes. Diabetes. 2004; 53(2): 294-305.
215） Zierath JR. Invited review: Exercise training-induced changes in insulin signaling in skeletal muscle. J Appl Physiol. 2002; 93(2): 773-81.
216） Wadden TA, Butryn ML, Wilson C. Lifestyle modification for the management of obesity. Gastroenterology. 2007; 132(6): 2226-38.
217） Marcus BH, Dubbert PM, Forsyth LH, et al. Physical activity behavior change: issues in adoption and maintenance. Health Psychol. 2000; 19(1 Suppl): 32-41.
218） Garrett S, Elley CR, Rose SB, O'Dea D, Lawton BA, Dowell AC. Are physical activity interventions in primary care and the community cost-effective? A systematic review of the evidence. Br J Gen Pract. 2011; 61(584): e125-33.
219） Muller-Riemenschneider F, Reinhold T, Willich SN. Cost-effectiveness of interventions promoting physical activity. Br J Sports Med. 2009; 43(1): 70-6.
220） Muller-Riemenschneider F, Reinhold T, Nocon M, Willich SN. Long-term effectiveness of intervenetions promoting physical activity: a systematic review. Prev Med. 2008; 47(4): 354-68.
221） Nyenwe EA, Dagogo-Jack S. Metabolic syndrome, prediabetes and the science of primary prevention. Minerva Endocrinol. 2011; 36(2): 129-45.
222） Wadden TA, West DS, Delahanty L, et al. The

Look AHEAD study: a description of the lifestyle intervention and the evidence supporting it. Obesity. 2006; 14(5): 737-52.
223） Herman WH, Hoerger TJ, Brandle M, et al. The cost-effectiveness of lifestyle modification or metformin in preventing type 2 diabetes in adults with impaired glucose tolerance. Ann Intern Med. 2005; 142(5): 323-32.
224） Hernan WH, Brandle M, Zhang P, et al. Costs associated with the primary prevention of type 2 diabetes mellitus in the diabetes prevention program. Diabetes Care. 2003; 26(1): 36-47.
225） McCall A, Raj R. Exercise for Prevention of Obesity and Diabetes in Children and Adolescents. Clin Sports Med. 2009; 28(3): 393-421.
226） DPPRG. Within-trial cost-effectiveness of lifestyle intervention or metformin for the primary prevention of type 2 diabetes. Diabetes Care. 2003; 26(9): 2518-23.
227） Loveman E, Frampton GK, Shepherd J, et al. The clinical effectiveness and cost-effectiveness of long-term weight management schemes for adults: a systematic review. Health Technol Assess. 2011; 15(2): 1-182.
228） Wu S, Cohen D, Shi Y, Pearson M, Sturm R. Economic analysis of physical activity interventions. Am J Prev Med. 2011; 40(2): 149-58.
229） Heran BS, Chen JM, Ebrahim S, et al. Exercise-based cardiac rehabilitation for coronary heart disease. Cochrane Database Syst Rev. 2011; 7: CD001800.
230） Giada F, Biffi A, Agostoni P, et al. Exercise prescription for the prevention and treatment of cardiovascular diseases: part I. J Cardiovasc Med. 2008; 9(5): 529-44.
231） Thomas DE, Elliott EJ, Naughton GA. Exercise for type 2 diabetes mellitus. Cochrane Database Syst Rev. 2006; 3: CD002968.
232） Strasser B, Siebert U, Schobersberger W. Resistance training in the treatment of the metabolic syndrome: a systematic review and meta-analysis of the effect of resistance training on metabolic clustering in patients with abnormal glucose metabolism. Sports Med. 2010; 40(5): 397-415.
233） Umpierre D, Ribeiro PA, Kramer CK, et al. Physical activity advice only or structured exercise training and association with HbA1c levels in type 2 diabetes: a systematic review and meta-analysis. JAMA. 2011; 305(17): 1790-9.

【要旨日本語訳】

身体活動・運動と非感染性疾患

現代の環境は，明らかに，肉体労働を減らし，身体的な心地よさを高め，受動的な娯楽を楽しむ余裕を作り出すように設計されている。その結果，身体的不活動と体を動かさない娯楽は，脱工業化社会のいたるところで見られるようになった。人間の代謝，循環，筋・骨格システムは，生き残るために相当な身体活動を要する環境の中で進化してきた。このことを考えると，身体的不活動が多くの病気の原因となっていることは驚くにあたらない。疫学研究のエビデンスによれば，身体的不活動は重大なリスクであり，年齢，遺伝的要因，これまでの過ごし方（例えば，生活習慣），体組成，現在の生活習慣（例えば，食事，アルコール消費，喫煙）などとは独立して，すべての個人に対して重大な健康上の問題を引き起こす。身体的不活動は加齢変化を加速させ，心血管疾患，2 型糖尿病，他の病的変化（例えば，衰弱，骨粗鬆症，サルコペニア，肥満）などの非感染性疾患の頻度を増加させる。身体的不活動による非感染性疾患死亡率の相対危険度の上昇は，小児期より認められ，年齢とともに上昇する。しかし，身体活動・運動は非感染性疾患，あるいは座業がちな生活と加齢による他の病的な変化の発症を遅らせる，あるいは予防する。本総説では，健康維持，加齢に関連する疾病，非感染性疾患の予防に身体活動・運動が欠かせない要素であることを支持している観察研究および無作為化比較試験（RCT）を概説する。

（この日本語訳は，読者の利便性を考慮して著者の許可のもとに編集委員会が作成したもので，論文の一部ではありません。日本語訳が著者の意図にあっていない可能性がありますので，正確な意味を確認するためには原文をご確認ください）