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Physical activity, exercise, and chronic diseases: A brief review

Elizabeth Anderson, J. Larry Durstine *

Department of Exercise Science, University of South Carolina, Columbia, SC, USA

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ABSTRACT

Chronic diseases are the leading cause of death worldwide with increasing prevalence in all age groups, genders, and ethnicities. Most chronic disease deaths occur in middle-to low-income countries but are also a significant health problem in developed nations. Multiple chronic diseases now affect children and adolescents as well as adults. Being physically inactive is associated with increased chronic disease risk. Global societies are being negatively impacted by the increasing prevalence of chronic disease which is directly related to rising healthcare expenditures, workforce complications regarding attendance and productivity, military personnel recruitment, and academic success. However, increased physical activity (PA) and exercise are associated with reduced chronic disease risk. Most physiologic systems in the body benefit positively from PA and exercise by primary disease prevention and secondary disease prevention/treatment. The purpose of this brief review is to describe the significant global problem of chronic diseases for adults and children, and how PA and exercise can provide a non-invasive means for added prevention and treatment.

Introduction

A chronic disease is an illness that is not contagious, usually of long duration, progresses slowly, and is typically a result of genetics, environment, or poor lifestyle.[1] In 1990, more than 28 million (57%) of all global deaths were caused by chronic disease.[2] This number increased to 36 million (63%) of all global deaths in 2008[3] and 39 million (72%) of all global deaths in 2016[4] (Fig. 1). Even though life expectancy estimates have consistently risen for the last two centuries,[5,6] current estimations support a potential decline in life expectancy for future generations due to an increase in various chronic diseases such as lower respiratory disease, obesity, cancer, cardiovascular disease (CVD), diabetes, and stroke.[7] Presently, the literature supports that the incorporation of daily physical activity (PA) and exercise into one's lifestyle will reduce risk for chronic diseases and mortality while providing a means for primary disease prevention.[8] Furthermore, once a chronic illness is diagnosed, treatment is better managed when PA and exercise are part of the disease medical management plan. In either case of disease prevention or treatment, PA and regular exercise provide a higher quality of life and perhaps increased longevity.[9]

Although altering disease risk factors reduces overall chronic disease risk, modifiable risk factors such as sedentary behavior are associated with an increased risk for chronic disease.[10] Non-modifiable risk factors are traits that cannot be changed such as age, ethnicity, and genetics. However even though not altered directly, genes are strongly influenced by the environment and lifestyle affecting gene expression.[11] Modifiable risk factors are positively influenced by lifestyle such as daily PA, regular exercise, healthy diet, social engagement, spirituality, and stress management.[12] However, other modifiable risk factors exist that are not directly related to lifestyle but negatively influence chronic disease risk such as education level, socioeconomic status, and employment. PA and regularly practiced exercise positively influence risk factors for chronic diseases such as CVD, type 2 diabetes, obesity, and cancer.[13–19] Thus, the purpose of this brief review is to describe the global chronic disease problem for adults and children, describe the social-economic impact of chronic disease, and how PA and exercise can provide a non-invasive role for added chronic disease prevention and treatment. To achieve this purpose, a literature search was conducted using Pubmed, Medline, and Google Scholar databases. Search terms used were physical activity, exercise, multiple chronic diseases, chronic disease prevalence measures, and healthcare economy. In addition, the reference lists from systematic reviews incorporating PA and exercise and chronic disease were also reviewed.

The Rise of Chronic Disease

Diseases have always plagued humans. Infectious diseases remain a primary focus for prevention and treatment.[20] Over time, the incidence

* Corresponding author. 921 Assembly St., Columbia, SC, 29208, USA.
E-mail address: LDURSTIN@mailbox.sc.edu (J.L. Durstine).

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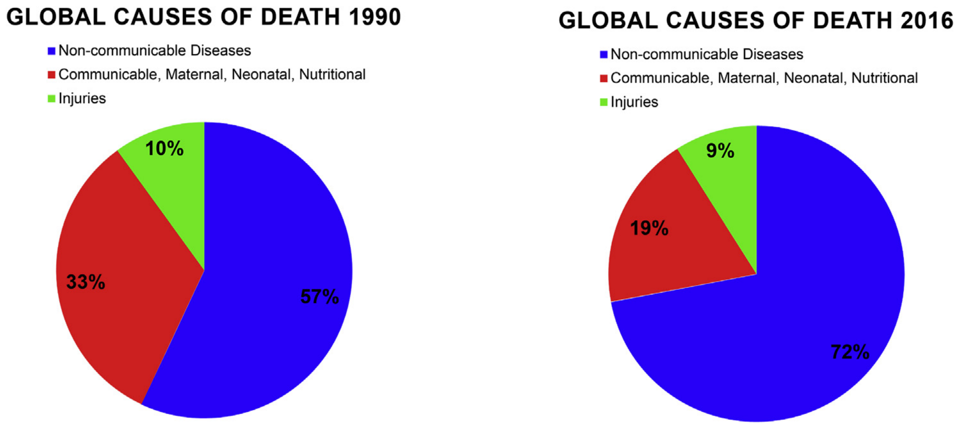

Fig. 1. Global Causes of Death.
Global causes of death have shifted from communicable to non-communicable diseases. As communicable disease prevention and treatment has improved, deaths caused by non-communicable disease have increased and continues to rise.
The information for developing this figure was taken from Murray and Lopez. The Lancet. 1997 and Naghavi et al., The Lancet. 2017.

and mortality rates for infectious diseases have dropped with advancements of vaccinations, antibiotics, sanitation, and the development of procedures for general infectious disease prevention.[21] The reduction of infectious diseases is associated with decreased morbidity and mortality resulting in an increase in life expectancy.[22] However, unanticipated consequences followed the gain in life years including a shift in the world's health burden from infectious to non-communicable diseases (NCDs) such as CVD.[4]

Many developing countries now experience the burden of both infectious and chronic disease rather than seeing a replacement of infectious disease with chronic disease. For example, India has the highest number of diabetic cases in the world[23] while also having the highest number of certain infectious diseases such as tuberculosis every year.[24] In this same regard, infectious diseases in South Africa account for almost the same number of deaths as chronic disease.[25]

In the past, chronic diseases were usually considered a problem only in developed countries.[26] However, 80% of deaths in low- and middle-income countries are now caused by chronic diseases.[26–28] Low- and middle-income countries are shown to have four times the mortality rate from NCDs than high-income countries.[22] Ischemic heart disease and stroke represented 85% of CVD deaths and 28% of all-cause mortality in developing nations.[26] Diabetes prevalence is expected to increase from about 400 million to 600 million globally by the year 2035 with most of this increase occurring in low-to middle-income countries.[29] Cancer prevalence crosses all global economic gaps with 57% of the reported cancer cases occurring in low-to middle-income countries and 43% in developed nations.[30] In China for example, cancer is the leading cause of death and is accounts for 25% of all deaths.[31,32]

Another global trend, especially in low-to middle-income countries, is the rate at which obesity prevalence has increased in recent decades. Currently, about 2 billion adults globally (approximately 25–33% of the world's population) are overweight and another 33% are obese. Obesity is associated with negative health implications and is a well-established risk factor for chronic diseases including CVD, type 2 diabetes, and certain cancers.[33] In the United States, obesity prevalence (BMI $\geq$30) has more than doubled in the last two decades as has severe obesity (BMI $\geq$40). These trends lead to future predictions of a 33% increase in obesity and a 9% increase in severe obesity by 2030.[34] Similar trends are seen across the globe. For instance, obesity prevalence in North and South America more than doubled between 1980 and 2015 with a 64% prevalence of overweight.[35] In Europe, approximately 60% of the population are considered overweight and 23% are obese.[35]

Countries once unaffected by increasing obesity now struggle with elevated obesity rates. For example, China has reported a significant increase in the number of obesity cases.[36] While the proportion of the Chinese population classified as obese is relatively low (5%), China currently is ranked as second in the world with 250 million adults classified as overweight and another 40 million obese.[36] Furthermore, the prevalence of overweight and obese children in China has more than doubled in the last 20 years.[37] India has 135 million people affected by obesity with prevalence rates varying between states from 12 to 31%.[38] These rates are expected to increase especially in middle-to low-income countries.[39] Other obesity-related NCD rates such as CVD, type 2 diabetes, and cancer will also continue to rise and present a significant global health problem[10,40–42] (Fig. 2).

Socio-Economic Impact of Chronic Disease

Chronic diseases are an increasing worldwide concern that has tremendous social implications. In 2013, global healthcare costs for CVD, stroke, type 2 diabetes, breast cancer, and colon cancer were an estimated $54 billion in international currency (INT).[43] Globally, approximately $21 billion INT in productivity losses are due to physical inactivity and chronic disease. Physical inactivity cost alone is associated with chronic disease and early death and is estimated at $145 billion INT.[43]

Increased occurrence of chronic diseases also has had a significant impact on the workforce. Individuals having chronic diseases are either not employed or work fewer hours and are less productive when compared to healthy workers.[44] As chronic disease incidence rates increase, the likelihood of experiencing productivity losses and increases in welfare expenditures continue to rise.[45]

Global military workforces are dramatically affected. Militaries from around the world are experiencing a major decline in the ability to recruit, and obesity is the primary challenge for this recruiting dilemma. In North America, Asia, Europe, and Australia, approximately 50% of all military-aged adults (18–29 years) are overweight or obese.[46] Young adults are reported to have low aerobic fitness that is associated with obesity. As a result, young adults wanting to enter the military will have difficulty meeting required physical fitness tests.[46] In addition, young adults show less interest in enlisting as a result of an inactive lifestyle.[46]

A decline in academic performance is associated with the rise in chronic disease in children, adolescents, and young adults. Higher course grades and academic success are associated with regular classroom attendance.[47] However, present data supports an inverse relationship between school attendance and standard test scores with being overweight and obese. More research is needed to determine whether these findings are due to social and behavioral factors related to obesity or the condition itself.[48] Diabetes is also linked to lower academic test scores as well as a lower ability to focus.[48] Lower test scores in grade school, high school, and college are associated with a decline in college degree attainment. In college and university settings, an association was reported between lower graduation rates with overweight, obesity, and/or other chronic diseases.[49]

Because chronic diseases are related to reduced academic success, global society is affected. For example, college graduates are less likely to

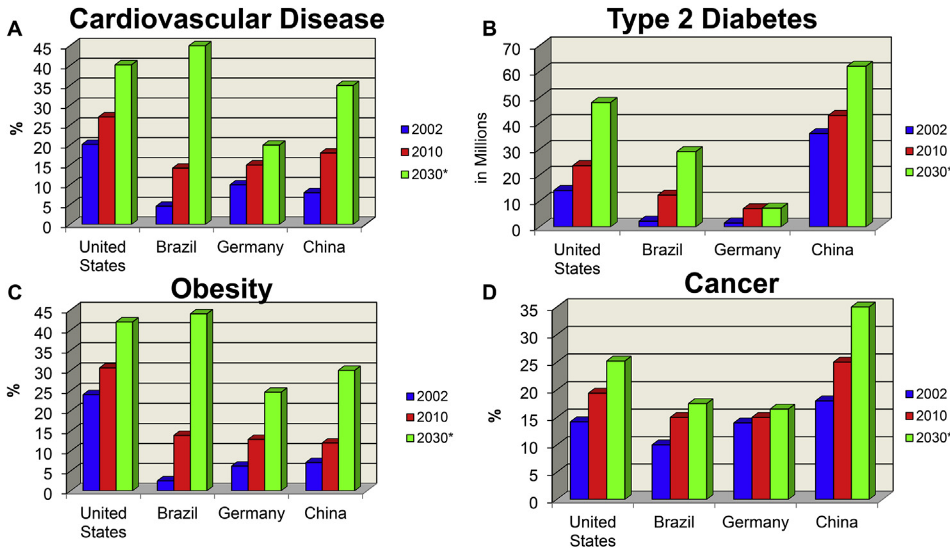

Fig. 2. Chronic Disease Trends.
Chronic disease trends from 2002 to 2010 and an estimation for 2030 including A) Cardiovascular disease, B) type 2 diabetes, C) obesity, and D) cancer in the United States, Brazil, Germany, and China.
Figure taken from Durstine, Gordon, Wang, Luo. J Sport Health Sci. 2013. (Permission obtained).

utilize welfare programs,[50] likely to vote at all levels of government,[51] and likely to volunteer and donate to charities.[52] As the global prevalence of chronic disease continues to rise, healthcare expenditures will also rise, productivity losses will become commonplace, national defenses will have greater difficulty in recruiting, academic success will likely be reduced, and global society will suffer.

Youth and Chronic Disease

Middle-aged and older adults have historically been associated with a greater risk for chronic disease when considering that advanced age is a well-established risk factor.[9] Nevertheless, a rise in chronic diseases are found in younger populations.[53] Presently, a greater research focus is placed on the obesity rise in children and adolescents. In the United States, the prevalence of obese children (≥95th percentile) aged 2–19 years has dramatically increased from 5% in the 1960s, to 11% in 1994, to 15% in 2000,[54] to 17% in 2014,[55] and to 19% in 2016.[56] Globally, similar trends are seen for overweight and obesity prevalence in children.[53] Gender differences are also noted; young girls frequently have higher obesity prevalence than young boys. However, overweight, obesity, and gender differences do vary by country and culture, and is a global concern[53] (Fig. 3).

Overweight and obesity in youth are associated with an increased risk for other chronic health problems. Children and adolescents are at an increased risk for hypertension when body weight is elevated, especially if body weight exceeds the 95th percentile.[57] The prevalence of high blood pressure in adolescents varies between countries but is more prevalent in middle-to low-income nations.[58] In Portugal, the prevalence of high blood pressure and borderline high blood pressure is about 8% in preschool aged children (3–6 years old) who are overweight/obese.[59] Globally, hypertension prevalence in youth aged 8–17 years is approximately 11%.[55,58] Overweight and obesity in youth is also associated increased risk for abnormal blood lipid levels including elevated total cholesterol and low-density lipoprotein (LDL)-cholesterol, and low levels of high-density lipoprotein (HDL)-cholesterol. The prevalence of abnormal blood lipid levels in adolescents between 12 and 19 years is 20% among overweight and obese youth.[60]

Metabolic syndrome (MetS) is the clustering of chronic conditions that relate to one another and is associated with an increased CVD risk. The conditions associated with the diagnosis of MetS include high blood pressure, hyperglycemia, central obesity, elevated LDL-cholesterol, elevated triglycerides, and low HDL-cholesterol. Present findings support non-alcoholic fatty liver disease as having a role in insulin resistance in obese adolescents.[61] Describing, diagnosing, and treating MetS is very different for children than for adults, and implications for care are not completely understood.[62] However, MetS in children and adolescents is a serious health problem. Because the mechanisms for MetS in children is not completely understood, prevalence and incidence estimations for youth are difficult to determine. Nevertheless, attempts to develop prevalence estimations have ranged in obese youth from 19 to 35%,[55,60] and these values are increasing worldwide[61] requiring immediate attention to provide proper treatment in children having cardiometabolic

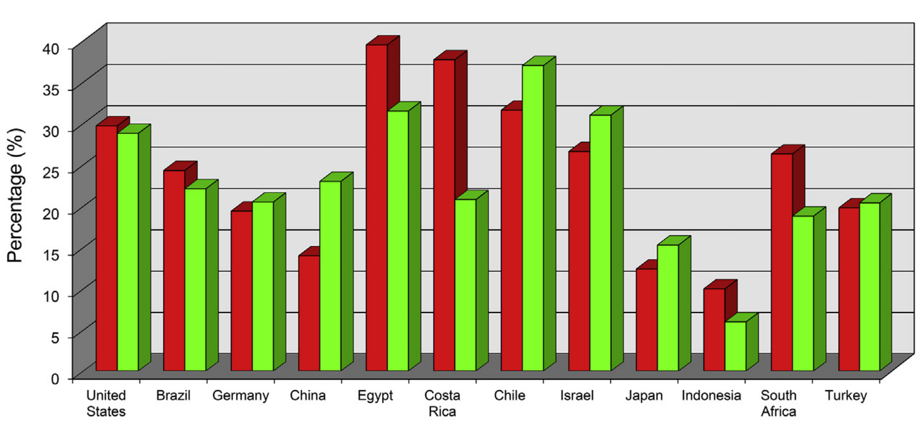

Fig. 3. Prevalence of Overweight and Obesity in Children - 2013.
Overweight and obesity prevalence varies between countries and cultures of the world. In 2013, Egypt and Costa Rica had the highest prevalence of young obese girls while Chile and Israel have the highest prevalence of young obese boys.
The information for developing this figure was taken from Ng et al., The Lancet. 2014.

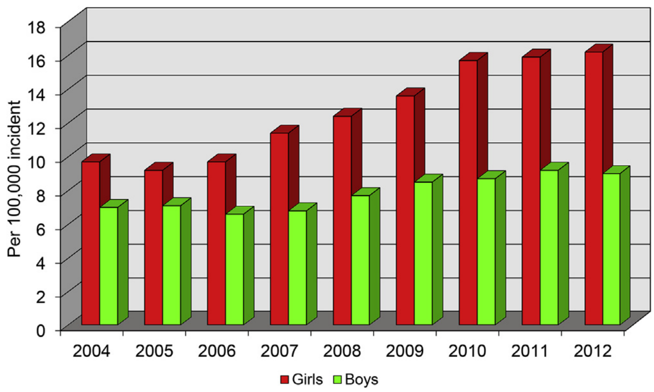

Fig. 4. Youth Type 2 Diabetes Incidence in the United States.
The increase in Type 2 diabetes incidence in youth.
The information for developing this figure was taken from Mayer-Davis et al. NEJM. 2017.

risk factors.[62]

Prediabetes and type 2 diabetes have become an increasing concern among young people, especially among overweight and obese youth.[63,64] In the United States for 2008, approximately 25% of adolescents between the ages of 12–19 years had prediabetes.[55,60] Between 2004 and 2012, the United States incidence rate for type 2 diabetes in children and youth between the ages of 10–19 years increased by almost 5% each year with greater incidence rates in young girls[65] (Fig. 4). Most children diagnosed with diabetes have poor glycemic control and have higher treatment failure rates.[66] Similar trends for pediatric type 2 diabetes are seen throughout the world. The United Kingdom had an incidence increase of 6 children per 100,000 each year between 1994 and 1998 to 33 children per 100,000 each year between 2009 and 2013.[63] Type 2 diabetes in Asia overtook type 1 diabetes as the predominant form of diabetes in children from Hong Kong and Taiwan.[67]

While childhood cancer mortality rates in the United States have fortunately declined, incidence rates unfortunately continue to rise (Fig. 5). The incidence rates of pediatric cancers rose from an annual increase of 0.6% in 1975 to 1.2% in 2010.[68] Even though evidence supports a link between obesity and multiple types of cancer in adults,[40] the same link in children is not well established. Preliminary data does suggest that certain childhood cancers may indeed be related to obesity,[69] but further research in this area is needed. Although, evidence does support that children are at an increased risk of mortality if they are obese at diagnosis and during treatment for cancer.[70,71] Childhood cancer survivors have a greater risk for adult obesity and other chronic diseases including cancer relapse within 10 years.[71] As both childhood cancer rates and childhood obesity rates rise, mortality rates and the risk for adult obesity also increase, as does the risk for relapse and/or other future chronic diseases.

Physical inactivity

Physical inactivity is associated with increased chronic disease risk.[72–75] Moreover, the literature supports that lower morbidity and mortality rates are associated with maintaining moderate levels of PA and physical fitness.[17] Support data come from epidemiologic and longitudinal studies reporting reduced disease risk following lifestyles incorporating daily PA and having higher cardiorespiratory fitness.[76–78]

Many countries and organizations such as the American College of Sports Medicine and the World Health Organization (WHO) have released PA guidelines to provide science-based recommendations for PA and exercise. These guidelines are for young children, adolescents, adults, elderly, and for individuals with chronic diseases. These guidelines consider different PA dimensions (mode, frequency, duration, and intensity) and domains (leisure time, transportation, occupation, and domestic activity) to allow for individualization.[55,60] The different PA domains impact health and should be considered separately. For instance, increasing one PA domain (such as occupation activity) tends to cause another domain (such as leisure time activity) to decline[55,60] and could cause an overall increase in sedentary time. Increasing sedentary time and sleep is inversely related to poor health and premature mortality.[79,80]

Physical inactivity prevalence is the percentage of individuals who do not perform sufficient daily PA to meet the PA and exercise guidelines of at least 150 min of moderate-intensity aerobic PA per week or at least 75 min of vigorous PA per week for adults[81] and at least 60 min of moderate-to vigorous-intensity daily PA for children aged 5 to 17.[82] Recent findings show an increase in physical inactivity globally.[78] This increase in physical inactivity is associated with technology advances including increased use of television, computer, mobile devices, and video games.[83] In the United States, only 42% of children between the ages of 6–11 years meet the WHO PA guidelines. Approximately 14% of adolescents report being regularly physically inactive while only 8% of 12- to 19-year-olds meet recommended PA levels.[55,60] In this same regard, 30% of adults did not engage in enough PA during leisure time. Inactivity prevalence does increase with age: 25% of young adults (18–44 years), 33% of middle-aged adults (45–64 years), 36% of older adults (65–74 years), and 53% of the elderly (≥75 years) are reported

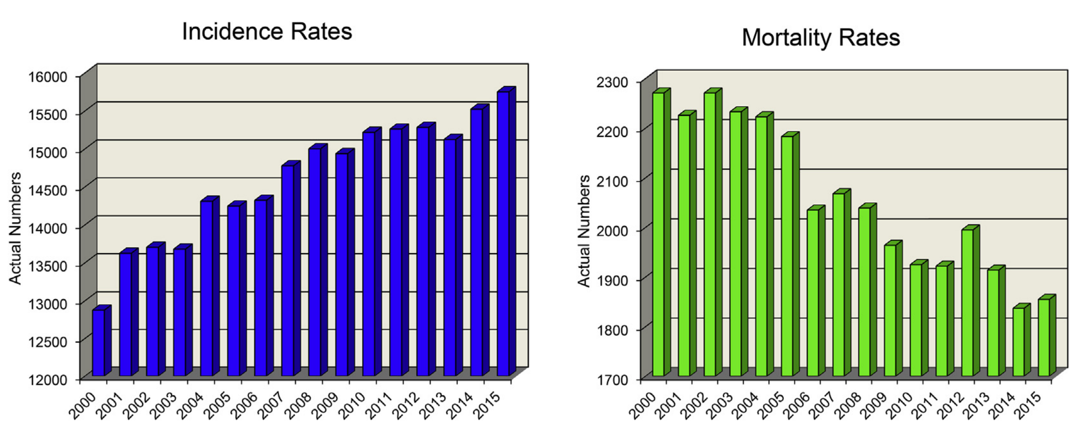

Fig. 5. Childhood Cancer Incidence and Mortality Rates in the United States.
Incidence and Mortality rates in childhood cancer in the US between 2000 and 2015, including all types of cancer between the ages of 0–19 years, both male and female patients of all races and ethnicities.
The data provided for developing this figure was taken from The United States Cancer Statistics [1999–2015] at the Center for Disease Control and Prevention.

inactive.[60,84]

Low PA levels result in harmful and even detrimental consequences. For example, if type 2 diabetic patients increase their sedentary time by just 60 min/day, mortality risk could increase by 13%.[72] Additional problems arise with a physically inactive lifestyle including impaired circulation, osteoporosis, arthritis and/or other skeletal disabilities, diminished self-concept, greater dependence on others for daily living, reduced opportunity and ability for normal social interactions, and overall diminished quality of life.[85]

Health benefits of PA and exercise

Chronic disease prevention, rehabilitation/treatment, and other health benefits of daily PA and exercise are continually being investigated with new information being found and reported.[3,74,86,87] A question often asked is how PA and exercise provide for chronic disease prevention and treatment. Because PA and exercise impact many health concerns in diverse ways, the answer to this question is dependent upon each condition and the severity of the disease. One way to understand how PA and exercise can improve health is best realized when comparing the effects of PA to medication use on heart rate at rest and during exercise. For example, beta-blockers are typically used to treat different CVDs and will lower resting, submaximal, and maximal exercise heart rates. Daily PA and exercise also result in lower resting and submaximal heart rates but not maximal heart rate. The use of beta blockers and PA and exercise participation both have the same effect on heart rate except for maximal heart rate. While conventional medications treat symptoms or alter physiologic functioning in a synthetic or non-physiologic fashion, PA and exercise cause the physiologic systems of the body to function optimally. Thus, daily PA and exercise act as a natural treatment for many diseases. For example, PA and exercise participation improves myocardial function[88,89] by increasing myocardial strength and oxygen delivery[90] while decreasing myocardial oxygen demand.[91] Other cardiovascular improvements associated with daily PA and exercise include lower systolic blood pressure and lower blood catecholamine levels at rest and at all submaximal exercise levels, hence aiding in prevention and treatment of CVD risk factors. These adaptations cause improved systemic functioning and overall individual health without the potential side effects of traditional medicines. PA and exercise participation function both in prevention and treatment for chronic disease.[92] The cardiovascular system is not the only physiologic system to benefit from PA and exercise. The scientific literature supports that most if not all physiologic systems are positively altered by PA and exercise.[17,87,93,94] Thus, exercise can be viewed as a medicine.

Current research literature supports the concept of a dose-response curve for PA and exercise with high person-to-person variability.[17,95,96] The concept of an exercise dose-response curve for health benefits was first introduced for PA and exercise in two landmark epidemiological studies.[97,98] These studies demonstrated that increases in PA and physical fitness are associated with decreased all-cause mortality. Other clinical investigations also successfully depicted the dose-response curve.[99] For example, older men and women have significantly lower mortality risk when moderate cardiorespiratory fitness levels are maintained.[100]

Other means for optimizing bodily functioning by PA and exercise are found in the literature. Quality of life is increased when PA and exercise are included as part of the medical management plan for individuals living with chronic disease.[101–103] Improved functional capacity and muscular strength, reduced inflammation, increased HDL-cholesterol, and body weight reductions are a result of PA and exercise in children and adults.[104] The implementation of daily PA and exercise prevention interventions support an 80% reduction in CVD risk,[15] 90% reduction in type 2 diabetes risk,[18] 33% reduction in cancer risk,[17] and in some cases reductions in all-cause mortality.[13] Results from exercise-based cardiac rehabilitation programming found no effect on all-cause mortality but a greatly reduced cardiac mortality.[19,103,105] Also reported is that an exercise-based cardiac rehabilitation program, when compared to a usual care control group, reduced the need for percutaneous transluminal coronary angioplasty by 19%, reductions in nonfatal myocardial infarctions by 21%, and cardiac mortality reductions by 26%.[106] A review of 63 studies incorporating exercise programming as part of cardiac rehabilitation demonstrate reduced cardiovascular mortality by 8–10% and hospital re-admission by 26–31%.[19] Furthermore, myocardial infarction patients enrolled in 3–6 months of cardiac rehabilitation programming experienced an 11–36% increase in aerobic functional capacity, improved quality of life, and decreased risk for subsequent cardiac events.[15,16]

Health improvements seen with PA and exercise are not limited to the cardiovascular system. After becoming physically active, type 2 diabetics improve their overall insulin sensitivity and positively altered skeletal muscle proteins and enzymes associated with glucose metabolism and insulin signaling.[107] As a result, structured exercise programming is an important part of a diabetic's medical management plan.[104,108] Another health benefit example is the inverse relationship found between cancer mortality and PA and exercise. Cancer mortality rates are reduced by 7–17% with increased PA.[14] Depression and anxiety symptoms are also improved with daily PA and exercise.[109]

Additional health benefits exist for preventing disease complications and improved quality of life. Daily PA and exercise enhances bone health by increasing bone mineral density. These interventions are recommended in the prevention and treatment of osteoporosis and to decrease the risk of future bone fractures.[110,111] Also, PA and exercise improve the immune system enabling the body to fight infectious diseases resulting in less overall susceptibility to sicknesses.[112] As part of this immune adaptation, lymphatic function is enhanced and inflammation is reduced by decreasing inflammatory cell accumulation.[113]

In conjunction with a proper nutritional diet, PA and exercise exert synergistic effects to improve infertility which is often associated with obesity. Infertility linked to hypogonadism in obese men is improved with daily PA and exercise.[114] Ovulation and pregnancy rates are increased by PA and exercise in overweight and obese women who struggle with infertility.[115] PA and exercise have a positive influence during pregnancy for both the mother and the baby. Present literature supports daily PA and exercise as safe and improves maternal and fetal well-being.[116,117] Women who exercise while pregnant avoid excessive weight gain[116] and improve fetus nervous system.[118] PA and exercise during pregnancy can also decrease time spent in labor[119] and reduce the risk of having a large (≥4 kg body weight) newborn.[120]

PA and exercise induce molecular adaptations in multiple brain regions, improving functional and structural neural properties, allows for enhanced learning and skill acquisition,[121–123] and improves cognition in healthy adults[124] and in neurologically disabled adults.[123,125] An inverse relationship exists between the amount of PA and exercise with risk for developing dementia (including Alzheimer's) and Parkinson's disease.[122] PA and exercise is proposed to delay the onset of those conditions and is recommended as a preventative measure for cognitive decline and as part of the treatment/management plan.[122,126]

The portions of the brain most adaptable to change (i.e., memory/learning, emotion, etc.) are the first enhanced by PA and exercise.[123] Clearly, neurological deficits in addition to mental health conditions improve with PA and exercise[127] which in turn prevents or reduces other health conditions associated with poor stress management,[128] depression, and anxiety.[129,130]

Conclusion

Chronic diseases are the leading cause of death worldwide as disease incidence rates continue to rise. Most chronic disease deaths occur in middle-to low-income societies as well as in developed countries. As the prevalence of these diseases rise in adults, chronic diseases such as type 2 diabetes and obesity rise in youth and adolescents. Including PA and exercise into daily lifestyle activities provides multiple health benefits, promote societal growth, and provide long-term chronic disease prevention and treatment while improving overall global health. Thus, PA and exercise provide a non-invasive means for added chronic disease prevention and treatment. Though additional physiologic, biochemical, and molecular information regarding PA and exercise health benefits are useful, important areas for future research include how to get more people to overcome PA and exercise barriers, better understand the interaction of medications with PA and regular exercise, determine the mechanisms for MetS in children, design research projects that yield better MetS prevalence and incidence estimations for youth, and determine the mechanisms for certain childhood cancers and their relationships to other diseases such as obesity.

Conflicts of interest

The authors have no conflicts of interest to report.

Each authors' contributions

Each author contributed equally to the drafting of this manuscript. JLD provided an initial draft for the Introduction, – The Rise of Chronic Disease, – Health Benefits of Exercise, created Fig. 2, and was responsible for the overall editorial development. EA expanded on the initial drafts for the previously mentioned sections and wrote the sections on – Youth and Chronic Disease, – Physical Inactivity, – Socio-Economic Impact of Chronic Disease, and the Conclusion. EA created Figs. 1, Fig. 3, Fig. 4, and Fig. 5.

Submission statement

The manuscript has not been published and is not under consideration for publication elsewhere.

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