

## REVIEW

# Physical Activity in the Prevention of the Most Frequent Chronic Diseases: an Analysis of the Recent Evidence

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## Abstract

**Background:** Physical activity is widely recognized as a means for the primary prevention of chronic diseases as well as in patients' treatment and rehabilitation. Moreover, activity has beneficial effects on an individual's health and well-being. Despite the benefits of regular physical activity, the percentage of physically inactive adults in the world is high. Environmental and policy approaches aimed to increase physical activity require continual stress of the epidemiological evidence from studies investigating disease mechanisms as well as controlled clinical trials. **Purpose:** To update the evidence that physical activity/exercise is important for reducing the chronic diseases (cardiovascular and heart, diabetes, cancer, obesity, osteoporosis, and fall-related injuries, depression and emotional stress) and for mechanisms that may operate in the relation between physical activity and a disease risk. **Methods:** Research studies published from 2004 through to March 2007 were identified through a review of the literature available on the NLM PubMed, Medline, Current Contents, and Elsevier-Science Direct databases. **Results:** Recent evidence on physical activity/exercise and reduction of chronic major diseases incidence and rehabilitation of patients replicates previous findings. The strongest evidence exists for colon cancer, breast cancer, and cardiovascular diseases. The maximal magnitudes of the risk reduction reported were: 75% for breast cancer, 49% for cardiovascular and heart diseases, 35% for diabetes, 22% for colorectal cancer. Increased physical activity also prevented the weight gain associated with aging at least 2-times greater in individuals who were more active compared with those who were inactive. Limited new findings has been reported for the beneficial role of physical activity in fall-related injures, depression and emotional distress. **Conclusion:** Recent evidence confirms previous findings that engaging in moderate physical activity is very important for the primary prevention of chronic diseases, decreasing all causes of mortality and that exercise is one of the determinants for physical and psychological well-being. The current evidence provides further support that physical activity can suppress concentrations of  $17\alpha$ -estradiol in women.

**Key Words:** Physical exercise - cancer - cardiovascular diseases - type 2 diabetes - obesity - osteoporosis - mental health - prevention - mechanisms

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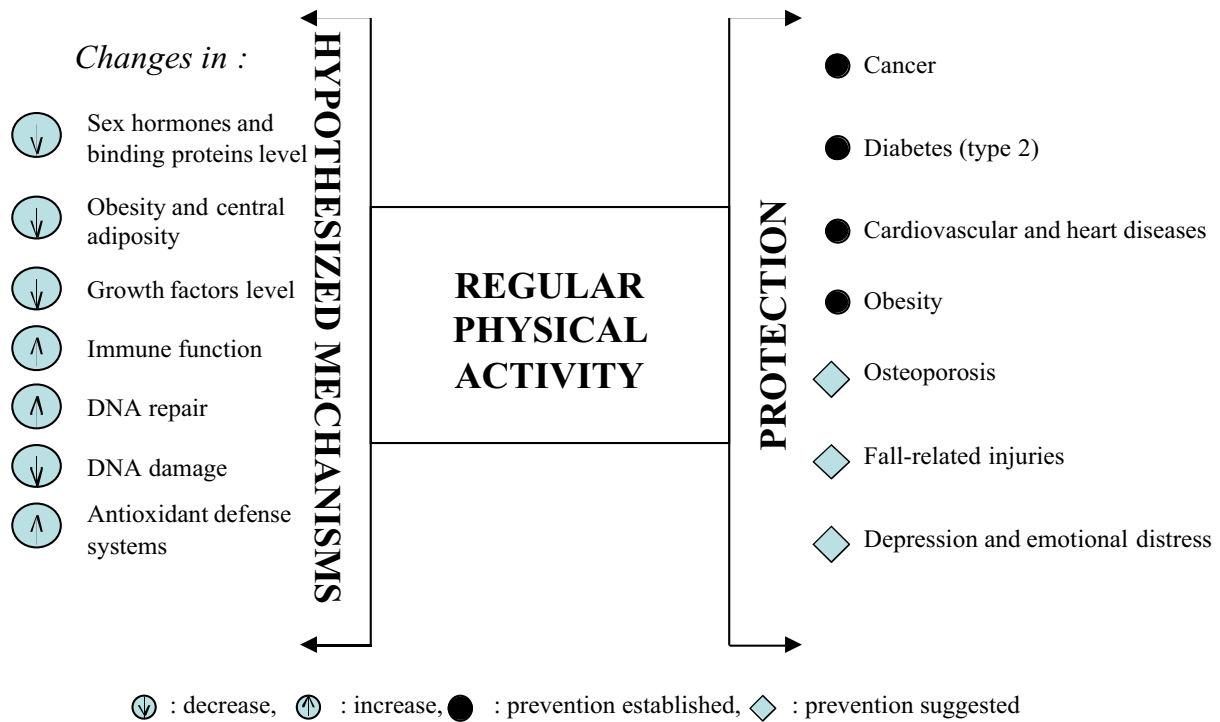
## Introduction

Regular physical activity is associated with enhanced health and well-being. The results of numerous studies have revealed that regular physical activity is widely recognized as a mean of preventing the occurrence of many chronic diseases and reduced risk of all-cause mortality (Blair et al., 1995; Lee et al., 1995; American College, 1998; Hulens et al., 2002; WHO, 2002; Lebrun et al., 2006). Research has shown reduced risk of cardiovascular and heart diseases, type 2 diabetes, some types of cancer, osteoporosis, fall-related injures, depression, and obesity (Bauman, 2004). For this reason, it has been observed a worldwide increase in health enhancing physical activity interest among researchers.

In spite of the importance of physical activity for health, most people have a sedentary lifestyle. It was estimated in 2000 that 74% of Americans failed to meet

recommended amounts of physical activity (i.e., 30 minutes per day of moderate intensity activity on  $\geq 5$  days per week, or 20 minutes of vigorous intensity activity on  $\leq 3$  days per week (Khan et al., 2002; Centers for Disease, 2003). Also, the recent 'World Health Report' of the World Health Organization (2003) states that more than 60% of adults can be classified as inactive in worldwide. In Poland, sedentary lifestyle is also common for the majority of society: 72.9% of adults declare a sedentary lifestyle and only 5.9% indicate a high level of physical activity (Drygas et al., 2001).

Very interesting data comes from meta-analyses of studies that quantified the impact of physical inactivity on the incidence of disease and estimated its direct cost (Colditz, 1999; Bricker et al., 2001; Stephenson et al., 2000). The studies have reported relative risks (RR) for inactive people versus active for conditions attributable to physical inactivity. The increased relative risks were



**Figure 1. Protective Effects of Physical Activity on Chronic Diseases and Hypothesized Biological Mechanisms for its Health Benefits**

reported for ischemic heart disease, osteoporosis and related injuries, and colon cancer (RR=2.0); diabetes, hypertension (type 2) (RR=1.5) (Colditz, 1999), stroke (RR=2.0) (Bricker et al., 2001), depression (RR=1.3) (Stephenson et al., 2000), breast cancer (RR=1.5) (Friedenreich, 2001). It is worth adding that physical inactivity and poor diet were estimated to be the second leading cause of total US death in 2000 (16.6%) following smoking (18.1%) (Mokdad et al., 2004). According to estimation by Garrett et al. (2004) of the direct cost of physical inactivity in 1.5 million adult Americans in 2000, 31% of cost related to colon cancer, heart disease, osteoporosis, and stroke as well as 12% costs of depression and anxiety were attributable to a lack of physical activity. Total costs of expenditures for medical treatment of six major diseases attributable to physical inactivity were high (\$ 83.6 million). The estimated total cost in USA (\$161 million) is very similar to direct health care costs in Australia (161 million), provided by the Australian Institute of Health and Welfare's Disease Costs and Impact Study attributed to physical inactivity in 1993-94 (Stephenson et al., 2000). Promotion of increased physical activity is an increasingly important public health priority. National physical activity campaigns have been organized in order to increase levels of physical activity through education in diverse media, classroom-based health education, community events, creation of walking trails, sports events (Khan et al., 2002; Ruskowska-Majzel et al., 2005).

Thus, it is important continually to update the evidence of health benefits from regular physical activity and sport participation as each year new studies identify strong and consistent associations. The purpose of the study was to cover novel findings on the association between physical activity and risk factors of chronic diseases coming in the

latest years, as illustrated schematically in Figure 1.

## Methods

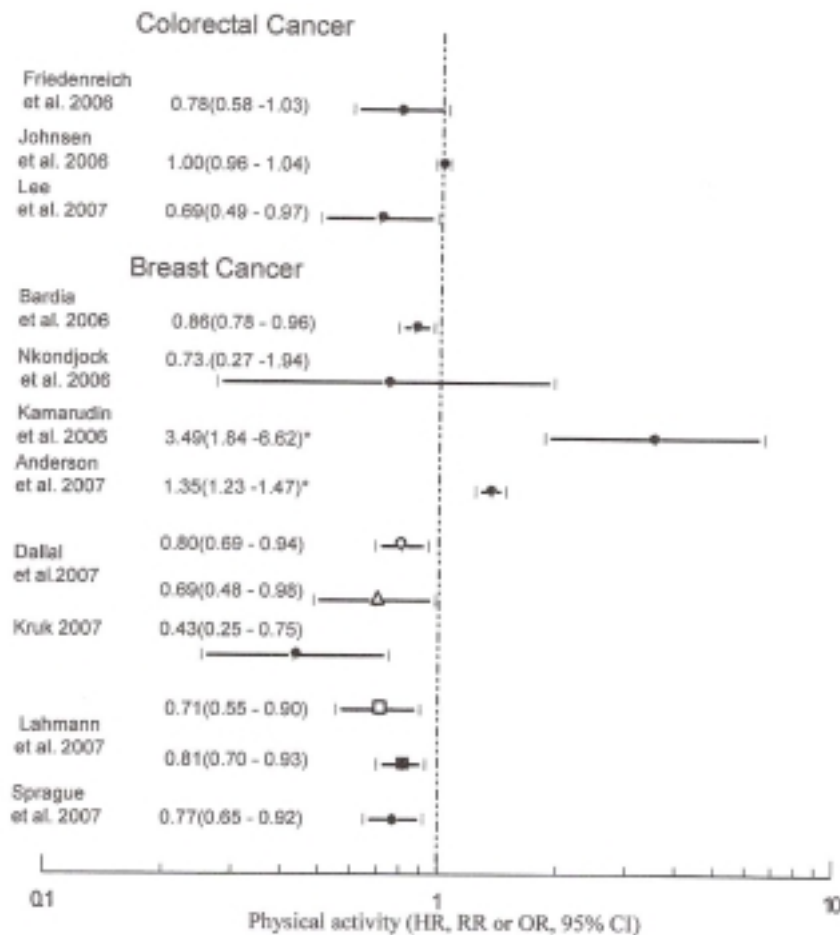
Literature searches of computer databases were performed from the period from 2004 including March 2007 (NLM, PubMed, Medline, Current Contents, Elsevier-Science Direct).

The search strategy included the terms physical activity, exercise, or physical fitness in sequence with the terms cardiovascular disease, heart disease, diabetes, cancer, fall-related injuries, obesity, osteoporosis, depression and emotional distress. Recently published articles on the mechanisms through which exercise exerts effects on chronic diseases were also identified. The relation between a potential risk factor for a disease and exercise/physical activity is most frequently explored in the literature by evaluating relative risk (RR) or odds ratio (OR).

## Results

### Cancer

The majority of epidemiologic studies have found an inverse association between physical activity and cancer risk. Levels of evidence on physical activity/exercise and cancer prevention are classified as follows: convincing, probable, possible and insufficient (Friedenreich & Orenstein, 2002; Hsia et al., 2005). Among the site-specific cancer studies consistence of scientific evidence for colon and breast cancer is strong and the most consistent and was classified as convincing (average risk reductions ranges from 40 to 50% for colon and from 30 to 40% for breast cancer), for endometrium evidence is weaker and less consistent and classified as 'probable' (average risk



**Figure 2. Relative Risk Estimates and 95% Confidence Intervals (CI) for Cancer Disease and Physical Activity.** All risk estimates are given for activity with the highest level compared with the lowest level (open square, premenopausal; closed square, postmenopausal; open circle, invasive cancer; open triangle, in situ cancer)

reductions ranges from 30 to 40%), for prostate and lung 'possible' (average risk reductions ranges from 10 to 30% for prostate and 30-40% for lung) (Friedenreich & Orenstein, 2002).

The protective effect of physical activity on cancer risk has been observed across different population and study design (reviewed recently by Monninkhof et al., 2007 and Kruk & Aboul-Enein 2006b, 2007).

Recent studies reaffirm the inverse correlation between physical activity and the cancer risk for colon and breast (Figure 2).

In the European study conducted by Friedenreich et al. (2006) (cohort of 413,044 participants, 1,094 cases of colon cancer and 599 cases of rectal cancer) multivariate HR of colon cancer was decreased by 22% among the most active participants compared with inactive and negative trend in the risk of colon cancer associated with physical activity was observed. The author found stronger risk reduction among active individuals with a BMI under 25kg/m<sup>2</sup> (HR=0.63, 95% CI=0.39-1.01) compared with the inactive. The most beneficial effect of physical activity was detected for right-sided colon cancer among moderately active and active participants with a BMI under 25kg/m<sup>2</sup> compared with inactive having BMI>30kg/m<sup>2</sup> (HR=0.38, 95% CI=0.21-0.68). However, author found no association between any type of physical activity and the rectal cancer risk.

In contrast, the study of a Danish middle-aged population (26,122 men, 28,356 women, 157 men and 140 women were diagnosed with colon cancer follow-up time 1993 to 2003) by Johnsen et al. (2006). The researchers found no association between the risk of colon cancer and occupational or recreational activity measured in energy expenditure or the time spent on six types of activity (sports, cycling, walking, gardening, house-work, do-it-yourself work) 'during summer and winter'. However, the authors found a borderline significant risk reductions when they examined the linear effect of number of activities in which participants were involved and the risk was adjusted for occupational activity (RR=0.88, 95% CI=0.78-1.00, P<sub>trend</sub>=0.053 for men and 0.87, 95% CI=0.76-1.00, P<sub>trend</sub>=0.051 for women).

In the most recent population-based study of Lee et al. (2007) of 65,022 Japanese men (154 proximal colon, 166 distal colon, 149 rectal cancer cases identified during 6 years of follow-up) a significant inverse correlation between the level of physical activity (time spending daily on heavy physical work or strenuous exercise, walking and standing) and the risk of developing colorectal cancer was found among men, only. In particular, the authors observed strong risk reduction in men for colon cancer (OR=0.58, 95% CI=0.39-0.87, P<sub>trend</sub>=0.006) and for proximal colon cancer (OR=0.29, 95% CI=0.14-0.60, P<sub>trend</sub><0.001). A lack of association for rectal cancer

corroborates findings of Friedenreich et al. (2006).

Evidence for an association between physical activity and breast cancer is weaker and less consistent than that found for colon cancer. The evidence from the majority of epidemiologic studies indicates a stronger and more consistent effect for risk reduction among postmenopausal women (Friedenreich, 2004).

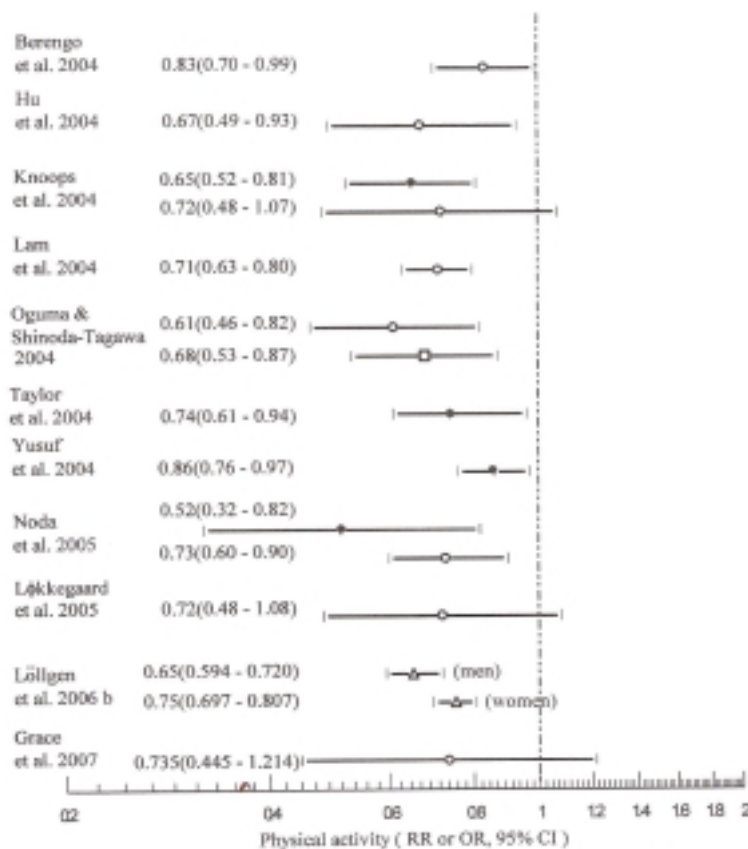
Recent reports confirm previous evidence (Fig. 2). Of eight recently published studies seven studies found statistically significant reduction in the relative breast cancer risk. The maximal magnitudes in the risk decrease change from 20 to 72% (Bardia et al., 2006; Kamarudin et al., 2006; Anderson et al., 2007; Dallal et al., 2007; Kruk, 2007; Lahmann et al., 2007; Sprague et al., 2007). In the Iowa Women's Health Study (USA) of 41,836 postmenopausal women (2,548 incident cases identified through 18 years follow-up) presented by Bardia et al. (2006) high levels of recreational activities were inversely associated with breast cancer risk. In addition, the authors found that risk reductions vary by estrogen receptor/progesterone receptor status of the tumor and a BMI value. A higher risk reduction was discovered in a case-control study in Kuala Lumpur (Malaysia), (203 breast cancer cases, 203 controls) carried out by Kamarudin et al. (2006). In their study women who did not exercise regularly have 3.5 times higher risk of getting breast cancer in comparison to those who exercised regularly. Also, the authors of a population-based case-control study of Polish women (Anderson et al., 2007) (2,386 cases, 2,502 controls, aged

25-74 years) reported increased by 35% RR for women of which average lifetime physical activity was <220 MET scores/wk for every year of life compared with those physically active (≥220 MET scores/wk).

In turn, in the California Teachers Study by Dallal et al. (2007) (110,599 women, 2,649 invasive and 593 in situ breast cancer cases) a 20% reduction of the risk of invasive breast cancer among women reported long-term strenuous activity (>5 hours/wk per year) and a 31% reduction of in situ cancer risk compared with those of short-term activity (≤5 hours/wk per year). The authors observed a linear decrease in the risk of breast cancer with increasing amounts of physical activity (Ptrend=0.02 and 0.04, respectively).

The next study, in the Region of Western Pomerania, found that high level of lifetime total physical activity (>150 MET-hours/wk per year) was associated with a significant 57% risk reduction relative to that detected in the low activity group of participants (<110 MET-hours/wk per year) (Kruk, 2007). Also, lifetime activity for household and recreational activities revealed significant risk reductions: OR=0.54, 95% CI=0.31-0.94, Ptrend=0.002, and OR=0.40, 95% CI=0.22-0.70, Ptrend<0.001, respectively.

In turn, Lahmann et al. (2007) examined data from nine European countries (218,169 women aged 20-80 years, 3,423 incident invasive breast cancer). The authors found that higher levels of household physical activity were associated with reduction of breast cancer risk (a



**Figure 3. Relative Risk Estimates and 95% Confidence Intervals (CI) for Cardiovascular and Heart Diseases and Physical Activity.** All risk estimates are given for activity with the highest level compared with the lowest level (open square, stroke; open circle, cardiovascular; closed circle, coronary heart disease; open triangle, all cause mortality and cardiovascular mortality)

29% reduction in premenopausal women and a 19% reduction in postmenopausal women). However, they observed no relation of recreational and occupational physical activity to breast cancer risk.

In a population-based case-control study (USA) by Sprague et al. (2007) examining 1,689 in situ and 6,391 invasive breast cancer cases and 7,630 controls, ages 20 to 69 years, women without a first-degree family history of breast cancer engaged more than 6 hours/wk in strenuous recreational activity over their lifetime had a 23% reduction in the risk of invasive breast cancer compared with those reporting no recreational activity. The authors also observed the protective effect of physical activity early in life in postmenopausal years and in the recent past among women without family history of the disease. Lifetime strenuous occupational activity was not associated neither with invasive nor in situ breast cancer.

In contrast, Nkondjock et al. (2006) in a study carried out on a cohort of 80 French-Canadian families with 250 members involving 89 cases-carriers of mutated BRCA gene and 48 non-affected carriers found no benefit from physical activity in women with BRCA1 and BRCA2 mutations.

Several world public health organizations have issued activity guidelines for adult physical activity preventing the cancer development. The recommended guidelines depend on kind of organization and may be summarized as follows: 30–60 minutes per day of moderate to vigorous intensity physical activity through four days/wk or 20–30 minutes of vigorous physical activity at least three days/wk (AICR, 2005) or one hour/day of moderate activity and one hour/wk of vigorous activity (Cancer Care Ontario, 2003).

### *Cardiovascular diseases*

Cardiovascular diseases (CVD) include high blood pressure (hypertension), coronary heart disease (CHD), stroke, rheumatic heart disease and other forms of heart disease. The protective effect of physical activity and regular exercises on risk factors of the CVD morbidity and mortality, hypertension, blood glucose level, cholesterol and triacylglycerols levels has been reported for different study design and population (see reviews in Hagberg et al., 2000; Bauman, 2004; Faff, 2004; Oguma & Shinoda-Togawa, 2004; Taylor et al., 2004; Dylewicz et al., 2005; Löllgen et al., 2006a; Löllgen et al., 2006b). It is worth to add that the review of Faff (2004) summarizes a role of both physical activity and physical fitness in reduction of the mortality from cardiovascular diseases. Based on literature data author states that 'not only in the young or middle-aged but also in the older people the increase in the level of physical activity coincides with the reduced morbidity and mortality from a coronary disease as well as with reduced rate of deaths from all causes'. In addition, numerous studies reported that exercise training in heart failure patients improves quality of their life and is recommended as a part of the standard treatment (reviewed in Smart & Marwick, 2004; Taylor et al., 2004).

A summary of the findings relating exercise/physical activity to CVD or CHD risk, from studies published in

2004–2007 and from recently published meta-analysis is presented in Figure 3.

In a systematic review and meta-analysis presented by Taylor et al. (2004) of 48 studies (8,940 patients from Europe, North America and Asia/Australia) on the effectiveness of exercise-based cardiac rehabilitation, a significant 26% reduction in cardiac mortality (OR=0.74) was found among cardiac rehabilitation individuals compared with usual care patients. Another noteworthy systematic review that evaluated results from 81 studies with a total number of 2,387 patients, that examined a role of exercise training in heart failure by Smart & Marwick (2004), found that exercise caused significant increment in maximal oxygen consumption (of a measure of functional capacity in patients with heart failure), thereby may be beneficial.

Very interesting are the previous published data from 30 articles evaluated by Oguma & Shinoda-Tagawa (2004). The results indicate that physical activity was associated with significantly reduction of CHD and stroke among women in a dose-response relation (RR: 0.78, 0.53, 0.61,  $P < 0.0001$ ; 0.73, 0.68,  $P < 0.0001$ , respectively). The authors also observed that walking 1 hour/week was associated with reduction of CVD risk among women.

Moreover, Faff (2004) gives a detailed description of finding on association between physical activity and physical fitness and decreased mortality from CVD based on the literature of this subject published till 2002. The author has suggested that physical activity coincides with the reduced morbidity and mortality from a coronary diseases independently on age being performed. As shown by the analyzed results, physical activity and fitness exert beneficial effects on the CVD risk factors, such as the level of cholesterols, triacylglycerols, elevated blood pressure, and improve insulin sensitivity and glycemic control.

The next interesting finding from the INTERHEART study carried out by Yusuf et al. (2004) including 15,152 cases and 14,820 controls from 52 countries analyzed the effect of physical activity on the CHD risk factors. The authors found that subjects regularly involved in moderate activities such as walking, cycling, swimming-vigorous for 4 hours or more per week had significantly decreased multivariable ORs compared with those inactive. In multiple risk factors analysis relative to acute myocardial infarction a strong association of the magnitude of risk with healthy lifestyle was found. For example, a 14% reduction of the risk observed among physically active women was increased to 40% (OR=0.60, 99% CI=0.51–0.71) in those who exercised regularly and consumed fruit and vegetables daily, and further to 80% among those who also avoided smoking. The authors stated that regular physical activity is inversely correlated with cardiovascular disease 'in both sexes and at all ages in all regions' though a potential limitation as selection bias was possible in the study.

Importance of physical activity in relation to all causes mortality including CVD was also shown in a meta-analysis of 30 prospective cohort studies published till 2004 by Löllgen et al (2006a, 2006b). The authors estimated that physical activity at moderate levels was

associated with a significantly reduced risk in both genders, women (RR=0.653) and men (RR=0.748) versus inactive subjects.

The recent studies reaffirm that physical activity is associated with reduction of the mortality from CVD (Figure 3). In the prospective large study middle-aged subjects (15,853 men and 16,824 women) living in eastern and western Finland (Barengo et al., 2004), CVD mortality was lower by 9-17% in men and by 11-17% in women who were moderately or highly physically active during leisure time compared with those inactive. Also, a 23% benefit from occupational activities was found in both genders. Yet, in this study, women who reported walking or cycling to and from work daily 15-29 min had a 22% reduced risk.

In the Finish prospective follow-up (18.4 years) study by Hu et al. (2004) (3,316 participants aged 25-74 years, with type 2 diabetes, 903 deaths due to CVD) 17% and 33% reductions for CVD mortality were observed due to moderate and high leisure-time physical activity versus low activity, respectively (Ptrends<0.005). Moreover, occupational and commuting (walking or cycling) physical activity showed a declining CVD death risk at increased intensity levels.

The next study carried out in Europe by Knoop et al. (2004) of elderly individuals, aged 70-90 years, 2,152 subjects at risk, 371 deaths due to CVD, 122 deaths due to CHD, also provides the favorable impact of physical activity.

Likewise, a high reduction of CVD-related mortality due to leisure-time physical activity was reported in Caucasian population (24,079 dead cases and 13,054 live controls) (Lam et al., 2004). In this study, the inverse correlation between physical activity and the risk of a cardiovascular cause of death was found in both sex, however, the gradient of the activity-mortality relationship was steeper in men than in women.

Another studies have also confirmed that a causal relation between physical activity and CVD diseases may exist (Lökkegaard et al., 2005; Noda et al., 2005; Grace et al., 2007). In the Danish prospective population based study (447 participants) by Lökkegaard et al. (2005), a borderline significant 28% reduction of CVD for exercising more than 4 hours/wk was found as compared with those inactive. The next study by Noda et al. (2005) examined the impact of exercise on mortality from CVD in Asian population (Japan) aged 40-79 years (31,023 men, 42,242 women). The authors demonstrated that both the walking time and the sports time are inversely correlated with mortality from total stroke, ischemic stroke, CHD, and total CVD. For example, both men and women combined who reported  $\geq 1$ hour/day walking had a 16%-29% reduced risk after adjusting for multiple covariates (HR=0.71, 95% CI=0.54-0.94; P=0.02 for ischemic stroke, and hazard ratio (HR) HR=0.84, 95% CI=0.75-0.95, Ptrend=0.006 for total CVD). Increasing walking time was also inversely associated with ischemic stroke and CVD risk with significant trends (Ptrends: 0.02 and 0.006, respectively). More stronger significant inverse association between sports participation time and mortality risk from CHD and total CVD were also seen in their study, as shown

in Figure 3.

Very interesting are the recently published data by Grace et al. (2007) obtained by examining 964 residents of Canada (355 diabetes, 144 with CVD, 75 diabetes and CVD, 390 non diabetes individuals), aged 35-74 years. The results of this study indicate that non-diabetes individuals participated in a greater range of total physical activity and more frequently compared with diabetes (P difference between groups 0.001 and 0.013, respectively). Moreover, diabetes individuals had lower exercise capacity compared with non-diabetes. It is well recognized that decreased exercise capacity is independent risk factor for cardiovascular and all-cause mortality (for review see Dylewicz et al., 2005). However, the authors reported a nonsignificant decreased risk of cardiovascular disease in subjects who were physically active in the last three months compared with those who were inactive (Figure 3).

Finally, this short review provides additional epidemiologic evidence that increasing physical activity reduces cardiovascular diseases risk. Taking into account the finding discussed above on amplitude of intensity and duration of daily exercise it seems reasonable to state that the data confirm the previous recommendation (De Backer et al., 2003; Thompson et al., 2003) i.e., physical activity at moderate-intensity at least 30 min on most days should be sufficient to diminish cardiovascular disease risk.

#### *Type 2 diabetes mellitus*

Diabetes mellitus (type 2) constitutes a widespread health problem in the world. In 2000 it was estimated 171 million prevalent diabetes mellitus, and there is a prognosis that the number people with the disease diagnose will increase to 366 million in 2030 (Forgarty et al., 2005). The data of numerous studies, based on evidence from large prospective cohort trials and randomized controlled trials, have revealed that physical activity can prevent type 2 diabetes (for review see Nakhanakhup et al., 2006). For example, Hsia et al. (2005) identify an association between increased physical activity and lower incidence of type 2 diabetes in postmenopausal Caucasian women (74, 240 participants). A 26% reduction of diabetes risk was observed for the highest quintile of walking (energy expenditure 10.1-40.8 MET-hours/wk) compared with the least active women (HR=0.74, 95% CI=0.62-0.89) and 33% reduction of the risk for total physical activity (HR=0.67, 95% CI=0.56-0.82 for an energy expenditure level of 23.4-143.0 MET-hours/wk versus the lowest level (0-2.3 MET-hours/wk). Both tests of linear trend across physical activity categories were significant (Ptrend<0.001 and Ptrend=0.002, respectively). The research noted a less clear relationship between risk for the disease and activity in African-American, Hispanic, and Asian/Pacific Islander women.

A significant decrease in the risk of diabetes mellitus for physically active subjects was also found in a recent paper by Grace et al. (2007) (OR=0.645, 95% CI=0.456-0.911).

According to report of Nakhanakhup et al. (2006), the following exercise components are recommended for type 2 diabetic patients: walking, running, bicycling or



swimming at least 30 min in each training session by 3-5 days a week at the intensity 40-60% of VO<sub>2</sub>max or 50-70% of maximum heart rate or 90 min per week at intensity >60% of VO<sub>2</sub> max or >70% of maximum heart rate. The authors state that such dose of physical activity may ensure achieving cardiorespiratory and metabolic improvements.

### Obesity

Many epidemiological studies have been conducted to show the hypothesized relationship between a high BMI and development of several diseases, for example, cardiovascular diseases including hypertension, non-insulin-dependent diabetes mellitus, site-specific cancer such colon and prostate in men, breast cancer, endometrium, cervix, and ovarian in women (Carmichael & Bates, 2004; Kuhl, 2005). Recently, much attention has focused on the relation between BMI and cancer. For example, Zhu et al. (2005) examining an association between BMI and breast cancer on African American women (304 cases, 305 controls) at the ages of 20 to 64 years, found that both pre- and postmenopausal women with BMI of 25 to 29.9 and 30 kg/m<sup>2</sup> or higher had increased breast cancer risk: 1.75 (95% CI=1.02-3.02) and 2.32 (95% CI=1.33-4.03) in comparison to women having BMI<25kg/m<sup>2</sup>. The positive correlation between obesity and breast cancer risk was reported, for example, by Silvera et al. (2005) basing on the National Breast Screening Study of 49,613 Canadian women (2,545 cases). The researches found that obese postmenopausal women (BMI ≥30kg/m<sup>2</sup>) in the highest quartile of energy intake (≥2406 kcal/day) were at greater risk of breast cancer compared to women who consumed <1,630 kcal/day (HR=1.72, 95% CI=1.01-2.93). For literature reviews on the relation between diet, obesity and breast cancer risk see Carmichael and Bates (2004) and Linos et al. (2007). In turn Burke et al. (2007) reported that trials of a 4-month multiple factors programs (The Activity, Diet and Blood Pressure) participants at risk hypertension and BMI>25kg/m<sup>2</sup> achieved a greater improvements in time spent in physical activity (about 37min/wk) as compared to participants of usual care. Decreased weight body was in participants suffering from hypertension maintained long term suggesting long-term benefits also followed by long-term reduction of cardiovascular risk.

The prevalence of obesity continues to increase in affluent countries, particularly in USA and West Europe. In USA, it is evaluated that 21% of American adults were obese, i. e., having BMI ≥30kg/m<sup>2</sup> in 2001 (Mokdad et al., 2003) and over 50% are overweight (BMI=25-29,9 kg/m<sup>2</sup>) (American Cancer Society, 2003). In Europe, prevalence of obesity obeys 10-20% of all men and 15-25% of all women (Carmichael & Bates, 2004). The large Canadian Study representing all Canadian provinces and territories found that 50% of the males subjects and about 33% of the females are overweight (Rohan et al., 2007). The direct costs of obesity have been valuated basing on the methods developed by Colditz (1999). In USA the cost was estimated being 7% of total health care costs, in France-approximately 2%.

Physical activity is considered as an important factor in contributing to weight loss. For example, the Littman

et al. study (2005) of over 15,000 American adults between 53 and 57 years on association between physical activity and weight change found that increasing MET-hours of energy expenditure and number of sessions a week of high-, moderate-, and even low-intensity activities, such as jogging, fast cycling and aerobics, over 10 years prevented the weight gain after age 45 years associated with aging (the ORs of losing weight more than 5% than gaining in women with BMI>25, 25-<30 and ≥30 kg/m<sup>2</sup> were 3.47, 7.38 and 3.05 times higher among those who were more active in comparison with those who were inactive). Among men, the reduction was significant only for those with BMI 25-<30 and ≥30 kg/m<sup>2</sup> (ORs=2.42 and 2.34, respectively).

A recent cohort study the National Runners' Health Study (Williams & Wood, 2006) of 8,080 male and 4,871 female runners found that age-related weight gain occurs even in the most active subjects when their physical activity is constant. This study noticed that vigorous physical activity may need to be increased by 4.4 km/wk in men and 3.9 km/wk in women during a year to avoid of the gain in weight associated with aging. However, a study of Drøyvold et al. (2004) (11-year follow-up study of 9,357 normal weight healthy women aged 20-49 years) found that individuals with high level of leisure time physical activity gained BMI of 0.18 kg/m<sup>2</sup> less than those with low level of physical activity over 11 years. In turn, analyses of BMI of 64,911 male runners aged between 18 and 55 years by Williams and Pate (2005) found that vigorous physical activity must increase with age in order to prevent middle-age men's adiposity.

During the past decades the increased obesity prevalence has been observed in youth. A systematic semi-quantitative review by Ferreira et al. (2007) found that physical activity of subjects was most positive correlated with father's physical activity, time spent outdoor and school related policies regarding activity. This finding is in accordance with evidence collected in the last several years showing that physical activity in adolescence is an important contributing factor to adult activity because people establish many of their lifestyle choices as they proceeded through adolescence (Hallal et al., 2006).

Protective effects of physical activity on overweight and obesity are well documented by Jethon & Wierzbicka-Damska (2005). The authors concluded that physical exertion without help of diet is moderately effective in reduction of a body weight among overweighted or obese individuals. For reviews of recommendations of amount of physical activity required to achieve weight maintenance the study by Williams & Wood (2006) and references therein are illustrative.

### Osteoporosis and fall-related injuries

Osteoporosis consists a major health problem of ageing population, especially in postmenopausal women. The disease is associated with increased susceptibility to fractures due to decreased bone density (Renno et al., 2005). Another risk factor in the elderly is the susceptibility to falls (Brown & Jose, 2002). The incidence of osteoporosis fractures are the highest in North Europe and USA (Roy et al., 2003). Rates of the osteoporosis are

higher in Scandinavia than in Southern European countries due to the climate, which limits physical activity and exposure to sunlight-important to vitamin D synthesis and bone formation. For women, the costs associated with osteoporosis are higher than for myocardial infarction, stroke, and breast cancer in some countries (Forgarty et al., 2005).

It is known from literature data that regular physical activity could influence bone strength and mineral density (Chien et al., 2000) due, probably, to beneficial impact on bone turnover caused by skeletal muscle activity (Langberg et al., 2000). Study done by Lindsey and co-workers (Lindsey et al., 2005) tested a association between physical performance measures and bone mineral density in healthy 116 elder women (mean 68.3 years). This study found that step length, walking speed, balance and grip strength were significantly associated with bone mineral density; women with longer step lengths and faster normal and brisk gait speeds had higher bone density.

Recent studies support these observation that physical exercise may play an important role in improving the range of variables evaluated in subjects with osteoporosis (Liu-Ambrose et al., 2005; Uusi-Rasi et al., 2006). The first study by Uusi-Rasi et al. (2006) based on a prospective 6-year study of 107 gymnasts and 110 controls found that the long-term recreational gymnastics is beneficial in age related functional decline and bone loss. The second study by Liu-Ambrose and co-workers (2005) reported that physical exercise programs positively influenced psychological well-being and reduced the chronic pain of osteoporosis and back pain in postmenopausal women with low bone mass. The authors state that only resistance and agility training may significantly correlate with change in health-related quality of life determined by physical, emotional and social well-being. The methods used to measure the quality of life in patients with osteoporosis are reviewed by Lips and van Schoor (2005). Moreover, the authors strongly underline the important role of group-based exercise programs in improvement of health-related quality of life.

Another concern is a role of exercise in health-related quality of life of patients with vertebral fractures. The interventions of exercise for preventing falls in elderly people were recently reviewed by several researchers (Rejeski & Mihalko, 2001; Gillespie et al., 2007). For example, Gillespie et al. (2007) reviewed data of 62 controlled trials involving 21,668 subjects, published since 1966 to 2003 year. In conclusion the authors stated that 'interventions to prevent falls that are likely to be effective are now available; less is known about their effectiveness in preventing fall-related injures'.

There is consensus from studies that examined the influence of physical exercise on bone strength that to improve meaningfully quality of life the patients with fractures should be encourage to spend several hours/wk in stretching, strength training and aerobic activities (Papaioannou et al., 2006).

The existing literature represents the view that high physical activity during childhood and early adolescence is an important factor for development of maximal bone mass (Kannus et al., 1995; Ford et al., 2004; Hallal et al.,

2006; Rikkinen et al., 2006; Park et al., 2007). For example, Park et al. (2007) examined relationship between bone health and the quality and quantity of habitual physical activity among a cohort of 172 Japanese aged 65-83 years. The authors found that men and women in the lowest quartile of moderate-exercise duration (<8.5 min/day) were, respectively, 2.2 and 3.5 times more at risk of fracture in comparison to those in the highest quartile (>24.5 min/day). In addition, women in the two lowest quartiles of step count (<5171 step count) had 4.9 and 8.3 times higher the risk than those in the highest quartile (>8,746 step count). Based on these finding the authors propose the following recommendations for bone health in older age: engage in low- and moderate-intensity habitual physical activity taking more than 7,000 steps/day with a duration more than 15 min/day at an intensity >3 METs.

A very recent study (Bolanowski et al., 2006) of the Polish gymnasts (115 females, aged 27-75 years) showed that Tai Chi exercise, a popular low-weight bearing exercise regularly practiced by elderly Chinese population, improves the skeletal status in postmenopausal women and recommended this kind of exercise as a means in the prevention of osteoporosis in this group of high risk women.

#### *Depression and emotional distress*

In the past two decades, numerous investigators have reported a possible association between psychosocial stress and the development of cancer, particularly breast cancer risk (Copper & Faragher, 1993; Grinsberg et al., 1996; Kiecolt-Glaser & Glaser, 1999; Kruk & Aboul-Enein, 2004; Kroenke & Kubzansky, 2005). Moreover, more often than not, depression, anxiety, emotional stress, sadness were considered as factors risk for several diseases: arthritis, dermatologic disorders, diabetes or hypertension (Cassileth et al., 1984). Depression is twice as prevalent in females as males; the disease affects about 9.5% of USA adult population each year (Craft, 2005). In USA costs spent on lost productivity and medical treatment of this chronic disease each year are estimated to be 40 billion dollars.

There is also a consensus that physical activity is independently associated with lower psychological distress (Cassileth et al., 1984; Mutrie, 2000; Kruk & Aboul-Enein, 2004; Craft, 2005; Lim & Taylor, 2005; Jerma et al., 2006). The recent finding confirms consistency of data that exercise reduces mental strain and depression.

For example, a study by Lim & Taylor (2005) of 8,881 Australian community-dwelling people, aged 65 years and over, found that 49% of all older people who reported having adequate physical activity with the prevalence rate highest than employed individuals and regular physical activity experienced beneficial effects on both the physical and psychological well-being. For example, subjects having adequate physical exercise were at least 1.5 times more able to travel independently by car, bus, or train than those without adequate exercise. In turn, Craft (2005) in a quasi-experimental design with a small number of participants (19 individuals) found that a 9-week exercise



intervention caused a reduction in the symptoms of depression. The author postulated that coping self-efficacy is responsible for physical activity interaction.

The finding was confirmed by the recent study of Jerma et al. (2006) carried out in Australia 'aimed to evaluate the effectiveness of a mind, body and spiritually based health promotion program in increasing physical activity, as well as improving mental and spiritual health in women'. Results revealed that symptoms of depression decreased significantly among the interaction group compared with the controls. Moreover, the authors observed that although the intervention group and the comparison group had a similar spiritual component in their program spiritual health scores were significantly higher at week 8 of exercise in the intervention group than at baseline. It is noteworthy to mention that the above study is the first that examined the relationship between physical activity and spiritual health.

### Possible Mechanisms Underlying Physical Exercise Activity Interactions

The health benefits of a physically active lifestyle are very well documented in the literature but mechanisms through which exercise exerts protective effects for some chronic diseases have not been yet elucidated fully, although several possible mechanisms have been proposed (Friedenreich & Orenstein, 2002; IARC, 2002; Taylor et al., 2004; Rundle, 2005; McTiernan et al., 2006). The mechanisms are summarized in Fig. 1. As a comprehensive review of biological mechanisms that may be involved between the association between physical activity and the chronic diseases protection or therapy is beyond the scope of this paper, therefore only the most recent evidences will be presented at present.

One of the most frequently reported mechanism is that physical activity can decrease endogenous sexual hormones (estradiol, estrone, testosterone) levels and increase generation of sex hormone-binding globulin (SHBG) (Hoffman-Goetz et al., 1998; McTiernan et al., 1998; Kaaks & Lukanova, 2002; de Waard & Thijssen, 2005; Jasienska et al., 2006). There is a consensus among investigators that physical activity modifies the time for exposure to endogenous sex hormones through alteration in age at menarche and the menstrual cycle. The most recent finding by Jasienska et al. (2006) from Polish regularly menstruating women (139 individuals) aged 24-37 years found that increased habitual physical activity decreased statistically significantly salivary levels of estradiol: mean estradiol concentrations were, respectively, 21.1 pmol/L, 17.9 pmol/L and 16.6 pmol/L in the low, the moderate and in the high activity group. The ovarian steroid hormone have been recognized as an important factor risk in the breast cancer development (reviewed e.g. by Kruk & Aboul-Enein, 2006a). Also, a study by Bardia et al. (2006) showed that higher recreational physical activity decreased the risk of breast cancer in postmenopausal women. The observed protective effect was accompanied by variation of estrogen receptor/progesterone receptor status.

Additionally, the highly significant relationship

between adiposity and elevated levels of estrogens and androgens was observed by McTiernan et al. (2006). The authors found statistically important association between physical activity, BMI and levels of estrone, free estradiol, testosterone, prolactin and SHBG in 267 postmenopausal women. Body mass index was positively associated with concentration of estrone, estradiol, testosterone and prolactin, and negatively associated with SHBG. For example, women with high BMI and low physical activity had a mean estrone concentration of 28.8 pg/mL, those with high BMI and high physical activity, 19.9 pg/mL. Estrone is responsible for induction of the proliferation benign and malignant cells and leads to secretion of mitogenic growth factors by direct stimulation (Henderson & Feigelson, 2000). Moreover, Bentz et al. (2005) found that physical activity may influence on the estrogen metabolism favoring its transformation in the body to the low estrogenic products 2-hydroxyestrone (2-OHE1). The product shows weak binding affinity to the estrogen receptor and, thereby, exerts antiproliferative effect on mammary cells. In contrast, the second possible product of the estrogen metabolism, 16  $\alpha$ -hydroxyestrone (16 $\alpha$ -OHE1) acts as a stimulus of tumors. A low 2-OHA1/16  $\alpha$ -OHE1 ratio is postulated as a factor of increased risk for breast cancer.

Obesity plays a key role in modulation of insulin resistance mainly through its endocrine function. Low levels of SHBG and higher concentrations of insulin are related to higher BMI and obesity. Insulin may influence postmenopausal breast cancer by increasing free estradiol concentration and decreasing levels of SHBG (Chlebowski et al., 2004; Gonullu et al., 2005). Increased physical activity, reduction of BMI and caloric intake are means for reduction of insulin and insulin-like growth factors (IGFs). High concentrations of IGF-1 are correlated with increased risk of breast, colorectal, prostate and lung cancers (Friedenreich & Orenstein, 2002; Gonullu et al., 2005). In addition exercise may increase prostaglandin F (PGF) concentration which inhibits colonic cell proliferation and increases gut motility (Friedenreich & Orenstein, 2002). Moreover, insulin resistance and IGF-1 may act synergistically in development of breast cancer (see Friedenreich & Orenstein, 2002; Malin et al., 2004, and papers cited therein).

Exercise exerts effect on cardiovascular risk factors mainly through reduction of plate aggregation, improvement of cardiac function, increase of blood flow and oxygen delivery to skeletal muscle, improvement of cardio-respiratory fitness, reduction of body weight, lowering of blood pressure, improvement of lipid profil in plasma, increase in insulin sensitivity and urinary sodium excretion (Hambrecht et al., 1993; Hambrecht et al., 2000; Charkoudian & Joyner, 2004).

Furthermore, the beneficial role of physical activity on a person's health may also result from its effects on the inflammatory process. Kasapis & Thompson (2005) in their systematic review of data published between 1975 and 2004 conclude that regular physical activity may reduce resting high-sensitivity C-reactive protein (CRP) level by several mechanisms, including decrease in

production of pro-inflammatory cytokines such as necrosis factor- $\alpha$  (TNF- $\alpha$ ) and interleukin 6 (IL-6). The cytokines exert deleterious effects on glucose homeostasis, beta-cell functioning (Purohit et al., 2002), stimulation of estrogen synthesis (Gonullu et al., 2005). This suggestion is confirmed by the recent study by Panagiotakos et al. (2005) (874 men, 903 women examined) who found that high level physical activity (expended  $>7$  kcal/min) resulted in a 29% decrease of C-reactive protein levels, 20% TNF- $\alpha$ , and 32% of IL-6 compared with the sedentary subjects. The role of physical activity in antitumour immune defenses include also an increase of the number and activity of macrophages, lymphokine-activated killer cells and IL-1 and IL-2 (Shephard et al., 1995).

Regular moderate exercise increases also levels of antioxidant enzymes and plays an important role against oxidative stress caused by oxygen free radicals (OFR) if they are generated in excess, chemical carcinogens, and ionizing radiation (for details see Toyokuni et al., 1995; Brown & Bicknell, 2001 and Kruk & Aboul-Enein, 2006a). Oxygen free radicals are known to react rapidly with proteins, lipids, carbohydrates and nucleic acids (e.g. DNA) (Kruk, 1998). Consequences of DNA damage are mutations that initiate tumor and sustain progression. The role of oxygen free radicals in cancer development was reviewed previously by Dreher and Junod (1996). Moderate physical exercises theoretically can reduce DNA damage and increase DNA-repair activity through up-regulating the activities of antioxidant defense systems responsible for removing ROS (Rundle, 2005). The role of physical activity in reduction of oxidative stress caused by OFR has been detailed in our previous paper (Kruk & Aboul-Enein, 2007).

## Summary and Discussion

Risk factors established for different types of chronic diseases include non-modifiable factors (family history, advanced age, race/ethnicity, gender, socioeconomic status) and those modifiable such as physical inactivity, smoking, overweight or obesity, diet, excess consumption of alcohol (Oguma et al., 2002; American Cancer Society, 2003; Jenun et al., 2005). Lack of awareness and knowledge about recognized risk factors may have influence on an individual's risk perception. For this reason world-wide public campaign attempt to raise awareness of the chronic diseases risk factors, especially of those which are modifiable. According to data of WHO each year a lack of physical activity causes 1.9 million premature deaths in the world and 600,000 in Europe alone; physical inactivity has been accepted as a leading risk factor in 'World Health Reports' by WHO (2002, 2003). In Australia and USA costs of illness caused by physical inactivity were estimated as high (for coronary heart disease 18% and 22%, colon cancer 19% and 22%, non-insulin dependent diabetes mellitus 13% and 12%, breast cancer 9% and 5%, falls 18% and 18% (Stephenson et al., 2000; Lim and Taylor, 2005).

Regardless of difficulties during the accurate assessment of physical activity components (intensity,

duration, frequency) in epidemiological studies for main types of physical activity: occupational, domestic (housework, yard work, child care, chores), transportation (walking, bicycling), leisure-time (in time devoted for sports, exercise, hobby), the strength of the evidence conforming the protective role of exercise in health protection is high (Myers, 2005; US Centers for Disease Control, 2005).

Recently, much attention has focused on investigation of effects of regular moderate physical activity and fitness on the life satisfaction of the chronic illness patients (for definitions of physical activity and physical fitness see Caspersen et al, 1985). According to data from a study of 13,000 Germans by Jennen & Uhlenbruck (2004) complementary strategies in both the prevention and rehabilitation of diseases and life satisfaction are: regular daily exercise, daily mental training and a very close relationship with children and grandchildren. It should be noted that fitness is suggested as a powerful predictor of mortality and a weak predictor of the chronic diseases risk factors (Faff, 2004; Myers et al., 2005). Improvement of fitness of an equivalent 1 MET, (equivalent energy expenditure of 1000 kcal/wk (Thompson et al, 2003) or the 30 minutes moderate exercise a day on most days of the week) causes a 20% reduction in all cause mortality (Myers et al., 2005). Such an amount of energy expenditure can be easily achieved, for example, by walking, modest intensity cycling, swimming or household work (Thompson et al, 2003).

Due to continuation of life increase maintaining the health of older people is an important public health strategy. The health benefits coming from regular physical activity, such as improving survival and functional ability as well as quality of life of older adults are well recognized. Details of the strategy of physical activity promotion are well discussed by Lim & Taylor (2005). It is important to underline that clinicians who care for older people with health problems provide advice on the possible benefits of increased physical activity as a routine part of clinical care.

Another noteworthy evidence for the role of physical activity/exercise is treatment/rehabilitation of patients with chronic diseases. Cancer patients suffer from a reduced quality of life such as emotional well-being (e.g. depression, anxiety) and physical functioning (e.g. fatigue, pain). The current knowledge of exercise intervention for treatment of patients with cancer shows that moderate exercise has a positive effect and is safe (Fialka-Moser, 2003; Carmack Taylor et al., 2004; Watson and Mock, 2004). The benefits of being active of breast cancer patients and survivors is obvious and confirmed in the recent studies (Wilmoth et al, 2004; Holmes et al., 2005; Mutoie et al, 2007). The authors state that physical activity reduces fatigue, depression, weight gain and loss of functional capacity, increases cardiorespiratory fitness and physical functioning, thereby improves quality of life after diagnosis of cancer. Moreover, regular physical activity can reduce the risk of mortality even by 50% among physically active women relative to that detected among those inactive post-diagnosis (Holmes et al., 2005). (For reviews of evidence for exercise therapy in the treatment

of cancer and other chronic diseases see recent reviews (Kujala, 2004; Jethon & Murawska-Cialowicz, 2005; McNeely et al., 2006; Ignarro et al., 2007).

Physical activity is qualified as a leading health indicator. Several global and national strategic initiatives were developed in order to promote a healthy lifestyle, especially interventions increasing physical activity in all age groups (Khan et al., 2002; Ruszkowska-Majzel et al., 2005; Martin et al., 2006; Yancey et al., 2007). Despite a strong link between physical inactivity and chronic diseases risk a growing body of evidence originating from representative samples found that a low percentage of adults identified a lack of physical activity as a risk factor for the diseases. This view is supported by a low knowledge of the influence of lifestyle on the health problems even among well educated young people of the world, especially in some countries of Eastern Europe, Asia, Africa and Latin America (Peacey et al., 2006). This indicates a general lack of knowledge among the public that increase of the disease incident rates is due in part to physical inactivity.

In conclusion, available studies provide further evidence that physical activity is associated with enhanced health and decreased risk of several chronic diseases and all cause-mortality. Limited new findings have been published for the role of exercise in mental health and fall-related injuries. However, the type and magnitude of physical activity associated with optimal health benefits have not been defined precisely. Further efforts in order to promote exercise, and weight control as a part of lifestyle that reduce chronic diseases risk should be enhanced.

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