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Physical activity: One of the cornerstones in the management of type 2 diabetes mellitus

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Abstract

Disease prevention not only entails stopping the development of the disease before it occurs, but also includes measures aimed at slowing down the progression of the established disease. Diabetes mellitus should be seen as an interacting occurrence between people and their environment. Thus the primary concern in prevention and treatment of type 2 diabetes mellitus should include changes in those structural, social and economic factors that are important determinants of lifestyle. Exercise has long been a cornerstone in the management of diabetes based on its potential to improve metabolic control and diminish complications. Presently the lack of understanding pertaining to exercise and its benefits, associated with type 2 diabetes mellitus as well as the absence of education and intervention programmes makes good diabetes management difficult to achieve. Exercise is undervalued in the management of type 2 diabetes mellitus. This may be due to a lack of understanding and motivation on the part of the person with diabetes mellitus as well as the absence of clear recommendations, encouragement and follow-up actions by health-care workers. Health-care workers should address these issues because most people with type 2 diabetes mellitus have the potential to derive benefit from regular, moderate levels of exercise.

Keywords: Type 2 diabetes, physical activity, exercise, sedentary behaviour, physical inactivity, glycaemic control.

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Introduction

Diabetes mellitus is a chronic disorder of carbohydrate, fat and protein metabolism. It represents a heterogeneous group of disorders that have hyperglycemia as a common feature. There are two distinct forms of diabetes, termed type-1 diabetes mellitus formerly labelled as “insulin dependent” and type 2 diabetes mellitus previously known as “non-insulin dependent diabetes mellitus”. Type 2 diabetic patients need insulin for their wellbeing but not for their survival. The value of this simple and useful classification relies on the

recognition of the mechanisms underlying the development of the two types of diabetes mellitus (Eves & Plotnikoff, 2006)

The identification of diabetes as type-1 diabetes mellitus is primarily achieved by clinical observation and simple investigations, although the condition can be further defined by genetic and immunological markers. Insulin dependence, the hallmark of type-1 diabetes, necessitates insulin injections in order to survive. Type-1 diabetes mellitus appears to be an auto-immune disease in which the body attacks and ultimately destroys insulin-producing pancreatic beta cells in an inflammatory reaction (American College of Sports Medicine, 2001). The pathogenesis in type 2 diabetes mellitus is such that although the pancreas produces insulin, the body does not utilise the insulin correctly. This is primarily due to insulin resistance in peripheral tissue, where the insulin-receptors within the body cells are insensitive to insulin resulting in glucose not readily entering the tissues (Seidell, Bjorntorp, Sjostrom, Sannerstedt, Krotkiewski & Kvist, 1989), thus ultimately leading to hyperglycemia or elevated blood glucose concentrations (Levene, 2003). This increase in blood glucose in turn stimulates the beta cells of the pancreas to secrete more insulin in an attempt to maintain a normal blood glucose concentration.

Insulin resistance is often associated with hypertension, lipid disturbances and obesity (Kumar, Cotran & Robins, 2003). Apart from genetic dispositions, diet and obesity, animal experiments as well as epidemiological data suggest that a lack of physical activity may contribute to insulin resistance (Watkins, Amiel, Howell & Turner, 2003). In comparison to type-1 diabetes mellitus much less is known about the potential pathogenesis of type 2 diabetes mellitus, despite it being the most common type. There is no evidence that auto-immune mechanisms are involved. Lifestyle clearly plays a role and obesity has been identified as a co-morbidity factor of type 2 diabetes mellitus (Polonsky, Sturis, & Bell, 1996; Ostenson, 2001). Although considered to be a disease in adulthood, there has been an epidemic increase in the incidence of type 2 diabetes mellitus in obese children, particularly among Black Africans, Hispanics, Native Americans, and Asians (Kumar, Cotran & Robins, 2003). Diabetes has been called the “new world syndrome”(Zimmet, McCarty & de Courten, 1997), a symptom of globalization with social, cultural, economic and political significance (Zimmet, 2000).

Apart from the impact on health, the economic cost of diabetes mellitus and its complications, the impact is enormous both in health-care and loss of productivity to society (Zimmet, 2000). Diabetes mellitus will, in the future, constitute a heavy burden both for individuals affected and for the society in which they live (Zimmet, Alberti & Shaw, 2001). This article aims to review the epidemiological evidence suggesting the beneficial effects of exercise related to

diabetes mellitus. The article also features on the management of diabetes using exercise as a therapeutic modality.

Prevalence of diabetes mellitus

The incidence of type 2 diabetes mellitus is increasing markedly in adult populations around the world (Hjelm, Mufunda, Nambozi & Kemp, 2003). This is viewed as a growing chronic health problem, the complications of which cause significant morbidity and mortality (Nathan, 1993). Diabetes mellitus constitutes a growing global public health problem, with an increasing incidence from 30 million people ten years ago to about 135 million today (Amos, McCarty & Zimmet, 1997) to an estimated 300 million in 2025 (World Health Organisation, 1998a; World Health Organisation, 1998b). As populations age and urbanize, and as obesity becomes more prevalent (Macbeth & Shetty, 2001; Harris, Petrella & Leadbetter, 2003), the incidence of type 2 diabetes mellitus increases proportionally.

The prevalence of type 2 diabetes mellitus is at its highest among the Pima Indians living in Arizona (Santeusanio, Di Loreto, Lucidi, Murdolo, De Cicco, Parlanti, Piccioni & De Feo, 2003) and Polynesians. South Asians and West Africans are in the middle range, with European populations in the lowest range. Europeans could reflect a population predisposition to genetic susceptibility, and/or exposure to environmental factors (McMichael, 2001). The persistent elevated rates of type 2 mellitus among South Asian migrants several generations after migration to the UK, suggest that genetic factors play an important role (McKeigue, 1997). A similar elevation in type 2 prevalence rates among urbanized Indian, Chinese and African migrants in Mauritius is testimony to the importance of environmental (lifestyle) factors, (Zimmet, Alberti & Shaw, 2001) as does the five-fold difference in type 2 diabetes mellitus prevalence between rural and urban populations in Tamil Nadu in South India (McKeigue, 1997). Care of diabetics in the African continent is fraught with numerous problems. The prevalence of diabetes mellitus among African adults appears to be lower than that reported in most industrial countries; however it is estimated that at least one million people in Africa suffer from type 2 diabetes mellitus (McLarty, Pollitt, & Swai, 1990). The continents identified with the largest potential future increase are Asia and Africa, where diabetes mellitus could increase two to three fold (Amos, McCarty & Zimmet, 1997). South Africa has diabetes mellitus prevalence of 4.5% and an impaired glucose tolerance prevalence of 51% (Erasmus, Blanco, Okesina, Matsha, Gqweta & Mesa, 2001).

Recent studies have indicated that the prevalence of type 2 diabetes mellitus is an increasing health concern among black South Africans. The age-adjusted prevalence of diabetes in urban settings in 2001 was found to be 8% in Cape Town and 5.3% in Durban (Nthangeni, Steyn, Alberts, Steyn, Levitt, Laubscher,

Bourne, Dick & Temple, 2002). Among peri-urban Xhosa speaking the age-adjusted prevalence was found to be 4.5% (Erasmus, et al., 2001) and in rural Kwa-Zulu Natal, 4.2% (Motala, Pirie, Gouws & Omar & Grey, 2001). Diabetes care in South Africa is incongruent with the greatest need for care. From observation, highly trained health-care workers tend to be concentrated in metropolitan areas and render service to the affluent minority as opposed to rendering service in the rural, resource-poor areas of the country. This may have several implications. For example, people from poor-resource setting will not have insight and education into the benefits of physical activity related to diabetes management and the positive effect it will have on their glucose levels. People residing in these areas may not understand the different types of exercises that are available and how to execute them. Therefore education on general exercise (frequency, duration and set), different exercise types and execution of the type of exercise should be developed (in the form of handouts or booklets) and provided to patient at public hospital in resourced-poor setting.

Aetiology of type 2 diabetes mellitus

The main factors associated with the development of type 2 diabetes mellitus are genetic predisposition, increasing age, increased body fat and environmental factors such as urbanization and industrialization (Sowers, 2003; Lim, Kang & Stewart, 2004). Increased longevity and changes in lifestyle from a traditional healthy and active life to a modern, sedentary, stressful life coupled with the overconsumption of energy-dense food (Zimmet, 2000; Hjelm, Mufunda, Nambozi & Kemp, 2003) is also part of the aetiology. Despite the variation in the prevalence of type 2 diabetes mellitus among populations and at the individual level, the most overt environmentally mediated epidemiological feature of type 2 diabetes mellitus is the strong positive correlation with relative body fat (Figure 1). Genetic factors exacerbate this condition and epidemiological studies indicate that type 2 diabetes mellitus appears to stem from a collection of multiple genetic defects, each multiple genetic defects contributes to its own pre-disposing risk and each modified by environmental factors. The two metabolic defects that characterize type 2 diabetes mellitus are a derangement in beta-cell secretion of insulin and an inability of peripheral tissue to respond to insulin (insulin resistance) (Kumar, Cotran & Robins, 2003).

Type 2 diabetes mellitus is generally viewed as a lifestyle disorder, most prevalent among populations with heightened genetic susceptibility (Zimmet, 1995). Recent epidemiological evidence indicates that a majority of the world's populations are prone to type 2 diabetes mellitus in the wake of increasing obesity (Stern, 1991), with Caucasians being a possible exception. This plausible evolutionary explanation relies on the old concept of hunter-gatherer genes that accounts for the rapid rise of type 2 diabetes in some populations. Neel (1962) postulated the theory of the existence of the "thrifty gene" (Neel, 1962).

According to Neel's theory early people lived in feast-famine cycles and the thrifty gene would have had selective advantages because it increased the ability of the body to store fat (energy) that could later be metabolized during periods of food shortage (Dowse & Zimmet, 1993).

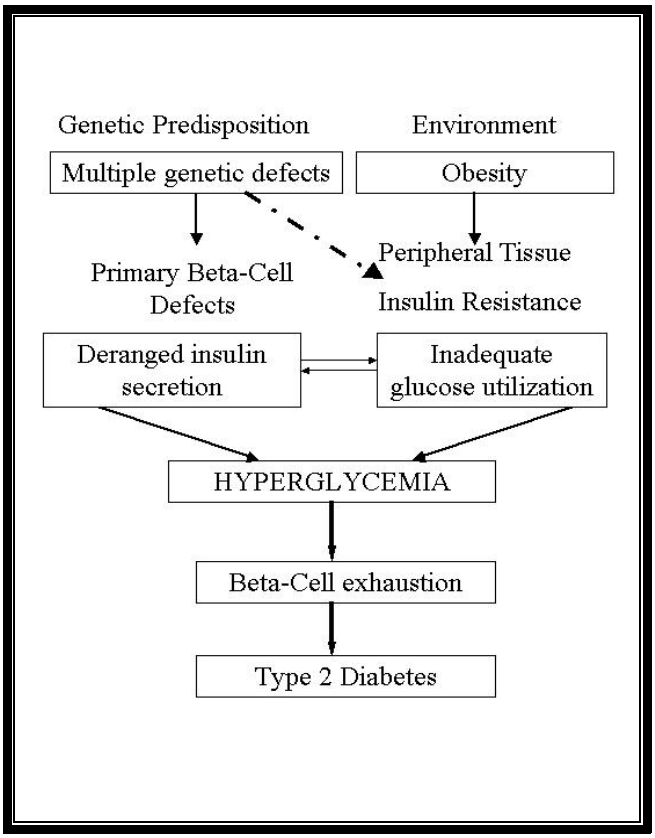

Figure 1: Pathogenesis of type 2 diabetes mellitus. Genetic predisposition and environmental influences converge to cause hyperglycemia and overt diabetes (Redrawn from Kumar et al., 2003).

In summary, type 2 diabetes mellitus has a heterogeneous and multi-genetic, complex aetiology (Zimmet, McCarty & de Courten, 1997; Groop & Orho-Melander, 2001). Most people who have type 2 diabetes mellitus are obese, have disturbances in lipid metabolism and suffer from hypertension (Toews & el-Guebaly, 1989; Schersten, 1997). Diabetes mellitus needs to be treated using a holistic approach embracing dietary adjustments, physical activity and exercise, medication (if needed) and education.

General exercise guidelines in type 2 diabetes mellitus

The therapeutic effect of exercise on type 2 diabetes mellitus is different to that in type-1 diabetes. Approximately 80% of people with type 2 diabetes are obese

and insulin resistant and only about 35% require insulin therapy (Durstine, & Moore, 2003). Physicians often prescribe exercise in combination with diet and oral antidiabetic agents to achieve and maintain weight reduction and improve glycaemic control. Research has proven that regular physical activity protects against the development of type 2 diabetes in high-risk populations (Pan, Li, Hu, Wang et al., 1997; Tuomilehto et al., 2001). Together with the treatment and prevention of obesity by dietary restriction, increased physical activity is an important component of lifestyle modification for people with impaired glucose tolerance, with a family history of type 2 diabetes, or with other risk factors for its development (Horton, 2006). Exercise-induced-hypoglycemia and acute regulation of blood glucose are less of a problem in type 2 diabetes than in type-1 diabetes, however cardiovascular disease and musculoskeletal injuries are generally greater in persons with type 2 diabetes mellitus. People with type 2 diabetes mellitus can develop the same diabetes complications as those with type-1 diabetes mellitus, which includes retinopathy, nephropathy, neuropathy and macrovascular disease, and must be screened for the mentioned complications prior to commencement of an exercise program (Horton, 2006).

Guidelines for general exercise training and prescription: Effects on the exercise response

Under normal circumstances, in people without diabetes there is coordination between the hormonal and metabolic processes which results in the maintenance of glucose homeostasis. Insulin and counter-regulatory hormone concentrations in people with diabetes do not respond to exercise in the normal manner and the balance between peripheral glucose utilization and hepatic glucose production may be disturbed (Hornsby & Albright, 2003). The effects of diabetes on a single exercise session is dependent on several factors, including: use and type of medication to lower blood glucose levels (oral or insulin hypoglycemic agents); timing of medication administration; blood glucose level prior to exercise; timing, amount, and type of previous food intake, presence and severity of diabetic complications; use of other medication secondary to diabetic complications and the intensity, duration and type of exercise (Hornsby & Albright, 2003).

General recommendations for exercise prescription

Exercise prescription for people with diabetes must be individualized according to medication usage schedule, presence and severity of diabetes complications, and goals and expected benefits of the exercise programme (Hornsby & Albright, 2003). Physical activity for those without significant complications or limitations should include appropriate endurance and resistance exercise for developing and maintaining cardio-respiratory fitness, body composition, and muscular strength and endurance. In general, one hour of exercise requires an

additional 15g of carbohydrate either before or after exercise. If exercising is vigorous and is of long duration, an additional 15 to 30g of carbohydrate is needed every hour. Exercise is a contraindication if there is active retinal hemorrhage or there has been recent therapy for retinopathy; illness or infection is present; blood glucose is above 13.8mmol/l (250mg/dl) and ketones is present (blood glucose should be lowered before initiation of exercise); or blood glucose is 4.4 to 5.5 mmol/l (80 to 100 mg/dl) because the risk of hypoglycemia is great (in this situation, carbohydrate should be eaten and blood glucose allowed to increase before initiation of exercise) (Durstine & Moore, 2003). Exercise precautions includes the following: keeping a source of rapidly acting carbohydrate available during exercise; consuming adequate fluids before, during and after exercise; practicing good foot care by wearing proper shoes and cotton socks, and inspecting feet after exercise; and carrying medical identification (Hornsby & Albright, 2003).

General effects of acute exercise in patients with type 2 diabetes mellitus blood glucose levels and insulin sensitivity

In healthy non-diabetic individuals, exercise has very little impact on blood glucose levels. In individuals with type 2 diabetes mellitus, exercise with either moderate or heavy intensity is associated with decreases in blood glucose levels. A single bout of exercise often decreases plasma glucose levels (Wallberg-Henriksson, Rincon & Zierath, 1998), which progresses into the post-exercise periods. The blood glucose lowering effect of exercise in individuals with type 2 diabetes mellitus can be explained by the insulin-dependent activation of glucose transportation by exercise (Wallberg-Henriksson & Holloszy, 1984), as well as increased insulin sensitivity.

Hormone levels

Moderate to heavy exercise reduces insulin secretion and inversely the plasma insulin levels are reduced (Wallberg-Henriksson et al., 1998). Glucagon and adrenaline levels increase during exercise. Glucose homeostasis is generally maintained during exercise because the increase in glucose utilization is matched by an increase in hepatic glucose production. The exercise-induced increase in glucagon and the fall in insulin levels can control the increase in glucose production. The important role of pancreatic hormones is the control of hepatic glucose production during exercise, the increase in glucose uptake in peripheral tissues is controlled primarily by insulin-independent mechanisms (Kumar et al.,2003).

Glucose transport

The total skeletal muscle glucose transporter protein (GLUT 4) levels are increased in exercise trained middle aged individuals with either normal glucose tolerance or in individuals with type 2 diabetes mellitus, compared to sedentary individuals (Houmard, Egan, Neufer & Friedman et al., 1991). These individuals have improved insulin sensitivity, which is explained by increased GLUT 4 expression. Exercise is also a stimulator of glucose transportation (Wallberg-Henriksson & Holloszy, 1984). In humans, insulin sensitivity is related to the degree of physical activity (Horton, 2006). Exercise also enhances insulin sensitivity in obese individuals and those with type 2 diabetes mellitus (Bjorntorp, De Jounge, Sjostrom & Sullivan, 1970). In patients with type 2 diabetes mellitus, regular exercise training may enhance cellular glucose uptake. This improvement in insulin sensitivity may overcome defects in the insulin signal transduction pathway, seen in muscle tissue taken from individuals with type 2 diabetes mellitus (Bjornholm, Kawano, Lehtihet & Zierath, 1997).

General long term effects of exercise in patients with type 2 diabetes mellitus

Metabolic control and insulin sensitivity

Aerobic power is inversely related to modest, favourable changes in glycosylated haemoglobin and glucose tolerance (Wallberg-Henriksson et al., 1998; Albright, Franz, Hornsby, Kriska Marrero, Ullrich & Verity, 2000). In certain studies (Saltin, Lindgarde, Houston & Horlin et al., 1979; Reitman, Vasquez, Klimes & Nagulesparan, 1984; Krotkiewski, Lonnroth, Mandroukas, Wroblewski, Rebuffe-Scrive, Holm, Smith & Bjorntorp, 1985; Santiago, 1986; Lampman & Schteingart, 1991), duration of physical activity ranged from 6 weeks to 12 months, and improved glucose tolerance was shown in early stages of type 2 diabetes (Rogers, Yamamoto, King, Hagberg et al., 1988). Some studies also showed that mild-to-moderate physical activity ranging from 12 weeks up to 2 years did not improve glucose control in type 2 diabetic subjects (Minuk, Vranic, Marliss, Hanna et al., 1981; Skarfors, Wegener, Lithell & Selinus, 1987). It was also noted that older diabetic individuals (e.g., over 55years) may not show the same exercise-induced blood glucose changes as usually seen in younger diabetic individuals (Zierath & Wallberg-Henriksson, 1992). Favourable changes in glucose tolerance usually deteriorates within 72 hours of the last exercise bout in those with type 2 diabetes (Schneider, Amorosa, Khachadurian & Ruderman, 1984) and are a reflection of the last individual exercise bout, rather than training per se (Koivisto, Yki-Jarvinen & DeFronzo, 1986). Hence, regular physical activity is recommended for persons with type 2 diabetes to sustain glucose-lowering effects.

Body Weight

In individuals with type 2 diabetes mellitus and obesity a diet-induced decrease in body weight is associated with the beneficial effect of improved metabolic control and reduced risk of ischaemic heart disease (Schneider, Vitug & Ruderman, 1986). Patient compliance with weight loss programmes is often low and diet therapy alone is generally not sufficient to maintain weight loss on a long term basis (Schneider & Ruderman, 1990). Programmes which combine diet therapy and exercise are more successful in achieving bodyweight reduction in participants (Albright et al., 2000; Bogardus, Ravussin, Robbins & Wolfe et al., 1984).

Cardiovascular Risk Factors

Exercise is associated with a decrease in serum triglycerides levels, particularly very low-density lipoproteins, and an increase in high density lipoprotein cholesterol (Wallberg-Henriksson et al., 1998). Physical activity has also been reported to lower blood pressure in hypertensive individuals (Albright et al., 2000; Wallberg-Henriksson et al., 1998). The latter adaptation occurs independent of weight loss and changes in body composition. Physical training has also shown to increase cardiovascular fitness and physical working capacity in individuals with type 2 diabetes mellitus (Eriksson, 1999).

Resistance training for the management of type 2 diabetes mellitus

Resistance training has been recognised as a useful therapeutic tool for the treatment of a number of chronic diseases (Pu et al., 2001; Spruit, Gosselink, Troosters, De Paepe & Decramer, 2002; Schmitz, Jensen, Kugler, Jeffery & Leon, 2003; Segal, Reid, Courneya & Malone et al., 2003; Kongsgaard, Backer, Jorgensen, Kjaer & Beyer, 2004; Haykowsky, Eves, Figgures & McLean et al., 2005) and has been demonstrated to be safe and efficacious for the elderly (Singh, Ding, Manfredi, Solares et al., 1999) and obese (Cuff, Meneilly, Martin & Ignaszewski et al., *20*03) individuals. Resistance training has been reported to enhance insulin sensitivity (Ades, Savage, Brochu & Tischler et al., 2005; Poehlman, Dvorak, DeNino, Brochu & Ades, 2000), daily energy expenditure (Hunter, McCarthy & Bamman, 2004; Ades et al., 2005) and quality of life (Kell, Bell & Quinney, 2001).

Resistance training also has the potential for increasing muscle strength (Hunter et al., 2004; Ouellette, LeBrasseur, Bean & Phillips et al., 2004), lean muscle mass (Ryan et al., 2001), and bone mineral density (Nelson et al., 1994) which could enhance functional status and glycaemic control and assist in the prevention of osteoporosis and sarcopenia. Resistance training requires equipment, knowledge of exercise techniques and initial instruction, unlike

aerobic exercise, such as walking. Tesch, Colliander and Kaiser (1986) demonstrated that muscle biopsy specimens form resistance-trained, non-diabetic men contained glycogen concentration 50-100% higher than those of physically inactive men in the general population. Certain exercise studies have shown that as little as 4 weeks of resistance training increases muscle glycogen synthesis in elderly, previously sedentary and healthy individuals (Miller, Pratley, Goldberg & Gordon et al., 1994). Resistance training could help in the management of diabetes mellitus by increasing skeletal muscle mass, since muscle is the principal source of glucose disposal (DeFronzo, Jacot, Jequier & Maeder et al., 1981; Shulman, Bloch & Rothman, 1995). In a cross-sectional study comparing healthy male athletes with sedentary control subjects, a significant correlation ($r=0.54$) was observed between muscle mass and insulin sensitivity (Yki-Jarvinen, Koivisto, Taskinen & Nikkila, 1984). Resistance training clearly produces significant skeletal muscle hypertrophy even in elderly individuals (Fiatarone, Marks, Ryan, Meredith et al., 1990) with associated increases in insulin sensitivity (Yki-Jarvinen et al., 1984).

Conclusion

Despite evidence pointing to the benefits of exercise there is still a lack of participation among patients who are at risk of or who have type 2 diabetes mellitus. The reasons for the non-participation in regular exercise includes the patients' lack of knowledge about the benefits of exercise, a lack of motivation and the absence of clear guidelines from health-care professionals. In most South African communities the rate of diabetes is on the increase and is becoming unmanageable due to a lack of education and proper interventional programmes. A study undertaken by Paul and Van Heerden (2004), investigated the knowledge, attitudes, beliefs and practices relating to exercise among type-1 diabetes mellitus patients in government hospitals in Kwa-Zulu Natal. The study undertaken my Paul and van Heerden (2004) showed that patients visiting government hospitals were provided with a basic check-up, including glucose capillary tests and blood pressure measurement and were very briefly advised on exercise, if at all. It was also noted that no education relating to diet or medication was provided. The results showed that even though many people were positive about exercising, they were unable to exercise due to the lack of knowledge on the appropriate type, duration and frequency.

Diabetes-related studies in South Africa has been limited to risk profiles of various populations (Joffe & Seftel, 1994; Levitt, Steyn, Lambert, Reagon, Lombard, Fourie, Rossouw & Hoffman, 1999; Motala, Pirie, Gouws, Omar & Grey, 2001) and dietary habits (Nthangeni *et al*., 2002) of diabetics. Ultimately all persons with diabetes, irrespective of geographic and/or socio-economic settings should have the opportunity to benefit from the many valuable therapeutic effects of exercise (Campaigne, 1997).

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