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Narrative review on effects of physical training on risk of cardiometabolic diseases

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Abstract:

Cardiometabolic diseases as defined by various expert bodies are a varied range of noncommunicable diseases that have slowly creeped in the community by inducing a dreadful combination of central adiposity, reduced insulin sensitivity, hypertension, and dyslipidemia which lead to cardiometabolic diseases, diabetes, renal disorders, and/or metabolic syndrome (MetS). Several authors have brought it to notice that alterations in lifestyle and environment leading to the disruption of circadian rhythm trigger the pathophysiology leading to the development of multiple risk factors and cardiometabolic diseases. Statements very critically state that though MetS cannot be considered as an absolute risk indicator, patients with it are twice at the risk of developing cardiac ailment and at five times the risk of developing insulin-resistant diabetes in the near future. Collaboratively, be it WHO statement of 1999, "the National Cholesterol Education Program ATP3 2005," or further ratification by "the International Diabetes Federation" 2006, "the American Association of Clinical Endocrinologist" 2003, "European Group for the study of Insulin Resistance," "the European Society of Cardiology," and the American College of Cardiology American Heart Association as discussed in this brief review, all are continuously insisting on prevention and conducting awareness programs for the same. The electronic database (PubMed/MEDLINE, Embase, etc.,) was searched for available literature on different guidelines for exercise prescription (Frequency, Intensity, Time, Type [FITT]) in January–April 2021. After reviewing the literature by different authors, a brief review was conceptualized from the same. The different protocols suggested for health and fitness by different guidelines have been presented here with the effect of physical activity discussed with literature support with respect to physiology, prevention, prophylaxis, and treatment. The burden of lifestyle disorders is increasing tremendously and is also increasing the economic cost on society. It is high time that we understand the seriousness and start observing the well-stated advice offered by several guidelines over many years and stay physically active.

Keywords:

Cardiometabolic diseases, fitness, guidelines, health, physical activity

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Introduction

Cardiometabolic diseases as defined by various expert bodies are a varied range of noncommunicable diseases (NCD) that have slowly creeped in the community by inducing a dreadful combination of central adiposity, reduced insulin sensitivity, hypertension, and dyslipidemia which lead to cardiometabolic diseases, diabetes, renal disorders, and/or metabolic syndrome (MetS). Several authors have brought it to notice that alterations in lifestyle and environment leading to the disruption of circadian rhythm trigger the pathophysiology leading to the development of multiple risk factors and cardiometabolic diseases.[1-3] There are statements that very critically state that though MetS cannot be considered as an absolute risk indicator, patients

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with MetS have twice the risk of developing cardiac ailment and are at five times the risk of developing insulin-resistant diabetes in the near future. Hence, collaboratively, be it WHO statement of 1999, "(the National Cholesterol Education Program) ATP3 2005," or further ratification by "International Diabetes Federation" 2006, "the American Association of Clinical Endocrinologist" 2003, "European Group for the study of Insulin Resistance," "the European Society of Cardiology (ESC)," and the American College of Cardiology American Heart Association all are continuously insisting on prevention and conducting awareness programs for the same. Ironically, the experts worldwide, even after knowing the facts and practically visualising the serious consequences, are still highly ignorant about the precise information in the joint interim statements published from time to time. Thus, an attempt has been made to discuss them all together in this review. The various diagnostic criteria are represented in Table 1.[4-7] Visualizing the grave situation, one should be all the more cautious as these statements are released with a disclaimer that the thresholds should be made more sensitive and this should be a continuous evolutionary process, showing that with every passing decade the situation is becoming all the more gloomy.

Impact of sedentary lifestyle on cardiometabolic risk

The younger generation of society is slowly falling in the clutches of this dreaded syndrome which primarily originates from sedentary lifestyle and its associated risk. With the change in lifestyle which has high screen time along with prolonged reclining posture, young adults are going through several chronic stressors and problems related to insomnia. This is making them prone to develop autonomic system dysfunction in long run. Moreover, an unhealthy diet is also inducing obesity additionally.[2,8-12] It is more alarming than the COVID pandemic which has impacted the gross domestic

Table 1: Diagnostic criteria for metabolic syndrome by different guidelines

Guidelines by	Year	Diagnostic criteria	Criteria	Parameter Threshold
WHO[5]	1999	Presence of insulin resistance with any two or more of others	Abdominal obesity	Waist/hip ratio >0.9 (men) or >0.85 (women) or BMI >30 kg/m^2
				WC ≥94 cm in men and
			Insulin resistance	Glucose >6.1 mmol/L (110 mg/dl)
				2 h glucose >7.8 mmol/L (140 mg/dl) (essential)
			Hypertension	BP >140/90 mmHg
			Hyperlipidemia	HDL-C <0.9 mmol/L (35 mg/dl) in men
				HDL-C <1.0 mmol/L (40 mg/dl) in women
				Triglycerides >1.7 mmol/L (150 mg/dl)
NCEP ATP3[5]	2005	Presence of any three or more of the following	Abdominal obesity	WC >102 cm (men) or >88 cm (women)
			Insulin resistance	Blood glucose >5.6 mmol/L (100 mg/dl) or drug therapy for elevated blood glucose
			Hypertension	BP >130/85 mmHg or drug therapy for hypertension
			Hyperlipidemia	HDL-C <1.0 mmol/L (40 mg/dl) in men <1.3 mmol/L (50 mg/dl) in women or on drug therapy for low HDL
				Triglycerides >1.7 mmol/L (150 mg/dl) or drug therapy for elevated triglycerides
IDF[5]	2006	Waist >94 cm (men) or >80 cm (women) along with the presence of two or more	Abdominal obesity	Waist >94 cm (men) or >80 cm (women) (essential)
			Insulin resistance	Blood glucose greater than 5.6 mmol/L (100 mg/dl) or diagnosed diabetes
			Hypertension	BP >130/85 mmHg or drug treatment for hypertension
			Hyperlipidemia	HDL-C <1.0 mmol/L (40 mg/dl) in men, <1.3 mmol/L (50 mg/dl) in women or treatment for low HDL-C
				Blood triglycerides >1.7 mmol/L (150 mg/dl) or drug treatment for elevate trigylceride
European Guidelines on cardiovascular disease prevention[36]	2016	To keep below the ranges to reduce the risk factor	Abdominal obesity	BMI >20-25 kg/m^2
				WC >94 cm in men and >80 cm in women
			Insulin resistance	HbA1c >7% (>53 mmol/mol)
			Hypertension	>140/90 mmHg
			Hyperlipidemia	HDL-C <40 mg/dL in men and <45 mg/dL in women
				Triglycerides >150 mg/dL
ACC/AHA[7]	2019	A tally of 3 makes the diagnosis	Abdominal obesity	WC as ≥40 inches (≥102 cm) in men and ≥35 inches (≥88 cm) in women (by ethnically appropriate cutpoints) along with BMI
			Insulin resistance	HbA1c >6.5%
			Hypertension	BP >130/80 mmHg
			Hyperlipidemia	HDL-C <40 mg/dL in men; <50 mg/dL in women
				Triglycerides >150 mg/dL, nonfasting

NCEP: National Cholesterol Education Program, IDF: International diabetes federation, BMI: Body mass index, WC: Waist circumference, HDL: High-density lipoprotein, HDL-C: HDL-cholesterol, HbA1c: Glycated hemoglobin, BP: Blood pressure, ACC: American College of Cardiology, AHA: American Heart Association

product globally, as this epidemic is increasing the burden and the cost of healthcare by hampering society's physical, mental, social well-being as well as affecting its equity day by day. It has been concluded and suggested by several authors that this needs continuous evaluation and surveillance.[5] By the year 2015, it was predicted that an alarming number of "603.7 million adults and 107.7 million children," would have slowly fallen a prey to this condition and as per the data suggested by the author since 1980, the disease burden of obesity has also entrapped more than 70 countries and is still counting, with the rate of increase observed more in childhood obesity than in adult.[13] The consensus statement insisted that abdominal obesity remains the most important component of all the complex pathophysiologies causing MetS,[4] and according to the recent Center For Disease Control and Prevention report, 38% of the US adults were physically inactive and 50% of them have a Hb1c >7.0% or higher.[14]

It is jointly agreed that the major culprit in increasing the prevalence of syndrome X noncommunicable disorder is sedentary lifestyle, stress, and diet.[5,9-11] It is more prevalent in the urban population and is further affecting disability-adjusted life years and increasing the burden on society as it causes further risk of developing stroke, atherosclerosis, and other life-threatening disorders. Stress which is long term and becomes chronic slowly tends to disrupt the hypothalamo–pituitary–adrenal axis and limbic system and induces a pro-inflammatory state in the body and impairs the quality of life. Moreover, the disruption of balance between the sympathetic and parasympathetic nervous system due to this state alters the various hormonal activities, leads to changes related to oxidative stress in the body, and also changes the dietary pattern. All of these along with several other pollutants and stressors form a milieu which thrusts the chances of early mortality in an individual.[9,10,15-17] Moreover, it has been admitted that it is no more the disease of the elite. Where the prevalence is increasing in the Western countries at supersonic speed with the increase in the incidence of sedentary lifestyle and unhealthy diet, mimicking the west, the Asian men and women have also demonstrated the greatest prevalence even though they had a lower body mass index (BMI).[14,18] It has been brought to notice that college-going students who are considered to be moderate on physical activity level, objective measures in studies categorize these young adults as having low level of fitness and are thus at high risk of cardiometabolic diseases.[19-21]

As observed in various guidelines as well as suggested by several authors, it is obesity and its related factors such as diet, sleep, and physical inactivity which need to be targeted to reduce the risk further.[4,5,18,20-22]

It is astonishing to view the rising trend in adult BMI in a population-based measurement study with 19.2 million participants conducted by NCD risk factor collaboration from the year 1975 to 2014. They have suggested that if the same trend continued the prevalence would surpass grave numbers in 2025 estimating them to reach 18% in males and over 21% in females and also further targeting the younger generation. It was reported in 2011 that South Asians had high prevalence of MetS and another report in 2012 suggested equally high prevalence of the same in American adults by quoting that almost one-third of them had it already. Adding a word of precaution here, that researchers have also identified some metabolically active obese individuals and they claim that these individuals do not develop more features of this syndrome other than obesity.[5,23] However, contradictory views coexist which state that no form of obesity is considered to be healthy and all obese are at risk of developing further morbidities[24-26] considering the pro-inflammatory state which exists.

As per the "WHO Global status report on NCDs 2010," 3.2 million people surrender to death due to sedentary lifestyle and have 20%–30% increase in risk for all-cause mortality, and as specified earlier, it is not only an observation only in high-income groups but also in middle income and is most commonly observed in women.[27]

Data Source and Search Strategy

The electronic database (PubMed/MEDLINE, Embase, etc.,) was searched for available literature on different guidelines for exercise prescription (FITT) in Jan-April 2021. Four authors S, PM, AB, and KG conducted a literature search using keywords such as guidelines, cardiometabolic risk, MetS, and recommendation. Inconsistencies were verified by RHR, MA, and VM.

Study Selection and Screening

The included studies were only guidelines of reputed organizations. The search was organized in discussion in the flow of physical inactivity and associated cardiometabolic risk as discussed by various authors, effect of physical activity on the risk factors, regular physical training adaptations, and recommendations as per different guidelines. The PRISMA flow diagram also postulates information further inculcated in the selection process of studies [Figure 1].

Information was gathered in an electronic spreadsheet shared by the reviewers and included year-wise guidelines, diagnostic criteria, and physical activity recommendations as shown in Tables 1 and 2.

Table 2: Recommendations as per guidelines to lower the risk of developing metabolic syndrome

Guidelines and year of publication	Physical activity	Resistance training
CSEP[40]	150 min per week moderate-to-vigorous aerobic exercise per week	At least twice a week for major muscle group
WHO recommendation for 18-64 years[39]	Minimum 150-300 min of moderate-intensity aerobic or 75-150 min of vigorous-intensity aerobic throughout the week or a combination of both. Minimum 10 min bout of exercise duration	Major muscle group on two or more days a week
EAPC of the ESC 2016[37]	150-300 min a week moderate intensity or 75-150 min/week vigorous intensity, also accumulated in short bouts of at least 10 min to overall weekly goals	8-12 reps at 60%-80% of 1 RM minimum two times per week, balance and gait training
2019 ACC/AHA[7]	90-150 min of moderate exercise per week at 65%-75% of heart rate reserve or 75 min of vigorous-intensity aerobic exercise per week	Dynamic resistance exercise 90-150 min/week, 50%-80% of 1 Rep max
CDC and prevention[41]	At least, 150 min accumulated over a week moderate Intensity or 75-min vigorous intensity	At least, twice a week
American Diabetes Association 2019[38]	Moderate intensity, 3 days per week for 20-45 min to accumulate to minimum of 150 min per week	Yes

CSEP: Canadian Society for Exercise Physiology, EAPC: European Association of Preventive Cardiology, ESC: European Society of Cardiology, CDC: Center for disease control, ACC: American College of Cardiology, AHA: American Heart Association, 1RM: one-repetition maximum

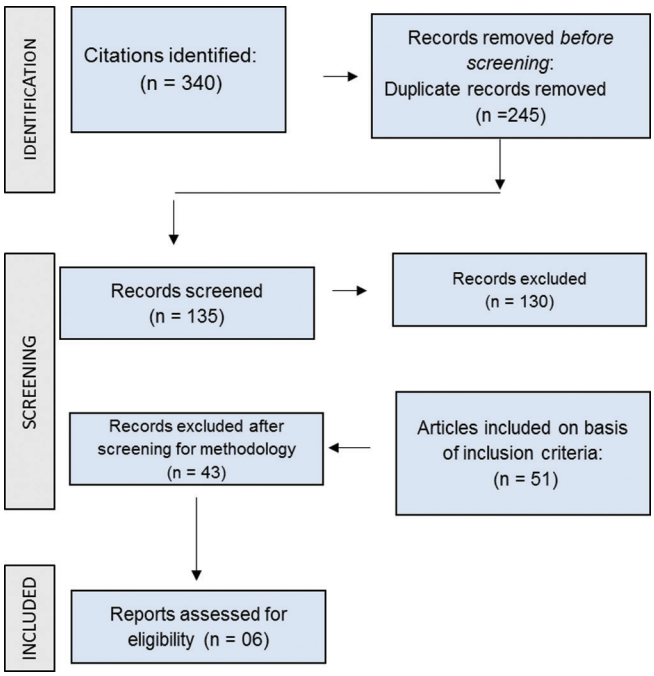

Figure 1: PRISMA flowchart

Data Extraction and Study Quality Assessment

The investigators (AB, PM, MA, and S) independently extracted key data from the included guideline in a standardized template database, and the other authors (KG, VM, and RHR) reviewed and validated the extracted data. Peer discussions helped to remove the biasness; however, there was no blinding of reviewers and journals. All the reviewers equally contributed scanning for guidelines and depicting the findings. As the data from reputed guidelines were only included, which are conventionally based on unbiased and well-documented literature, and clinical review, the average quality of all the guidelines included was more than good.

Study Characteristics and Discussion

The primary aim of this narrative review is to enlist the different protocols suggested for health and fitness by different guidelines and the recommendations suggested by them.

Finally, six major guidelines were identified and selected for this review. The procedure is depicted in the flowchart [Figure 1].

Ekelund *et al*. collectively evaluated data from 14 studies with 20,871 children and young adults of the age 4–18 years from "the International Children's Accelerometry Database." By reanalysis of raw data obtained through accelerometry of the amount of time spent on physical inactivity and moderate and vigorous physical activity, they concluded that time spent in moderate-to-vigorous exercise significantly associated with better cardiometabolic risk parameters, such as waist circumference, systolic blood pressure (BP), high-density lipoprotein cholesterol and insulin, independent of age, gender, sedentary time, and waist circumference (when not used as outcome measure).[22,28] There are also other studies which reiterate that aerobic as well as aerobic plus resistance training reduces the prevalence of the development of MetS after 9 months of training and also caused reduction in MetS parameters such as waist circumference and systolic BP.[29] Authors have also seen better cardiometabolic profiles regardless of obesity or normal weight as an effect of involvement in regular physical exercise.[30,31]

Campbell *et al*. conducted and represented one systematic review and two meta-analyses between 2012 and 2017

having large number of studies in itself, after having searched around 260 articles, to conclude that there is "no better effect of high-intensity interval training (HIIT) than moderate-intensity aerobic exercise on cardiometabolic parameters in adults between the age of 20 and 77 years," with moderate strength of evidence. However, they lamented that there is no specific definition for HIIT in literature and to observe a significant effect on the long-term effectiveness on physiological mechanisms of the body and acceptability of a protocol, a clinical trial should at least last for 6 months in duration. To be more specific, they found literature supporting improvement seen in normal-weight individuals for cardiorespiratory fitness and $VO2_{max}$ but not for the other factors signifying cardiometabolic syndrome such as blood glucose indices, BP, and anthropometric measures. However, patients in the overweight and obese category of BMI showed a significant improvement in both the indices of BP and also body composition along with insulin sensitivity.[32] Moreover, physical activity has been found to be protective for reducing the risk for cancer as well as depression.[27]

Exercise has over years demonstrated improvement in insulin sensitivity with most of the time showing a dose–response relationship, though not always and also not associated with aerobic fitness and improvement in $VO2_{max}$ in certain studies. However, with the various central and peripheral adaptations happening with exercise, it has been reported that the role of increased expression of insulin receptor substrate-1 and GLUT4 translocation to sarcolemma and T tubules and thus increase glucose uptake, as a consequence of deactivation of TBC1D1, is vital. Whereas, TBC1D4 phosphorylation causes its deactivation and activates the GLUT4 translocation postexercise, in both the cases the insulin sensitivity increases.

With regular physical training, this is a phenomena that happen at a continuous pace at rest in human body and thus increases the insulin sensitivity even at rest.[33] The intramyocellular triglyceride concentrations are high in both obese and after endurance training, but the insulin sensitivity is different in both. Lipid intermediates, namely diacylglycerols (DAGs) and ceramides, play a crucial role in this mechanism. Endurance athletes generally have a high DAG content in comparison to physically inactive obese as well as normal-weight individuals. High-ceramide content may disrupt the normal phosphorylation and activation mechanism and also affect GLUT4 translocation and thus affect insulin sensitivity. However, physical training reduces ceramide levels and this plays a vital role on specifically "the saturated fatty acid content (but not unsaturated fats) in skeletal muscle" and thus affects glucose tolerance.[33] Moreover, another aspect which draws attention here is that with aging there is more risk of cardiometabolic disorders related to frailty and sarcopenia. This induces reduction in muscle power and increased visceral fat and simultaneous reduction of myokines and increase in adipokines, respectively. These have also shown to have been positively impacted as dose-dependent physical activity has shown reduction in morbidity and mortality even in elderly above the age of 70 years.[34]

Another mechanism postulated is the improvement in β-cell activity with exercise, which is otherwise compromised by overstimulation as a consequence of impaired insulin sensitivity. This is studied by various authors by analyzing the "Disposition Index (DI = SI × acute insulin response to glucose."[33] Analyzing the seriousness of syndrome X, it was discovered that all kinds of adipocytes were not same; there were some which were brown, beige, and white. Out of them, the cellular content of mitochondria which varied in brown and beige adipocytes increased their potential for thermogenesis with an increase amount of adiponectin and thus having a positive effect on glucose tolerance as well as β-cell activity,[35] and thus, fat cells and their metabolic role are also equally important in controlling MetS. Although there is still dearth of literature and further elucidation is recommended, there are also studies which have suggested that there are some myokines stimulated in an active muscle or after exercise which induces browning of fat and thermogenesis.[36]

Implications

Guidelines for physical activity: Prevention, prophylaxis, and treatment

Almost similar exercise prescription is advised by most of the guidelines for physical activity as represented in Table 2.[5-7,14,37-41] The Canadian Society for Exercise Physiology has asked one to remain active most of the time with limiting sedentary time to <8 hours/day and interrupted by as many breaks in between. Moreover, it is equally important to take a good quality sleep of 7–9 h with consistent sleep and wake up timings.[40] This is definitely stressing on the sleep cycle and circadian rhythm.

The "European Association for Cardiovascular Prevention and Rehabilitation" guidelines recommend physical activity to lower the cardiovascular risk. "The European Association of Preventive Cardiology" of the ESC insists that a dose–response relationship exists and to set physical activity goals and self-monitoring is of utmost importance along with behavioral strategies.[42]

As shown in Table 2, most of the guidelines have resistance training added to the regime of aerobic exercise to improve insulin resistance. Most of the

recommendations also have the same guidelines for adults who demonstrate the MetS criteria; however, once further complications develop they advocate to observe special precautions and further customization of the exercise protocol.

Conclusion

The burden of lifestyle disorders is increasing tremendously and is also increasing the economic cost on the society. It is high time that we understand the seriousness and start observing the well-stated advice offered by several guidelines over many years and stay physically active.

Furthermore, observing the variation in the different guidelines, there is a dire need to develop a common accurate as well as authentic monitoring criterion, for measuring the activity level of an individual so that its impact can be studied further. Moreover, this needs to come as an obligatory measure from the government and public health departments and monitored as a part of "Public Health Enforcement Majeure."

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There are no conflicts of interest.

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