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The Role of Cardiovascular Fitness in the Prevention of Chronic and Degenerative Disease in U.S. Population.

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- INTRODUCTION

The advent of COVID-19 pandemic has vastly underlined the importance of good health in humans as a key factor for correct immune function, and decreased susceptibility to SARS-CoV-2 infection. At the time of this writing, the United States of America is the world-leading country in terms of COVID-19 reported infections (48,413,265)[1] and related deaths (778,336)[1] (covid19.who.int). Since the SARS-CoV-2 virus initial outbreak in the United States, in the earlier months of 2020, strong links between patients' comorbidities or chronic conditions and mortality from COVID-19 complication have been shown[2]. The prevalence of adults with multiple chronic conditions (MCC) in the United States reached 27.2% (26.5-27.9; 95% CI)[4], in 2018[4], with 51.8% of civilian, noninstitutionalized adults being diagnosed with at least one chronic condition in 2018[4]. The latest reported prevalence of MCC affected adults in the U.S. is critical in understand the underlying epidemic in regards of such conditions, especially when compared to the data reported from previous years. The findings reported in previous research showed MCC prevalence to be 21.8% in 2001, and 26.0% in 2010[7]. Although life expectancy at birth, in the United States, did not significantly change in the past decade[3], the increasing rates of both comorbidities and chronic health conditions of the U.S. population suggest that, as improvements in the medical field mitigated the negative impact of chronic disease on life expectancy, increased lifespan and health may be attainable if the mentioned health threatening risk factors were prevented amongst the American population. Although the constant growth of risk factors has been reported consistently throughout the decades, by both national and international official institutions, such as the Center of Disease Control and Prevention[5] (www.CDC.gov) and the World Health Organization[6] (www.WHO.int), the COVID-19 pandemic underlined the importance in preventing such conditions[8] in order to be less susceptible to diseases as well as to increase populations healthy lifespan. This manuscript reflects on how high intensity exercise may play a role in prevention and/or amelioration of chronic, degenerative conditions in the U.S. population.

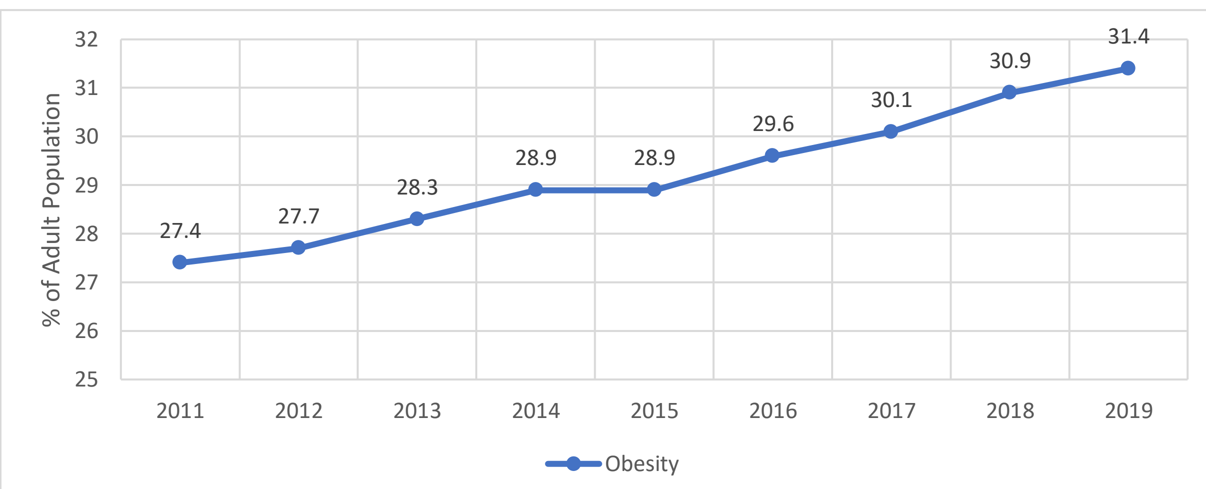
- CHRONIC CONDITIONS vs. DEGENERATIVE DISEASES

The National Center for Chronic Disease Prevention and Health Promotion (NCCDPHP) is a department of the CDC focusing on the analysis of chronic disease prevalence in the United States and preventing such conditions amongst the US population. The institution reports the following conditions as the most prevalent and of major health impact in the U.S.[7].

- Hypertension
- Coronary heart disease
- Stroke
- Diabetes
- Cancer
- Arthritis
- Kidney disease
- Chronic obstructive pulmonary disease
- Asthma

Chronic conditions have been associated with behavioral factors who have shown to expose subjects to a significantly greater risk to develop these conditions; the list of major risk factors include tobacco use, poor nutrition, lack of physical activity and excessive alcohol consumption[5] (CDC, April 2021). Although tobacco use has been declining from 20.9% smoking prevalence in 2005 to the drastically reduced data showing 14.0% of American smoking in 2019[9], the rate of degenerative diseases such as obesity[10] and diabetes[11] have been reported to be at a constant increase over the years[10,11](Figure 1). Insight as the one mentioned suggests how nutrition and physical activity may play a major role in preventing the onset of degenerative diseases and related chronic conditions.

Figure 1. Percent of Adults with Obesity in the US[9] (2011-2019)



Obesity is defined as body mass index (BMI) ≥ 30.0; BMI was calculated from self-reported weight and height (weight [kg]/ height [m²). Respondents reporting weight < 50 pounds or ≥ 650 pounds; height < 3 feet or ≥ 8 feet; or BMI: <12 or ≥ 100 were excluded. Pregnant respondents were also excluded.

OBESITY, METABOLIC DISEASE AND DIABETES

The increase in prevalence of obesity has become a major health problem in all populations worldwide. Obesity is associated with large decrease in life expectancy, this is especially true for young adults with obesity rather than the older[12]. Obesity is diagnosed using the Body Mass Index (BMI)[6] method. BMI is calculated by dividing the subject's weight in kilograms by his height in meters squared.

$$BMI = \frac{kg\ of\ BW}{(height\ in\ m)^2}$$

In recent years waist circumference measurement has shown to be a valid predictor for body fat[13], similarly to BMI, but is currently considered a better indicator for cardiometabolic disease risk since. This is due to the greater ability of this method to evaluate central obesity in subjects with low BMI but with intra-abdominal fat accumulation[14]. Other limitations related to these methods is their inability to evaluate fat-free mass, which is of major importance in assessing cardiometabolic disease risk[15]. Based on the different methods of assessing risk of obesity related co-morbidities can be observed in Figure 2a and 2b[15,16,17].

Figure 2a. Measures of Central Adiposity

Body Mass Index (BMI)[16]			
Men and Women	18.5-24.9 kg/m^2	25-29.9 kg/m^2	≥ 30 kg/m^2
Classification	Normal Weight	Overweight	Obese
Co-morbidities risk	Low	Increased	High

Figure 2b. Measures of central Adiposity

Waist Circumference[17]			
Men	< 94 cm	94-101.9 cm	≥ 102 cm
Women	< 80 cm	80-87.9	≥ 88 cm
Classification	Normal fat distribution	Moderate central fat accumulation	High central fat accumulation
Co-morbidities risk	Low	Increased	High

Metabolic Syndrome (MetS) was defined in 2009 by the Int. Diabetes Federation Task Force on Epidemiology and Prevention; the National Heart, Lung and Blood Institute; the World Heart Federation; the Int. Association for the Study of Obesity; the Int. Arthrosclerosis Society;

and the American Heart Association[20]. By definition, a subject is considered to have MetS if 3 or more of the associated components were present (figure 3).

Figure 3. Individual components of Metabolic Syndrome[20]

<table>
<tr><th colspan="2">Components of MetS[20]</th><td rowspan="12">Individuals reporting the presence of 3 or more components have MetS</td></tr>
<tr><td rowspan="2">Waist Circumference</td><td>Men ≥ 102 cm</td></tr>
<tr><td>Women ≥ 88 cm</td></tr>
<tr><td colspan="2">Fasting Blood Glucose ≥ 100 mg/dl (5.5 Mmol/L)</td></tr>
<tr><td colspan="2">Treatment with hypoglycemic agents or insulin</td></tr>
<tr><td colspan="2">Systolic Blood Pressure ≥ 130 mm/Hg</td></tr>
<tr><td colspan="2">Diastolic Blood Pressure ≥ 85 mm/Hg</td></tr>
<tr><td colspan="2">Treatment with antihypertensive drugs</td></tr>
<tr><td colspan="2">Serum triglycerides ≥ 150 mg/dl (1.7 mmol/L)</td></tr>
<tr><td colspan="2">Treatment for hypertriglyceridemia (niacin/fibrates)</td></tr>
<tr><td rowspan="2">HDL-C</td><td>Men < 40 mg/dl (1.0 mmol/L)</td></tr>
<tr><td>Women <50 mg/dl (1.3 mmol/L)</td></tr>
</table>

MetS has shown to be more prevalent among overweight and obese adults compared to normal weight adults (CDC 2020) and currently represents an important risk factor for all-cause mortality among all populations[18]. In 2017, the Journal of American Heart Association reported that MetS was associated with a 70% increase in risk of sudden cardiac death where the risk did not vary between different sex nor race groups[19]. Metabolic syndrome has been showed to be one of the main risk factors involved in the onset of Type-2 Diabetes[21,22]. Diabetes is a medical condition that affects individuals by not being able to regulate efficiently glucose concentration in the blood; patients usually need to follow a healthy diet and take medications to regulate their glucose concentration in the blood. Having high glucose concentration (hyperglycemia) in the blood for long periods of time may impair the ability of the patient to provide energy, hydrate and store glucose within cells, leading to the   Diabetes has become one of the most prevalent chronic conditions in the United States, with 34.2 million Americans being affected by this condition (CDC, 2018)[5,23]. Diabetes is the leading degenerative disease being attributed as the underlying cause of serious complications such as heart disease, stroke, blindness, kidney failure[23] and was the 7th leading cause of death in America in 2017[23].

EXERCISE TO PREVENT OBESITY AND RELATED METABOLIC DISEASE

Since obesity, metabolic syndrome and type 2 Diabetes are officially recognized as major chronic and degenerative diseases, it is important to understand the link between these conditions and educate the populations at risk to improve their healthy lifespan and increase quality of life. There is a seven times greater risk of diabetes in obese people, and a threefold increase in risk for overweight people when these two groups are compared to healthy weight individuals[24]. Additionally, being overweight or obese the most modifiable risk factor for type 2 diabetes[25], the key in the prevention of such condition may be in correct weight management through proper nutrition and exercise. The ACSM's recommendation for Physical Activity has as main goals regarding the prevention of chronic degenerative disease the improvement of overall health including, but not limited to, the regulation of blood pressure and the prevention of weight gain[26]. ACSM Guidelines suggest that adults aged 18-65 yr should:

- Participate in moderate intensity aerobic physical activity for at least 150 minutes/week, or vigorous intensity aerobic activity for 75 minutes/week[26].
- All adults should perform activities that maintain or increase muscular strength and endurance for a minimum of two days/week[26].
- Increased health benefits can be obtained by engaging in moderate intensity physical activity beyond the equivalent of 300 minutes/week[26].

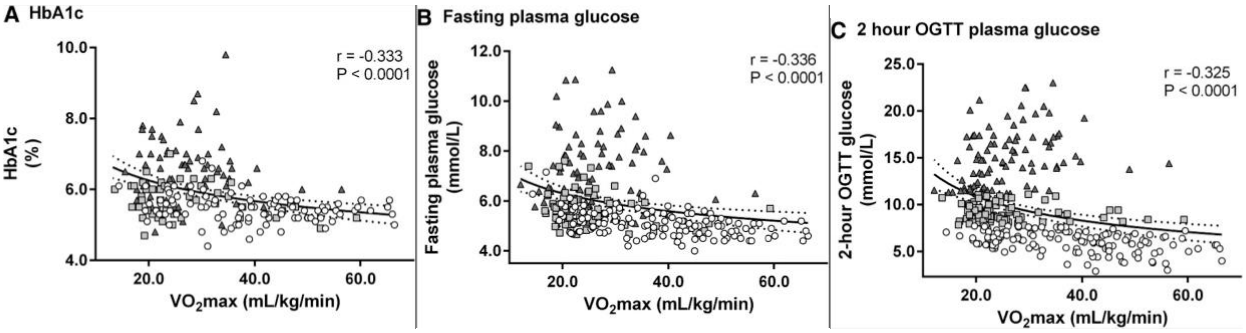
Although the dose-dependent response of exercise was noted on the ACSM's Guidelines, insight from the incidence of morbidities in the U.S. suggests that American adults are not following such recommendations.

Evidence from Letite et al. indicates that training to specifically improve/maintain cardiorespiratory fitness (VO_2max) may be more relevant in the prevention of type 2 diabetes, insulin resistance and obesity[27]. Ferreira et al found that VO_2max was inversely associated with arterial stiffness, and this was independent of the metabolic syndrome[28]. In an 8-year experimental study with before-after design, Najafipour F, Mobasseri M, Yavari A, et al, indicated that constant progressive aerobic exercise (from 50% HRmax at baseline up to 80% HRmax for maintenance) for duration >52 weeks reported health markers improvements among all dependent variables being considered, with significant improvements in VO_2max, and significantly lower BMI and HbA1c levels in trained group compared to control[29]. In the same study, significant decrease in HbA1c levels were found after the last 2 years of the intervention to have significantly decreased (1.39%)[29]. Yan et al. reported that after a 12-week aerobic training program, HbA1c was reduced by 1.1% with a significant increase in VO_2max noted on the same study; however, this study showed no significant difference in pre- and post-intervention BMI, giving interesting insight on how HbA1c levels improvements may be obtained by focusing on cardiovascular fitness[30]. The proposed model of VO_2max-focused training for decreasing risk factors in the onset of developing type-2 diabetes may be adopted in assessing exercise programs for individuals at risk of developing cardio-metabolic disease as well as to people who already suffer from chronic conditions.

In 2001, Wilmore et al. were able to show significant relationship between cardiovascular fitness improvement and decrease in risk factors for both CVD and type-2 diabetes (T2D) in 502 healthy, previously sedentary individuals[31]. The study analyzed changes in maximal O_2 uptake in subjects who engaged in 3 days/week, 30-minute aerobic activity on cycle ergometer. The subjects started exercising at the heart rate (HR) associated with 55% of their VO_2max. After 14 weeks of training, exercise intensity progressively increased to the HR associated with 75% of VO_2max and it was maintained for longer cycling sessions for 50 minutes sessions. Baseline HR, VO_2max, lipid profile, lipoprotein, body composition (CT scan), resting blood glucose and insulin, and intra venous glucose tolerance test values were recorded. Following the 20 weeks of training, there were significant increases in VO_2max (+16%) and power output at 60%VO_2max with significant decrease in the HR at 50. These changes were significant as well as the reduction in the factors for CVD and Type-2 diabetes[31]. Although Wilmore JH et al. finally underline that risk prevention in developing such conditions was to be related to reduced BMI values at the end of the intervention, the manuscript was still able to provide significant evidence in support of the mitigating effects of improved cardiovascular fitness on lipidology and obesity. Whether VO_2max improvements are related to training-induced increase in muscle mass, improvements in the O_2 carrying capacity and affinity, or decreased fat mass, finally, all are main components in the reduction of cardiometabolic risk.

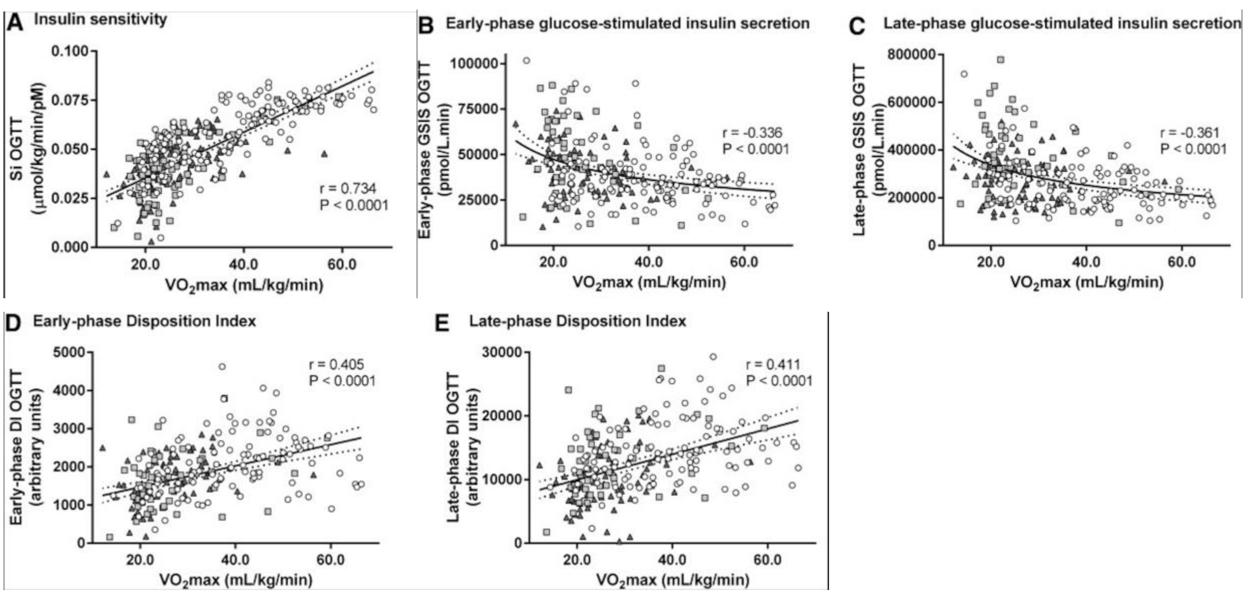
In a cohort study on 313 subjects with heterogenous age, sex and glycemic control, Solomon et al. reported significant correlation between poor VO_2max with high HbA1c, high fasting glucose, high 2-h post. high oral glucose tolerance test glucose levels, high early- and late-phase glucose stimulated insulin secretion[32] (Figure 3 & 4)[32].

Figure 3[32].



Cardiorespiratory fitness is associated with markers of glycemic control. VO_{2max} was measured during incremental workload and exhaustive aerobic exercise in subjects representative of a heterogeneous population with respect to age, BMI, adiposity, and glucose tolerance status (white circles, NGT; light-gray squares, IGT; and dark-gray triangles, T2D). Regression analysis demonstrated inverse curvilinear log-log relationships between VO_{2max} and HbA_{1c} ($\log_{10}y = -0.14 \log_{10}x + 0.98$) (*A*), fasting glucose ($\log_{10}y = -0.17 \log_{10}x + 1.03$) (*B*), and 2-h glucose during OGTT ($\log_{10}y = -0.39 \log_{10}x + 1.55$) (*C*). Solid and dotted lines represent the regression curves and 95% CI, respectively, and show unadjusted data.[32]

Figure 4[32].



Cardiorespiratory fitness is associated with Si_{OGTT}, $GSIS_{OGTT}$, and DI_{OGTT}. VO_{2max} was measured during incremental workload and exhaustive aerobic exercise in subjects representative of a heterogeneous population with respect to age, BMI, adiposity, and glucose tolerance status (white circles, NGT; light-gray squares, IGT; and dark-gray triangles, T2D). VO_{2max} was directly associated with Si_{OGTT} ($y = 0.00117x + 0.0119$) (*A*) but had an inverse curvilinear log-log relationship with early-phase ($\log_{10}y = -0.39 \log_{10}x + 5.18$) (*B*) and late-phase ($\log_{10}y = -0.42 \log_{10}x + 6.07$) (*C*) $GSIS_{OGTT}$. Finally, there were direct linear relationships between VO_{2max} and early-phase ($y = 27.8x + 916$) (*D*) and late-phase ($y = 200x + 5{,}966$) (*E*) DI_{OGTT}, a measure of pancreatic β-cell insulin secretory compensation for changing insulin sensitivity. Solid and dotted lines represent the regression curves and 95% CIs, respectively, and show unadjusted data.[32]

CONCLUSION

Cardiovascular and cardiorespiratory fitness must be taken in consideration when addressing chronic and degenerative disease prevention. Being physically active may not be sufficient in preventing the onset of risk factors for cardiometabolic diseases. Although scientific evidence indicates aerobic fitness and, specifically, VO_2max represent valid and significant factors all individuals should aim to improve through exercise and training, additional investigation is required to address specific, obtainable guidelines dedicated to populations at risk to develop cardiometabolic disease.

REFERENCES:

1. "United States of America: Who Coronavirus Disease (Covid-19) Dashboard with Vaccination Data." *World Health Organization*, World Health Organization 12/5/2021
2. Sanyaolu, Adekunle et al. "Comorbidity and its Impact on Patients with COVID-19." *SN comprehensive clinical medicine*, 1-8. 25 Jun. 2020, doi:10.1007/s42399-020-00363-4
3. Kochanek KD, Anderson RN, Arias E. Changes in life expectancy at birth, 2010–2018. NCHS Health E-Stat. 2020.
4. Boersma P, Black LI, Ward BW. Prevalence of Multiple Chronic Conditions Among US Adults, 2018. Prev Chronic Dis 2020;17:200130. DOI: http://dx.doi.org/10.5888/pcd17.200130external icon.
5. *Centers for Disease Control and Prevention*, Centers for Disease Control and Prevention, https://www.cdc.gov/.
6. *World Health Organization*, World Health Organization, https://www.who.int/.
7. Ward BW, Schiller JS. Prevalence of multiple chronic conditions among US adults: estimates from the National Health Interview Survey, 2010. Prev Chronic Dis. 2013 Apr 25;10:E65. doi: 10.5888/pcd10.120203. PMID: 23618545; PMCID: PMC3652717.
8. "People with Certain Medical Conditions." *Centers for Disease Control and Prevention*, Centers for Disease Control and Prevention, https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/people-with-medical-conditions.html.
9. Current cigarette smoking among adults in the United States. *Centers for Disease Control and Prevention* (2020).
10. Nutrition, physical activity, and obesity - behavioral risk factor surveillance system. *Centers for Disease Control and Prevention*

11. Centers for Disease Control and Prevention.National Center for Chronic Disease Prevention and Health Promotion, Division of Nutrition, Physical Activity, and Obesity.Data, Trend and Maps
12. Engin A. The Definition and Prevalence of Obesity and Metabolic Syndrome. Adv Exp Med Biol. 2017;960:1-17. doi: 10.1007/978-3-319-48382-5_1. PMID: 28585193.
13. *Lean ME, Han TS, Deurenberg P. Am J Clin Nutr. 1996 Jan; 63(1):4-14*
14. *Seidell JC, Han TS, Feskens EJ, Lean ME. J Intern Med. 1997 Nov; 242(5):401-6.*
15. Han, Thang S, and Mike Ej Lean. "A clinical perspective of obesity, metabolic syndrome and cardiovascular disease." *JRSM cardiovascular disease* vol. 5 2048004016633371. 25 Feb. 2016, doi:10.1177/2048004016633371
16. Impact of the metabolic syndrome on mortality from coronary heart disease, cardiovascular disease, and all causes in United States adults. *Malik S, Wong ND, Franklin SS, Kamath TV, L'Italien GJ, Pio JR, Williams GR. Circulation. 2004 Sep 7; 110(10):1245-50.*
17. Waist circumference as a measure for indicating need for weight management. *Lean ME, Han TS, Morrison CE. BMJ. 1995 Jul 15; 311(6998):158-61.*
18. Shi TH, Wang B, Natarajan S. The Influence of Metabolic Syndrome in Predicting Mortality Risk Among US Adults: Importance of Metabolic Syndrome Even in Adults With Normal Weight. Prev Chronic Dis 2020;17:200020. DOI: http://dx.doi.org/10.5888/pcd17.200020external icon
19. Hess, Paul L et al. "The Metabolic Syndrome and Risk of Sudden Cardiac Death: The Atherosclerosis Risk in Communities Study." *Journal of the American Heart Association* vol. 6,8 e006103. 23 Aug. 2017, doi:10.1161/JAHA.117.006103
20. Alberti KG, Eckel RH, Grundy SM, Zimmet PZ, Cleeman JI, Donato KA, Fruchart JC, James WP, Loria CM, Smith SC Jr. Harmonizing the metabolic syndrome: a joint interim statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity. *Circulation*. 2009;120:1640–1645.
21. Laaksonen DE, Lakka HM, Niskanen LK, Kaplan GA, Salonen JT, Lakka TA: Metabolic syndrome and development of diabetes mellitus: application and validation of recently suggested definitions of the metabolic syndrome in a prospective cohort study. *Am J Epidemiol* 156: 1070–1077, 2002
22. The Metabolic Syndrome as Predictor of Type 2 Diabetes.
Carlos Lorenzo, Mayor Okoloise, Ken Williams, Michael P. Stern, Steven M. Haffner. Diabetes Care Nov 2003, 26 (11) 3153-3159; DOI: 10.2337/diacare.26.11.3153

23. DRI. “Diabetes Statistics.” *Diabetes Research Institute Foundation*, University of Miami Miller School of Medicine, *National Institutes of Health* *SEARCH for Diabetes in Youth study; https://www.diabetesresearch.org/diabetes-statistics.
24. Abdullah A, Peeters A, de Courten M, et al. The magnitude of association between overweight and obesity and the risk of diabetes: a meta-analysis of prospective cohort studies. Diabetes Research & Clinical Practice 2010;89(3):309-19.
25. Gatineau , Mary, et al. “Adult Obesity and Type 2 Diabetes - Gov.uk.” *Public Health England*, July 2014.
26. “Physical Activity Guidelines Resources.” *ACSM_CMS*, 2018.
27. Leite, Silmara Ao et al. “Low cardiorespiratory fitness in people at risk for type 2 diabetes: early marker for insulin resistance.” *Diabetology & metabolic syndrome* vol. 1,1 8. 21 Sep. 2009, doi:10.1186/1758-5996-1-8
28. Ferreira I, Henry RM, Twisk JW, van Mechelen W, Kemper HC, Stehouwer CD. Amsterdam Growth and Health Longitudinal Study. The metabolic syndrome, cardiorespiratory fitness, and subcutaneous trunk fat as independent determinants of arterial stiffness: the Amsterdam Growth and Health Longitudinal Study. *Arch Intern Med.* 2005;25:165(8):875–82. doi: 10.1001/archinte.165.8.875.
29. : Najafipour F, Mobasseri M, Yavari A, et al. Effect of regular exercise training on changes in HbA1c, BMI and VO2 max among patients with type 2 diabetes mellitus: an 8-year trial. BMJ Open Diab Res Care 2017;5:e000414. doi:10.1136/ bmjdrc-2017-000414
30. Yan H, Prista A, Ranadive SM, et al. Effect of Aerobic Training on Glucose Control and Blood Pressure in T2DDM East African Males. ISRN Endocrinol 2014;864897:1–6.
31. Wilmore, J H et al. “Relationship of changes in maximal and submaximal aerobic fitness to changes in cardiovascular disease and non-insulin-dependent diabetes mellitus risk factors with endurance training: the HERITAGE Family Study.” *Metabolism: clinical and experimental* vol. 50,11 (2001): 1255-63. doi:10.1053/meta.2001.27214
32. Solomon, Thomas P J et al. “Association between cardiorespiratory fitness and the determinants of glycemic control across the entire glucose tolerance continuum.” *Diabetes care* vol. 38,5 (2015): 921-9. doi:10.2337/dc14-2813