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VO_2max as a Vaccination Against Lifestyle Diseases – Impact on Longevity, Disease Incidence, and a Marker of Fitness

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Abstract

Introduction:

Cardiorespiratory fitness (VO_2max) is a key marker of health and physical fitness. It could be referred to as a "vaccination against lifestyle diseases," as higher VO_2max protects the body from multiple chronic conditions.

Materials and Methods:

This review analyzed original articles, review papers, and meta-analyses indexed in PubMed, JACC, OUP, ScienceDirect, and PMC. The analysis focused on epidemiological, clinical, and mechanistic aspects of VO_2max in relation to longevity, metabolic health, and cardiovascular risk.

Literature Review:

VO_2max serves as the "gold standard" for physical fitness assessment, integrating respiratory, cardiovascular, and muscular function. Low VO_2max is strongly associated with higher all-cause and cardiovascular mortality, while higher VO_2max confers protective effects. Epidemiological studies indicate that even moderate improvements in VO_2max reduce mortality risk and contribute to longer life. Low VO_2max is linked to higher incidence of lifestyle-related diseases, including cardiovascular diseases, type 2 diabetes, chronic inflammation, cancer, and multimorbidity in older adults. Regular exercise, including moderate-intensity aerobic training and high-intensity interval training (HIIT), substantially increases VO_2max across populations, including older adults. These adaptations result from central and peripheral mechanisms, improving cardiac output, muscle perfusion, and mitochondrial function. VO_2max acts as a "biological vaccination," reducing chronic low-grade inflammation, improving insulin sensitivity, lowering blood pressure, and positively influencing lipid profiles.

Summary:

VO_2max is a critical health marker and predictor of longevity. Higher cardiorespiratory fitness reduces the risk of lifestyle-related diseases more effectively than many classical risk factors. Regular physical activity, particularly HIIT, improves VO_2max and provides a protective effect analogous to a "vaccine" against lifestyle diseases. VO_2max should be considered a key public health indicator and incorporated into routine clinical practice and preventive health programs.

Keywords:

VO_2max; Cardiorespiratory fitness; Lifestyle diseases; Longevity; Cardiovascular health; Physical activity; High-intensity interval training

Introduction

Cardiorespiratory fitness, most commonly assessed by maximal oxygen uptake (VO_2max), is a well-established marker of health and physical fitness. Numerous epidemiological studies have shown that a high VO_2max is associated with a reduced risk of cardiovascular diseases, type 2 diabetes, cancer, and increased longevity [1]. In this context, VO_2max is sometimes referred to as a "vaccination against lifestyle diseases," as its high value protects the body from many chronic health conditions.

Aim of the study

The aim of this review is to present the role of VO_2max in the prevention of lifestyle-related diseases, its significance as a predictor of longevity, and to summarize current scientific evidence in this area.

Materials and Methods

This review was conducted based on an analysis of the scientific literature. Only original articles, review papers, and meta-analyses published in journals indexed in PubMed, JACC, OUP, ScienceDirect, and PMC were included. The analysis covered epidemiological, clinical, and mechanistic aspects of the relationship between VO_2max, longevity, and metabolic-cardiovascular health.

Literature Review

VO_2max as a Marker of Fitness and Health

Maximal oxygen uptake (VO_2max) is widely regarded as the "gold standard" for assessing physical fitness, as it integrates the function of the respiratory, cardiovascular, and muscular systems [2]. Its value reflects the body's capacity to transport and utilize oxygen during progressively intense exercise, serving as a comprehensive indicator of physiological fitness. VO_2max is a strong and independent predictor of overall and cardiovascular morbidity and mortality. In a meta-analysis, which included 102,980 participants, individuals with the lowest fitness levels ($\leq$25.3 $ml \cdot kg^{-1} \cdot min^{-1}$ in men and $\leq$19.4 $ml \cdot kg^{-1} \cdot min^{-1}$ in women) had a significantly higher risk of death compared to those with high fitness levels ($\geq$35.5 $ml \cdot kg^{-1} \cdot min^{-1}$ in men and $\geq$30.1 $ml \cdot kg^{-1} \cdot min^{-1}$ in women). Importantly, each 1-MET increase in VO_2max ($\approx$3.5 $ml \cdot kg^{-1} \cdot min^{-1}$) was associated with a 13% reduction in all-cause mortality

and a 15% reduction in cardiovascular mortality [3]. In an another study, including over 37,000 participants, subjects were divided into quintiles of cardiorespiratory fitness. Those in the lowest quintile (<30 ml·kg^{-1}·min^{-1} for men and <27 ml·kg^{-1}·min^{-1} for women) exhibited a several-fold higher risk of premature death compared to participants in the highest quintile (>45 ml·kg^{-1}·min^{-1} for men and >38 ml·kg^{-1}·min^{-1} for women) [4]. Similarly, Mandsager et al. (2018), analyzing data from 122,007 patients undergoing exercise testing, reported that individuals with the highest fitness ("elite performers," VO_2max >97.7th percentile for age and sex, often >50–55 ml·kg^{-1}·min^{-1}) had the lowest mortality risk. The difference in survival between the highest and lowest fitness groups exceeded the mortality differences associated with classical risk factors such as smoking or diabetes [5]. Strasser & Burtscher propose considering low VO_2max (<25 ml·kg^{-1}·min^{-1} in adults) as a clinical risk factor, comparable in importance to hypertension or dyslipidemia. In summary, VO_2max is not only a measure of physical fitness but also one of the strongest markers of health and prognosis in the general population. Values below ~25–30 ml·kg^{-1}·min^{-1} are associated with a significantly increased risk of chronic diseases and premature death, whereas values above 45–50 ml·kg^{-1}·min^{-1} confer protective effects and can be considered a "physiological reserve of health."

VO_2max and Lifestyle-Related Diseases

Lifestyle-related diseases, including cardiovascular diseases, type 2 diabetes, chronic metabolic disorders, and certain cancers are leading causes of death and disability worldwide. There is a clear relationship between VO_2max levels and the risk of developing these conditions.

Cardiovascular diseases.

Low cardiorespiratory fitness is a strong risk factor for coronary artery disease, myocardial infarction, and heart failure. Kodama et al. (2009) confirmed that individuals with low VO_2max had higher cardiovascular mortality, independent of other factors such as hypertension or smoking. Ross et al. (2016) emphasize that VO_2max assessment should be considered alongside other key cardiovascular risk markers, as it provides unique prognostic information [6].

Type 2 diabetes and metabolic disorders.

VO_2max is closely linked to insulin sensitivity and glycemic control. Individuals with low cardiorespiratory fitness are at higher risk of developing type 2 diabetes [7]. Improving VO_2max through exercise increases glucose tolerance and reduces insulin resistance, making it an important element of prevention and metabolic therapy [8].

Cancer and inflammatory states.

Low VO_2max promotes a chronic low-grade inflammatory state, considered a key driver of cancer and other chronic lifestyle diseases. Regular physical activity that enhances cardiorespiratory fitness reduces inflammatory markers, further explaining the protective role of high VO_2max against carcinogenesis [9].

Aging and multimorbidity.

Low VO_2max is associated with increased risk of multimorbidity and premature disability in older adults. In population terms, low fitness can be considered a "lifestyle disease itself," representing a common denominator for many chronic pathologies [2].

VO_2max and Longevity

Epidemiological studies demonstrate a strong link between VO_2max and lifespan. Unlike many traditional risk factors, cardiorespiratory fitness provides independent and powerful prognostic information for survival. In the meta-analysis by Kodama et al. (2009), each 1-MET increase in fitness (≈3.5 $ml \cdot kg^{-1} \cdot min^{-1}$) was associated with a 13% reduction in all-cause mortality and a 15% reduction in cardiovascular mortality. Even modest improvements in VO_2max can therefore have a meaningful impact on prognosis and contribute to additional healthy years of life. [3] Nes et al. (2014) reported that participants in the lowest VO_2max quintile (<30 $ml \cdot kg^{-1} \cdot min^{-1}$ for men and <27 $ml \cdot kg^{-1} \cdot min^{-1}$ for women) had significantly higher mortality compared to those in the highest quintile (>45 $ml \cdot kg^{-1} \cdot min^{-1}$ for men and >38 $ml \cdot kg^{-1} \cdot min^{-1}$ for women), independent of age, sex, BMI, or blood pressure [4]. Mandsager et al. (2018) observed a clear survival gradient according to VO_2max. Individuals in the highest fitness category ("elite performers," >97.7th percentile) had the lowest risk of death. Importantly, there was no upper threshold beyond which higher VO_2max became detrimental [5]. In summary, high VO_2max is among the strongest predictors of longevity. Maintaining values above 40–45 $ml \cdot kg^{-1} \cdot min^{-1}$ is associated with significantly longer survival compared to low fitness (<25–30 $ml \cdot kg^{-1} \cdot min^{-1}$). Regular exercise that improves VO_2max is one of the most effective interventions for promoting healthy lifespan.

Interventions to Improve VO_2max

VO_2max is largely modifiable, and its levels can be substantially increased through appropriately designed physical activity, both in the general population and among patients with chronic conditions [10].

High-intensity interval training (HIIT).

HIIT produces the most pronounced improvements in VO_2max. In a classic study by Wisløff et al. (2007) in heart failure patients, intervals at 90–95% HRmax increased VO_2max by an average of 46%, significantly more than moderate continuous training. Even individuals with severe health limitations can achieve substantial gains in cardiorespiratory fitness [11].

Moderate-intensity aerobic training.

Regular moderate-intensity aerobic exercise (e.g., brisk walking, cycling, swimming) also improves VO_2max,

though to a lesser extent than HIIT. Myers et al. (2019) emphasize that any regular physical activity improves cardiovascular health and cardiorespiratory fitness, provided it is consistent [12].

General population and older adults.

Cohort studies show that even older adults can achieve meaningful VO_2max improvements through regular training. Benefits were observed in studies focusing on cardiovascular prevention, where systematic exercise reduced mortality and improved longevity [13].

Adaptive mechanisms.

VO_2max improvements arise from both central and peripheral adaptations. Ross et al. (2016) highlight that these include increased cardiac output, improved skeletal muscle perfusion, and enhanced mitochondrial density and oxidative capacity. Regular exercise thus acts as a "biological vaccination," strengthening protective mechanisms against lifestyle diseases [6].

In summary, interventions to increase VO_2max include both moderate aerobic activity and high-intensity interval training, the latter being especially effective in high-risk populations. Benefits are observed at all ages and across baseline fitness levels, making exercise a universal tool for prevention and therapy.

3.5. VO_2max as a "Vaccination Against Lifestyle Diseases"

The literature increasingly describes high VO_2max as a "vaccination" against lifestyle diseases. Like vaccines protect against infections, maintaining high cardiorespiratory fitness safeguards the body against chronic conditions associated with modern lifestyles, including cardiovascular, metabolic, oncologic, and neurodegenerative diseases.

Protective mechanisms.

High VO_2max confers protection by reducing chronic low-grade inflammation ("inflammaging"), improving insulin sensitivity, lowering blood pressure, and beneficially modifying lipid profiles [2]. Regular exercise that increases VO_2max induces cardiovascular and metabolic adaptations that counteract the development of major lifestyle-related diseases.

Epidemiological evidence.

Population studies show that individuals with the highest VO_2max have a markedly lower risk of premature death than those with low fitness. In Mandsager et al. (2018), "elite performers" (>97.7th percentile VO_2max for age and sex) exhibited the lowest mortality risk, independent of classical risk factors. The authors likened high VO_2max to a preventive "vaccine"—the higher the fitness, the greater the protection against lifestyle diseases [5].

VO_2max as a preventive marker.

Ross et al. (2016) proposed treating VO_2max as a key public health biomarker, alongside blood pressure, cholesterol, and body mass index. Regular monitoring of VO_2max could serve as a "population-level vaccination tool," as its increase reduces morbidity and mortality [6].

Clinical implications.

Lavie et al. (2019) emphasize that improving cardiorespiratory fitness should be a priority in public health interventions. Maintaining VO_2max above threshold values (≈40–45 $ml \cdot kg^{-1} \cdot min^{-1}$ for men and 35–38 $ml \cdot kg^{-1} \cdot min^{-1}$ for women) functions as a "preventive buffer" protecting against aging and chronic diseases [7].

Summary

VO_2max is a key marker of health and a predictor of longevity. Epidemiological and clinical evidence demonstrates that higher cardiorespiratory fitness reduces the risk of lifestyle-related diseases and premature death more effectively than many classical risk factors. Regular physical activity, especially high-intensity interval training, is an effective strategy to improve VO_2max and thereby serve as a "vaccination" against lifestyle diseases.

Based on current evidence, VO_2max should be regarded as one of the most important public health indicators and incorporated into routine clinical practice and preventive health programs.

Disclosure

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